Oral hygiene and COVID-19

Is there a link?

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Background

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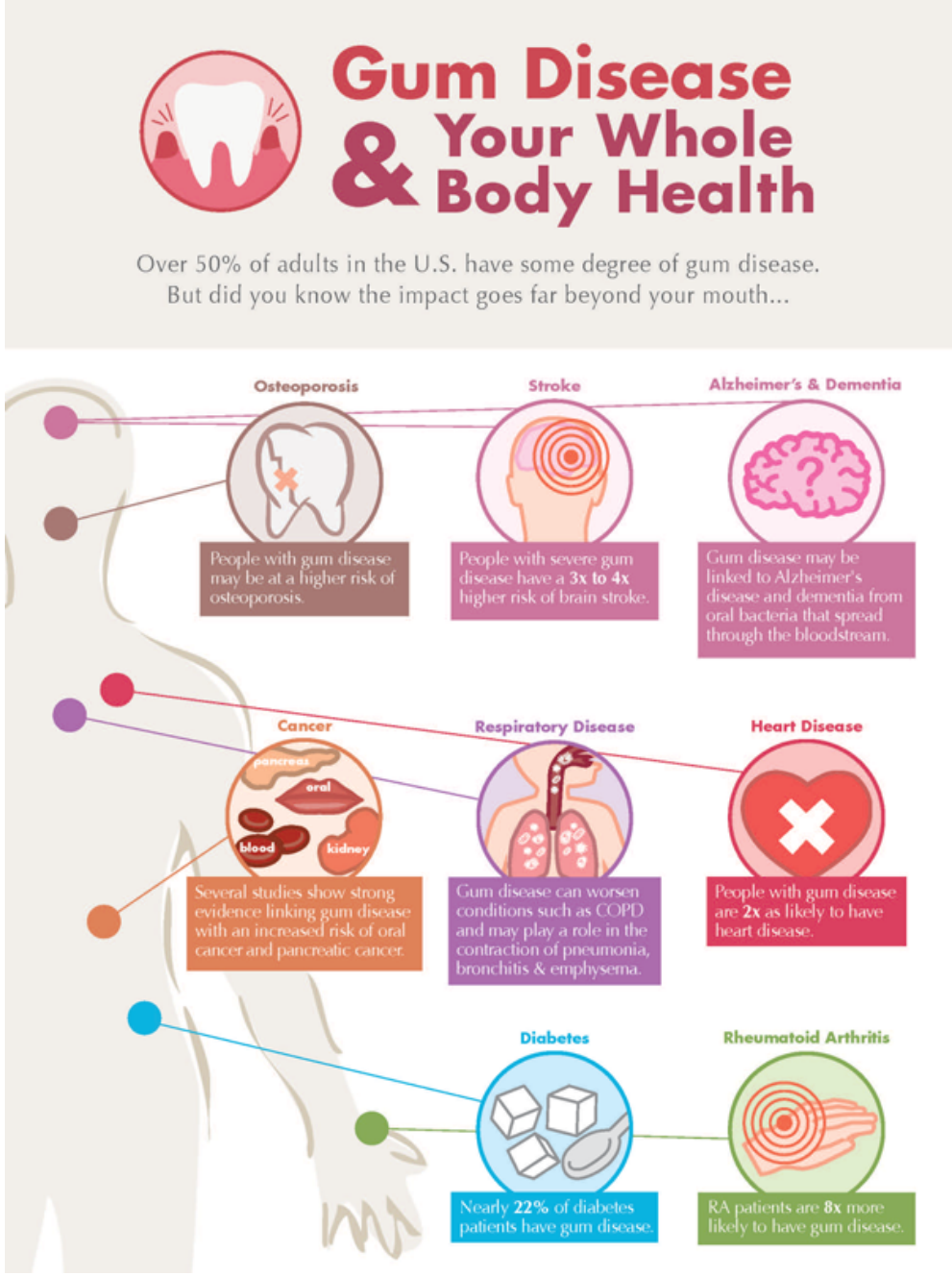
Oral systemic link

Studies have shown that severe gum disease increases the risk of:

- Osteoporosis
- 4 times higher risk of a stroke
- Alzheimer's and dementia
- Cancer
- Respiratory disease
- Heart disease
- Diabetes
- Rheumatoid arthritis



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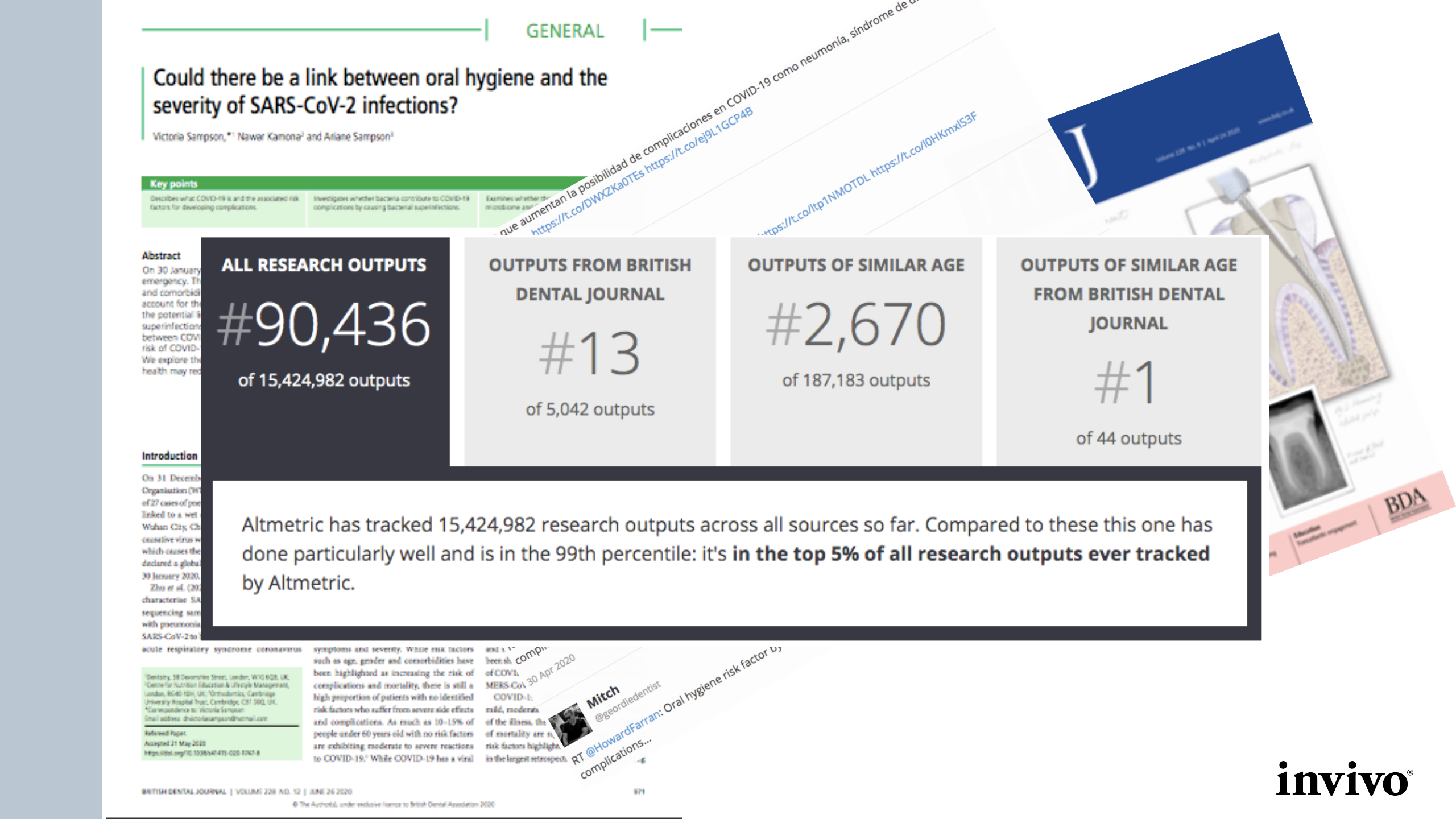
GENERAL
Could there be a link between oral hygiene and the severity of SARS-CoV-2 infections?
Victoria Sampson,*[1] Nawar Kamona[2] and Ariane Sampson[3]
Key points
Abstract
Introduction
ALL RESEARCH OUTPUTS
#90,436
of 15,424,982 outputs
OUTPUTS FROM BRITISH DENTAL JOURNAL
#13
of 5,042 outputs
OUTPUTS OF SIMILAR AGE
#2,670
of 187,183 outputs
OUTPUTS OF SIMILAR AGE FROM BRITISH DENTAL JOURNAL
#1
of 44 outputs
Altmetric has tracked 15,424,982 research outputs across all sources so far. Compared to these this one has done particularly well and is in the 99th percentile: it's in the top 5% of all research outputs ever tracked by Altmetric.
Mitch
@geordiedentist
30 Apr 2020
RT @HowardFarran: Oral hygiene risk factor b
complications...
BRITISH DENTAL JOURNAL | VOLUME 228 NO. 12 | JUNE 26 2020
BDA

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- Bioregulatory practitioner
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Is there a link between oral hygiene and the severity of SARS-CoV-2 Infections?

V. SAMPSON [1], N.KAMONA, A. SAMPSON

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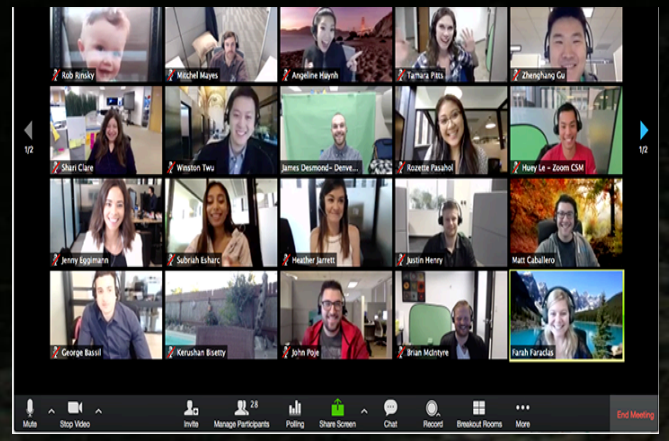
Dentistry post COVID-19?



Is there a link between oral hygiene and the severity of SARS-CoV-2 Infections?

- What is COVID-19?
- Risk factors for developing COVID-19 complications?
- Causes of a severe COVID-19 infection?
- Does bacteria play a role in COVID-19?
- Do COVID-19 patients suffer from bacterial super infections?
- Link between oral microbiome and COVID-19 complications?
- Link between oral health and COVID-19 complications?

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COVID-19: What is it?

World Health Organisation, 2020

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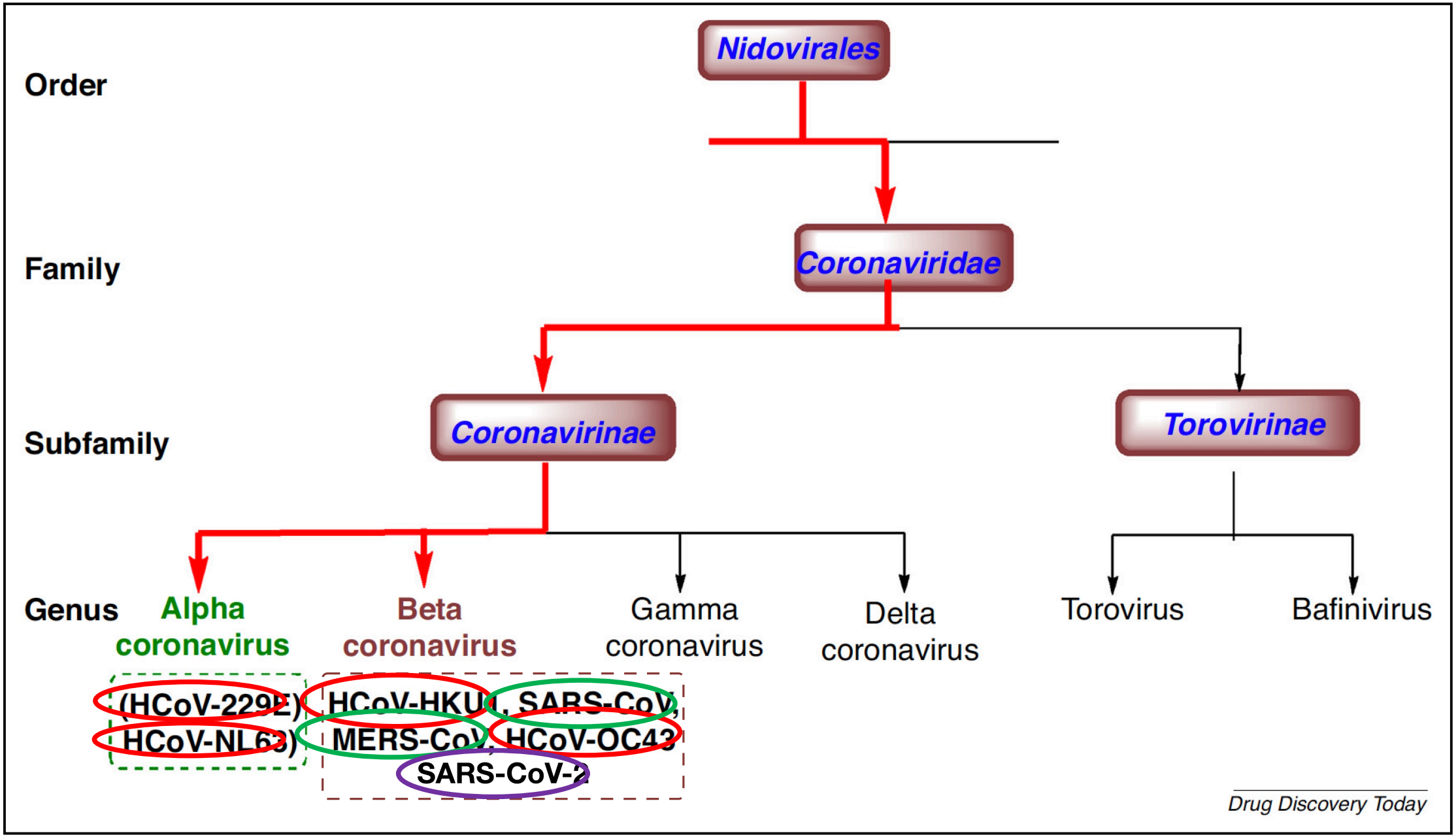
Order
Nidovirales
Family
Coronaviridae
Subfamily
Coronavirinae
Torovirinae
Genus
Alpha coronavirus
Beta coronavirus
Gamma coronavirus
Delta coronavirus
Torovirus
Bafinivirus
(HCoV-229E)
HCoV-NL63)
HCoV-HKU1, SARS-CoV
MERS-CoV, HCoV-OC43
SARS-CoV-2
Drug Discovery Today

COVID-19: Risk factors

1. Age (mean = 69 years)
2. Gender (70% men)
3. Underlying comorbidity (48% of cases)
    - Hypertension (30%)
    - Diabetes (19%)
    - Heart disease (8%)
    - Obesity (47.6%)

Perico et al, 2020
Zhou et al, 2020

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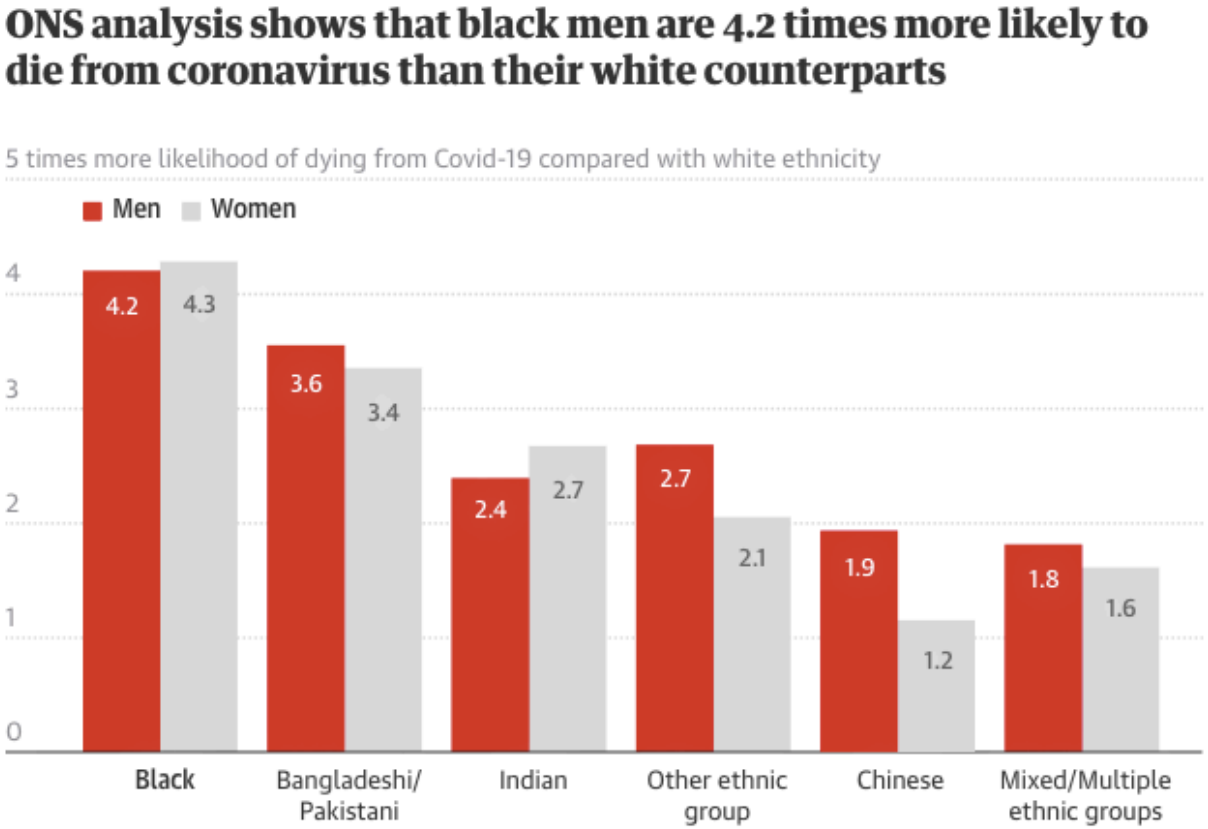
COVID-19: Risk factors



Office for National Statistics UK, 2020

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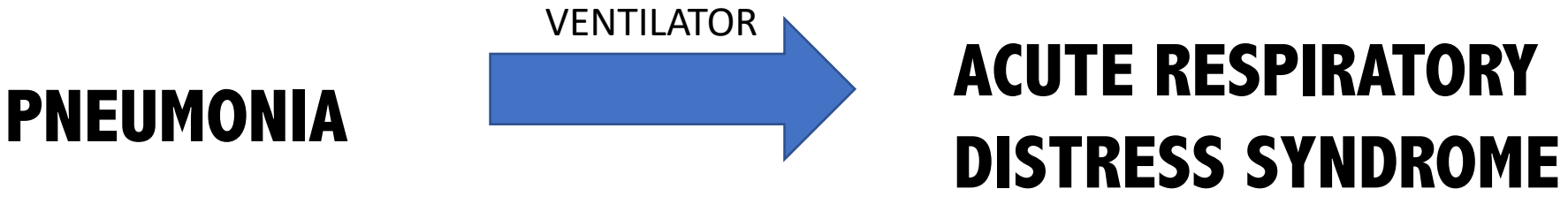
COVID-19: Complications

1. Pneumonia
2. Sepsis
3. Septic shock
4. Acute respiratory distress syndrome (ARDS) (41.8%)
5. Blood clots



Acute respiratory distress syndrome is the primary cause of death in COVID-19 infected patients.

Chaomin et al, 2020

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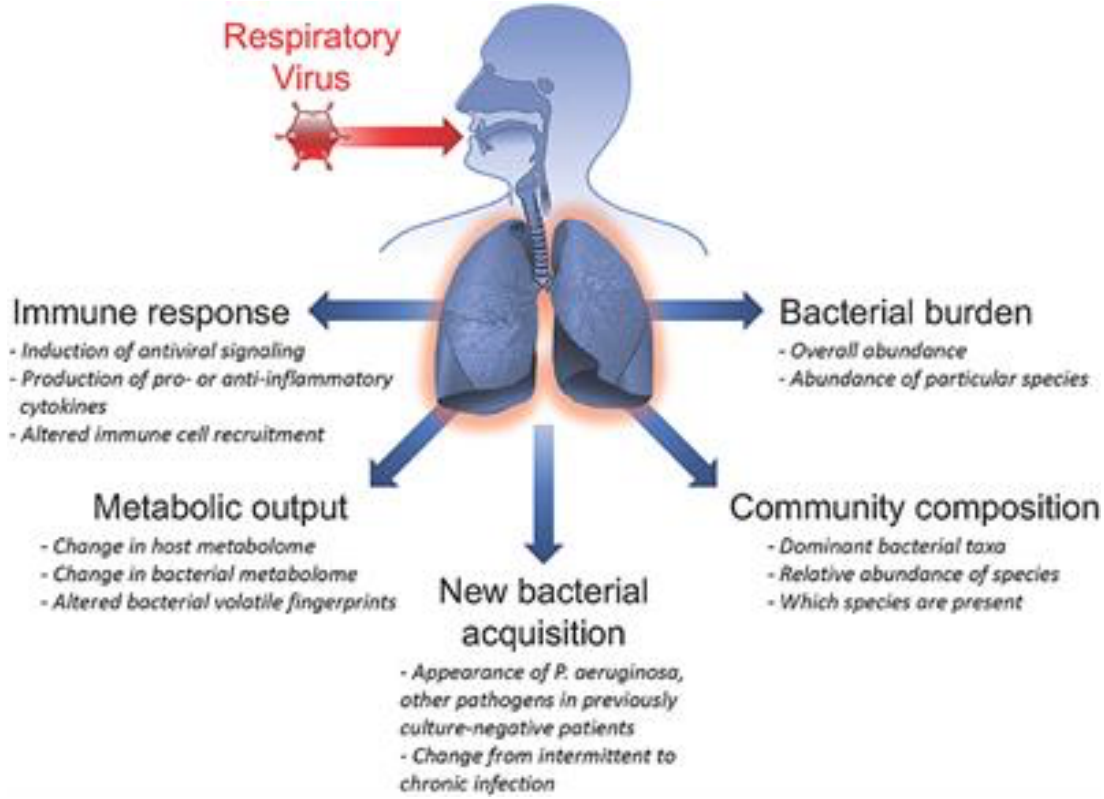
COVID-19: Risk factors

1. Age (mean = 69 years)
2. Gender (70% men)
3. Underlying comorbidity (48% of cases)
    - Hypertension (30%)
    - Diabetes (19%)
    - Heart disease (8%)
    - Obesity (47.6%)



- Oral microbiome/ oral bacterial load

Perico et al, 2020
Zhou et al, 2020

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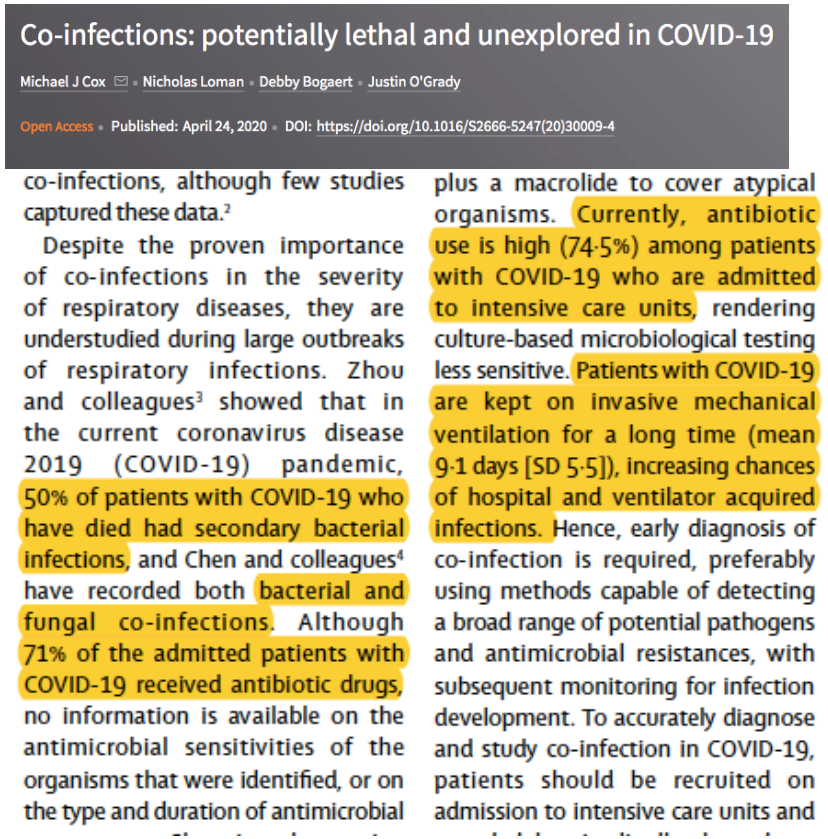
COVID-19: Oral Microbiome

1) Bacterial Superinfections: > 50% COVID-19 patients who die

- Most fatalities in 1918 influenza outbreak due to subsequent bacterial infection
- > 50% of severe COVID-19 patients had secondary bacterial infections when they died
- > 71% admitted into hospital required antibiotics
- 74.5% of patients admitted to ICU required antibiotics



Co-infections: potentially lethal and unexplored in COVID-19

Michael J Cox ✉ • Nicholas Loman • Debby Bogaert • Justin O'Grady

Open Access • Published: April 24, 2020 • DOI: https://doi.org/10.1016/S2666-5247(20)30009-4

co-infections, although few studies captured these data.[2]

Despite the proven importance of co-infections in the severity of respiratory diseases, they are understudied during large outbreaks of respiratory infections. Zhou and colleagues[3] showed that in the current coronavirus disease 2019 (COVID-19) pandemic, 50% of patients with COVID-19 who have died had secondary bacterial infections, and Chen and colleagues[4] have recorded both bacterial and fungal co-infections. Although 71% of the admitted patients with COVID-19 received antibiotic drugs, no information is available on the antimicrobial sensitivities of the organisms that were identified, or on the type and duration of antimicrobial

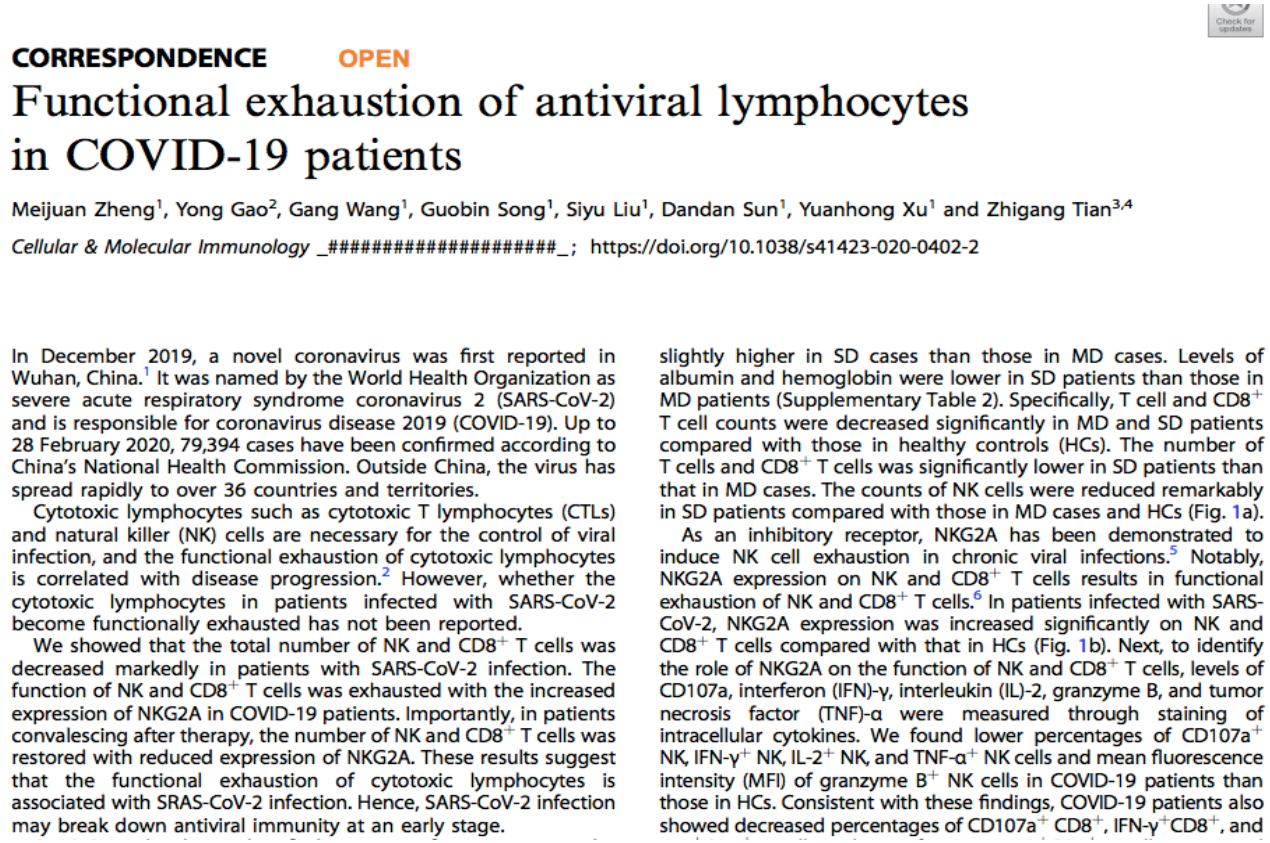
plus a macrolide to cover atypical organisms. Currently, antibiotic use is high (74·5%) among patients with COVID-19 who are admitted to intensive care units, rendering culture-based microbiological testing less sensitive. Patients with COVID-19 are kept on invasive mechanical ventilation for a long time (mean 9·1 days [SD 5·5]), increasing chances of hospital and ventilator acquired infections. Hence, early diagnosis of co-infection is required, preferably using methods capable of detecting a broad range of potential pathogens and antimicrobial resistances, with subsequent monitoring for infection development. To accurately diagnose and study co-infection in COVID-19, patients should be recruited on admission to intensive care units and

Cox et al, 2020

COVID-19: Oral Microbiome

1) Bacterial Superinfections: > 50% COVID-19 patients who die

- Severe COVID-19 patients displayed high neutrophil count and low lymphocyte count
- Mild COVID-19 patients displayed low neutrophil count and high lymphocyte count



CORRESPONDENCE OPEN

Functional exhaustion of antiviral lymphocytes in COVID-19 patients

Meijuan Zheng[1], Yong Gao[2], Gang Wang[1], Guobin Song[1], Siyu Liu[1], Dandan Sun[1], Yuanhong Xu[1] and Zhigang Tian[3,4]

Cellular & Molecular Immunology _####################_; https://doi.org/10.1038/s41423-020-0402-2

In December 2019, a novel coronavirus was first reported in Wuhan, China.[1] It was named by the World Health Organization as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and is responsible for coronavirus disease 2019 (COVID-19). Up to 28 February 2020, 79,394 cases have been confirmed according to China's National Health Commission. Outside China, the virus has spread rapidly to over 36 countries and territories.

Cytotoxic lymphocytes such as cytotoxic T lymphocytes (CTLs) and natural killer (NK) cells are necessary for the control of viral infection, and the functional exhaustion of cytotoxic lymphocytes is correlated with disease progression.[2] However, whether the cytotoxic lymphocytes in patients infected with SARS-CoV-2 become functionally exhausted has not been reported.

We showed that the total number of NK and $CD8^+$ T cells was decreased markedly in patients with SARS-CoV-2 infection. The function of NK and $CD8^+$ T cells was exhausted with the increased expression of NKG2A in COVID-19 patients. Importantly, in patients convalescing after therapy, the number of NK and $CD8^+$ T cells was restored with reduced expression of NKG2A. These results suggest that the functional exhaustion of cytotoxic lymphocytes is associated with SRAS-CoV-2 infection. Hence, SARS-CoV-2 infection may break down antiviral immunity at an early stage.

slightly higher in SD cases than those in MD cases. Levels of albumin and hemoglobin were lower in SD patients than those in MD patients (Supplementary Table 2). Specifically, T cell and $CD8^+$ T cell counts were decreased significantly in MD and SD patients compared with those in healthy controls (HCs). The number of T cells and $CD8^+$ T cells was significantly lower in SD patients than that in MD cases. The counts of NK cells were reduced remarkably in SD patients compared with those in MD cases and HCs (Fig. 1a).

As an inhibitory receptor, NKG2A has been demonstrated to induce NK cell exhaustion in chronic viral infections.[5] Notably, NKG2A expression on NK and $CD8^+$ T cells results in functional exhaustion of NK and $CD8^+$ T cells.[6] In patients infected with SARS-CoV-2, NKG2A expression was increased significantly on NK and $CD8^+$ T cells compared with that in HCs (Fig. 1b). Next, to identify the role of NKG2A on the function of NK and $CD8^+$ T cells, levels of CD107a, interferon (IFN)-γ, interleukin (IL)-2, granzyme B, and tumor necrosis factor (TNF)-α were measured through staining of intracellular cytokines. We found lower percentages of $CD107a^+$ NK, IFN-γ^+ NK, IL-2^+ NK, and TNF-α^+ NK cells and mean fluorescence intensity (MFI) of granzyme B^+ NK cells in COVID-19 patients than those in HCs. Consistent with these findings, COVID-19 patients also showed decreased percentages of $CD107a^+$ $CD8^+$, IFN-γ^+CD8^+, and

Zheng et al, 2020

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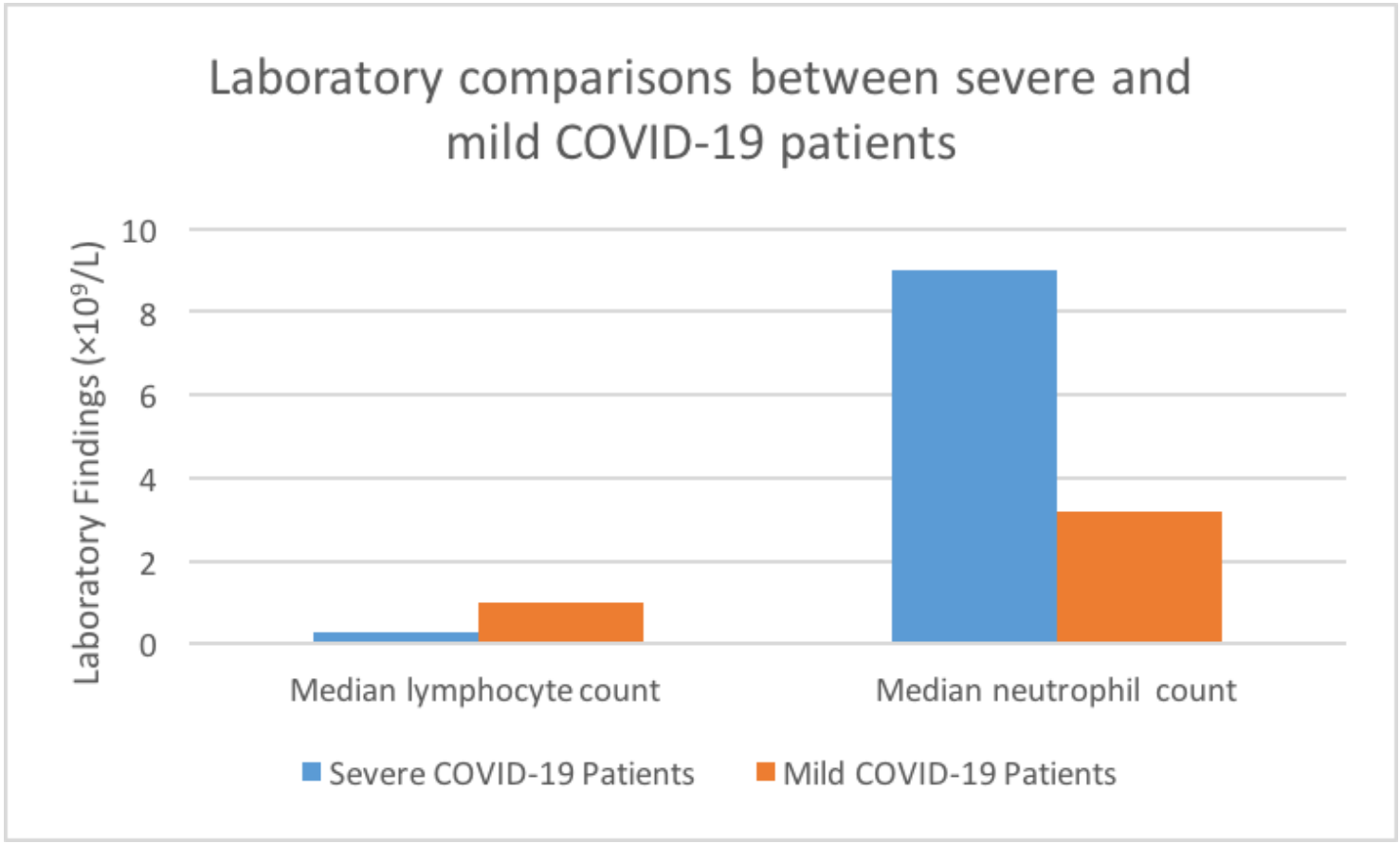
COVID-19: Oral Microbiome

1) Bacterial Superinfections: > 50% COVID-19 patients who die



Chen et al, 2020

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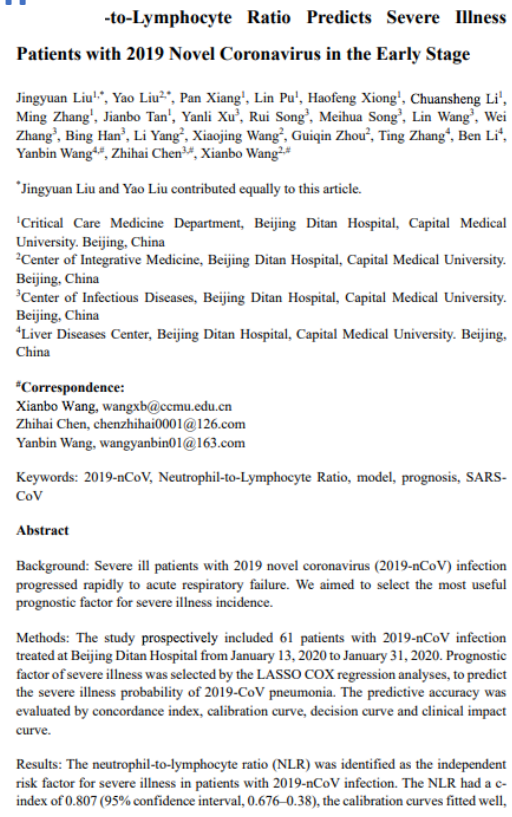
COVID-19: Oral Microbiome

2) Heightened bacterial load during COVID-19 infection

- > 80% of severe COVID-19 patients had high bacterial load
- > 80% required antibiotics to treat bacterial superinfections
- Neutrophil-to-lymphocyte ratio was best predictor of severe COVID-19 infections



-to-Lymphocyte Ratio Predicts Severe Illness Patients with 2019 Novel Coronavirus in the Early Stage

Jingyuan Liu[1,*], Yao Liu[2,*], Pan Xiang[1], Lin Pu[1], Haofeng Xiong[1], Chuansheng Li[1], Ming Zhang[1], Jianbo Tan[1], Yanli Xu[3], Rui Song[3], Meihua Song[3], Lin Wang[3], Wei Zhang[3], Bing Han[3], Li Yang[2], Xiaojing Wang[2], Guiqin Zhou[2], Ting Zhang[4], Ben Li[4], Yanbin Wang[4,#], Zhihai Chen[3,#], Xianbo Wang[2,#]

[*]Jingyuan Liu and Yao Liu contributed equally to this article.

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Zhihai Chen, chenzhihai0001@126.com
Yanbin Wang, wangyanbin01@163.com

Keywords: 2019-nCoV, Neutrophil-to-Lymphocyte Ratio, model, prognosis, SARS-CoV

Abstract

Background: Severe ill patients with 2019 novel coronavirus (2019-nCoV) infection progressed rapidly to acute respiratory failure. We aimed to select the most useful prognostic factor for severe illness incidence.

Methods: The study prospectively included 61 patients with 2019-nCoV infection treated at Beijing Ditan Hospital from January 13, 2020 to January 31, 2020. Prognostic factor of severe illness was selected by the LASSO COX regression analyses, to predict the severe illness probability of 2019-CoV pneumonia. The predictive accuracy was evaluated by concordance index, calibration curve, decision curve and clinical impact curve.

Results: The neutrophil-to-lymphocyte ratio (NLR) was identified as the independent risk factor for severe illness in patients with 2019-nCoV infection. The NLR had a c-index of 0.807 (95% confidence interval, 0.676–0.38), the calibration curves fitted well,

Liu et al, 2020

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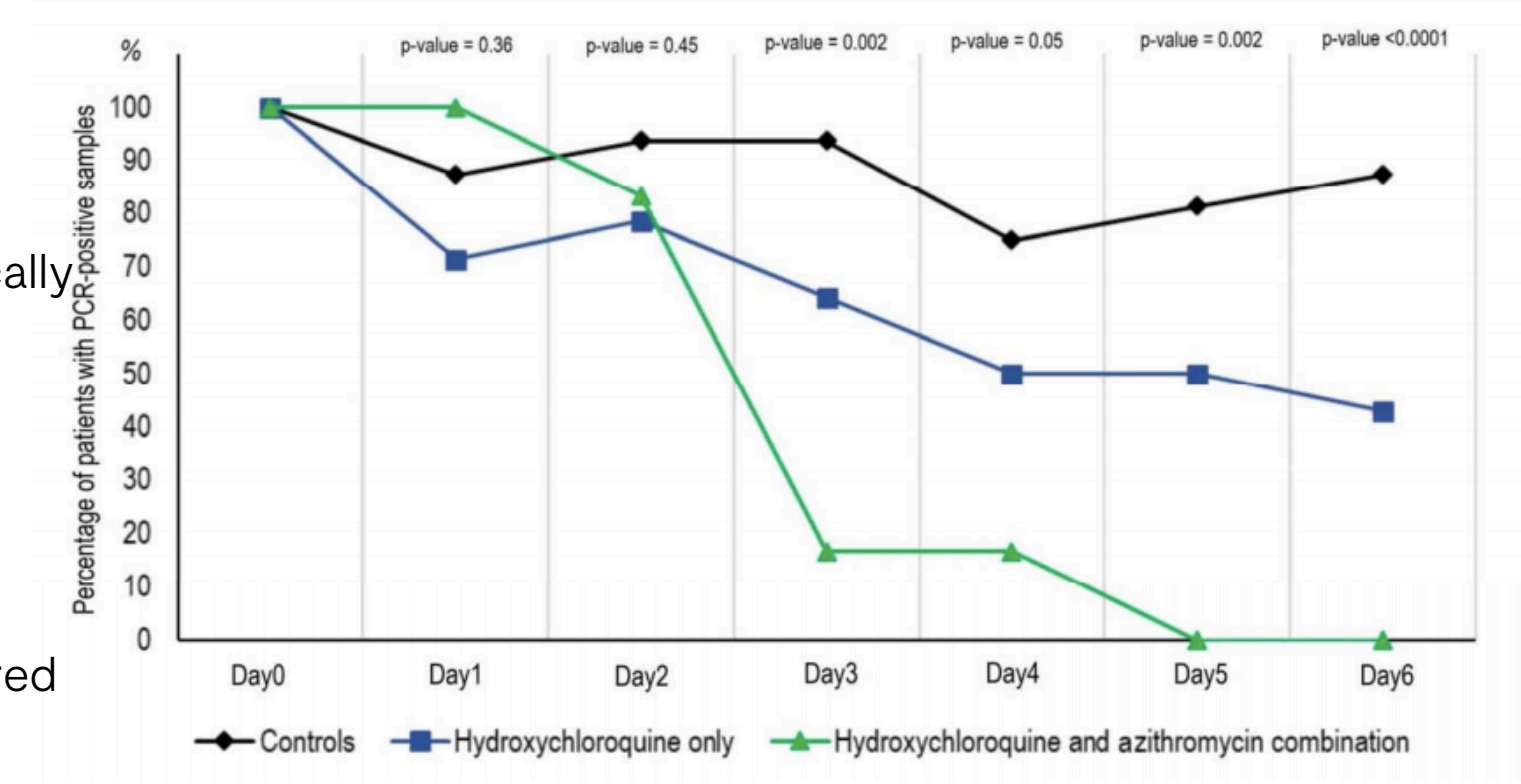
COVID-19: Oral Microbiome

3) Improved treatment outcomes with combination of antiviral and antibiotic

- 100% of patients who had combination of hydroxychloroquine and azithromycin cured virologically after 6 days
- 57.1% of patients who had hydroxychloroquine alone cured after 6 days
- 12.5% of control patients cured virologically after 6 days.



Gautret et al, 2020

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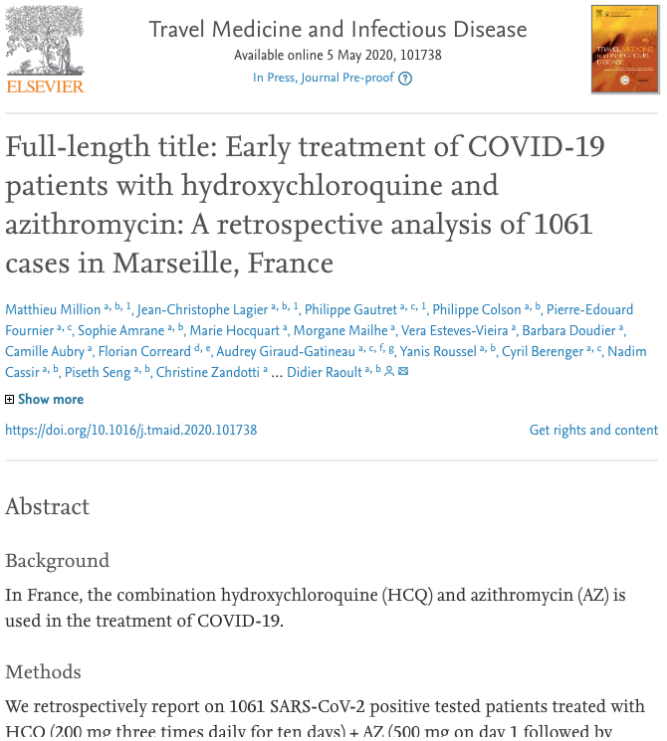
COVID-19: Oral Microbiome

3) Improved treatment outcomes with combination of antiviral and antibiotic

- 91.7% of 1061 patients were virologically cured within 10 days on a combination of antiviral and antibiotic



Travel Medicine and Infectious Disease
Available online 5 May 2020, 101738
In Press, Journal Pre-proof

Full-length title: Early treatment of COVID-19 patients with hydroxychloroquine and azithromycin: A retrospective analysis of 1061 cases in Marseille, France

Matthieu Million [a, b, 1], Jean-Christophe Lagier [a, b, 1], Philippe Gautret [a, c, 1], Philippe Colson [a, b], Pierre-Edouard Fournier [a, c], Sophie Amrane [a, b], Marie Hocquart [a], Morgane Mailhe [a], Vera Esteves-Vieira [a], Barbara Doudier [a], Camille Aubry [a], Florian Correard [d, e], Audrey Giraud-Gatineau [a, c, f, g], Yanis Roussel [a, b], Cyril Berenger [a, c], Nadim Cassir [a, b], Piseth Seng [a, b], Christine Zandotti [a] ... Didier Raoult [a, b]

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https://doi.org/10.1016/j.tmaid.2020.101738

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Abstract

Background

In France, the combination hydroxychloroquine (HCQ) and azithromycin (AZ) is used in the treatment of COVID-19.

Methods

We retrospectively report on 1061 SARS-CoV-2 positive tested patients treated with HCQ (200 mg three times daily for ten days) + AZ (500 mg on day 1 followed by

Million et al, 2020

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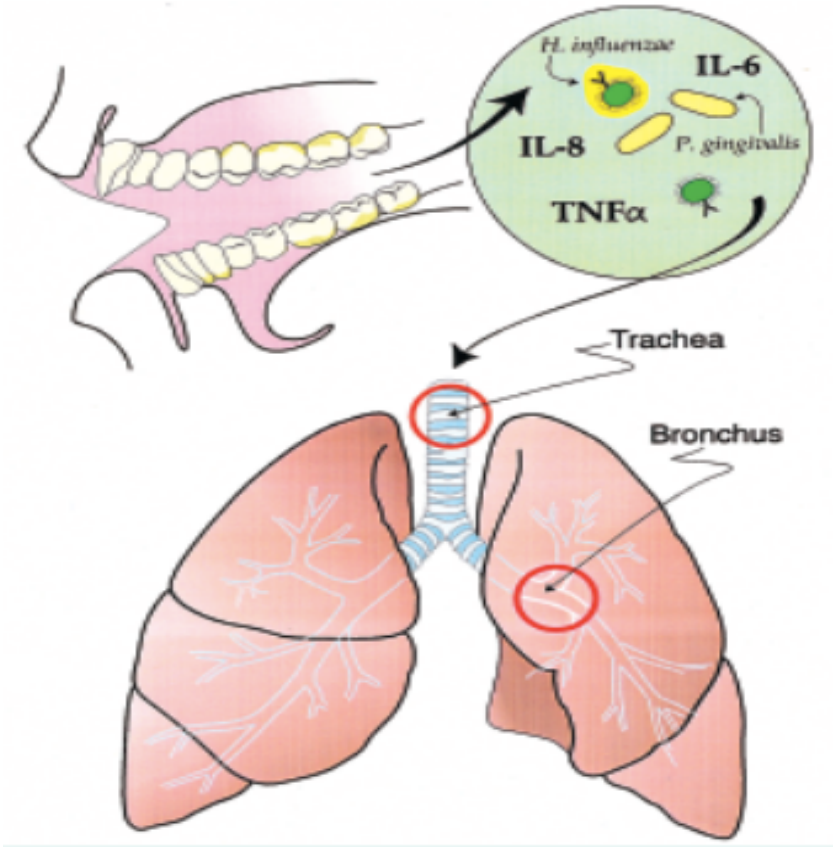
COVID-19: Oral Microbiome

4) Bacterial introduction through the mouth



<u>Mechanisms of oral bacteria introduction</u>

- Aspiration of oral pathogens into lungs
- Periodontal disease-associated enzymes modify oral mucosal surfaces to allow for adhesion and colonization of respiratory pathogens
- Respiratory epithelium altered by periodontal associated cytokines to promote infection by respiratory pathogens

Scannapieco et al, 2020

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COVID-19: Oral Microbiome

4) How do risk factors associated with COVID-19 alter the oral microbiome?

Bacteria in oral biofilm aspirated into respiratory tract help initiate or progress pneumonia or sepsis

- Diabetes, hypertension and heart disease associated with higher numbers of F.nucleatum, P.intermedia and P.gingivalis

- Patients with periodontal disease are at:
  - 25% increased risk cardiovascular disease (DeStefano, 1993) (M Paizan, 2014)
  - x3 risk diabetes mellitus (P. Preshaw 2012)
  - 20% increased risk hypertension (Aguilera et al, 2019)
  - x3 risk of obesity (Vecchia et al, 2004)

Periodontal disease causes systemic inflammation, producing high levels of interleukin 2,6,10
The same inflammatory markers heightened in COVID-19

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COVID-19: Oral Microbiome

5) Periodontal disease and increased risk of respiratory infections

- Reduction of periodontal disease significantly reduces risk of pneumonia
- *P. intermedia* induces severe bacterial pneumonia
- *P. intermedia* enhances adhesion of respiratory pathogens to lower airway cells

the supernatant of PINU499 were significantly lower than that of *S. pneumoniae*-infected mice without PiSup ($P < 0.01$). The survival rates of *S. pneumoniae*-infected mice with *P. gingivalis* supernatant (PgSup) were significantly higher than those of *S. pneumoniae*-infected mice without PgSup ($P < 0.05$), whereas there was no significant difference between the survival rates of *S. pneumoniae*-infected mice with and without *F. nucleatum* supernatant (FnSup).

DISCUSSION

The present study is the first to demonstrate that the products of *P. intermedia* induce severe bacteremic pneumococcal pneumonia as well as the enhancement of pneumococcal adhesion to lower airway cells. Several lines of evidence support this notion.

First, *S. pneumoniae*-infected mice with PiSup exhibited significantly lower survival rates, with earlier increases in *S. pneumoniae* bacterial loads in the lungs, spleen, and blood, than those of *S. pneumoniae*-infected mice without PiSup. Significant increases in inflammatory cytokines were observed in the early phases of *S. pneumoniae*-infected mice with PiSup, indicating the severity of bacteremia compared to that of *S. pneumoniae*-infected mice without PiSup. Although belated bacteremia was observed in *S. pneumoniae*-infected mice without PiSup, a high bacterial load in the lungs was observed only in *S. pneumoniae*-infected mice with PiSup. These data suggest that PiSup enhances *S. pneumoniae* invasion into blood circulation, as well as *S. pneumoniae* adhesion and proliferation in the lungs.

Second, PiSup enhanced pneumococcal adhesion to lower airway cells *in vitro*. We also observed the upregulation of PAFR expression in airway cells upon PiSup stimulation and attenuation of pneumococcal adhesion by CV-3988, suggesting that PiSup enhances pneumococcal adhesion via PAFR up-regulation.

Nagaoka et al, 2020
Yang et al, 2020

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5) Periodontal disease and increased risk of respiratory infections

Table 1: **Bacterial secondary infections in a familial cluster of pneumonia indicating person-to-person transmission [10]** GN=Gram-negative, GP=GP, FAC-ANE=facultatively anaerobic (aerobic, but capable of switching to fermentation if oxygen is absent). Is there a link to anaerobic coinfection (like Prevotella, which is again present here)? Many more species, just listed top 30 here.

NReads	Bacteria	Type	Diseases
16594	Lautropia	GN FAC-ANE	oral cavities of HIV-infected children [11]
14330	Cutibacterium	GP anaerobic	chronic blepharitis and endophthalmitis,
9618	Escherichia	GN FAC-ANE	
5558	Haemophilus	GN FAC-ANE	pneumonia, meningitis and bloodstream infection
4649	Scytonema	cyanobacteria	
3798	Hyphomicrobium	GN aerobic	
3289	Capnocytophaga	GN FAC-ANE	usually occur with dog or cat bites
2440	Burkholderia	GN aerobic	melioidosis [12]
2098	Variovorax	GN aerobic	
1811	Campylobacter	GN aerobic	diarrhoea [7]
1781	Pseudomonas	GN FAC-ANE	
1659	Staphylococcus	FAC-ANE	Boils, impetigo, food poisoning, cellulitis, and toxic shock syndrome
1604	Schaalia	GP aerobic	
1541	Streptococci	GP aerobic	pharyngitis, pneumonia, sepsis, endocarditis, etc
1174	Mycoplasma	Lack a cell wall	respiratory Mycoplasma pneumoniae [13]
1047	Phyllobacterium	GN aerobic	
997	Moraxella	GN aerobic	otitis media in infants and children [14]
940	Flavobacterium	GN aerobic	fish pathogens
931	Bacillus	GP FAC-ANE	Inhalation or respiratory anthrax
659	Neisseria	GN aerobic	infection and persistence in the upper respiratory tract [15]
493	Prevotella	GN anaerobic	aspiration pneumonia, lung abscess, pulmonary empyema, etc
463	Fusobacterium	GN anaerobic	periodontal, tonsillitis, peritonsillar abscess, etc
358	Veillonella	GN anaerobic	rare cases of meningitis, osteomyelitis, and periodontal disease
328	Cupriavidus	GN aerobic	Infection in 87 yr Chinese man [16]
325	Corynebacterium	GP aerobic	diphtheria toxin [17]
318	Sphingomonas	GN aerobic	
314	Micrococcus	GP aerobic	anaphylactoid [18]
307	Loriellopsis	cyanobacteria	
297	Calothrix	cyanobacteria	
281	Lysinibacillus	GP	Sepsis [19]
278	Methylobacterium	GN aerobic	opportunistic pathogens in immunocompromised patients
277	Treponema	?	syphilis, bejel, and yaws

Chakraborty S, 2020

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COVID-19: Oral Microbiome

6) Poor oral hygiene and increased risk of respiratory infections

- Pneumonia is greatest cause of death in patients over 70 (*Takeyoshi et al, 2020)*
- Improved oral care statistically proven **to half the incidence of pneumonia related deaths** in patients over 70 (*Takeyoshi et al, 2020)*
- Improved oral care can significantly reduce incidence of ventilator-associated pneumonia in ICU

(Abe et al, 2006)

- Samples of bronchoalveolar lavages from hospitalized pneumonia patients display microorganisms of denture plaque and periodontal disease *(Quagliarello, V)*
- **One in 10 pneumonia-related deaths in elderly could be prevented by improving oral hygiene**

Sjogren, P 2008

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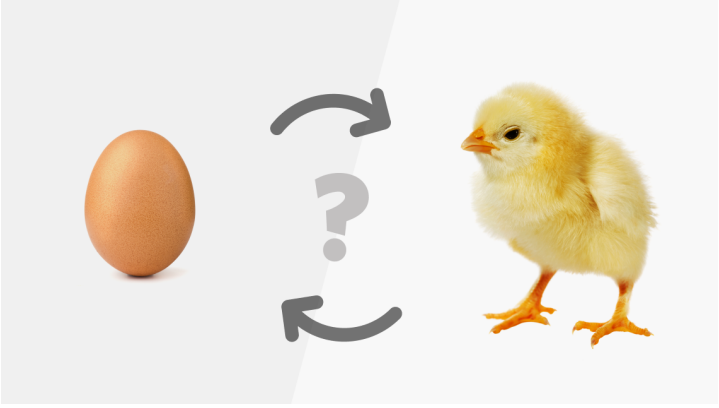
COVID-19: Oral Microbiome

7) Altered gastrointestinal microbiome- an extension of the mouth

Patients hospitalized with severe COVID-19:

- Reduction in commensal bacteria
- Increase in *Clostridia spp, Actinomyces spp, Bacteroides spp, Streptococcus*
- Reduction in *Lactobacilli* and *Bifidobacteria*

Marcialis M, 2020



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COVID-19: Oral Microbiome

7) Recap

- Four main comorbidities associated with increased risk of complications and death from COVID-19 are associated with altered oral biofilms and periodontal disease
- Periodontopathic bacteria are implicated in systemic inflammation, bacteraemia, pneumonia and death
- P.intermedia, a bacteria in periodontally diseased patients can induce severe pneumonia and increase risk of death
- Bacteria present in metagenome of severely infected Covid-19 patients had high levels of oral commensal organisms (P.intermedia)
- > 80% of patients in ICU exhibited high bacterial load, high levels of neutrophils and low levels of lymphocytes
- 74.5% of patients admitted to ICU required antibiotics
- Treatment has been successful with a dual regime of an antiviral and an antibiotic
- The gastrointestinal tract's microbiome is significantly altered in severe cases of COVID-19

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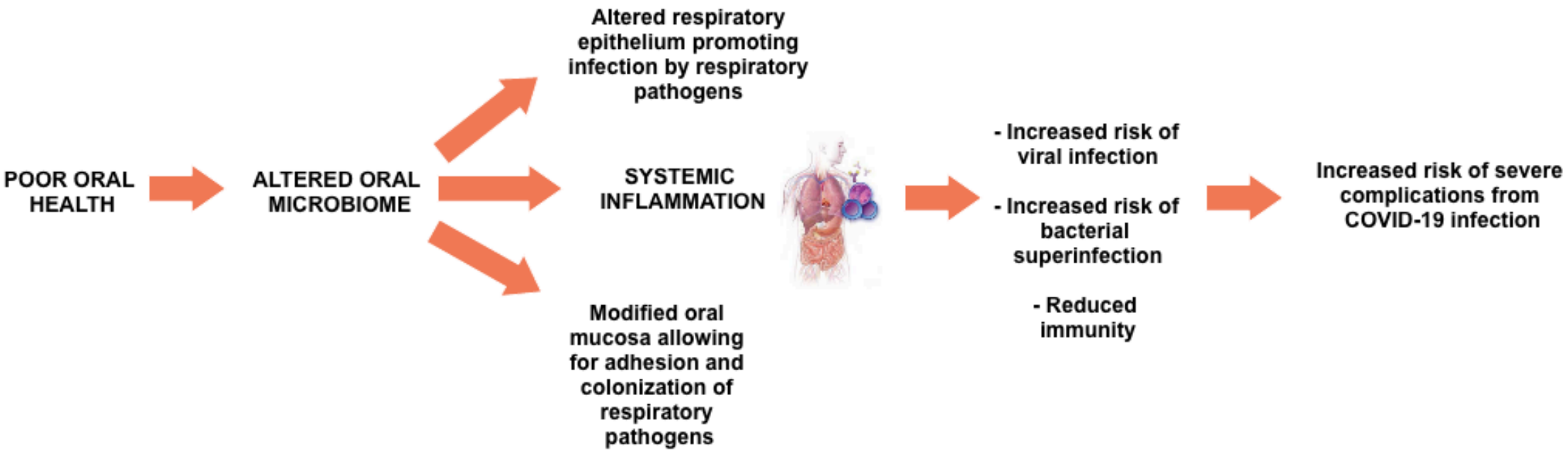
COVID-19: What can we do for patients?

8) Oral hygiene recommendations



V Sampson, 2020

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COVID-19: What can we do for patients?

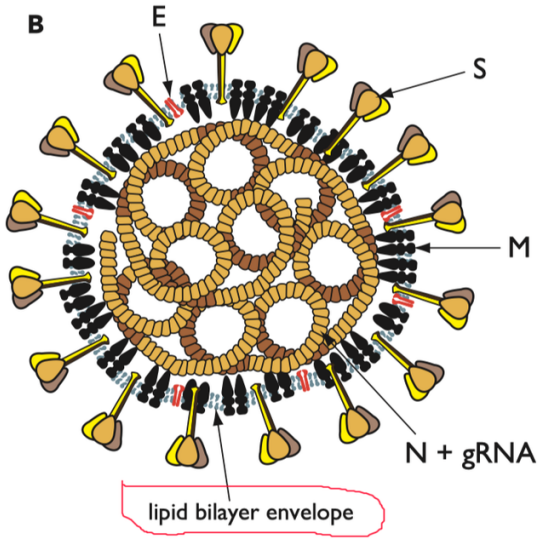
2. Oral hygiene improvement at home:

- Change toothbrush head every 3-4 months
- If patient has had COVID-19, change toothbrush immediately afterwards
- Prescription of high fluoride toothpaste for high risk patients. If patient is shielded or vulnerable, deliver toothpaste
- Interdental cleaning
- Brush twice a day minimum
- Denture hygiene- chemical and mechanical cleaning nightly

COVID-19: What can we do for patients?

2. Oral hygiene improvement at home

- Recommend the use of a toothpaste that contains SLS (Sodium Lauryl Sulfate)



Brushing your teeth could help prevent the spread of coronavirus, a leading dentist has said.

Most toothpastes contain the same detergents as antibacterial hand gels, Professor Martin Addy said. As the virus is most commonly spread by salvia and cough droplets, this could help kill germs before they have a chance to move on, he noted.

He also recommends that health care workers on the frontline of the pandemic brush their teeth before putting on personal protective equipment (PPE).

Prof Addy, emeritus professor of dentistry at the University of Bristol, said: 'From my own knowledge and listening to experts, a major source of droplets are derived from saliva.

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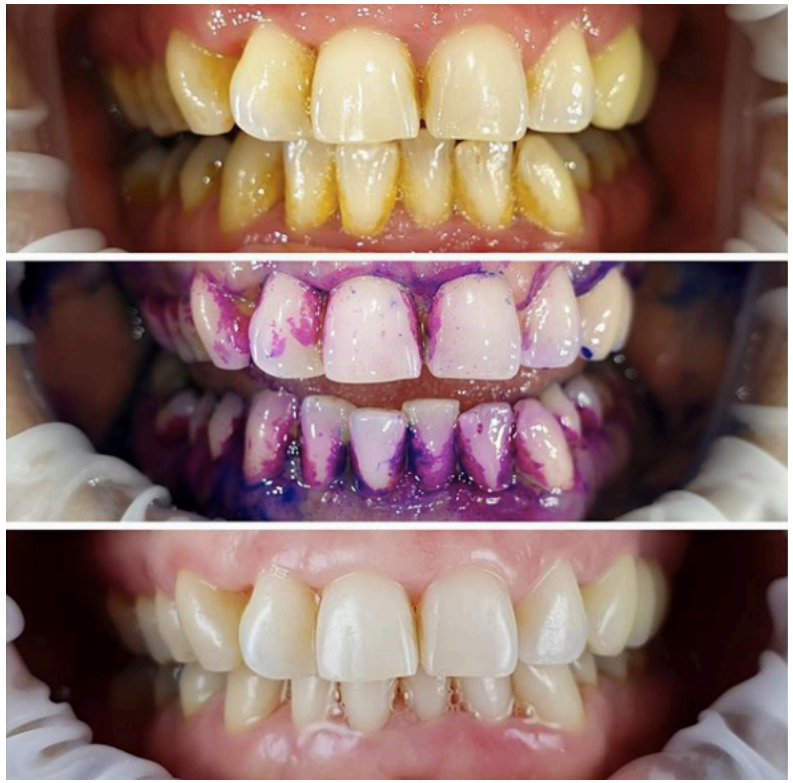
3. Oral risk reduction in the clinic

- Guided Biofilm Therapy for all patients for regular removal of biofilm



EMS, 2020

EMS

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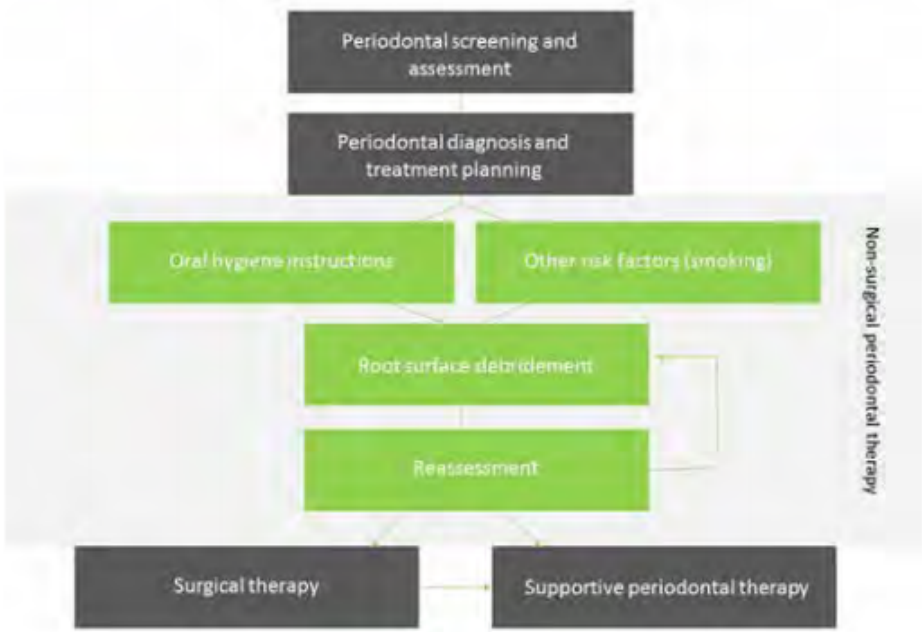
3. Oral risk reduction in the clinic

- Removal of plaque retentive factors (such as poorly done fillings and calculus)
- Non surgical periodontal treatment for patients who have periodontal disease (deep cleaning)
- Management/ removal of modifiable systemic risk factors (smoking, poor diet, stress, obesity, diabetes)



British Society of Periodontics, 2016

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4. Improvement of diet and possible introduction of pre/probiotics?

- Mechanically ventilated patients given probiotics developed less ventilator associated pneumonia deaths

- Preexisting altered gut or oral microbiomes should be corrected/ treated to reduce the risk of dysbiosis during COVID-19 infection and therefore the risk of complications

Webb G, 2020

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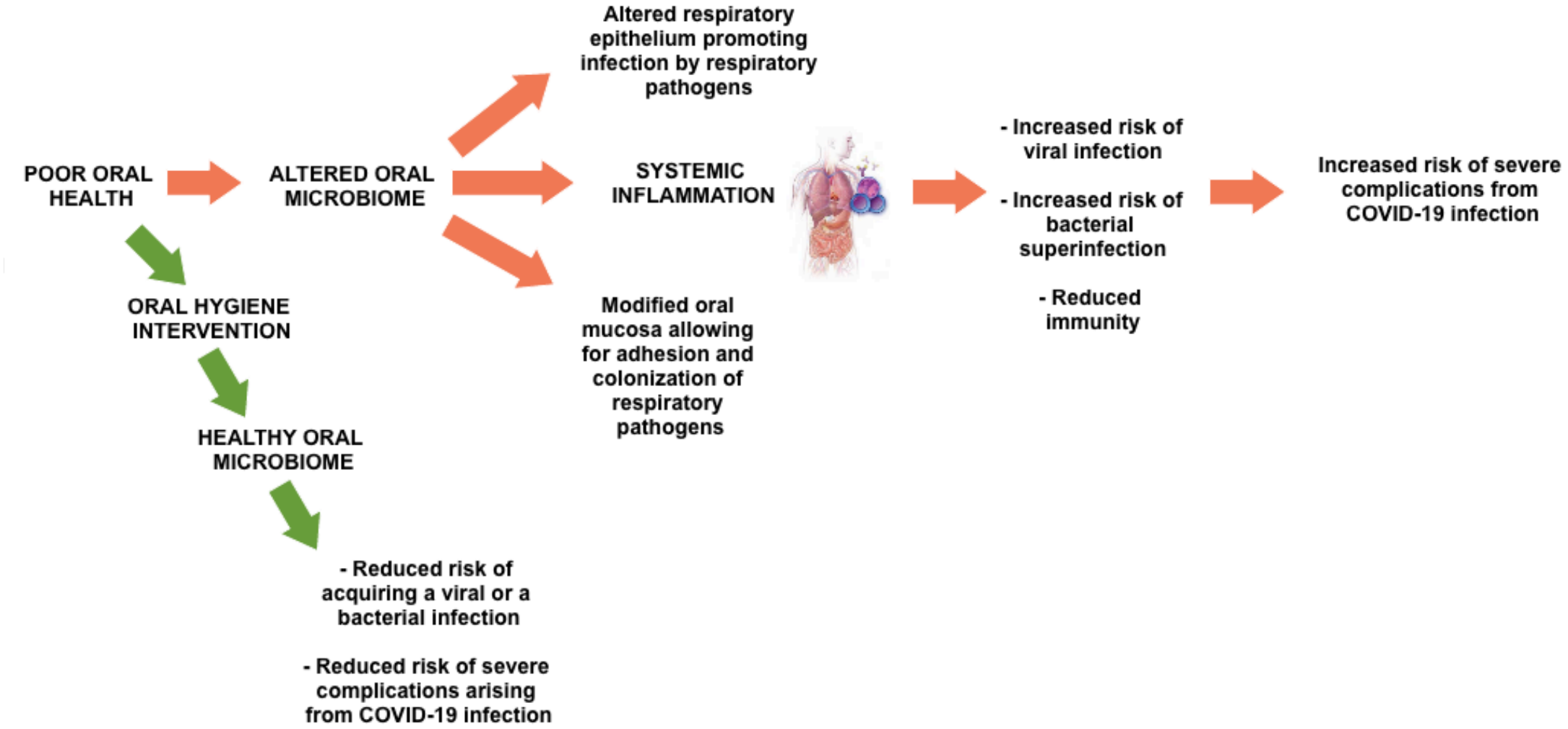

V Sampson, 2020

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References

1. **World Health Organisation. [Online] 2020. https://www.who.int/emergencies/diseases/novel-coronavirus-2019.**
2. *A novel coronavirus from patients with pneumonia in China.* **Zhu, Na, et al. 382, s.l. : New England Journal of Medicine, 2020.**
3. *Angiotensin-converting enzyme 2 (ACE2) as a SARS-CoV-2 receptor: molecular mechanisms and potential therapeutic target.* **Zhang, H. 2020, Intensive Care Medicine.**
4. *Clinical Management of severe acute respiratory infection when novel coronavirus infection is suspected.* **World Health Organization. s.l. : WHO, 2020.**
5. *Early transmission dynamics in wuhan, China, of novel coronavirus infected pneumonia.* **Li, Q. s.l. : New England Journal of Medicine, 2020.**
6. *The epidemiology and pathogenesis of coronavirus disease (COVID-19) outbreak.* **Rothan, Hussin. s.l. : Journal of Autoimmunity, 2020.**
7. *COVID-19 Infection: Implications for Perioperative and Critical Care Physicians.* **Greenland, J, Michelow, M and Wang, L. 2020, Anaesthesiology.**
8. *Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospectove study.* **Zhou, F. s.l. : Lancet, 2020.**
9. *Should COVID-19 Concern Nephrologists? Why and to What Extent? The Emerging Impasse of Angiotensin Blockade.* **Perico, L, Benigni, A and Remuzzi, G. s.l. : Nephron, 2020.**
10. *A pathological report of three COVID-19 cases by minimally invasive autopsies.* **Yao, X and He, Z. s.l. : Zhonghua Bing Li Xue Za Zhi, 2020.**
11. *Risk Factors Associated With Acute Respiratory Distress Syndrome and Death in Patients With Coronavirus Disease 2019 Pneumonia in Wuhan, China.* **Chaomin, Wu. s.l. : JAMA Internal Medicine, 2020.**
12. *Is SARS just ARDS?* **Rubenfield, Gordon. s.l. : American Medical Association, 2016.**
13. *Molecular immune pathogenesis and diagnosis of COVID-19.* **Xiaowei, Li. s.l. : Journal of Pharmaceutical Analysis, 2020.**
14. **Avadhanula, V.** *Respiratory Viruses Augment the Adhesion of Bacterial Pathogens to Respiratory Epithelium in a Viral Species- and Cell Type-Dependent Manner.* s.l. : Journal of Virology.
15. *Infection with human coronavirus NL63 enhances streptococcal adherence to epithelial cells.* **Golda, A. s.l. : Journal of General Virology, 2011.**
16. *Functional exhaustion of antiviral lymphocytes in COVID-19 patients.* **Zheng, M. s.l. : Cellular and molecular immunology, 2020.**
17. **Liu, J.** *Neutrophil-to-Lymphocyte Ratio Predicts Severe Illness Patients with 2019 Novel Coronavirus in the Early Stage.* Critical Care Medicine, Beijing Ditan Hospital. s.l. : Beijing Ditan Hospital, 2020.
18. *Clinical characteristics of 113 deceased patients with coronavirus disease 2019: retrospective study.* **Chen, T. s.l. : British Medical Journal, 2020.**
19. *Covid-19 infection: the perspectives on immune responses.* **Yufang, S. s.l. : Cell Death and Differentiation, 2020.**
20. *A systematic review of the preventative effect of oral hygiene on pneumonia and respiratory tract infection in elderly people in hospitals and nursing homes: effect estimates and methodological quality of randomised controlled trials.* **Sjogren, P. s.l. : Journal of American Geriatric Society, 2008.**
21. *Defining the normal bacterial flora of the oral cavity.* **Jorn, A. s.l. : Journal of Clincial Microbiology, 2005.**
22. *The respiratory tract microbiome and lung inflammation: a two-way street.* **Huffnagle, G, Dickson, R and Lukacs, N. 10, s.l. : Mucosal Immunology, 2017, Vol. 2.**
23. *Role of Oral Bacteria in Respiratory Infection.* **Scannapieco, A. 7, s.l. : Journal of Periodontology, 1999, Vol. 70.**
24. *The Periodontopathic Bacterium Fusobacterium nucleatum Induced Proinflammatory Cytokine Production by Human Respiratory Epithelial Cell Lines and in the Lower Respiratory Organs in Mice.* **Hayata, M, et al. 49, s.l. : Cellular Physiology and Biochemistry, 2019, Vol. 53.**
25. *Can oral bacteria affect the microbiome of the gut?* **Olsen, I. s.l. : Journal of Oral Microbiology, 2019.**
26. *akahashi K, Nishimura F, Kurihara M, et al. Subgingival microflora and antibody responses against periodontal bacteria of young Japanese patients with type 1 diabetes mellitus.* **Takahashi, K. s.l. : Journal of International Academy of Periodontology, 2001.**
27. *Dental disease and the risk of coronary heart disase and mortality.* **DeStefano, F. s.l. : British Medical Journal, 1993.**
28. *Is There an Association between Periodontitis and Hypertension?* **Paizan, Mara. s.l. : Curr Cardiol Rev.**
29. *Periodontitis and diabetes: a two-way relationship.* **Preshaw, P. s.l. : Diabetologia, 2012.**
30. *Periodontitis is associated with hypertension: a systematic review and meta-analysis.* **Aguilera, Eva, et al. 1, s.l. : Cardiovascular Research, 2019, Vol. 116.**
31. **Gong, J.** *Correlation Analysis Between Disease Severity and Inflammation-related Parameters in Patients with COVID-19 Pneumonia.* Department of Integrated Traditional Chinese and Western Medicine,, Tongji Hospital. s.l. : Tongji Hospital, 2020.
32. *Prevotella intermedia Induces Severe Bacteremic Pneumococcal Pneumonia in Mice with Upregulated Platelet-Activating Factor Receptor Expression.* **Nagaoka, K. s.l. : American Society for Microbiology, 2014.**
33. *Oral care reduces pneumonia in older patietns in nursing homes.* **Yoneyama, Takeyoshi. s.l. : The American Geriatric Society, 2002.**
34. *Professional oral care reduced influenza infection in elderly.* **Abe, S, et al. 43, s.l. : Arch Gerentol Geriatr, 2006.**
35. *Modifiable risk factors for nursing home-acquired pneumonia.* **Quagliarello, V. s.l. : Clin Infect Dis, 2005.**
36. *Bronchopneumonia and oral health in hospitalised older patients .* **Imsand, M. s.l. : British Society of Gerodontology, 2008.**
37. *Oral Care reduced incidence of ventilator associate pneumonia in ICU populations.* **Mori, H. s.l. : Intensive Care Journal, 2005.**
38. *Hydroxychloroquine and azithromycin as a treatment of COVID-19: results of an open-label non-randomized clinical trial.* **Gautret. s.l. : International Journal of Antimicrobial Agents, 2020.**
39. **Chakraborty, S.** *Metagenome of SARS-Cov2 patients in Shenzhen with travel to Wuhan shows a wide range of species - Lautropia, Cutibacterium, Haemophilus being most abundant - and Campylobacter explaining diarrhea.* s.l. : OSF Preprints, 2020.

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Oral hygiene and COVID-19

Is there a link?

Thank you for listening

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