

A SELECTION OF TEN READINGS ON TOPICS RELATED TO FAMILY MEDICINE IN 2023 AND BEYOND

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Selection of readings made by A/Prof Goh Lee Gan

READING 1 – CONCISE REVIEW OF COVID-19 VACCINES

Samaranayake LP,¹ Seneviratne CJ,² Fakhruddin KS.³ Coronavirus disease 2019 (COVID-19) vaccines: A concise review. Oral Dis. 2022 Nov;28 Suppl 2:2326-2336. PMID: 33991381.

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ABSTRACT

The development of a successful vaccine against severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), the agent of coronavirus disease 2019 (COVID-19), in an unmatched period of 10 months, is a tribute to human ingenuity in the face of a vicious pandemic. A return to pre-pandemic "normalcy" depends on the successful delivery of the vaccine to a majority (~70 percent) so as to develop herd immunity critical to arrest the community spread of infection. Vaccination against COVID-19 is particularly important for dentistry as the dental team works in an environment replete with aerosol-generating procedures (AGP) that facilitate virus spread. Hence, a COVID-19 vaccine is likely to be an obligatory requirement for dental practice, and the latest addition to the extensive list of vaccines required for dental professionals for the safe delivery of dental care. Here, we review the currently available major candidate vaccines against SARS-CoV-2 and their benefits and risks. These include the vaccines developed on next-generation platforms (mRNA, DNA, and viral vector vaccines), and the classic platforms (the live-attenuated virus, and the protein subunit vaccines). The review concludes with a summary of impending issues and challenges facing the provision of COVID-19 vaccines for all stakeholders in dentistry.

READING 2 – OMICRON COVID-19 VARIANT

Chia TRT,¹ Young BE,¹ Chia PY.¹ The Omicron-transformer: Rise of the subvariants in the age of vaccines. Ann Acad Med Singap. 2022 Nov;51(11):712-729. doi: 10.47102/annals-acadmedsg.2022294.

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ABSTRACT

INTRODUCTION: Omicron is the latest SARS-CoV-2 variant of concern, the pathogen that causes COVID-19. Since its emergence in late 2021, Omicron has displaced other circulating variants and caused successive waves of infection worldwide throughout 2022. Omicron is characterised by the rapid emergence of many subvariants and high rates of infection in people with vaccine- and/or infection-induced immunity. This review article will consolidate current knowledge regarding Omicron subvariants, the role of boosters, and future vaccine development.

METHOD: This narrative review is based on a literature search using PubMed. Search terms related to Omicron were used and priority was given to published peer-reviewed articles over pre-prints.

RESULTS: Studies indicate that vaccinations and boosters are important to reduce disease severity, hospitalisation, and death from Omicron. A variety of factors, such as differing host factors, circulating variants, and forces of infection, can influence the benefit of repeated booster administration. Next-generation bivalent vaccines have now been approved in some countries including Singapore and have demonstrated the ability to induce broad variant protection. Future third-generation vaccines involving mucosal vaccines and/or pan-sarbecovirus vaccines may provide broader and longer-lasting protection.

CONCLUSION: Due to current high levels of vaccine- and infection-induced immunity, it is likely that rates of severe illness, hospitalisation, and death due to Omicron will continue to moderate. Nevertheless, the virus is ever-changing, and public health policies, especially those related to vaccinations, will also have to continually evolve and adapt as COVID-19 transitions to endemicity.

READING 3 – PUBLIC ACCEPTABILITY OF COVID-19 CONTROL MEASURES IN SINGAPORE, HONG KONG, AND MALAYSIA

Voo TC,¹ Ballantyne A,² Ng CJ,³ Cowling BJ,⁴ Xiao J,⁵ Phang KC,⁶ Kaur S,⁷ Jenarun G,⁸ Kumar V,⁹ Lim JM,⁹ Tun ZM,⁹ Wong NCB,⁹ Tam CC.¹⁰ Public acceptability of COVID-19 control measures in Singapore, Hong Kong, and Malaysia: A cross-sectional survey. *Int J Infect Dis.* 2022 Jul;120:51-58. doi: 10.1016/j.ijid.2022.04.021. Epub 2022 Apr 14.

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ABSTRACT

BACKGROUND: Several countries have implemented control measures to limit the spread of SARS-CoV-2, including digital contact tracing, digital monitoring of quarantined individuals, and testing of travellers. These raise ethical issues around privacy, personal freedoms, and equity. However, little is known regarding public acceptability of these measures.

METHODS: In December 2020, we conducted a survey among 3,635 respondents in Singapore, Hong Kong, and Malaysia to understand public perceptions on the acceptability of COVID-19 control measures.

FINDINGS: Hong Kong respondents were much less supportive of digital contact tracing and monitoring devices than those in Malaysia and Singapore. Around three-quarters of Hong Kong respondents perceived digital contact tracing as an unreasonable restriction of individual freedom; <20 percent trusted that there were adequate local provisions preventing these data being used for other purposes. This was the opposite in Singapore, where nearly 3/4 of respondents agreed that there were adequate data protection rules locally. In contrast, only a minority of Hong Kong respondents viewed mandatory testing and vaccination for travellers as unreasonable infringements of privacy or freedom. Less than 2/3 of respondents in all territories were willing to be vaccinated against COVID-19, with a quarter of respondents undecided. However, support for differential travel restrictions for vaccinated and unvaccinated individuals was high in all settings.

INTERPRETATION: Our findings highlight the importance of sociopolitical context in public perception of public health measures and emphasise the need to continually monitor public attitudes toward such measures to inform implementation and communication strategies.

READING 4 – COPING WELL WITH COVID-19 – LESSONS LEARNED

Kim J,^{#,1} Moon J,^{#,1} Yoo HC,¹ Jung TY,² Kim W.³ Why Have the Republic of Korea, Taiwan, and Singapore Coped Well with COVID-19 and What Are the Lessons Learned from Their Experiences? *Yonsei Med J.* 2022 Mar;63(3):296-303. doi: 10.3349/ymj.2022.63.3.296.

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ABSTRACT

This study investigated how three Asian countries-Republic of Korea (ROK), Republic of China (Taiwan), and Singapore-considered as standouts, responded to the coronavirus disease 2019 (COVID-19) in terms of governance system, health sector innovation, and social distancing to draw lessons that other countries can learn from.

The countries were commonly in success of the response in early stage of the pandemic thanks to their effective and efficient strategies paired with advanced information and communications technology (ICT). Consequently, the three jurisdictions reported lower confirmed cases as well as fatality rate of the infectious disease compared to other high-income countries. In addition, the countries' previous experiences with other pandemics, including influenza A, Middle East respiratory syndrome, and severe acute respiratory syndrome enabled them to establish resilient public health systems and gain public acceptance to governmental control or surveillance during national infectious disease-related crises outbreaks.

Advanced ICT infrastructure and digital technology were used as effective tools for testing, tracing, and treatment of the pandemic in collaboration with the private sector as a crucial player.

The ROK, Taiwan, and Singapore adopted different strategies between containment and mitigation policy to flatten the epidemic curves effectively according to their own situation and judgement.

Despite the exemplary aspect of the three nations in coping with the COVID-19 pandemic, a few limitations were also observed in terms of vaccination and unequal consequences of the pandemic among people. These should be further discussed in order to be prepared for future pandemics.

READING 5 – SHOULD FRAIL OLDER ADULTS BE VACCINATED? RESULTS OF SINGAPORE STUDY

Gao J,¹ Lun P,¹ Ding YY,¹ George PP.¹ COVID-19 Vaccination for Frail Older Adults in Singapore – Rapid Evidence Summary and Delphi Consensus Statements. *J Frailty Aging.* 2022;11(2):236-241. doi: 10.14283/jfa.2022.12.

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ABSTRACT

OBJECTIVE: This study aimed to synthesise available evidence on the effectiveness and safety of COVID-19 vaccines for frail older adults through a rapid review, supplemented with geriatricians' consensus statements.

METHODS: References were identified through MEDLINE and Web of Science on 1 February 2021 using relevant terms related to COVID-19, vaccine, and older adults. Searches were also conducted on reference lists of review articles and Google Scholar. The content was updated on 8 April via hand searching. We included studies on Phase III randomised controlled trials and data from real world administration of vaccines. A two-round Delphi study was conducted with 15 geriatricians to elicit their thoughts and recommendations regarding COVID-19 vaccination for frail older adults.

RESULTS: Five Phase III randomised controlled efficacy trials reported vaccine efficacy ranging from 66.7 percent to 95 percent among participants aged 16 to 95. The vaccine efficacy for participants aged 65 and above is 94.7 percent and 86.4 percent for Pfizer-BioNTech and Moderna respectively. Sputnik V reported a vaccine efficacy of 91.8 percent for participants 60 and above. Serious adverse events were reported by 0.27-1 percent of participants who received at least one dose of the four vaccines. For the Delphi study, 16 out of 24 statements achieved consensus. The Delphi panel opined that

frail or very old adults, except those with limited life expectancy, should be vaccinated due to their vulnerability. They also agree that vaccination decisions should be made by patients when possible, with the involvement of next-of-kin should the frail older adult be unable to do so. Lastly, the panel thought that frail older adults should be included in future clinical trials.

CONCLUSION: In early clinical trials, there is paucity of evidence on efficacy and safety of current COVID-19 vaccines among frail older adults. Geriatricians' consensus indicate that frail older adults should be vaccinated except where life expectancy is limited. Future trials assessing efficacy and safety should include frail older adults.

READING 6 – ADOPTION OF PREVENTIVE BEHAVIOUR STRATEGIES DURING COVID-19 IN SINGAPORE

Ozdemir S,¹ Ng S,¹ Chaudhry I,¹ Finkelstein EA.¹ Adoption of Preventive Behaviour Strategies and Public Perceptions About COVID-19 in Singapore. *Int J Health Policy Manag.* 2022 May 1;11(5):579-591. doi: 10.34172/ijhpm.2020.199.

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ABSTRACT

BACKGROUND: The unprecedented severity of coronavirus disease 2019 (COVID-19) constitutes a serious public health concern. However, adoption of COVID-19-related preventive behaviours remain relatively unknown. This study investigated predictors of preventive behaviours.

METHODS: An analytical sample of 897 Singaporean adults who were quota sampled based on age, gender, and ethnicity were recruited through a web-enabled survey. Outcomes were adoption, or increased frequency, of preventive behaviours (avoiding social events; avoiding public transport; reducing time spent shopping and eating out; wearing a mask in public; avoiding hospitals/clinics; keeping children out of school; washing hands/using sanitisers; keeping surroundings clean; avoiding touching public surfaces; working from/studying at home). Public perceptions regarding COVID-19 (chances of getting COVID-19; perceived likelihood of COVID-19-related intensive care unit (ICU) admission; government trust; self-efficacy; perceived appropriateness of COVID-19 behaviours; response efficacy), anxiety, and demographic characteristics (age; ethnicity; marital status; education; chronic conditions; current living arrangements) were investigated as predictors of preventive behaviours adopted during COVID-19 in binomial and ordered logistic regressions.

RESULTS: Though adoption of preventive behaviours among Singaporeans varied, it was, overall, high, and consistent with government recommendations. Nearly a quarter reported moderate to severe anxiety (General Anxiety Disorder 7-item – GAD-7 scores). Respondents who perceived higher COVID-19 risks had higher government trust, higher self-efficacy, and perceived that others acted appropriately reported increased adoption/frequency of preventive measures. The strongest indicator of behavioural change was response efficacy. Respondents who were older, highly educated, anxious, and married reported higher adoption/frequency of preventive measures.

CONCLUSION: To successfully influence appropriate preventive behaviours, public health messages should highlight response efficacy, increase self-efficacy, and promote trust in governmental response. The focus should be on demographic segments with low adoptions, such as younger individuals and those with low education.

READING 7 – FACTORS ASSOCIATED WITH COVID-19 VACCINATION INTENT IN SINGAPORE, AUSTRALIA, AND HONG KONG

Shah S,¹ Gui H,¹ Chua PEY,² Tan JB,³ Suen LK,⁴ Chan SW,⁵ Pang J.⁶ Factors associated with COVID-19 vaccination intent in Singapore, Australia and Hong Kong. Vaccine. 2022 May 9;40(21):2949-2959. doi: 10.1016/j.vaccine.2022.03.062. Epub 2022 Apr 5.

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ABSTRACT

BACKGROUND: The COVID-19 pandemic has caused significant morbidity and mortality globally. As vaccines have been developed under expedited conditions, their safety and efficacy are being questioned by some populations leading to vaccine hesitancy, resulting in delayed vaccine uptake and herd immunity. This study aims to adopt a combination of Health Belief Model and other independent risk factors associated with high vaccine acceptance.

METHODS: An anonymised cross-sectional survey was distributed between 15 January and 3 February 2021 across Singapore, Hong Kong, and Australia among adult respondents through a certified online panel. Exploratory factor analysis and confirmatory factor analysis were carried out to assess perception constructs followed by multivariate regression modelling to assess factors associated with high vaccine acceptance against SARS-CoV-2.

RESULTS: A total of 3,133 anonymised participants from Singapore (n = 1,009), Australia (n = 1,118) and Hong Kong (n = 1,006) completed the survey. While age and gender were not significantly associated, Asian ethnicity, current smokers, and self-efficacy were significant associated factors of increased vaccine acceptance. While specific practices like taking micronutrients more frequently and cleaning and disinfecting their house more often were positively associated with increased vaccine acceptance, seeking medical help for COVID-19 symptoms like loss of smell/taste and overall COVID-19 knowledge score were negatively associated. Increased likelihood of vaccine acceptance was seen among those that obtained COVID-19 information less frequently and used digital media or non-health-related sources such as influencers as a source of information. Among the eight perception constructs, perceived susceptibility and perceived response efficacy were positively associated, while perceived barriers were negatively associated with high vaccine acceptance.

CONCLUSION: While demographic parameters have weak association with vaccine acceptance, perceptions and practice parameters can help to better understand and influence vaccine acceptance. Study findings should provide guidance on the risk communication strategy to enhance vaccine acceptance for vaccination and boosters against new SARS-CoV-2 variants.

READING 8 – MYOCARDITIS FOLLOWING COVID-19 VACCINATION

Lee ASY,¹ Balakrishnan IDD,² Khoo CY,² Ng CT,² Loh JX,² Chan LL,² Teo LLY,² Sim DKL.² Myocarditis Following COVID-19 Vaccination: A Systematic Review (October 2020-October 2021). *Heart Lung Circ.* 2022 Jun;31(6):757-765. doi: 10.1016/j.hlc.2022.02.002. Epub 2022 Feb 25.

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ABSTRACT

INTRODUCTION: Reports of SARS-CoV-2 coronavirus (COVID-19) vaccine-related myocarditis, particularly after mRNA vaccines, have raised concerns amongst the general public. This review examined the literature regarding myocarditis post-COVID-19 vaccination, drawing from vaccine safety surveillance databases and case reports.

METHODS: Combinations of search terms were used in PubMed and COVID-19-specific repositories – LitCovid and the Cochrane COVID-19 Study Register – between 1 October 2020 and 31 October 2021. Manual searches of GoogleScholar and screening of article bibliographies were also performed.

RESULTS: Information was obtained from five vaccine safety surveillance databases. Fifty-two (52) case reports totalling 200 cases of possible COVID-19 vaccine-related myocarditis were summarised. Vaccine surveillance databases differed in reporting formats and vaccination rates; however, gross estimates suggested low overall incidence rates of 2-5 per million mRNA vaccines. The incidence appeared to be higher in younger male populations, with onset of symptoms within a few days, usually after the second dose. Some with prior COVID-19 infections had onset after the first dose. Cases with prior unrelated myocarditis were also noted. Almost all presented with chest pain (98.0 percent). Troponin elevation was universally described and cardiac magnetic resonance imaging was commonly reported based on the updated Lake Louise criteria. Clinical course was mild in the majority, with response to anti-inflammatory treatment.

CONCLUSION: COVID-19 vaccine-related myocarditis is an important but rare adverse event. More research is needed into its pathogenesis and reasons for its predominance in young males, while gaps in data exist in those aged <16 years, as well as those with prior COVID-19 infections and prior myocarditis.

READING 9 – COVID-19 VACCINE ACCEPTANCE AND HESITANCY

Koh SWC,^{1,2} Liow Y,^{3,4} Loh VWK,⁴ Liew SJ,⁴ Young D,⁴ Chan YH.⁵ COVID-19 vaccine acceptance and hesitancy among primary healthcare workers in Singapore. *BMC Prim Care.* 2022 Apr 15;23(1):81. doi: 10.1186/s12875-022-01693-z.

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ABSTRACT

BACKGROUND: Factors affecting COVID-19 vaccine acceptance and hesitancy among primary healthcare workers (HCW) remain poorly understood. This study aims to identify factors associated with vaccine acceptance and hesitancy among HCW.

METHODS: A multi-centre online cross-sectional survey was performed across six primary care clinics from May to June 2021, after completion of staff vaccination exercise. Demographics, profession, years working in healthcare, residential status, presence of chronic medical conditions, self-perceived risk of acquiring COVID-19, and previous influenza vaccination were collected. HCW who accepted vaccine were then asked to rank their top five reasons for vaccine acceptance; HCW who were vaccine hesitant had to complete the 15-item 5C scale on psychological antecedents of vaccination.

RESULTS: Five hundred fifty seven out of 1,182 eligible HCW responded (47.1 percent). Twenty-nine were excluded due to contraindications. Among 528 respondents, vaccine acceptance rate was 94.9 percent (n = 501). There were no statistically significant differences in COVID-19 vaccine acceptance between sex, age, ethnicity, profession, number of years in healthcare, living alone, presence of chronic diseases, self-perceived risk, or previous influenza vaccination. The top three reasons for COVID-19 vaccine acceptance ranked by 501 HCW were to protect their family and friends, protect themselves from COVID-19, and due to high risk of acquiring COVID-19 because of their jobs. HCW with suspected or confirmed COVID-19 exposure were 3.4 times more likely to rank "high risk at work" as one of the top reasons for vaccine acceptance ($\chi^2 = 41.9$, $p < 0.001$, OR = 3.38, 95 percent CI 2.32-4.93). High mean scores of "Calculation" (5.79) and low scores for "Constraint" (2.85) for 5C components among vaccine hesitant HCW (n = 27) highlighted that accessibility was not a concern; HCW took time to weigh vaccine benefits and consequences.

CONCLUSION: COVID-19 vaccine hesitancy is a minute issue among Singapore primary HCW, having achieved close to 95 percent acceptance rate. COVID-19 exposure risk influences vaccine acceptance; time is required for HCW to weigh benefits against the risks. Future studies can focus on settings with higher hesitancy rates, and acceptance of booster vaccinations with the emergence of delta and omicron variants.

READING 10 – FATIGUE AND COGNITIVE IMPAIRMENT IN POST-COVID-19 SYNDROME

Ceban F,¹ Ling S,² Di Vincenzo JD,² Lui LMW,³ Gill H,³ Teopiz KM,³ Rodrigues NB,³ Subramaniapillai M,³ Lee Y,⁴ Cao B,⁵ Lin K,⁶ Mansur RB,⁷ Ho RC,⁸ Rosenblat JD,⁹ Miskowiak KW,¹⁰ Vinberg M,¹¹ Maletic V,¹² McIntyre RS.¹³ Fatigue and cognitive impairment in Post-COVID-19 Syndrome: A systematic review and meta-analysis. *Brain Behav Immun.* 2022 Mar;101:93-135. doi: 10.1016/j.bbi.2021.12.020. Epub 2021 Dec 29.

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ABSTRACT

IMPORTANCE: COVID-19 is associated with clinically significant symptoms despite resolution of the acute infection (i.e., post-COVID-19 syndrome). Fatigue and cognitive impairment are amongst the most common and debilitating symptoms of post-COVID-19 syndrome.

OBJECTIVE: To quantify the proportion of individuals experiencing fatigue and cognitive impairment 12 or more weeks following COVID-19 diagnosis, and to characterise the inflammatory correlates and functional consequences of post-COVID-19 syndrome.

DATA SOURCES: Systematic searches were conducted without language restrictions from database inception to 8 June 2021 on PubMed/MEDLINE, The Cochrane Library, PsycInfo, Embase, Web of Science, Google/Google Scholar, and select reference lists.

STUDY SELECTION: Primary research articles that evaluated individuals at least 12 weeks after confirmed COVID-19 diagnosis and specifically reported on fatigue, cognitive impairment, inflammatory parameters, and/or functional outcomes were selected.

DATA EXTRACTION & SYNTHESIS: Two reviewers independently extracted published summary data and assessed methodological quality and risk of bias. A meta-analysis of proportions was conducted to pool Freeman-Tukey double arcsine transformed proportions using the random-effects restricted maximum-likelihood model

MAIN OUTCOMES & MEASURES: The co-primary outcomes were the proportions of individuals reporting fatigue and cognitive impairment, respectively, 12 or more weeks following COVID-19 infection. The secondary outcomes were inflammatory correlates and functional consequences associated with post-COVID-19 syndrome.

RESULTS: The literature search yielded 10,979 studies, and 81 studies were selected for inclusion. The fatigue meta-analysis comprised 68 studies, the cognitive impairment meta-analysis comprised 43 studies, and 48 studies were included in the narrative synthesis. Meta-analysis revealed that the proportion of individuals experiencing fatigue 12 or more weeks following COVID-19 diagnosis was 0.32 (95 percent CI, 0.27, 0.37; $p < 0.001$; $n = 25,268$; $I^2 = 99.1$ percent). The proportion of individuals exhibiting cognitive impairment was 0.22 (95 percent CI, 0.17, 0.28; $p < 0.001$; $n = 13,232$; $I^2 = 98.0$). Moreover, narrative synthesis revealed elevations in proinflammatory markers and considerable functional impairment in a subset of individuals.

CONCLUSIONS & RELEVANCE: A significant proportion of individuals experience persistent fatigue and/or cognitive impairment following resolution of acute COVID-19. The frequency and debilitating nature of the foregoing symptoms provides the impetus to characterise the underlying neurobiological substrates and how to best treat these phenomena.