Original Article

Dental hygienists and dentists as providers of brush biopsies for oral mucosa screening

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Abstract

Background: Oral cancer is a severe and potentially fatal disease usually starting in the squamous epithelium lining the oral cavity. Together with oropharyngeal carcinoma, it is the fifth to sixth most common malignancy worldwide. To limit the increase in the global oral cancer incidence over the past two decades, the World Health Assembly adopted a resolution urging member states to integrate preventive measures such as engagement and training of dental personnel in screening, early diagnosis, and treatment into their national cancer control programs.

Aim: The aim of this study was to investigate if dental hygienists (DHs) and dentists (Ds) in general dental practice care can be entrusted to perform brush sampling of oral potentially malignant disorders (OPMDs), and to evaluate their level of comfort in performing brush biopsies.

Methods: Participants were five DHs and five Ds who received one day of theoretical and clinical training in oral pathology to identify OPMDs (leukoplakia [LP], erythroplakia [EP], and oral lichen planus [OLP]), and perform brush sampling for PAP cytology and high-risk human papillomavirus (hrHPV) analysis.

Results: Out of 222 collected samples, 215 were adequate for morphological assessment and hrHPV analysis. All the participants agreed that sample collection can be incorporated in DHs and Ds routine clinical duties, and most of them reported that sample collection and processing was easy/quite easy.

Conclusion: Dentists and DHs are capable of collecting satisfactory material for cytology and hrHPV analysis. All the participating DHs and Ds were of the opinion that brush sampling could be handled routinely by DHs and Ds in GDP.

Keywords
Cancer, erythroplakia, leukoplakia, oral lichen planus, potentially malignant oral disorders, oral

1 | Introduction

In 2007, the World Health Assembly (WHA) adopted a resolution on oral health to ensure that member states integrate measures against oral cancer into their national cancer control programmes. Among other measures, the resolution envisaged a broad involvement of oral-health professionals or primary health care personnel with relevant training in detection, early diagnosis, and treatment...
of cancers in oral cavity. Oral cancers cause a significant health-care burden on the global scale, with some 275,000 new cases reported annually. In Sweden, this number gravitates towards 1200 new cases and roughly 350 patients with oral/oropharyngeal cancer die each year. A 5-year overall survival rate of approximately 55% drops to only 3%–4% if the disease is detected at advanced stage. Moreover, approximately 30% of patients treated for oral/pharyngeal cancers suffer a relapse, and have an increased risk of new primary tumours. The incidence of oral cancer is increasing because of aging population, and due to hrHPV- driven carcinogenesis, while incidence of tumours caused by the traditional etiological factors remains constant. Oral cancer is often preceded by oral potentially malignant disorders (OPMDs), among which leukoplakia (LP), erythroplakia (EP), and oral lichen planus (OLP) predominate. The prevalence of oral mucosal changes varies between 11% and 62% in different populations. The diagnosis of OPMDs is clinical as well as histopathological. Homogenous and non-homogenous LP is common in middle-aged and older men with tobacco habits and excessive alcohol intake. The risk for malignant transformation of LP was reported to be 3.5%, but the rate varied between studies from 0.13% to 34%. The global prevalence of EP is reported to be 0.01%–0.21%, mostly occurring in men aged 50–70 years, with malignant transformation rates ranging from 14% to 50%. Atrophic and erosive OLP, most frequently seen in men, have a risk of malignant transformation of 0.5%–2%. Tumours could be prevented through a routine screening and early detection of OPMD. Oral cytology is non-invasive, fast and less costly, than incisional biopsies but not yet a standard procedure despite reports clearly showing that brushing is a diagnostic accurate method for identifying oral cancer. As dental hygienists (DHs) and dentists (Ds) regularly see their patients, they should be able to identify patients at increased risk. After being referred to a specialist these patients could be enrolled in a follow-up program at the primary point of care. In difference to a previous study, focusing on evaluating the level of comfort in clinicians for using different adjunctive screening devices, including brush biopsies, this study was the first to investigate in depth the role for DHs in screening for premalignant oral lesions in the primary care settings. For the primary point of care to be responsible for the continuous surveillance of OPMDs, they require an easy, fast, and affordable, non-invasive method which brush biopsies fulfill. Cytological analysis of brush samples is a time-consuming method, often plagued by large interobserver variability. It requires specialist skills what makes it expensive, and difficult to introduce brush biopsies on a wider scale. However, cytology assisted by the artificial intelligence (AI)-based technologies opens opportunities for radical improvement. A deep learning-based AI method allows cost-effective, fast, non-invasive and objective characterization of cellular changes. It is concluded that a pipeline for nuclei classification and localization using deep learning can contribute to minimize the subjectivity of the human analysis and also support the detection of cancer at early stages. Through integration of explainable AI techniques, enabling cytologists to interpret and support the AI system, it is possible to develop an interactive tool with which medical and dental expertise can offer the best possible diagnostics at minimal cost.

## 1.1 | Aims

The overall aim of this project was:

To investigate whether DHs and Ds in general dental practice (GDP) are capable to collect enough cell material for cytological diagnosis by brush sampling of OPMDs as part of the national strategy for oral cancer screening and prevention.

The specific aims of this project were:

- To test the ability of DHs and Ds in a dental setting to perform brush sampling for possible automated cytological diagnosis of OPMDs;
- To evaluate the level of comfort in performing brush biopsies for screening of oral lesions among the participating DHs and Ds.

## 2 | MATERIALS AND METHODS

An inquiry regarding the interest to participate in the study was sent out to all 20 GDPs in the Dalarna county, Sweden. Five clinics expressed their interest to participate. One DH and one D were recruited from each clinic. Prior to study start all the participants were engaged in a one day course conducted by 2 senior consultants in orofacial medicine which included: (1) information about the purpose of the study and how it is organized, (2) information and discussion regarding Good Clinical Practice (GCP) adapted for those who work with clinical trials in dentistry (3) lectures on clinical oral pathology including oral examination, in order to learn to identify OPMDs and (4) practical training on how to perform and handle the brush samples for cytology and HPV diagnosis.

All patients over the age of 18 booked for an appointment with the DHs or Ds (regardless of the reason for their visit), were offered to be enrolled in the study. In total, 200 adult patients were intended to be recruited using convenience sampling. To be included in the study, patients had to be without cognitive impairment and to have the ability to understand information about the study, as well as to be able to sign a written consent form.

Clinical examination and documentation were carried out in accordance with the research protocol which included collecting data on the person’s age, gender, tobacco habits, medications, and country of birth. Data on alcohol habits was collected through the Alcohol Use Disorders Identification Test (AUDIT).

Ten samples from healthy individuals and ten from patients with OPMD were planned to be collected by each of the Ds and DHs, which is in total 100 samples from healthy individuals and 100 samples from patients with OPMD. Two brush samples were obtained from each patient, one for cytological analysis and one for hrHPV analysis.

For cytological assessment, specimens were collected using a special brush (Cytobrush Plus GT Medscand, Cooper Surgical) which was rubbed against oral mucosa for approximately 30s (Figure 1).
The cytobrush was placed immediately in a vial of PreservCyt transport medium (Hologic), spun around the walls of the vial for approximately 10 s and then removed. Collected specimens were stored at room temperature until transport to the laboratory at the Department of Pathology & Cytology Dalarna, County Hospital Falun, Falun, Sweden, where they were processed within 4 weeks from the day of collection. At the laboratory, a ThinPrep TP5000 processor (Hologic, Inc.) was used to prepare liquid based cytology (LBC) slides (one slide per patient) according to the manufacturer’s protocol. Slides were stained using Gemini AS slide stainer (Thermo Scientific) according to regressive Papanicolaou (PAP) staining technique as described by Soost et al. Microscopic examination of LBC preparations was performed by a senior cytology specialist (B.V.) using a bright field optical microscope BX43 (LRI Olympus), according to the previously described protocol. Slides were examined at x10 objective from the left to right edge of the preparations with a minimum of 20% overlap between examined fields. Cells with somewhat atypical morphology were marked, and cell morphology was further analysed at 40× objective. When assessing the sample adequacy, a minimum of 10 fields was counted at 40× objective along a diameter that includes the center of the preparation. A cutoff of at a minimum of 5000 well-visualized/preserved squamous cells per slide was applied as in analogy to the previously established criteria for cervical swab evaluations. Representative images of the LBC preparations from a healthy control are shown in Figure 2. Images were obtained using Olympus BX43 light microscope, EP50 digital camera and an Imageview Cam-HD 6.3 series software (LRI Olympus).

Figure 3 shows a brush sample from a histopathologically diagnosed lesion with severe dysplasia and HPV 16 infection. The oral epithelial cells from the lesion show severe dysplasia (published with permission from Tandläkartidningen Hirsch J-M, Haj-Hosseini N, Kruger Weiner C, Hasseus B, Lindblad J (2021) Icke-invasiv kontroll av cellförändringar i munslehminnan. Tandläkartidningen 113 (9):48–55). Orange cells, hyperkeratinized surface cells in which the nucleus is missing. Blue cells with hyperchromatic nuclei with low nuclear cytoplasmic ratio interpreted as severe dysplastic epithelial cells. Dysplastic cells with relatively irregular shape, elongated which usually indicates an ongoing process in which an epithelial cell loses its cell polarity and cell–cell adhesion and acquires migratory and invasive properties, a so-called epithelial-mesenchymal transition.

**FIGURE 1** Cytobrush rubbed against the mucosa.

**FIGURE 2** (A–C) Representative images of the LBC preparations from a healthy control A-4×; B-10× and C-40× magnification. (D–F) Representative images of liquid-based cytology preparations from a subject with the tentative diagnosis of oral lichen planus. D-4×; E-10× and F-40× magnification.
The second brush sample was sent to the Department of Immunology, Genetics and Pathology, Medical Genetics and Genomics, Uppsala University (UU), Uppsala, Sweden, for hrHPV analysis. The cells were transferred on to an Indicating FTA Elute Genomics, Uppsala University (UU), Uppsala, Sweden, for hrHPV Immunology, Genetics and Pathology, Medical Genetics and Genomics, Uppsala University. The cells were transferred on to an Indicating FTA Elute Genomics, Uppsala University (UU), Uppsala, Sweden, for hrHPV analysis. The cells were transferred on to an Indicating FTA Elute Genomics, Uppsala University (UU), Uppsala, Sweden, for hrHPV Immunology, Genetics and Pathology, Medical Genetics and Genomics, Uppsala University.

The hrHPV analysis detects and quantifies the following human papilloma virus (HPV) types: 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, and 59. It also measures a human single copy gene (Homo sapiens hydroxymethylbilane [HMBS]), which serves as a control. For this purpose, the samples must contain enough cellular material so that the analysis can be informative. The limit of detection for both HMBS and HPV was set to ten DNA copies per polymerase chain reaction (PCR).

Following the primary investigation, patients with confirmed lesions (suspected LP, EP, or OLP) were referred to the Department of Orofacial Medicine, Falun Hospital, Falun, Region Dalarna, where the sampling procedure using a brush technique was repeated and a punch biopsy was performed as routine by a specialist in orofacial medicine. For histopathological diagnosis, the punch biopsy was referred to the Department of Oral Pathology, Faculty of Odontology, Malmö University, Malmö, Sweden.

A questionnaire was designed and distributed as an online email survey to the participating DHs and Ds, in order to evaluate their level of comfort with being involved in the continuous clinical follow-up of OPMDs using non-invasive brush sampling for cytology. The questionnaire included background questions regarding number of years in the profession and previous courses on mucosal changes (answer options "yes"/"no"). Other questions concerned identification of mucosal change, taking the sample, taking care of the sample, motivating the patient to agree to a biopsy, and the referral procedure. The answer alternatives for these questions were "easy," "quite easy," "quite difficult," and "difficult." Finally, the participating DHs and Ds were asked for their opinion on whether this follow-up could be included as a part of the daily work at a GDP (answer options "yes"/"no"), how long it took to take the sample, as well as time (in min) for sampling including photographing mucosal lesions.

### 2.1 | Statistics

The data were analysed using IBM SPSS Statistics for Windows, Version 26.0 (IBM Corp.). Descriptive analyses of frequencies, and distributions were performed. Chi-square tests were calculated when comparisons were made between DHs and Ds. Statistical significance was set at $p < 0.05$.

### 2.2 | Ethical considerations

The study involved minimal risk for patients, with only brush samples and, in referred patients, a 5 mm tissue biopsy (punch biopsy) taken from the oral mucosa. The samples were saved according to the existing procedure for pathology in Falun and at Dalarna Biobank (No: RD20-00418), and at the Institute for Immunology, Genetics, and Pathology at Uppsala University.

The results are presented at group level and in such a manner that they cannot be linked to a particular person. The study was approved by the Swedish Ethical Review Authority (No: 2019-03904) and registered at Clinicaltrials.gov (NCT04081038).

### 3 | RESULTS

In total, 100 patients were included in the study, 71% of whom were female. The mean age was 52.2 years (standard deviation [SD] 17.1), 52.9 years (SD 16.4) in females and 50.5 years (SD 19.1) in male patients. In total, 200 brush samples were collected by participating DHs and Ds in GDP, two from each patient. Of the patients, 67 were healthy and 33 had suspected OPMDs. Among the 33 patients with suspected OPMDs and referred to special care for punch biopsy, a further 22 brush samples were collected by a specialist. There was good correlation between the clinical diagnoses set by the DHs, Ds, and specialist with the histopathological diagnosis (see Table 1).

More detailed comparison of the cytopathological and histopathological diagnoses is beyond the scope of this study and remains as (ongoing) future work.

Table 2 shows the number of patient samples obtained per occupational group. In total, DHs collected more samples than Ds (57 vs. 43, $p = 0.005$). The DHs identified fewer patients with lesions than did the Ds (12 vs. 21; $p = 0.003$). All patients referred to specialist

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**FIGURE 3** Brush sample from a histopathologically diagnosed lesion with severe dysplasia and HPV 16 infection.
Of the 122 samples (100 samples collected in GDP and 22 samples in specialist care), 119 (98%) contained enough cell material to perform analysis. The samples were scanned, and the images were found to be suitable for training, validation, and test sets for developing a neural network model for cell detection and classification.

Representative images of the cytological preparations are provided in Figure 1.

For hrHPV analysis, 75 of the 122 samples were analysed, and 71 samples (95%) contained enough cell material to perform hrHPV analysis. All samples were negative for hrHPV.

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<table>
<thead>
<tr>
<th>Clinical diagnosis GDP&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Clinical diagnosis DOM&lt;sup&gt;b&lt;/sup&gt;</th>
<th>Histopathological diagnosis</th>
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</thead>
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<tr>
<td>Erosive changes</td>
<td>Lichenoid reaction</td>
<td>Candida-infected oral mucosa. Lichenoid reaction cannot be ruled out</td>
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<tr>
<td>Oral lichen with erosive changes</td>
<td>Oral lichen planus</td>
<td>Lichenoid reaction</td>
</tr>
<tr>
<td>Bal like mucosal swelling</td>
<td>Mucosal hyperplasia</td>
<td>Mucosal hyperplasia</td>
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<td>White lesion</td>
<td>Benign hyperkeratosis</td>
<td>Benign hyperkeratosis</td>
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<tr>
<td>Reticular lichen</td>
<td>Lichenoid reaction</td>
<td>Lichenoid reaction</td>
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<tr>
<td>Mucosal changes with white streaks</td>
<td>Lichenoid reaction</td>
<td>Lichenoid reaction</td>
</tr>
<tr>
<td>Whitish mucosal change</td>
<td>Hyperkeratosis</td>
<td>Benign hyperkeratosis</td>
</tr>
<tr>
<td>Whitish mucosal change</td>
<td>Hyperkeratosis or normal mucosa</td>
<td>Benign hyperkeratosis</td>
</tr>
<tr>
<td>Lichenoid reaction</td>
<td>Lichenoid reaction</td>
<td>Lichenoid reaction</td>
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<tr>
<td>Snuff lesion</td>
<td>Benign hyperkeratosis</td>
<td>Benign hyperkeratosis</td>
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<td>Gingival lichen</td>
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<td>Stalked whitish lesion</td>
<td>Mucosal hyperplasia</td>
<td>Mucosal hyperplasia</td>
</tr>
<tr>
<td>Whitish mucosal change</td>
<td>Leukoplakia</td>
<td>Benign hyperkeratosis</td>
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<tr>
<td>Erosive lichen</td>
<td>Lichenoid reaction</td>
<td>Candida infected mucosa. Lichenoid reaction</td>
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<td>White non scrapable change</td>
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<td>Leukoplakia</td>
<td>Nonspecific inflammation, hyperkeratosis due to friction injury</td>
<td>Benign hyperkeratosis with unobtrusive hints of verrucous hyperplasia</td>
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<td>Hyperkeratosis</td>
<td>Hyperplasia</td>
<td>Benign hyperkeratosis</td>
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<td>Whitish widespread change</td>
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<td>Tongue lining with slight epithelial dysplasia</td>
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<td>Lichen-like change</td>
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<td>Lichenoid reaction</td>
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<td>Gingivitis</td>
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<tr>
<td>Lichenoid reaction</td>
<td>Lichenoid reaction</td>
<td>Lichenoid reaction</td>
</tr>
<tr>
<td>Ulcerated mucosal change</td>
<td>Irritation hyperplasia</td>
<td>Lichenoid reaction</td>
</tr>
</tbody>
</table>

<sup>a</sup>General Dental Practice.<br><sup>b</sup>Department of Orofacial Medicine.

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<table>
<thead>
<tr>
<th>Number of patients</th>
<th>Dental hygienists</th>
<th>Dentists</th>
<th>Total</th>
<th>Specialist dentist</th>
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</thead>
<tbody>
<tr>
<td>Patients with healthy samples</td>
<td>45 (67.2%)</td>
<td>22 (32.8%)</td>
<td>67</td>
<td>-</td>
</tr>
<tr>
<td>Patients with mucosal changes</td>
<td>12 (36.4%)</td>
<td>21 (63.6%)</td>
<td>33</td>
<td>22</td>
</tr>
<tr>
<td>Total</td>
<td>57 (57.0%)</td>
<td>43 (43.0%)</td>
<td>100</td>
<td>22</td>
</tr>
</tbody>
</table>

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TABLE 1 The clinical diagnosis set by dental hygienists, dentists, by specialist in orofacial medicine and the histopathological diagnosis.
Of the ten participants, nine (five DHs and four Ds) responded to the questionnaire regarding work experience in years, and comfort in performing brush sampling. Table 3 presents data on the participants’ years of work, previous courses on mucosal changes, and experience of sampling. The mean number of years of work in the profession was 21.4 (DHs) and 23.0 years (Ds). All participants thought that sampling can be included in the duties of DHs and Ds, and most thought that sampling and taking care of the samples was easy or quite easy. Seven out of ten of the participants thought the referral procedure was easy or quite easy. The time spent on taking the sample was somewhat longer for the DHs, especially when the process included taking photographs. A general comment was that much of the time spent on sampling was due to the fact that this was a study, which involved extra administrative tasks, and that the brush test itself only took about 5–10 min.

4 | DISCUSSION

The objective of this study was to explore if DHs and Ds were able to obtain sufficient cell material for cytological analysis by collecting brush samples.

The results have demonstrated that DHs and Ds in GDP are capable and well suited to obtain cell samples for diagnostic purposes and for cell characterization as well as hrHPV analysis. The results have shown that all but three brush samples contained enough cells to allow cytological analysis, and it was possible to extract DNA for hrHPV PCR from all but four samples. The clinical picture as judged by the primary care staff as showing a mucosal derangement was, by the specialist considered, relevant for further investigation, and for incisional biopsies. Based on the histopathological diagnosis the clinical picture was considered as normal and not associated with any disease.

The aim was to collect 200 brush samples in total. Due to the Covid-19 pandemic, with limited patient contact, the collection of samples ceased when samples from altogether 67 healthy patients and 33 patients with suspected OPMDs had been obtained in GDP. However, the number of samples was considered sufficient for the purpose of this study as 99% of the samples were adequate for cyto- logical and 95% were adequate for HPV diagnosis. Before the study was initiated all participants had one day of information and education which included half a day training in oral clinical pathology which could have been extended with a few more hours. This would have possibly resulted in more samples from mucosal changes.

Sweden has a long tradition of screening for cervical cancer in primary care. Cell sampling for cytology and HPV analysis is performed by midwives, who send the samples to the laboratory for testing. The evaluation of the resulting report, naturally, is in the hands of a specialist who is responsible for evaluation and organizing follow-up measures if required. Our long time goal is to implement this model in clinical practice for continuous follow-up of OPMDs in general dental care by DHs and Ds by using cytological diagnosis of oral mucosal changes which has been reported to be a safe, simple and fast method with high sensitivity and specificity. The modification of the Bethesda system for oral cytology can be used as a standardized system for the oral cytological assessment.

All the participants thought that brush sampling could very well be carried out as part of routine in GDP. This notion is further underlined by the answers in the questionnaire, distributed to all participants, where a majority found the brush samples easy or quite easy to perform. The participating DHs spent more time on collecting the samples compared to the Ds, and probably this was because in Sweden, DHs have no assistants, whereas Ds do.
Furthermore, the fact that this was a study, with some extra administration and with information having to be given to the patient, also contributed to the extra time DHs spent on sampling while the extra administration can easily be handled by the Ds as assistant.

None of the participants found it difficult to identify mucosal changes, and, according to the specialist at the specialist clinic, all referred patients with mucosal changes were correctly referred. As EP and LP are clinical diagnoses, an incisional biopsy is necessary to establish a histopathological diagnosis that coincides with the clinical diagnosis. Three samples diagnosed as lichenoid reactions in the tissue samples did not clearly demonstrate a microscopic picture to support the diagnoses of LP and EP. However, it is mandatory to confirm a tentative clinical diagnosis with a tissue biopsy to be able to decide on the correct treatment.

All the collected samples were negative for hrHPV and the clinical diagnosis of OPMDs was not clearly established, confirming the challenges in identifying OPMDs as described previously. When an OPMD diagnosis is made, the patient should always be enrolled into a follow-up program to ensure that high grade cellular changes and oral cancer are diagnosed promptly. This is important, as it is not possible to predict which oral EP, LP, or OLP will progress to neoplasia – notably squamous cell carcinoma. An efficient, fast and cost-effective way to do this is by performing brush biopsies, a non-invasive technique with sufficient sensitivity and specificity that does not require surgery. It can be performed in GDP, as demonstrated by the results of this study. The report from the cytological examination should always include a copy to the responsible specialist in the same way as in case of screening for cervical cancer by the midwives in primary care. If cellular changes are significant, the patient should be reviewed by a specialist for further evaluation and treatment, which normally includes surgical interventions. Based on the collective findings, the specialist must decide on further management of the patients. If a future plan involves follow-up based on the cytological diagnosis this could very well entail continuous follow-up with brush sampling in GDP, as outlined above.

Even though the specialists in orofacial medicine considered all the referred patients as relevant for further investigation, based on the experience of this study, extended training in clinical oral pathology is suggested in advance of introducing brush sampling in GDP. Dental hygienists collected more samples than Ds did, but the Ds collected fewer samples with lesions, indicating a difficulty in identifying lesions adequate for brush sampling. Therefore, it is also suggested to initiate a discussion regarding the curriculum for the degree of dental hygiene with the responsible parties. A DH must demonstrate the ability to independently perform oral examinations, and to recognize the need for interventions. Previous studies regarding DHs conducting screening of oral lesions are few. Based on the answers from 369/3000 responders, an online email survey concluded that continuing education is needed for DHs to be able to be responsible for continuous surveillance of OPMDs. To summarize, in advance of replacing tissue biopsies with brush biopsies for cytology, the recommendation is still to handle continuous surveillance of oral lesions at a specialist clinic, which may explain the high propensity to refer patients to a specialist. The Swedish agency for health technology assessment and assessment of social services (SBU) have investigated the reliability of brush samples in combination with cytology when assessing oral mucosal lesions. The overall results showed that the sensitivity and specificity of diagnosis of oral cancer or potentially malignant changes was high. However, the sampling was mostly carried out by specialists, which makes the transferability of the results when implemented in general dental care uncertain. Our results show that brush sampling in general dental care worked very well in the five general dental practices which took a part in the study.

In the future, even self-sampling, as available for screening for cervical cancer (which has been shown to work well), may be an option. Furthermore, to organize screening, there is a need for a fast and inexpensive sampling procedure, including sampling, sending, and assessing samples in a safe way, and quickly reporting the results. It is therefore important that the process of preparing and scanning the microscope slides is efficient. Introducing an objective and non-invasive diagnostic method such as AI-assisted digital cytology may be of a great significance for the efficient OPMDs surveillance and follow-up after cancer treatment. With a reliable AI system, we expect that the workload of cytopathologists may decrease. More frequent brush sampling could be economically advantageous for both the society and the patient, enabling an earlier diagnosis and easier follow-up.

5 | CONCLUSION

Based on the results of this limited study, we found that DHs and Ds in GDP are capable to collect enough cell material for cytological analysis. All the participating DHs and Ds were of the opinion that brush sampling could be handled routinely by DHs and Ds in GDP.

6 | CLINICAL RELEVANCE

6.1 | Scientific rationale for the study

To organize screening using a fast and inexpensive sampling procedure, including sampling, sending, and analysing samples in a safe way, and quickly reporting the results, in order to prevent death from oral cancer.

6.2 | Principal findings

In order to better prepare DHs to identify suspected OPMDs, the curriculum in clinical oral pathology needs to be expanded, and in parallel, postgraduate and clinical training should be organized.
6.3 | Practical implications

Based on the results of this limited study, we suggest that follow-up of oral lesions, previously diagnosed through routine incisional biopsies at a specialist center, could be handled routinely by DHs and Ds in GDP, using a brush sampling technique. With occurrence or recurrence of abnormal cytology, the patients should be referred to the specialist center.

AUTHOR CONTRIBUTIONS

Conceptualization, K.E, CRS, VB, JL, JMH; methodology, K.E, CRS, VB, JL, JMH; software, K.E; validation, K.E, CRS, VB, JL, JMH; formal analysis, K.E; investigation, K.E, CRS, VB, JL, JMH; resources, K.E; data curation, K.E, CRS, VB, JL, JMH; writing—original draft preparation, K.E; writing—review and editing, K.E, CRS, VB, JL, JMH; visualization, K.E, CRS, VB, JL, JMH; project administration, K.E; funding acquisition, K.E. All authors have read and agreed to the published version of the manuscript.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest. The funder had no role in the design of the study; in the collection, analysis, or interpretation of data; in the writing of the manuscript; or in the decision to publish the results.

DATA AVAILABILITY STATEMENT

Data are available on request.

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