Evidence to support safe return to clinical practice by oral health professionals in Canada during the COVID-19 pandemic: A report prepared for the Office of the Chief Dental Officer of Canada

July 2021 update

This evidence synthesis was prepared for the Office of the Chief Dental Officer, based on a comprehensive review under contract by the following:

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Foreword to the third update

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July 13, 2021

Following the successful completion of the original document on 31 July 2020, the Office of the Chief Dental Officer of Canada (OCDOC) commissioned McGill University to produce three updates during the year following the first report. This is the third of those update reports, covering relevant literature published between March 1st and June 30th, 2021. It is intended as an addendum to the original document and its previous updates, and should thus be used in conjunction with them. This 3rd update document will reside alongside the original report and the 1st and 2nd updates in the public domain, to be accessible to decision makers as they carry out their respective responsibilities.

As with the original document and its previous updates, McGill University drafted a comprehensive knowledge update concerning key issues that inform the provision of oral health care by relevant providers in Canada during the COVID-19 pandemic. The OCDOC then reconvened the representative multidisciplinary knowledge-based group from the national oral health professional and federal government health domains. The group's role was to work collaboratively to contribute to the generation of a single high-level national evidence update document by the team from McGill.

The organizations participating in this collaboration included:

Federal Health Portfolio

- Public Health Agency of Canada
- Health Canada, COVID-19 Task Force

National oral health regulatory federations

- Federation of Dental Hygiene Regulators of Canada
- Canadian Dental Regulatory Authorities Federation
- Canadian Dental Assisting Regulatory Authorities
- Canadian Alliance of Dental Technology Regulators
- Canadian Alliance of Regulators for Denturism

National oral health professional associations

- Canadian Dental Association
- Denturist Association of Canada
- Canadian Dental Assistants Association
- Canadian Dental Hygienists Association
- Canadian Dental Therapists Association

National oral health academic association

- Association of Canadian Faculties of Dentistry

OCDOC Mandate: to advance population-level oral health through health promotion, disease prevention and professional/technical guidance with an emphasis on vulnerable populations.

Introduction

During May and June 2020, a research team completed a rapid review of the literature to support the safe practice of Canadian dental professionals during the COVID-19 pandemic. Following input from stakeholders on the draft report in mid-July, the report was finalized and submitted July 31 and then published on the Canada.ca website in both official languages in September 2020. The review covered literature published from January 1, 2000, to June 30, 2020. With the rapid pace of new publications linked to the COVID-19 pandemic, the Chief Dental Officer of Canada determined that updates to the report were needed three times during the year following the first report. These updates covered scientific literature published between July 1, 2020, and October 31, 2020, between November 1, 2020, and February 28, 2021, and finally between March 1, 2021, and June 30, 2021. This is the third (and last) of those update reports adding relevant literature published during the period March 1st to June 30th 2021. The results of the two previous updates are found in this document and are identified as such.

This update document uses the same structure as the original report, addressing the same nine questions. In response to each question, we include: the rationale for the question (the same as the previous report); the summary response provided in the previous report; and then a summary of the new literature. The references are only those identified for the relevant update period and appended tables contain only material from newly identified references. Readers should return to the original report and previous updates for lists of references and other material pertinent to those documents.

Project goal

To create a knowledge product around which the Office of the Chief Dental Officer of Canada can convene a representative knowledge-based group of the national oral health professional domain, in order to generate a single high-level national expert document which Canada's oral health regulatory authorities may then choose to consult in developing consistent guidance for their respective registrants at the Provincial/Territorial level. Further, educators, program officials and policy makers may also choose to consult this document as they carry out their respective responsibilities.

When reading this report it is important to recognize three essential points:

- With the exception of the first two topics, which are related to the disease COVID-19 itself, the remaining topics concerning interventions in oral health care and the literature searches reflect reference to oral health care. The report therefore focuses on evidence directly related to oral health care. However, where relevant, we also refer the reader to Health Canada websites for pertinent information (https://www.canada.ca/en/public-health/services/diseases/coronavirus-disease-covid-19.html).
- This document does not provide guidelines or recommendations. This is the role of the relevant federal, provincial, and territorial authorities. The role of this document is to highlight high quality evidence that such authorities and others in leadership roles can use as they decide what guidance to give oral health professionals in Canada. Topics supported by limited or no evidence throughout the original report and its updates should be viewed as potential gaps for future research.

This document focuses on evidence that is categorized as high quality using internationally recognized hierarchies of evidence [1] [2] [3]. These are in descending order:

1. Systematic reviews and meta-analyses
2. Randomised controlled trials with definitive results (confidence intervals that do not overlap the threshold clinically significant effect)
3. Randomised controlled trials with non-definitive results (a point estimate that suggests a clinically significant effect but with confidence intervals overlapping the threshold for this effect)
4. Cohort studies

5. Case-control studies
6. Cross sectional surveys
7. Case reports
8. Expert opinion

Specific objectives

1. To update the previously published comprehensive review of the literature concerning key issues that inform the provision of oral health care by relevant providers in Canada during the COVID-19 pandemic. Those key areas are:
    a. Which patients are at greater risk of the consequences of COVID-19 and so consideration should be given to delaying elective in-person oral health care?
    b. What are the signs and symptoms of COVID-19 that oral health professionals should screen for prior to providing in-person health care?
    c. What evidence exists to support patient scheduling, waiting and other non-treatment management measures for in-person oral health care?
    d. What evidence exists to support the use of various forms of personal protective equipment (PPE) while providing in-person oral health care?
    e. What evidence exists to support the decontamination and re-use of PPE?
    f. What evidence exists concerning the provision of aerosol-generating procedures (AGP) as part of in-person oral health care?
    g. What evidence exists to support transmission mitigation strategies during the provision of in-person oral health care?
    h. What evidence exists to support space ventilation strategies that reduce the risk of transmission?
    i. What evidence exists to support the disinfection of surfaces in spaces in which oral health care is provided?

2. To prepare a written report documenting the updated findings of the aforementioned literature searches. The report is prepared in a manner that provides clear and concise information to decision-makers (individuals providers or organizational) highlighting where strong to no levels of scientific evidence exist to support different approaches.

Methods used to identify and include relevant literature

The same methodological approach was used for this update as was used in the original report and previous updates. In summary, search words and phrases were identified for each of the above topic areas a) to i), and searches were performed for English language articles, in standard scientific literature databases for the period March 1 to June 30, 2021. Two steps were then used to include publications in this report/process: i) step 1 was a review of abstracts to decide on the relevance of publication content for the topic areas; and ii) step 2 was to include only those publications reporting the results of prospective cohort studies, randomized controlled trials, systematic reviews and/or meta-analyses. Steps 1 and 2 were done by one author and a random number of publications were reviewed in the same way by a second author so as to ensure reliability of the findings. An additional, separate search was performed of the bibliography supporting relevant national, provincial and state guidelines concerning oral health care provision during the COVID-19 pandemic in Canada and the USA. Any publications identified in this bibliography that were not in our aforementioned search, but which fulfilled the quality criteria in step 2 and were published during the relevant period were also included in this update report.

With respect to step 1, concerning relevant subject areas, as well as searching for COVID-19 and SARS-CoV-2, we also searched for similar respiratory tract viruses such as SARS, MERS, H1N1 and influenza. In reporting the results of our work, we have made clear whether the evidence concerns COVID-19, SARS-CoV-2, SARS, MERS, H1N1, influenza and sometimes other pathogens. In reality, much of the work reported is in the form of systematic reviews that cover a range of relevant pathogens and diseases. In the updates, for questions with a robust body of evidence about COVID-19, we did not update evidence about other respiratory diseases or viruses (indicated for a topic when applicable).

With respect to step 2, concerning the inclusion of only that evidence fulfilling certain levels of quality, this was taken to enable this review to focus only on strong evidence in support of various approaches and concepts. This means that any evidence we highlight is of high quality. However, where we state that there is no evidence using our quality criteria, it does not mean there is no evidence at all, rather it means that evidence that exists is not of high enough quality to be included in our review. This is particularly important to note in the context of the current pandemic wherein there are a very high number of publications emerging from rapidly performed research, which for good reasons, may not be of the quality ideally desired. There are also many documents containing the opinions of experts, which are valuable in the circumstances, but which are recognized to be low in the hierarchy of quality of evidence.

Report structure

This report will address each of topics a) to i) in turn. For each topic, we provide the rationale for the question (which is the same as in the original report and previous updates); the summary response provided in the previous updates; and then a summary of the new literature, stating how strong the evidence is. The main body of the report contains only these summaries; however, each topic has an appendix containing a tabular summary of included papers, with summary data where appropriate. Readers of this report who are interested in more detailed information will need to access the relevant papers themselves. We also make clear where evidence is related to COVID-19/SARS-CoV-2 or related to similar respiratory tract viruses such as SARS, MERS, H1N1 and influenza. Finally, where pertinent, we refer readers to relevant Health Canada websites.

Summary of update reports

First update

This section provides an overview of the findings reported in the different sections. For more detailed information and for the references, see the relevant sections.

We identified a large number of new systematic reviews and meta-analyses concerning the symptoms of people diagnosed with COVID-19 and the risk factors for serious consequences such as hospitalization, ventilation and death among those patients. Many of these reviews and analyses confirmed data presented in the previous report. The evidence is strong that the most common signs and symptoms experienced by people diagnosed with COVID-19 are fever, cough, fatigue and muscle aches, shortness of breath, sputum, headache, sore throat and gastrointestinal symptoms, including diarrhea. New strong evidence has emerged reporting loss of sense of smell and altered sense of taste as common symptoms. With respect to risk factors for serious consequences of COVID-19, the evidence is strong for increased risk among people with cardiovascular diseases, hypertension, diabetes, chronic respiratory diseases, liver and kidney diseases, obesity and smokers. Newly added risk factors are people with cancer and cerebrovascular conditions. In terms of sociodemographic factors, the evidence is strong that increased age augments the risk of serious consequences, with this increased risk beginning to emerge particularly for those 60 years and older. There is now good evidence in the international literature indicating men being at increased risk for COVID-19 and its consequences, although it is not clear why - is it biological or because of their work, socializing habits and/or smoking and alcohol consumption? However, it is important to note that in Canada, the incidence of COVID-19 is higher in women. There is also some evidence to indicate that when studies control for socioeconomic factors, there are no racial differences in serious consequences for COVID-19.

While the evidence concerning the disease itself is increasingly strong, the evidence supporting different interventions pertinent to oral health care remains minimal and weak and relatively little work has been published in the period since the first report. In terms of clarifying guidance for oral health professionals, one systematic review highlights the categories of actions in pre-treatment, during treatment and post-treatment phases of care that organizations around the world have concentrated on, although this does not mean the relevant actions are based on evidence, rather that these are common areas to consider. Another review of guidelines for dental care during the pandemic noticed an increasing focus on preventive and non-Aerosol Generating Procedures (AGPs) and another highlighted the need to develop an evidence-based classification of AGPs and non-AGPs in dentistry rather than the theoretical approaches used thus far.

In terms of PPE, the picture remains unclear in terms of evidence directly related to oral health care, although the evidence does suggest using combined forms of facial covering (e.g., face visor and N95 mask) is better than just one, as no single interventions are fully effective in preventing transmission. There is emerging evidence that N95 masks can be microwaved and re-used at least once without loss of function but there remains no evidence supporting various mitigating approaches such as use of pre-treatment mouthwash, rubber dam and high-volume evacuation. There is evidence that chlorhexidine mouthwash reduces bacterial colony-forming units but none on this or other mouthwashes concerning viruses or disease transmission.

There is emerging evidence concerning the risk factors for Health Care Workers (HCWs) contracting COVID-19, plus the impacts of the disease on them, which are both relevant in terms of considering how to mitigate risks and impacts. Suggestions concerning reducing hours and increasing mental support services have been made for HCWs.

Second update

This section provides an overview of the findings reported in the different sections. For more detailed information and for the references, see the relevant sections.

Our second update identified another large collection of systematic reviews and meta-analyses documenting comorbidities that increase the risk of severe complications in case of infection by SARS-Cov-2. Most results are similar and/or complementary to previous versions of this report (e.g., higher risk for severe COVID-19 in individuals with hypertension, cardiac lesions and diabetes mellitus), but we have also highlighted reports that clarify risk related to pregnant women (the authors recognize that use of the term **pregnant women** is not gender inclusive. However, the systematic reviews on pregnant women referenced in this evidence synthesis did not include gender diverse people who are pregnant, limiting findings referenced to pregnant women only), who are at higher risk of the same complications for other individuals, including severe COVID-19 and ICU admission. Neonates can be affected negatively if born to mothers who are COVID-19-positive, including lower weight at birth and more frequent admission to a neonatal unit. Many reviews reinforce well-established evidence concerning COVID-19 signs and symptoms, but some reviews introduce a new concept of major relevance in our field: oral mucosal lesions associated to COVID-19.

Newer systematic reviews highlight the effective use of telehealth approaches to reduce in-person dental appointments, provide patient information and train professionals. They also reinforce the need for specific COVID-19 questionnaires before dental care, ventilated waiting rooms/common spaces, social distancing and regular disinfection of non-treatment and operatory areas but evidence does not support the use of laboratory screening tests for SARS-Cov-2 in dental care settings.

Other reviews compared different masks and respirators and suggested that FFP3 and FFP2 may be comparable to N95 to protect professionals from COVID-19. Again, face shields with lateral protection seem essential for dental care providers, combined with at least type 3 medical masks or respirators. However, there is little evidence to support different methods to reuse PPE, with recommended use only in cases of shortage.

A hierarchy of risk for contamination was suggested by evidence identified in this update, with higher risk associated with the use of ultrasonic scalers, high-speed handpieces, air-water syringe, air polishers, as well as handpieces and lasers for oral surgery (including extractions and osteotomy). Reviews have recommended the use of alternative techniques to minimise aerosols (e.g., atraumatic restorative treatment with hand instruments and silver diamine fluoride instead of conventional restorative treatment), and pre-appointment use of several types of mouthwashes to minimize risks of transmission.

Little evidence was gathered to support the use of air cleaning systems as a means to mitigate the transmission of COVID-19 in dental operatory rooms. More studies are still needed to determine disinfection methods for surfaces and objects in an oral healthcare facility, although a novel finding, however, is the efficacy of sodium hypochlorite as a disinfecting medium for impressions and dental prostheses.

Third update

The findings of this last update include several confirmatory SRs regarding comorbidities and conditions linked to a higher risk for fatal and severe COVID-19, further strengthening the evidence in this domain. We identified new information about certain conditions, which can lead to worse outcomes in case of SARS-CoV-2 infection, including psychiatric disorders, obstructive sleep apnea, pulmonary aspergilosis, multiple sclerosis and Parkinson's disease. Besides previously identified and now well-known signs and symptoms of COVID-19 (e.g., fever, cough, olphactory loss), there is some evidence that the condition may sometimes lead to skin manifestations .

This update identified some limited evidence in support of specific telehealth-based approaches to limit the presence of patients during the pandemic, as well as artificial intelligence for patient screening to decide whether in-person appointments are appropriate. We also identified a classification system that is usable by oral healthcare providers to assist in the screening of possible COVID-19 cases.

New evidence to support the use of different PPE was limited and confirmed some of the findings of our previous updates. No new studies concerning the reprocessing and re-use of PPEs were eligible for this update, in line with the current non-recommendation of those approaches due to sufficient supplies. In this context it is important to recognize that while re-use of certain PPE was considered at the beginning of the pandemic when supplies were often short, it is now not recommended to re-use PPE in Canada (see https://www.canada.ca/en/health-canada/services/drugs-health-products/covid19-industry/medical-devices/personal-protective-equipment/medical-masks-respirators/reprocessing.html).

Included studies reinforced the need for adequate ventilation and filtration to control contamination during AGPs, with optimal results in hospital settings by combining both. Few studies have approached space ventilation strategies directly, but some provide specific recommendations based on the use of natural ventilation, air vents and filtering units. The time to remove aerosols seems to reduce considerably if ventilation is combined with filtering units.

The mitigation and management of aerosols specific to oral health care settings is still based on limited evidence, although the following website provides a good overview of how COVID-19 is transmitted (https://www.canada.ca/en/public-health/services/diseases/2019-novel-coronavirus-infection/health-professionals/main-modes-transmission.html). However, in this most recent update, we identified new evidence to support some pre-procedural mouthwashes, rubber dam and high-volume evacuators. Included studies recommend the minimization of aerosols as much as possible in different dental treatments, including the use of hand scalers and manual excavation instead of high-speed handpieces where viable. New evidence has emerged that high-power lasers may result in a considerable volume of particles in the air; thus, studies suggest more complex barrier methods when they are used, both in clinical and laboratory settings.

Finally, limited evidence supports a wide array of surface disinfecting agents against SARS-CoV-2, but also reminds us that this virus is able to survive for several days on vinyl, steel and glass, which are common materials in any oral healthcare environment. Given the paucity of evidence on SARS-CoV-2, the reader may opt to refer to previous studies on other enveloped viruses for further information on those agents:

https://www.canada.ca/en/health-canada/services/drugs-health-products/disinfectants/covid-19.html

https://www.canada.ca/en/health-canada/services/drugs-health-products/covid19-industry/disinfectanst-sanitizers-cleaners-soaps.html

Report results

a. Which patients are at greater risk of the consequences of COVID-19 so consideration should be given to delaying elective in-person oral health care?

a.1. Findings from the first update

We identified multiple systematic reviews, meta-analyses and a few cohort studies adding to the knowledge and understanding of which patient groups are at greater risk of severe consequences of having COVID-19. The large majority of these studies confirmed findings we described in the previous report. Nevertheless, there have been some important additional findings with strong evidence supporting them. Recently published reviews and meta-analyses confirmed the increased risk for serious consequences of COVID-19 including hospitalization, ventilation and death for people with cardiovascular diseases [4] [5] [6] [7] [8] [9] [10] [11] [12] [13] [14] [15] [16] [17], hypertension [4] [5] [6] [7] [8] [9] [10] [11] [12] [17] [18] [19] [20], respiratory diseases [5] [7] [10] [11] [12] [18] [21] [22] [23], diabetes [4] [5] [7] [8] [10] [11] [19] [20] [21] [24] [25] [26] [27] [28], liver [12] [29] [30] [31] and kidney diseases [5] [8] [11] [12] [14] [22] [32] [33] [34] [35] [36] [37] [38] [39] plus for smokers [18]. New information adds to the list of at-risk people who are obese [20] [40] [41] [42] [43], have cancer [11] [44]

[45] [46] [47] and cerebrovascular conditions [10] [11] [12] [13] [17] [48] [49] [50] [51].

Concerning age and sex, again there has been additional high-quality evidence published. It is clear that increased age increases the risk of serious consequences [20] [49] [52] [53] with one review clarifying that the peak increase in risk is for serious consequences starts to occur for those 50-59 years of age but the largest risk increase is for the 60-69 year olds compared to those in their 50s, although the risk keeps increasing with older age [52]. With respect to sex, it is now clear from the international literature that the incidence of COVID-19 is greater in men than women [10] [19] [54] [55]. However, it is important to note, as shown on the webpage Covid-19 epidemiological and economic research data, that in Canada, the incidence of COVID-19 is higher in females compared to males, although this varies by age group. In terms of disease outcomes, again the international literature shows men are at increased risk for serious consequences of COVID-19 including death [20] [54] [56] [57] [58]. However, these studies also pointed out that it is not clear why men are at greater risk for worse outcomes. They could be at increased risk because of the nature of their work, their socializing habits, their smoking, alcohol consumption and/or levels of comorbidities [20] [58]. In Canada, there have been more hospitalizations and deaths among women but more men admitted to intensive care units (again see COVID-19 epidemiological and economic research data. It is also important to recognize that certain groups in the population face greater risk due to social, economic and occupational vulnerabilities (see Vulnerable populations and COVID-19 l). Further research needs to be performed to better understand the different levels of risk experienced by various groups in the population.

Canada covid-19 weekly epidemiology report. Further research needs to be performed to better understand this phenomenon.

With respect to COVID-19 in pregnancy, the evidence remains relatively limited because the numbers are considerably smaller than in the broader population studies. Nevertheless, there is limited, emerging evidence that pregnant women with COVID-19 are at increased risk for complications with their pregnancy [59] [60] [61] [62]. There is also emerging limited evidence concerning the problems suffered by neonates who are COVID-19 positive [59] [60] [63] [64] [65]. With respect to the possibility of vertical transmission from mother to foetus, one systematic review reported zero such cases [64] while two others reported rates of 2-3.2% of neonates testing positive for SARS-Cov-2 among babies born to mothers who were also SARS-Cov-2 positive [61] [66].

a.2. Findings from the second update

This second update returned several systematic reviews (SRs) within this topic. As for the November 2021 update, most of those SRs confirm previous strong evidence regarding the risk for complications of COVID-19 associated with now well-known comorbidities. Probably the most studied comorbidity linked to higher risk of severe COVID-19, ICU admission and death is hypertension, which was identified by 49 new SRs [67] [68] [69] [70] [71] [72] [73] [74] [75] [76] [77] [78] [79] [80] [81] [82] [83] [84] [85] [86] [87] [88] [89] [90] [91] [92] [93] [94] [95] [96] [97] [98] [99] [100] [101] [102] [103] [104] [105] [106] [107] [108] [109] [110] [111] [112] [113] [114] [115]. Twenty-six SRs further confirm the higher rates of severe COVID-19 among CVD patients, with a higher risk for ICU admission and death [67] [68] [69] [71] [72] [74] [76] [77] [78] [81] [82] [84] [86] [87] [88] [91] [92] [98] [99] [101] [107] [113] [114] [115] [116] [117]. Specific CVD and conditions tackled by recent SRs include congestive heart failure [10] [75] [107] [118] [119] [120] [121], cardiac arrythmia [75] [119] [120] [122], myocardial injury [119] [123], history of heart transplant [124], general [89] [125] [126] and acute cardiac injury [67] [75] [97] [110] [120] [123] [127] [128] [129] [130], and coronary heart disease [93] [103] [105] [115] [131]. In all cases, the risk of severe COVID-19 and subsequent death raises considerably.

As found in previous versions of this report, a history of respiratory diseases raises the risk for severe COVID-19 and death (six SRs) [69] [105] [114] [132] [133] [134] . Specific conditions associated with increased risk for poor outcomes of COVID-19 were asthma (11 SRs) [72] [85] [88] [91]

[94] [100] [133] [135] [136] [137] [138] [139], COPD (15 SRs) [67] [77] [84] [86] [90] [98] [113] [114] [116] [140] [141] [142] [143] [144] [145] and ARDS (12 SRs) [67] [71] [72] [108] [110] [120] [130] [146] [147] [148] [149] [150]. Three SRs suggest higher risk for severe COVID-19 in patients with a history of pneumonia [73] [112] [133]. This update also reinforces findings for diverse types of cancer [67] [69] [72] [84] [86] [88] [94] [100] [101] [103] [107] [113] [114] [116] [151] [152] [153] [154] [155] [156] [156] [157] [158] [159] [160] [161] [162] [163], cerebrovascular diseases [67] [69] [72] [77] [84] [86] [88] [113] [114] [115] [164] [165] [166] [167], acute [67] [86] [120] [123] [130] [168] [169] [170] [171] [172] [173] [174] [175] [176] [177] [178] [179] and chronic kidney diseases (including patients who received transplants and hemodialysis) [67] [69] [82] [86] [88] [94] [100] [103] [105] [107] [113] [116] [140] [142] [169] [174] [175] [178] [179] [180] [181] [182] [183], being linked to severe COVID-19 and higher odds for death. A history of diabetes mellitus has been associated with a higher risk of severe COVID-19 and consequences like cerebrovascular accidents, ICU admission, invasive ventilation and mortality [67] [68] [69] [70] [71] [72] [73] [74] [76] [77] [78] [80] [81] [82] [84] [86] [87] [88] [90] [91] [92] [93] [94] [95] [96] [97] [98] [99] [100] [101] [102] [103] [104] [105] [106] [107] [108] [110] [112] [113] [114] [115] [116] [132] [142] [184] [185] [186] [187] [188] [189] [190].

More specific findings of this update include a higher severity of and mortality through COVID-19 among individuals affected by dementia [191] [192] [193] [194] and other nervous system diseases [164] [195]; liver disease (mostly chronic) [67] [69] [113] [114] [196] [197] [198] [199] [200] [201] [202] [203]; and thromboembolism, both arterial [204] [205] [206] [207] [208] [209] and venous [210] [211] [212] [213] [214] [215] [216] [217] [218] [219] [220] [221]. Evidence seems less consensual regarding autoimmune disease, with conflicting results [88] [100] [222].

Important factors linked to severe COVID-19 outcomes include advanced age [69] [71] [72] [78] [79] [90] [101] [105] [106] [109] [134] [141] [180] [206] [223] [224] [225] [226] [227], obesity [94] [96] [100] [101] [114] [142] [190] [228] [229] [230] [231] [232] [233] [234] [235] [236] and smoking (current or previous) [67] [77] [78] [81] [86] [94] [103] [104] [145] [237]

[238] [239] [240] [241] [242] [243] [244] [245] [246], all of which were mentioned in our previous reports. Interestingly, a history of bariatric surgery seems protective against COVID-19-related death and hospital admission [247]. In this update, we found no evidence for the role of a specific sex/gender as a risk factor for complications of COVID-19 [67] [69] [71] [72] [73] [77] [78] [79] [87] [90] [92] [101] [103] [104] [105] [130] [141] [223] [226] [248] [249] [250] [251] [252]. Regarding the role of race in COVID-19 outcomes, some SRs suggest modest differences in the risk for severe disease and mortality with higher risk among Asians compared other groups [71] [253] [254] [255]. Interestingly, newer SRs suggest different risks to acquire COVID-19 in people with different blood types, the highest risk being for those with blood type A and Rh-positive; however, the odds for severe COVID-19 and death are the highest among blood type AB individuals [256] [257] [258].

Stronger evidence is now emerging concerning pregnant women, neonates and children. Pregnant women are at higher risk for hospital admission (including ICU and invasive ventilation) if affected by COVID-19, compared to non-pregnant women [259] [260] [261] [262]. The risk is further increased if some of the abovementioned conditions are present, e.g., obese women, increased maternal age, pre-existing hypertension and diabetes [259] [263]. Neonates are at higher risk for complications if their mothers are COVID-19-positive, including admission to a neonatal unit, low birth weight and fetal distress, besides the possibility of acquiring the disease from their mothers (vertical transmission) [259] [260] [261] [263] [264] [265] [266] [267] [268]. Regarding children, although they are less prone to complications from COVID-19 [148] [269] [270] [271] [272] [273] [274], a history of cancer [275] or obesity [276] increases the risk for severe disease in this age group. We found no evidence fulfilling our inclusion criteria concerning the association between congenital and genetic syndromes (e.g., Down syndrome, intellectual disabilities) with the outcomes of COVID-19. This as a major knowledge gap that should be explored in future prospective studies.

We found moderate evidence suggesting more complications with COVID-19 among individuals who have tuberculosis, influenza, chronic hepatitis, HIV, rheumatic diseases, intestinal diseases, dyslipidemia, secondary infections and vitamin D insufficiency. Also, individuals who underwent surgical procedures while affected by COVID-19 seem to face higher mortality rates [277].

A good document summarizing the key risk factors for severe COVID-19 disease can be found at: People who are at high risk for severe illness from COVID-19.

a.3 Findings from the third update

Fourteen SRs with meta-analyses endorse the higher risk of severe COVID-19 and subsequent mortality among people with cardiovascular disease (CVD) [278] [279] [280] [281] [282] [283] [284] [285] [286] [287] [288] [289] [290] [291]. Hypertension is again highlighted as a risk condition for more severe COVID-19 cases, with higher odds of ICU admission and death (15 SR with meta-analysis [278] [279] [292] [280] [281] [282] [293] [294] [295] [283] [284] [285] [287] [290] [291]). Other specific CVD linked to a higher risk of severe and lethal COVID-19 were congestive heart failure [296] [297] [289] [298]), cardiac arrythmias [299] [297] [300] [298], myocardial and cardiac injuries [298] [301] [293], ST- Segment Elevation Myocardial Infarction (STEMI) [302] [303], acute cardiac injury [288] [289] [290] [298] [304], coronary heart disease [297] [295], and both left and right ventricular dysfunction [305] [306]. Moreover, the occurrence of cardiac arrest in COVID-19 patients results in more frequent mortality compared to non-infected patients [305].

Six new SRs with meta-analyses further endorsed previous evidence that pre-existing respiratory diseases in general can increase the risk for severe COVID-19 outcomes and subsequent mortality [279] [292] [304] [281] [22] [293]. The same can be stated for specific respiratory diseases, i.e., asthma [307] [308] [309] [310] [311] [312], COPD [307] [313] [304] [308] [282] [297] [295] [284] [314] [310] [285] [290] [291], ARDS [278] [315] [280] [281] [22] [295] [288] [290], obstructive sleep apnea [316], and pulmonary aspergillosis [317] [318].

A large body of evidence confirms the link between diabetes mellitus and severe and lethal COVID-19 [278] [319] [320] [279] [292] [280] [281] [321] [282] [322] [293] [323] [294] [295] [324] [325] [283] [326] [327] [284] [319] [328] [285] [287] [329] [290] [291] [330]. People with cancer are also at higher risk for the same poor outcomes, with even higher mortality during active chemotherapy [307] [331] [332] [333] [280] [304] [282] [334] [293] [335] [331] [336] [284] [337] [338] [291] [330].

Six SRs and meta-analyses concluded that cerebrovascular diseases in general are linked to higher odds for severe COVID-19 [279] [282] [293] [295] [287] [291]. Two SRs with meta-analyses came to the same conlsusion for dementia, with higher mortality rates for people with this condition [339] [340].

A single SR with meta-analysis concluded that patients who suffer from certain psychiatric disorders (i.e. mood disorders, schizophrenia, schizotypal and delusional disorders) may be at higher risk to become infected by SARS-CoV-2 [341]. The same patients may be at higher risk of severe and lethal COVID-19 outcomes, at least when they are in advanced age or have comorbidities.

A single SR with meta-analysis provided evidence that COVID-19 increases the odds of developing Guillain-Barré syndrome, although this remains rare [342]. Acute liver lesions were also identified as potential complications of COVID-19 by two SRs with meta-analyses [22] [288].

Again, chronic [292] [304] [282] [293] [295] [324] [343] [344] [283] [345] [287] [291] and acute kidney diseases [304] [281] [22] [295] [346] [347] [345] [288] [290] [348] were highlighted as risk factors for severe COVID-19 and subsequent hospital admission and death. Severe COVID-19 was also more frequent among people with liver disease [278] [304] [349] [293] [350].

Ten SRs with meta-analyses point out that current and previous smokers are at higher risk of death if infected by SARS-CoV-2 [278] [304] [281] [321] [351] [352] [293] [297] [295] [291]. Twelve SRs with meta-analyses identified obesity as a risk factor for severe COVID-19, hospitalization (including ICU admission and invasive ventilation) and death, even in young patients [353] [354] [355] [356] [357] [295] [324] [358] [359] [360] [287] [361].

Age was again confirmed as a risk factor for severe COVID-19 and mortality, mostly in the presence of comorbidities [339] [292] [362] [304] [363] [364] [293] [297] [294] [324] [284] [365] [288] [290] [291]). Three SRs with meta-analyses described Black and East Asian individuals as being at higher risk of COVID-19, with a non-Caucasian ethnicity being linked to a higher risk of consequent mortality [363] [321] [293]. Two SRs with meta-analyses highlighted that seroprevalence of SARS-CoV-2 varies considerably among different regions of the world, with highest rates in Southeast Asian, African and Eastern Mediterranean regions [363] [293].

Arterial thrombosis has been linked to higher risks of severe and fatal COVID-19 [366] [296] [367] [368] [369] [370], while venous thrombosis (including pulmonary embolism) was highlighted as a risk factor for ICU admission among COVID-19 patients [371] [372] [217] [373] [374].

Some SRs with meta-analyses link pre-existing conditions to worse outcomes among COVID-19 patients, including higher mortality with dyslipidemia [375] and hemoglobinopathies [376]. Diseases and conditions linked to a higher risk of lethal and severe COVID-19 included multiple sclerosis [377], Parkinson’s disease [378], femoral and hip fractures [379] [380], rheumatic diseases [381], immunosuppression [333] [330], previous HIV infection [382] [383] [384] [385] [386] and different degrees of frailty [387] [388] [389] [390]. The previous use of NSAIDs exerted no difference on the course of COVID-19, however [391].

Nutritional issues (i.e. deficiencies of vitamin D [392] [393] [394] [395] [396] [397] and micronutrients [398]) were identified by some SRs with meta-analyses as being correlated with severe and/or fatal COVID-19.

An emerging issue refers to the recurrence of COVID-19, which was described in 15% of a sample of 3,644 patients by a SR with meta-analysis [399].

Pregnant women infected with COVID-19 were slightly more likely to be admitted to ICU, particularly with increased maternal age, high body mass index and comorbidities [400] [281] [401] [402] [294] [403]. Neonates born to COVID-19-positive women were more likely to be admitted to neonatal units and have lower birth weight (1 SR with meta-analysis [281]). Two SRs with meta-analyses concerning COVID-19 in children stated that, although the prevalence is lower than in adults [294], comorbidities like cancer can increase the risk for severe and fatal infection in this group [333].

b. What are the signs and symptoms of COVID-19 that oral health care professionals should screen for prior to providing in-person health care?

b.1. Findings from the first update

We identified multiple systematic reviews and meta-analyses plus prospective cohort studies adding to the now strong literature on the signs and symptoms of COVID-19. The additional literature we identified largely confirmed the summary and list of symptoms provided in the earlier report (fever, cough, shortness of breath, fatigue and muscle weakness and aches, headache and digestive symptoms such as diarrhea [5] [9] [10] [19] [404] [405] [406] [407] [408] [409]), although notable new information has been added. This includes new signs and symptoms now recognized as among those often shown by people with COVID-19, including anosmia (lost sense of smell; 39-88%) [406] [407] [410] [411] and dysgesia (altered sense of taste; 81%) [411]. There were also important additions to the previous list of signs and symptoms, including loss of appetite (34%) [5], myocardial injury (16%) [412], dizziness (6%) [19] and confusion/agitation (5%) [407]. On top of this, there has been additional literature concerning symptoms experienced by children with COVID-19, including fever (53%), cough (39%) and sore throat (14%) [413]. The evidence concerning the symptoms experienced by pregnant women with COVID-19 remains relatively limited compared to the general population but new information now available includes estimates of the proportion of pregnant women with viral pneumonia (71-89%) [60], fever (44-63%) [60] [65] [414], cough (36-71%) [60] [65] [414], dyspnea (13-34%) [65] [414] and myalgia or fatigue (11%) [60].

b.2. Findings from the second update

This second update found a large body of evidence confirming previously described signs and symptoms of COVID-19, including fever, cough, dyspnea, sore throat, muscle pain, headache, abdominal pain, diarrhea, agitation/confusion, dizziness, loss of appetite, as well as olfactory and gustatory impairment. Ischemic strokes also seem more frequent among COVID-19 patients [115] [164] [415] [416] [417] [418] [419].

Newly described findings include expectoration with blood (hemoptysis), chest pain and tightness [67] [69] [130] [420], and ocular manifestations (conjunctival symptoms) [421]. Specific laboratory and imaging findings can be seen in COVID-19 patients (please refer to **Appendix B for more information**).

Of special interest for oral healthcare providers, a single SR describes oral mucosal lesions associated with COVID-19 [422]. Patients may present irregular ulcers, small blisters and petechiae affecting palate, tongue, lips, gingiva or buccal mucosa. Desquamative gingivitis was also observed. Whereas mild cases seem to develop oral mucosal lesions before or at the onset of respiratory symptoms, patients who required medication and hospital admission may have those lesions between 7 and 24 days after symptoms started.

A good document concerning signs and symptoms of COVID-19 can be found at the following link: COVID-19 signs, symptoms and severity of disease: A clinician guide.

b.3 Findings from the third update

This third update found several SRs with meta-analyses confirming previous information about the signs and symptoms of COVID-19. Fever is highlighted as one of the most common signs, reaching a medium grade for almost half of the cases [280] [377] [281] [423] [424] [293] [297] [294] [365] [425] [291].

Newer signs to consider include cutaneous manifestations, often morbilliform, varicelliform, and urticarial [426]. COVID-19 also has been linked to neurological symptoms [427] [425] [428] and higher pulse rate [291].

We also identified recent SRs with meta-analyses quantifying asymptomatic patients as being 31% of COVID-19-positive nursing home residents [364] and 5% to 12.9% of children [281] [429] [430].

As the pandemic evolves, new data on long-term, post-COVID-19 symptoms were reported by a single SR with meta-analysis [431]. After recovery from COVID-19, 55% of patients report chronic fatigue and pain, while almost a quarter report neurological complaints and olfactory dysfunctions (24% each), and abdominal breathing (21%).

c. What evidence exists to support patient scheduling, waiting and other non-treatment management measures for in-person oral health care?

c.1. Findings from the first update

Again, several relevant systematic reviews were identified. One relevant publication reviewed COVID-19 transmission risk and protection protocols published by organizations in countries throughout the world and in academic journals [432]. They categorized the approaches they found common to all protocols in these publications into pre-, during and post-dental treatment measures as per Table 1 below. It is important to note that this summary of factors common to all reviewed dental COVID-19 protocols does not necessarily reflect any evidence to support their inclusion, or exactly what the advice for each factor is, rather it is a list of factors in dental COVID-19 dental protocols that were common to all review publications.

Table 1. Measures recommended in dental protocols identified in systematic review by Banakar et al [432].

Stage of care	Measures recommended
Pre-dental treatment Before entering a dental office At the dental office	Patient triage, identification potential COVID-19 cases, delay of non-urgent dental care, management of dental appointments, active and culturally safe screening of dental staff. Active and culturally safe screening of patients, physical distancing in the dental office, cleaning and disinfection measures for patients, use of facemasks by everyone entering the dental office, patient education, use of personal protective equipment (PPE) by the dental team and management of the dental operatory room.
During dental treatment	Maintaining hand hygiene, offering preoperative anti-microbial mouth rinse to patients, using rubber dams, high-volume saliva ejectors, and extraoral dental radiographs, using 4-handed dentistry, avoiding aerosol-generating procedures, one-visit treatment and environmental cleaning and disinfection procedures.
Post-dental treatment	Cleaning and disinfecting reusable facial protective equipment, as well as management of laundry and medical waste.

This list of factors to consider and the categorization of the stages of pre-, during and post-dental treatment was very similar to those documented in two other systematic reviews on the subject [433] [434]. A review of guidelines for pediatric dentistry during the COVID-19 pandemic published throughout the world made similar observations but in addition, focused on the need for preventive and non-AGPs [435]. The authors mentioned focusing on using approaches including telehealth, using fluoride varnish and resin or sealing non-cavitated caries, using atraumatic restorative technique (ART), interim therapeutic restorations, indirect pulp capping, the Hall technique and silver diamine fluoride [435].

c.2. Findings from the second update

Some included studies bring new information about telehealth, reaching moderate levels of evidence. The possibility of reducing physical contact and providing continuous care makes telehealth appropriate, with potential to reduce COVID-19-related morbidity and mortality [436]. Oral health-specific approaches were highlighted as useful for the present pandemic by two reviews [437] [438]. Examples of contributions by teledentistry include fewer in-person appointments and remote triage of the elderly, with good cost-effectiveness and acceptability by patients, caregivers, families and care facilities [439]. The use of remote appointments was also highlighted as favorable for evaluating cleft lip and palate patients, including their post-treatment follow-up [440]. Generic telehealth methods have been pointed as a way to guarantee better access to care during a lockdown [441] and to evaluate chronic pain patients in certain circunstances [442]. One review suggested that the use of mobile apps in health care can increase the effectiveness of tasks such as training personnel and managing patients at risk or with symptoms of COVID-19 [443].

Recommended practices for patient management before entering the dental office include triage of possibly infected patients [444] [445] and restricting dental treatment to urgent care during high levels of infectious disease in the local community [438]. In-office approaches should include active screening with temperature measurement, minimum number of patients in waiting rooms, physical distancing, good ventilation and no shared objects among waiting patients and staff [444] [445] [446] [447]. Emergency treatment of COVID-19 patients should follow high levels of personal protection and be conducted within specifically equipped facilities [445]. A recent review questions the use of laboratory tests (e.g., ELISA and rapid serological assays) for SARS-Cov-2 in an oral healthcare setting, and recommend simpler approaches instead, including an interview, checking temperature to rule our possible active COVID-19 cases and strict infection control [448].

In terms of disinfection of dental operative settings, disinfecton/cleaning of dental chairs after each patient is recommended, while disinfecton/cleaning of all other surfaces (e.g., operatory light, counters and delivery units) twice a day is also recommended [445]. Personal belongings and jewelry should not be worn by dental professionals during patient management. Another review suggests cleaning and disinfection of waiting and treatment areas between patients, including doorknobs, chairs, floor, desks, restrooms and elevators [444].

c.3 Findings from the third update

Moderate evidence from SRs confirm the usefulness of teledentistry and telehealth-based approaches during the pandemic. New evidence concerning promising uses include the surveillance of oral epithelial dysplasia [449] and speech therapy interventions in children with palatal clefts [450]. A prospective study highlights the potential use of artificial intelligence for the screening of dental patients to minimize emergency service overuse and thus COVID-19-related risks [451].

An SR [452] recommends three criteria to use in the context of providing emergency care in a hospital setting when the emergency care has to be provided prior to receiving the result of a diagnostic test. These criteria help assign relevant patients to high risk of having COVID-19 versus low risk of having COVID-19. Relevant patients are considered as high risk of having COVID-19 in the presence of one of more of the following criteria:

(i) fever plus one or more sign/symptom of respiratory disease and previous stay in an area reporting local transmission of COVID-19 disease within 14 days prior to symptom onset;

(ii) any acute respiratory illness and contact with a confirmed COVID-19 case within 14 days prior to symptom onset; or

(iii) severe respiratory infection requiring hospitalization, without an etiology that fully explains the clinical presentation.

After application of the three criteria, suspected cases are confirmed by COVID-19 RT-PCR test and chest imaging [452]. Those tests should be done before admission in the surgical ward when possible; the absence of conclusive tests should lead the patient to be treated as a COVID-19 patient.

At the dental office, recommended approaches during the pandemic remain similar to what was reported in our previous updates. This includes using remote approaches, limited scheduling and postponing treatment during the active phases of the pandemic [424] [453] [454], using COVID-19 screening questionnaires and emergency care under negative pressure or isolation [424] [453], and prioritizing non-aerosol procedures (e.g., caries excavation in children) [455]. A new recommendation refers to waste disposal, which should be preferably done in double-layer, yellow, leak-resistant clinical waste bags, with a "gooseneck" knot [454].

Recommendations for masks and frequent handwashing as a prevention method by the population in general and patients visiting health care settings remain. An SR with meta-analysis [456] concerning the prevention of influenza demonstrated optimal transmission prevention with 5 to 10 handwashings daily, whereas 10 or more did not result in further effect. A new SR did not reveal a significant preventive effect for influenza if face masks used by people in the community is the only public health measure [457].

An SR provided relevant data about the most frequent environments for the transmission of COVID-19, with these being public travel, 58.1%; close contacts, 43.1%; and community spread, 27.4% [294]. Those aspects, besides the potential transmission by fomites [458] [424] [459], should be kept in mind for infection control and patient screening. In terms of oral health care staff adopting appropriate preventive measures, a recent randomized RCT among dental students demonstrated that a behavioural intervention based on “dissonance induction” (i.e., making a subject recognize inconsistencies between COVID-19 prevention guidelines and their beliefs/practices) was more effective than an intervention based on “assessment reactivity” (i.e., enquiring about preventive behaviour to elicit future attention to adequate COVID-19 prevention practices) in students adopting preventive measures [460]. In this study, the group of students intervened by “assessment reactivity” performed like a negative control group (i.e., no behavioural intervention).

Important information about the transmission of COVID-19 and means to prevent or reduce transmission can be found at these two websites:

https://www.canada.ca/en/public-health/services/diseases/2019-novel-coronavirus-infection/health-professionals/main-modes-transmission.html

https://www.canada.ca/en/public-health/services/publications/diseases-conditions/routine-practices-precautions-healthcare-associated-infections/part-d.html#D.V

d. What evidence exists to support the use of various forms of personal protective equipment (PPE) while providing in-person oral health care?

d.1. Findings from the first update

We identified several systematic reviews with relevant information. One investigated the use of powered air-purifying respirators (PAPR) compared to N95 masks and other devices in the prevention of viral infection of health care workers, focusing on SARS-Cov-2, SARS-Cov-1, MERS and Ebola viruses. This review reported no difference in HCW infection rates using PAPR versus other respirator devices. They did note however, increased heat tolerance for HCWs using PARP but more difficulty communicating and with mobility [461]. Another review investigated the benefits for oral

and maxillofacial surgeons of using N95 versus surgical masks when performing AGPs [462]. They concluded that most studies comparing the two showed no difference in infection rates of HCWs but there was some evidence suggesting that N95 masks may be better when performing an AGP with a patient known to be COVID-19 positive or whose status is unknown [462]. Another review of N95 and surgical masks and eyewear use in dental care reported that combined use of two or more measures (for example, mask and facial visor) is effective as a barrier to aerolized microbes, although this can be affected by multiple factors such as airflow dynamics, aerolized particle size, prolonged wearing and wetness of masks and poor fit. Importantly, they noted that no intervention on its own has been demonstrated effective at preventing infection [463]. We identified no research evidence that referred specifically to KN95 masks.
Another review investigated the physical and mental health impacts of COVID-19 on HCWs during the pandemic [464] and reported that working in a high-risk setting, having a COVID-19-diagnosed family member, inadequate hand hygiene, improper PPE use, close contact with patients ≥ 12 times daily, extended contact hours (≥15 daily) and unprotected exposure are associated with increased risk of COVID-19-related impacts for HCWs [464]. They also noted that prolonged PPE usage led to cutaneous manifestations and skin damage, that HCWs experienced high levels of depression, anxiety, insomnia and distress, and that female HCWs and nurses are disproportionately affected [464]. All this suggests the need for vigilance with infection control procedures, shorter work hours and mental health support for HCWs [464].

d.2. Findings from the second update

Again, this update identified several relevant new SRs. This update found moderate evidence regarding protection of health care workers against COVID-19. In general, reviews stress the critical role of proper donning and doffing of PPE [465] [466]. Again, reviews highlight the adversities of prolonged use of PPE, with skin damage on the nasal bridge being the most common problem [467].

Several reviews approached specific PPE items, including:

- Face shields and eye protection: Their use should be combined with a mask or respirator [466] [468] and provide lateral facial protection [469].
- Respirators and masks: FFP3 respirators were recommended for treating COVID-19 suspected and confirmed patients in an SR [445]. Both FFP3 and FFP2 are at least equivalent to N95 [104]. An SR [465] found that powered air-purifying respirators (PAPR) may be more protective than N95 masks, although harder to don. Gowns are more protective against respiratory viruses, and risk can be further reduced by using a combination of sealed gown fitted tightly around neck and wrists, plus gloves. According to the same review, gloves lead to lower risk for contamination when worn by different methods: with tabs to facilitate doffing (same with masks), one-step removal with gowns, double gloving, and sanitizing with quaternary ammonium compounds or bleach before and after doffing. Type 3 medical masks are recommended as the standard protocol in a dental operatory, although they may not be very effective to prevent influenza-like illness [466] [470] [471].

Despite the evidence that complex PPEs and procedures (e.g., PAPR, doffing after sanitation) may be more protective in ideal settings, we lack data about their performance in diverse "real life" scenarios. Future studies should clarify whether more complexity may lead to higher risk of inadequate use of PPEs and thus higher risk of contamination in oral healthcare settings.

Several reviews compared N95 to medical masks [444] [445] [466] [468] [470]. General findings show that N95 masks may be superior in moderate- to high-risk clinical settings, with further reduction in the risk of COVID-19 infection and other respiratory viruses. Some reviews recommend that dental professionals, including oral and maxillofacial surgeons, should wear N95 masks when small-sized aerosolized particles are expected [466]. Although face masks (medical or not) may reduce primary respiratory infection risk [472], COVID-19-specific studies are still needed.

The Health Canada website also has information concerning PPE.

d.3 Findings from the third update

In general, this third update has found few sources of evidence dealing with PPE for patient care, but included some data about complications for health care workers (including oral health professionals, nurses and physicians) e.g., headache, dry skin, dyspnoea, hyperhidrosis and dermatitis [473] [474].

Updated evidence still supports face masks as important to reduce COVID-19 infection risk among the general population [475]. For health professionals, data resonate with previous updates by indicating that conventional surgical masks may not be an effective barrier for health professionals during the use of AGPs [476], compared to N95 respirators [477]. The recommendation of gowns and gloves as relevant protection methods against COVID-19 infection remain, as observed with SARS-CoV-1 and SARS- CoV-2 [477].

e. What evidence exists to support the decontamination and re-use of PPE?

e.1. Findings from the first update

We identified one additional systematic review on this subject [478]. The review investigated the use of microwave and heat-based decontamination of N95 masks and found that microwave irradiation may provide safe and effective viral decontamination for N95 masks while conserving function but that autoclaving did not do the latter so is not supported. The authors did however note that more research needs to be performed in "real world settings" to confirm their conclusions [479].

e.2. Findings from the second update

Few included sources of evidence approached possible ways to re-use PPE. One scoping review did not recommend routine decontamination of facemasks, but rather in situations of shortage only [466]. Some specific decontamination methods before re-use of masks include:

- Ultraviolet C radiation (UV-C): able to inactivate SARS-CoV-2 and other respiratory viruses [466] in respirators and masks, without damaging them [468].
- Hydrogen peroxide vapor (H_2O_2): able to decontaminate without reducing the performance of respirators and masks [466] [468].
- Dry heat: as with H_2O_2, dry heat can decontaminate respirators and masks without damaging them [468].

e.3 Findings from the third update

We identified no new sources of evidence under this topic for the 3rd update. In this context it is important to note that re-using and reprocessing PPE in Canada was only, considered at the beginning of the pandemic when there were shortages of certain PPE. Re-use and reporocessing of PPE is no longer recommended in Canada.

Relevant information from Health Canada can be found at:

https://www.canada.ca/en/health-canada/services/drugs-health-products/covid19-industry/medical-devices/personal-protective-equipment/medical-masks-respirators/reprocessing.html

f. What evidence exists concerning the provision of aerosol-generating procedures (AGP) as part of in-person oral health care?

f.1. Findings from the first update

We identified two systematic reviews with relevant subject matter published during the period July to October inclusive. One systematic review confirmed that SARS-Cov-2 is present in saliva and as well as sputum and the nasopharynx and concluded that saliva could be used to test for COVID-19 [480]. Another rapid systematic review was performed with the aim of classifying aerosol generating procedures (AGPs) [481]. They identified a list of procedures with strong agreement in the literature that they were AGPs. This list did not include dental procedures and the authors hypothesized that this non-inclusion of dental procedures is because they comprise a wide range of acts some of which are AGPs and others are not [481]. This raises the important point that the dental professions need to identify AGPs versus non-AGPs within dental procedures and this needs to be based on sound principles and science. This is important because it has implications for the use of PPE and other interventions while performing dental procedures.

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f.2. Findings from the second update

We identified limited evidence regarding this topic. Three reviews indicate that wastewater can be a source of infection by SARS-Cov-2 [482] [483] [484], although we identified no study fulfilling our inclusion criteria with recommendations for oral healthcare settings. Even with the paucity of direct evidence, it seems reasonable to highlight the importance of the careful management of water processors and sedimentation tanks in dental offices and laboratories, whose interior should be seen as a potential reservoir of the virus.

Regarding transmission by droplets, particles smaller than 5 µm can move beyond 8 meters and stay suspended for more than 2 hours [446]. Environmental conditions may affect the viability of SARS-Cov-2, with longest lifespan at low temperatures and high humidity.

Two SRs recommend a hierarchy of contamination risk for dental procedures, as follows [485]:

- Higher: Ultrasonic scaler, highspeed air-rotor, air-water syringe, air polishing, extractions using motorized handpieces;
- Moderate: slow-speed handpieces, prophylaxis, extractions;
- Lower: air-water syringe (water only) and hand scaling.

High-risk procedures also include laser surgery and osteotomies, commonly used in oral and maxillofacial surgery [462] [486] [487].

f.3 Findings from the third update

A limited body of evidence refers to AGP in this third update, with most sources focusing on transmissibility itself. Two SRs reinforce the role of sustained speaking and breathing (not only coughing or loud speech) as potential sources of air droplets contributing to airborne transmission of COVID-19 [488] [489]. Saliva itself can be considered as a potential carrier of SARS-CoV-2. A new SR highlighted a sensitivity of 83% for detecting COVID-19 with the saliva of symptomatic patients (compared to 97% and 87% from bronchoalveolar secretion and nasopharygeal swabs, respectively) [490]. Another SR reported good contamination control in a hospital setting providing care for COVID-19 patient with the combination of negative pressure isolation rooms, strict PPE and sterilisation protocols and structured training for care provision [476].

Specific studies on oral health care include a SR comparing high- and low-power lasers, with more aerosol generation with the first [491]. According to the authors, when using high-power lasers in dental offices and laboratories oral health care providers should consider more complex infection control procedures.

As in previous updates, we identified evidence concerning other infectious agents (SARS, MERS, H1N1, influenza and bacteria) resulting in recommendations by authors of these studies of a hierarchy of procedures to use during the pandemic, [492] [455] [454]. These include preferring manual caries excavation and hand scaling rather than high-speed handpieces and ultrasonic scaling, whenever possible.

g. What evidence exists to support transmission mitigation strategies during the provision of in-person oral health care?

g.1. Findings from the first update

As previously mentioned, we identified a systematic review confirming that SARS-Cov-2 is present in saliva and as well as in sputum and the nasopharynx [480]. This is important to consider in the context of this topic concerning mitigating strategies. We also identified several systematic reviews published in the relevant period investigating a number of mitigating strategies during the provision of dental care and other health care procedures. A Cochrane review looked at a range of mitigating strategies including high volume evacuation, dental isolation combination systems, rubber dam and disinfectants, including disinfectant coolants [493]. The authors observed that all the studies included in their review investigated interventions' effects on colony forming units of bacteria, not viruses or respiratory disease transmission. They nevertheless concluded that there was probably benefit in using all the tested interventions but that the evidence to support them was weak [493]. Another Cochrane review investigated the potential protective effect against COVID-19 transmission of health care workers using antimicrobial mouthwashes and/or nasal sprays and identified no studies, although they did note a few relevant on-going randomized trials [494]. Another systematic review investigated the specific question “Does hydrogen peroxide mouthwash (at any concentration) have a virucidal effect?” and identified no research fulfilling their quality criteria addressing this question, thereby concluding that there is no evidence to support the use of hydrogen peroxide mouthwash to control viral load [495]. A rapid systematic review noted the possible beneficial effect of hypertonic saline nasal washes and mouth washes to mechanically reduce viral load and so potentially reduce risk of transmission from patients with COVID-19 to others [496]. Finally, another systematic review investigated the potential benefits of anti-microbial mouthwashes in managing COVID and found no clinical studies, only in vitro evaluations of chlorhexidine, povidone-iodine and C31G. The review noted that all these mouthwashes demonstrated reduced viral load in in vitro studies but recognized the lack of clinical evidence [497].

In summary, there remains no evidence concerning interventions to mitigate viral or COVID-19 transmission during dental treatments but there is good evidence supporting Chlorhexidine mouthwash reducing bacterial load (this was identified in the previous version of this report). Evidence for other interventions is weak and equivocal.

g.2. Findings from the second update

Newer systematic and scoping reviews indicate different methods to mitigate contamination during dental treatment, although evidence could be classified as limited. Two SRs recommend the use of chemomechanical caries removal, extraoral radiographs and hand scalers whenever possible [444].

High-volume evacuators (HVE) have also been recommended as a valid approach to reduce contamination during AGP, although included reviews gathered data from studies about bacterial contamination [444] [447] [466] [498]. The same has been stated for the use of a rubber dam, which is another effective method to reduce airborne particles and thus microbial contamination [445] [466] [447] [498].

Some of the reviews and clinical studies included in this update approach the use of different antimicrobial mouthrinses to reduce contamination in the mouth and pharynx. In general, the pre-procedural use of those mouthrinses is considered a valid method to reduce contamination by aerosols during dental treatment [444] [466] [498] [499], although the real benefit in COVID-19 patients remains unclear [500]. Povidone- iodine (PVP-I) and essential oils (EO) showed efficacy against SARS-CoV-2 in a small RCT (5 participants/mouthwash), when used as a prophylaxis for viral spread. In that trial, participants recruited from a COVID-19 reference center used either substances for 4-6 days (gargling for 30 sec, 3x/day), reaching negative viral load in most cases at 4 days [501]. There is evidence that reinforces the virucidal effect of PVP-I against other respiratory viruses [502], whereas EO, chlorhexidine (CHX) and cetylpyridinium chloride (CPC) mouthrinses are able to reduce airborne bacteria during AGP [498].

A recent RCT displays promising results for CPC-, dipotassium glycyrrhizinate- and tranexamic acid-based mouthrinses used 3x daily for 7 to 10 days before dental implant placement, as methods to reduce airborne bacterial contamination [503]. Finally, a systematic review states that there is no evidence to support whether mouthwashes containing chlorine compounds, including chlorine dioxide and sodium chlorite, can prevent or manage COVID-19 [504].

g.3 Findings from the third update

Evidence concerning methods to mitigate contamination during dental procedures remains limited. Besides some interventions mentioned above (avoiding/minimizing AGPs, including minimal use of high-speed handpieces, air-water syringe and ultrasonic scalers), two SRs enforce the advantage of high-volume evacuators whenever possible [454] [505]. One of those reviews state that the use of rubber dam along with a high-volume evacuator will further reduce the risk of contamination [454].

A few SRs and clinical studies suggest some benefit from mouthrinses before dental procedures. Agents tested against SARS-CoV-2 and with potential advantage include: povidone-iodine, hydrogen peroxide, chlorhexidine digluconate, ColdZyme, cetylpyridinium chloride, and essential oils [506] [507] [508] [509].

h. What evidence exists to support space ventilation strategies that reduce the risk of transmission?

h.1. Findings from the first update

We identified one systematic review published in the relevant period and with pertinent information [493]. This Cochrane systematic review of multiple interventions to reduce aerosols during dental procedures reported one study with only two participants suggesting a stand-alone ventilation system may reduce aerosols during cavity preparation and ultrasonic scaler use [493]. It also reported another study with 50 participants suggesting laminar flow with a HEPA filter may reduce aerosols at 76cm from the floor and 20-30cm from a patient's mouth. However, they stated that no studies reported on viral contamination or disease transmission, rather they concerned bacterial contamination and the evidence was of low certainty [493].

h.2. Findings from the second update

In the period, there were just three SRs and a scoping review about ventilation as a way to reduce COVID-19 transmission. Air purifiers with HEPA filters and room ventilation (30 min) between patients have been recommended as a protocol to reduce the risk of infection, as well as irradiation with UVC [444] [445]. Recommendations for HEPA filters included at least 99.995% retention for particles of 0.01 µm or more [510]. In case of emergency dental treatment of COVID-19-positive patients, the operatory room should be under negative pressure or continuous air exchange [447]. Although the role of air exchange is recommended for any patient [483], the exact degree of protection provided by those approaches is still unclear. Recommended air exchange rates depend on whether the patient is diagnosed with COVID-19, with at least 1.5 and 6.0 air change/hr for negative and positive patients, respectively [510].

h.3 Findings from the third update

Only a single SR [454] and 1 prospective study [511] approached this topic, with limited evidence regarding air cleaning in dental offices. The authors of those studies recommended the following measures to prevent cross-infection by SARS-CoV-2: (i) adequate natural ventilation of the operatory and waiting area, (ii) placing supply-air vents in the waiting area to promote air flow from clean areas into potentially contaminated spaces, (iii) return-air vents in the operatory or waiting room, and (iv) properly directed extractor fans (not towards doors), and fixed-split and portable air conditioning (without recirculation) without incorporated humidifiers [454].

Both references [454] [511] recommend the use of portable high efficiency particulate air (HEPA) filtration units in operating rooms. HEPA units should be adjacent to the patient's chair, but not behind professionals. One of the studies reported complete removal of aerosols in 4 to 12 minutes by combining a HEPA unit with ventilation, whereas the latter alone would take 30 minutes [511].

i. What evidence exists to support the disinfection of surfaces in spaces in which oral health care is provided?

i.1. Findings from the first update

We identified one additional systematic review covering surface disinfection published during this period [512]. This review investigated the use of surface decontamination against SARS-Cov-2 and against airborne pathogens and directly transmitted viral pathogens in dental settings. They found no evidence that fulfilled their quality criteria concerning SARS-Cov-2. However, they reported finding good quality evidence that 70% ethanol and 0.5% sodium hypochlorite used as surface disinfectants reduce the possibility of surface transmission of respiratory viruses. They recommended applying these disinfectants on surfaces for 1 minute to reduce the risk of contamination with SARS-Cov-2 [512].

i.2. Findings from the second update

This second update gathered more SRs about this topic than the previous update. Moderate evidence suggests the disinfection of impressions, trays and dental prostheses with 1% NaOCl for 1 minute as a way to reduce SARS-CoV infectivity [513]. A scoping review reinforces the need for routine disinfection of any dental prosthetic material with intermediate level disinfectants as well as methods to mitigate patients' gag reflex (e.g., proper suction and anaesthesia) [447].

Some reviews gathered limited evidence that certain disinfectants may reduce contamination by bacteria and other respiratory viruses on diverse surfaces, including door handles, chairs, desks and other surfaces that may touched regularly. The most frequent disinfectants studied were 0.1% sodium hypochlorite, 62-70% isopropyl alcohol, 0.5% hydrogen peroxide [444] [445] [514]. Single SRs indicated successful viral inactivation with glutaraldehyde and iodine-containing detergents [514], whereas 0.05-0.2% benzalkonium chloride and 0.02% chlorhexidine digluconate were less able to inactivate various coronaviruses [483]. Finally, irradiation by ultraviolet-C (UV-C) has been stated as an effective method to inactivate pathogenic bacteria [515] and viruses [514]. Most of those agents may be useful against SARS-Cov-2, although this second update could not gather any direct evidence.

It is important to note that Health Canada has lists of surface disinfectants and hand sanitizers that it states are supported by evidence and likely to be effective against SARS-CoV-2. However, since disinfecting agents may damage dental materials and equipment and other surfaces, it is important to review their compatibility before use.

i.3 Findings from the third update

Four SRs provided limited evidence regarding surface disinfecting agents of potential use in oral healthcare environments against SARS-CoV-2 [516] [459] [454] [517]. The virus can survive up to 28 days at room temperature over certain surfaces (i.e., polymer and paper banknotes, vinyl, steel and glass); thus, those surfaces should receive special attention. Dangerous viral loads can remain for up to 21 days on most of those surfaces. This can be mitigated by low temperatures combined to low humidity, and sunlight.

An SR recommended disinfecting surfaces ideally 10 or more minutes after AGPs, as a fallow time to permit the settling of suspended viral particles. It also recommends a combination of 70–80% ethanol (minimum 1-minute exposure time) + 0.5% hydrogen peroxide + freshly prepared 0.1% (1 g/L) sodium hypochlorite, to be used at 2–3-hour intervals [454].

Specific disinfectants successfully tested against SARS-CoV-2 include 1% sodium hypochlorite, which can also be used to flush water lines (2 min between patients and 1L by the end of the day), but not on lithium disilicate restorations (reason: decrease in bonding) [454]. Another SR highlights that combining n-propyl or isopropyl alcohols to detergents may not be a good approach, since they result in more skin irritation than the agents separately [517].

Two SRs also suggested there is some limited evidence to support the previously mentioned usefulness of the following agents/methods against other viruses: vaporized hydrogen peroxide [518], 2% glutaraldehyde, 0.25% peracetic acid, and autoclaving [454].

As with previous updates, we refer readers to Health Canada's website on surface disinfectants and hand sanitizers:

https://www.canada.ca/en/health-canada/services/drugs-health-products/disinfectants/covid-19/list.html#tbl1

Glossary of abbreviations

Abbreviation	Explanation
AGP	Aerosol-generating procedures
CDC	Centers for Disease Control and Prevention
CFU	Colony-Forming Unit
CHX	Chlorhexidine
COVID-19	Coronavirus disease 2019
HVE	High-Volume Evacuation
H1N1	Influenza A
ICU	Intensive Care Unit
IgM	Immunoglobulin M
MERS	Middle East Respiratory Syndrome
PPE	Personal Protective Equipment
RCT	Randomized Controlled Trials
SARS	Severe Acute Respiratory Syndrome
SARS-CoV-2	Severe Acute Respiratory Syndrome Coronavirus-2
SR	Systematic Review
TMD	Temporomandibular disorders
UVGI	Ultra-violet Germicidal Irradiation

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Appendix A: Key findings for topic a) patients at greater risk of the consequences of COVID-19

The following diseases, conditions and groups have strong evidence for risk.

Heart diseases and conditions

Cardiovascular disease (CVD)

Main finding	Source
Higher risk for COVID-19: (i) severity: odds 1.79 to 3.37x greater, RR= 3.00 (ii) mortality: odds 3.15 to 4.85x greater *Severe Heart Disease* (i) mortality: odds 0.67x greater Prevalence: 5% to 16%	SR and meta-analysis: Abate at al. [278]; SR and meta-analysis: Cheng at al. [279]; SR and meta-analysis: Giri et al. [280]; SR and meta-analysis: Hatmi et al. [281]; Meta- analysis: Hoang et al. [282]; SR and meta-analysis: Mirjalili et al. [283]; SR and meta-analysis: Parohan et al. [284]; Meta- analysis: Sinclair et al. [285]; SR and meta-analysis: Szarpak et al.[286]; SR and meta-analysis: Thakur et al. [287]; SR and meta-analysis: Tiruneh et al. [288]; SR and meta-analysis: Toloui et al. [289]; SR and meta-analysis: Wu Y et al. [290]; SR and meta-analysis: Yue-liang et al. [291]

Congestive heart failure

Main finding	Source
Higher risk for COVID-19: (i)severity: 19.07% (ii) mortality: 47.8%, odds 2.70x greater, RR=5.13 Prevalence in patients with COVID-19: 14.4% to 85%	Meta-analysis: Greca et al.[296]; SR and meta-analysis: Lee KH et al. [297]; SR and meta-analysis: Toloui et al.[289]; SR and meta-analysis: Zhao YH et al. [298]

Cardiac arrythmias

Main finding	Source
Higher risk for COVID-19: (i) severity: RR=12.1 (ii) mortality: 40.3%, odds 1.95x greater, RR=3.8 Prevalence in patients with COVID-19: 15.3% to 18%	SR and meta-analysis: Garcia-Zamora et al. [299]; SR and meta-analysis: Lee KH et al. [297]; SR and meta-analysis: Tondas et al. [300]; SR and meta-analysis: Zhao YH et al. [298]

Myocardial injury

Main finding	Source
Higher risk for COVID-19: (i) mortality: 61.7% Prevalence in patients with COVID-19: 21.2%	SR and meta-analysis: Zhao YH et al. [298]

Cardiac injury

Main finding	Source
Higher risk for: (i) severe COVID-19: RR: 1.80 (ii) mortality: odds 6.87x greater	SR and Meta-analysis: Dy et al. [301]; SR and meta-analysis: Kim et al. [293]

ST- Segment Elevation Myocardial Infarction (STEMI)

Main finding	Source
Patients with ST-Segment Elevation Myocardial Infarction (STEMI): mortality 1.17 to 1.52x greater	SR and meta-analysis: Chew et al. [302]; SR and meta-analysis: Rattka et al.[303]

Acute cardiac injury

Main finding	Source

Higher risk for COVID-19: (i) severity: 19.46%, odds 3.48x greater (ii) mortality: odds 25.16x greater, RR= 6.91 Prevalence in patients with COVID-19: 1% to 6.4%	SR and meta-analysis: Goel at al. [304]; SR and meta-analysis: Tiruneh et al. [288]; SR and meta-analysis: Toloui et al. [289]; SR and meta-analysis: Wu Y et al. [290]; SR and meta-analysis: Zhao YH et al. [298]

Coronary heart disease

Main finding	Source
Higher risk for COVID-19: (i) severity: odds 2.87x greater (ii) mortality: odds 2.70x greater	SR and meta-analysis: Lee KH et al. [297]; SR and meta-analysis: Li X et al. [295]

Cardiac arrest

Main finding	Source
Higher risk for COVID-19: (i) mortality: 89.9% (ii) compared with non-infected COVID-19: odds 2.34x greater	SR and meta-analysis: Ippolito et al. [305]

Ventricular dysfunction

Main finding	Source
Higher risk for COVID-19: (i) mortality: 48.5% vs 27.4% in patients with or without right ventricular dysfunction (odds 3.10x greater) (ii) mortality: 56.3% vs 30.6% in patients with or without ventricular dilatation (odds 2.43x greater) (iii) mortality: 52.9% vs 14.8% in patients with or without right ventricular dysfunction (odds 5.75x greater)	SR and meta-analysis: Ippolito et al. [305]; SR and meta-analysis: Paternoster et al.[306]

Hypertension

Main finding	Source
Higher risk for COVID-19: (i) severity: 35.9%, odds 1.98 to 3.11x greater, RR= 1.70 to 2.02 (ii) ICU admission: 15% (iii) mortality: odds 2.67 to 3.67x greater Prevalence: 15% to 32.2%	SR and meta-analysis: Abate et al. [278]; SR and meta-analysis: Cheng at al. [279]; SR and meta-analysis: Du et al. [292]; SR and meta-analysis: Giri et al. [280]; SR and meta-analysis: Hatmi et al. [281]; Meta- analysis: Hoang et al. [282]; SR and meta-analysis: Kim et al. [293]; SR and meta-analysis: Li J et al.[294]; SR and meta-analysis: Li X et al. [295]; SR and meta-analysis: Mirjalili et al.[283]; SR and meta-analysis: Parohan et al. [284]; Meta- analysis: Sinclair et al. [285];

	SR and meta-analysis: Thakur et al.[287]; SR and meta-analysis: Wu Y et al. [290]; SR and meta-analysis: Yue-liang et al. [291]

Respiratory diseases and conditions

Respiratory disease (general)

Main finding	Source
Higher risk for COVID-19: (i) severity: odds 1.98 to 5.67x greater; RR=1.55 (ii) mortality: odds 3.72x greater Prevalence in patients with COVID-19: 7% to 34%	Meta-analysis:SR and meta-analysis: Cheng at al. [279]; SR and meta-analysis: Du et al. [292]; SR and meta-analysis: Goel at al.[304]; SR and meta-analysis: Hatmi et al. [281]; SR and meta-analysis: Khateri et al. [22]; SR and meta-analysis: Kim et al. [293]

Respiratory disease (Asthma)

Main finding	Source
Higher risk for COVID-19: (i) poor outcomes: odds 0.92x greater (ii)severity: 2.3% vs 2.2% for non-severe patients (odds 1.04 to 1.13x greater)	SR and meta-analysis: Alkhatami et al. [307]; SR and meta-analysis: Gulsen et al. [308]; SR and meta-analysis: Kaur A et al. [309]; SR and meta-analysis: Reyes et al.[310]; SR and meta-analysis: Soreoto

(iii) mortality: odds 0.87 to 0.96x greater (v) incidence of asthma with age in COVID-19 patients: odds 0.77x greater Prevalence in patients with COVID-19: 3%, odds 0.08x	et al.[311]; SR and meta-analysis: Wu T et al. [312]

Chronic obstructive pulmonary disease (COPD)

Main finding	Source
Higher risk for: (i) severe COVID-19 (risk difference: odds 2.88x to 8.35x greater, RR= 3.63 to 4.22 (ii) severity: 5.2% vs 1.4% for non-severe patients (odds 2.58x greater) (iii) ICU admission (odds 1.35x greater) (iv) COVID-19 mortality: 30% (odds 2.29 to 3.55x greater, RR= 3.18) (v) mortality associated with males: RR= 1.20 Prevalence in patients with COVID-19: 2.2%	SR and meta-analysis: Alkhatami et al. [307]; SR and meta-analysis: Gerayeli et al. [313]; SR and meta-analysis: Goel at al. [304]; SR and meta-analysis: Gulsen at al.[308]; Meta- analysis: Hoang et al. [282]; SR and meta-analysis: Lee KH et al. [297]; SR and meta-analysis: Li X et al. [295]; SR and meta-analysis: Parohan et al.[284]; SR and meta-analysis: Rabbani et al.[314]; SR and meta-analysis: Reyes et al. [310]; Meta- analysis: Sinclair et al.[285]; SR and meta-analysis: Wu Y et al. [290]; SR and meta-analysis: Yue-liang et al.[291]

Acute respiratory distress syndrome (ARDS)

Main finding	Source
Higher risk for COVID-19: (i) severity: 26% to %; odds: 39.59x to 42.69x greater (ii) mechanical ventilation: MDM:-7.0 (iii) ICU admission: MDM: 3.1 (iv) mortality: odds 1.25 to 62.85x greater, RR =7.99 Prevalence in patients with COVID-19: % to 30.93%	SR and meta-analysis: Abate et al. [278]; SR and meta-analysis: Dmytriw et al. [315];SR and meta-analysis: Giri et al. [280]; SR and meta-analysis: Hatmi et al. [281]; SR and meta-analysis: Khateri et al. [22]; SR and meta-analysis: Li X et al.[295]; SR and meta-analysis: Tiruneh et al.[288]; SR and meta-analysis: Wu Y et al. [290]

Diabetes mellitus

Main finding	Source
Higher risk for COVID-19: (i) severity: 10.8% to 48%, odds 1.60 to 3.39x greater, RR= 1.54 to 2.10 (ii) mortality: 82%, odds 0.54 to 2.60x greater, RR= 1.3	SR and meta-analysis: Abate et al. [278]; SR and meta-analysis: Saha et al. [319]; SR and meta-analysis: Chamorro-Pareja et al. [320]; SR and meta-analysis: Cheng at al. [279]; SR and meta-analysis: Du et al. [292]; SR and

Comparing diabetic vs non-diabetic patients: (i) severity: 34.8% vs 22.8% (odds 1.43x greater) (ii) mortality: 20% to 21.3% vs 6.1% to 11% (odds 1.82 to 2.3x greater) (iii) ARDS as complication: 34.4% vs 17.2% (odds 2.38x greater) (iv) Acute Cardiac Injury as complication: 22% vs 12.8% (odds 2.59x greater) (v) AKI as complication: 19.1% vs 10.2% (odds 1.97x greater) COVID-19 is associated with diabetic ketoacidosis (DKA), hyperglycaemic hyperosmolar state (HHS) and euglycemic DKA (EDKA) Prevalence of mortality among diabetic patients in: (i) Europe: 28% (ii) United States: 20% (iii) Asia: 17% High to moderate certainty of evidence for associations among diabetes and COVID-19:	meta-analysis: Giri et al. [280]; SR and meta-analysis: Hatmi et al. [281]; SR and meta-analysis: Hewitt et al. [321]; Meta- analysis: Hoang et al. [282]; SR and meta-analysis: Kaminska et al. [322]; SR and meta-analysis: Kim et al. [293]; SR and meta-analysis: Lazarus et al. [323]; SR and meta-analysis: Li J et al. [294]; SR and meta-analysis: Li X et al. [295]; SR and meta-analysis: Li Y et al. [324]; SR and meta-analysis: Lontchi-Yimagou et al. [325]; SR and meta-analysis: Mirjalili et al.[283]; SR and meta-analysis: Palaiodimos et al.[326]; SR and meta-analysis: Papadopoulus et al. [327]; SR and meta-analysis: Parohan et al. [284]; SR and meta-analysis: Saha et al. [319]; SR and meta-analysis: Schlesinger et al. [328]; Meta- analysis: Sinclair et al. [285]; SR and meta-analysis: Thakur et al. [287]; SR and meta-analysis: Varikasuvu et al. [329]; SR and meta-analysis: Wu Y et al. [290]; SR and meta-analysis: Yue-liang et al. [291]; SR and meta-analysis: Zhang L et al. [330]

(i) between male sex (odds 1.28x greater) (ii) older age (>65 years) (odds 3.49x greater) (iii) pre-existing comorbidities: - cardiovascular disease (odds 1.56x greater) - CKD (odds 1.28x greater) - COPD (odds 1.40x greater) Prevalence in patients with COVID-19: 9.55% to 48%	

Cancer

Main finding	Source
Higher risk infection in patients with COVID-19 with different types of cancer: (i) lung cancer:2.1% Higher risk for COVID-19: (i) severity: 16%, odds 1.48 to 2.73x greater, RR=1.64 to 2.91 (ii) mortality: 1% to 41%, odds 0.20 to 3.54x greater (iii) mortality of patients > 60 years with cancer and COVID-19:	SR and meta-analysis: Alkhatami et al. [307]; SR and meta-analysis: Lei et al. [331]; SR and meta-analysis: Kamal et al. [332]; SR and meta-analysis: Belsky et al. [333]; SR and meta-analysis: Giri et al. [280]; SR and meta-analysis: Goel at al. [304]; Meta- analysis: Hoang et al. [282]; SR and meta-analysis: Kaur H et al.[334] ; SR and meta-analysis: Kim et al.[293]; SR and meta-analysis: Kong et al. [335]; SR and meta-analysis:

(iv) mortality of patients with comorbidities, cancer and COVID-19: - Hypertension: odds 1.6x greater - Cardiovascular diseases: odds 2.2x greater - COPD: odds 11.4x greater (v) mortality lung cancer: 18% to 60%, odds 1.47 to 1.8x greater (viii) mortality in patients with active chemotherapy: odds x greater (ix) mortality hematological cancer: 37.48% (x) mortality breast cancer: 14.2% Prevalence in patients with COVID-19: odds 0.07x -in Europe: odds 0.22x greater -in Asia-Pacific: odds 0.04x greater -in North America: odds 0.05x greater - patients > 60 years with cancer and COVID-19: odds 0.10x greater	Lei et al.[331]; SR and meta-analysis: Liu GE et al. [336]; SR and meta-analysis: Parohan et al. [284]; SR and meta-analysis: Tagliamento et al. [337]; SR and meta-analysis: Venkatesulu et al. [338]; SR and meta-analysis: Yue-liang et al.[291]; SR and meta-analysis: Zhang L et al. [330]

- patients ≤60 years with cancer and COVID-19: odds 0.05x greater	

Cerebrovascular diseases and conditions

Cerebrovascular diseases (general)

Main finding	Source
Higher risk for COVID-19: (i) severity: odds 2.47 to 3.92x greater, RR= 2.12 to 2.86 Prevalence in patients with COVID-19: 43%	SR and meta-analysis: Cheng at al.[279]; Meta- analysis: Hoang et al. [282]; SR and meta-analysis: Kim et al. [293]; SR and meta-analysis: Li X et al.[295]; SR and meta-analysis: Thakur et al. [287]; SR and meta-analysis: Yue-liang et al. [291]

Nervous system diseases and conditions

Dementia

Main finding	Source
Higher risk for COVID-19: (i) poor outcomes: in elderly adults with COVID-19 (odds 2.96x greater) (ii) mortality in elderly patients with hip fracture: RR=1.13	SR and meta-analysis: Alcock et al. [339]; SR and meta-analysis: Saragih et al. [340]

(iii) mortality rates of dementia vs non-dementia elderly adults with COVID-19: 39% vs 20%	

Chronic kidney diseases (CKD)

CKD (general)

Main finding	Source
Higher risk for COVID-19: (i) severity: odds 1.27 to 4.24x greater, RR= 1.76 to 2.00 (ii) hospitalization: odds 4.29x greater (iii) mortality: 19.18%, odds 0.55 to 5.58x greater Prevalence in patients with COVID-19: 4.5% to 9.7%	SR and meta-analysis: Du et al. [292]; SR and meta-analysis: Goel at al. [304]; Meta- analysis: Hoang et al. [282]; SR and meta-analysis: Kim et al. [293]; SR and meta-analysis: Li X et al. [295]; SR and meta-analysis: Li Y et al. [324]; SR and meta-analysis: Lin YC et al. [343]; SR and meta-analysis: Menon et al. [344]; SR and meta-analysis: Mirjalili et al.[283]; SR and meta-analysis: Singh Jet al [345]; SR and meta-analysis: Thakur et al. [287]; SR and meta-analysis: Yue-liang et al. [291]

Acute kidney disease (AKI)

Main finding	Source

Higher risk for COVID-19: (i) severity: 20%, odds 8.28 to 16.013x greater (ii) hospitalization: 10% (iii)mortality: odds 13.52 to 22.86x greater Prevalence in patients with COVID-19: 7% to 12.78%	SR and meta-analysis: Goel at al. [304]; SR and meta-analysis: Hatmi et al. [281]; SR and meta-analysis: Khateri et al. [22]; SR and meta-analysis: Li X et al. [295]; SR and meta-analysis: Menon et al.[346]; SR and meta-analysis: Nasiri et al. [347]; SR and meta-analysis: Singh J et al.[345] ; SR and meta-analysis: Tiruneh et al. [288]; SR and meta-analysis: Wu Y et al. [290]; SR and meta-analysis: Xu et al. [348]

Smoking

Main finding	Source
Higher risk to severe COVID-19: - current smokers: odds 0.74 to 1.40x greater, RR= 1.23 - Compared to never-smokers, patients with a smoking history: odds 1.53x greater - Underlying Cardiovascular Disease: 9.7%, odds 2.87x greater	SR and meta-analysis: Abate et al.[278]; SR and meta-analysis: Goel at al. [304]; SR and meta-analysis: Hatmi et al. [281]; SR and meta-analysis: Hewitt et al. [321]; SR and meta-analysis: Hou et al. [351]; SR and meta-analysis: Kang et al. [352]; SR and meta-analysis: Kim et al. [293]; SR and meta-analysis: Lee KH et al. [297]; SR and meta-analysis: Li X et al. [295];

Higher risk to ICU admission: 24% Higher risk to COVID-19 mortality: - current smokers: 43%, odds 1.79x greater, RR= 1.19 to 2.19 - previous smoking history (ex-smoking): odds 1.91x greater - compared to former smokers, current smokers' patients: increased mortality COVID-19 (RR= 2.19) - median age: 77 years - female: 48% Prevalence in patients with COVID-19: 9% to 14%	SR and meta-analysis: Yue-liang et al.[291]

Obesity

Main finding	Source
Higher risk for COVID-19: (i) poor outcome or hospitalization: odds 1.51 to 1.73x greater (ii) severity: odds 1.31 to 3.03x greater	SR and meta-analysis: Bansal et al. [353]; SR and meta-analysis: Chowdhury et al. [354]; Meta- Analysis: Das et al. [355]; SR and meta-analysis: Foldi et al. [356]; SR and meta-analysis: Helvaci et al. [357];

(iii) severity: associated with visceral fat area (odds 1.9x greater) (iv)severity when associated with comorbidities: odds 1.56x greater (iii) ICU admission: odds 1.35 to 2.81x greater; SMD 0.46 (iv) invasive mechanical ventilation: SMD 0.38; odds 1.77x greater (v) in younger patients: odds 3x greater (vi) associated to ARDS: odds 2.89x greater Higher risk for COVID-19 mortality: (i) odds: 0.96 to 3.52x greater Prevalence in patients with COVID-19: 25%	SR and meta-analysis: Li X et al. [295]; SR and meta-analysis: Li Y et al. [324]; SR and meta-analysis: Pranata et al. [358]; Meta-analysis: Pranata et al. [359]; SR and meta-analysis: Seidu et al.[360]; SR and meta-analysis: Thakur et al. [287]; SR and meta-analysis: Zhang X et al. [361]

Liver diseases and conditions

Liver diseases (general)

Main finding	Source

Higher risk for COVID-19: (i) severity: 32%; odds 1.02x greater, RR=1.84. *Metabolic dysfunction-associated fatty liver disease* Higher chance for COVID-19: (i) severity: 28% *Non-alcoholic fatty liver disease* (i) severity: 36%, odds 2.60x greater (ii) ICU admission: 24%, odds 1.66x greater (iii)mortality: odds 1.01x greater	SR and meta-analysis: Abate et al. [278]; SR and meta-analysis: Goel et al. [304]; SR and meta-analysis: Hegyi et al. [349]; SR and meta-analysis: Kim et al. [293]; SR and meta-analysis: Singh A et al. [350]

Acute liver diseases

Main finding	Source
Prevalence in patients with COVID-19: 19% to 22.8%	SR and meta-analysis: Khateri et al. [22]; SR and meta-analysis: Tiruneh et al. [288]

Effect of age

Main finding	Source

Prevalence of COVID-19: (i) <20 years: 20% lower than that of working age adults (20-64 years) RR=0.77 (ii)20 years: 2.1% (iii)20 – 49 years: 5.8% (iv)50-64 years: 5.2% (v) ≥65 years: 2.6% (vi) ≥65 years: lower than that of working age adults (20-64 years) RR=0.76 (vii) Among aged care residents: 45% High risk for severe COVID-19: (i) age>=60 years (51%, odds 2.62 to 5.73x greater) (ii) age ≥65 vs <65 years old (odds 4.59x greater) Associated to: - diabetes: 22.95% - hypertension: 48.95% - cardiovascular diseases: 19.95% High risk for severe COVID-19 (ICU admissions): (i) age ≥60 years: 22%	SR and meta-analysis: Alcock et al. [339]; SR and meta-analysis: Du et al. [292]; SR and meta-analysis: Dumitrascu et al. [362]; SR and meta-analysis: Goel at al. [304]; SR and meta-analysis: Chen X et al. [363]; SR and meta-analysis: Hashan et al.[364]; SR and meta-analysis: Kim et al. [293]; SR and meta-analysis: Lee KH et al. [297]; SR and meta-analysis: Li J et al. [294]; SR and meta-analysis: Li Y et al. [324]; SR and meta-analysis: Parohan et al. [284]; SR and meta-analysis: Singhal et al. [365]; SR and meta-analysis: Tiruneh et al. [288]; SR and meta-analysis: Wu Y et al. [290]; SR and meta-analysis: Yue-liang et al. [291] , ,

(ii) Among aged care residents: 37% High risk for COVID-19 mortality: (i) age ≥60 years: 11%, odds 6.00x greater, MD= 13.32 (ii) age ≥60 years with hip fracture: 34% (9% in non-infected patients), RR=4.42 for early mortality (iii) age ≥70 years: 86.6%, odds 3.61x greater (iv) age >= 70 and < 70 years with CKD and COVID-19 (odds 8.69x greater) than in the >= 70 years (odds 2.44x) (v) age >= 80 years: 84.4% (vi) advanced age + frailty: odds 1.79x greater (vii) Among aged care residents: 23% (viii) older age: odds 1.05x greater	

Effect of sex

Main finding	Source
High risk for severe COVID-19:	SR and meta-analysis: Abate et al.[278]; SR and meta-analysis:

(i) male: 58.1% to 65.09%, odds 1.31 to 1.51x greater; RR 1.02 to 1.26 (ii)male vs. female: 7% vs. 6.6%, odds 1.50x High risk for COVID-19 mortality: (i) male: 37% (odds 1.54 to 1.72x greater, RR= 1.67) (ii) female: odds 0.97x greater	Du at al. [292]; SR and meta-analysis: Goel at al. [304]; SR and meta-analysis: Chen X et al.[363]; SR and meta-analysis: Zaki et al. [458]; SR and meta-analysis: Kim et al.[293]; SR and meta-analysis: Lee KH et al. [297]; SR and meta-analysis: Li J et al.[294]; SR and meta-analysis: Li X et al. [295]; SR and meta-analysis: Li Y et al. [324]; SR and meta-analysis: Parohan et al. [284]; Meta-analysis: Sinclair et al. [285]; SR and meta-analysis: Wu Y et al. [290]; SR and meta-analysis: Yue-liang et al.[291]; SR and meta-analysis: Zhang L et al. [330]

Effect of race

Main finding	Source
Prevalence of COVID-19: - Black: RR 2.70 - Asian: RR 1.91, odds 0.06x greater -non-Hispanic white: odds 0.30x greater -Hispanic: odds 0.27x greater	SR and meta-analysis: Chen X et al.[363];SR and meta-analysis: Hewitt et al. [321]; SR and meta-analysis: Kim et al. [293]

-non-Hispanic black: 0.15x greater - others or unknown: odds 0.21x greater - White: lower risk of infection compared with Black and Asian people. - Compared with non-Hispanic white, Hispanic ethnicity was associated with a lower risk of the critical outcome (RR= 0.83). - Compared with non-Hispanic white, non-Hispanic black was not associated with a lower risk of the critical outcome (RR= 0.84). - Compared with non-Hispanic white, Asian ethnicity was not associated with a lower risk of the critical outcome (RR= 1.33). Higher risk for COVID-19: (i) mortality: Non-Caucasian ethnicity RR=1.67	

Arterial thrombosis/coagulopathies

Main finding	Source
Higher risk for COVID-19: (i)mortality: odds 2.39x greater (ii) mortality: hypercoagulability (23.1%)	SR and meta-analysis: Gabbai-Armelin et al. [366]; Meta-analysis: Greca et al. [296]; Meta-analysis: Mitra et al.

(iii) thrombotic events + comorbidities: 85% (iv) thrombotic events + Elevated D-dimer: 70% (v) thrombotic events + Cardiovascular complications: 100% (vi) Platelet count and D-dimer level were significant predictors of disease severity and older men had higher risks of severe coagulopathic disease (vii) *Disseminated intravascular coagulation* - Prevalence: 3% - Mortality: odds 2.46x greater Prevalence in patients with COVID-19: 22%	[367]; Meta-analysis: Moonla et al.[368]; SR and meta-analysis: Xiong et al. [369]; SR and meta-analysis: Zhou X et al. [370]

Venous thromboembolism (VTE), vein thrombosis (DVT) and/or pulmonary embolism (PE)

Main finding	Source
Prevalence in patients with COVID-19: - VTE: 18% to 26% - DVT: 14% to 15.43% - PE: 4.85% to 11% - PE with or without DVT: 12%	Meta- analysis: Birocchi et al. [371]; SR and meta-analysis: Gratz et al.[372]; SR and meta-analysis: Porfidia et al. [217]; SR and meta-analysis: Ng et al. [373]; SR and meta-analysis: Sarfraz et al. [374]

Higher risk for COVID-19, ICU admission: - VTE: 24% - DVT: 7% - PE: 19%	

HIV

Main finding	Source
Higher risk for COVID-19: (i) severity: 2.5%, RR= 1.24 (ii) hospitalization: 28.4% (iii) ICU admission: 3.5% (iv)mortality: 5.3% to 14.1%, odds 1.19x greater, RR= 1.78 (v) HIV + COVID+ hypertension: 24% (vi) HIV + COVID+ diabetes: RR= 0.96 (v) HIV + COVID+ chronic cardiac disease: RR= 5.2 (v) HIV + COVID+ CKD: RR= 8.43 Prevalence in patients with COVID-19: 0.9% to 1.2% - United States: 1.43% - Spain: 0.26% - China: 0.99%	SR and meta-analysis: Haryanto et al.[382]; SR and meta-analysis: Lee et al. [383]; SR and meta-analysis: Liang et al. [384]; SR and meta-analysis: Ssetongo et al.[385]; SR and meta-analysis: Ssetongo 2 et al.[386]

Vitamin D insufficiency

Main finding	Source
Higher risk for COVID-19: (i) severe: odds 1.75 to 2.57x greater, RR= 2.00 (ii) ICU admission: odds 0.36x greater (iii)mortality: odds 1.05 to 3.08x greater, RR= 2.45 (iv) mortality in male gender: odds 0.93 to 1.22x greater (v) mortality in diabetic patients: odds 0.88x greater (vi) not statistically significant when reviewed 31 studies (8209 patients). (vii) individuals with Vitamin-D deficiency were 80% more likely to acquire COVID-19 infection as compared to those who have sufficient Vitamin D levels (odds 1.80x greater)	SR and meta-analysis: Akbar et al. [392]; SR and meta-analysis: Bassatne et al.[393];SR and meta-analysis: Kazemi et al.[394]; SR and meta-analysis: Oscanoa et al. [395]; SR and meta-analysis: Shah et al.[396]; SR and meta-analysis: Teshome et al. [397]

Frailty patients

Main finding	Source
Impact of clinical frailty scale (CFS) sub-categories (1-3, 4-5 and 6-9), by increasing severity of frailty and to	SR and meta-analysis: Kastora et al. [387]; SR and meta-analysis: Yang et al.[388]; SR and meta-analysis: Zhang XM et

identify factors associated with increased mortality from COVID-19: - CFS 4- 5 patient group had significantly increased mortality when compared to patients with CFS 1-3 (odds 1.95x greater) - CFS 6- 9 patient group had mortality increase when compared to patients with CFS 1-3 (odds 3.09x greater) - male gender, Ischaemic Heart Disease, Hypertension and Chronic Kidney Disease were associated with increased COVID-19 mortality. - Frailty was significantly associated with increased risk of all-cause mortality among patients with COVID-19 (odds 1.81x greater) - Prevalence frailty + COVID-19: 51% - Severity: odds 691.76x greater - Hospitalization: odds 2.62x greater - Mortality: odds 1.99x greater - Most common: • Age 60-70 years (odds 1.85x greater) • Age ≥70 years (8.45x greater)	al. [389]; SR and meta-analysis: Zhao J et al. [390] l

• Male (odds 1.88x greater) • Occupation of retirees (odds 4.27x greater)	

Pregnant women

Main finding	Source
Higher risk for severe COVID-19: (i) ICU admission: 6.9% Higher risk for COVID-19 pregnant mortality: (i) 1.3%, odds 1.37x greater (ii) obesity: RR 2.48 (iii) gestational diabetes: RR 5.71 (iv) asthma: RR 2.05 Compared with mild COVID-19, severe COVID-19 was strongly associated with: (i)preeclampsia: odds 4.16x greater) (ii) preterm birth: odds 4.29x greater (iii) gestational diabetes: odds 1.99x greater	SR and meta-analysis: Chmielewska et al. [400]; SR and meta-analysis: Hatmi et al. [281]; SR and meta-analysis: Karimi et al. [401]; SR and meta-analysis: La Verde et al. [402]; SR and meta-analysis: Li J et al. [294]; SR and meta-analysis: Wei et al. [403]

(iv) low birth weight: odds 1.89x greater Pre-existing maternal comorbidity, higher risk for: (i) admission to ICU: RR= 5.09 (ii) invasive ventilation: RR= 4.34 (iii) mortality: RR= 2.26 Delivery in pregnant women with covid-19: (i) spontaneous preterm birth: 26.8% to 52.45%, odds 1.82x greater (ii) stillbirth: odds 1.28 to 2.11x greater (iii) preeclampsia: 6.2%, odds 1.33x greater (iv) caesarean section: 58.3% to 86.66% (v) vaginal delivery: 25% (vi)fetal death: 4.6% to 7% (vii) abortion: 16.7% (viii) post-partum hemorrhage: 39.1% (ix) premature rupture membrane: 20.7% (x) fetal growth retardation: 11.7% (xi) obstetric complications: 51.7%	

Pregnant women vs non-pregnant women (i) Pregnant women with COVID-19 were less likely to be obese (RR= 0.68) (ii) Pregnant women with COVID-19 were less likely to have a smoking history (RR= 0.32) (iii) non-pregnant women with COVID-19- had a higher frequency of comorbidity compared to COVID-19-infected pregnant women: -chronic cardiac disease (RR= 0.58) - renal disease (RR= 0.45) - malignancy (RR= 0.82). (iv) pregnant women were significantly higher risk for: - ICU admission (RR= 2.26) - invasive mechanical ventilation (RR= 2.68)	SR and meta-analysis: Khan et al.[519]

The following diseases, conditions and groups have limited to moderate evidence for risk.

Obstructive Sleep Apnea

Main finding	Source
Higher risk for COVID-19: (i) poor outcome: odds 1.72x greater	SR and meta-analysis: Haryanto et al. [316]

(ii) severity: odds: 1.70x greater (ii) mechanical ventilation: odds 1.67x greater (iii) ICU admission: odds 1.76x greater (iv) mortality: odds 1.74x greater	

Pulmonary Aspergillosis

Main finding	Source
Higher risk for COVID-19: (i) ICU admission: 54.9% (ii) mortality: 10.2% to 51.2%, odds 2.83x greater	SR and meta-analysis: Mitaka et al. [317];SR and meta-analysis: Singh S et al. [318]

Effect of Demographic Region

Main finding	Source
Seroprevalence in the general population: Higher risk for COVID-19: - South- East Asia (India): 19.6% - Asia: RR= 1.42 - Africa: 16.3% - Eastern Mediterranean: 13.4%	SR and meta-analysis: Chen X et al.[363]; SR and meta-analysis: Kim et al.[293]

- Americas: 6.8% -North America: RR= 1.23 - Europe: 4.7%, RR= 1.19 - Western Pacific: 1.7%	

Mental Disorders

Main finding	Source
COVID-19 patients suffered from: (i) Mood disorders: 43.1% (ii) Schizophrenia, schizotypal and delusional disorders: 16.1% Higher risk for COVID-19: (i) poor outcomes: in elderly adults with COVID-19) (ii)severity: odds 1.76x greater (iii) mortality: odds 1.52x greater (iv)mortality: - Mood disorders: 15.9% - Schizophrenia, schizotypal and delusional disorders: 22.3% Among COVID-19 patients with mental disorders + comorbidities:	SR and meta-analysis: Toubasi et al. [341]

(i)diabetes: 24.5% (ii)hypertension: 35.4% (iii)CVD: 11.5% (iv)cerebrovascular disease: 9.1% (v) CKD: 9.6%	

Guillain- Barre Syndrome (GBS)

Main finding	Source
(i) Compared with non-infected contemporary or historical controls, patients with SARS-CoV-2 infection (odds 3.27x greater) (ii) In SARS-CoV-2-infected patients, olfactory nerve involvement: 41.4% (iii) In SARS-CoV-2-infected patients, olfactory or concomitant cranial nerve involvement: 42.8% Prevalence in patients with COVID-19: 0.15%, 15 cases per 100,000 SARS-CoV-2 infections	SR and meta-analysis: Palaiodimu et al. [342]

Use of non-steroidal anti-inflammatory drugs (NSAIDs)

Main finding	Source
(i) No difference in the hazard for the development of a fatal course of COVID-19 between NSAID users	SR and meta-analysis: Kow et al. [391]

and non-NSAID users (odds 0.73 to 0.86x greater)	

Dyslipidemia

Main finding	Source
Higher risk for: (i) mortality: 60%, odds 1.69x greater Prevalence in COVID-19 patients: 17.5%	SR and meta-analysis: Zuin et al.[375]

Multiple Sclerosis

Main finding	Source
Higher risk for: (i) severe COVID-19: odds x greater (ii) hospitalization: 20.7% (iii) ICU admission: odds x greater (iv) mortality: 3%	SR and meta-analysis: Barzegar et al.[377]

Parkinson’s disease

Main finding	Source
Higher risk for: (i) poor outcomes: odds 2.64x greater	SR and meta-analysis: Putri et al.[378]

(ii) severe COVID-19: odds 2.61x greater (iii) mortality: RR= 2.63	

Femoral fractures

Main finding	Source
Higher risk for: (i) severe COVID-19: odds x greater (ii)mortality: among patients with and without COVID-19 (odds 6.31x greater) (iii) mortality: surgically treated patients with COVID-19 (odds 5.99x greater) (iv) mortality: among patients with hip fracture (34.74%, RR= 4.59) (v) mortality: among patients with hip fracture 30-day (38%)	SR and meta-analysis: Patralekh et al.[379]; Meta-analysis: Raheman et al.[380]

Immunosuppressed patients

Main finding	Source
Higher risk for COVID-19: (i) severity: 16% (ii) ICU admission: 8% (iii) mortality: 2%	SR and meta-analysis: Belsky et al.[333]; SR and meta-analysis: Zhang L et al. [330]

Rheumatic diseases

Main finding	Source
Higher risk for COVID-19: (i) severity: odds 1.53x greater (ii) hospitalization: 1.36x greater (iii)ICU admission: odds 1.94x greater (iii) mortality: odds 1.29x greater	SR and meta-analysis: Wang Q et al. [381]

Hemoglobinopathies

Main finding	Source
Higher risk for COVID-19: (i) mortality: odds 1.07x greater Prevalence in patients with COVID-19: odds 4.4x	SR and meta-analysis: Haghpanah et al.[376]

Micronutrient deficiency

Main finding	Source
Higher risk for COVID-19: (i) ICU admission: odds 0.26x greater Incidence among COVID-19 patients: odds 0.37x	SR and meta-analysis: Wang MX et al.[398]

COVID-19 recurrence

Main finding	Source
Of 3,644 patients recovering from COVID-19 and being discharged: -15% patients were re-positive with SARS-CoV-2 during the follow-up. - Among recurrence cases, it was estimated 39% subjects underlying at least one comorbidity.	SR and meta-analysis: Hoang et al.[399]

Neonates

Main finding	Source
Higher risk for neonates born to mothers with covid-19: (i) admitted to the neonatal unit (67.06%) (ii) low birth weight: 42.8%	SR and meta-analysis: Hatmi et al.[281]

Children

Main finding	Source
Higher risk for COVID-19: (i) ICU admission: 8.1% (ii) mechanical ventilation: 5.99% (iii) mortality: 3.8% (iv) mean age: 4.6 years (v) 50.3% males	SR and meta-analysis: Li J et al. [294]

Pediatric patients with cancer and COVID-19: - risk of severity: 24% - risk of mortality: 9% Pediatric patients with comorbidities and COVID-19: Higher risk for: (i) severity: 5.1% (ii) severity in obese: RR=2.87 (iii) mortality: RR=2.81	SR and meta-analysis: Belsky et al.[333]

General considerations

Main finding	Source
COVID-19 mortality rates (general): -14% to 17.1% -for general patients admitted to the hospital (excluding critical care): 11.5% -for patients with critical illness: 40.5%	SR and meta-analysis: Macedo et al. [520]; SR and meta-analysis: Wu Y et al. [290]

Appendix B: Key findings for topic b) clinical signs and symptoms of COVID-19

The following signs, symptoms, groups and situations have strong evidence for risk.

Fever

Main finding	Source
High risk for COVID-19: (i) severity: odds 0.79 to 1.96x greater (ii) patients with Multiple Sclerosis: 69.8% (iii) associated with chills: 14.45% (iv) HIV patients: 71.1% (v) elderly patients: 83.95% Prevalence of: - Medium grade fever: 44.33% - Low grade fever: 38.16% - High grade fever: 14.71% Prevalence in patients with COVID-19: 78.1% to 92%	SR and meta-analysis: Giri et al. [280]; SR and meta-analysis: Barzegar et al. [377]; SR and meta-analysis: Hatmi et al. [281]; SR and meta-analysis: Islam et al. [423]; SR and meta-analysis: Amiri et al. [424]; SR and meta-analysis: Kim et al.[293]; SR and meta-analysis: Lee KH et al.[297]; SR and meta-analysis: Li J et al. [294]; SR and meta-analysis: Singhal et al. [365]; SR and meta-analysis: Vakili et al.[425]; SR and meta-analysis: Yue-liang et al. [291]

Cough

Main finding	Source
High risk for COVID-19: (i) severity: odds 0.65 to 1.45x greater (ii) patients with Multiple Sclerosis: 63.9% (iii)elderly patients: 60.95%	SR and meta-analysis: Cares-Marambio et al. [521]; SR and meta-analysis: Giri et al. [280]; SR and meta-analysis: Barzegar et al. [377]; SR and meta-analysis: Hatmi et al. [281]; SR and meta-analysis:

Prevalence in patients with COVID-19: 14% to 73%	Amiri et al. [424]; SR and meta-analysis: Kim et al.[293]; SR and meta-analysis: Li J et al. [294]; SR and meta-analysis: Singhal et al. [365]; SR and meta-analysis: Vakili et al. [425]; SR and meta-analysis: Yue-liang et al.[291]

Dyspnea/shortness of breath

Main finding	Source
High risk for COVID-19: (i) severity: odds 4.20 to 8.68x greater, RR= 2.90 (ii) patients with Multiple Sclerosis: 39.5% (iii) elderly patients: 42.95% Prevalence in patients with COVID-19: 32.6% to 48.96%	SR and meta-analysis: Booth et al.[522]; SR and meta-analysis: Cares-Marambio et al. [521]; SR and meta-analysis: Giri et al. [280]; SR and meta-analysis: Barzegar et al. [377]; SR and meta-analysis: Hatmi et al. [281]; SR and meta-analysis: Kim et al. [293]; SR and meta-analysis: Li J et al. [294]; SR and meta-analysis: Singhal et al. [365]; SR and meta-analysis: Vakili et al. [425]; SR and meta-analysis: Yue-liang et al. [291]; SR and meta-analysis: Zhang L et al.[330]

Myalgia or fatigue (muscle ache)

Main finding	Source
High risk for COVID-19: (i) severity: odds 1.40 to 4.82x greater, RR= 1.43 (ii) patients with Multiple Sclerosis: 51.2% Prevalence in patients with COVID-19: 13% to 52%	SR and meta-analysis: Booth et al.[522]; SR and meta-analysis: Cares-Marambio et al. [521]; SR and meta-analysis: Giri et al. [280]; SR and meta-analysis: Barzegar et al.[377]; SR and meta-analysis: Hatmi et al. [281]; SR and meta-analysis: Amiri et al. [424]; SR and meta-analysis: Kim et al.[293]; SR and meta-analysis: Li J et al. [294]; SR and meta-analysis: Vakili et al.[425]; SR and meta-analysis: Yassin et al.[428]; SR and meta-analysis: Yue-liang et al.[291]

Headache

Main finding	Source
High risk for COVID-19: (i) severity: odds 1.36x greater Prevalence in patients with COVID-19: 6% to 12.1%	SR and meta-analysis: Hatmi et al. [281]; SR and meta-analysis: Amiri et al. [424]; SR and meta-analysis: Vakili et al. [425]; SR and meta-analysis: Yassin et al. [428]; SR and meta-analysis: Yue-liang et al. [291]

Gastrointestinal symptoms

Main finding	Source
Higher chance for COVID-19: (i) severity: odds 2.07x greater (ii) ICU admission: odds 1.01x greater (iii) mortality: 3.5%, odds 0.92x greater (iv) mortality: China (0.9%), USA (10.8%) Prevalence in patients with COVID-14.8%	SR and meta-analysis: Bolia et al.[523]; SR and meta-analysis: Hatmi et al. [281]; SR and meta-analysis: Menon et al. [524]; SR and meta-analysis: Shehab et al.[525]

Diarrhea

Main finding	Source
High risk for COVID-19: (i) severity: odds 3.97x greater Prevalence in patients with COVID-19: 7.8% to 19.08%	SR and meta-analysis: Bolia et al. [523]; SR and meta-analysis: Hatmi et al. [281]; SR and meta-analysis: Li J et al. [294]; SR and meta-analysis: Shehab et al.[525]; SR and meta-analysis: Zarifian et al.[526]

Abdominal pain

Main finding	Source
High risk for COVID-19: (i) severity: odds 2.76x greater Prevalence in patients with severe COVID-19: 4.5%, odds 7.17x greater	SR and meta-analysis: Hatmi et al.[281]; SR and meta-analysis: Li J et al. [294]; SR and meta-analysis: Yue-liang et al. [291]

Nausea and vomiting

Main finding	Source
High risk for COVID-19: (i)severity: odds 15.55x greater Prevalence in patients with COVID-19: 4.7% to 19.7%	SR and meta-analysis: Bolia et al.[523]; SR and meta-analysis: Booth et al.[522]; SR and meta-analysis: Hatmi et al. [281]; SR and meta-analysis: Li J et al. [294]; SR and meta-analysis: Shehab et al. [525]; SR and meta-analysis: Vakili et al.[425]; SR and meta-analysis: Zarifian et al. [526]

Chill

Main finding	Source
High risk for COVID-19:	SR and meta-analysis: Booth et al.[522]; SR and meta-analysis: Yue-liang et al. [291]

(i)severity: odds 2.30 to 6.32x greater	

Anosmia/hyposomnia

Main finding	Source
Prevalence in patients with COVID-19: 18.3% to 38.2%, odds 10.21x greater When compared with patients with Olfactory dysfunction (OD), patients without OD: High risk for COVID-19: (i) hospitalization: odds 5.28x greater (ii)Mechanical Ventilation: odds 7.01x greater (iii) mortality: odds 7.0x greater	SR and meta-analysis: Goshtasbi et al.[527]; SR and meta-analysis: Mutiawati et al.[528]; SR and meta-analysis: Vakili et al.[425]; SR and meta-analysis: Yassin et al. [428]

Gustatory impairment

Main finding	Source
Prevalence in patients with COVID-19: 19.6% to 5.4%	SR and meta-analysis: Vakili et al.[425]; SR and meta-analysis: Yassin et al.[428]

Anorexia/loss of appetite

Main finding	Source
High risk for COVID-19: (i) severity: odds 0.58 to 2.25x greater, RR=2.07 Prevalence in patients with COVID-19: 10.2% to 28.9%	SR and meta-analysis: Kim et al. [293]; SR and meta-analysis: Vakili et al.[425]; SR and meta-analysis: Yue-liang et al. [291]; SR and meta-analysis: Zarifian et al.[526]

Nasal congestion

Main finding	Source
Prevalence in patients with COVID-19: 3.7% to 22%	SR and meta-analysis: Hatmi et al. [281]; SR and meta-analysis: Amiri et al. [424]

Stroke

Main finding	Source
Higher chance for COVID-19: (i) severity: in patients with acute ischemic stroke vs non-severe patients (RR=2.91)	SR and meta-analysis: Lu et al. [529]; SR and meta-analysis: Syahrul et al. [530]; SR and meta-analysis: Tan et al.[531]

(ii) ICU admission: in patients with acute ischemic stroke vs non-severe patients (RR=4.47) (iii) mortality: hemorrhagic stroke (44.72%) and ischemic stroke (36.23% to 38%) Prevalence in patients with COVID-19: -ischemic stroke: 1.11% to 1.7% -hemorrhagic stroke: 0.46% -ischemic stroke (71.58%) was more prevalent than hemorrhagic stroke (28.42%)	

Dizziness

Main finding	Source
High risk for COVID-19: (i) severity: RR=2.06 Prevalence in patients with COVID-19: 6.7% to 11.3%	SR and meta-analysis: Kim et al. [293]; SR and meta-analysis: Vakili et al.[425]; SR and meta-analysis: Yassin et al.[428]

Chest pain/chest tightness

Main finding	Source

High risk for COVID-19: (i) severity: odds 4.09x greater Prevalence in patients with COVID-19: 16%	SR and meta-analysis: SR and meta-analysis: Cares-Marambio et al. [521]; SR and meta-analysis: Yue-liang et al. [291]

Sputum

Main finding	Source
High risk for COVID-19: (i) severity: odds 11.40x greater (ii) mortality: odds 2.08x greater	SR and meta-analysis: Booth et al. [522]; SR and meta-analysis: Zhang L et al. [330]

Laboratory abnormalities

Main finding	Source
- Fibrinogen: MD 0.42 - C- reactive protein: MD 35.74; odds 3.99x greater risk for severe disease - Ferritin: MD 506.15 - Procalcitonin: MD 0.07, odds 2.91 to 5.28x greater risk for severe disease - Leukocytosis: odds 3.44x greater risk for severe disease	SR and meta-analysis: Chaudhary et al. [532]; SR and meta-analysis: Haryanto et al.[533]; SR and meta-analysis: Heidari- Beni et al. [534]; Meta-analysis: Huang et al. [535]; SR and meta-analysis: Kiss et al. [536]; SR and meta-analysis: Yue-liang et al.[291]; SR and meta-analysis: Zarifian et

- Lymphocytopenia: odds 4.39x greater risk for severe disease - Aspartate aminotransferase: odds 3.02x greater risk for severe disease - Lactic dehydrogenase: odds 8.33x greater risk for severe disease	al.[526]; SR and meta-analysis: Zhang L et al.[330]

D-dimer (elevated)

Main finding	Source
Higher risk for COVID-19: (i) severity: 77%, MD 0.43 to 0.60 (ii) mortality: 75%	SR and meta-analysis: Chaudhary et al.[532]; SR and meta-analysis: Haryanto et al.[533] ; SR and meta-analysis: Zhan et al. [537]; SR and meta-analysis: Zhao R et al. [538]

Neurological symptoms

Main finding	Source
- Prevalence in COVID-19 patients: (i)severity: 31% (ii) mortality: 6.2% (iii) most prevalent comorbidity: cerebrovascular disease (2.5% to 4.3%)	SR and meta-analysis: Tandon et al. [427]; SR and meta-analysis: Vakili et al. [425]; SR and meta-analysis: Yassin et al.[428]

Pregnant women

Fever

Main finding	Source
Higher risk for COVID-19 mortality: Fever alone: 100% Comparing pregnant women and non-pregnant women with COVID-19: The risk of experiencing fever (RR= 0.74)	SR and meta-analysis: Karimi et al. [401]; SR and meta-analysis: Khan et al. [519]

Cough

Main finding	Source
Higher risk for COVID-19 mortality: cough alone: 100%	SR and meta-analysis: Karimi et al. [401]

Dyspnea

Main finding	Source
Higher risk for COVID-19 mortality: 58.3%	SR and meta-analysis: Karimi et al. [401]

Myalgia or fatigue

Main finding	Source
Higher risk for COVID-19 mortality: 50% Comparing pregnant women and non-pregnant women with COVID-19: The risk of experiencing myalgia (RR= 0.92)	SR and meta-analysis: Karimi et al.[401]; SR and meta-analysis: Khan et al. [519]

Diarrhea

Main finding	Source
Comparing pregnant women and non-pregnant women with COVID-19: The risk of experiencing diarrhea (RR= 0.40)	SR and meta-analysis: Khan et al.[519]

Gastrointestinal symptoms

Main finding	Source
Higher risk for COVID-19 mortality: 8.3%	SR and meta-analysis: Karimi et al.[401]

Chest discomfort

Main finding	Source

Comparing pregnant women and non-pregnant women with COVID-19: The risk of experiencing chest discomfort (RR= 0.86)	SR and meta-analysis: Khan et al.[519]

Headache

Main finding	Source
Prevalence in COVID-19 patients: 6% Comparing pregnant women and non-pregnant women with COVID-19: The risk of experiencing headache (RR= 0.77)	SR and meta-analysis: Hatmi et al.[281]; SR and meta-analysis: Khan et al. [519]

Expectoration

Main finding	Source
Comparing pregnant women and non-pregnant women with COVID-19: The risk of experiencing expectoration (RR= 0.45)	SR and meta-analysis: Khan et al.[519]

Sore throat

Main finding	Source
Higher risk for COVID-19 mortality: 8.3%	SR and meta-analysis: Karimi et al. [401]

Children

Multisystem inflammatory syndrome (MIS-C)

Main finding	Source
Common: - gastro-intestinal symptoms (84.3% to 87.3%) - neurologic symptoms (22.9%) - cardiovascular symptoms (45% to 31%) - myocarditis (55.3% to 61.8%) - coronary vessel abnormalities (17.2%) - ventricular dysfunction (38%) - coronary aneurism (20% to 21.7%) - ECG abnormalities (28.1%) - Cardiac arrythmias (33.3%) - shock (65.8%),	SR and meta-analysis: Dhar et al.[539]; SR and meta-analysis: Haghighi- Aski et al. [540]; SR and meta-analysis: Yashuara et al.[429]

Prevalence in COVID-19 patients: - prevalence in Hispanic patients: 34.6% - prevalence in Black patients: 31.5% High risk for: (i)mortality: 1% to 1.9%	

Fever

Main finding	Source
Common (45.86% to 47%)	SR and meta-analysis: Islam et al.[423]; SR and meta-analysis: Mansourian et al. [541]

Cough

Main finding	Source
Common (37%)	SR and meta-analysis: Mansourian et al.[541]

Gastro-intestinal symptoms

Main finding	Source
Common (87.3%)	SR and meta-analysis: Yashuara et al. [429]

Diarrhea

Main finding	Source
Common (19%)	SR and meta-analysis: Mansourian et al. [541]

Dyspnea

Main finding	Source
Common (odds 6.61x greater)	Meta-analysis: Zhou B et al.[430]

Pharyngalgia

Main finding	Source
Common (13%)	SR and meta-analysis: Mansourian et al. [541]

Laboratory abnormalities

Main finding	Source
Common: - lymphopenia (9%) - lymphocytosis (26%) - neutropenia (34%) - D-dimer (36%) -low oxygen saturation (38%)	SR and meta-analysis: Hatmi et al. [281]; SR and meta-analysis: Mansourian et al.[541]

Radiological features

Main finding	Source
Common: - abnormal chest X-ray (odds 3.33x greater)	Meta-analysis: Zhou B et al. [430]

General considerations

Main finding	Source
- 5% to 12.94% were asymptomatic - 79.6% presented mild/moderate symptoms -7.46% presented severe symptoms - the mean age 9.3 years	SR and meta-analysis: Hatmi et al. [281]; SR and meta-analysis: Yashuara et al. [429]; Meta-analysis: Zhou B et al.[430]

The following diseases, conditions and groups have limited to moderate evidence for risk.

Dysgeusia

Main finding	Source
Prevalence in patients with COVID-19: 36.6%, odds 8.61x greater	SR and meta-analysis: Mutiawati et al. [528]

Ageusia

Main finding	Source
Prevalence in patients with COVID-19: 49.8%	SR and meta-analysis: Hatmi et al. [281]

Expectoration

Main finding	Source
High risk for COVID-19: (i) severity: odds 1.36x greater	SR and meta-analysis: Yue-liang et al.[291]

Rhinorrhea

Main finding	Source
Prevalence in patients with COVID-19: 7.5%,	SR and meta-analysis: Li J et al.[294]

Cutaneous manifestations

Main finding	Source
Prevalence in patients with COVID-19: -morbilliform (30.6%)	SR and meta-analysis: Lee et al.[426]

-varicelliform (18.8%) -urticarial (13.2%) -chilblains- like (12.5%) -acro- ischemic (9%) The most common: morbilliform, varicelliform, and urticarial	

Impairment of consciousness (also termed "confusion" or "agitation" or "delirium")

Main finding	Source
High risk for COVID-19: (i) mortality: odds 1.50 to 2.39x greater Prevalence in patients with COVID-19: 27%	SR and meta-analysis: Pranata et al. [542]

Lymphopenia/lymphadenopathy

Main finding	Source
High risk for COVID-19: (i) severity: 32%	SR and meta-analysis: Hatmi et al. [281]

Thrombocytopenia

Main finding	Source
High risk for COVID-19: (i) mortality: odds 7.37x greater (ii) mortality Thrombocytopenia + ARDS: odds 3.49x greater Prevalence in patients with COVID-19: 12.4%	SR and meta-analysis: Zong et al. [543]

Radiological features

Main finding	Source
High risk for COVID-19: (i)severity: bilateral lung involvement with severe clinical presentation: odds 3.44x	SR and meta-analysis: Hashemi- Madani et al.[544]

Vital signs outcomes

Main finding	Source
- Prevalence in critical COVID-19 patients: (i) Higher body temperature: VDM=0.29 (ii) Higher body pulse: VDM= 4.19	SR and meta-analysis: Yue-liang et al.[291]

Asymptomatic

Main finding	Source
- Prevalence in COVID-19 patients: (i) Among aged care residents: 31%	SR and meta-analysis: Hashan et al. [364]

Long-term symptoms

Main finding	Source
Prevalence in patients post-COVID-19 infection: - abdominal lung functions: 20.7% - neurological complaints: 24.13% - olfactory dysfunctions: 24.13% - specific widespread symptoms (chronic fatigue and pain): 55.17%	SR and meta-analysis: Salamanna et al.[431]

Appendix C: Key findings for topic c) non-disease-specific approaches to assist with non-treatment patient management measures for in-person oral health care

The following approaches and settings have moderate evidence for risk.

Teledentistry

Main finding	Source
Oral epithelial dysplasia (OED): Remote consultations with patient-provided clinical photographs may be a useful way of maintaining a level of surveillance in this group of patients. (89–100% agreement).	SR and meta-analysis: McCarthy et al.[449]
Children with Cleft Palate: The use of telepractice for providing speech pathology interventions for children with cleft palate is useful, as audiovisual materials, the use of interactive videos for speaking children and educational videos for parents.	SR: Palomares-Aguilera et al. [450]

Telehealth

Main finding	Source
Telehealth or virtual care clinics to evaluate patients	SR: Murphy et al. [545]

with fracture: 18% to 100% of efficiency	SR: Parker et al. [546]
Remote consultations in general practice are likely to be used more by younger, working people, non-immigrants, older patients, and women. Internet-based consultations more used by younger, affluent, and educated groups.	SR: Samarrai et al. [547]
Telehealth is important during COVID-19 pandemic and after, for Otolaryngologists, due the risk of infection resulting from the examination of the head and neck and AGP due to the predilection of viral particles for the nasal cavities and pharynx.	Prospective study : Borders et al.[548]
Clinical Swallowing outcomes via Telehealth: Investigated the reliability of outcome measures derived from clinical swallowing tele-evaluations in real-world clinical practice. Advantages: - reliability were "excellent" for most raters across all tasks (ICCs of .63 and 1.00) - Subjective observations of oral intake and objective measures	

taken can be reliably measured via telehealth in clinical practice. Disadvantages: - infrequent instances of suboptimal video quality -reduced camera stability -camera distance -obstruction of the patient's mouth during tasks.	

Artificial Intelligence

Main finding	Source
Artificial Intelligence techniques optimize on clinical settings in terms of quality, accuracy and most importantly time: - early screening - diagnosis - prognosis of the disease Were identified in total: -14 models for screening - 38 diagnostic models for detecting COVID-19 - 50 prognostic models for predicting ICU need, ventilator need, mortality risk, severity assessment or hospital length stay.	SR: Adamidi et al. [549]

Use of screening algorithm, within a newly integrated Electronic Health Record (EHR). Advantages: - stratify risk in order to identify patients who are likely to have a poor outcome if care is delayed; - reduce patients with non-emergent needs seeking care in the emergency rooms; - prevent overuse of dental emergency services; - follow up visit to the dental emergency clinic post screening was 30% with or without algorithmic usage; - when utilizing the algorithm, the rates of patients that did need emergency care based on Acuity Level was 63%.	Prospective study: Perelman et al.[451]

Hospital environment

Main finding	Source
Management of emergency surgical patients under COVID-19 pandemic: A patient is defined "suspected" for COVID-19 infection if he presents: • fever and at least one sign/symptom of respiratory	SR: De Simone et al. [452]

disease and a history of travel to or residence in a country area or territory reporting local transmission of COVID-19 disease during the 14 days prior to symptom onset; • any acute respiratory illness, having been in contact with a confirmed COVID-19 case in the last 14 days prior onset of symptoms; • severe respiratory infection, with no other etiology that fully explains the clinical presentation, requiring hospitalization. Suspected clinical diagnosis of COVID-19 is confirmed through: • The *COVID-19 RT-PCR test* • The *chest imaging* that includes chest radiograph, computed tomography scan or lungs ultrasound.	

Dental office

Before entering a dental office

Main finding	Source
Identification of suspected patients or carriers of Covid-19: (i) Urgent dental care: pharmacological and phone tracking with video treatment. (ii) Elective dental care postpone of	SR and meta-analysis: Amiri et al. [424]; Scoping review: Lourenço et al. [453]

treatment for 14 days or/and initial screening via telephone. (iii) only maintaining urgency treatments in positive epidemiological areas for the COVID-19 disease *Orthodontic procedures:* (i)limited scheduling of patients.	SR: Singh et al. [454]

At the dental office

Main finding	Source
Patient Assessment - As soon as the patient is scheduled for dental treatment, a comprehensive medical history, screening questionnaire for COVID-19, and true emergency questionnaire should be completed. - 72,2% of the authors, suggested either an epidemiological and clinical questionnaire or a simple clinical exam. -Emergency dental care: using negative pressure rooms or rooms for isolation of airborne infection.	SR and meta-analysis: Amiri et al. [424]; Scoping review: Lourenço et al. [453]
Pediatric Dentistry: (i)Greater rigor in the use of PPE may cause strangeness for children.	SR: Sales et al. [455]

(ii) the management of patient's behavior before and during the treatment and new approaches to perform the procedures will be demanded. (iii)non-aerosol techniques and minimally invasive procedures will be preferable. *Orthodontic Procedures:* (i)limiting the number of HCP during procedure. *Endodontic Procedures:* (i) endodontists demonstrated adequate knowledge of main symptoms of COVID-19 and the risks of infection during dental procedures (98.5%). (ii) Most professionals have suspended elective dental care during quarantine; while, about half of them, performed only emergency procedures in their workplaces. (iii) in their daily practice, 72.1% of endodontists implemented biosecurity measures in preventing COVID-19.	SR: Singh et al. [454] SR : Sarria- Guzman et al. [550]

Post dental treatment

Main finding	Source
Waste management Clinical waste should segregate in double-layer yellow leak-resistant clinical waste bags (with a "gooseneck" knot).	SR: Singh et al. [454]

Specific precautions

Frequent handwashing

Main finding	Source
Existing data pooled from RCTs reveal a reduction in occurrence of Influenza with the Handwash with facemask in community settings: 64.9%	SR and meta-analysis: Aggarwal et al. [457]
Effect of disease prevention *Could reduce the risk of disease infection:* - hand washing more than 4 times/day compared to not (odds 0.61x greater)	SR and meta-analysis: Xun et al.[456]

- hand washing ≤4 times/day compared with hand washing 5-10 times/day (Odds 0.75x greater) - hand washing ≤4 times/day compared with hand washing >10 times/day (odds 0.65x greater) - hand washing ≤10 times/day with hand washing >10 times/day (odds 0.59x greater) *No statistically significantly reduce the risk of disease infection:* - hand washing more than 10 times/day compared to 5-10 times/day (odds 0.86x greater) Patients could not identify the symptoms, routes of transmission or prevention actions against SARS-CoV-2 infection. The only preventive measures indicated were washing hands and sanitize with alcohol.	SR: Sarria- Guzman et al. [550]

Masks or respirators

Main finding	Source
Existing data pooled from RCTs do not reveal a reduction in occurrence of Influenza with the	SR and meta-analysis: Aggarwal et al. [457]

use of facemask alone in community settings: 10.9%	

Specific settings, general considerations

Main finding	Source
-COVID-19 incubation period is similar SARS: median 5- 6 days but can take up to 14 days to show symptoms. -COVID-19 meantime between symptoms onset and hospitalization: median 4.4 days. -fomite transmission was examined in high-frequency touch surfaces (circulating banknotes, disposable chopsticks, hospital staff PPE, and others).	Scoping review: Zaki et al.[458]; SR and meta-analysis: Amiri et al. [424]; SR: Onakpoya et al. [459]
The status of dentists and other oral health practitioners' knowledge, attitude, and awareness about COVID-19: (i) 85.5% of the dentists had a high level of awareness about virus transmission modes (as sneezing, coughing, shaking hands, and contacting infected surfaces).	SR and meta-analysis: Jafari et al.[551]

(ii)80.7% of the dentists gave the correct answers to the questions related to virus transmission modes. (iii) 79.9% of the dentists had a positive attitude about virus transmission modes (like continuous handwashing, social distancing, and mask wearing).	
The common mode of COVID-19 transmission: -travel related: 58.1% -close contacts: 43.1% -community spread: 27.4%	SR and meta-analysis: Li J et al. [294]
RCT done among 1517 undergraduate dental students tested the effectiveness of 'dissonance induction' (DI) and 'assessment reactivity' (AR) in improving adherence to World Health Organization (WHO) measures as compared to a control group: - DI group were found to be significantly higher (15.11 ± 4.1) compared to the AR (13.13 ± 2.01) and control (12.87 ± 2.97) groups - DI is an easy intervention to bring an immediate and significant change in adherence to precautionary measures.	RCT: Chandu et al. [460]

Appendix D: Key findings for topic d) PPE for providing in-person healthcare

The following personal protective approaches have limited to moderate evidence for risk, though strong evidence for SARS-CoV-2 and other diseases.

Risk factors for health care workers (HCW)

Main finding	Source
Adverse events among HCW due to PPE use during the COVID-19: - headache (55.9%) - dry skin (54.4%) - dyspnoea (53.4%) - pressure injuries (40.4%) - itching (39.8%) - hyperhidrosis (38.5%) - dermatitis (31.0%; 0.6 to 6.7 cases per 10 000 person/year) Factors related with a greater risk of adverse events among HCW due to PPE use during the COVID-19: - females had a higher risk of adverse events (odds 1.87 to 3.20x greater) - comorbidities such as diabetes mellitus, obesity, pre-existing headache, and smoking	SR and meta-analysis: Galanis et al. [473]; SR: Larese Filon et al. [474]

- the longer duration of shifts wearing PPE (odds 1.24 to 4.26x greater)	

Risk factors for oral health care workers

Main finding	Source
Adverse events among HCW due to PPE use during the COVID-19: - occupational contact dermatitis: Higher incidence compared to other HCWs. For dentists (11 cases per 10 000 person/year) For dental technicians (13.8 cases per 10 000 person/year)	SR: Larese Filon et al. [474]

Face masks

Main finding	Source
Wearing face masks may reduce COVID-19 infection risk (RR=0.12)	SR: Tabatabaeizadeh [475];

Surgical masks

Main finding	Source
Conventional surgical masks do not offer protection against high-risk AGPs.	R: Sobti et al. [476]

N95 masks

Main finding	Source
Significantly protective of HCW from contracting SARS-CoV-1 and SARS- CoV-2: odds 0.11x greater	SR and meta-analysis: Chan et al.[477]

Gowns

Main finding	Source
Significantly protective of HCW from contracting SARS-CoV-1 and SARS- CoV-2: odds 0.59x greater	SR and meta-analysis: Chan et al.[477]

Gloves

Main finding	Source
Significantly protective of HCW from contracting SARS-CoV-1 and SARS- CoV-2: odds 0.39x greater	SR and meta-analysis: Chan et al. [477]

Appendix E: Key findings for topic e) decontamination and re-use of PPE

The following decontamination and personal protective approaches no have new information for evidence for risk.

Appendix F: Key findings for topic f) the provision of aerosol-generating procedures (AGP)

The following aerosol-generating procedures have limited evidence for risk in relation to SARS-CoV-2.

Droplet transmission

Main finding	Source
-*Coughing*: 82% of the droplet nuclei produced when coughing is within a sufficiently small range (0.74–2.12 micrometres, μm) to contribute to airborne disease transmission. Coughing increases the contagiousness, especially in close contact, of symptomatic cases relative to asymptomatic ones. - *Speaking*: the particles generated by speaking tend to involve a broader size distribution, including some particles that are larger in size than produced by other aerosol-generating behaviours in the 3.5 and 5 μm range. The viral transmission of influenza can occur from speaking but it is untested as to whether the finding applies to COVID-19. - *Breathing*: 42% of a large proportion of particles produced	SR: Chacon et al.[488] ; SR: Chen et al. [489]

during breathing were of diameters < 0.8µm, of which size and concentration tend to be unaffected by such environmental factors as temperature and humidity. The viral transmission of influenza strains can occur through breathing-related activities. - *Sustained phonation*: particles between 3.5 and 5 µm in size became more prominent in sustained phonation compared to speech and other explored AGPs. - *Loud phonation*: the act of voicing loudly does not seem to have an impact on the size of particles generated. Highly infectious COVID-19 individuals shed tens to thousands of SARS-CoV-2 virions/min via droplets and aerosols while breathing, talking and singing. *Overall sensitivity of respiratory specimens for COVID-19 detection among symptomatic patients:* (i)97% for bronchoalveolar (ii)92% for double naso/oropharyngeal swabs (iii)87% for nasopharyngeal swabs (iv)83% for saliva (v) 82% for DTS (vi)44% for oropharyngeal swab	SR and meta-analysis: Khiabani et al.[490]

Bio-aerosol transmission/contamination

Main finding	Source
Medical interventions: No have studies examining transmissibility with other safety protocols, nor any studies quantifying the risk of aerosol generation with nasopharyngeal or oropharyngeal swabs for detection of SARS-CoV-2. *Bio-aerosol transmission/contamination associated with nasopharyngeal or oropharyngeal swab testing*: Using a dedicated sampling room with negative pressure isolation room, PPE, strict sterilisation protocols, structured training with standardised collection methods and a structured collection and delivery system= 0% HCW infection rate among eight nurses conducting over 11 000 nasopharyngeal swabs. Most orthopaedic procedures are high-risk AGPs.	SR: Agarwal et al.[552] SR : Sobti et al. [476]

Consensus of AGP on oral and dental procedures

Main finding	Source
The use of laser in Dentistry: (i) high-power lasers form more aerosols than low-power lasers (ii) high-power lasers need to be controlled to minimize the risks of cross-infection.	SR: Lago et al.[491]

The following aerosol-generating procedures have limited evidence for risk in relation to SARS, MERS, H1N1, influenza and bacteria.

Consensus of AGP on oral and dental procedures

Main finding	Source
During dental periodontal procedures: Hierarchy of procedure contamination risk: (i) Higher: Higher power settings (ii) Moderate: Ultrasonic scaling, air polishing and prophylaxis procedures produce contamination (splatter, droplets and aerosol) in the presence of suction, with a small amount of evidence showing droplets taking between 30 min and 1 h to settle. (iii) Lower: hand scaling	SR: Johnson et al. [492]

(iv) Distribution of contamination varied in relation to operator position (v) Distribution of contamination was found on the operator, patient and assistant with higher levels around the head of the operator and the mouth and chest of the patient	
During pediatric procedures: (i)non-aerosol techniques and minimally invasive procedures will be preferable.	SR: Sales et al. [455]
During Orthodontic procedures: (i)avoiding or restricting AGPs whenever possible; (ii)avoiding the use of high-speed dental handpieces, air-water syringe and ultrasonic scalers; (iii)using rubber dams and HVE during AGPs; (iv)utilization of the 4-handed or 6-handed cooperation technique; (v)avoiding intraoral radiographs like IOPA or occlusal views that can stimulate gag reflexes and induce coughing; (vi)using handpieces with anti-retractive valves.	SR: Singh et al. [454]

Appendix G: Key findings for topic g) mitigation strategies (for example, rubber dam, mouth rinses etc.) during the provision of in-person oral health care

The following interventions have limited evidence for risk in dental procedures in relation to SARS-CoV-2.

Mouth rinse solutions

Different types of solution

Main finding	Source
(i) The main oral antiseptics that have been tested against SARS-CoV-2 were: - PVP-I - H_2O_2 - chlorhexidine digluconate (CHX) - ColdZyme - CPC.	SR: Mateos-Moreno et al. [506]

Povidine-iodine (PVP-I)

Main finding	Source
(i)The current evidence supports the virucidal properties of 0.5% PVP-I is effective in reducing SARS-CoV-2 in the nasal cavity,	SR: Chopra et al.[507]; SR: Mateos-Moreno et al.[506]

nasopharynx, oral cavity, and oropharynx. (ii)The preoperative use of PVP-I mouthrinse/gargle is important in preventing the spread of infection during the COVID-19 pandemic. (iii) PVP-I have been tested against other coronaviruses and SARS-CoV-2. The effect of decreasing salivary load with PVP-I and CPC mouth-rinsing was observed to be sustained at 6 h time point. Within the limitation of the current study, the use of PVP-I and CPC formulated that commercial mouth-rinses may be useful as a pre-procedural rinse to help reduce the transmission of COVID-19.	RCT: Seneviratne et al.[508]

Hydrogen Peroxide (HP)

Main finding	Source
(i) Nose/mouth/throat washing with hydrogen peroxide may enhance those local innate responses to viral infections and help protect against the current SARS-CoV-2. (ii)HP have been tested against other coronaviruses and SARS-CoV-2.	SR: Mateos-Moreno et al.[506]

Chlorhexidine (CHX)

Main finding	Source
CHX is a simple and safe addition to current COVID-19 prevention. Using CHX as an oral rinse and posterior oropharyngeal spray in hospitalized COVID-19 patients: (i) SARS-CoV-2 was eliminated from the oropharynx of patients who used CHX as an oral rinse (62.1%) versus of the control group patients (5.5%). (ii) Patients who used a combination of oral rinse and oropharyngeal spray, 86.0% eliminated oropharyngeal SARS-CoV-2, versus 6.3% of control patients. (iii) CHX have been tested against SARS-CoV-2.	Prospective Cohort Study : Huang et al. [509]; SR : Mateos-Moreno et al.[506]

Cetylpyridinium chloride (CPC)

Main finding	Source
(i) CPC have been tested against other coronaviruses and SARS-CoV-2.	SR: Mateos-Moreno et al.[506]

The following interventions have limited evidence for risk in dental procedures in relation to other coronaviruses and bacteria.

General considerations

Main finding	Source
Various risk reduction interventions that have been consistently recommended: (i)avoiding or restricting AGPs whenever possible; (ii)avoiding the use of high-speed dental handpieces, air-water syringe and ultrasonic scalers; (iii)limited scheduling of patients; (iv)limiting the number of HCP during procedure; (v)using rubber dams and HVE during AGPs; (vi)utilization of the 4-handed or 6-handed cooperation technique; (vii)avoiding intraoral radiographs like IOPA or occlusal views that can stimulate gag reflexes and induce coughing; (viii)using handpieces with anti-retractive valves.	SR: Singh et al. [454]

High-volume evacuator

Main finding	Source
(i) HVE used with intraoral evacuator (Iso Vac) was found to be most effective in mitigating spatter. (ii) HVE+ rubber dam: reduces the contamination risk.	SR: Singh et al. [454]
(i)During oral prophylaxis using ultrasonic scalers, the use of HVE+ intraoral suction device resulted in significant reductions in CFUs compared with the use of the intraoral suction device alone (P < .001). (ii)The highest amounts of CFUs were found in the operating zone and on patients during HVE and combination treatment periods.	RCT: Suprono et al. [505]

Rubber dam

Main finding	Source
(i) During AGPs procedures dental treatment: the use with HVE reduces the contamination risk.	SR: Singh et al. [454]

Laser

Main finding	Source
The use of laser in Dentistry: low-power lasers form less aerosols than high-power lasers but must be protected to minimize the risks of cross-infection.	SR: Lago et al. [491]

Mouth rinse solutions

Different types of solution

Main finding	Source
(i) The main oral antiseptics that have been tested against other coronaviruses are: - povidone-iodine (PVP-I) - essential oils - cetylpyridinium chloride (CPC) -sodium bicarbonate - sodium chloride -baby shampoo -hydrogen peroxide (H_2O_2).	SR: Mateos-Moreno et al. [506]

Hydrogen Peroxide (HP)

Main finding	Source
(i)HP is produced physiologically by oral bacteria and plays a significant role in the balance of oral	SR: Mateos-Moreno et al.[506]

microecology since it is an important antimicrobial agent.	

Essential oil (EO)

Main finding	Source
(i) EO have been tested against other coronaviruses.	SR : Mateos-Moreno et al. [506]

Appendix H: Key findings for topic h) space ventilation strategies to reduce the risk of transmission

The following ventilation settings have limited evidence for risk in relation to SARS-CoV and microorganisms.

Air cleaning systems in dental office

Main finding	Source
Preventive engineering control measures that may reduce the risk of infection: (i)ensuring adequate natural ventilation of the operatory and waiting area with new air, (ii)allowing air flow from the clean area into the less clean area by placement of supply-air vents in reception or corridor area	SR: Singh et al. [454]

(iii)return-air vents in the waiting area or rear of the patient operatory, (iv) portable high efficiency particulate air (HEPA) filtration units placed adjacent to the patient's chair, but not behind the dental healthcare personnel. (v)use of properly directed extractor fans (not towards doors), fixed-split and portable air conditioning (without recirculation) without incorporated humidifiers.	
(i)Aerosol accumulation may occur in dental treatment rooms with poor ventilation. (ii) Accumulated aerosol particles could not be removed by ventilation alone within 30-min in rooms with Equivalent ventilation provided by the PAC (ACH_{vent}<15). (iii)Addition of Portable Air Cleaner (PAC) with a HEPA filter significantly reduced aerosol accumulation and accelerated aerosol removal. (iv)Accumulated aerosols could be completely removed in 4 to 12-min by ventilation combined with PAC. (iv)Effectiveness of the PAC was especially prominent in rooms with poor ventilation.	Prospective study : Ren et al. [511]

Appendix I: Key findings for topic i) disinfection of surfaces in spaces in which oral health care is provided

The following approaches and interventions have limited to moderate evidence for risk in relation to SARS-CoV-2.

General Considerations

Main finding	Source
(i) The longest SARS-CoV-2 survival time is 28 days at room temperature (RT) on different surfaces: -polymer banknotes - vinyl - steel - glass - paper banknotes. (ii) SARS-CoV-2 human infection from contaminated surfaces, dangerous viral load on surfaces for up to 21 days was determined on: -polymer banknotes -steel -glass - paper banknotes. (iii) For viruses other than SARS-CoV-2, the longest period of survival was 14 days, on: - glass.	SR: Marzoli et al. [516]

(iv) Environmental conditions can affect virus survival: -low temperatures and low humidity: support prolonged survival of viruses on contaminated surfaces independently of surface type. - exposure to sunlight: reduces the risk of surface transmission. - Laboratories reported the highest frequency of contaminated surfaces (20.5%, 17/83).	SR: Onakpoya et al. [459]

Disinfection methods

Main finding	Source
(i)Surface inactivation of SARS-CoV-2 can be achieved by standard disinfection methods involving the use of: 70–80% ethanol (minimum 1-minute exposure time) + 0.5% hydrogen peroxide + freshly prepared 0.1% (1 g/L) sodium hypochlorite, at 2–3-hour intervals. (ii)A fallow period or minimum post AGP downtime of 10 minutes has been recommended to allow for settling of larger droplets before initiation of environmental cleaning.	SR: Singh et al.[454]

(iii) Heat-automated high-level disinfection using washer-disinfector may be employed for decontamination of photographic retractors.	

Disinfectants

Chlorine

Main finding	Source
- 1%NaOCl solution for 1 minute: reduce SARS-CoV infectivity and to minimize the risk of cross-contamination through prosthetic materials; - 1%NaOCl solution: increase in surface roughness and color alteration on acrylic resin (not clinically significant); - 1% NaOCl solution: decrease in bonding strength on lithium disilicate.	SR: Singh et al. [454]
Flushing dental unit water lines for at least 2 minutes at patient intervals or sucking about 1 L of 1% sodium hypochlorite through the suction line at the end of the day	SR : Singh et al. [454]

reduces the risk of cross-contamination.	

Alcohols

Main finding	Source
- n-propanol alone: low irritation potential - 60% n-propanol: significant damage effects of repeated exposure in healthy (as well as atopic skin in vivo) - n-propanol or isopropanol + detergents: greater irritation potential, compared with a quantitatively identical application of the same irritant alone.	SR and meta-analysis : Tasar et al.[517]

Detergents

Main finding	Source
- n-propanol or isopropanol + detergents (ie, sodium lauryl sulfate): greater irritation potential for frequent handwashing with detergents, compared with a quantitatively	SR and meta-analysis : Tasar et al. [517]

identical application of the alcohol alone.	

The following approaches and interventions have limited evidence for risk in relation to different viruses and bacteria.

Disinfectants

Hydrogen peroxide

Main finding	Source
Efficacy of Vaporized Hydrogen Peroxide (VHP) fogging against dental environment pathogens: - VHP generation was effective for the bacteria and some viruses. - aerosolized hydrogen peroxide found a greater log kill with the use of VHP generators. - The VHP generators can play a role in dental bio-decontamination.	SR: Ahmed et al. [518]

Glutaraldehyde

Main finding	Source
Sterilization and disinfection of orthodontic armamentarium: cold sterilization using 2% glutaraldehyde for heat-sensitive items: orthodontic markers, ultrasound bath and thermal disinfection.	SR: Singh et al.[454]

Peracetic acid

Main finding	Source
Sterilization and disinfection of orthodontic armamentarium: cold sterilization using 0.25% peracetic acid for heat-sensitive items: orthodontic markers, ultrasound bath and thermal disinfection.	SR: Singh et al. [454]

Autoclaves

Main finding	Source
Sterilization and disinfection of orthodontic armamentarium: - autoclave sterilization preferably for pliers, arch wires and minis crews. -high-level chemical disinfection or cold sterilization using 2%	SR: Singh et al. [454]

glutaraldehyde or 0.25% peracetic acid for heat-sensitive items such as orthodontic markers; ultrasound bath and thermal disinfection.	

Appendix J: **Methods used to identify and include relevant literature**

This report was structured as a rapid review of the evidence to support safe provision of oral health care during the COVID-19 pandemic. Different search strategies were tailored for nine key areas (“a” to “i”); available evidence was divided according to those key areas.

J.1. Eligibility criteria

J.1.1. Study types and design

This report and subsequent updates included studies in the field of COVID-19/SARS-CoV-2, but extended inclusion to studies on closely related respiratory viruses (key areas “c” to “i”), comprising SARS, MERS, H1N1, influenza, common cold and sometimes other pathogens. For questions with a robust body of evidence about COVID-19, we did not update evidence about other respiratory diseases or viruses (key areas “a” and “b”). Eligible study designs were: systematic reviews (SR) (with meta-analysis or not), scoping reviews, randomized controlled trials (RCT) and prospective cohort studies. We considered only manuscripts written in English as potential sources of study data.

The large amount of included studies for key areas “a” and “b” led us to stricter criteria, as detailed at session J.3.2.1. The paucity of literature on SARS-CoV-2 infection control has led us to extend inclusion criteria for key areas “f”, “g”, “h” and “i”. Therefore, studies related to airborne bacterial contamination were also included for those areas.

J.1.2. Types of conditions and interventions

Each key review area approached a distinct set of conditions and/or interventions of relevance for oral health care. In brief, those were conditions leading to higher risk of morbidity or mortality by COVID-19, approaches to protect healthcare professionals and patients from infection in different moments (i.e. physical distancing, aerosol-generating procedures, asepsis/disinfection and PPE). We expect conditions and interventions of relevance for the viruses mentioned above to be potentially relevant for COVID-19/SARS-CoV-2, even if as with poorer generalizability – studies reporting them would be considered as weaker sources of evidence.

Specific conditions and interventions were:

a. Comorbidities and other health conditions able to increase the risk of COVID-19-related complications, including death;
b. Clinical signs and symptoms expected with COVID-19 and observable by dental professionals before rendering in-person care;
c. Non-treatment approaches to provide in-person dental care, including patient scheduling, waiting and others (for example, teledentistry-based interventions);
d. Different PPE for in-person dental care, based on studies from different areas of health (not restricted to dental professions);

e. Decontamination of PPE, aiming at their possible re-use;
f. Aerosols generated by dental procedures, and their relevance for the transmission of COVID-19;
g. Methods to mitigate cross-infection by aerosols during in-person provision of oral health care, including rubber dam and pre-operatory mouth washes;
h. Spatial ventilation strategies to reduce the risk of transmission;
i. Disinfection of surfaces where oral health care is provided.

Since, at the time of preparing this review, there is no available vaccine for COVID-19, we have not considered that kind of intervention. We did not include prophylactic antiviral regimens for the same reason, for either patients or health care professionals. Since there is potential for vaccines and antivirals to become parts of dental professionals' routine after their development, we may consider including them in future updates.

J.1.2. Outcomes

This review considered any outcome related to the severity of COVID-19 as relevant, including signs/symptoms, complications and incident comorbidities, disease-specific severity indexes, and survival/death. Whenever relevant, measures of contamination (for example, % contaminated per group, or microbial counts on disinfected surfaces) and adverse effects (for example, rash caused by prolonged mask wearing) were considered.

Whenever relevant for each study key area, a brief description of patient and professional perception was provided. This would be done quantitatively (by numbers, for example, % of dentists who disinfect impressions before sending to the laboratory) or qualitatively (by a concise narrative of key perceptions).

J.2. Search strategy

J.2.1. Electronic searches

We performed systematic literature searches separated by key areas in the following databases: CINAHL, Embase (Ovid), MEDLINE (Ovid) and SCOPUS, restricting our search to a period of 4 months (March 1 2021 and June 30 2021). Different search strategies were prepared for key areas "a" to "i" and adapted for each database. Given their similar nature, some pairs of key areas employed a single search (i.e, "a"+"b"; "c"; "d"+"e"; "f"+"g"; "h" and "I"), totalling six searches.

Please refer to Table J1 at the end of this Appendix for the terms used in the electronic searches.

J.2.2. Researching other resources

We reviewed the list of references of all papers included in the report to identify other potentially relevant studies ("reference mining").

J.3. Data collection and analysis

J.3.1. Selection of studies

Two researchers (L.A. and R.S.) examined the titles and abstracts from each search to decide on their exclusion. A third researcher (P.A.) tackled any disagreement between the two reviewers during the selection of titles and abstracts.

Potential inclusion (including cases of insufficient information for exclusion) led to the revision of full text versions by two researchers (R.S. and P.A.). For full text selection, any disagreement was decided by a consensus meeting with a third researcher (L.A.). Although we always reached consensus, the third researcher would have the final decision in cases of persisting disagreement.

In the case of having two or more manuscripts describing the same study, those references would count as a single included study.

J.3.2 Data extraction/management, and quality of studies

Studies were classified according to the level of evidence provided: SR>RCT>prospective cohort. Scoping reviews were considered due to the breadth of information rather than strength of evidence. Since this is a rapid review on a vast number of key areas, no in-depth quality assessment was performed – instead, we classified sources of evidence as “strong”, “limited” or “none” for each specific condition/intervention.

J.3.2.1 Eligibility Criteria for Key areas A and B

Our search yielded several redundant studies for key areas A and B. That led us to restrict our eligibility criteria, by including only systematic reviews, with meta-analyses or not. As decision criteria for inclusion, this report considered as a systematic review just those studies with:

(a) a well-defined goal and/or research question, based on participant/patient type, exposure and outcome variables;

(b) systematic study selection, by using reproducible methods (including clear search strategy and eligibility criteria);

(c) quality assessment of reviewed literature (for example, application of standard quality assessment questionnaires for clinical studies);

(d) any strategy to synthetize obtained data (including meta-analysis) or at least a critical description primary study data, if studies cannot be pooled.

Primary studies for key area A were restricted to prospective ones. This enabled us to focus on high-level evidence. The latter restriction was not applied to key area B, given the non-analytical nature of the question.

Scoping reviews were still eligible for key areas C to I, to achieve broader information for those areas with more scarce evidence. Retrospective studies were excluded from this update, however.

J.2. Description of studies

J.2.1. Results of the search

The search strategy retrieved 4,486 study titles and abstracts. After examining those references, 4,269 clearly did not meet the inclusion criteria and were excluded. Two hundred and seventeen full text reports of potentially relevant studies were obtained for further evaluation. After excluding 15 full reports, our sample totaled 202 study reports.

According to each section, articles were included. Appendix Table J2 shows the selection of the publication for inclusion in the systematic review.

Appendix Table J2. Yield of the six electronic search strategies, in terms of the number of reports.

Key areas	**Total**	**Excluded**	**Included**
A + B	1,485	1,309	176
C	635	614	21
D + E	448	443	5
F + G	603	589	14
H	1,077	1,075	2
I	238	233	5
No data	No data	No data	Total =223*

* Several articles were included for more than one topic (e.g.: 14 articles were identified for topics A and B; 7 articles for two or more different topics) hence the total in the table surpasses 100% of the included articles (n = 223 and 202, respectively).

J.2.2. Included Studies

Regarding study design, the majority of our inclusions were SR and/or meta-analyses (n=193, 95.5%). We have also included five Prospective Cohort Studies (n=5, 2.48%), two scoping reviews (n=2, 1%), as well two RCT (n=2, 1%).

J.2.3. Measures of treatment effect and Unit of analysis issues

Included studies underwent qualitative analysis and separate data extraction, without further efforts for quantitative synthesis. Please refer to the main document and Appendices A to I for the description and results of included studies.