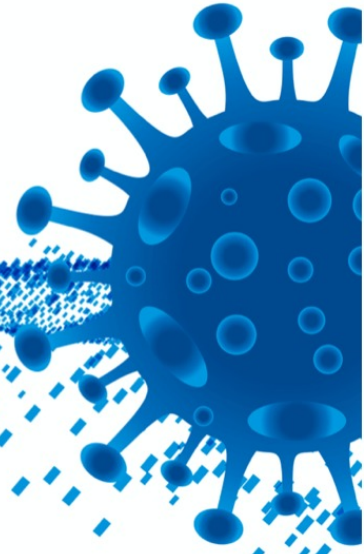


COVID-19 **MD**



# COVID-19

Clinical Guidelines Dentistry

| **Update**

Scientific paper drawn up by the COVID-19 MD group aiming the dissemination of the knowledge about the clinical practice in Dentistry in the context of COVID-19.

The expression *Clinical Guidelines* refers to a scientific methodology and type of publication arising from it. This document should not, thus, be understood as legislation nor as any type of imposition of regulatory or legal nature. It is a scientific contribution to the broadening of the knowledge about the professional practice in the context of COVID-19, hopefully serving its recipients.



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This document consists of a partial update of the full document COVID-19 | Clinical Guidelines for Dental Medicine, published in April 2020<sup>[1]</sup>. Updating a document of this magnitude may involve replacing it in its entirety or maintaining the matrix with the relevant changes (partial update). The previously published recommendations that justified changes are duly presented below, having been the subject of discussion and deliberation by the COVID-19 MD group.

It should be noted that the process of updating a Clinical Guidance Standard is governed by the following purposes<sup>[2,3]</sup>:

- Change or adding bibliographic references;
- Change of the clinical recommendation, in order to reflect the context of current practice; this change can alter the cost-benefit of a given recommendation;
- Important changes in results;
- Changes in health service settings; changes in available resources;
- Ensure that the recommendations take into account the latest government policies;
- Reflect people's involvement in care decisions;
- Patient-centered language.

A quality clinical decision rests on three assumptions:

- The patient's interests; if the clinical decision doesn't satisfy him/her, it will have failed miserably its main goal;
- The practitioner's experience as a key element unifying his/her acumen, knowledge and even intuition, the so-called human factor;
- The scientific evidence as a basis of reliable, objective and essential information.

The Clinical Guidelines presented here intend to be that basis of information and knowledge, objectives which are key to support the clinical decision.

Every theatre of clinical practice has its own specificities. In this context, these Clinical Guidelines do not constitute hermetic orders to abide by, but only a robust body of knowledge allowing the practitioner to set up the implementing protocol which best suits the characteristics of each clinic.

It should also be added that the adoption of these guidelines doesn't guarantee zero risk of acquisition of the infection.

## List of Abbreviations

ADA = American Dental Association

CDC = Centers for Disease Control and Prevention

CHX = Chlorhexidine gluconate

CPC = Cetylpyridinium chloride

ACE2 = Angiotensin-Converting Enzyme 2

IL = Interleukin

IPVD = Povidone-iodine

PPE = Personnel protective equipment

PXH = Hydrogen peroxide

rt-PCR = Reverse transcription polymerase chain reaction

## Preliminary remark

Despite the appearance of COVID-19 a year, there is still a gap in the quality of the scientific evidence that is published. The amount of information in this area is excessive, in a desperate attempt to find answers to a virus that is still so unknown to us. As such, this update followed the methodology of the initially published NOC (protocol provided by the English National Institute for Health and Care Excellence (NICE), namely the interim process and methods for developing rapid guidelines on COVID-19 ([nice.org.uk](https://www.nice.org.uk) <sup>[4]</sup>).



# Introduction

Addition of 5 sections, without any change in the previously published information.

- Oral manifestations;
- Saliva;
- Impact of COVID-19 on the Dental sector;
- Telemedicine;
- Vaccination.

## Oral manifestations

### Periodontal Disease

Periodontal disease can be compared to a silent pandemic which pathophysiology is complex and multifactorial. COVID-19 is classified as a pandemic, where the development of symptoms may be associated with a “cytokine burst”. This event involves an increase in the levels of inflammatory factors, namely interleukins (IL), gamma interferon and tumor necrosis factors. In patients diagnosed with periodontal disease, there is an increase in the levels of IL-6 and IL-17, produced at the level of gingival tissues and with repercussions at the systemic level<sup>[5,6]</sup>. This “cytokine burst”, present in both pathologies, suggests a possible relationship between both, in order to understand whether the presence of one of them is a risk or predictive factor. That said, the need and importance of periodontal support consultations is reinforced<sup>[5,7,8]</sup>.

In Periodontal Disease, the supporting tissues are destroyed by bacterial infection, with the transition from a healthy sulcus to a periodontal pocket. When it comes to periodontal pocket, viral species are detected (herpes simplex 26-78%; epstein-barr 46-58%; cytomegalovirus 42-58%). This suggests that periodontal pockets provide an environment compatible with viral infection and survival<sup>[8,9]</sup>. In addition, gingival crevicular fluid can also constitute a reservoir for SARS-CoV-2<sup>[9,10]</sup>.

### Oral Injuries

The spread of COVID-19 correspond to the detection of a wide range of oral manifestations. On this basis, concerns were raised about the possible causes of these

injuries: whether caused directly by the SARS-CoV-2 virus or indirectly by the failure of the infected host's immune system<sup>[11,12,13,14]</sup>. Oral signs and symptoms associated with COVID-19 include changes in taste, unspecific oral ulcerations, desquamative gingivitis, petechiae, and opportunistic infections, such as infection by candida albicans. Oral lesions have different clinical aspects, varying in location, size, appearance of color and quantity<sup>[11]</sup>.

Abanoub Riad<sup>[15]</sup> and his co-workers published several cases, in which they suggest that the presence of oral mucositis in positive SARS-CoV-2 patients may be related to direct damage to cells infected by the virus or as an opportunistic infection resulting from immune dysregulation.

The name “COVID tongue” emerged in an attempt to categorize clinical characteristics associated with infection by SARS-CoV-2, a virus that is still unknown. However, the oral manifestations detected in the tongue are nonspecific and relatively common in the general population, namely glossitis, aphthous stomatitis, irregular depapillation (associated with lesions of the geographical tongue), therefore, this label should be interpreted cautiously in order to avoid false diagnoses<sup>[16, 17]</sup>.

## Saliva

The functional receptor for SARS-CoV-2 is known to be the receptor for the angiotensin II-converting enzyme (ECA2). This receptor was found in the ducts of the epithelial cells of the salivary glands, especially in the minor glands. Therefore, the early contamination of the salivary gland ducts produces infected saliva, which can culminate in the appearance of oral symptoms prior to lung injuries<sup>[18, 19, 20]</sup>. In addition to this route of entry of the virus into the oral cavity, there are two others, the SARS-CoV-2 from the upper respiratory tract or bloodstream<sup>[21, 22]</sup>.

Recent research has put saliva as a potential diagnostic tool for SARS-CoV-2 infection due to its easy access and interconnection with systemic diseases<sup>[19, 23, 24, 25]</sup>.

Regarding the diagnosis of infection by SARS-CoV-2 via salivary samples, there are several advantages over the collection of nasopharyngeal samples. These include the fact that the technique is minimally invasive, easy, inexpensive, and the harvest can be performed by the individual himself (not requiring specialized personnel) and with a minimal risk of cross-infection<sup>[19, 20, 21, 24, 26, 27, 28]</sup>. In addition, the collection of saliva provides a sample of sufficient size to test different biomarkers<sup>[22]</sup>. However, the

interpretation of the results published in the literature has to be performed with caution, since results with different sensitivity and detection rates have been revealed in symptomatic and asymptomatic patients. In another words, in asymptomatic patients, salivary samples are more sensitive and have a higher SARS-CoV-2 virus detection rate than nasopharyngeal samples. In symptomatic individuals the results are exactly the opposite<sup>[19]</sup>.

The collection of saliva can be performed in the posterior oropharyngeal region (the individual encourages the production of sputum, including the collection of pharyngeal and not exclusively oral secretions); or collection of oral saliva from the salivary glands exclusively<sup>[27]</sup>.

Haya Altawalah and her co-workers<sup>[29]</sup> conducted a cross-sectional study, whose objective was to evaluate the potential of salivary detection of SARS-CoV-2 by rt-PCR as an alternative to nasopharyngeal samples. The results suggest a high sensitivity (83.43%) and specificity (96.71%) for the salivary rt-PCR test when compared to the nasopharyngeal standard sample. These results corroborate those of previous publications. The k coefficient points to strong concordance analyzes for the diagnosis of SARS-CoV-2 via nasopharyngeal and salivary samples<sup>[29]</sup>.

László Márk Czumbel and his co-workers<sup>[30]</sup> in a meta-analysis, emphasize the need for standardization of procedures related to the collection and processing of salivary samples as a means of diagnosing SARS-CoV-2 infection, despite highlighting saliva as a promising method.

Another issue to be addressed in future investigations is related to the technique of collecting the salivary sample and whether different collection methods influence the sensitivity of the test for the detection of SARS-CoV-2 infection<sup>[21]</sup>. It should be noted that the technique of extracting viral RNA, detected viral load, the number of crops, which saliva to collect and when to collect it must also be standardized. For example, it is known that the viral load in saliva is higher in the first days of infection and that it tends to decrease exponentially when the virus already has pulmonary involvement<sup>[22]</sup>. There are studies that are beginning to highlight the potential diagnosis of samples of gingival crevicular fluid<sup>[31]</sup>.

# Impact of COVID-19 on the Dental sector

The panorama of dental medicine has experienced major changes, not only economically, but also in the psychological field of the dental team. And, if before the pandemic, the dental medicine consultation was a safe place, with the adaptations introduced today, it is even more<sup>[32, 33]</sup>.

Economically, this impact translates into an increase in the cost of personal protective equipment<sup>[34]</sup> and a decrease in the number of consultations given. Since then, the appointment times were increased, in order to consider a period of disinfection and ventilation of the office<sup>[35]</sup>. On the other hand, the expectation of a possible economic crisis often culminates in postponing treatments<sup>[36]</sup>.

The challenges of this new era have forced dentistry and medicine to reinvent itself. This adaptation includes the introduction of new technologies, so that the interests of patients are protected and safeguarded. Telemedicine is an example of this reinvention.

## Telemedicine

Telehealth consists of using electronic and technological strategies to provide long-distance clinical support and promote the education of patients and professionals<sup>[37]</sup>. Telemedicine is defined as the use of video conferencing for diagnosis and medical advice about a certain pathology<sup>[37, 38]</sup>. These concepts are not new and date back to 1997. Nevertheless, the lockdown has forced the world to, as a result of the pandemic by COVID-19, allow the rapid development of this medical approach<sup>[37]</sup>. The word “tele” means distance, so telemedicine presupposes compliance with one of the most important measures to prevent the spread of the virus: social distance<sup>[39]</sup>.

There are several advantages in the area of Telemedicine, namely: Teleconsultation; Tlediagnosis, Teletriaging and Telemonitoring<sup>[39]</sup>.

COVID-19 has a real impact on oral health, not only because of the role that salivary glands play as potential reservoirs of the SARS-CoV-2 virus, but also because of the injuries that can manifest in the oral cavity of infected individuals. In the latest publications that relate oral health to infected individuals, vesicle-bullous and maculopapular lesions are described<sup>[40, 41]</sup>. So, the early detection of these lesions by an oral medicine specialist can play a key role in screening individuals suspected of being infected with SARS-CoV-2<sup>[8, 40]</sup>.

The systems available for the application of Telemedicine are still restricted, but they represent an easily accessible, viable and useful tool for both healthcare professionals and patients. This communication can be via messaging applications (WhatsApp, Instagram, SMS, Messenger) or video calling systems (WhatsApp, Skype, FaceTime)<sup>[40]</sup>. Petruzzi et al.<sup>[42]</sup> confirmed the 82% agreement between the diagnosis of cases by teleconsultation and clinical and pathological examination.

One of the specialties that will most benefit from this remote system is Orthodontics, especially in appliance control appointments<sup>[43]</sup>. Still, it is an area with limitations as it is often dependent on the quality of the image that patients provide. For a correct diagnosis, the images must be representative of the entire region of the mouth to be analyzed, as well as without any filter<sup>[40]</sup>.

It should be noted that Telemedicine is not a substitute for face-to-face appointment because it has a palliative approach<sup>[40]</sup>. However, once explored and well implemented, it is a complement to the practice of conventional dentistry<sup>[34]</sup>. In pandemic situations, Telemedicine prevents the spread of the virus among healthcare professionals and patients<sup>[13]</sup>.

## Vaccination

In April 2020, efforts to develop a SARS-CoV-2 vaccine grew exponentially and culminated in more than 100 proposals under study<sup>[44]</sup>.

Currently, the European Medicines Agency has approved the use of vaccines from BioNTech/Pfizer<sup>®</sup>, Moderna's<sup>®</sup> and AstraZeneca<sup>®</sup>. The Janssen vaccine is in the process of approval and Sanofi vaccines - GSK<sup>®</sup> and CureVac<sup>®</sup> have not yet started the authorization process.

The formulation of each type of vaccine depends on how the virus's genetic material is used - recombinant proteins, replicative or non-replicating viral vectors, DNA, mRNA, live attenuated vaccines or with the virus inactive<sup>[44, 45, 46]</sup>.

Vaccines provoke an immune response through specific antibodies in the long term, although existing studies are still insufficient to attest to this claim<sup>[47]</sup>.

It is important to note that within the concentrations of viral particles in the vaccine that can confer immunity, side effects must be taken into account. Thus, higher concentrations tend to have more pronounced side effects, and the effectiveness is

maintained<sup>[44]</sup>. The most common side effects are fatigue, flu-like syndrome, vomiting, nausea, fever, arthralgia, headache, anaphylaxis - stressed the importance of vaccination<sup>[48, 49, 50]</sup>.

For vaccines already approved, their prescription consists of two doses at intervals of 21 days, 28 days or 12 weeks respectively for BioNTech/Pfizer<sup>®</sup><sup>[48]</sup>, Moderna's<sup>®</sup><sup>[49]</sup> and AstraZeneca<sup>®</sup><sup>[50]</sup>. The effectiveness of the three vaccines is very similar. The BioNTech/Pfizer<sup>®</sup> and Moderna's<sup>®</sup> vaccines suggest an efficacy greater than 90% after the second dose<sup>[51]</sup>, while the AstraZeneca<sup>®</sup> vaccine suggested a 70% efficacy in the initial studies. However, new publications show a greater effectiveness of this vaccine when applied with an interval of 12 weeks instead of 4 weeks<sup>[52]</sup>.

It is not correct to say that there is a vaccine that overlaps another, since the three approved vaccines have led to a decrease in severe cases of hospitalization and in cases of death by COVID-19.

However, it is necessary to maintain the preventive rules for compliance with social distance, respiratory etiquette and the use of a mask.

# Materials and Methods

Update of the sections "Bibliographic Research" (date of the research; search terms), "Inclusion/Exclusion Criteria", "Selection and Assessment of Evidence" and "Research Results".

## Questions (Appendix II, section 1)

Reformulation of questions 2.4. and 2.5. of the Pre-Intervention Stages group.

## Bibliographic Research

An update of the systematic research of the *MEDLINE* (via *PubMed*), *Cochrane Library* and *Trip Database* databases was conducted, with known technical limitations, during the period ranging between **April 2020 and March 2021**. The search included the following keywords individually and in different combinations (Appendix II, section 2): "SARS"; "MERS"; "SARS-CoV-2"; "COVID-19 OR Covid-19 OR coronavirus\*"; "influenza"; "dentistry"; "**COVID tongue**"; ["ventilator" AND ("oral hygiene" OR "dentistry)]; [{"aerosol\*" OR air) AND "SARS"]. In a second phase we cross-checked the results of the first research with the algorithm created by the *National Institute for Health and Care Excellence* (NICE)<sup>[4]</sup>.

## Inclusion/Exclusion Criteria

The following have been defined as inclusion criteria (Appendix II, section 3):

**Patients (P):** patients infected or not with the virus SARS-CoV-2.

**Intervention (I):** any type of dental procedure, with or without the generation of aerosols, in a context of pandemic by SARS-CoV-2.

**Comparison (C):** any type of dental procedure, with or without the generation of aerosols, before the pandemic by SARS-CoV-2.

**Outcomes (O):** control of SARS-CoV-2 virus transmission; monitoring of patients infected with SARS-CoV-2; prevention measures; disinfection measures; risk of the

procedures carried out in dentistry in the contraction of the infection by SARS-CoV-2; training for the health professionals and administrative staff for the new post-pandemic situation; interpersonal contact at times of pandemic by SARS-CoV-2; which personal protective equipment (PPE) to wear, its effectiveness and how to wear it; **oral manifestations of the disease; oral health-SARS-CoV-2 interaction; vaccination.**

The following have been defined as exclusion criteria(Appendix II, section 4):

**Criterion A:** creation of a Clinical Database;

**Criterion B:** other pathologies;

**Criterion C:** triage of opting for hospital treatment/treatment at home;

**Criterion D:** genetic studies/genome;

**Criterion E:** pharmacology;

**Criterion F:** articles written in languages other than Portuguese, English, Spanish and French;

**Criterion G:** others that are not included in the previous ones.

## Selection and Assessment of Evidence

The research, the triage by title, the abstract and the full analysis of the text of the article were conducted/written by two proofreaders (AV; CM). Any disagreements have been solved through direct confrontation in the form of oral discussion. In situations where an agreement could not be reached, resort was had to a third proofreader (AM).

We have made a summary critical assessment of the literature, but we have not formally assessed the risk of the presence of biases resorting to specific scales.

However, we have always briefly and simply indicated the kind of information underlying the clinical recommendations produced by us.

## Ranking of Evidence and Class of Recommendation

The objective of the Clinical Guidelines lies on formulating recommendations based on the evidence which has clinical applicability. The levels of evidence (Appendix II, section 5) rank the different kinds of articles depending on the intrinsic methodology, while the classes of recommendation (Appendix II, section 5) rank the force of the action. In this context, it is expectable that strong recommendations present less frequent variations. The review of scientific evidence allows to gage the ratio risk/benefit of a given action<sup>[25]</sup>.



## Research Results

After duplicates have been removed, the research of the databases resulted in a total of 132,876 references, of which 132 641 did not match the inclusion criteria, being consequently ineligible, and were classified as excluded. We obtained the full articles of the 274 potentially eligible references, selected through systematic and manual research.

After the assessment, 123 studies were excluded for the reasons described in Appendix I, section 4.

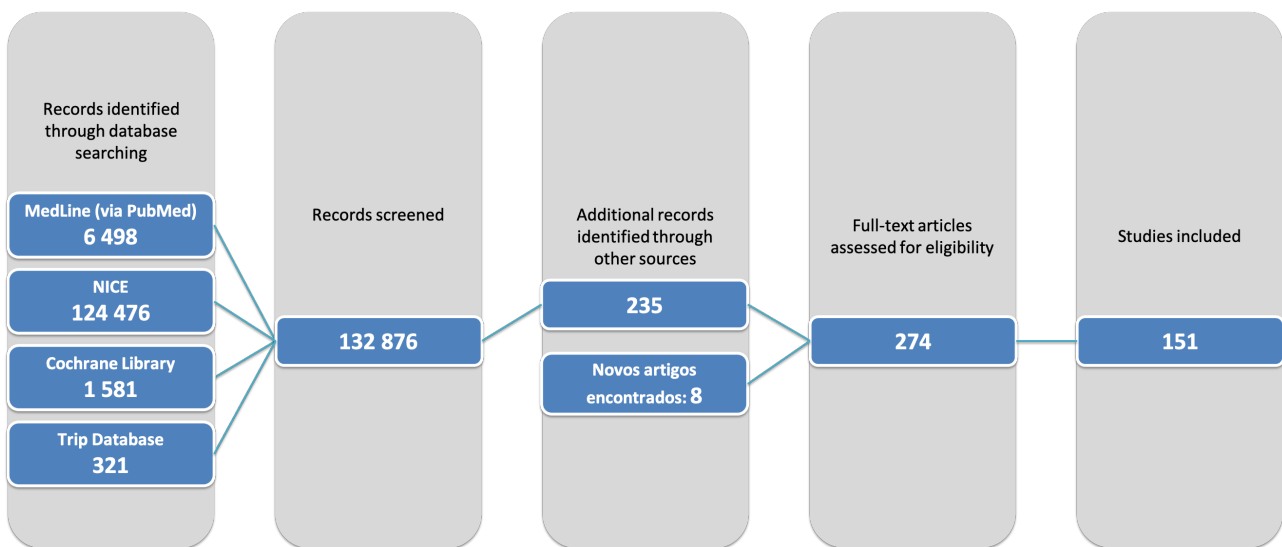


Figure 2 - Result of the Systematic Research.

# The Pre-Intervention Stages

Consolidation of scientific evidence on the sections The Schedule | The management of the appointments; questions 1.4. and 1.5.

Adjustment of the clinical recommendation previously proposed in questions 2.1., 2.4. and 2.5.

## The Schedule

### The management of the appointments

#### **UPDATE OF THE EVIDENCE THAT SUPPORTS THE QUESTION, WITH CHANGES IN THE LEVEL AND CLASS OF THE RECOMMENDATION**

The dental health care personnel main concern is the protection of the patient as well as of all those involved in the management and operation of the clinic in a safe way, keeping the levels of effectiveness of treatment and meeting the patient's demands<sup>[53]</sup>. *(Level III, Class IIa)*.

#### **UPDATE OF THE EVIDENCE THAT SUPPORTS THE QUESTION 1.4., WITHOUT CHANGING THE LEVEL AND CLASS OF THE RECOMMENDATION**

---

Should the patient be alerted to avoid paying the consultation in cash?

**Answer:** Yes, the patient must be alerted to pay using, preferably, the POS terminal or any other electronic means<sup>[54, 55]</sup>. *(Level IV, Class IIa)*

## UPDATE OF THE EVIDENCE THAT SUPPORTS THE QUESTION 1.5., WITHOUT CHANGING THE LEVEL AND CLASS OF THE RECOMMENDATION

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What are you supposed to do if a patient asks for a teleconsultation?

**Answer:** The option of providing a teleconsultation is the sole responsibility of the doctor and the clinic. Given the specificity of the necessary treatments in most specialties of dentistry requiring the presence and contact with the patient, the decision must be made case-by-case. The digital consultation may be established by electronic mail or video through several digital platforms, through applications for cellphones, among others, **always respecting the patient's privacy as if it were a face-to-face consultation**<sup>[56, 57,</sup>

<sup>58, 59]</sup>. (*Level III, Class II*)

## Questionnaire to be completed

### ADJUSTMENT OF THE CLINICAL RECOMMENDATION AND UPDATE OF THE EVIDENCE THAT SUPPORTS THE QUESTION 2.1.

Which questions must be asked while making an appointment by telephone?

Previously proposed recommendation:

- The questions asked referred to the last 15 days; With regard to taste and smell, the question focused only on sudden loss, not distinguishing between total and partial loss;

**Answer:** The following questions must be asked:

- **Do you have (or have you had) fever over the last 14 days?** (temperature  $\geq 38$  °C)
- **Do you have (or have you had) cough or trouble breathing over the last 14 days?**
- **Do you have/experience (or have you had/experienced) a general discomfort, physical fatigue, diarrhea or headaches over the last 14 days?**
- **Do you complain from (or have you experienced) a total or partial loss of smell or taste over the last 14 days?**
- **Does any of your family members or close contacts suffer from (or has any of them referred) any of those symptoms over the last 14 days?**
- Have you been in contact with anyone suspect or having tested positive for COVID-19?
- Have you already been diagnosed with COVID-19? **If the answer is affirmative: Are you still in isolation period (14 days)?**

If any of the answers is affirmative, the doctor must be informed about the health condition and weigh up the urgency of the patient's treatment<sup>[54, 55, 60-73]</sup>. (*Level IIb, Class I*)

## **ADJUSTMENT OF THE CLINICAL RECOMMENDATION AND UPDATE OF THE EVIDENCE THAT SUPPORTS THE QUESTION 2.4.**

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The patient reports that he was infected with SARS-CoV-2, **but he no longer has symptoms**, how to proceed?

Previously proposed recommendation:

- If the patient has had no symptoms for at least 3 days (fever, cough, fatigue, shortness of breath), has been in isolation at home and tested negative for SARS-CoV-2 with a test (rRT-PCR for SARS-CoV- 2), this patient can now go to the consultation.

**Answer:** If the patient has not had a fever for at least 3 days (without using antipyretics), has significantly improved cough, fatigue, and shortness of breath, and has been in isolation at home for at least 10 days in asymptomatic, mild or moderate cases, or 20 days in the most severe cases, you do not need to present a negative laboratory test for SARS-CoV-2 and you can go to the consultation<sup>[73, 74, 75]</sup>.

For professionals at high risk of exposure such as health professionals or caregivers of close proximity to vulnerable people, the previous criteria should add the need for a negative test for SARS-CoV-2 with a test (rRT-PCR for SARS- CoV-2) If the laboratory test result for SARS-CoV-2 is positive, the isolation is prolonged until 20 days have elapsed since the onset of symptoms, at which point the isolation end is determined, without the need for additional testing. laboratory testing. (*Level IV, Class IIa*)

## **ADJUSTMENT OF THE CLINICAL RECOMMENDATION AND UPDATE OF THE EVIDENCE THAT SUPPORTS THE QUESTION 2.5.**

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How to **proceed with the appointment of a patient considered a suspected or confirmed case of COVID-19** and who is in isolation at home?

Previously proposed recommendation:

- A patient in a period of isolation by COVID-19 and in need of urgent medical and dental treatment can only abandon isolation with the authorization of the Health Delegate or Assistant Physician of the Local Family Health Unit. Only with this authorization will the patient be able to go to the clinic or dental

office and be treated according to the individual protection rules in force for all medical and dental procedures.

**Answer:** A patient undergoing a period of isolation due to COVID-19 in need of urgent dental treatments can only leave the isolation after authorization by the Local Health Delegate. This clearance is the only one allowing the patient to visit the clinic or dental practice and to be treated according to the standards of individual protection in force for every dental procedure<sup>[73, 76-78]</sup>. **In the imperative need to observe a suspected or confirmed case of COVID-19, in urgent situations, consider scheduling the appointment, at the end of the morning or in the afternoon, at specific times, so that there is no sharing of the waiting room, always consulting the patient with the use of PPE for high-risk procedures<sup>[55]</sup>. (Level IV, Class IIa)**

# The Peri-Intervention Stages

Consolidation of scientific evidence on the sections Definition of Risk of the Procedure; question 15.3. Personal Protective Equipment (PPE); questions 17.1., 17.2., 17.3. and 17.5

Adjustment of the clinical recommendation previously proposed in questions 18.1.

## Definition Of Risk of the Procedure

### UPDATE OF THE EVIDENCE THAT SUPPORTS THE QUESTION 15.3., WITH CHANGING THE LEVEL AND CLASS OF THE RECOMMENDATION

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How should the general procedures in a clinic be ranked in terms of risk?

**Answer:** At the dental clinics there are several levels of equipment to be worn according to the risk to which one is exposed. Considering every patient as a potentially infected individual, the risk of contagion must be considered real and you must not underrate it. The risk is defined by the proximity of exposure as a result of the kind of tasks one performs and by the recurrence of the exposure. We can consider the following levels of risk of the procedure:

- Low risk: sporadic contact with people, considering that social distance is kept and that there is no contact with potentially infected people;
- Moderate risk: constant interaction with people, having, however, the possibility of keeping safety distancing, adopting a respiratory etiquette and wearing masks;
- High risk: frequent and close contact with patients (the distance from them being less than 1 m), but without performing aerosol-generating procedures;
- Very high risk: frequent and close contact with patients (the distance from them being less than 1 m), but with aerosol generation [79-82].

At the clinic, the administrative and secretariat staff may present a moderate or low risk, however, assistants, hygienists and doctors present a high or very high risk of exposure [79,82-84]. **(Level III, Class I)**

# Personal Protective Equipment (PPE)

## PPE donning

### **UPDATE OF THE EVIDENCE THAT SUPPORTS THE QUESTION 17.1., WITH CHANGING THE LEVEL AND CLASS OF THE RECOMMENDATION**

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17.1 Must the PPE to be worn be defined by the risk involved in the procedure ?

**Answer:** The risk of the procedure to be performed defines the type of PPE to be worn. However, when it comes to select the PPE, you must consider factors other than its function, like its fitting, how comfortable it is to put on and wear, the possibility of decontamination, being disposable and its cost. The professional must select the combination of elements of the PPE that best fit, given that he/she might have to wear them for long periods and, therefore, they must be as comfortable as possible. As a general rule, the type of PPE must be selected according to the following levels of risk of the procedure<sup>[79,82,85-96]</sup>. **(Level Ib, Class I)**

- Low risk - basic equipment (uniform or disposable gown, dedicated shoes or shoe covers and surgical mask);
- Moderate risk - degree 1 protection PPE;
- High risk - degree 2 protection PPE;
- Very high risk - degree 3 protection PPE.

(read donning of the PPE - Appendix III, section 2)

### **UPDATE OF THE EVIDENCE THAT SUPPORTS THE QUESTION 17.2., WITH CHANGING THE LEVEL AND CLASS OF THE RECOMMENDATION**

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17.2 What is the appropriate PPE according to the levels of protection?

**Answer:** The selection of the equipment is conditioned by the level of risk and the degree of protection inherent in the procedure to be carried out. Additionally, every equipment must be certified for use in the EU. It is necessary to undergo some training for its donning and, mainly, for its removal, since many of the cases of contamination of the health professionals occur during the removal of the contaminated equipment. *(Level III, Class I)* The basic equipment must be worn upon entering the clinic after hand hygiene. It must be kept on at all



times and only replaced by a better PPE, according to one of the three degrees of strategic occupational protection to be applied at the dental clinics<sup>[82,84-86,88-92,98-99]</sup>: **(Level IIa, Class I)**

## **UPDATE OF THE EVIDENCE THAT SUPPORTS THE QUESTION 17.3., WITH CHANGING THE LEVEL AND CLASS OF THE RECOMMENDATION**

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17.3 Which type of masks are there? And what is the indication for its clinical use?

**Answer:** Face masks are medical devices destined to minimize the transmission of infectious agents between professionals and patients. These masks must comply with EN 14683:2019. They are classified in different types (Type I, Type II and Type IIR) according to their capacity of bacterial filtration and resistance to fluids and splatters. Type IIR mask displays a bacterial filtration effectiveness >98% and resistance to fluids >160 KPa, being called surgical mask, while the Anglo-Saxons call it *Fluid Resistant Surgical Mask* (FRSM). Self-filtering masks or respirators are destined to personal protection against one or more risks. They are encompassed by the PPE and comply with EN 149:2001+A1:2019, for <sup>85</sup> standards of effectiveness of filtration and total leak into the interior of the mask, and are classified as: FFP1 (*Filter Face Piece* 1) of low effectiveness, leak into the interior 22% and infiltration into the material 20%; FFP2 (N95 of US – NIOSH certification) of medium effectiveness, leak into the interior 8% and infiltration into the material 6%; FFP3 (N99 of US – NIOSH certification) of high effectiveness, leak into the interior 2% and infiltration into the material 1%. Surgical masks must be worn essentially to protect third parties, whereas the valveless respirators allow a bidirectional protection and these must be the ones to be worn by the health professionals. In a context of epidemiologic prevention, the use of respirators equipped with valves is not recommended<sup>[100]</sup>. The respirators are individual protection devices and are more recommended for use by the health professionals to provide a higher protection in contexts with a higher infective load<sup>[81,82,87,89,97,77-87]</sup>. **(Level III, Class II)**

## **UPDATE OF THE EVIDENCE THAT SUPPORTS THE QUESTION 17.5., WITHOUT CHANGING THE LEVEL AND CLASS OF THE RECOMMENDATION**

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17.5 How are you supposed to put the PPE on?

**Answer:** There are different ways of putting the PPE on, but every single one of them aiming to prevent the secondary transmission of diseases. The process of donning must be carried out near the area where it is supposed to be worn, it improves the safety of the whole process when it is carried out with the active assistance of a team member. Face masks, surgical masks or respirators must be put on and adjusted with your hands properly washed

and after putting on the surgical cap. Every mask must provide for the best sealing possible. For that, it must be well tight and adjusted over the nasal bridge and facial contour in order to prevent the entrance of <sup>86</sup> contaminated air through the side of the mask or respirators. An adaptation test must be conducted at the end. You must conduct a qualitative assessment of the adaptation by softly inhaling in order to detect any strong odor. On the other hand, you must check the sealing, first by producing negative pressure, inhaling to create vacuum inside, which is supposed to cause a slight flattening of the respirator's surface if the sealing is effective; immediately thereafter you must conduct the test of positive pressure, blowing moderately to cause the bulging of the respirator's surface in case of sealing<sup>[104, 108, 109, 111]</sup>. As you enter the clinic, you must put on the first protective "layer", starting with the removal of the ornaments and the hand washing. Next, you put the bouffant cap and the mask on. Then you must assess the procedure to be performed and put the appropriate PPE on: (Level IV, Class I)

- Wash your hands;
- Adapt the respirator and make the adjustment test;
- Put the disposable waterproof gown or the waterproof coverall on;
- Put the foot protection (shoe or boot covers) on;
- Disinfect the hands using ABAS;
- Put on gloves – make sure they are well fitted-over the gown/coverall;
- Put the goggles on, where required;
- Put a surgical cap/bouffant cap or hood of the coverall on;
- Put a face shield protection on, where required;
- Disinfect the inner gloves using ABAS and put the second pair of gloves on, where required degree 3 protection;
- Check the adaptation of every element. **(Level IIa, Class I)**

NOTE: The elements of the PPE that you need depend on the level of risk and the adequate degree of protection. Donning a full PPE obeys to a systemization, the dentist being ideally helped by an assistant having previously washed his/her own hands; in order to create surgical conditions of sterilization the assistant must perform the hand disinfection in between two steps<sup>[82,84,85,87,88,90,98,111]</sup>.

## Treatment

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### 18.1. How can you reduce microbiological burden in intraoperative stage?

Previously proposed recommendation:

- Rinse and gargle with antimicrobial solutions capable of oxidizing this type of virus (1% hydrogen peroxide, 0.2% povidone iodine) for 30 to 60 s before starting the consultation;

**Answer:** In the current pandemic context, it has been recommended the implementation of mouthrinses with antiseptic solutions prior to the execution of intraoral surgical procedures, in an attempt to reduce the viral load of SARS-CoV-2. The American Dental Association (ADA) and the US Center for Disease Control and Prevention (CDC) have issued recommendations in this regard, despite the low level of evidence, advising the use of oral antimicrobials through mouthrinses with hydrogen peroxide (PXH), povidone-iodine (IPVD), chlorhexidine gluconate (CHX), essential oils or cetylpyridinium chloride (CPC).

To date, there has been no clinical study to support the virucidal effects of any oral solution as a preoperative protocol. The evidence was based only on *in silico* and *in vitro* studies, which established the principle of proof of the rationale of action of some of these antimicrobials, through the disruption of various metabolic pathways, oxidation or rupture of the SARS-CoV-2 envelope.

More recently, several literature reviews have emerged<sup>[112-115]</sup> that reported the first clinical studies that define the validation of these agents against SARS-CoV-2. An uncontrolled prospective study detected only a transient unsustainable decrease until 2 h in the viral load after mouthrinses with CHX (0.12%) in the saliva of COVID patients<sup>[116]</sup>. A series of 4 uncontrolled cases detected an effective reduction in the 2 patients with the highest viral load up to 3 hours after mouthwash with IPVD (1%, 1min)<sup>[117]</sup>. Another prospective, uncontrolled study with 10 cases, reported that mouthrinses with PXH (1%, 30 sec.) did not reduce the intraoral viral load<sup>[118]</sup>. Finally, a randomized controlled trial with 16 patients evaluated the influence of IPVD (0.5%), CHX (0.2%) and CPC (0.075%). A decrease in viral load was detected in a sustainable way until 6 h, after CPC and IPVD mouthrinses<sup>[119]</sup>.

These studies have significant limitations, derived from the applied methodology, sample size or validation biases, compromising reliable extrapolations. However, in the absence of more robust evidence, the following can be advised in the light of the most current data:

- **the recommendation hydrogen peroxide mouthrinses is questionable and should not continue to be supported, until further evidence is available. (Level III, Class IIb)**

- rinse with solutions of povidone-iodine (0.5%) or cetylpyridinium chloride (0.075%) for 30 seconds, before any oral procedure that generates aerosols and/or droplets. (*Level Ib, Class IIa*)
- pre-operative mouthrinses with antimicrobial solutions should be an integral part of the microbial load control protocol in the dental office, namely, in a rational articulation with surgical aspiration and effective ventilation systems to minimize the infectiousness of aerosolization.

## After-Intervention Stages

Consolidation of scientific evidence on the questions 20.6., 20.12., 20.13., 20.15., 26.1. e 27.2.

### End of the Consultation and Disinfection of the Medical Office

#### UPDATE OF THE EVIDENCE THAT SUPPORTS THE QUESTION 20.6., WITHOUT CHANGING THE LEVEL AND CLASS OF THE RECOMMENDATION

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How should X-ray positioners be disinfected?

**Answer:** After the consultation, positioners should be washed with water and detergent, and after that they should be placed in ultrasonic container. Sterilizing procedures should observe the manufacturer's recommendations<sup>[120-125]</sup>. (*Level IV, Class IIa*)

#### UPDATE OF THE EVIDENCE THAT SUPPORTS THE QUESTION 20.12., WITHOUT CHANGING THE LEVEL AND CLASS OF THE RECOMMENDATION

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Regarding surface disinfection (equipment and workbenches), which product is more efficient and for how long should contact time be? be the contact time?

**Answer:** Surface disinfection can be performed using a disinfectant detergent to achieve a faster procedure, i.e. a product containing compatible detergent and disinfectant (2 in 1). Generally, commercially available products (such as virucidals), duly certified by the relevant authorities should be used. They can have different presentations: liquid, gel, foam or spray. Alternatively, the use of alcohol-based solutions (70%, at least 1 min), hydrogen peroxide (0.5-1% at least 1 min), sodium hypochlorite (0.1-0.5%, at least 10 min) has also been proven as being effective. Metal surfaces which are not compatible with sodium hypochlorite due to the risk of corrosion, should be disinfected with alcohol-based solutions or another suitable product for, at least, 1 min<sup>[33, 34, 126-132]</sup>. (*Level III, Class I*)

**UPDATE OF THE EVIDENCE THAT SUPPORTS THE QUESTION 20.13., WITHOUT CHANGING THE LEVEL AND CLASS OF THE RECOMMENDATION**

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Is UV radiation an effective sterilization method?

**Answer:** UV radiation is effective when combined with surface disinfectants with virucidal properties<sup>[130, 133]</sup>. (*Level Ia, Class IIa*)

**UPDATE OF THE EVIDENCE THAT SUPPORTS THE QUESTION 20.15., WITHOUT CHANGING THE LEVEL AND CLASS OF THE RECOMMENDATION**

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Is it necessary to make the suitable aeration of the clinical office before starting the following consultation?

**Answer:** The aeration of the clinical office is recommended by most authors. However, the time necessary to this aeration depends on the room's volume and on the available ventilation features, among other factors, and it is not fully clarified. Some authors refer natural aeration for, at least, 10 minutes or the implementation of an HVAC system<sup>[130, 134-144]</sup>. (*Level IV, Class IIa*)

# Sterilizing

## Material Cleaning, Disinfection and Sterilization

### Standards

#### **UPDATE OF THE EVIDENCE THAT SUPPORTS THE QUESTION 26.1., WITHOUT CHANGING THE LEVEL AND CLASS OF THE RECOMMENDATION**

Does contamination with SARS-CoV-2 imply a change of the procedures used to clean, decontaminate and sterilize materials and instruments?

**Answer:** It does not imply a change of good practice, however the recommended procedures should be reminded. Non-rotary instruments should be pre-processed (decontaminated) with a suitable disinfectant or with a 5% sodium hypochlorite solution (pay attention to metals), for 30 minutes; washed with water, placed in the ultrasonic container with an enzymatic disinfectant for the recommended time and at the recommended temperature; after getting dry, they should be placed in a sterilization sleeve (in kits or individually) and placed in the autoclave. Rotary instruments should be submitted to a pre-treatment with a 70% alcohol solution, a detergent washing and, after getting dry, they should be lubricated, placed in the sterilization sleeve and in the autoclave. After the autoclave and before being used again, rotary instruments can be lubricated again, manually or in dedicated equipment. Instruments which get in contact with the patient's oral mucous membranes and fluids (e.g., dental mirror, tweezers, restorative material applicators) should be considered as semi-critical and should be sterilized using thermal methods (steam and pressure - autoclave; chemical vapor - formaldehyde; dry heat); semi-critical instruments sensitive to heat should not be reused, they should be discarded instead. Surgical instruments and other instruments which penetrate soft tissues or bones (forceps, periodontal cures, bone drills, etc.) should be considered as critical and, if they are reusable, they should be sterilized in the autoclave<sup>[120-122, 129, 145, 146]</sup>. (*Level IIIb, Class IIa*)

# Accidental Exposure

## How to act in the event of Accidental Exposure

### **UPDATE OF THE EVIDENCE THAT SUPPORTS THE QUESTION 27.2., WITHOUT CHANGING THE LEVEL AND CLASS OF THE RECOMMENDATION**

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In the event of an accidental exposure to biological contaminants from a COVID-19 patient, which procedure should be adopted?

**Answer:** Regarding the hands (without protection or with gloves which have lost their protection barrier, ex accidental perforation), you should perform their immediate antiseptics with ABAS. The skin is the most external barrier of the human body. Health professionals working with COVID-19 patients are prone to damages of their skin and mucosa barriers. To minimize the break of skin and mucosa barriers, health professionals should observe the standards related to the use of PPE and avoid an excessive exposure. Regarding mucous membranes, namely the ocular conjunctiva, an immediate washing with water or a saline solution should be performed. In the case of a suspected exposure when removing the goggles, the periocular area should immediately be cleaned with a cotton ball soaked in ethanol at 70%. Bear in mind that the excess of ethanol can cause conjunctiva and cornea irritation. Additionally, we recommend the implementation of measures related to skin and mucosa care during work<sup>[147, 148]</sup>. (*Level IV, Class I*)



## Conclusion

Given the inherent dynamics of SARS-CoV-2 infection and the still unclear knowledge of its pathophysiological mechanisms, it is extremely important to constantly update the dentist and his team for advances in the protection and control of cross-infection in this area. The likelihood of seeing an asymptomatic patient is real, so all patients should be treated as potentially infected. This probability comes not only from the natural history of the disease COVID-19 itself, but also from the incubation period of the virus, which can vary from 0 to 24 days, with the majority of patients developing mild symptoms. Therefore, dental consultation should contribute to the mitigation of the virus<sup>[34, 140-151]</sup>

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### What PPE to adopt in the post-pandemic context?

This issue is possibly one of the most worrisome for dentists and their team. The reality is that PPE recently adopted in the context of the SARS-CoV-2 pandemic is not new or specifically created for this virus. These already existed and were simply ignored in the exercise of the profession. The risk of transmitting infectious diseases via aerosol is a reality that places the dental team at a high risk of contamination. It is up to health professionals to have common sense in making decisions about which PPE they adopt. Of course, there are minimums to be met, namely the use of long-sleeved uniforms and shoes for exclusive clinical use, disposable/reusable overall in consultations with the production of aerosol, a pair of gloves, eye and capillary protection.

## Updating

Taking into account the still short experience of coexistence with COVID-19, these Clinical Guidelines shall be object of continuous updating, and they can also be kept, revised or completely redrafted.

## Acknowledge

The authors would like to acknowledge NSK, Tokyo, Japan for supporting the translation of this Clinical Guidelines.

# Appendix I

## Materials and Methods

## Section 1 | Questions

### PRE-

2.4. The patient reports that he was infected with SARS-CoV-2, **but he no longer has symptoms**, how to proceed?

2.5. How to **proceed with the appointment of a patient considered a suspected or confirmed case of COVID-19** and who is in isolation at home?

## Section 2 | Bibliographic Research

Table 1 - Algorithm established by the proofreader - Stage 1 (AV; CM)

1	SARS.ti,ab,kw
2	MERS.ti,ab,kw
3	SARS-Co-2.ti,ab,kw
4	COVID-19 or COVID-19 or coronavirus*.ti,ab,kw
5	OR/3,4
6	Influenza.ti,ab,kw
7	Dentistry/
8	AND/1,7
9	AND/2,7
10	AND/5,7
11	AND/6,7
12	Aerosol.ti,ab,kw
13	Air.ti,ab,kw
14	OR/12, 13
15	AND/1, 14
16	Ventilator.ti,ab,kw
17	Oral hygiene.ti,ab,kw
18	OR/16, 17
19	AND/7, 18

Table 2 - Algorithm adapted from NICE - Stage 2<sup>[1]</sup>

1	exp coronavirus/
2	((corona* or corono*) adj1 (virus* or viral* or virinae*)).ti,ab,kw.
3	<i>((coronavirus* OR coronaviridae* OR coronavirinae* OR Coronavirus* OR Coronovirus* OR Wuhan* OR Hubei* OR <b>huaian</b> OR "2019-nCoV" OR 2019nCoV OR nCoV2019 OR "nCoV-2019" OR "COVID-19" OR COVID19 OR "CORVID-19" OR CORVID19 OR "WN-CoV" OR <b>Inco</b> OR "HCoV-19" OR HCoV19 OR CoV OR "2019 novel*" OR ncov OR "n-cov" OR "SARS-CoV-2" OR "SARSCoV-2" OR "SARSCoV2" OR "SARS-CoV2" OR SARSCov19 OR "SARS-Cov19" OR "SARSCov-19" OR "SARS-Cov-19" OR <b>ncolor</b> OR Ncorona* OR Ncorono* OR NcovWuhan* OR NcovHubei* OR NcovChina* OR NcovChinese*) .ti, ab, kw.) all</i>
4	(((respiratory* adj2 (symptom* or disease* or illness* or condition*)) or "seafood market*" or "food market*") adj10 (Wuhan* or Hubei* or China* or Chinese* or Huanan*)).ti,ab,kw.
5	((outbreak* or wildlife* or pandemic* or epidemic*) adj1 (China* or Chinese* or Huanan*)).ti,ab,kw.
6	"severe acute respiratory syndrome*".ti,ab,kw.
7	or/1-6
8	limit 7 to yr="2019 -Current"

## Section 3 | Articles Included

Reference	Author, year	Participants	Intervention	Comparison	Outcome	Notes
1	Guerra F. 2020	Patients COVID 19 positive or negative	Any type of dental procedure, with or without aerosol production, in a pandemic situation due to SARS-CoV-2	Any type of dental procedure, with or without aerosol production, before the SARS-CoV-2 pandemic	Dental Medicine practice and practice guidelines after general confinement	-
2	NICE. 2014	-	-	-	NICE Guidelines elaboration manual	-
3	Rosenfeld RM. 2009	-	-	-	Guideline development manual	
4	NICE. 2020	-	-	-	Guidelines for the preparation of quick NOC	-
5	Sahni V, 2020	-	-	-	Possible relationship between COVID-19 and Periodontal Disease - cytokine expression	Letter to Editor
6	Takahashi Y. 2020	-	-	-	Possible worsening of symptoms by COVID-19 due to the presence of periodontal bacteria; Contribution of oral hygiene care to prevention	-
7	Manzalawi R. 2020	Pacients SARS-CoV-2 positives	-	-	Gingival bleeding as a sign of infection by SARS-CoV-2	Case report
8	Di Spirito F. 2020	-	-	-	Oral manifestations associated with SARS-CoV-2 infection and the importance of early diagnosis of oral lesions by specialists in oral medicine and pathology	Letter to Editor
9	Badran Z. 2020	-	-	-	Periodontal pockets as possible reservoirs for the SARS-CoV-2 virus	-
10	Xiang Z. 2020	-	-	-	Oral locations as potential reservoirs for SARS-CoV-2 and implications for changes in host microbiota	-
11	Amorim dos Santos J. 2020	Pacients SARS-CoV-2 positives	-	-	Prevalence of oral lesions / changes in positive SARS-CoV-2 patients	-
12	Bemquerer LM. 2021	-	-	-	Correlation between oral dermatological lesions in positive SARS-CoV-2 patients	Letter to Editor
13	Corchuelo J. 2020	Pacients SARS-CoV-2 positives (asymptomatic)	-	-	Presence of oral lesions in asymptomatic positive SARS-CoV-2 patients	Case report
14	Brandão TB. 2021	Pacients SARS-CoV-2 positives	-	-	Presence of oral lesions in positive SARS-CoV-2 patients; possible consideration of the oral cavity as a target for infection with this virus	Case series
15	Riad A. 2020	Pacients SARS-CoV-2 positives	-	-	SARS-CoV-2 positive patients with mucositis: possible relationship?	Case series

16	Pérez-Sayáns M. 2021	-	-	-	COVID-19 language; pathognomonic of COVID-19?	Letter to Editor
17	Hathway RW. 2021	-	-	-	Tongue COVID-19	Letter to Editor
18	Santosh ABR. 2020	-	-	-	Possible transmission of COVID-19 disease through saliva in asymptomatic patients	Letter to Editor
19	Sarode GS. 2020	Pacients SARS-CoV-2 positives	-	-	Efficacy of salivary and nasopharyngeal samples in the detection of SARS-CoV-2	-
20	Medeiros da Silva RC. 2020	-	-	-	Salivary samples as a means of diagnosing SARS-CoV-2 infection	-
21	Fernandes LL. 2020	Pacients SARS-CoV-2 positives	Salivary samples	-	Salivary samples as a means of diagnosing SARS-CoV-2 infection	-
22	Michailidou E. 2020	-	-	-	Salivary samples as a means of diagnosing SARS-CoV-2 infection, salivary diagnostic methods	-
23	Kashiwagi K. 2021	-	-	-	Salivary samples as a means of diagnosing SARS-CoV-2 infection, via RT-PCR	Case report
24	Hamid H. 2020	-	-	-	Salivary samples as a means of diagnosing SARS-CoV-2 infection	-
25	Chen L. 2020	-	-	-	Salivary samples as a means of diagnosing SARS-CoV-2 infection and classification of oral symptoms	-
26	Hung K. 2020	-	Salivary samples	Nasopharyngeal samples	Salivary samples as a means of diagnosing SARS-CoV-2 infection	-
27	Azzi L. 2021	-	Salivary samples	Nasopharyngeal samples	Salivary samples as a means of diagnosing SARS-CoV-2 infection; virus detection techniques in samples	-
28	Fakheran O. 2020	-	-	-	Salivary samples as a means of diagnosing SARS-CoV-2 infection	-
29	Altawalah H. 2020	Patients with suspected infection by SARS-CoV-2	Salivary samples	Nasopharyngeal samples	SARS-CoV-2 detection via RT-PCR	Cross-sectional study
30	Czumbel LM. 2020	Pacients SARS-CoV-2 positives	Salivary samples	Nasopharyngeal samples	Consistency and reliability of viral RNA detection in salivary samples	Metanalysis
31	Gupta S. 2021	Pacients SARS-CoV-2 positives	Amostra do fluido crevicular	Amostras nasofaríngeas e salivares	Detection of viral RNA	-
32	Brandolin BA. 2020	-	-	-	Impact of COVID-19 in dentistry	-
33	Banakar M. 2020	-	-	-	SARS-CoV-2 infection prevention protocol	-
34	Bizzoca ME. 2020	-	-	-	Changes in Dentistry practice during the pandemic by COVID-19	-
35	Kathree BA. 2020	-	-	-	Impact of COVID-19 in dentistry	-
36	Coulthard P. 2020	-	-	-	Impact of COVID-19 in dentistry	-



37	Wijesooriya NR. 2020	-	-	-	Changes and adaptations in the practice of Dentistry after the emergence of COVID-19: education, telemedicine	-
38	Crawford E. 2020	-	-	-	Efficacy and usefulness of telemedicine	-
39	Ghai S. 2020	-	-	-	Telemedicine	-
40	Telles-Araujo GT. 2020	-	-	-	Telemedicine as a means of supporting the COVID-19 pandemic	-
41	Tapia ROC. 2020	Pacients SARS-CoV-2 positives	-	-	Description of oral lesions	Case series
42	Petruzzi M. 2016	-	-	-	Telemedicine	-
43	Saccomanno S. 2020	-	-	-	Orthodontics and Telemedicine	-
44	Zhu F. 2020	Adult patients who have not contracted COVID-19 disease	Ad5 vectored COVID-19 vaccine ( $5 \times 10^{10}$ , $1 \times 10^{11}$ , and $1 \cdot 5 \times 10^{11}$ viral particles)	-	Adverse effects 7 days after vaccine administration	Dose-escalation, open-label, non-randomised, first-in-human trial
45	Zhao J. 2020	-	-	-	Updates vaccination COVID-19	-
46	Awadasseid A. 2021	-	-	-	Updates vaccination COVID-19	-
47	Kim KD. 2020	-	-	-	Updates vaccination COVID-19	-
48	DGS. 2020	-	-	-	Norma: 021/2020: Vaccination Campaign against COVID-19 COMIRNATY® Vaccine	-
49	DGS. 2021	-	-	-	Norma:001/2021: Vaccination Campaign against COVID-19 COVID-19 Vaccine MODERNA®	-
50	DGS. 2021	-	-	-	Norma:003/2021: Vaccination Campaign against COVID-19 COVID-19 Vaccine AstraZeneca®	-
51	Centers for Disease Control and Prevention. 2021	-	-	-	Updates vaccination COVID-19	-
52	Bernal JL. 2021	-	-	-	Vaccination with BNT162b2 mRNA and ChAdOx1 adenovirus vector	-
53	Farronato M. 2020	-	-	-	Oral cavity as a route of transmission of the SARS-CoV-2 virus to the entire body via the ECA2 receptor	-
54	Bioseguridad para la Atención Odontológica COVID 19 2020	-	-	-	Measures aimed at prevention: Telemedicine, Instructions for consultation, entrance to the clinic, reception, waiting room, bathroom	-
55	DGS. 2020	-	-	-	Guideline 022/2020: COVID-19: Procedures in Clinics, Offices or Oral Health Services of Primary Health Care, Social and Private Sector.	-
56	Lurie N. Carr BG. 2020	-	-	-	Telemedicine in disaster response and support	-

57	Reeves JJ, Hollandsworth HM. 2020	-	-	-	Describe the implementation of an important technological support system to optimize clinical management during the COVID-19 pandemic.	-
58	Lv N. 2020	-	-	-	Monitoring of emergency consultations during COVID-19	-
59	León S. 2020	-	-	-	Inequalities in access to health care for the elderly	-
60	Spagnuolo G, de Vito D. 2020	-	-	-	Care to be taken before scheduling an emergency appointment	-
61	Meng L. 2020	-	-	-	Infection control in consultation with MD + recommendations	-
62	Peng X. 2020	-	-	-	Mechanisms of transmission of Covid-19 virus in the profession of dentistry, as well as prevention measures pre, peri and postoperative	-
63	DGS. 2020	-	-	-	Standard 007/2020: SARS-CoV-2 Infection Prevention and Control (COVID-19): PPE	-
64	Smales FC. 2003	-	-	-	Maintenance of MD consultations in sars-cov1	-
65	Li RW. 2004	-	-	-	Recommendations on management sars-cov-1 patients (possible cases, unprotected contacts, contacts with SARS-cov 1 patients in less than 10 days or assintomáticos patients, cross infection control measures	Coughing and sneezing can produce aerosols from 0.001 µm to 10,000 µm
66	Samaranayake LP. 2004	-	-	-	Implications of SARS-cov-1 in dentistry: patient identification, hygiene hands, PPE's	Referem bochecho com chx entre 0,12 e 2% antes da consulta
67	Huang Z. 2020	-	-	-	Establish management strategies and procedures action protocol in the radiology department during the outbreak of COVID-19	Strategies for staff and patients
68	Lai T. 2020	-	-	-	Proposed model to be adopted in the ophthalmology consultation to prevent covid cross infection (pre, peri)	Includes questionnaire to be made to the patient before the consultation
69	Maragakis, L. 2020	-	-	-	Questionnaire that helps the patient understand whether or not may be infected with SARS-CoV-2 and should or should not schedule an appointment.	-
70	Repici A. 2020	-	-	-	Use of PPE's according to the patient's risk; patient's clothing; OS PPE's: depending on the risk; how to wear and remove. Treatments negative pressure room	High and low endoscopy. Possible extrapolation to dentistry?
71	Zhang Y. 2020	-	-	-	Procedures adopted in a hospital in China in control of infected patients COVID-19	The questionnaire at the end seems to me relevant for the classification of individuals at risk - I leave it up to the experts to consider the relevance of the evidence for inclusion in the recommendations.

72	DGS. 2020	-	-	-	Norma 020/2020: COVID-19: Definição de Caso de COVID-19.	-
73	DGS. 2020	-	-	-	Norma 004/2020: COVID-19: Patient Approach with Suspected or Confirmed COVID-19.	-
74	ADA. 2020	-	-	-	Minimize COVID-19 transmission risk	-
75	ECDC. 2020	-	-	-	Criteria for the identification of COVID-19	-
76	DGS. 2020	-	-	-	Orientação 010/2020: Infection with SARS-CoV-2 (COVID-19) - Social Distancing and Isolation	-
77	OMD. 2020	-	-	-	Treatment of patients with COVID-19 or high risk of contagion	-
78	OMD. 2020	-	-	-	Preventive care and Dentistry Appointments	-
79	OSHA. 2020	-	-	-	Guidelines for the preparation of post-pandemic different working sectors	Definition of risk of the procedures, the various classes
80	CDC. 2020	-	-	-	Guidelines monitoring of risk in professional environments	
81	Handbook of COVID19 Prevention and Treatment. 2020	-	-	-	Prevention of SARS-CoV-2: Isolation of areas, team management, individual protection, hospital protocols and digital support	-
82	-	-	-	-	COVID-19: Infection, prevention	-
83	CAL/OSHA	-	-	-	Aerosol-borne diseases	-
84	Pan Y. 2020	-	-	-	Routes of transmission of the virus and measures to contain the spread of the virus	-
85	Zhang W, 2020	-	-	-	Prevention and control of corona virus in dental clinics - control of medical teams, screening of patients	-
86	Association of Occupational health Professionals in Healthcare (AOHP) 2020	-	-	-	Infection through bioaerosols	-
87	Verbeek JH, Rajamaki B, et al. 2019	Total of 1950 patients in 17 trials	21 interventions concerning PPE entire body, dressing and remove PPE; Compliance of health professionals	PPE: How to dress and remove without self-contamination by health professionals, evaluate training methods for health workers to improve compliance	Breathable PPE with low quality evidence, 2 pairs of gloves for removing PPE, face-to-face training have better rates in preventing self-contamination	Possible extrapolation for Dentistry
88	ECDC. 2020	-	-	-	Guidelines for PPE placement and removal criteria when treating patients suspected of SARS-CoV-2 infection	-

89	ECDC. 2020	-	-	-	PPE needed to care for suspected or confirmed SARS-CoV-2 infection patients	-
90	ECDC. 2020	-	-	-	Uso seguro de EPI aquando tratamiento de pacientes infecciosos	-
91	Sociedad Española de Patología Digestiva; Asociación Española de Gastroenterología. 2020	-	-	-	Safe use of PPE when treating infectious patients	Possible extrapolation for Dentistry
92	Howard BE. 2020	-	-	-	Risk of aerosol production in the context of COVID-19	-
93	Zimmermann M. 2020	-	-	-	Monitoring of patients undergoing surgery in the context of a pandemic	-
94	Alharbi A. 2020	-	-	-	Guidelines for care in the context of dental medicine in the context of a pandemic	-
95	Ayyed AB. 2020	-	-	-	Guidelines for care in the context of dental medicine in the context of a pandemic	-
96	FalahchaiM. 2020	-	-	-	Guidelines for care in the context of dental medicine in the context of a pandemic	-
97	Park, S.H. 2020	-	-	-	Personal protective equipment in the context of a pandemic	-
98	Samaranayake LP. 2020	-	-	-	Effectiveness of personal protective equipment	-
99	Jamal M. 2020	-	-	-	Guidelines for care in the context of dental medicine in the context of a pandemic	-
100	Agência Nacional de Vigilância Sanitária				Respiratory Protection Primer against Biological Agents for Health Workers	
101	Chughtai AA, Seale H, et al. 2020	-	-	-	Regulation for the use of masks by health professionals in hospitals	
102	Wang Q. 2020	-	-	-	Personal protective equipment in the context of a pandemic	-
103	3M	-	-	-	Features description FFP2, KN95, and N95	-
104	Infarmed	-	-	-	Surgical masks vs. Filtering Breathing Apparatus	Description features
105	Zangmeister CD. 2020	-	-	-	Effectiveness of mask material against SARS-CoV-2	-
106	Kahler CJ. 2020	-	-	-	Mask protection mechanism against SARS-CoV-2	-
107	Udwadia ZF. 2020	-	-	-	Personal protective equipment in the context of a pandemic	-
108	Bradford SP. 2020	-	-	-	Surgical masks and N95: filters and effectiveness	-

109	Villani FA. 2020	-	-	-	Prevention in dentistry practices in the context of a pandemic	-
110	Regli A. 2020	-	-	-	Surgical masks and N95: filters and effectiveness	-
111	Gallagher JE. 2020	-	-	-	Personal protective equipment in the context of a pandemic	-
112	Reis INR. 2021	-	-	-	Efficacy of preoperative mouthwashes in reducing the transmission of SARS-CoV-2	-
113	Castro-Ruiz C. 2020	-	-	-	Efficacy of povidone-iodine in reducing the risk of transmission of SARS-CoV-2	Narrative review
114	Carrouel F. 2021	-	-	-	Efficacy of preoperative mouthwash solutions in reducing salivary viral load	Critical review
115	Ather A. 2021	-	-	-	Efficacy of preoperative mouthwashes in reducing the transmission of SARS-CoV-2	Scoping Review
116	Yoon JG. 2020	-	-	-	Clinical importance of high doses of salivary SARS-CoV-2	-
117	Martínez Lamas L. 2020	-	-	-	Efficacy of povidone-iodine in reducing the risk of transmission of SARS-CoV-2	In vivo
118	Gottsauner MJ. 2020	-	-	-	Effectiveness of hydrogen peroxide in reducing salivary viral load	Prospective clinical pilot study
119	Seneviratne CJ. 2020	-	-	-	Efficacy of preoperative mouthwash solutions in reducing salivary viral load	Randomized control trial
120	Hokett SD. 2000	-	-	-	Effectiveness of sensor protections	-
121	Rutala, WA. 2019	-	-	-	Disinfection and cleaning guidelines	-
122	CDC. 2020	-	-	-	Infection prevention guidelines	-
123	Hamedani S. 2020	-	-	-	Guidelines for safe imaging protocols in the context of a pandemic by COVID-19	-
124	Doriguêto PVT. 2020	-	-	-	Guidelines for safe imaging protocols in the context of a pandemic by COVID-19	-
125	Ilhan B. 2020	-	-	-	Guidelines for safe imaging protocols in the context of a pandemic by COVID-19	-
126	CDC. 2003	-	-	-	Infection control in dental institutions	Adaptation to SARS-CoV-2
127	DGS.2020	-	-	-	Orientação 014/2020: SARS-CoV-2 infection (COVID-19): Cleaning and disinfecting surfaces in public or similar establishments	-
128	Colaneri M. 2020	-	-	-	Environmental contamination by SARS-CoV-2 in a hospital environment	-

129	United States Environmental Protection Agency Washington, D.C. 20460 Office Of Chemical Safety And Pollution Prevention List N	-	-	-	Online list of disinfectants against SARS-CoV-2	-
130	Gurzawska-Comis K. 2020	-	-	-	Guidelines on the prevention of nosocomial infection during the pandemic by COVID-19	-
131	Poggio C. 2020	-	-	-	Guidelines on the prevention of nosocomial infection during the pandemic by COVID-19	-
132	Bali RK. 2020	-	-	-	Guidelines for exercising the profession of maxillofacial surgeons in the context of a pandemic	-
133	Dexter F. 2020	-	-	-	Desinfecção de instrumentos combinada entre desinfetantes e luz UV	-
134	CDC. 2005	-	-	-	Mycobacterium transmission prevention guidelines	-
135	Administração Central do Sistema de Saúde IP. 2008	-	-	-	Technical Specifications for HVAC Installations.	ET 06/2008 V.2014
136	CDC. 2003	-	-	-	Appendix B - air quality and cross infection control	-
137	New York Stat Department of Health. 2014	-	-	-	Guidelines for building hospitals and clinics.	-
138	US Department of Veterans Affairs. Office of Construction & Facilities Management. 2014	-	-	-	Guide to dental clinics	-
139	Harrel SK, 2004	-	-	-	Aerosols in Dentistry: implications for infection control	-
140	Helmis CG. 2007	-	-	-	Air quality in the dentistry office	-
141	Li Y. 2007	-	-	-	The role of ventilation in the airborne transmission of infectious agents in the built environment - a systematic multidisciplinary review	-
142	Raghunath N, 2016	-	-	-	Aerosols in Clinical Practice	-
143	Qian H. 2018	-	-	-	Ventilation control for air transmission of human exhaled bio-aerosols in buildings	-
144	Amato A. 2020	-	-	-	Guidelines for the prevention and reduction of the risk of transmissibility of SARS-CoV-2	-

145	Handbook of COVID19 Prevention and Treatment. 2020	-	-	-	Prevention of SARS-CoV-2: Isolation of areas, team management, individual protection, hospital protocols and digital support	-
146	Volgenant CMC. 2021	-	-	-	Guidelines for the prevention and reduction of the risk of transmissibility of SARS-CoV-2. Approach includes limiting aerosol production.	-
147	Chinese Center for Disease Control and Preventions	-	-	-	Key points for the prevention of health professionals against SARS-CoV-2	-
148	Cabrera-Tasayco FDP. 2020	-	-	-	Biosafety required in the dental office with the appearance of the SARS-CoV-2 virus	Literature review
149	Ather A. 2020	-	-	-	Epidemiology, symptoms and routes of transmission of SARS-CoV-2. Recommendations for patient screening, cross-infection control and dental office care	-
150	Zimmermann M. 2020	-	-	-	Protective measures for the patient and medical team in the provision of care in the area of maxillofacial surgery	-
151	Turkistani KA. 2020	-	-	-	Risks and precautions that dentists and their teams should take when providing dental care Duarte the pandemic by COVID-19	Systematic Review
152	Perry DJ. 2007	-	-	-	Evidence Levels	-
153	Kirchhof, P. 2016	-	-	-	Recommendations Classes	-

## Section 4 | Articles Excluded

Table 4 | Articles Excluded

Author (1° e 2°), Year	Criteria	DOI/PMID
Pylińska-Dąbrowska D, Starzyńska A, <i>et al.</i> 2020	G	10.3390/jcm9103344
Sebastian P, Jorge P, <i>et al.</i> 2021	G	10.1016/j.jobcr.2021.01.006
Jungo S, Moreau N, <i>et al.</i> 2021	A	10.1371/journal.pone.0246586
Estrich CG, Mikkelsen M, <i>et al.</i> 2020	A	10.1016/j.adaaj.2020.09.005
Allen-Tejerina AM, Rallis KS, <i>et al.</i> 2020	B	10.1016/j.eururo.2020.10.003
Yee R, Truong TT, <i>et al.</i> 2021	G	10.1128/JCM.02686-20
Costa Dos Santos Junior G, Pereira CM, <i>et al.</i> 2020	D	10.1021/acs.analchem.0c04679
Carraturo F, Del Giudice C, <i>et al.</i> 2020	B	10.1016/j.envpol.2020.115010
Yang H, Hu J, <i>et al.</i> 2020	G	10.1016/j.pdpdt.2020.101943
Barbato L, Bernardelli F, <i>et al.</i> 2020	G	10.1111/odi.13646
Vargas-Buratovic JP, Verdugo-Paiva F, <i>et al.</i> 2020	G	10.5867/medwave.2020.05.7916.
Ashtiani RE, Tehrani S, <i>et al.</i> 2020	G	10.1111/jopr.13261
Shi AH, Guo W, <i>et al.</i> 2020	G	PMID: 32582908
Hertrampf K, Flörke C, <i>et al.</i> 2020	G	10.1111/odi.13529
Zhao B, An N, <i>et al.</i> 2020	G	10.1017/ice.2020.29
Rupf S, Hannig M. 2020	G	10.1007/s00784-020-03351-z
Harmooshi NN, Shirbandi K, <i>et al.</i> 2020	G	10.1007/s11356-020-09733-w
Khamis AH, Jaber M, <i>et al.</i> 2020	D	10.1016/j.jfma.2020.12.003
Abduljabbar T, Alhamdan RS, <i>et al.</i> 2020	D	10.1055/s-0040-1716986
Guo F, Tang B, <i>et al.</i> 2020	G	10.3389/fmed.2020.577468



Esteki R, Asgari N, <i>et al.</i> 2020	D	<a href="https://doi.org/10.29089/2020.20.00115">https://doi.org/10.29089/2020.20.00115</a>
Xiong X, Wu Y, <i>et al.</i> 2020	G	10.1016/j.ajodo.2020.07.005
Cueno ME, Imai K. 2021	D	10.3389/fmed.2020.594439
Davies A, Howells R, <i>et al.</i> 2020	G	10.1111/ipd.12773
Saltaji H, Sharaf KA. 2020	G	10.1016/j.ajodo.2020.04.006
Graham J, Parschal J, <i>et al.</i> 2020	G	PMID: 32650332
Carter A. 2020	G	10.1038/s41432-020-0103-9
Shi J, Wen J, <i>et al.</i> 2020	G	10.11607/ijp.7139
Purschke M, Elsamaloty M, <i>et al.</i> 2020	G	10.1364/AO.401602
Cumbo E, Gallina G, <i>et al.</i> 2020	G	10.3390/ijerph17165736
Zhao B, An N, <i>et al.</i> 2020	G	10.1017/ice.2020.292
Siles-Garcia AA, Alzamora-Cepeda AG, <i>et al.</i> 2020	G	10.1017/dmp.2020.252
González-Olmo MJ, Delgado-Ramos B, <i>et al.</i> 2020	G	10.1186/s12903-020-01274-5
Moffat RC, Yentes CT, <i>et al.</i> , 2021	G	10.1177/2380084420969116
Kara C, Çelen K, <i>et al.</i> 2020	B	10.1177/1535370220953771
Bordea IR, Xhajanka E, <i>et al.</i> 2020	G	10.3390/microorganisms8111704
Patel M. 2020	G	10.1016/j.heliyon.2020.e05402
Roychoudhury S, Das A, <i>et al.</i> 2020	G	10.3390/ijerph17249411
Coulthard P, Thomson P, <i>et al.</i> 2020	G	10.1038/s41415-020-2404-y
Patel J. 2020	D	10.1016/j.jds.2020.05.005
Elisetti N. 2020	B	10.1016/j.mehy.2020.110355
Troeltzsch M, Berndt R. 2020	G	10.1016/j.mehy.2020.110419
Santos CN, Rezende KM, <i>et al.</i> 2020	D	10.1590/1807-3107bor-2020
Farooq I, Ali S, <i>et al.</i> 2020	G	10.12669/pjms.36.7.3125
Marcenes W. 2020	G	10.1922/CDH_Dec20editorialMarcenes03
France K, Hangorsky U, <i>et al.</i> 2021	G	10.1002/jdd.12496
Brondani M, Donnelly L. 2021	B	10.1177/2380084420961089

Klemmedson D. 2020	G	10.1016/j.adaj.2020.08.005
Dave PK, Rojas-Cessa R, <i>et al.</i> 2020	D	10.3390/bios11010014
Kohmer N, Westhaus S, <i>et al.</i> 2020	D	10.1002/jmv.26145
Bwire GM, Majigo MV, <i>et al.</i> 2021	D	10.1002/jmv.26349
Bouayad A. 2020	D	10.1002/rmv.2135
Rongqing Z, Li M, <i>et al.</i> 2019	D	10.1093/cid/ciaa523
Toor SM, Saleh R, <i>et al.</i> 2020	D	10.1111/imm.13262
Elzein R, Bader B, <i>et al.</i> 2021	G	10.1016/j.jflm.2021.102123
Kapoor P, Chowdhry A, <i>et al.</i> 2021	D	10.1038/s41405-021-00064-7
Manaktala N, Pralhad S, M R. 2021	G	10.1186/s13037-021-00282-w
Harahwa TA, Lai Yau TH, <i>et al.</i> 2020	G	10.1515/dx-2020-0058
Capocasale G, Nocini R, <i>et al.</i> 2021	G	10.1002/cre2.332
Li G, Chang B, <i>et al.</i> 2020	G	10.1016/j.jiph.2020.09.013
Moraes RR, Correa MB, <i>et al.</i> 2020	G	10.1371/journal.pone.0242251
Marshall S, Duryea M, <i>et al.</i> 2020	G	10.1016/j.ajodo.2020.08.010
Al Kawas S, Al-Rawi N, <i>et al.</i> 2020	G	10.1186/s12903-020-01281-6
Gherlone E, Polizzi E, <i>et al.</i> 2020	G	PMID: 33135082
Brüssow H. 2020	D	10.1111/1462-2920.15302
Harrison AG, Lin T, <i>et al.</i> 2020	G	10.1016/j.it.2020.10.004
Beauquis J, Petit AE, <i>et al.</i> 2021	G	10.1177/0022034521990314
Abbas B, Wajahat M, <i>et al.</i> 2020	G	10.1055/s-0040-1722107
Marouf N, Cai W, <i>et al.</i> 2021	B	10.1111/jcpe.13435
Rohani B. 2020	B	10.1111/odi.13761
Riad A, Kassem I, <i>et al.</i> 2020	B	10.1111/odi.13675
Lucaciu O, Tarczali D, <i>et al.</i> 2020	G	10.1016/j.jds.2020.04.012
Dar-Odeh N, Elsayed S, <i>et al.</i> 2020	G	10.1016/j.jds.2020.11.007
Mohammadpour H, Ziai A, <i>et al.</i> 2020	D	PMID: 33262797

Dacic SD, Miljkovic MN, <i>et al.</i> 2020	G	10.3855/jdc.13147
Ghani F. 2020	G	10.29271/jcsp.2020.supp2.101
Farook FF, Mohamed Nuzaim MN, <i>et al.</i> 2020	G	10.1055/s-0040-1718641
Belchior Fontenele MN, Pedrosa MDS. 2020	B	10.1177/0145561320982686
Umer F, Arif A. 2021	G	10.1177/2380084421989693
da Hora Sale SPH, Lopes de Gusmão Sales P, <i>ET AL.</i> 2020	G	10.23736/S0026-4970.20.04372-1
MacDonald DS, Colosi DC, <i>et al.</i> 2021	G	10.1016/j.oooo.2020.10.017
Goswami M, Chawla S. 2020	G	10.1016/j.jobcr.2020.06.014
Gómez-Ochoa SA, Franco OH, <i>et al.</i> 2021	G	10.1093/aje/kwaa191
Matic N, Stefanovic A, <i>et al.</i> 2021	G	10.1007/s10096-020-04090-5
Babady NE, McMillen T, <i>et al.</i> 2021	G	10.1016/j.jmoldx.2020.10.018
Burton MJ, Clarkson , <i>et al.</i> 2020	G	10.1002/14651858.CD013627
Ortega KL, Rech BO, <i>et al.</i> 2020	G	10.1016/j.jhin.2020.10.003
Cavalcante-Leão BL, de Araujo , <i>et al.</i> 2021	G	10.4317/jced.57406
Jarvis MC. 2020	G	10.1038/s4110.3389/fpubh.2020.590041415-020-1843-9
Comber L, O Murchu E <i>et al.</i> 2020	G	10.1002/rmv.2184
Fink JB, Ehrmann S, <i>et al.</i> 2020	G	10.1089/jamp.2020.1615
Clementini M, Raspini M, <i>et al.</i> 2020	G	10.1111/odi.13649
Yuan XN, Meng QY, <i>et al.</i> 2020	D	10.19723/j.issn.1671-167X.2020.05.002
Gallagher JE, Johnson IG, <i>et al.</i> 2020	G	10.1038/s41405-020-00053-2
Ehtezazi T, Evans DG, <i>et al.</i> 2021	G	10.1038/s41415-020-2504-8
Chen B, Jia P, <i>et al.</i> 2021	G	10.1007/s10311-020-01174-8
Holliday R, Allison , <i>et al.</i> 2021	G	10.1016/j.jdent.2020.103565
Yang M, Chaghtai A, <i>et al.</i> 2021	G	10.1186/s12903-021-01417-2

Sette-de-Souza PH, Soares Martins JC, <i>et al.</i> 2020	G	10.26355/eurrev_202010_23245
Pruthi G, Parkash, <i>et al.</i> 2020	G	10.1016/j.jobcr.2020.10.010.
Azim AA, Shabbir <i>et al.</i> 2020	G	10.1111/iej.13406
Rutkowski JL, Camm DP, <i>et al.</i> 2020	C	10.1563/aaid-joi-D-20-00316
Batista RCS, Arruda CVB, <i>et al.</i> 2020	G	10.1155/2020/7945309
Sarapultseva M, Hu , <i>et al.</i> 2021	B	10.1177/2380084421993099
Comisi JC, Ravenel TD, <i>et al.</i> 2021	G	10.1111/jerd.12717
Arakeri G, Rao Us . 2021	G	10.1016/j.bjoms.2020.09.018
Eden E, Frencken J, <i>et al.</i> 2020	G	10.1038/s41415-020-2153-y
Butera A, Maiorani C <i>et al.</i> 2020	G	10.3390/jcm9123914
Kaur H, Kochhar AS. 2020	G	10.1016/j.mehy.2020.110281
Bizzoca ME, Campisi , <i>et al.</i> 2020	G	10.1186/s12903-020-01301-5
Mendez J, Villasanti U. 2020	G	PMID: 33017527
Seron MA, Strazzi-Sahyon HB, <i>et al.</i> 2020	G	10.1590/0103-6440202003760
Imran E, Khurshid Z <i>et al.</i> 2020	G	10.1055/s-0040-1717001
Frankenberger R, Van Meerbeek B. 2021	G	10.3290/j.jad.b931433
Filho JMP, Spanemberg JC <i>et al.</i> 2020	G	10.1016/j.jormas.2020.11.001
Chan JF, Yuan S, <i>et al.</i> 2020	G	10.1093/cid/ciaa644
Tang JW. 2021	G	10.1016/j.jviromet.2020.114033
Madas BG, Fűri P <i>et al.</i> 2020	G	10.1038/s41598-020-79985-6
Vergara-Buenaventura A, Castro-Ruiz C. 2020	G	10.1016/j.bjoms.2020.08.016
Marquès M, Domingo JL. 2021	G	10.1016/j.envres.2020.110559
Smith SH, Somsen GA <i>et al.</i> 2020	G	10.1063/5.0027844
Allison JR, Currie CC, <i>et al.</i> 2021	G	10.1111/joor.13098
Kumar PS, Geisinger , <i>et al.</i> 2020	G	10.1002/JPER.20-0567



## Section 5 | Level of Evidence and Classes of Recommendation

Evidence Levels Adapted and translated from Perry, DJ, et al. 2007<sup>[184]</sup>

Level of Evidence	Descriptive
<b>Level Ia</b>	Evidence from systematic reviews or meta-analyses of randomized controlled trials
<b>Level Ib</b>	Evidence from, at least, one randomized controlled trial
<b>Level IIa</b>	Evidence from, at least, one well-designed non-randomized controlled trial
<b>Level IIb</b>	Evidence from, at least, one other type of quasi-experimental well-designed trial
<b>Level III</b>	Evidence from descriptive non-experimental well-designed trials, such as comparative studies, correlation studies and case studies
<b>Level IV</b>	Evidence from reports of expert committees or experiments performed by respected entities

*Classes of recommendation Adapted and translated from Kirchhof P, et al. 2016<sup>[185]</sup>*

Class of recommendation	Descriptive	Indication
<b>Class I</b>	Evidence and/or general agreement that a given procedure or treatment is beneficial, useful, and effective	<b>Recommended/Indicated</b>
<b>Class II</b>	Conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of a procedure or treatment	
<b>Class IIa</b>	Evidence/opinion is in favor of usefulness/efficacy	<b>Should be considered</b>
<b>Class IIb</b>	Usefulness/efficacy is less well established by evidence/opinion	<b>May be considered</b>
<b>Class III</b>	Evidence and/or general agreement that a procedure/treatment is not useful/effective and in some cases may be harmful	<b>Not recommended</b>

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