

## A SELECTION OF TEN READINGS ON TOPICS RELATED TO PANDEMIC TO ENDEMIC, MYTHS, LONG COVID, AND VACCINE HESITANCY

FPSCI 23 – SATURDAY, 05 OCT 2024: 2.00pm – 5.30pm  
All are available as PMC free full text

Selection of readings made by A/Prof Goh Lee Gan

### READING 1 – IMPACT OF COVID-19 ON CARDIOVASCULAR DISEASE

Vosko I,<sup>1</sup> Zirlik A,<sup>1</sup> Bugger H.<sup>1</sup> Impact of COVID-19 on Cardiovascular Disease. *Viruses*. 2023 Feb 11;15(2):508.

doi: 10.3390/v15020508. PMID: 36851722.

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#### ABSTRACT

Coronavirus disease 2019 (COVID-19) is a viral infection with the novel severe acute respiratory distress syndrome corona virus 2 (SARS-CoV-2). To date, more than 670 million people have suffered from COVID-19 worldwide, and roughly 7 million death cases were attributed to COVID-19. Recent evidence suggests an interplay between COVID-19 and cardiovascular disease (CVD). COVID-19 may serve as a yet underappreciated CVD risk modifier, including risk factors such as diabetes mellitus or arterial hypertension. In addition, recent data suggest that previous COVID-19 may increase the risk for many entities of CVD to an extent similarly observed for traditional cardiovascular (CV) risk factors. Furthermore, increased CVD incidence and worse clinical outcomes in individuals with preexisting CVD have been observed for myocarditis, acute coronary syndrome, heart failure (HF), thromboembolic complications, and arrhythmias. Direct and indirect mechanisms have been proposed by which COVID-19 may impact CVD and CV risk, including viral entry into CV tissue or by the induction of a massive systemic inflammatory response. In the current review, we provide an overview of the literature reporting an interaction between COVID-19 and CVD, review potential mechanisms underlying this interaction, and discuss preventive and treatment strategies and their interference with CVD that were evaluated since the onset of the COVID-19 pandemic.

### READING 2 – COVID-19 UPDATE 2023

Biancolella M,<sup>#,1</sup> Colona VL,<sup>#,2</sup> Luzzatto L,<sup>#,3,4</sup> Mattiuz G,<sup>4</sup> Watt JL,<sup>5</sup> Conticello SG,<sup>6,7</sup> Kaminski N,<sup>8</sup> Mehriani-Shai R,<sup>9</sup> Ko AI,<sup>10,11</sup> Gonsalves GS,<sup>12</sup> Vasilioiu V,<sup>13</sup> Novelli G,<sup>#,14-16</sup> Reichardt JKV.<sup>#,17</sup> COVID-19 annual update: a narrative review. *Hum Genomics*. 2023 Jul 24;17(1):68.

doi: 10.1186/s40246-023-00515-2. PMID: 37488607.

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## ABSTRACT

Three and a half years after the pandemic outbreak, with WHO having formally declared the emergency over, COVID-19 is still a significant global issue. Here, we focus on recent developments in genetic and genomic research on COVID-19, and we give an outlook on state-of-the-art therapeutical approaches, as the pandemic is gradually transitioning to an endemic situation.

The sequencing and characterisation of rare alleles in different populations has made it possible to identify numerous genes that affect either susceptibility to COVID-19 or the severity of the disease. These findings provide a beginning to new avenues and pan-ethnic therapeutic approaches, as well as to potential genetic screening protocols. The causative virus, SARS-CoV-2, is still in the spotlight, but novel threatening virus could appear anywhere at any time. Therefore, continued vigilance and further research is warranted.

We also note emphatically that to prevent future pandemics and other worldwide health crises, it is imperative to capitalise on what we have learnt from COVID-19: specifically, regarding its origins, the world's response, and insufficient preparedness. This requires unprecedented international collaboration and timely data sharing for the coordination of effective response and the rapid implementation of containment measures.

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## **READING 3 – GEOEPIDEMIOLOGICAL PERSPECTIVE OF COVID-19 PANDEMIC**

**Vallée A.<sup>1</sup> Geoepidemiological perspective on COVID-19 pandemic review, an insight into the global impact. *Front Public Health*. 2023 Oct 19;11:1242891.**

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## ABSTRACT

The COVID-19 pandemic showed major impacts, on societies worldwide, challenging healthcare systems, economies, and daily life of people. Geoepidemiology, an emerging field that combines geography and epidemiology, has played a vital role in understanding and combatting the spread of the virus. This interdisciplinary approach has provided insights into the spatial patterns, risk factors, and transmission dynamics of the COVID-19 pandemic at different scales, from local communities to global populations. Spatial patterns have revealed variations in incidence rates, with urban-rural divides and regional hotspots playing significant roles. Cross-border transmission has highlighted the importance of travel restrictions and coordinated public health responses. Risk factors such as age, underlying health conditions, socioeconomic factors, occupation, demographics, and behaviour have influenced vulnerability and outcomes. Geoepidemiology has also provided insights into the transmissibility and spread of COVID-19, emphasising the importance of asymptomatic and pre-symptomatic transmission, super-spreading events, and the impact of variants. Geoepidemiology should be vital in understanding and responding to evolving new viral challenges of this and future pandemics.

#### READING 4 – INTERACTIONS BETWEEN COVID-19 AND DIABETES

Heshmati HM.<sup>1</sup> Interactions between COVID-19 infection and diabetes. *Front Endocrinol (Lausanne)*. 2024 Jan 10;14:1306290.

doi: 10.3389/fendo.2023.1306290. PMID: 38292772.

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#### ABSTRACT

At the start of 2020, the Coronavirus disease 2019 (COVID-19) caused a major pandemic affecting human health and economy around the world. The virus responsible for the disease is "severe acute respiratory syndrome coronavirus 2" (SARS-CoV-2). It invades the target cells by binding to angiotensin-converting enzyme 2 (ACE2). ACE2 is expressed in several organs including endocrine glands. Multiple endocrine and metabolic systems including the endocrine pancreas have been impacted by COVID-19. COVID-19 can promote obesity through alterations in lifestyle (e.g., unhealthy diet and reduced physical activity due to confinement and isolation) leading to type 2 diabetes and/or can directly impair the function of the endocrine pancreas particularly through a cytokine storm, promoting or aggravating type 1 or type 2 diabetes. The increased ACE2 receptors of high adiposity commonly associated with type 2 diabetes and the chronic hyperglycaemia of diabetes with its negative impact on the immune system can increase the risk of COVID-19 infection and its morbidity/mortality. In conclusion, there are bidirectional interactions between COVID-19 and diabetes (e.g., COVID-19 infection can impact diabetes and diabetes can impact COVID-19 infection). The services offered by healthcare systems for the management of diabetes have been adapted accordingly.

#### READING 5 – COVID-19 PANDEMIC MAY RESULT IN RISE OF DIABETES PANDEMIC

Conte C,<sup>1,2</sup> Cipponeri E,<sup>2</sup> Roden M,<sup>3-5</sup> Diabetes Mellitus, Energy Metabolism, and COVID-19. *Endocr Rev*. 2024 Mar 4;45(2):281-308. PMID: 37934800.

doi: 10.1210/edrv/bnad032. PMID: 37934800.

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#### ABSTRACT

Obesity, diabetes mellitus (mostly type 2), and COVID-19 show mutual interactions because they are not only risk factors for both acute and chronic COVID-19 manifestations, but also because COVID-19 alters energy metabolism. Such metabolic alterations can lead to dysglycaemia and long-lasting effects. Thus COVID-19 has the potential to cause a further rise of the diabetes pandemic. This review outlines how preexisting metabolic alterations spanning from excess visceral adipose tissue to hyperglycaemia and overt diabetes may exacerbate COVID-19 severity. We also summarise the different effects of SARS-CoV-2 infection on the key organs and tissues orchestrating energy metabolism, including adipose tissue, liver, skeletal muscle, and pancreas. Lastly, we provide an integrative view of the metabolic derangements that occur during COVID-19. Altogether, this review allows for better understanding of the metabolic derangements occurring when a fire starts from a small flame, thereby help reducing the impact of COVID-19.

## READING 6 – NUTRITIONAL DEFICIENCIES THAT MAY PREDISPOSE TO LONG COVID

Schloss JV.<sup>1</sup> Nutritional deficiencies that may predispose to long COVID. *Inflammopharmacology*. 2023 Apr;31(2):573-583. PMID: 36920723.

doi: 10.1007/s10787-023-01183-3. PMID: 36920723.

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### ABSTRACT

Multiple nutritional deficiencies (MND) confound studies designed to assess the role of a single nutrient in contributing to the initiation and progression of disease states. Despite the perception of many healthcare practitioners, up to 25 percent of Americans are deficient in five or more essential nutrients. Stress associated with COVID-19 further increases the prevalence of deficiency states. Viral infections compete for crucial nutrients with immune cells. Viral replication and proliferation of immunocompetent cells critical to the host response require these essential nutrients, including zinc. Clinical studies have linked levels of more than 22 different dietary components to the likelihood of COVID-19 infection and the severity of the disease. People at higher risk of infection due to MND are also more likely to have long-term sequelae, known as Long COVID.

## READING 7 – VIRAL PERSISTANCE, REACTIVATION, AND MECHANISMS OF LONG COVID

Chen B,<sup>1</sup> Julg B,<sup>2</sup> Mohandas S,<sup>3</sup> Bradfute SB<sup>4</sup>; RECOVER Mechanistic Pathways Task Force. *Viral persistence, reactivation, and mechanisms of long COVID*. *Elife*. 2023 May 4;12:e86015. PMID: 37140960.

doi: 10.7554/eLife.86015. PMID: 37140960.

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### ABSTRACT

COVID-19 caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection has infected hundreds of millions of individuals. Following COVID-19 infection, a subset can develop a wide range of chronic symptoms affecting diverse organ systems referred to as post-acute sequelae of SARS-CoV-2 infection (PASC), also known as long COVID. A National Institutes of Health-sponsored initiative, RECOVER: Researching COVID to Enhance Recovery, has sought to understand the basis of long COVID in a large cohort. Given the range of symptoms that occur in long COVID, the mechanisms that may underlie these diverse symptoms may also be diverse. In this review, we focus on the

emerging literature supporting the role(s) that viral persistence or reactivation of viruses may play in PASC. Persistence of SARS-CoV-2 RNA or antigens is reported in some organs, yet the mechanism by which they do so and how they may be associated with pathogenic immune responses is unclear. Understanding the mechanisms of persistence of RNA, antigen, or other reactivated viruses and how they may relate to specific inflammatory responses that drive symptoms of PASC may provide a rationale for treatment.

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## READING 8 – COVID-19 VACCINE DEVELOPMENT

**Excler JL,<sup>1</sup> Saville M,<sup>2</sup> Privor-Dumm L,<sup>3</sup> Gilbert S,<sup>4</sup> Hotez PJ,<sup>5</sup> Thompson D,<sup>6</sup> Abdool-Karim S,<sup>7</sup> Kim JH.<sup>8,9</sup> Factors, enablers and challenges for COVID-19 vaccine development. *BMJ Glob Health*. 2023 Jun;8(6):e011879. PMID: 37277195.**

**doi: 10.1136/bmjgh-2023-011879. PMID: 37277195.**

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### ABSTRACT

The COVID-19 pandemic triggered a sense of vulnerability and urgency that led to concerted actions by governments, funders, regulators, and industries to overcome traditional challenges for the development of vaccine candidates and to reach authorisation. Unprecedented financial investments, massive demand, accelerated clinical development, and regulatory reviews were among the key factors that contributed to accelerating the development and approval of COVID-19 vaccines. The rapid development of COVID-19 vaccines benefited from previous scientific innovations such as mRNA and recombinant vectors and proteins. This has created a new era of vaccinology, with powerful platform technologies and a new model for vaccine development. The lessons learnt highlight the need for strong leadership, to bring together governments, global health organisations, manufacturers, scientists, private sectors, civil societies, and philanthropy, to generate innovative, fair, and equitable access mechanisms to COVID-19 vaccines for populations worldwide and to build a more efficient and effective vaccine ecosystem to prepare for other pandemics that might emerge. With a longer-term view, new vaccines must be developed with incentives to build expertise for manufacturing that can be leveraged for low/middle-income countries and other markets to ensure equity in innovation, access, and delivery. The creation of vaccine manufacturing hubs with appropriate and sustained training, in particular in Africa, is certainly the way of the future to a new era of public health to safeguard the health and economic security of the continent and guarantee vaccine security and access, with the need for such capacity to be sustained in the interpandemic period.

## READING 9 – POST-PANDEMIC STRATEGIES FOR DEVELOPMENT AND APPROVAL OF COVID-19 VACCINES AND THERAPEUTICS

**Ao D,<sup>#,1</sup> He X,<sup>#,1</sup> Liu J,<sup>1</sup> Xu L.<sup>2</sup> Strategies for the development and approval of COVID-19 vaccines and therapeutics in the post-pandemic period. *Signal Transduct Target Ther.* 2023 Dec 21;8(1):466. PMID: 38129394.**

**doi:10.1038/s41392-023-01724-w. PMID: 38129394.**

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### ABSTRACT

The spread of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) resulted in significant casualties and put immense strain on public health systems worldwide, leading to economic recession and social unrest. In response, various prevention and control strategies were implemented globally, including vaccine and drug development and the promotion of preventive measures. Implementing these strategies effectively curbed the transmission of the virus, reduced infection rates, and gradually restored normal social and economic activities. However, the mutations of SARS-CoV-2 have led to inevitable infections and reinfections, and the number of deaths continues to rise. Therefore, there is still a need to improve existing prevention and control strategies, mainly focusing on developing novel vaccines and drugs, expediting medical authorisation processes, and keeping epidemic surveillance. These measures are crucial on combatting the Coronavirus disease (COVID-19) and achieve sustained, long-term prevention, management, and disease control. Here, we summarise the characteristics of existing COVID-19 vaccines and drugs and suggested potential future directions for their development. Furthermore, we discuss the COVID-19-related policies implemented over the past years and present some strategies for the future.

## READING 10 – ACCEPTANCE OF COVID-19 VACCINATION INCREASED WILLINGNESS TO ACCEPT OTHER VACCINES

**Kłoda K,<sup>1</sup> Mierzecki A,<sup>2</sup> Mastalerz-Migas A,<sup>3</sup> Babicki M.<sup>3</sup> Beneficial effects of SARS-CoV-2 vaccination resulting from the COVID-19 pandemic with regard to the uptake of influenza virus, pneumococcal, and herpes zoster adult vaccination - a narrative literature review. *Ann Agric Environ Med.* 2023 Dec 22;30(4):587-594. PMID: 38153058.**

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### ABSTRACT

**INTRODUCTION AND OBJECTIVE:** Analysis of factors influencing COVID-19 vaccination coverage in various countries raised the question whether the recent pandemic affected the vaccination rates of other pathogens in adults. Therefore, the aim of this review article was to analyse the literature to find potentially beneficial effects of the introduction of the large-scale vaccinations resulting from the COVID-19 pandemic, with regards to the influenza virus, pneumococcal, and herpes zoster adult vaccinations, in order to identify factors and strategies to increase the uptake of these vaccines.

**REVIEW METHODS:** The review of the literature was based on scientific articles indexed in the PubMed Database published between 2022-2023, during the COVID-19 pandemic. Data search was performed from 24-30 July 2023.

**BRIEF DESCRIPTION OF THE STATE OF KNOWLEDGE:** It was found that the COVID-19 pandemic has had a beneficial effect on the acceptance and coverage of influenza and pneumococcal vaccination in the vulnerable elderly populations, and among healthcare workers in the case of influenza. Furthermore, the COVID-19 outbreak affected the designs of vaccine clinical trials, resulting in a lower frequency of age-related exclusion criteria, broadening the group of vaccine recipients.

SUMMARY: Acceptance of COVID-19 vaccination increased willingness to accept other vaccines. The attitude to vaccination is a personal decision-making process based on previous experience and interpersonal interactions, greatly affected by information and recommendation from medical professionals. The COVID-19 pandemic vaccination implementation opened new opportunities to develop prevention efforts and build vaccination strategies in middle-income countries.