Nigeria Immunization Technical Advisory Group (NGI-TAG)

Interim Recommendations on the Use of COVID-19 Vaccines in Nigeria

Should the COVID-19 vaccines be introduced for use among targeted Nigerian populace? If so, which COVID vaccines should the country introduce? What groups should be prioritized to receive the vaccines first?

Contents

Acronyms

ACRONYMS	DEFINITIONS
ACE	Angiotensin Converting Enzyme
ADE	Antibody Dependent Enhancement
AEFI/AESI	Adverse Events Following Immunization
AFENET	African Field Epidemiological Network
ARDS	Acute Respiratory Distress Syndrome
BMGF	Bill and Melinda Gates Foundation
CEPI	Coalition for Epidemic Preparedness Innovations
CHAI	Clinton Health Access Initiative
DCL/IVAC	Direct Consulting and Logistics/International Vaccines Access Centre
DHS	Demographic and Health Survey
DM	Diabetes Miletus
ECG	Electrocardiogram
EOC	Emergency Operations Centre
EPI	Expanded Program on Immunization
ESRD	End-Stage Renal Disease
EUA	Emergency Use Assessment
EUL	Emergency Use Listing
FMoH	Federal Ministry of Health
GAVI	Global Alliance on Vaccines and Initiative
HCWs	Health Care Workers
HICs	High Income Countries
HIV	Human Immunodeficiency Virus
HRF	Hypoxemic Respiratory Failure
ICU	Intensive Care Unit
LMICs	Low-Middle Income Countries
MERS	Middle East Respiratory Syndrome
MICS/NICS	Multiple Indicator Cluster Survey/National Immunization Coverage Survey
MIS-C	Multisystem Inflammatory Syndrome in Children
MoF	Ministry of Finance
mRNA	Messenger RNA
NAAT	Nucleic Acid Amplification Test
NAFDAC	National Agency for Food and Drug Administration
NBS	National Bureau of Statistics
NCDC	National Center for Disease Control
NGI-TAG	National Immunization Technical Advisory Group
NLPS	National Longitudinal Phone Survey
NPHCDA	National Primary Health Care Development Agency
NPIs	Non-Pharmaceutical Interventions
PEG	Polyethylene Glycol
PICO	Population, Intervention, Comparator, and Outcomes Format
PPE	Personal Protective Equipment
PTF	Presidential Task Force
RBD	Receptor Binding Domain

RDT	Rapid Diagnostic Test
RNA	Ribonucleic Acid
RSA	Republic of South Africa
SAGE	WHO Strategic Advisory Group of Experts on Immunization
SARS	Severe Acute Respiratory Syndrome
SARS CoV2	Severe Acute Respiratory Syndrome Coronavirus 2
SOP	Standard Operating Procedure
SORMAS	Surveillance Outbreak Response Management & Analysis System
UCC	Ultra-Cold Chain
UK	United Kingdom
UNICEF	United Nations International Children Emergency Funds
USA	United States of America
WB	World Bank
WG	Working Group
WHO	World Health Organization

Executive Summary

Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), the causative virus of COVID-19 disease, has caused a pandemic of a proportion only seen over a century ago when the Spanish flu ravaged the world in 1918. This virus causes an acute respiratory syndrome with varying involvement of other organ systems. The case fatality rates vary across nations and do clearly correlate with the health systems capacities in the different regions. Similarly, the transmissibility has been significantly different, with the USA, UK, Brazil, and Europe having the highest proportion of transmission and fatalities. No one is immune from being infected by this virus. However, it is noteworthy that adults, mainly those aged 50 years and above, have been the most vulnerable to this viral infection and children are mostly asymptomatic or display mild symptoms of the disease.

The first case of COVID-19, in Nigeria, imported from Italy, was confirmed on 27th February 2020. Subsequently, there was an increasing number of COVID-19 cases with the peak of the first wave at 790 cases on 1 July 2020 and the current surge as high as 2,314 on January 22, 2021, with total confirmed cases of 143,516 and total deaths of 1,710, as of February 12, 2021. These figures are a significant underestimation due to sub-optimal testing of the population for COVID-19. Lagos State remains the epicenter with almost a third of the country's total number of cases, but there has been progressive spread to all the other states of the country. The rapid rate of spread during the present resurgence (second wave) in many countries, including Nigeria, has been alarming. There has been a significant fatality among the frontline health workers, including Nigeria. The case fatality rate (CFR) of COVID-19 in Nigeria is 1.2%.

COVID-19 is a disease that is still being studied with several unanswered questions. While it is now known that the immunological and inflammatory responses in the pathophysiology of the disease are the core drivers of the severity of the illness, controlling these have been more problematic in individuals with pre-existing morbidities. The various pharmaceutical measures to prevent and/or cure the disease have not produced total and prompt elimination of SARS CoV2. Still, the prompt institution of dexamethasone and anti-coagulants beneficially modulate the severity of the disease. Various other pharmaceutical and phytopharmaceutical agents, including but not limited to the antiviral drug, remdesivir, and Ivermectin are being evaluated for the management of this disease. However, what have proven to be beneficial in limiting the transmission of the disease thus far are the non-pharmaceutical measures including, the use of face mask, social distancing, handwashing and other physical barrier methods.

As a result, the world is forced to turn again to the proven means of preventing infection: vaccination. I In an unprecedented move the global community of researchers backed by government and industry has produced several safe and effective vaccines in less than one year. Vaccines usually take 5 - 10 years to acquire the WHO prequalification license for public use. Therefore, the global community must choose between the raging COVID-19 disease fatalities and the associated fatalities due to financial and economic derailments and accepting to apply these vaccines. Therefore, the vaccines are being evaluated for Emergency Use Authorization (EUA) by the WHO.

The Federal Ministry of Health has alerted on the health care system's imminent lack of capacity to cope with the fast-growing daily new cases of COVID-19. The populace's failure to adhere to non-pharmaceutical measures to prevent transmission of the disease is a major additional reason why the introduction of vaccination is a major consideration. The National Primary Health Care Development Agency (NPHCDA) has therefore posed the following questions to NGI-TAG:

"Should the COVID-19 vaccines be introduced for use among targeted Nigerian populace?" "If so, which COVID vaccines should the country introduce?" "What groups should be prioritized to receive the vaccines first?"

In line with NGI-TAG Standard Operating Procedure, the Chairman commissioned a COVID-19 Working Group (WG) to address the questions posed by NPHCDA. The WG was tasked with developing the recommendation framework, conducting a systematic search and data assessment, and proposing the first draft of recommendations/options on COVID-19 vaccines for NGI-TAG consideration. The recommendation framework considered four (4) categories of issues: vaccine and immunization characteristics; disease epidemiology; economic and operational considerations; and health policy and programmatic issues. The systematic search and data assessment were conducted in four (4) steps:

- Framing queries and data ranking
- Searching relevant peer-reviewed articles
- Quality assessment of selected articles
- Synthesizing and making sense of the evidence

The WG was co-chaired by Dr Dorothy Esangbedo and Dr Idris Muhammed and composed of three (5) core members and one (1) non-core member. The members' expertise cut across Public Health, Epidemiology, Infectious Disease, Internal Medicine, Pharmacology, Pediatrics, Immunology, and Virology. The COVID-19 WG with support from the secretariat organized six (6) meetings to deliver on the assignment. In addition to this, other coordination activities were performed continuously by the secretariat through regular emails and phone calls.

As at 2nd of February 2021, there were 238 COVID-19 vaccine candidates out of which 75 were in pre-clinical and 67 in clinical trial stages respectively. Ten (10) COVID-19 vaccine candidates in Phase 3 clinical trial were prioritized for the systematic search on vaccine safety. While good safety profile was reported for all the vaccines, only Pfizer-BioNTech and Moderna vaccines had published efficacy data and reported 95% protection against COVID-19 in persons 16 years of age or older and 94.1% efficacy against symptomatic COVID-19 in persons 18 years or older, respectively. There is paucity of information on the safety of co-administration of COVID-19 vaccines with other vaccines. It is therefore recommended that there should be a minimum interval of 14 days between administration of COVID-19 vaccines and any other vaccine. The duration of protection of administering COVID-19 vaccines in the general population is currently unknown. However, previous longitudinal studies of patients with SARS-CoV-2 infection reported substantial waning of neutralizing antibody titers between 1 year and 2 years after infection. Based on available data for Pfizer-BioNTech, Moderna and AstraZeneca-Oxford vaccines, COVID-19 vaccines are better tolerated in older adults than younger adults and have similar immunogenicity across all age groups. Also, vaccination is strongly recommended for persons with co-morbidities. There is limited data on persons above 85 years of age, children, adolescents below the age of 16 years, pregnant women, lactating women, people living with HIV, persons who have previously had SARS-

Cov-2 infection, persons with current acute COVID-19, and persons who previously received passive antibody therapy for COVID-19. The recommended schedule for the Pfizer-BioNTech and Moderna vaccines, both on the WHO EUL, is 2 doses (21 or 28 days apart respectively). On the 10th of February 2021, AstraZeneca-Oxford vaccine was also granted WHO EUA with a recommended schedule of 2 doses at 8 to 12 weeks apart.

To answer the questions posed to NGI-TAG, **"Should the COVID-19 vaccines be introduced for use among targeted Nigerian populace?"** The answer is yes. The second question is **"If so, which COVID vaccines should the country introduce?"** For now, Nigeria should immediately introduce any of the vaccines with WHO EUA and NAFDAC approval. Top vaccine candidates for the country to consider are the vaccines on the WHO EUL, the Pfizer-BioNTech, Moderna and AstraZeneca-Oxford vaccines. There are several other vaccines already approved by other NRAs which are currently being administered in the respective countries. These vaccines may be considered for use in the country as soon as NAFDAC approves their safety and efficacy profile with due consideration of WHO evaluation of the vaccine for EUA.

The third question posed to NGI-TAG was: ***"What groups should be prioritized to receive the vaccines first?"*** The recommendation is that the following groups should be prioritized in the following order:

- COVID-19 health care frontline workers
- frontline health care workers
- Individuals 50 years old and above
- Individuals 16 years old and above with co-morbidities such as diabetes hypertension, and obesity
- Frontline Workers in other essential social services – such as the police and airport workers
- Other individuals 16 years and older with co-morbidities.

It is also recommended that pregnant women should consult their health care providers to determine if the benefit of the vaccine outweighs the risk. This is based on evidence from the epidemiology of the disease in the country. Finally, NGI-TAG strongly recommends that Nigeria should support as a matter of urgency, local vaccine production and scale-up of government support in the areas of phytopharmacology, virology, ecology, and medical innovations through adequate planning of financial budget lines and release of funds at and as when due.

1 Introduction

The WHO was alerted to a cluster of pneumonia cases "of unknown cause" in Wuhan, Hubei province, China on 31 December 2019 and by 11 January 2020, China confirmed its first death in Wuhan from an illness which is now named Covid-19 disease. By 6 March 2020, over 100,000 [1] cases have been recorded around the world and on 11 March 2020, WHO declared it a 'Public Health Emergency of International Concern', a pandemic [1]. The rapid rate of transmission of the disease and the increasing impact on the public and health-care-related services worldwide was alarming and on 23 March 2020, the United Nations warned that the pandemic is threatening the whole of humanity and requires "war time" plan in times of human crisis. [1-3]

The epidemiological impact of this disease continues to increase at an alarming rate to this day. As of 12 February 2021, there has been a total of 108,313,118 cases worldwide reported to the WHO from 224 countries and territories, and 2,379,137 deaths. The USA accounts for about a quarter of the cases and USA deaths record got as high as 4,000 fatalities in 24 hours.[4]

The impact of COVID-19 on the health care system includes reduction in the resources for the treatment of other diseases. A literature review done from March to 1 June 2020, regarding the impact of COVID-19 on the health care provided to patients in Italy revealed that COVID-19 pandemic was associated with a reduced access to inpatient and outpatient health care services, with a lower volume of elective surgical procedures. There has also been deliberate avoidance of health facilities by many, out of fears of contacting the disease in health facilities. [5]

There is varying acceptance of the existence of the disease, and/or its transmissibility and fatality potential by the populace. As a result, there has been an abysmal compliance with the non-pharmaceutical measures aimed at preventing transmission which include wearing of face mask, maintaining a distance of at least 6 meters between individuals, avoidance of crowded gatherings, frequent handwashing and use of hand sanitizers. [6-9]

Schools, colleges, and universities across the world have responded to the potential of transmission of the disease within their facilities by closing and/or shifting to online/remote teaching, learning and assessment.[10, 11] This shift has been a major challenge in resource poor countries, especially in Africa. Global stock markets crashed, and governments and several central banks rolled out massive economic support measures across the world. Philanthropic companies and individuals have been visibly helping the disenfranchised individuals as the world economy is brought to its knees. [12, 13]

The causative virus of COVID-19, SARS CoV2, continues to mutate and new and more contagious variants of the virus have been detected in UK, Brazil, South Africa, Uganda, and Ghana and still spreading. [14] It is therefore critical that as the COVID-19 variants become more prominent across countries, the Government of Nigeria identifies the strain most common in the country and plan accordingly to secure and distribute the vaccine that is found to be most effective against these variants. The Nigeria Centre for Disease Control is coordinating efforts to increase genomic surveillance of the COVID-19 virus, to identify circulating variants. This includes genetic sequencing of viruses in positive cases among travelers from the United Kingdom and South Africa. So far, some cases have been identified in Nigeria with the B.1.1.7 variant which was first identified in the United Kingdom. [15]

The strain of coronavirus, called D614G, emerged in Europe and has become the most common in the world. Research at the University of North Carolina at Chapel Hill and the University of Wisconsin-Madison shows the D614G variant replicates faster and is more transmissible than the variant that originated in China at the beginning of the pandemic. However, while the D614G strain spreads faster, in animal studies it was not associated with more severe disease, and the strain is slightly more sensitive to neutralization by antibody drugs. [16, 17]

A study conducted in about 2000 people in South Africa, revealed that Astra Zeneca had a low efficacy (<25%) against mild and moderate COVID-19 infection, which would not meet minimal international standards for emergency use. However, scientists are hopeful it might still prevent severe disease and death. COVID-19 vaccines made by Johnson & Johnson and Novavax have also been shown to offer weaker protection against B.1.351 (also known as 501.V2), the SARS-CoV-2 variant that now causes the vast majority of all infections in South Africa, than against older variants. The vaccines' efficacy against mild disease in South Africa was 57% for J&J and 49% for Novavax—lower than in any other country they were tested. But the J&J vaccine, which was put to the test in the largest of the studies, convincingly protected against severe disease and death, even against the B.1.351 variant. [18]

The first case of COVID-19 in Nigeria was confirmed 27th February 2020, an imported case from Italy. There is no evidence yet that the variants have any impact on current vaccines, therapeutics and diagnostics. This is being monitored by ongoing surveillance and research, and the information may change. [15] Subsequently, there was an increasing number of COVID-19 cases with the daily peak of the first wave at 790 cases on 1 July 2020 and the current surge as high as 1,478 on January 21, 2021 with total confirmed cases of 114,691 and total deaths of 1,478, figures considered to be a significant underestimation due to sub-optimal testing of the population for COVID-19. Lagos State remains the epicenter with almost 50% of the total number of cases in the country but there has been progressive spread to all the other states of the country. The rapid rate of spread during the present resurgence (second wave) in many countries including Nigeria has been alarming. There has been significant fatality among the frontline health workers, including in Nigeria. [15]

Further to the above, the National Primary Health Care Development Agency (NPHCDA) has therefore posed these questions to NGI-TAG:

- "Should the COVID-19 vaccines be introduced for use among targeted Nigerian populace?"
- "If so, which COVID vaccines should the country introduce?"
- "What groups should be prioritized to receive the vaccines first?"

1.1 Context of the question

The Federal Ministry of Health has alerted on the imminent incapacity of the health care system to cope with the fast growing daily new cases of COVID-19. The failure of the

populace to adhere to non-pharmaceutical measures to prevent transmission of the disease is an additional reason why introduction of vaccination is a major consideration. However, the global supply of COVID-19 vaccines is constrained because manufacturing capacity is unable to meet global demand. The supply situation creates an access challenge where countries without prior investment in vaccines development or manufacturing were at risk of not accessing vaccines. In addition, bilateral agreements between High Income Countries (HICs) and vaccine manufactures to secure advance doses, put Low-and-Middle-Income Countries (LMICs) at a disadvantage for access. In response, the COVAX Facility was set up as part of the Access to COVID-19 Tools (ACT) Accelerator program [19] to provide a procurement pool that would guarantee vaccine access for all countries regardless of ability to pay or secure advance purchase agreements. [20, 21]
The epidemiology of COVID-19 and the vaccine scarcity dictate that the available vaccines should necessarily be administered to the most vulnerable groups in the population.

1.2 General Information on the subject

Human coronavirus was first diagnosed in 1965 by Tyrrell and Bynoe from the respiratory tract sample of an adult with a common cold. [22, 23] It belongs to the *Coronaviridae* family, subdivided into four groups: α, β, γ, and δ coronaviruses. The α- and β-coronaviruses can infect mammals, while γ- and δ- coronaviruses tend to infect birds. Coronaviruses cause a range of disorders, from common cold to lethal infections, such as the Severe Acute Respiratory Syndrome (SARS), Middle East Respiratory Syndrome (MERS) and Coronavirus Disease 2019 (COVID-19). [23] The coronavirus infection first appeared in the form of Severe Acute Respiratory Syndrome Coronavirus (SARS-CoV-2) in Guangdong province, China, in 2002. [24-26]

The novel coronavirus, SARS CoV2, is a β-coronavirus which causes Coronavirus Disease 2019 (COVID-19). The identity of this virus is based on the results of sequencing and evolutionary analysis of the viral genome. [27, 28] [27, 28] SARS CoV2 structure consists of a positive-stranded RNA genome of approximately 29,000 base pairs covered with distinctive spike proteins about 9-12 nm in size on its surface giving it its crown-like appearance. These spike proteins facilitate viral entry into the host cell. [29]

Thousands of genomes have been sequenced since the first whole genomic sequence was published in January 2020. [30, 31] [30, 31] Mutations in the spike protein have emerged recently, such as the B.1.1.7 and B.1.351 which are spreading fast globally, demonstrating increased infectivity and severity in some reports. [32]

SARS CoV2 is a zoonotic infection, for which current data suggest that bat is the animal vector responsible for transmitting the virus to humans [33, 34] probably through consumption of pangolin (a Chinese delicacy) [35]. The history of the genome study also indicates that it emanated between 17 October to 11 December 2019. [35, 36]

The basic reproductive ratio or basic reproduction number (R_0), the number of infected contacts per infected individual for COVID-19, varies from country to country with average estimate of 3.30 to 5.47. [37] The primary mode of transmission is person-to-person contact through large respiratory droplets containing the SARS-CoV-2 virus generated by sneezing, coughing, singing, and speaking. Transmission is also possible through aerosols and fomites that have been contaminated by respiratory secretions. [38]

Geographic spread is facilitated by air transportation. However, the route of transmission in the community can be sporadic, cluster or community spread. This is facilitated by overcrowding and enclosed spaces with poor ventilation. [38] No one is immune to this virus. SARS CoV2 uses the human angiotensin converting enzyme 2 (ACE 2) receptor sites to latch onto respiratory cells. The receptor-binding domain (RBD) in the spike protein is the most variable part of the coronavirus genome as mutations occur in these receptor- binding domain of SARS Cov2. Six RBD amino acids in the spike protein have been shown to be critical for binding to ACE2 receptor sites. Five of these six residues differ between SARS-CoV-2 and SARS-CoV-2. SARS-CoV-2 seems to have an RBD that binds with high affinity to ACE2 from humans, ferrets, cats, and other species with high receptor homology. [39, 40]

The natural immunity to SARS-CoV-2 consists of both B-cell (antibody) and T-cell specific immune responses. Serological studies have mostly focused on the spike protein and the nucleoprotein components, although there are other antigen components being studied. The antibodies to the RBD of the spike protein are predicted to be neutralizing and protective. The relative importance of B- and T-cell responses in the clearance of the virus and in the maintenance of protection remains unclear. However, there is an association between the magnitude of immune response and the severity of disease. This may be related to the size of viral load experienced by the patient. [40, 41]

Studies have demonstrated that some individuals have some level of cross-reactive immunity to SARS-CoV-2 without ever having been infected by the virus. The cross-reacting immunity includes T-cells recognition of SARS-CoV-2 nucleoprotein and non-spike protein seen in 40-60% of the population but the individuals have no antibodies. Also, cross-reactive antibodies have been found in the younger population of unexposed individuals and in a significant proportion of the population in some sub-Saharan countries. This may explain to some extent the lower mortality seen in the African continent and in children. The hypothesis is that previous exposure to other low-pathogenic coronaviruses may be responsible for this. [29, 42]

The duration of immunity remains to be fully determined. In non-SARS, non-MERS human respiratory CoV infections, protection is transient, and the waning antibody contributes to susceptibility to reinfection within 1 year. SARS-CoV-2 shares about 86% homology with SARS-CoV-1. [29] Early studies suggested SARS antibody declined within 3 years after infection. However, more recent studies have demonstrated that SARS neutralizing antibodies can still be detected 12–17 years after infection and T-cell responses are still measurable 15 years later. However, there is no evidence currently available on the protective role of this immunity against subsequent infection. [29, 43]

COVID-19 vaccine development and some diagnostic methods for SARS CoV2 infection rely on the development of effective immunological response to SARS CoV2. Studies have demonstrated ineffective innate cell immunopathology in SARS CoV2 infection and association with a high risk of fatal COVID-19. The adaptive immunity developed by humans to SARS CoV2 consists of SARS-CoV-2-specific antibodies, CD4+ T cells, and CD8+ T cells. T cell responses have been associated with reduced disease, thus implying that SARS-CoV-2-specific CD4+ T cell and CD8+ T cell responses may be important for the control and resolution of primary SARS-CoV-2 infection. [29]

The neutralizing antibodies component of adaptive immune response have generally not correlated with severity of COVID-19 disease as was also observed for Middle Eastern respiratory syndrome (MERS). [44] However, neutralizing antibodies have been noted to be associated with protective immunity against secondary infection with SARS-CoV2 or SARS-CoV in non-human primates. An understanding of the complex immune responses in SARS CoV2 infection by studying antibody, memory B cell, CD4+ T cell, and CD8+ T cell memory in an integrated manner is important for understanding the durability of the protective immunity. [44-47]

Severe COVID-19 in humans takes a slow course for fatal cases (median 19 days after symptoms appear). This suggests that protective immunity against symptomatic or severe secondary COVID-19 take days to develop and may include reactivation of memory cells such as circulating memory T cells and memory B cells. It is notable that memory B cells specific for the Spike protein or RBD were detected in almost all COVID-19 cases, with no apparent half-life at 5 to 8 months post-infection. [47-49]

A confirmed case of COVID-19 disease is based on a positive Nucleic Acid Amplification Test (NAAT); or a positive SARS-CoV-2 Antigen-Rapid Diagnostic Test (RDT) that meets either the probable case definition or suspect criteria; or an asymptomatic person with a positive SARS-CoV-2 Antigen-RDT who is a contact of a probable or confirmed case. [15, 50, 51]

Majority of human infections with SARS-CoV-2 are asymptomatic or minimally symptomatic. The median incubation period is 5.7 (range 2-14) days. [52] The likelihood of serious illness developing increases with the age of the patient and in the presence of co-morbidities such as obesity, hypertension and diabetes. [29]

Frontline healthcare workers are exposed to large numbers of infectious particles either through single contact or by repeated exposure and this is inferred to be responsible for a worse outcome. The dominant severe pathology is pneumonia and acute respiratory distress syndrome which develop about one to three weeks after onset of symptoms. Other organ systems can be affected including coagulopathy, cardiovascular dysfunction, gastrointestinal disturbance, central nervous system pathologies and multi-organ failure. Slow progression to severe disease does occur in many cases, and *there is evidence that this can often be associated with relatively low viral load in the respiratory tract by this stage*. It has therefore been proposed that immune and inflammatory responses are the key pathophysiological events leading to respiratory failure and the various fatalities caused by SARS CoV2 infection. This is supported by post-mortem histopathological evidence, and that treatment with steroids improves the outcome of respiratory failure. The present understanding is that anti-viral therapy is likely to be effective only if administered early in the course of the infection. [53-56]

Data reviewed by WHO supports potential benefits of AZD1222 outweigh the known and potential risks of taking vaccines. As sufficient vaccine supply will not be immediately available to immunize everyone who could benefit from it, countries are recommended to use the WHO Prioritization Roadmap and the WHO Values Framework as guidance for their prioritization of target groups. [57] As long as vaccine supplies are very limited in settings with community transmission, the Roadmap recommends that priority be given initially to health workers and older people with and without comorbidities. Protecting health workers has a threefold purpose: (i) to protect the individual health workers; (ii) to protect critical essential services during the COVID-19 pandemic; and (iii) to prevent onward transmission to vulnerable people. Protecting older people will have the greatest public health impact in terms of reducing the number of deaths. As more vaccines become available, additional priority groups should be vaccinated as outlined in the WHO Prioritization Roadmap, taking into account national epidemiological data, vaccine-specific characteristics as outlined in product information approved by regulatory authorities, and other relevant considerations. [57]

The currently approved vaccines for use form a response to the crown-like protein "spike" on the SARS-CoV-2 virus. The variants have some changes to the spike, making them better able to target cells, like the variant B.1.1.7 first identified in the United Kingdom (UK), or to increase resistance to antibodies, like the variant B.1.351 first identified in the Republic of South Africa (RSA). [58, 59]

Preliminary results of laboratory tests have demonstrated that both the Moderna and Pfizer-BioNtech COVID-19 vaccine will remain effective against the variant B.1.1.7. Oxford-AstraZeneca are also confident that their current vaccine will be effective against this variant, based on a recent study report.

The current vaccines appear to have mixed efficacy against B.1.351. The AstraZeneca-Oxford vaccine trial in RSA did not show protection against mild to moderate illness caused by the local variant B.1.351. The trial was not large enough to show whether or not it provided protection against severe illness against the local variant. RSA halted plans to roll out the AstraZeneca-Oxford coronavirus vaccine and will start vaccinations with the Johnson & Johnson COVID-19 vaccine.[60, 61]

It is vitally important to determine the vaccine's effectiveness when it comes to preventing more severe illness caused by the B.1.351 variant. Additional studies will also allow us to confirm the optimal vaccination schedule and its impact on vaccine efficacy. [62] CEPI has announced funding for additional clinical research to optimize and extend the use of existing vaccines, which could include "mix-and-match" studies of different vaccines used in combinations that may improve the quality and strength of the immune response. Such studies could be useful in optimizing the use of available vaccine. [63]

SARS-CoV-2 infections in children and adolescents rarely cause severe illness or deaths. [64] Their symptoms are usually mild and may be non-specific. Fever, gastrointestinal disturbance, respiratory features are the most common symptoms. A few cases of a hyper-inflammatory and/or toxic shock-like syndrome that present over two months after the infection have been described. This Multisystem Inflammatory Syndrome in Children (MIS-C) is now thought to be a rare late manifestation of SARS CoV-2 infection, perhaps occurring in genetically susceptible individuals and/or because of co-morbidities. This reason also highlights the need

for careful monitoring for any such rare disease manifestations in the evaluation of safety of COVID-19 vaccines. [64, 65]
When matched, pregnant women vs age-matched non-pregnant women, pregnancy is associated with an increased rate of hospitalizations, ICU care, and mechanical ventilation, but not death.[66, 67] The neonates of infected mothers were more likely to require ICU care but no evidence of increased mortality. The information on breastfeeding is sparce. The virus has been detected in breast milk but no evidence that the neonate was infected from breast milk.[68, 69]

Global and national policy developments on COVID-19 pandemic aim at reduction of deaths, the demand on health care system, as well as the reduction of collateral damage to the economy, society, mental health, and other outcomes through reversal of the rate of epidemic growth, mitigation of transmission rate and ultimately the elimination of the disease. To date, WHO has not issued a Position Paper on COVID-19. However, in accordance with its mandate to provide guidance, coordination, and leadership for global health matters, the WHO has published over 200 articles in the past one year on policy guidance and coordination of the various thematic areas presented by the COVID-19 pandemic. These include an interim guidance: *Guiding principles for immunization activities during the COVID-19 pandemic*; followed on 15 May 2020 by immunization in the context of COVID-19 pandemic and on 20 May 2020, the *Framework for decision-making: implementation of mass vaccination campaigns in the context of COVID-19. These* documents describe the principles to consider for maintaining routine immunization activities, and issues to consider on the implementation of mass vaccination campaigns for the prevention of vaccine-preventable diseases and high-impact -diseases (VPD/HID) as well as assessing the risks and benefits of conducting outbreak-response vaccination campaigns. [70-72]

Also published on 1 June 2020, was the *Guideline on maintaining essential health services: operational guidance for the COVID-19 context interim guidance*.[73] The document recommends practical actions that can be taken at national, sub regional, and local levels to reorganize and safely maintain access to high-quality, essential health services during the pandemic. It also outlines indicators that can be used to monitor essential health services and describes considerations on when to stop and restart services in line with the intensity of COVID-19 transmission. [73]

There have been various conspiracy theories about the pandemic in the social media, a major influence of public perception, attitude and behavior about the novel coronavirus, and the various non-pharmaceutical and pharmaceutical interventions to control transmission including vaccine hesitancy. In response to this, the WHO published on 20 December 2020, an interim guideline on *COVID-19, Global Risk Communication and Community Engagement Strategy. [74]*

WHO SAGE values framework for the allocation and prioritization of COVID-19 vaccination was published on 13 September 2020. The document is a guide on the prioritization of groups for vaccination when vaccine supply is limited. [29]

2 Methodology

2.1 Establishment and functioning of a Working Group

In line with NGITAG SOP, the chairman commissioned a working group to make a proposal to NGITAG on the introduction of COVID-19 vaccine amongst Nigerian targeted Populace in Nigeria. The WG was mainly tasked to develop the recommendation framework, conduct a systematic search and data assessment and propose a first draft of recommendations/options on COVID-19 vaccines for NGITAG consideration. The working group was chaired by Dr. Dorothy Esangbedo and composed of 4 core members and 1 non-core members with various expertise in Public Health, Pediatrics, Immunology and Virology. The group was supported by 6-member committee secretariat~~s~~. The working group TORs is attached to this document as Annex 1. To be able to deliver on the assignment, the COVID-19 Technical Working Group with support from the secretariat organized various meetings. In addition to this, other coordination activities were constantly performed by the secretariat through regular emails and phone calls.

2.2 Recommendation framework

In order to guide the evidence, search, the working group developed a recommendation framework, outlining the issues and specific data needed to inform the decision on the MoH request. The recommendation framework considered 4 categories of issues. Specific elements and data to search were identified and ranked for each issue. The main issues highlighted by the recommendation framework are as follow: 1) Vaccine and immunization characteristics; 2) Disease; 3) Economic and operational considerations; 4) Health policy and programmatic issues. Key elements considered for each issue are listed below:

- **Vaccine and immunization characteristics**: Safety, efficacy, and effectiveness; vaccine indirect effects; vaccine characteristics
- **Disease:** Burden of disease; clinical characteristics of disease; use and costs of health care; alternative measures; regional and international considerations
- **Economic and operational considerations:** Vaccine related costs and resource use; vaccine availability; vaccine affordability; socio-economic and social impact of disease; economic impact on immunization programme
- **Health policy and programmatic issues:** Interaction with other existing strategies; Feasibility; Vaccine registration and regulation; Impact on resources; Ability to evaluate; Acceptability; Equity; Social considerations.

A detailed recommendation framework is attached as Annex 2.

2.3 Evidence Search and Assessment

(This is a brief description on the WG method of working; full documentation of the process will be in annexes).

Following the development of the recommendation framework, the working group has taken different steps in order to gather, assess and select evidence that will support the recommendation on COVID-19 vaccines and Target group. Below is a brief description of the method used by the group:

Step 1: Framing queries and data ranking
In order to enable a systematic and rigorous data search, for each specific data identified in the recommendation framework, specific queries were formulated, using the PICO format where appropriate. Data needed through these queries were then screened and ranked as critical, important and not important. Only data ranked as Critical and Important were selected for literature search. Selected queries were categorized as those requiring a systematic search in databases and those for which information could be found in grey literature and reference documents such as unpublished NPHCDA reports and local data, WHO position papers, and vaccine manufacturers' websites.

Step 2: Searching relevant peer-reviewed articles
For queries requiring systematic search, a clear search strategy was formulated. Depending on the queries one or more search were performed mainly on Pubmed database. Articles obtained were screened (titles and abstracts) for relevance to the question and those available in full text were retrieved and qualified for the next step of quality assessment. The search process and results were documented and attached to this document as Annex (table 1 and 2).

Step 3: Quality Assessment of selected articles
Extracted full articles went through a more detailed assessment using well-known quality check tools SIGN and CASP. The appropriate checklist was used depending on the study design type. Each appraisal exercise looked at the methodological quality, the results relevance to the specific query as well as its applicability in local setting. Articles were qualified for use or rejected based of the scoring and other consideration such scarcity of studies dealing with a specific issue. Assessment outcomes are also recorded in Table 3 and 4 of Annex.

Step 4: Synthetizing and making sense of the evidence
Qualified articles were first summarized focusing on presenting findings to specific queries without providing any judgment. Secondly a comprehensive analysis of the overall body of the evidence guided by the policy question was done to enable the decision and options to be presented to NGITAG members.

3 Presentation of the evidence

In this section each query related to specific data (it may have more than one query for a specific data) indicated in the NITAG recommendation framework will be indicated and the source of evidence on the same will be mentioned alongside. It will be in bullet points to facilitate the reporting but afterwards the working group will put in in prose form. Note this section only presents the findings, the discussion (e-g judgment/sense -making in the country context takes place in the next section). Considering the issues outlined in the discussion, recommendations/options were then proposed in the subsequent section.

3.1 Vaccine and immunization characteristics

3.1.1 Safety

What is the safety profile and listed adverse effects of COVID-19 vaccines in the general population? [Systematic Search/WHO website]

Vaccines Under Consideration (Table 1/2)					
	fizer-BioNTech Vaccine	**Moderna Vaccine**	**straZeneca-Oxford Vaccine**	**Sinovac Vaccine**	**Sinopharm/BIBO Vaccine**
Name of Vaccine	BNT162b2	mRNA-1273	*ChAdOx1 nCoV-19 vaccine (**AZD1222**)* *Indian Brand* COVISHIELD™	*SARS-CoV-2 vaccine (inactivated)*	Inactivated SARS-CoV-2 vaccine (Vero cell)
Type of Vaccine	COVID-19 mRNA	COVID-19 mRNA	Adenoviral non-replicating vaccine *Recombinant, replication-deficient chimpanzee adenovirus vector encoding the SARS-CoV-2 Spike (S) glycoprotein. Produced in genetically modified human embryonic kidney (HEK) 293 cells	*Inactivated virus*	Inactivated virus
anufacturer of Vaccine	fizer/BioNTech + Fosun Pharma	oderna + National Institute of Allergy and Infectious Diseases (NIAID)	*AstraZeneca + University of Oxford*	*Sinovac Research and Development Co., Ltd*	inopharm+ China National Biotec Group Co + Beijing Institute of Biological Products
Country of Vaccine anufacture	America / Germany	America	Britain** Node in India,	China	China
HO EUL/PQ Status	Finalized	Finalized	Finalized for UK brand Not yet for India node	ssessment in progress	Assessment in progress

Dose and Vaccine Schedule (CDC)	.3 mL (30 mcg of mRNA) 2 Doses, 21 days apart	0.5 mL (100 mcg of mRNA) 2 Doses, 28 days apart	0.5ml 2 doses, 28 days apart (WHO EUA Recommendation: 8 to 12 weeks apart)	2 dose, 14 days apart	2 doses, 21 days apart
Authorized age groups (CDC)	ages ≥16 years	ages ≥18 years	Ages >/= 18 years	Pending official data	Pending official data
Phase 1/2 Report	ChiCTR2000034825 NCT04523571	NCT04283461 Interim Report Study Report	PACTR202005681895696	Study Report	Study Report
Phase 2/3 Reports		NCT04649151	Study Report		

Summary of Trial Results					
	Pfizer-BioNTech Vaccine	Moderna Vaccine	AstraZeneca-Oxford Vaccine	Sinovac Vaccine	Sinopharm/BIBO Vaccine
Title of Article	Safety and Efficacy of the BNT162b2 mRNA Covid-19 Vaccine (Phase 3)	Efficacy and Safety of the mRNA-1273 SARS-CoV-2 Vaccine (Phase 3)	Safety and efficacy of the ChAdOx1 nCoV-19 vaccine (AZD1222) against SARS-CoV-2: an interim analysis of four randomised controlled trials in Brazil, South Africa, and the UK (Phase 3)	Safety, tolerability, and immunogenicity of an inactivated SARS-CoV-2 vaccine in healthy adults aged 18–59 years: a randomised, double-blind, placebo-controlled, phase 1/2 clinical trial	Safety and immunogenicity of an inactivated SARS-CoV-2 vaccine, BBIBP-CorV: a randomised, double-blind, placebo-controlled, phase 1/2 trial (Phase 1/2)

				(Phase 1/2)	
Author/Year/Grade	Fernando P. Polack, M.D., Stephen J. Thomas, M.D., Nicholas Kitchin, M.D., Judith Absalon, M.D., Alejandra Gurtman, M.D., Stephen Lockhart, D.M., John L. Perez, M.D., Gonzalo Pérez Marc, M.D., Edson D. Moreira, M.D., Cristiano Zerbini, M.D., et al / 2020 / 10 (11)	Lindsey R. Baden, M.D., Hana M. El Sahly, M.D.,corresponding author Brandon Essink, M.D., Karen Kotloff, M.D., Sharon Frey, M.D., Rick Novak, M.D., David Diemert, M.D., et al / 2020 / 10(11)	Voysey, M., Clemens, S. A. C., Madhi, S. A., Weckx, L. Y., Folegatti, P. M., Aley, P. K., et al / 2020 / 10(11)	Zhang, Y., Zeng, G., Pan, H., Li, C., Hu, Y., Chu, K., et al / 2020 / 10(11)	Shengli Xia., Yuntao Zhang, Yanxia Wang., Hui Wang., Yunkai Yang, George Fu Gao., et al. / 2020 / 10(11)
Type of Article	RCT	RCT	RCT	RCT	RCT
Link of Article	https://www.nejm.org/doi/full/10.1056/NEJMoa2034577	https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7787219/	https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)32661-1/fulltext#seccestitle10 https://www.seruminstitute.com/pdf/covishield_ChAdOx1_nCoV19_corona_virus_vaccine_insert.pdf (Indian brand)	https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(20)30843-4/fulltext	https://doi.org/10.1016/S1473-3099(20)30831-8
Objective	We assessed the safety and efficacy of two 30-	A randomized, double-blind trial to evaluate	We evaluated the safety and efficacy of	We investigated CoronaVac (Sinovac	We aimed to assess the safety and immunogenicity of an

	µg doses of BNT162b2, administered intramuscularly 21 days apart, as compared with placebo.	the efficacy and safety of mRNA-1273.	the ChAdOx1 nCoV-19 vaccine in a pooled interim analysis of four trials.	Life Sciences, Beijing, China), an inactivated vaccine candidate against COVID-19, containing inactivated Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), for its safety, tolerability and immunogenicity.	inactivated Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) vaccine candidate, BBIBP-CorV, in humans.
Vaccine Safety Result	The safety profile of BNT162b2 was characterized by short-term, mild-to-moderate pain at the injection site, fatigue, and headache. The incidence of serious adverse events was low and was similar in the vaccine and placebo groups.	Vaccine recipients had higher rates of local reactions (e.g., pain, erythema, swelling) and systemic reactions (e.g., headache, fatigue, myalgia) than placebo recipients. Most reactions were mild to moderate and resolved over 1–3 days.	Across all four studies, the vaccine had a good safety profile with serious adverse events and adverse events of special interest balanced across the study arms. Serious adverse events occurred in 168 participants, 79 of whom received ChAdOx1 nCoV-19 and 89 of whom received MenACWY or saline control. There were 175	Between April 16 and April 25, 2020, 144 participants were enrolled in the phase 1 trial, and between May 3 and May 5, 2020, 600 participants were enrolled in the phase 2 trial. 743 participants received at least one dose of investigational product (n=143 for phase 1 and n=600 for phase 2; safety population). In the	42 (29%) of 144 vaccine recipients had at least one adverse reaction within 7 days of either vaccination, compared with eight (17%) of 48 placebo recipients. In the group aged 18–59 years, at least one adverse reaction occurred within the first 7 days after either vaccination in 11 (46%) of 24 vaccine recipients in the 2 µg cohort (compared with three [38%] of eight placebo recipients; p>0·99), eight (33%) of 24 vaccine recipients in the 4 µg cohort (compared with two [25%] of eight placebo recipients; p>0·99), and 11 (46%) of 24 vaccine recipients in the 8 µg

			events (84 in the ChAdOx1 nCoV-19 group and 91 in the control group), three of which were considered possibly related to either the experimental or a control vaccine.	phase 1 trial, the incidence of adverse reactions for the days 0 and 14 cohort was seven (29%) of 24 participants in the 3 ug group, nine (38%) of 24 in the 6 μg group, and two (8%) of 24 in the placebo group, and for the days 0 and 28 cohort was three (13%) of 24 in the 3 μg group, four (17%) of 24 in the 6 μg group, and three (13%) of 23 in the placebo group. The seroconversion of neutralising antibodies on day 14 after the days 0 and 14 vaccination schedule was seen in 11 (46%) of 24 participants in the 3 μg group, 12 (50%) of 24 in the 6 μg group, and none (0%) of 24 in the	cohort (compared with one [13%] of eight placebo recipients; p=0·2). In the group aged 60 years and older, at least one adverse reaction occurred within the first 7 days of either vaccination in one (4%) of 24 vaccine recipients in the 2 μg cohort (compared with one [13%] of eight placebo recipients; p=0·44), six (25%) of 24 vaccine recipients in the 4 μg cohort (compared with zero placebo recipients; p=0·3), and five (21%) of 24 vaccine recipients in the 8 μg cohort (compared with one [13%] of eight placebo recipients; p>0·99).

				placebo group; whereas at day 28 after the days 0 and 28 vaccination schedule, seroconversion was seen in 20 (83%) of 24 in the 3 µg group, 19 (79%) of 24 in the 6 µg group, and one (4%) of 24 in the placebo group. In the phase 2 trial, the incidence of adverse reactions for the days 0 and 14 cohort was 40 (33%) of 120 participants in the 3 µg group, 42 (35%) of 120 in the 6 µg group, and 13 (22%) of 60 in the placebo group, and for the days 0 and 28 cohort was 23 (19%) of 120 in the 3 µg group, 23 (19%) of 120 in the 6 µg group, and 11 (18%) of 60 for the placebo group.	

				Seroconversion of neutralising antibodies was seen for 109 (92%) of 118 participants in the 3 µg group, 117 (98%) of 119 in the 6 µg group, and two (3%) of 60 in the placebo group at day 14 after the days 0 and 14 schedule; whereas at day 28 after the days 0 and 28 schedule, seroconversion was seen in 114 (97%) of 117 in the 3 µg group, 118 (100%) of 118 in the 6 µg group, and none (0%) of 59 in the placebo group.	
Adverse Events	Local Reactogenicity Among BNT162b2 recipients, mild-to-moderate pain at the injection site within 7 days after an injection was the most commonly reported local reaction.	Adverse events that were deemed by the trial team to be related to the vaccine or placebo were reported among 4.5% of participants in the placebo group and 8.2% in the mRNA-1273	Reports on the local and systemic reactogenicity of ChAdOx1 nCoV-19 have shown that it is tolerated and that the side-effects are less both in intensity and number in older	We found that two doses of CoronaVac at different concentrations and using different dosing schedules were well tolerated and moderately immunogenic in	Local Reactogenicity The most common injection site adverse reaction was pain, which was reported in 34 (24%) of 144 vaccine recipients after either vaccination, compared with three (6%) of 48 placebo recipients. For vaccine recipients in the group aged 18–59 years

	Pain was reported less frequently among participants older than 55 years of age (71% reported pain after the first dose; 66% after the second dose) than among younger participants (83% after the first dose; 78% after the second dose) A noticeably lower percentage of participants reported injection-site redness or swelling. In general, local reactions were mostly mild-to-moderate in severity and resolved within 1 to 2 days. Systemic Reactogenicity Systemic events were reported more often by younger vaccine recipients (16 to 55 years of age) than by older vaccine recipients (more than 55 years of age) in the	group. The most common treatment-related adverse events (those reported in at least 1% of participants) in the placebo group and the mRNA-1273 group were fatigue (1.2% and 1.5%) and headache (0.9% and 1.4%). In the overall population, the incidence of treatment-related severe adverse events was higher in the mRNA-1273 group (71 participants [0.5%]) than in the placebo group (28 participants [0.2%]) (Tables S8 and S15). The relative incidence of these adverse events according to vaccine group was not affected by age.	adults, with lower doses, and after the second dose. Although there were many serious adverse events reported in the study in view of the size and health status of the population included, there was no pattern of these events that provided a safety signal in the study. Three cases of transverse myelitis were initially reported as suspected unexpected serious adverse reactions, with two in the ChAdOx1 nCoV-19 vaccine study arm, triggering a study pause for careful review in each case. Independent clinical review of these cases has indicated that one in the experimental group	healthy adults aged 18–59 years. The incidence of adverse reactions in the 3 μg and 6 μg group were similar, indicating no dose-related safety concerns but more long-term follow-up is needed. Furthermore, most adverse reactions were mild, with the most common symptom being injection-site pain, which is in accordance with previous findings for another inactivated COVID-19 vaccine from Sinopharm (Beijing China).	(n=72), besides pain (nine [38%] in the 2 μg group, seven [29%] in the 4 μg group, and nine [38%] in the 8 μg group), additional injection site adverse reactions included swelling (two [3%] of 72) and itch (one [1%] of 72). For the vaccine recipients in the group aged 60 years and older (n=72), besides pain (one [4%] in the 2 μg group, four [17%] in the 4 μg group, and four [17%] in the 8 μg group), an additional injection site adverse reaction was induration (two [3%] of 72). We observed statistically higher reports for pain in the group aged 18–59 years than the placebo group (two [8%] of 24; p=0·017). Systemic Reactogenicity The most commonly reported systematic adverse reaction overall after either vaccination was fever, which was reported in five (4%) of 144 vaccine recipients, compared with three (6%) of 48 placebo recipients. For the group aged 18–59 years, fever was reported in all three dose cohorts of vaccine

	reactogenicity subset and more often after dose 2 than dose 1. The most commonly reported systemic events were fatigue and headache (59% and 52%, respectively, after the second dose, among younger vaccine recipients; 51% and 39% among older recipients), although fatigue and headache were also reported by many placebo recipients (23% and 24%, respectively, after the second dose, among younger vaccine recipients; 17% and 14% among older recipients). The frequency of any severe systemic event after the first dose was 0.9% or less. Severe systemic events were reported in less than 2% of vaccine recipients after either dose, except for fatigue (in		and one in the control group are unlikely to be related to study interventions, but a relationship remained possible in the third case. Careful monitoring of safety, including neurological events, continues in the trials.		recipients: one (4%) of 24 in the 2 µg cohort, one (4%) of 24 in the 4 µg cohort, and two (8%) of 24 in the 8 µg cohort. For this same age group (n=72), besides fever, the systematic adverse reactions included fatigue (two [3%]), inappetence (one [1%]), nausea (one [1%]), constipation (one [1%]), mucocutaneous abnormalities (two [3%]), headache (one [1%]), vomiting (one [1%]), and itch (non-injection site; one [1%]). For the vaccine recipients in the cohort aged 60 years or older (n=72), fever (one [1%]) and fatigue (one [1%]) were reported in the 8 µg cohort; and headache (one [1%]), diarrhea (one [1%]), and joint pain (one [1%]) in the 4 µg cohort. One placebo recipient was reported to have muscle pain. All adverse reactions were mild or moderate in severity. No serious adverse event was reported within 28 days post vaccination for all cohorts.

	3.8%) and headache (in 2.0%) after the second dose.				
Conclusion	A two-dose regimen of BNT162b2 conferred 95% protection against Covid-19 in persons 16 years of age or older. Safety over a median of 2 months was similar to that of other viral vaccines.	Two doses of a SARS-CoV-2 mRNA-based vaccine were safe and provided 94.1% efficacy against symptomatic Covid-19 in persons 18 or older.	ChAdOx1 nCoV-19 has an acceptable safety profile and is efficacious against symptomatic COVID-19, with no hospital admissions or severe cases reported in the ChAdOx1 nCoV-19 arm.	CoronaVac was well tolerated and induced humoral responses against SARS-CoV-2, which the supported the approval of emergency use of CoronaVac in China and in three phase 3 studies. The protective efficacy of CoronaVac remains to be determined.	The inactivated SARS-CoV-2 vaccine, BBIBP-CorV, is safe and well tolerated at all tested doses in two age groups. Humoral responses against SARS-CoV-2 were induced in all vaccine recipients on day 42. Two-dose immunisation with 4 μg vaccine on days 0 and 21 or days 0 and 28 achieved higher neutralising antibody titres than the single 8 μg dose or 4 μg dose on days 0 and 14.

Vaccines Under Consideration (Table 2/2)					
	The Gamaleya National Centre Vaccine (Sputnik-V) [75]	Janssen Pharmaceutical Vaccine [76]	Novavax Vaccine [77]	CanSinoBIO Vaccine [78]	Serum Institute of India Vaccine
Name of Vaccine	Gam-COVID-Vac Adeno-based (rAd26-S+rAd5-S)	Ad26.COV2.S	SARS-CoV-2 rS/Matrix M1-Adjuvant (Full length recombinant SARS CoV-2 glycoprotein nanoparticle vaccine	Recombinant novel coronavirus vaccine (Adenovirus type 5 vector)	RBD SARS-CoV-2 HBsAg VLP vaccine

			adjuvanted with Matrix M)		
Type of Vaccine	Viral vector (Non-replicating)	Viral vector (Non-replicating)	Protein subunit	Viral vector (Non-replicating)	Virus like particle
Manufacturer of Vaccine	Gamaleya Research Institute; Health Ministry of the Russian Federation	Janssen Pharmaceutical	Novavax	CanSino Biological Inc./Beijing Institute of Biotechnology	Serum Institute of India + Accelagen Pty + SpyBiotech
Country of Vaccine	Russia	America	America	China	India
WHO EUL/PQ Status	Timelines for data availability and submission to be clarified on 28-29 January.	Assessment yet to start.	No pre-submission meeting yet	Assessment yet to start.	Assessment yet to start.
Dose and Vaccine Schedule (CDC)	2 doses, 21 days apart	1 – 2 doses, 56 days apart Single dose – 66% effective at preventing moderate and severe forms of detectable illness 28 days after vaccination, 85 percent effective at preventing severe disease, and 100 percent effective at preventing hospitalizations and deaths.	2 doses, 21 days apart	1 dose	2 doses, 28 days apart

Authorized age groups (CDC)	Pending official data	Pending official data	Pending official data	Pending official data	
Phase 1 and 2 Reports	NCT04587219	NCT04509947 NCT04436276 Study Report Study Report	NCT04368988 Study Report Study Report	ChiCTR2000030906 NCT04313127 NCT04568811 NCT04552366 Study Report	ACTRN12620000817943 ACTRN12620001308987
Phase 2/3 Reports	NCT04640233		NCT04533399	Study Report	
Phase 3 Reports	NCT04530396 NCT04564716 NCT04642339 NCT04656613 Study Report	NCT04505722 NCT04614948	NCT04611802 EUCTR2020-004123-16-GB NCT04583995	NCT04526990 NCT04540419	
Title of Article	Safety and efficacy of an rAd26 and rAd5 vector-based heterologous prime-boost COVID-19 vaccine: an interim analysis of a randomised controlled phase 3 trial in Russia (Phase 3)	Safety and immunogenicity of the Ad26.COV2.S COVID-19 vaccine candidate: interim results of a phase 1/2a, double-blind, randomized, placebo-controlled trial (Phase 1/2 trial)	Phase 1–2 Trial of a SARS-CoV-2 Recombinant Spike Protein Nanoparticle Vaccine	Immunogenicity and safety of a recombinant adenovirus type-5-vectored COVID-19 vaccine in healthy adults aged 18 years or older: a randomised, double-blind, placebo-controlled, phase 2 trial	
Author/Year/Grade	Logunov, D. Y., Dolzhikova, I. V., Shcheblyakov, D. V., Tukhvatulin, A. I.,	Sadoff, Jerry, Mathieu Le Gars, Georgi Shukarev, Dirk Heerwegh, Carla	Cheryl Keech, M.D., Ph.D., Gary Albert, M.S., Iksung Cho, M.S., Andreana	Zhu, Feng-Cai, Xu-Hua Guan, Yu-Hua Li, Jian-Ying Huang, Tao Jiang, Li-Hua	

	Zubkova, O. V., Dzharullaeva, A. S., ... & Gam-COVID-Vac Vaccine Trial Group. / 2020 / 9(11)	Truyers, Anna Marit de Groot, Jeroen Stoop et al. / 2020 / 8(11)	Robertson, M.S., Patricia Reed, B.S., Susan Neal, Joyce S. Plested, Ph.D., Mingzhu Zhu, Ph.D., Shane Cloney-Clark, B.S., Haixia Zhou, Ph.D., Gale Smith, Ph.D., et al / 2020 / 8(11)	Hou, Jing-Xin Li et al. / 2020 / 8 (11)	
Type of Article	RCT	RCT	RCT	RCT	RCT
Link of Article	https://www.sciencedirect.com/science/article/pii/S0140673621002348	https://www.medrxiv.org/content/10.1101/2020.09.23.20199604v1	https://www.nejm.org/doi/full/10.1056/NEJMoa2026920?query=featured_home	https://doi.org/10.1016/S0140-6736(20)31605-6	
Objective	A heterologous recombinant adenovirus (rAd)-based vaccine, Gam-COVID-Vac (Sputnik V), showed a good safety profile and induced strong humoral and cellular immune responses in participants in phase 1/2 clinical trials. Here, we report preliminary results on the efficacy and safety of Gam-COVID-Vac from the	We designed a multi-center phase 1/2 a randomized, double-blinded, placebo-controlled clinical study to assesses the safety, reactogenicity and immunogenicity of Ad26.COV2.S, a non-replicating adenovirus 26 based vector expressing the stabilized pre-fusion spike (S) protein of SARS-CoV-2.	We initiated a randomized, placebo-controlled, phase 1–2 trial to evaluate the safety and immunogenicity of the rSARS-CoV-2 vaccine (in 5-μg and 25-μg doses, with or without Matrix-M1 adjuvant).	This is the first randomised controlled trial for assessment of the immunogenicity and safety of a candidate non-replicating adenovirus type-5 (Ad5)-vectored COVID-19 vaccine, aiming to determine an appropriate dose of the candidate	

	interim analysis of this phase 3 trial.			vaccine for an efficacy study.	
Vaccine Safety Result	The most common adverse events were flu-like illness in 156 (15·2%) and local reaction in 56 (5·4%) of 1029 participants in the vaccine group and 30 (8·8%) and four (1·2%) of 340 participants in the placebo group. There were three episodes of adverse events of grade 3 or worse, considered not associated with vaccination: an exacerbation of urolithiasis and acute sinusitis in the vaccine group and a flu-like illness in the placebo group. All these adverse events were resolved. In the participants older than 60 years, there were three serious adverse events reported in the vaccine group: renal colic and deep vein thrombosis	In cohorts 1 and 3 solicited local adverse events were observed in 58% and 27% of participants, respectively. Solicited systemic adverse events were reported in 64% and 36% of participants, respectively. Fevers occurred in both cohorts 1 and 3 in 19% (5% grade 3) and 4% (0% grade 3), respectively, were mostly mild or moderate, and resolved within 1 to 2 days after vaccination. The most frequent local adverse event (AE) was injection site pain and the most frequent solicited AEs were fatigue, headache and myalgia.	After randomization, 83 participants were assigned to receive the vaccine with adjuvant and 25 without adjuvant, and 23 participants were assigned to receive placebo. No serious adverse events were noted. Reactogenicity was absent or mild in the majority of participants, more common with adjuvant, and of short duration (mean, ≤2 days). One participant had mild fever that lasted 1 day. Unsolicited adverse events were mild in most participants; there were no severe adverse events. The addition of adjuvant resulted in enhanced	In the 1 × 1011 and 5 × 1010 viral particles dose groups, the RBD-specific ELISA antibodies peaked at 656·5 (95% CI 575·2–749·2) and 571·0 (467·6–697·3), with seroconversion rates at 96% (95% CI 93–98) and 97% (92–99), respectively, at day 28. Both doses of the vaccine induced significant neutralising antibody responses to live SARS-CoV-2, with GMTs of 19·5 (95% CI 16·8–22·7) and 18·3 (14·4–23·3) in participants receiving 1 × 1011 and 5 × 1010 viral particles, respectively.	

	(both associated with pre-existing comorbidities) and extremity abscess (due to physical injury and subsequent infection of the wound surface of the soft tissues of the finger). No association was found between serious adverse events and vaccine administration, with confirmation from the independent data monitoring committee.		immune responses, was antigen dose–sparing, and induced a T helper 1 (Th1) response. The two-dose 5-µg adjuvanted regimen induced geometric mean anti-spike IgG (63,160 ELISA units) and neutralization (3906) responses that exceeded geometric mean responses in convalescent serum from mostly symptomatic Covid-19 patients.	Specific interferon γ enzyme-linked immunospot assay responses post vaccination were observed in 227 (90%, 95% CI 85–93) of 253 and 113 (88%, 81–92) of 129 participants in the 1 × 1011 and 5 × 1010 viral particles dose groups, respectively. Solicited adverse reactions were reported by 183 (72%) of 253 and 96 (74%) of 129 participants in the 1 × 1011 and 5 × 1010 viral particles dose groups, respectively. Severe adverse reactions were reported by 24 (9%) participants in the 1 × 1011 viral particles dose group and one (1%) participant in the 5 × 1010 viral	

				particles dose group. No serious adverse reactions were documented.	
Conclusion	This interim analysis of the phase 3 trial of Gam-COVID-Vac showed 91·6% efficacy against COVID-19 and was well tolerated in a large cohort.	The safety profile and immunogenicity after only a single dose are supportive for further clinical development of Ad26.COV2.S at a dose level of 5x1010 vp, as a potentially protective vaccine against COVID-19.	At 35 days, NVX-CoV2373 appeared to be safe, and it elicited immune responses that exceeded levels in Covid-19 convalescent serum. The Matrix-M1 adjuvant induced CD4+ T-cell responses that were biased toward a Th1 phenotype.	The Ad5-vectored COVID-19 vaccine at 5 × 1010 viral particles is safe and induced significant immune responses in the majority of recipients after a single immunization.	

Is it safe to co-administer COVID-19 vaccines with other vaccines? [Systematic Search/WHO website]

	Pfizer-BioNTech Vaccine [79]	Moderna Vaccine [80]	AstraZeneca-Oxford Vaccine [81]
Type of Document	Interim recommendations for use of the Pfizer– BioNTech COVID-19 vaccine, BNT162b2, under Emergency Use Listing	Interim recommendations for use of the Moderna mRNA-1273 vaccine against COVID-19	Interim recommendations for use of the AZD1222 (ChAdOx1-S (recombinant)) vaccine against COVID-19 developed by Oxford University and AstraZeneca
Source	WHO	WHO	WHO
Link	https://www.who.int/publications/i/item/WHO-2019-nCoV-vaccines-SAGE_recommendation-BNT162b2-2021.1	https://www.who.int/publications/i/item/interim-recommendations-for-use-of-the-moderna-mrna-1273-vaccine-against-covid-19	https://www.who.int/publications/i/item/WHO-2019-nCoV-vaccines-SAGE_recommendation-AZD1222-2021.1

	There should be a minimum interval of 14 days between administration of this vaccine and any other vaccine against other conditions, until data on co-administration with other vaccines become available.	Given the lack of data on the safety and efficacy of mRNA COVID-19 vaccines administered simultaneously with other vaccines, the vaccine series should routinely be administered alone, with a minimum interval of 14 days before or after administration with any other vaccine. However, mRNA COVID-19 and other vaccines may be administered within a shorter period in situations where the benefits of vaccination are deemed to outweigh the potential unknown risks of vaccine coadministration (e.g., tetanus toxoid-containing vaccination as part of wound management, measles or hepatitis A vaccination during an outbreak) or to avoid barriers or delays to mRNA COVID-19 vaccination (e.g., in long-term care facility residents or healthcare personnel who received influenza or other vaccinations prior to/upon admission or onboarding). If mRNA COVID-19 vaccines are administered within 14 days of another vaccine, doses do not need to be repeated for either vaccine.	There should be a minimum interval of 14 days between administration of this vaccine and any other vaccine against other conditions. This recommendation may be amended as data on co-administration with other vaccines become available.

C. Which groups are more at risk of developing adverse events of COVID-19 vaccines? [Systematic Search/WHO website]

Paper 1

Title of Article/Author/Year/Grade: A Review of the Progress and Challenges of Developing a Vaccine for COVID-19 / Sharma, O., Sultan, A.A., Ding, H. and Triggle, C.R. / 2020 / 8(10)

Type of Article: Systematic Review
Link of Article:
https://www.frontiersin.org/articles/10.3389/fimmu.2020.585354/full?utm_source=F-AAE&utm_medium=EMLF&utm_campaign=MRK_1463957_35_Immuno_20201022_arts_A

Objective: This review will focus on the eight vaccine candidates that entered Phase 1 clinical trials in mid-May, including AstraZeneca/Oxford's AZD1222, Moderna's mRNA-1273 and Sinovac's CoronaVac vaccines, which are currently in advanced stages of vaccine development. In addition to reviewing the different stages of vaccine development, vaccine platforms and vaccine candidates, this review also discusses the biological and immunological basis required of a SARS-CoV-2 vaccine, the importance of a collaborative international effort, the ethical implications of vaccine development, the efficacy needed for an immunogenic vaccine, vaccine coverage, the potential limitations and challenges of vaccine development. [82]

Result: Pre-existing immunity to adenoviruses is a concern, particularly for those vaccine candidates utilizing human adenoviruses such as CanSino's Ad5 vaccine, as it may result in a reduced immune response to the vaccine. AstraZeneca/Oxford's AZD1222 is another adenoviral vector vaccine candidate but instead of utilizing a human adenovirus in its vaccine, it uses a genetically modified chimpanzee-derived adenovirus. This effectively addresses the concern about pre-existing immunity and consequently averts the negative impact on immune response generated to the vaccine. [82]

Conclusion: There are several vaccine candidates currently in clinical trials with AstraZeneca/Oxford's AZD1222, Moderna's mRNA1273 and Sinovac's CoronaVac vaccines advancing to Phase 3 clinical trials. With many placing their hopes on a vaccine against COVID-19 being available by the end of 2020 or early 2021, it is yet to be seen how the vaccine will be distributed, how national interests will unfold and whether the vaccine will ultimately prove to be safe and effective when administered to the global population at large. [82]

What are the contraindications to administering COVID-19 vaccines in the general population? [Systematic Search/WHO website]

	Pfizer-BioNTech Vaccine [79]	Moderna Vaccine [80]	AstraZeneca-Oxford Vaccine [81]
Type of Document	Interim recommendations for use of the Pfizer– BioNTech COVID-19 vaccine, BNT162b2, under Emergency Use Listing	Interim Clinical Considerations for Use of mRNA COVID-19 Vaccines Currently Authorized in the United States	Interim recommendations for use of the AZD1222 (ChAdOx1-S (recombinant)) vaccine against COVID-19 developed by Oxford University and AstraZeneca
Source	WHO	WHO	WHO

Link	https://www.who.int/publications/i/item/WHO-2019-nCoV-vaccines-SAGE_recommendation-BNT162b2-2021.1	https://www.who.int/publications/i/item/interim-recommendations-for-use-of-the-moderna-mrna-1273-vaccine-against-covid-19	https://www.who.int/publications/i/item/WHO-2019-nCoV-vaccines-SAGE_recommendation-AZD1222-2021.1
Contraindications	A history of severe allergic reaction (e.g. anaphylaxis) to any component of the vaccine is a contraindication to vaccination. In particular, BNT162b2 should not be administered to individuals with a known history of severe allergic reaction to polyethylene glycol (PEG) or related molecules as PEG is a component of the vaccine.	A history of anaphylaxis to any component of the vaccine is a contraindication to vaccination. mRNA-1273 vaccine should not be administered to individuals with a history of anaphylaxis to polyethylene glycol (PEG), a component of the vaccine. If anaphylaxis occurs after the first dose, a second dose of mRNA-1273 vaccine or of mRNA-BNT162b2 (Pfizer) should not be administered.	A history of anaphylaxis to any component of the vaccine is a contraindication to vaccination. People who have an anaphylactic reaction following the first dose of this vaccine should not receive a second dose of the same vaccine.
Precautions	Anaphylactic reactions after administration of BNT162b2 vaccine have been reported outside of clinical trials. A history of any immediate allergic reaction to any other vaccine or injectable therapy (i.e. intramuscular, intravenous, or subcutaneous vaccines or therapies) is considered as a precaution but not a contraindication to vaccination. For such persons, a risk assessment should be conducted to determine the type and severity	• A history of anaphylaxis to any other vaccine or injectable therapy (i.e. intramuscular, intravenous, or subcutaneous vaccines or therapies) is considered as a precaution but not a contraindication to vaccination. For such persons, a risk assessment should be conducted by a health professional with specialist expertise in allergic disorders. Such individuals may still receive vaccination. It remains uncertain	• No severe allergic reactions or anaphylaxis caused by AZD1222 have been recorded in the context of clinical trials. However, as for all vaccines, AZD1222 should be given under health care supervision, with the appropriate medical treatment available in case of allergic reactions. As for any other vaccine, an observation period of 15 min after vaccination should be ensured. • Anyone with an acute febrile illness (body temperature over 38.5 oC) should postpone vaccination until they are afebrile. However, the presence of a

	of reaction and the reliability of the information. Such individuals may still receive vaccination, but they should be counselled about the risks of developing a severe allergic reaction and the risks should be weighed against the benefits of vaccination. Such persons should be observed for 30 minutes after vaccination in health care settings where anaphylaxis can be immediately treated. In general, persons with an immediate allergic reaction to the first dose should not receive additional doses. For the purposes of this guidance, an immediate allergic reaction to a vaccine or medication is defined as any hypersensitivity-related signs or symptoms, such as anaphylaxis, urticaria, angioedema, respiratory distress (e.g. wheezing, stridor), that occur within hours of administration. However, subject to individual risk-benefit assessment, specialist services for	if there is an increased risk of anaphylaxis, but they should be counselled about the potential risk of anaphylaxis and the risks should be weighed against the benefits of vaccination. Such persons should be observed for 30 minutes after vaccination in health care settings where anaphylaxis can be immediately treated. • In general, persons with an immediate non-anaphylactic allergic reaction to the first dose should not receive additional doses, unless recommended after review by a health professional with specialist expertise. For the purposes of this guidance, an immediate non-anaphylactic allergic reaction is defined as any signs or symptoms, such as urticaria, angioedema or respiratory symptoms without any other symptoms (cough, wheezing, stridor), that occur within 4	minor infection, such as a cold, or low-grade fever should not delay vaccination.

	immunization may allow BNT162b2 to be provided under close medical supervision if it is the only available option for persons at high risk of severe COVID-19. As a small number of anaphylactic reactions have also been reported in vaccines without a history of severe allergic reactions, WHO recommends that BNT162b2 vaccine should be administered only in settings where anaphylaxis can be treated. Until more data and insights are available with regard to severe allergic reactions to BNT162b2 vaccination, all vaccines should be observed for at least 15 minutes after vaccination. Food, contact, or seasonal allergies are not considered a precaution. The vial stoppers are not made with natural rubber latex, and there is no contraindication or precaution to vaccination for persons with a latex allergy. In addition, as BNT162b2 does not contain eggs or gelatine, there is	hours of administration. However, subject to individual risk– benefit assessment, mRNA-1273 could be provided under close medical supervision if it is the only available option for persons at high risk of severe COVID-19. • As a small number of anaphylactic reactions have also been reported in vaccines without a history of anaphylaxis, WHO recommends that mRNA-1273 vaccine should be administered only in settings where anaphylaxis can be treated. Until more data and insights are available with regard to anaphylaxis after mRNA-1273 vaccination, all vaccines should be observed for at least 15 minutes after vaccination. • Food, insect venom and contact allergies and allergic rhinitis, eczema and asthma are not considered a precaution. The vial stoppers are not made with	

	no contraindication or precaution to vaccination for persons with allergies to these substances. Anyone with an acute febrile illness (body temperature over 38.5 oC) should postpone vaccination until they are afebrile.	natural rubber latex, and there is no contraindication or precaution to vaccination for persons with a latex allergy. In addition, as mRNA-1273 does not contain eggs or gelatine, there is no contraindication or precaution to vaccination for persons with allergies to any food substances. • Anyone with an acute febrile illness (body temperature over 38.5 oC) should postpone vaccination until they are afebrile.	

Title of Article/Author/Year: Evidence to recommendations for COVID-19 vaccines: Evidence framework. World Health Organization. 2020. WHO SAGE roadmap for prioritizing uses of COVID-19 vaccines in the context of limited supply. Geneva: World Health Organization; 2020 (https://www.who.int/publications/m/tem/who-WHO-roadmap-for-prioritizing-uses-ofcovid-19-vaccines-in-the-context-of-limited-supply accessed 30 December 2020).

Type of Article: WHO paper

Link of Article: (https://www.who.int/publications/i/item/WHO-2019-nCoV-SAGE-Framework- Evidence-2020-1, accessed 7 January 2021); file:///C:/Users/NPHCDA/Downloads/cdc_99850_DS1.pdf

Result: The interim recommendations for use of the Pfizer-BioNTech COVID-19 vaccine, BNT162b2, under Emergency Use Listing: Interim guidance revealed that; a history of severe allergic reaction (e.g., anaphylaxis) to any component of the vaccine is a contraindication to vaccination. In particular, BNT162b2 should not be administered to individuals with a known history of severe allergic reaction to polyethylene glycol (PEG) or related molecules as PEG is a component of the vaccine.

Conclusion: Contraindications to mRNA COVID-19 vaccination (Pfizer-BioNTech and Moderna COVID-19 vaccines); Contraindications to either of the mRNA COVID-19 vaccines: – Severe allergic reaction (e.g., anaphylaxis) after a previous dose of an mRNA COVID-19 vaccine or to any of its components – Immediate allergic reaction of any severity to a previous dose of an mRNA COVID-19 vaccine or any of its components (including polyethylene glycol [PEG]) – Immediate allergic reaction of any severity to polysorbate (due to potential cross-reactive hypersensitivity with the vaccine ingredient PEG) ▪ Persons with an immediate allergic reaction to the first dose of an mRNA vaccine should not receive additional doses of either of the mRNA COVID-19 vaccines.

3.1.2 Efficacy and effectiveness

a. What is the immunity or immune response of administering COVID-19 vaccines in the general population? [Systematic Search/WHO website]

Query 1: What is the immunity or immune response of administering COVID-19 vaccines in the general population? (Table 1/2)					
	Pfizer-BioNTech Vaccine [83]	Moderna Vaccine [84]	AstraZeneca-Oxford Vaccine [85]	Sinovac Vaccine [86]	Sinopharm/BIBO Vaccine [87]
Title of Article	Safety and Immunogenicity of Two RNA-Based Covid-19 Vaccine Candidates (Phase 3)	Safety and immunogenicity of SARS-CoV-2 mRNA-1273 vaccine in older adults. (Phase 3)	Safety and immunogenicity of ChAdOx1 nCoV-19 vaccine administered in a prime-boost regimen in young and old adults (COV002): a single-blind, randomised, controlled, phase 2/3 trial (Phase 2/3)	Safety, tolerability, and immunogenicity of an inactivated SARS-CoV-2 vaccine in healthy adults aged 18–59 years: a randomised, double-blind, placebo-controlled, phase 1/2 clinical trial (Phase 1/2)	Safety and immunogenicity of an inactivated SARS-CoV-2 vaccine, BBIBP-CorV: a randomised, double-blind, placebo-controlled, phase 1/2 trial (Phase 1/2)
Author/Year/Grade	Edward E. Walsh, M.D., Robert W. Frenck, Jr., M.D., Ann R. Falsey, M.D., Nicholas Kitchin, M.D.,	Anderson, E. J., Rouphael, N. G., Widge, A. T., Jackson, L. A., Roberts, P. C., Makhene, M., et al / 2020 / 7(11)	Ramasamy, M. N., Minassian, A. M., Ewer, K. J., Flaxman, A. L., Folegatti, P. M., Owens, D. R., et al / 2020 / 10(11)	Zhang, Y., Zeng, G., Pan, H., Li, C., Hu, Y., Chu, K., et al / 2020 / 10(11)	Xia S, Zhang Y, Wang Y, Wang H, Yang Y, Gao GF et al 2020. 10(11).

	Judith Absalon, M.D., Alejandra Gurtman, M.D., Stephen Lockhart, D.M., Kathleen Neuzil, M.D., Mark J. Mulligan, M.D., Ruth Bailey, B.Sc., Kena A. Swanson, Ph.D., Ping Li, Ph.D., et al. / 2020 / 9(11)				
Type of Article	RCT	RCT	RCT	RCT	RCT
Link of Article	https://www.nejm.org/doi/full/10.1056/NEJMoa2027906	https://www.nejm.org/doi/full/10.1056/NEJMoa2028436	https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)32466-1/fulltext	https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(20)30843-4/fulltext	https://doi.org/10.1016/S1473-3099(20)30831-8
Objective	We assessed the safety and efficacy of two 30-μg doses of BNT162b2, administered intramuscularly 21 days apart, as compared with placebo.	To test the safety and immunogenicity of SARS-CoV-2 mRNA-1273 vaccine in older adults since increased incidences of illness and	The coprimary outcomes of the trial are to assess efficacy as measured by the number of cases of symptomatic, virologically confirmed COVID-19 and safety of the vaccine as measured	We investigated CoronaVac (Sinovac Life Sciences, Beijing, China), an inactivated vaccine candidate against COVID-19, containing inactivated Severe	We aimed to assess the safety and immunogenicity of an inactivated Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) vaccine candidate, BBIBP-CorV, in humans.

		death from coronavirus disease 2019 (Covid-19) have been associated with an older age.	by the occurrence of serious adverse events. Secondary outcomes include safety, reactogenicity, and immunogenicity profiles of ChAdOx1 nCoV-19 in older adults (aged 56–69 years and ≥70 years), efficacy against severe and non-severe COVID-19, death, and seroconversion against non-spike proteins.	acute respiratory syndrome coronavirus 2 (SARS-CoV-2), for its safety, tolerability and immunogenicity.	
Immunogenicity Result	In each of 13 groups of 15 participants, 12 participants received vaccine and 3 received placebo. BNT162b2 was associated with a lower incidence and severity of systemic	Binding-antibody responses increased rapidly after the first immunization. By day 57, among the participants who received the 25-µg dose, the anti–S-2P geometric	The vaccine was safe and well tolerated, with reduced reactogenicity in older adults. Antibody responses against the SARS-CoV-2 spike protein were induced in all age groups and were boosted and maintained at 28 days after booster vaccination,	The seroconversion of neutralising antibodies on day 14 after the days 0 and 14 vaccination schedule was seen in 11 (46%) of 24 participants in the 3 µg group, 12 (50%) of 24 in the 6 µg group, and none (0%) of 24 in the placebo group;	Neutralising antibody geometric mean titres were higher at day 42 in the group aged 18–59 years (87·7 [95% CI 64·9–118·6], 2 µg group; 211·2 [158·9–280·6], 4 µg group; and 228·7 [186·1–281·1], 8 µg group) and the group aged 60 years and older (80·7 [65·4–99·6], 2 µg group; 131·5 [108·2–159·7], 4 µg group; and 170·87 [133·0–219·5], 8 µg group) compared with the placebo group (2·0 [2·0–2·0]). In phase 2, 448 participants were enrolled

	reactions than BNT162b1, particularly in older adults. In both younger and older adults, the two vaccine candidates elicited similar dose-dependent SARS-CoV-2–neutralizing geometric mean titers, which were similar to or higher than the geometric mean titer of a panel of SARS-CoV-2 convalescent serum samples.	mean titer (GMT) was 323,945 among those between the ages of 56 and 70 years and 1,128,391 among those who were 71 years of age or older; among the participants who received the 100-µg dose, the GMT in the two age subgroups was 1,183,066 and 3,638,522, respectively. After the second immunization, serum neutralizing activity was detected in all the participants by multiple methods. Bindi ng- and neutralizing-	including in the 70 years and older group. Cellular immune responses were also induced in all age and dose groups, peaking at day 14 after vaccination.	whereas at day 28 after the days 0 and 28 vaccination schedule, seroconversion was seen in 20 (83%) of 24 in the 3 µg group, 19 (79%) of 24 in the 6 µg group, and one (4%) of 24 in the placebo group. In the phase 2 trial, the incidence of adverse reactions for the days 0 and 14 cohort was 40 (33%) of 120 participants in the 3 µg group, 42 (35%) of 120 in the 6 µg group, and 13 (22%) of 60 in the placebo group, and for the days 0 and 28 cohort was 23 (19%) of 120 in the 3 µg group, 23 (19%) of 120 in the 6 µg group, and 11 (18%) of 60 for the placebo group.	(mean age 41·7 years [SD 9·9]) and were randomly assigned to receive the vaccine (8 µg on day 0 [n=84] or 4 µg on days 0 and 14 [n=84], days 0 and 21 [n=84], or days 0 and 28 [n=84]) or placebo on the same schedules (n=112). At least one adverse reaction within the first 7 days was reported in 76 (23%) of 336 vaccine recipients (33 [39%], 8 µg day 0; 18 [21%], 4 µg days 0 and 14; 15 [18%], 4 µg days 0 and 21; and ten [12%], 4 µg days 0 and 28). One placebo recipient in the 4 µg days 0 and 21 group reported grade 3 fever but was self-limited and recovered. All other adverse reactions were mild or moderate in severity. The most common systematic adverse reaction was fever (one [1%], 8 µg day 0; one [1%], 4 µg days 0 and 14; three [4%], 4 µg days 0 and 21; two [2%], 4 µg days 0 and 28). The vaccine-elicited neutralising antibody titres on day 28 were significantly greater in the 4 µg days 0 and 14 (169·5, 95% CI 132·2–217·1), days 0 and 21 (282·7, 221·2–361·4), and days 0 and 28 (218·0, 181·8–261·3) schedules than the 8 µg day 0

		antibody responses appeared to be similar to those previously reported among vaccine recipients between the ages of 18 and 55 years and were above the median of a panel of controls who had donated convalescent serum. The vaccine elicited a strong CD4 cytokine response involving type 1 helper T cells.		Seroconversion of neutralising antibodies was seen for 109 (92%) of 118 participants in the 3 μg group, 117 (98%) of 119 in the 6 μg group, and two (3%) of 60 in the placebo group at day 14 after the days 0 and 14 schedule; whereas at day 28 after the days 0 and 28 schedule, seroconversion was seen in 114 (97%) of 117 in the 3 μg group, 118 (100%) of 118 in the 6 μg group, and none (0%) of 59 in the placebo group.	schedule (14·7, 11·6–18·8; all p<0·001).
Conclusion	The immune responses elicited by BNT162b1 and BNT162b2 were similar. As has been observed	The 100-μg dose induced higher binding- and neutralizing-antibody titers than the 25-μg	Our findings show that the ChAdOx1 nCoV-19 vaccine was safe and well tolerated with a lower reactogenicity profile in older adults	CoronaVac was well tolerated and induced humoral responses against SARS-CoV-2, which suppored the approval of	The inactivated SARS-CoV-2 vaccine, BBIBP-CorV, is safe and well tolerated at all tested doses in two age groups. Humoral responses against SARS-CoV-2 were induced in all vaccine recipients on day 42. Two-dose

	with other vaccines and as is probably associated with immunosenescence, the immunogenicity of the two vaccine candidates decreased with age, eliciting lower overall humoral responses in adults 65 to 85 years of age than in those 18 to 55 years of age. Nevertheless, at 7 days and 14 days after the second dose, the 50% and 90% neutralizing GMTs that were elicited by 30 µg of BNT162b2 in	dose, which supports the use of the 100-µg dose in a phase 3 vaccine trial.	than in younger adults. Immunogenicity was similar across age groups after a boost vaccination. If these responses correlate with protection in humans, these findings are encouraging because older individuals are at disproportionate risk of severe COVID-19 and so any vaccine adopted for use against SARS-CoV-2 must be effective in older adults.	emergency use of CoronaVac in China and in three phase 3 studies. The protective efficacy of CoronaVac remains to be determined.	immunisation with 4 µg vaccine on days 0 and 21 or days 0 and 28 achieved higher neutralising antibody titres than the single 8 µg dose or 4 µg dose on days 0 and 14.

	older adults exceeded those of the convalescent serum panel. Antibody responses in both younger and older adults showed a clear benefit of a second dose.				

Query 1: What is the immunity or immune response of administering COVID-19 vaccines in the general population? (Table 2/2)				
	The Gamaleya National Centre Vaccine [75]	Janssen Pharmaceutical Vaccine [76]	Novavax Vaccine [77]	CanSinoBIO Vaccine [78]
Title of Article	Safety and immunogenicity of an rAd26 and rAd5 vector-based heterologous prime-boost COVID-19 vaccine in two formulations: two open, non-randomised phase 1/2 studies from Russia (Phase 1/2)	Safety and immunogenicity of the Ad26.COV2.S COVID-19 vaccine candidate: interim results of a phase 1/2a, double-blind, randomized, placebo-controlled trial (Phase 1/2 trial)	Phase 1–2 Trial of a SARS-CoV-2 Recombinant Spike Protein Nanoparticle Vaccine	Immunogenicity and safety of a recombinant adenovirus type-5-vectored COVID-19 vaccine in healthy adults aged 18 years or older: a randomised, double-blind, placebo-controlled, phase 2 trial
Author/Year/Grade	Denis Y Logunov, DSc., Inna V Dolzhikova, PhD., Olga V Zubkova, PhD., Amir I Tukhvatulin, PhD., Dmitry V Shcheblyakov, PhD., Alina S Dzharullaeva, MSc., et al. / 2020 / 7(11)	Sadoff, Jerry, Mathieu Le Gars, Georgi Shukarev, Dirk Heerwegh, Carla Truyers, Anna Marit de Groot, Jeroen Stoop et al. / 2020 / 8(11)	Cheryl Keech, M.D., Ph.D., Gary Albert, M.S., Iksung Cho, M.S., Andreana Robertson, M.S., Patricia Reed, B.S., Susan Neal, Joyce S. Plested, Ph.D., Mingzhu Zhu, Ph.D., Shane Cloney-Clark, B.S., Haixia Zhou, Ph.D., Gale Smith, Ph.D., et al / 2020 / 8(11)	Zhu, Feng-Cai, Xu-Hua Guan, Yu-Hua Li, Jian-Ying Huang, Tao Jiang, Li-Hua Hou, Jing-Xin Li et al. / 2020 / 8 (11)
Type of Article	RCT	RCT	RCT	RCT
Link of Article	https://www.thelancet.com/pdfs/journals/lancet/PIIS0140-6736(20)31866-3.pdf	https://www.medrxiv.org/content/10.1101/2020.09.23.20199604v1	https://www.nejm.org/doi/full/10.1056/NEJMoa2026920?query=featured_home	https://doi.org/10.1016/S0140-6736(20)31605-6
Objective	We aimed to assess the	We designed a multi-center phase 1/2 a randomized,	We initiated a randomized, placebo-controlled, phase	This is the first randomised controlled trial for

	safety and immunogenicity of two formulations (frozen and lyophilised) of this vaccine.	double-blinded, placebo-controlled clinical study to assesses the safety, reactogenicity and immunogenicity of Ad26.COV2.S, a non-replicating adenovirus 26 based vector expressing the stabilized pre-fusion spike (S) protein of SARS-CoV-2.	1–2 trial to evaluate the safety and immunogenicity of the rSARS-CoV-2 vaccine (in 5-µg and 25-µg doses, with or without Matrix-M1 adjuvant).	assessment of the immunogenicity and safety of a candidate non-replicating adenovirus type-5 (Ad5)-vectored COVID-19 vaccine, aiming to determine an appropriate dose of the candidate vaccine for an efficacy study.
Immunogenicity Result	At day 42, receptor binding domain-specific IgG titres were 14 703 with the frozen formulation and 11 143 with the lyophilised formulation, and neutralising antibodies were 49·25 with the frozen formulation and 45·95 with the lyophilised formulation, with a seroconversion rate of 100%. Cell-mediated responses were detected in all participants at day 28, with median cell proliferation of 2·5% CD4+ and 1·3% CD8+ with the frozen formulation, and a median cell proliferation of 1·3% CD4+ and 1·1% CD8+ with the lyophilised formulation	In cohorts 1 and 3 solicited local adverse events were observed in 58% and 27% of participants, respectively. Solicited systemic adverse events were reported in 64% and 36% of participants, respectively. Fevers occurred in both cohorts 1 and 3 in 19% (5% grade 3) and 4% (0% grade 3), respectively, were mostly mild or moderate, and resolved within 1 to 2 days after vaccination. The most frequent local adverse event (AE) was injection site pain and the most frequent solicited AEs were fatigue, headache and myalgia.	After randomization, 83 participants were assigned to receive the vaccine with adjuvant and 25 without adjuvant, and 23 participants were assigned to receive placebo. No serious adverse events were noted. Reactogenicity was absent or mild in the majority of participants, more common with adjuvant, and of short duration (mean, ≤2 days). One participant had mild fever that lasted 1 day. Unsolicited adverse events were mild in most participants; there were no severe adverse events. The addition of adjuvant	In the 1 × 1011 and 5 × 1010 viral particles dose groups, the RBD-specific ELISA antibodies peaked at 656·5 (95% CI 575·2–749·2) and 571·0 (467·6–697·3), with seroconversion rates at 96% (95% CI 93–98) and 97% (92–99), respectively, at day 28. Both doses of the vaccine induced significant neutralising antibody responses to live SARS-CoV-2, with GMTs of 19·5 (95% CI 16·8–22·7) and 18·3 (14·4–23·3) in participants receiving 1 × 1011 and 5 × 1010 viral particles, respectively. Specific interferon γ enzyme-linked immunospot assay

			resulted in enhanced immune responses, was antigen dose–sparing, and induced a T helper 1 (Th1) response. The two-dose 5-µg adjuvanted regimen induced geometric mean anti-spike IgG (63,160 ELISA units) and neutralization (3906) responses that exceeded geometric mean responses in convalescent serum from mostly symptomatic Covid-19 patients.	responses post vaccination were observed in 227 (90%, 95% CI 85–93) of 253 and 113 (88%, 81–92) of 129 participants in the 1 × 1011 and 5 × 1010 viral particles dose groups, respectively. Solicited adverse reactions were reported by 183 (72%) of 253 and 96 (74%) of 129 participants in the 1 × 1011 and 5 × 1010 viral particles dose groups, respectively. Severe adverse reactions were reported by 24 (9%) participants in the 1 × 1011 viral particles dose group and one (1%) participant in the 5 × 1010 viral particles dose group. No serious adverse reactions were documented.
Conclusion	In conclusion, these data collectively show that the heterologous vaccine based on rAd26-S and rAd5-S is safe, well tolerated, and does not cause serious adverse events in healthy adult volunteers. The vaccine is highly immunogenic and induces strong humoral and cellular immune responses in 100% of	The safety profile and immunogenicity after only a single dose are supportive for further clinical development of Ad26.COV2.S at a dose level of 5x1010 vp, as a potentially protective vaccine against COVID-19.	At 35 days, NVX-CoV2373 appeared to be safe, and it elicited immune responses that exceeded levels in Covid-19 convalescent serum. The Matrix-M1 adjuvant induced CD4+ T-cell responses that were biased toward a Th1 phenotype.	The Ad5-vectored COVID-19 vaccine at 5 × 1010 viral particles is safe, and induced significant immune responses in the majority of recipients after a single immunisation.

	healthy adult volunteers, with antibody titres in vaccinated participants higher than those in convalescent plasma.			

B. What are the underlying conditions (current diseases/ and conditions/age) that may interfere with the immune response? [Systematic Search/WHO website]

	Pfizer- BioNTech vaccine	Moderna m-RNA vaccine	AstraZeneca vaccine (viral replicating vaccine)
Link	https://www.nejm.org/doi/full/10.1056/NEJMoa2034577 (9/11)	https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7787219/ (9/11)	https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)32661-1/fulltext#seccestitle10 (7/11)
Title/ Author/ Grading	Safety and Efficacy of the BNT162b2 mRNA Covid-19 Vaccine; Polack et.al., 2020	Efficacy and Safety of the mRNA-1273 SARS-CoV-2 Vaccine; Baden et.al., 2020	Safety and immunogenicy of ChAdOx1 nCoV-19 vaccine administered in a prime-boost regimen in young and old adults (COV002); a single-blind, randomized controlled phase 2/3 trial.
Type of study	RCT	RCT	RCT
Results	A total of 43,548 participants underwent randomization, of whom 43,448 received injections: 21,720 with BNT162b2 and 21,728 with placebo. There were 8 cases of Covid-19 with onset at least 7 days after the second dose among participants assigned to receive BNT162b2 and 162 cases among those assigned to placebo; BNT162b2 was	At least one protocol-defined high-risk condition for severe COVID-19 was present in 22.3% of participants, and 4% of participants had two or more high risk conditions. Approximately 41.4% of the study population was considered at risk for progression to severe COVID-19 due to underlying comorbidities such as diabetes, chronic lung disease, severe obesity, significant	560 participants were enrolled between May 30 and August 8, 2020: 160 aged 18–55 years (100 assigned to ChAdOx1 nCoV-19, 60 assigned to MenACWY), 160 aged 56–69 years (120 assigned to ChAdOx1 nCoV-19: 40 assigned to MenACWY), and 240 aged 70 years and older (200 assigned to ChAdOx1 nCoV-19: 40 assigned to MenACWY). Local and systemic reactions were more common in participants given ChAdOx1 nCoV-19 than in those given the control vaccine, and similar in nature to those previously reported (injection-site pain, feeling feverish, muscle

	95% effective in preventing Covid-19 (95% credible interval, 90.3 to 97.6). Similar vaccine efficacy (generally 90 to 100%) was observed across subgroups defined by age, sex, race, ethnicity, baseline body-mass index, and the presence of coexisting conditions. Among 10 cases of severe Covid-19 with onset after the first dose, 9 occurred in placebo recipients and 1 in a BNT162b2 recipient. The safety profile of BNT162b2 was characterized by short-term, mild-to-moderate pain at the injection site, fatigue, and headache. The incidence of serious adverse events was low and was similar in the vaccine and placebo group.	cardiovascular disease, liver disease, or infection with HIV and/or aged ≥65 years. Primary efficacy analysis shows that mRNA-1273 vaccine is 94.4% efficacious (95%CI: 76.9–98.7%) beginning 14 days after the second dose in individuals aged 18–64 years at risk of severe COVID-19 due to underlying conditions. Efficacy %) in individuals aged 65 years and older with and without underlying conditions shows that mRNA-1273 is 86.4% efficacious (95%CI: 61.4–95.2). Point estimates were provided by subgroup of risk factor (chronic lung disease, cardiac disease, severe obesity, diabetes, liver disease and HIV). Vaccine efficacy was consistent across subgroups and comparable with the efficacy observed for the overall study population, though interpretation of the results is limited by small numbers of participants and cases.	ache, headache), but were less common in older adults (aged ≥56 years) than younger adults. In those receiving two standard doses of ChAdOx1 nCoV-19, after the prime vaccination local reactions were reported in 43 (88%) of 49 participants in the 18–55 years group, 22 (73%) of 30 in the 56–69 years group, and 30 (61%) of 49 in the 70 years and older group, and systemic reactions in 42 (86%) participants in the 18–55 years group, 23 (77%) in the 56–69 years group, and 32 (65%) in the 70 years and older group. As of Oct 26, 2020, 13 serious adverse events occurred during the study period, none of which were considered to be related to either study vaccine. In participants who received two doses of vaccine, median anti-spike SARS-CoV-2 IgG responses 28 days after the boost dose were similar across the three age cohorts. Neutralising antibody titres after a boost dose were similar across all age groups By 14 days after the boost dose, 208 (>99%) of 209 boosted participants had neutralising antibody responses. T-cell responses peaked at day 14 after a single standard dose of ChAdOx1 nCoV-19 (18–55 years)
Conclusion	The vaccine has a good safety profile and the	Both solicited injection-site and	ChAdOx1 nCoV-19 appears to be better tolerated in older adults than in younger

	immune response induced was optimal including individuals with co-morbidities. The two-dose regimen of BNT162b2 conferred 95% protection against Covid-19 in persons 16 years of age or older as well as people with co-morbidities.	systemic adverse events were more common among younger participants (18 to 64 years of age) than among older participants (≥65 years of age). After country implementation of vaccination programmes using mRNA vaccines in the United Kingdom and the USA, cases of anaphylactic reactions to the vaccine were observed in people with and without a history of anaphylactic reactions to other antigens	adults and has similar immunogenicity across all age groups after a boost dose. Further assessment of the efficacy of this vaccine is warranted in all age groups and individuals with comorbidities.

C. What is the duration of protection of administering COVID-19 vaccines in the general population (by age group and population type)? [Systematic Search/WHO website]

Article 1
Title of Article/Author: Immunological considerations for COVID-19 vaccine strategies
Link: https://www.nature.com/articles/s41577-020-00434-6
Type of Article: Informative Research
Objective: To discuss the immunological principles that are key in the development of COVID-19 vaccine strategies

Result: It will be necessary to consider that asymptomatic individuals, patients who have recovered from COVID-19 but generated poor immunity or whose immunity quickly waned, and individuals who received a rapidly developed 'pandemic' vaccine that provided suboptimal protection or rapidly waning immune responses may require a booster vaccination to ensure sufficient levels of population protection for herd immunity.

Conclusion: The durability of the antibody responses to SARS-CoV-2 remains unknown. However, previous longitudinal studies of patients with SARS-CoV-2 infection reported substantial waning of neutralizing antibody titres between 1 year and 2 years after infection. This is consistent with classical studies showing a relatively rapid waning of antibodies to the seasonal coronavirus 229. There are currently no immune correlates of protection for SARS-CoV-2 or other human coronaviruses. Thus, it is unclear what titre of neutralizing antibodies is sufficient to confer protection against infection. Establishing such correlates will be essential to guide the development of effective COVID-19 vaccines.

Article 2
Title of Article/Author: Assessing Durability of Vaccine Effect Following Blinded Crossover in COVID-19 Vaccine Efficacy Trials
Link: https://www.medrxiv.org/content/10.1101/2020.12.14.20248137v1.full
Type of Article: Case-Control
Objective: To assess the duration of COVID-19 vaccines in placebo to vaccine crossover populations

Result: Post-crossover estimates (persons who initially were on placebos and then offered the vaccine) of vaccine efficacy can provide insights about durability, identify waning efficacy, and identify late enhancement of disease, but are less reliable estimates than those obtained by a standard trial where the placebo cohort is maintained. As vaccine efficacy estimates for post-crossover periods depend on prior vaccine efficacy estimates, longer pre-crossover periods with higher case counts provide better estimates of late vaccine efficacy. Further, open-label crossover may lead to riskier behavior in the immediate crossover period for the unblinded vaccine arm, confounding vaccine efficacy estimates for all post-crossover periods.

Conclusion: The high efficacies reported in primary3 and interim4,5 analyses of multiple vaccine candidates, while universally welcomed, add complexity and uncertainty to the environment surrounding access to the vaccine for trial participants randomized to placebo. Continued blinded follow-up in the original arms is optimal to assess vaccine efficacy over time and is endorsed by the

FDA in their guidance pertaining to COVID-19 vaccine development. Early efficacy provides incomplete information about the totality of the risks and benefits of the vaccines. But at some point, consensus will emerge that the placebo volunteers should be offered vaccine. This paper argues that valuable information regarding durability and VAED can be obtained even after the placebo volunteers receive the vaccine and that studies should maintain rigorous blinded follow-up post crossover to recover this information.

Paper 3
Title of Article/Author: Frequently Asked Questions about COVID-19 Vaccination
Link: https://www.cdc.gov/coronavirus/2019-ncov/vaccines/faq.html
Type of Article: Grey Literature
Objective: To assess the duration of immunity from naturally occurring COVID-19 vs COVID-19 vaccines

Result: The protection someone gains from having an infection (called "natural immunity") varies depending on the disease, and it varies from person to person. Because this virus is new, we don't know how long natural immunity might last. Current evidence suggests that getting the virus again (reinfection) is uncommon in the 90 days after the first infection with the virus that causes COVID-19. We would not know how long immunity lasts after vaccination until we have more data on how well COVID-19 vaccines work in real-world conditions.

Conclusion: Experts are working to learn more about both natural immunity and vaccine-induced immunity.

Paper 4
Title of Article/Author: Immunity Against COVID-19 Will Take Weeks After Vaccination, Experts Say
Link: https://www.verywellhealth.com/covid-19-vaccine-immunity-time-5091651
Type of Article: Grey Literature
Objective: To understand the duration of immunogenicity of the COVID-19 vaccine

Result: Both the Pfizer and Moderna mRNA vaccines include a two-shot regimen. Pfizer's second dose is given 21 days after the first, while Moderna's second dose is given 28 days after the initial shot. For the Pfizer vaccine, the effectiveness hasn't been demonstrated until at least seven days after the second dose. For the Moderna vaccine, immunity may not be achieved until at least 14 days after the second dose.

Conclusion: Pfizer's vaccine offers immunity at least seven days after the second dose,1 and Moderna's vaccine offers immunity at least 14 days after the second dose. Although immunity is offered through the Pfizer-BioNTech and Moderna vaccines, building immunity against COVID-19 takes time and will still require social distancing and mask-wearing. While experts think it may last years, immunity duration is unknown. Therefore, more studies will need to be conducted.

Paper 5
Title of Article/Author: How long will immunity last after getting a coronavirus vaccine?
Link: https://www.bostonherald.com/2020/12/18/how-long-will-immunity-last-after-getting-a-coronavirus-vaccine/
Type of Article: Grey Literature
Objective: To understand the duration of immunogenicity of the COVID-19 vaccine

Result: Both Pfizer's and Moderna's mRNA two-dose vaccines are extremely effective and trigger immune responses mere days following vaccination. Pfizer's vaccine showed early protection 12 days after the first dose and 7 days after the second dose, according to data in the New England Journal of Medicine. High levels of antibodies in Moderna trial participants remained three months after the second dose.

Conclusion: It typically takes the body a few weeks to build robust immunity following vaccination, according to the US Centers for Disease Control and Prevention, providing a reminder that even after receiving a vaccine, wearing a mask and social distancing will be important.

Paper 6
Title of Article/Author: Safety and Efficacy of the BNT162b2 mRNA Covid-19 Vaccine (Pfizer vaccine)
Link: https://www.nejm.org/doi/full/10.1056/NEJMoa2034577?query=featured_coronavirus
Type of Article: RCT
Objective: To understand the required dosage of the Pfizer vaccine to confer 95% protection against Covid-19 in persons 16 years of age or older

Result: A total of 43,548 participants underwent randomization, of whom 43,448 received injections: 21,720 with the Pfizer vaccine and 21,728 with placebo. There were 8 cases of Covid-19 with onset at least 7 days after the second dose among participants assigned to receive the Pfizer vaccine and **162 cases** among those assigned to placebo; the Pfizer vaccine was 95% effective in preventing Covid-19. Similar vaccine efficacy (generally 90 to 100%) was observed across subgroups defined by age, sex, race, ethnicity, baseline body-mass index, and the presence of coexisting conditions. Among **10 cases of severe Covid-19 with onset after the first dose**, **9 occurred in placebo** recipients and **1 in a Pfizer vaccine** recipient. The safety profile of the Pfizer vaccine was characterized by short-term, mild-to-moderate pain at the injection site, fatigue, and headache. The incidence of serious adverse events was low and was similar in the vaccine and placebo groups.

Conclusion: A two-dose regimen of the Pfizer vaccine conferred 95% protection against Covid-19 in persons 16 years of age or older. Safety over a median of 2 months was similar to that of other viral vaccines.

Paper 7
Title of Article/Author: Durability of Responses after SARS-CoV-2 mRNA-1273 Vaccination
Link: https://www.nejm.org/doi/full/10.1056/NEJMc2032195?query=featured_coronavirus
Type of Article: Cohort Study
Objective: To understand the duration of immunogenicity of the COVID-19 vaccine.

Result: At the 100-μg dose, the Moderna mRNA-1273 produced high levels of binding and neutralizing antibodies that declined slightly over time, as expected, but remained elevated in all participants 3 months after the booster vaccination. At the day 119 **(4 months)** time point, the geometric mean titer (GMT) was **235,228** (95% confidence interval, 177,236 to 312,195) **in participants 18 to 55 years of age**, **151,761** (95% CI, 88,571 to 260,033) **in those 56 to 70 years of age**, and **157,946** (95% CI, 94,345 to 264,420) **in those 71 years of age or older**. Serum neutralizing antibodies continued to be detected in all the participants at day 119. No serious adverse events were noted in the trial, no prespecified trialhalting rules were met, and no new adverse events that were considered by the investigators to be related to the vaccine occurred after day 57.

Conclusion: Although correlates of protection against SARS-CoV-2 infection in humans are not yet established, these results show that despite a slight expected decline in titers of binding and neutralizing antibodies, **mRNA-1273 has the potential to provide durable humoral immunity**. Longitudinal vaccine responses are critically important, and a follow-up analysis to assess safety and immunogenicity in the participants for a period of 13 months is ongoing. Findings provide support for the use of a 100-µg dose of the Moderna mRNA-1273 vaccine in the phase 3 trial, which has shown a 94.5% efficacy rate.

D. Are there factors (e.g. vaccine co-administration) that interfere with the protection offered by COVID-19 vaccines?)? [Systematic Search/WHO website]

Paper 1
Title of Article/Author: COVID-19 and the Path to Immunity
Link: https://jamanetwork.com/journals/jama/fullarticle/2770758/
Type of Article: Informative Research
Objective: To understand the key features and evolution of B-cell– and T-cell–mediated adaptive immunity to SARS-CoV-2

Result: Potent neutralizing antibodies and T_H1-biased $CD4^+$ T-cell responses to the spike protein protect against SARS-CoV-2 infection in the lungs and nasal mucosa of nonhuman primates without evidence of immunopathological changes. In a study involving a human challenge to a circulating coronavirus (HCoV 229E), IgG and IgA antibodies waned over the first year after viral nasal challenge suggesting that protection against repeated infections with common cold coronaviruses lasts only 1 or 2 years. However, following experimental rechallenge with the same HCoV 229E strain at 1 year, no individuals who had been previously infected developed a cold and all had a shorter duration of detectable virus shedding. Thus, at least strain-specific immunity to clinical coronavirus disease may be preserved despite rapid waning of antibodies.

Conclusion: It is unknown whether memory T cells in the absence of detectable circulating antibodies protect against SARS-CoV-2. Thus, identification of SARS-COV-2–specific T cells or their molecular receptor footprint may have future utility to assess SARS-CoV-2 exposure before antibodies arise and after their decline. At present, a full understanding of T-cell contributions in the prevention of severe COVID-19 is limited. Relying on population-based natural immunity, especially for populations at risk of greater disease severity, is not wise. Boosting specific neutralizing antibodies and T_H1 immunity to high levels with an effective vaccine regardless of prior immune status may further protect these individuals. The induction of sufficient $CD4^+$ follicular helper T cells and inclusion of vaccine boosts, employed for several other vaccines where circulating antibody levels are critical for protection, may be needed to maintain levels of anti–SARS-CoV-2 neutralizing antibodies.

Paper 2
Link: https://onlinelibrary.wiley.com/doi/full/10.1111/cei.13495

Type of Article: Journal of Translational Immunology
Objective: To assess the impact of COVID-19 vaccine in immunosuppressed individuals

Result: While B cell responses to a variety of different vaccines are clearly inhibited by CD20 depletion despite some inhibition of CD20 T cells, inactivated herpes zoster vaccine can at least induce T cell responses. This may be relevant if the CD8 T cell response is a vital part of the coronavirus specific immunity, as reported for SARS-CoV-2. This feature may reduce concern about the limited antibody responses that may be generated following infection or after administration of a SARS-CoV-2 vaccine, as such asymptomatic people who have cleared SARS-CoV-2 and have a detectable anti-viral T cell response, but may not generate an antibody response. Although adenoviral vaccines have shown some value in generating neutralizing antibodies and cytopathic T cells in early human studies, live and attenuated viruses are contraindicated in immunosuppressed people.

Conclusion: It remains to be seen if SARS-CoV-2 DNA-RNA vaccines will be useful in people taking immunosuppressive agents. However, it is important that people with autoimmunity continue to be offered the benefit that high-efficacy immunotherapy can provide. With time, further knowledge will emerge that may help guide treatment selection within the COVID-19 and post-COVID-19 era.

Paper 3
Title of Article/Author: Emergence of Drift Variants That May Affect COVID-19 Vaccine Development and Antibody Treatment
Link: file:///C:/Users/fpg8/Downloads/pathogens-09-00324-v2.pdf
Type of Article: Systemic Review
Objective: To assess the impact of the COVID-19 vaccine on the COVID-19 variants

Result: Twelve distinct variants were found within B-cell epitopes of spike protein (S), nucleocapsid protein (N), and membrane protein (M), respectively. Also, twenty-one distinct variants were identified in T-cell epitopes. Large differences were observed in both the size and hydrophobicity in the middle of the epitope, which would compromise the binding affinity to antibodies trained by vaccines with wild-type spike protein. Most of the samples with the variant were collected in Europe, in particular the Netherlands (66 out of 112), Switzerland (29 out of 30), and France (21 out of 32). In these countries, the majority of infected patients possess the variant; therefore, vaccine design and convalescent plasma antibody treatment might require further considerations to accommodate the drift.

Conclusion: The highly prevalent COVID-19 variant in the European population may cause antigenic drift, resulting in vaccine mismatches that offer little protection to that group of patients. Innovative vaccine design methods, including using highly conserved internal epitopes, recombinant proteins spanning epitopes, or pooling multiple vaccines, will be required to combat the inherent antigenic drift.

Paper 4
Title of Article/Author: Factors that Influence the Immune Response to Vaccination
Link: https://cmr.asm.org/content/32/2/e00084-18
Type of Article: Informative Research and Systemic Review

Objective: To assess the impact of other factors that may interfere with the effectiveness of the COVID-19 vaccine

Result: There is solid evidence that intrinsic factors, such as genetics, sex, age at time of vaccination, and comorbidities, as well as vaccine-related factors, such as choice of vaccine products, adjuvants, and vaccination schedule, strongly influence vaccine responses. Good evidence also exists for the interaction between maternal antibodies and vaccine responses in infants. In contrast, the available data on the influence of other perinatal factors, such as birth weight or feeding method, or on the influence of infections, antibiotics, the microbiota, and nutrition are less robust. For smoking, alcohol consumption, psychological stress, and exercise, the data from different studies are inconsistent. Many studies report differences in vaccine responses depending on geographic region. However, many other factors, such as preexisting immunity, nutritional status, and other behavioral factors, as well as genetics and the microbiota, might confound this observation. The potential for confounding also exists for many of the other factors discussed in this review, as the response to vaccination is complex, likely involving the interplay of multiple different factors. It is therefore important not to overinterpret findings from single studies.

Conclusion: This review provides an overview of the current evidence for factors that might influence vaccine responses and identifies factors that require further investigation. Important topics for future studies include the influences of the microbiota (intestinal and respiratory), concurrent infections, and antibiotics on vaccine responses. Further important lines of investigation include the association between preexisting immunity and vaccine responses, as well as the influence of behavioral factors. Understanding these interactions in more depth will open new avenues for improving vaccine immunogenicity and effectiveness as well as designing vaccine schedules that optimize the benefits of vaccination.

Paper 5
Title of Article/Author: Interim Clinical Considerations for Use of mRNA COVID-19 Vaccines Currently Authorized in the United States
Link: https://www.cdc.gov/vaccines/covid-19/info-by-product/clinical-considerations.html
Type of Article: Grey Literature
Objective: To assess the impact of other factors that may interfere with the effectiveness of the COVID-19 vaccine

Result: Data from clinical trials indicate that mRNA COVID-19 vaccines can safely be given to persons with evidence of a prior SARS-CoV-2 infection. Vaccination should be offered to persons regardless of history of prior symptomatic or asymptomatic SARS-CoV-2 infection. **While there is no recommended minimum interval between infection and vaccination, current evidence suggests that the risk of SARS-CoV-2 reinfection is low in the months after initial infection but may increase with time due to waning immunity**. For persons receiving antibody therapies not specific to COVID-19 treatment (e.g., intravenous immunoglobulin, RhoGAM), administration of mRNA COVID-19 vaccines either simultaneously with or at any interval before or after receipt of an antibody-containing product is unlikely to substantially impair development of a protective antibody response. **mRNA COVID-19 vaccines may be administered to persons with underlying medical conditions who have no contraindications to vaccination. Clinical trials demonstrated similar safety and efficacy profiles in persons with some underlying medical conditions, including those that place them at increased risk for severe COVID-19**, compared to persons without comorbidities.

Conclusion: Given the lack of data on the safety and efficacy of mRNA COVID-19 vaccines administered simultaneously with other vaccines, the vaccine series should routinely be administered alone, with a minimum interval of 14 days before or after administration with any other vaccine. However, mRNA COVID-19 and other vaccines may be administered within a shorter period in situations where the benefits of vaccination are deemed to outweigh the potential unknown risks of vaccine coadministration (e.g., tetanus toxoid-containing vaccination as part of wound management, measles or hepatitis A vaccination during an outbreak) or to avoid barriers or delays to mRNA COVID-19 vaccination (e.g., in long-term care facility residents or healthcare personnel who received influenza or other vaccinations prior to/upon admission or onboarding).

If mRNA COVID-19 vaccines are administered within 14 days of another vaccine, doses do not need to be repeated for either vaccine. Data are not currently available to establish vaccine safety and efficacy in persons living with HIV or in persons with autoimmune conditions. While vaccine safety and efficacy data in this age group are limited, there are no biologically plausible reasons for safety and efficacy profiles to be different than those observed in persons 18 years of age and older. Adolescents aged 16–17 years who are part of a group recommended to receive a COVID-19 vaccine may be vaccinated with the Pfizer-BioNTech COVID-19 vaccine with appropriate assent.

Paper 6

Title of Article/Author: South Africa suspends use of AstraZeneca's COVID-19 vaccine after it fails to clearly stop virus variant
Link: https://www.sciencemag.org/news/2021/02/south-africa-suspends-use-astrazenecas-covid-19-vaccine-after-it-fails-clearly-stop
Objective: To assess the impact of different COVID-19 vaccine on variants

Results: The AstraZeneca-Oxford vaccine trial, which was conducted in ~2,000 participants in South Africa ran from June to November 2020 found that in starting the vaccination 2 weeks after the second dose—when participants presumably were fully immunized—19 cases of mild or moderate disease developed among the vaccinated, versus 23 in the placebo group, resulting in an efficacy of 21.9%. That is far below the 50% minimum required for emergency use authorization in many countries.
Researchers sequenced the viruses that infected trial participants and found a strong link between vaccine failure and B.1.351's explosion in South Africa. In people who received one dose of the vaccine before the variant began to spread widely, efficacy against mild and moderate disease was still a respectable 75%.

Conclusion: More research is needed to ensure the efficacy of the vaccines on COVID-19 variants. Researchers have begun to work on a second-generation candidate that targets the mutated spike protein of the B.1.351 variant.

Paper 7
Link: https://www.bbc.com/news/health-55951920
Type of Article: Grey Literature
Objective: To assess the impact of the Oxford Astra Zeneca vaccine on variants

Result: The Oxford-AstraZeneca vaccine gives people good protection against the new coronavirus variant which is now dominant in the UK. They found similar efficacy against the B117 "Kent" variant to the original virus, based on swabs from volunteers. Oxford researchers say their analysis found similar levels of efficacy against the old variant (84%) and the "Kent" B117 one (74.6%). Scientists behind the Pfizer-BioNTech and Moderna vaccines also say early research suggests their vaccines appear to protect against the dominant new variants in the UK. It is still unclear how well the vaccine works against other variants with more worrying mutations.

Conclusion: Coronaviruses are less prone to mutation than influenza viruses, but it is expected that as the pandemic continues, new variants will begin to become dominant among the viruses that are circulating and that eventually a new version of the vaccine, with an updated spike protein, would be required to maintain vaccine efficacy at the highest level possible.

E. What is the evidence of an effect of immunization on efficacy against COVID-19 (regardless of severity); mild symptomatic, moderate, and severe disease; hospitalizations and death. How does efficacy vary by age-group (children, younger adults, older adults), by sex, in pregnant and lactating women, and in specific co-morbidity risk groups? [Systematic Search/WHO website]

	Pfizer-BioNTech Vaccine	Moderna Vaccine	AstraZeneca – Oxford Vaccine
Type of document	WHO Guideline Document	WHO Guideline Document	WHO Guideline Document
Title of document	Interim recommendations for use of the Pfizer–BioNTech COVID-19 vaccine, BNT162b2, under Emergency Use Listing	Interim recommendations for use of the Moderna mRNA-1273 vaccine against COVID-19	Interim recommendations for use of the AZD1222 (ChAdOx1-S [recombinant]) vaccine against COVID19 developed by Oxford University and AstraZeneca
Source	WHO	WHO	WHO
Release date	8 January 2021	25 January, 2021	10 February, 2021
Link	https://www.who.int/publications/i/item/WHO-2019-nCoV-vaccines-SAGE_recommendation-BNT162b2-2021.1	https://www.who.int/publications/i/item/interim-recommendations-for-use-of-the-moderna-mrna-1273-vaccine-against-covid-19	https://www.who.int/publications/i/item/WHO-2019-nCoV-vaccines-SAGE_recommendation-AZD1222-2021.1
Populations for which supportive data are available from phase 2/3 clinical trials			
Older People	The risk of severe COVID-19 and death increases steeply with age. Data from the phase 3 trial indicate that the efficacy and safety of the vaccine are comparable across all age groups (above the age of 16). Vaccination is recommended for older persons.	The risk of severe COVID-19 and death increases steeply with age. Data from the phase 3 trial indicate that the efficacy and safety of the vaccine are comparable across all age groups (above the age of 18). Vaccination is recommended for older persons.	Because a relatively small number of participants aged 65 years or over were recruited into the clinical trials, there were few cases of COVID-19 in either the vaccine or the control group in this age category, and thus the confidence interval on the efficacy estimate is very wide. More precise efficacy estimates for this age

			group are expected soon, from both ongoing trials and vaccine effectiveness studies in countries that are using this vaccine. Immune responses induced by the vaccine in older persons are well documented and similar to those in other age groups. This suggests it is likely that the vaccine will be found to be efficacious in older persons. The trial data indicate that the vaccine is safe for this age group. The risk of severe disease and death due to COVID-19 increases steeply with age. Taking the totality of available evidence into account, WHO recommends the vaccine for use in persons aged 65 years and older.
Persons with comorbidities	Certain comorbidities have been identified as increasing the risk of severe COVID-19 disease and death. Phase 2/3 clinical trials have demonstrated that the vaccine has similar safety and efficacy profiles in persons with various underlying medical conditions, including those that place them at increased risk for severe COVID-19. The comorbidities studied in phase 2/3 clinical trials include hypertension; diabetes; asthma; and pulmonary, liver and kidney disease; as well as chronic (stable and controlled)	Certain comorbidities have been identified as increasing the risk of severe COVID-19 disease and death. The phase 3 clinical trial demonstrated that the vaccine has similar safety and efficacy profiles in persons with various underlying medical conditions, including those that place them at increased risk for severe COVID-19. The comorbidities studied in in the phase 3 clinical trial included chronic lung disease, significant cardiac disease, severe obesity, diabetes,	Certain comorbidities have been identified as increasing the risk of severe COVID-19 disease and death. The clinical trials demonstrated that the vaccine has similar safety and efficacy profiles in persons with various underlying medical conditions, including those that place them at increased risk for severe COVID-19. The comorbidities studied in the clinical trials included obesity, cardiovascular disease, respiratory disease and diabetes. Vaccination is recommended for persons with comorbidities that

	infection with human immunodeficiency virus (HIV), hepatitis C virus (HCV) and hepatitis B virus (HBV). Vaccination is recommended for persons with comorbidities that have been identified as increasing the risk of severe COVID-19.	liver disease and human immunodeficiency virus (HIV) infection. Vaccination is recommended for persons with such comorbidities that have been identified as increasing the risk of severe COVID-19.	have been identified as increasing the risk of severe COVID-19.
Populations for which limited, or no data exist from the phase 3 clinical trial			
Persons above 85 years of age	Persons above the age of 85 years and very frail older persons were not included in the clinical trials. However, the safety and immunogenicity data obtained in a large subset of older people with and without comorbidities suggest that the benefits of vaccination outweigh the potential risks. Vaccination is recommended for older persons without an upper age limit.	Extremely frail older persons and persons above the age of 95 years were not included in the clinical trials. However, the safety and immunogenicity data obtained in a large subset of older people with and without comorbidities suggest that the benefits of vaccination outweigh the potential risks. Vaccination is recommended for older persons without an upper age limit. For very frail older persons with a life expectancy anticipated to be less than 3 months, an individual risk–	Frail older adults might benefit from a higher dose of vaccine and we would not be able to assess this effect unless frailty was specifically queried in immunogenicity studies.

		benefit assessment will need to be conducted.	
Children and adolescents below the age of 16 years	There are currently no efficacy or safety data for children or adolescents below the age of 16 years. Until such data are available, individuals below 16 years of age should not be vaccinated.	There are currently no efficacy or safety data for children or adolescents below the age of 18 years. Until such data are available, individuals below 18 years of age should not be vaccinated with this vaccine.	There are currently no efficacy or safety data for children or adolescents below the age of 18 years. Until such data are available, vaccination of individuals below 18 years of age is not recommended.
Pregnant women	Pregnant women are at higher risk of severe COVID-19 compared to women of child-bearing age who are not pregnant, and COVID19 has been associated with an increased risk of preterm birth. The available data on BNT162b2 vaccination of pregnant women are insufficient to assess vaccine efficacy or vaccine-associated risks in pregnancy. However, it should be noted that the BNT162b2 vaccine is not a live virus vaccine, the mRNA does not enter the nucleus of the cell and is degraded quickly. Developmental and reproductive toxicology (DART) studies in animals have not shown harmful effects in pregnancy. Further studies are planned in pregnant women in the coming months. As data	Pregnant women are at higher risk of severe COVID-19 compared with women of childbearing age who are not pregnant, and COVID-19 has been associated with an increased risk of preterm birth. The available data on mRNA-1273 vaccination of pregnant women are insufficient to assess vaccine efficacy or vaccine-associated risks in pregnancy. However, it should be noted that the mRNA-1273 vaccine is not a live virus vaccine, and the mRNA does not enter the nucleus of the cell and is degraded quickly. Developmental and reproductive toxicology (DART) studies in animals have not shown harmful	Pregnant women are at higher risk of severe COVID-19 compared with women of childbearing age who are not pregnant, and COVID-19 has been associated with an increased risk of preterm birth. The available data on AZD1222 vaccination of pregnant women are insufficient to assess vaccine efficacy or vaccine-associated risks in pregnancy. However, it should be noted that AZD1222 is a nonreplicating vaccine. Animal developmental and reproductive toxicity (DART) studies are ongoing. Preliminary findings show no indication of harm to the development of the foetus. Further studies are planned in pregnant women in the coming months, including a pregnancy substudy and a pregnancy registry. As

	from these studies become available, recommendations on vaccination will be updated accordingly. In the interim, WHO recommends not to use BNT162b2 in pregnancy, unless the benefit of vaccinating a pregnant woman outweighs the potential vaccine risks, such as in health workers at high risk of exposure and pregnant women with comorbidities placing them in a high-risk group for severe COVID-19. Information and, if possible, counselling on the lack of safety and efficacy data for pregnant women should be provided. WHO does not recommend pregnancy testing prior to vaccination.	effects in pregnancy. Further studies are planned in pregnant women in the coming months. As data from these studies become available, recommendations on vaccination will be updated accordingly. In the interim, WHO recommends not to use mRNA-1273 in pregnancy, unless the benefit of vaccinating a pregnant woman outweighs the potential vaccine risks, such as in health workers at high risk of exposure and pregnant women with comorbidities placing them in a high-risk group for severe COVID-19. Information and, if possible, counselling on the lack of safety and efficacy data for pregnant women should be provided. WHO does not recommend pregnancy testing prior to vaccination. WHO does not recommend delaying pregnancy following vaccination.	data from these studies become available, recommendations on vaccination will be updated accordingly. In the interim, pregnant women should receive AZD 1222 only if the benefit of vaccination to the pregnant woman outweighs the potential vaccine risks, such as if they are health workers at high risk of exposure or have comorbidities that place them in a high-risk group for severe COVID-19. Information and, if possible, counselling on the lack of safety data for pregnant women should be provided. WHO does not recommend pregnancy testing prior to vaccination. WHO does not recommend delaying pregnancy because of vaccination.
Lactating Women	Breastfeeding offers substantial health benefits to lactating women and their breastfed children. Vaccine efficacy is expected to be similar in lactating women as in other adults. However, there are no data on the safety of COVID-19 vaccines in lactating women	Breastfeeding offers substantial health benefits to lactating women and their breastfed children. Vaccine efficacy is expected to be similar in lactating women as in other adults. However, there are no data on the safety of COVID-19 vaccines in	Breastfeeding offers substantial health benefits to lactating women and their breastfed children. Vaccine efficacy is expected to be similar in lactating women as in other adults. It is unknown whether AZD1222 is excreted in human milk. As the AZD1222 vaccine is a non-replicating vaccine, it is unlikely to pose

	or on the effects of mRNA vaccines on breastfed children. As the BNT162b2 vaccine is not a live virus vaccine and the mRNA does not enter the nucleus of the cell and is degraded quickly, it is biologically and clinically unlikely to pose a risk to the breastfeeding child. On the basis of these considerations, a lactating woman who is part of a group recommended for vaccination, e.g. health workers, should be offered vaccination on an equivalent basis. WHO does not recommend discontinuing breastfeeding after vaccination.	lactating women or on the effects of mRNA vaccines on breastfed children. As the mRNA-1273 vaccine is not a live virus vaccine and the mRNA does not enter the nucleus of the cell and is degraded quickly, it is biologically and clinically unlikely to pose a risk to the breastfeeding child. On the basis of these considerations, a lactating woman who is part of a group recommended for vaccination, e.g. health workers, should be offered vaccination on an equivalent basis. WHO does not recommend discontinuing breastfeeding after vaccination.	a risk to the breastfeeding child. On the basis of these considerations, a lactating woman who is part of a group recommended for vaccination, e.g., health workers, should be offered vaccination on an equivalent basis. WHO does not recommend discontinuing breastfeeding after vaccination.
Persons living with HIV	Persons living with HIV may be at higher risk of severe COVID-19. Among the phase 2/3 clinical trial participants with well controlled HIV, there were no reported differences in safety signals. HIV-positive persons who are well controlled on highly active antiretroviral therapy and are part of a group recommended for vaccination can be vaccinated. Available data on administration of the vaccine are currently insufficient to allow assessment of vaccine efficacy or	Persons living with HIV may be at higher risk of severe COVID-19. Among the phase 3 clinical trial participants with well controlled HIV, there were no reported differences in safety signals. HIV-positive persons who are well controlled on highly active antiretroviral therapy and are part of a group recommended for vaccination can be vaccinated. Available data on administration of the vaccine are currently	Persons living with human immunodeficiency virus (HIV) may be at higher risk of severe COVID-19. Persons living with HIV were not included in the primary analyses of the trials and safety data in subgroups of HIV-positive subjects are awaited. Data on administration of the vaccine are currently insufficient to allow assessment of vaccine efficacy or safety for persons living with HIV. It is possible that the immune response to the vaccine may be reduced, which

	safety for persons living with HIV who are not well controlled on therapy. It is possible that the immune response to the vaccine may be reduced, which may alter its effectiveness. In the interim, given that the vaccine is not a live virus, persons living with HIV who are part of a group recommended for vaccination may be vaccinated. Information and, where possible, counselling about vaccine safety and efficacy profiles in immunocompromised persons should be provided to inform individual benefit–risk assessment. It is not necessary to test for HIV infection prior to vaccine administration.	insufficient to allow assessment of vaccine efficacy or safety for persons living with HIV who are not well controlled on therapy. It is possible that the immune response to the vaccine may be reduced, which may alter its effectiveness. In the interim, given that the vaccine is not a live virus, persons living with HIV who are part of a group recommended for vaccination may be vaccinated. Information and, where possible, counselling about vaccine safety and efficacy profiles in immunocompromised persons should be provided to inform individual benefit–risk assessment. It is not necessary to test for HIV infection prior to vaccine administration.	may lower its clinical effectiveness. In the interim, given that the vaccine is nonreplicating, persons living with HIV who are part of a group recommended for vaccination may be vaccinated. Information and, where possible, counselling should be provided to inform individual benefit–risk assessment. It is not necessary to test for HIV infection prior to vaccine administration.
Immunocompromised persons	Immunocompromised persons are at higher risk of severe COVID-19. Available data are currently insufficient to assess vaccine efficacy or vaccine-associated risks in severely immunocompromised persons. It is possible that the immune response to the vaccine may be reduced, which may alter its effectiveness. In the interim, given	Immunocompromised persons are at higher risk of severe COVID-19. Available data are currently insufficient to assess vaccine efficacy or vaccine-associated risks in severely immunocompromised persons. It is possible that the immune response to the vaccine may be reduced, which may alter its effectiveness. In the interim,	Immunocompromised persons are at higher risk of severe COVID-19. Available data are currently insufficient to assess vaccine efficacy or vaccine-associated risks in severely immunocompromised persons, including those receiving immunosuppressant therapy. It is possible that the immune response to the vaccine may be reduced, which may lower its clinical effectiveness. In the

	that the vaccine is not a live virus, immunocompromised persons who are part of a group recommended for vaccination may be vaccinated. Information and, where possible, counselling about vaccine safety and efficacy profiles in immunocompromised persons should be provided to inform individual benefit–risk assessment	given that the vaccine is not a live virus, immunocompromised persons who are part of a group recommended for vaccination may be vaccinated. Information and, where possible, counselling about vaccine safety and efficacy profiles in immunocompromised persons should be provided to inform individual benefit–risk assessment.	interim, given that the vaccine is nonreplicating, immunocompromised persons who are part of a group recommended for vaccination may be vaccinated. Information and, where possible, counselling about vaccine safety and efficacy profiles in immunocompromised persons should be provided to inform individual benefit–risk assessment.
Person with autoimmune conditions	No data are currently available on the safety and efficacy of BNT162b2 in persons with autoimmune conditions, although these persons were eligible for enrolment in the clinical trials. Persons with autoimmune conditions who have no contraindications to vaccination may be vaccinated.	No data are currently available on the safety and efficacy of mRNA-1273 in persons with autoimmune conditions, although these persons were eligible for enrolment in the clinical trials. Persons with autoimmune conditions who have no contraindications to vaccination may be vaccinated.	No data are currently available on the safety and efficacy of AZD1222 in persons with autoimmune conditions. Persons with autoimmune conditions who are part of a group recommended for vaccination may be vaccinated.
Persons with a history of Bell's palsy	Cases of Bell's palsy were reported following vaccination in participants in the Pfizer-BioNTech clinical trials. However, there is currently no conclusive evidence that these cases were causally related to vaccination. Post-authorization safety surveillance will be important to assess any	Cases of Bell's palsy were reported following vaccination in participants in the manufacturer's clinical trial. However, there is currently no conclusive evidence that these cases were causally related to vaccination. Post-authorization	N/A

	possible causal association. In the absence of such evidence, persons with a history of Bell's palsy may receive BNT162b2 unless they have a contraindication to vaccination.	safety surveillance will be important to assess any possible causal association. In the absence of such evidence, persons with a history of Bell's palsy may receive mRNA-1273 unless they have a contraindication to vaccination.	
Persons who have previously had SARS-CoV-2 infection	Vaccination may be offered regardless of a person's history of symptomatic or asymptomatic SARS-CoV-2 infection. Viral or serological testing for prior infection is not recommended for the purpose of decision-making about vaccination. Available data from the phase 2/3 trials indicate that BNT162b2 is safe in people with evidence of prior SARS-CoV-2 infection. The added protection of vaccinating previously infected individuals is yet to be established. Despite the potential for reinfection, currently available data indicate that symptomatic reinfection within 6 months after an initial infection is rare. Thus, persons with PCR confirmed SARS-CoV-2 infection in the preceding 6 months may delay vaccination until near the end of this period. When more	Vaccination may be offered regardless of a person's history of symptomatic or asymptomatic SARS-CoV-2 infection. Viral or serological testing for prior infection is not recommended for the purpose of decision-making about vaccination. Available data from the phase 3 trials indicate that mRNA-1273 is safe in people with evidence of prior SARS-CoV-2 infection. The added protection of vaccinating previously infected individuals is yet to be established. Despite the potential for reinfection, currently available data indicate that symptomatic reinfection within 6 months after an initial infection is rare. Thus, persons with PCR confirmed SARS-CoV-2 infection in the preceding 6 months may choose to delay vaccination until near the end of this period. When	Vaccination may be offered regardless of a person's history of symptomatic or asymptomatic SARS-CoV-2 infection. Viral or serological testing for prior infection is not recommended for the purpose of decision-making about vaccination. Available data from the pooled analyses indicate that AZD1222 is safe in people with evidence of prior SARS-CoV-2 infection. In participants who were seropositive at baseline, antibody levels were boosted after dose 1, with no further boosting after dose 2. The added protection of vaccinating previously infected individuals is yet to be established. Currently available data indicate that symptomatic reinfection within 6 months after an initial infection is rare. Thus, persons with PCR-confirmed SARS-CoV-2 infection in the preceding 6 months may delay vaccination until near the end of this period. When more data on duration of immunity after

	data on duration of immunity after natural infection become available, the length of this time period may be revised.	more data on duration of immunity after natural infection become available, the length of this time period may be revised.	natural infection become available, the length of this time period may be revised.
Persons with current acute COVID-19	Vaccination of persons with acute symptomatic SARS-CoV-2 should be deferred until they have recovered from acute illness and the criteria for discontinuation of isolation have been met. There are no data to support a recommendation of a minimal interval between onset of symptoms and vaccination.	Vaccination of persons with acute COVID-19 should be deferred until they have recovered from acute illness and the criteria for discontinuation of isolation have been met.	Persons with acute PCR-confirmed COVID-19, including those with onset of PCR-confirmed infection between doses, should not be vaccinated until after they have recovered from acute illness and the criteria for discontinuation of isolation have been met. Persons with PCR-confirmed SARS-CoV-2 infection may delay vaccination for 6 months. When more data on duration of immunity after natural infection become available, the length of this delay may be revised.
Persons who previously received passive antibody therapy for COVID-19	Currently there are no data on the safety or efficacy of vaccination in persons who received monoclonal antibodies or convalescent plasma as part of COVID-19 treatment. Hence, as a precautionary measure, vaccination should be deferred for at least 90 days to avoid interference of the antibody treatment with vaccine-induced immune responses.	Currently there are no data on the safety or efficacy of vaccination in persons who received monoclonal antibodies or convalescent plasma as part of COVID-19 treatment. Hence, as a precautionary measure, vaccination should be deferred for at least 90 days to avoid interference of the antibody treatment with vaccine-induced immune responses.	Currently there are no data on the safety or efficacy of vaccination in persons who received monoclonal antibodies or convalescent plasma as part of COVID-19 treatment. Hence, as a precautionary measure, vaccination should be deferred for at least 90 days to avoid interference of the antibody treatment with vaccine-induced immune responses.

3.1.3 Vaccine indirect effects

A. What is the COVID-19 vaccines coverage threshold required for herd immunity? [Systematic Search/WHO website]

Paper 1

Title of Article/Author/Year/Grade: Global, regional, and national estimates of target population sizes for covid-19 vaccination: descriptive study. / Wang, W., Wu, Q., Yang, J., Dong, K., Chen, X., Bai, X., / 2020

Type of Article: Descriptive study

Link of Article: https://www.bmj.com/content/371/bmj.m4704

Objective: To provide global, regional, and national estimates of target population sizes for coronavirus disease 2019 (covid-19) vaccination to inform country specific immunization strategies on a global scale. [88]

Result: Herd immunity was estimated to be between 60-80% of the world population. Target population sizes for covid-19 vaccination vary markedly by vaccination goal and geographical region. Differences in demographic structure, presence of underlying conditions, and number of essential workers lead to highly variable estimates of target populations at regional and country levels. In particular, Europe has the highest share of essential workers (63.0 million, 8.9%) and people with underlying conditions (265.9 million, 37.4%); these two categories are essential in maintaining societal functions and reducing severe covid-19, respectively. In contrast, South East Asia has the highest share of healthy adults (777.5 million, 58.9%), a key target for reducing community transmission. Vaccine hesitancy will probably impact future covid-19 vaccination programmes; based on a literature review, 68.4% (95% confidence interval 64.2% to 72.6%) of the global population is willing to receive covid-19 vaccination. Therefore, the adult population willing to be vaccinated is estimated at 3.7 billion (95% confidence interval 3.2 to 4.1 billion). National estimates of the size of target populations suggest that six countries—China, India, the US, Pakistan, Brazil, and Nigeria—have the largest share of the total target population. [88]

Conclusion: The distribution of target groups at country and regional levels highlights the importance of designing an equitable and efficient plan for vaccine prioritization and allocation. Each country should evaluate different strategies and allocation schemes based on local epidemiology, underlying population health, projections of available vaccine doses, and preference for vaccination strategies that favour direct or indirect benefits. In the most optimistic scenario that this figure is actually reached, it would take about six to seven months to produce enough vaccines to achieve herd immunity by protecting at least 60-80% of the world population (4.7-6.2 billion). [88]

Paper 2

Title of Article/Author/Year/Grade: Challenges in creating herd immunity to SARS-CoV-2 infection by mass vaccination. / Anderson, R. M., Vegvari, C., Truscott, J., & Collyer, B. S. / 2020 / 6(10)

Type of Article: Rapid review

Link of Article: https://www.thelancet.com/article/S0140-6736(20)32318-7/fulltext

Objective: Determining the implications of herd immunity with the SARS-CoV-2 pandemic. [89]

Result: How much vaccine is required by any given country year by year to create herd immunity to block SARS-CoV-2 transmission, and how long this will take requires calculations with clearly defined assumptions. Vaccine delivery will probably scale up only gradually as manufacturing capabilities develop over 12–24 months post licensure of a COVID-19 vaccine. As such, the impact of vaccination on the transmission of SARS-CoV-2 will start slowly and build up over a few years to reach target coverage levels. The amount of vaccine required for a defined population will depend on evidence from phase 3 COVID-19 vaccine trials on efficacy and what can be assumed about the average duration of vaccine protection—it will be an assumption until the findings of phase 4 trials on duration of both protection against infection and severe disease are reported. For a vaccine with 100% efficacy that gives life-long protection, the level of herd immunity as a proportion of the population, p_c, required to block transmission is $[1 - 1 / R_0]$, where R_0 is the basic reproduction number. [89]

Given an R_0 value before lockdowns in most countries of between 2·5 to 3·5, we estimate the herd immunity required is about 60–72%. If the proportional vaccine efficacy, ε, is considered, the simple expression for p_c becomes $[1 - 1 / R_0] / \varepsilon$. If we assume ε is 0·8 (80%), then the herd immunity required becomes 75–90% for the defined range of R_0 values. For lower efficacies, the entire population would have to be immunised. These overall estimates ignore heterogeneities that can make these figures lower or higher in specific locations. [89]

Conclusion: Taking novel vaccines successfully through phase 1 to phase 3 trials within a year has been an outstanding achievement, but equally challenging over the coming year will be persuading governments and populations to use COVID-19 vaccines effectively to create herd immunity to protect all. [89]

Paper 3

Title of Article/Author/Year/Grade: Herd immunity and implications for SARS-CoV-2 control / Omer, S. B., Yildirim, I., & Forman, H. P. / 2020

Type of Article: Rapid review

Link of Article: https://jamanetwork.com/journals/jama/fullarticle/2772167

Objective: Determining the implications of herd immunity with the SARS-CoV-2 pandemic. [90]

Result: The population of the United States is about 330 million. Based on World Health Organization estimates of an infection fatality rate of 0.5%, about 198 million individuals in the United States are needed to be immune to reach a herd immunity threshold of approximately 60%, which would lead to several hundred thousand additional deaths. Assuming that less than 10% of the population has been infected so far,[10] with an infection-induced immunity lasting 2 to 3 years (duration unknown), infection-induced herd immunity is not realistic at this point to control the pandemic. SARS-CoV-2 vaccines will help to reach the herd immunity threshold, but the effectiveness of the vaccine(s) and the vaccine coverage are to be seen. [90]

Conclusion: Herd immunity is an important defense against outbreaks and has shown success in regions with satisfactory vaccination rates. Importantly, even small deviations from protective levels can allow for significant outbreaks due to local clusters of susceptible individuals, as has been seen with measles over the past few years. Therefore, vaccines must not only be effective, but vaccination programs must be efficient and broadly adopted to ensure that those who cannot be directly protected will nonetheless derive relative protections. [90]

3.1.4 Vaccine characteristics

A. In which presentations and formulations are COVID-19 vaccine available? Storage and handling requirements? [Manufacture's Website, WHO PP]

	Pfizer-BioNTech Vaccine	Moderna Vaccine	Astrazeneca-Oxford Vaccine	Sinovac Vaccine	Sinopharm/BIBO Vaccine
Name of Vaccine	BNT162b2	mRNA-1273	ChAdOx1 nCoV-19 vaccine (**AZD1222**)	SARS-CoV-2 vaccine (inactivated)	Inactivated SARS-CoV-2 vaccine (Vero cell)
Presentation	Multi-dose vial: up to 6 doses via vial	Multi-dose vials	5 ml preservative free, non-latex multidose vials	Multi-dose vial	Pre-filled 0.5ml syringes
Storage temperature	-80°C to -60°C	Between -25°C and -15°C	2°C — 8°C	2°C — 8°C	2°C — 8°C
Handling requirements	This vaccine requires ultra-low temperature freezer for storage up to 6 months. Temperature-controlled thermal shippers utilizing dry ice to maintain recommended temperature conditions of -70°C±10°C for up to 10 days will be needed for transportation. The vaccine can be stored for five days at refrigerated 2-8°C condition.	The mRNA-1273 COVID-19 vaccine is provided as a frozen suspension at −25 °C to −15 °C in a multidose vial containing 10 doses. The vaccine must be thawed prior to administration. After thawing, 10 doses (0.5 ml each) can be withdrawn from each vial. Vials can be stored refrigerated at 2–8 °C for up to 30 days prior to	Store in refrigerator (2 to 8°C). Shelf life = 6 months. Do not freeze. Keep vials in outer carton to protect from light. After first puncture cumulatively store up to 6 hours at room temperature or up to 48 hours at 2-8°C with total storage time not to exceed 48 hours. No dilution or reconstitution necessary.		BIBP-CorV can be transported and stored at normal refrigeration temperatures

	The Pfizer thermal shippers, in which doses will arrive, can be used as temporary storage units by refilling with dry ice for up to 15 days of storage. After storage for 15 days in the Pfizer thermal shipper, vaccination centers can transfer the vials to 2- 8°C storage conditions for an additional five days, for a total of 20 days. Once thawed and stored under 2-8°C conditions, the vials cannot be re-frozen or stored under frozen condition.	withdrawal of the first dose. Unopened vials may be stored for up to 12 hours in cool storage or at room temperature (8–25 °C). After the first dose has been withdrawn, the vial should be held between 2 °C and 25 °C and discarded after 6 hours.			

	The Gamaleya National Centre Vaccine (Sputnik V)	Janssen Pharmaceutical Vaccine	Novavax Vaccine	CanSinoBIO Vaccine
Name of Vaccine	Gam-COVID-Vac Adeno-based (rAd26-S+rAd5-S)	Ad26.COV2.S	SARS-CoV-2 rS/Matrix M1-Adjuvant (Full length recombinant SARS CoV-2 glycoprotein nanoparticle vaccine adjuvanted with Matrix M)	Recombinant novel coronavirus vaccine (Adenovirus type 5 vector)
Storage temperature	Frozen version (−18 ◦C) and lyophilized version (2–8 ◦C)	2–8◦C	2–8 ◦C	2–8 ◦C

A. What is the recommended form of administration and dosage for COVID-19 vaccines? [Manufacture's Website, WHO PP]

	Pfizer-BioNTech Vaccine	Moderna Vaccine	Astrazeneca-Oxford Vaccine	Sinovac Vaccine	Sinopharm/BIBO Vaccine
Name of Vaccine	BNT162b2	mRNA-1273	ChAdOx1 nCoV-19 vaccine (**AZD1222**)	SARS-CoV-2 vaccine (inactivated)	Inactivated SARS-CoV-2 vaccine (Vero cell)
Dose and Vaccine Schedule	0.3 mL (30 mcg of mRNA) 2 Doses, 21 days apart	0.5 mL (100 mcg of mRNA) 2 Doses, 28 days apart	WHO EUA Recommendation: 2 doses 8 to 12 weeks apart	2 doses, 14 days apart	2 doses, 21 days apart
Route of Administration	IM	IM	IM	IM	IM

	The Gamaleya National Centre Vaccine (Sputnik V)	Janssen Pharmaceutical Vaccine	Novavax Vaccine	CanSinoBIO Vaccine	Serum Institute of India Vaccine
Name of Vaccine	Gam-COVID-Vac Adeno-based (rAd26-S+rAd5-S)	Ad26.COV2.S	SARS-CoV-2 rS/Matrix M1-Adjuvant (Full length recombinant SARS CoV-2 glycoprotein nanoparticle vaccine adjuvanted with Matrix M)	Recombinant novel coronavirus vaccine (Adenovirus type 5 vector)	RBD SARS-CoV-2 HBsAg VLP vaccine
Dose and Vaccine Schedule (CDC)	Pending official data 2 doses, 21 days apart	1 – 2 doses, 56 days apart Single dose – 66% effective at preventing moderate and severe forms of detectable illness 28 days	2 doses, 21 days apart	1 dose	2 doses, 28 days apart

		after vaccination, 85 percent effective at preventing severe disease, and 100 percent effective at preventing hospitalizations and deaths			
Route of Administration	IM	IM	IM	IM	IM

C. What evidence exist to ensure flexibilities of the vaccine schedules for the vaccine program?

	Pfizer-BioNTech Vaccine	Moderna Vaccine	AstraZeneca-Oxford Vaccine	Sinovac Vaccine	Sinopharm/BIBO Vaccine
Name of Vaccine	BNT162b2	mRNA-1273	ChAdOx1 nCoV-19 vaccine (**AZD1222**)	SARS-CoV-2 vaccine (inactivated)	Inactivated SARS-CoV-2 vaccine (Vero cell)
Vaccine Schedule	21 days apart	28 days apart	28 days apart	14 days apart	21 days apart
Flexibility of Vaccine Schedule	WHO's recommendation at present is that the interval between doses may be extended up to 42 days (6 weeks), on the basis of currently available clinical trial data. Should additional data become available on longer intervals between doses, revision of this	WHO's recommendation at present is that, if judged necessary, the interval between doses may be extended to 42 days. The evidence base for this extension is not strong, but this was the longest interval for any participants in the primary efficacy	In light of the observation that two-dose efficacy and immunogenicity increase with a longer interdose interval, WHO recommends an interval of 8 to 12 weeks between the doses. If the second dose is inadvertently administered less than 4 weeks after the first, the dose does not need to be repeated. If administration of	N/A	N/A

	recommendation will be considered	analyses of the phase 3 trial	the second dose is inadvertently delayed beyond 12 weeks, it should be given at the earliest possible opportunity. It is recommended that all vaccinated individuals receive two doses.		

C. What is the recommended schedule for the control of COVID-19 disease?

	Pfizer-BioNTech Vaccine	Moderna Vaccine	AstraZeneca-Oxford Vaccine	Sinovac Vaccine	Sinopharm/BIBO Vaccine
Type of Document	WHO Guideline Document	WHO Guideline Document	WHO Guideline Document	Safety, tolerability, and immunogenicity of an inactivated SARS-CoV-2 vaccine in healthy adults aged 18–59 years: a randomised, double-blind, placebo-controlled, phase 1/2 clinical trial (Phase 1/2)	Safety and immunogenicity of an inactivated SARS-CoV-2 vaccine, BBIBP-CorV: a randomised, double-blind, placebo-controlled, phase 1/2 trial (Phase 1/2)
Title of Document	Interim recommendations for use of the Pfizer-BioNTech COVID-19 vaccine, BNT162b2, under Emergency Use Listing	Interim recommendations for use of the Moderna mRNA-1273 vaccine against COVID-19	Interim recommendations for use of the AZD1222 (ChAdOx1-S [recombinant]) vaccine against COVID19 developed by Oxford University and AstraZeneca	Zhang, Y., Zeng, G., Pan, H., Li, C., Hu, Y., Chu, K., et al / 2020 / 10(11)	Prof Shengli Xia, BSc., Yuntao Zhang, PhD., Yanxia Wang, BSc., Hui Wang, BSc., Yunkai Yang, BSc., Prof George Fu Gao, PhD., et al. / 2020 / 10(11)
Source	WHO	WHO	WHO	RCT	RCT
Link of Document	https://www.who.int/publications/i/item/WHO-2019-nCoV-vaccines-SAGE_recommendation-BNT162b2-2021.1	https://www.who.int/publications/i/item/interim-recommendations-for-use-of-the-moderna-mrna-1273-	https://www.who.int/publications/i/item/WHO-2019-nCoV-vaccines-SAGE_recommendation-AZD1222-2021	https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(20)30843-4/fulltext	https://doi.org/10.1016/S1473-3099(20)30831-8

		vaccine-against-covid-19			
Objective	To assess the safety and efficacy of two doses of BNT162b2, administered intramuscularly 21 days apart, as compared with placebo.	To test the safety and immunogenicity of SARS-CoV-2 mRNA-1273 vaccine in older adults since increased incidences of illness and death from coronavirus disease 2019 (Covid-19) have been associated with an older age.	The coprimary outcomes of the trial are to assess efficacy as measured by the number of cases of symptomatic, virologically confirmed COVID-19 and safety of the vaccine as measured by the occurrence of serious adverse events.	To investigate CoronaVac (Sinovac Life Sciences, Beijing, China), an inactivated vaccine candidate against COVID-19, containing inactivated Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), for its safety, tolerability and immunogenicity.	to assess the safety and immunogenicity of an inactivated Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) vaccine candidate, BBIBP-CorV, in humans.
Age/ Doses	16 years and above, 2 doses (21 days)	16 years and above 2 doses (28 days apart)	16 years and above 2 doses (28 days apart)	16 years and above 2 doses (28 days apart)	16 years and above 2 doses (28 days apart)

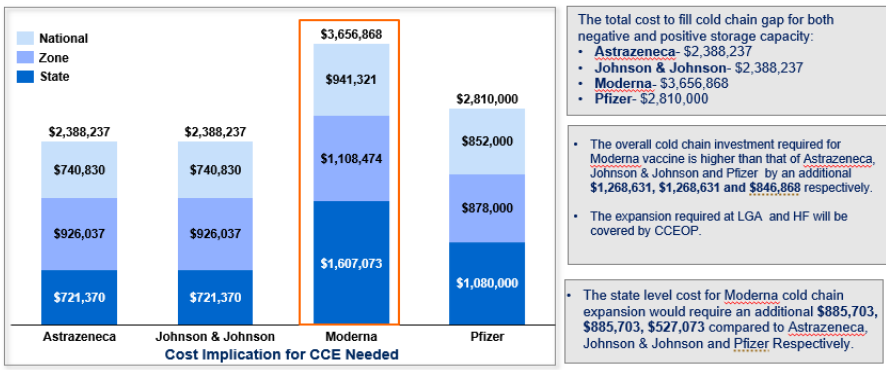
	The Gamaleya National Centre Vaccine	Janssen Pharmaceutical Vaccine	Novavax Vaccine	CanSinoBIO Vaccine	Serum Institute of India Vaccine
Title of Article	Safety and immunogenicity of an rAd26 and rAd5 vector-based heterologous prime-boost COVID-19 vaccine in two formulations: two open, non-randomised phase 1/2 studies from Russia	Safety and immunogenicity of the Ad26.COV2.S COVID-19 vaccine candidate: interim results of a phase 1/2a, double-blind, randomized,	Phase 1–2 Trial of a SARS-CoV-2 Recombinant Spike Protein Nanoparticle Vaccine	Immunogenicity and safety of a recombinant adenovirus type-5-vectored COVID-19 vaccine in healthy adults aged 18 years or older: a randomised, double-blind, placebo-controlled, phase 2 trial	

	(Phase 1/2)	placebo-controlled trial (Phase 1/2 trial)			
Author/Year/Grade	Denis Y Logunov, DSc., Inna V Dolzhikova, PhD., Olga V Zubkova, PhD., Amir I Tukhvatulin, PhD., Dmitry V Shcheblyakov, PhD., Alina S Dzharullaeva, MSc., et al. / 2020 / 7(11)	Sadoff, Jerry, Mathieu Le Gars, Georgi Shukarev, Dirk Heerwegh, Carla Truyers, Anna Marit de Groot, Jeroen Stoop et al. / 2020 / 8(11)	Cheryl Keech, M.D., Ph.D., Gary Albert, M.S., Iksung Cho, M.S., Andreana Robertson, M.S., Patricia Reed, B.S., Susan Neal, Joyce S. Plested, Ph.D., Mingzhu Zhu, Ph.D., Shane Cloney-Clark, B.S., Haixia Zhou, Ph.D., Gale Smith, Ph.D., et al / 2020 / 8(11)	Zhu, Feng-Cai, Xu-Hua Guan, Yu-Hua Li, Jian-Ying Huang, Tao Jiang, Li-Hua Hou, Jing-Xin Li et al. / 2020 / 8 (11)	
Type of Article	RCT	RCT	RCT	RCT	
Link of Article	https://www.thelancet.com/pdfs/journals/lancet/PIIS0140-6736(20)31866-3.pdf	https://www.medrxiv.org/content/10.1101/2020.09.23.20199604v1	https://www.nejm.org/doi/full/10.1056/NEJMoa2026920?query=featured_home	https://doi.org/10.1016/S0140-6736(20)31605-6	
Objective	to assess the safety and immunogenicity of two formulations (frozen and lyophilised) of this vaccine.	to assesses the safety, reactogenicity and immunogenicity of Ad26.COV2.S, a non-replicating adenovirus 26 based	We initiated a randomized, placebo-controlled, phase 1–2 trial to evaluate the safety and immunogenicity of the rSARS-CoV-2	Assessment of the immunogenicity and safety of a candidate non-replicating adenovirus type-5 (Ad5)-vectored COVID-19 vaccine, aiming to determine an	

		vector expressing the stabilized pre-fusion spike (S) protein of SARS-CoV-2.	vaccine (in 5-µg and 25-µg doses, with or without Matrix-M1 adjuvant).	appropriate dose of the candidate vaccine for an efficacy study.	
Doses	2 days (28 days)	Unconcluded (I dose or 2 doses (56 days apart) Single dose – 66% effective at preventing moderate and severe forms of detectable illness 28 days after vaccination, 85 percent effective at preventing severe disease, and 100 percent effective at preventing hospitalizations and deaths	2 doses (21 days apart)	One dose	

B. **What are the additional logistical and cold chain requirements of introducing COVID-19 vaccines into the current immunization program?** ***[NPHCDA reports and plans]***

There are cost implications for CCE needed to introduce Astrazeneca, Johnson & Johnson, Moderna and Pfizer vaccines considering current RI and NVIs



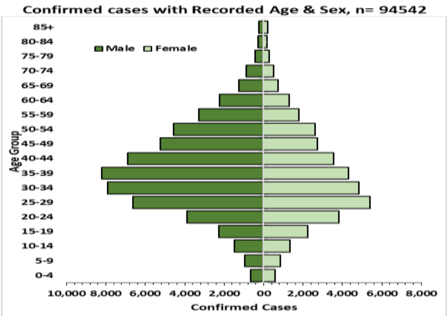
	RI, NVs, and Astrazeneca		RI, NVs and Johnson & Johnson		RI, NVs and Moderna		RI, NVs and Pfizer	
Supply Levels	(+2° C - +8° C)	(-20° C)	(+2° C - +8° C)	(-20° C)	(+2° C - +8° C)	(-20° C)	(+2° C - +8° C)	(-70° C)
National	106,436L	0L	106,436L	0L	0L	106,436L	0L	49,425L
Zone	106,436L	0L	106,436L	0L	0L	104,689L	0L	49,425L
State	58,905L	0L	58,905L	0L	0L	82,814L	0L	48,968L

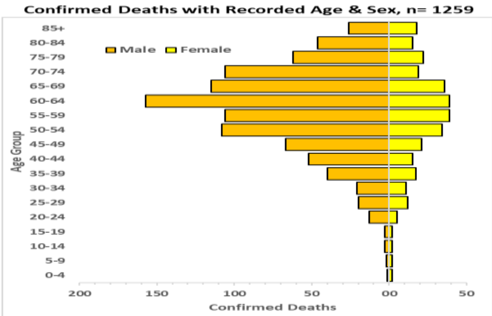
3.2 Disease

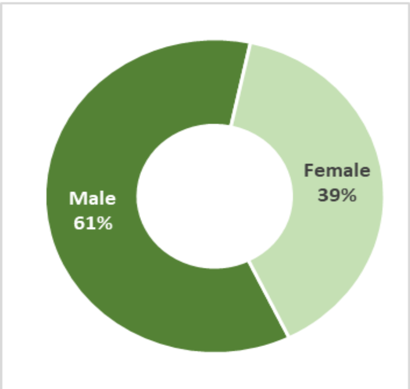
3.2.1 Burden of disease

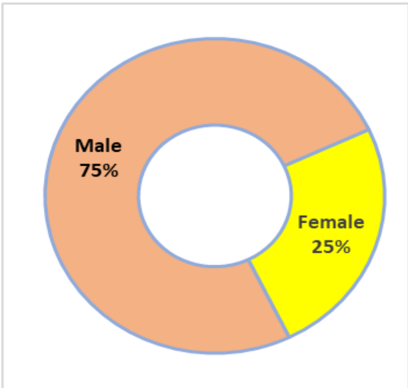
a. **What is the age specific incidence, prevalence and case fatality rate of COVID-19 in the country** ***[NPHCDA, NCDC, other reports and plans]?***

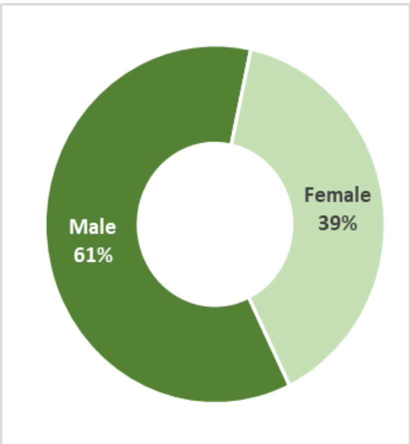
Title of Article/Author/Year/Grade: An update of COVID-19 outbreak in Nigeria/NCDC/2021
Type of Article: Official report
Source/Link of Article:
https://ncdc.gov.ng/diseases/sitreps/?cat=14&name=An%20update%20of%20COVID-19%20outbreak%20in%20Nigeria
Objective:
The write-up aims to convey the summary of COVID-19 epidemiology in Nigeria.
Result:
Cumulatively, since the outbreak began there have been 1,504 deaths reported with a case fatality rate (CFR) of 1.2% as at 26th of January 2021. [91]

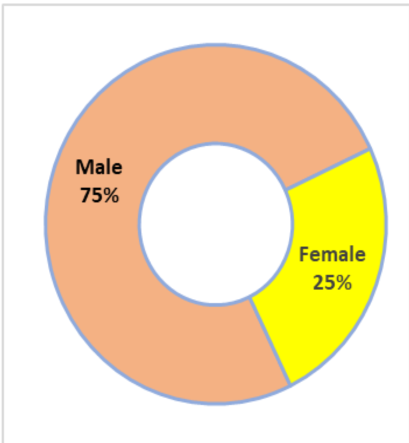

Confirmed cases with Recorded Age & Sex, n= 94542
Male
Female
85+
80-84
75-79
70-74
65-69
60-64
55-59
50-54
45-49
40-44
35-39
30-34
25-29
20-24
15-19
10-14
5-9
0-4
Age Group
10,000 8,000 6,000 4,000 2,000 00 2,000 4,000 6,000 8,000
Confirmed Cases

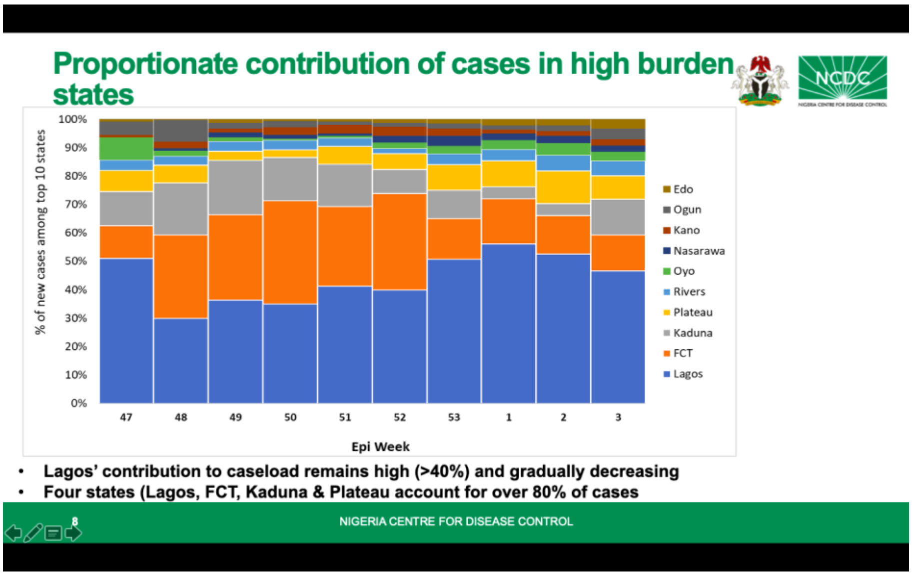

Confirmed Deaths with Recorded Age & Sex, n= 1259
Male
Female
85+
80-84
75-79
70-74
65-69
60-64
55-59
50-54
45-49
40-44
35-39
30-34
25-29
20-24
15-19
10-14
5-9
0-4
Age Group
200 150 100 50 00 50
Confirmed Deaths


Male
61%
Female
39%


Male
75%
Female
25%


Male
61%
Female
39%


Male
75%
Female
25%



1b. Number of outbreaks in Nigeria: Two waves in Nigeria so far. This can be considered as "outbreaks"

Conclusion:

- Cumulatively, since the outbreak began in Week **9 of** 2020 there have been **1,504** deaths reported with a case fatality rate (CFR) of **1.2%**
- Middle-aged and males more affected, worse CFR in males above 50 years of age.
- The number of COVID-19 confirmed cases in the country continues to rise. There is also an increasing number of persons who are asymptomatic or have mild symptoms

A. How frequently do COVID-19 outbreaks occur in the country *[NPHCDA, NCDC, other reports and plans]*. Are there areas or populations in the country that are at high risk of contracting COVID-19?

Title of Article/Author/Year/Grade: An update of COVID-19 outbreak in Nigeria/NCDC/2021
Type of Article: Official report
Source/Link of Article:
https://ncdc.gov.ng/diseases/sitreps/?cat=14&name=An%20update%20of%20COVID-19%20outbreak%20in%20Nigeria
Objective:
The write-up aims to convey the summary of COVID-19 epidemiology in Nigeria as at January 29, 2021.

Result: The pandemic is on-going, and high disease burden is seen in Lagos and Abuja. [91]

GENERAL FACT SHEET – DATA AS AT 7TH FEBRUARY 2021

Table 1: States with reported laboratory-confirmed COVID-19 cases, recoveries, deaths, samples tested and active cases

STATES	CONFIRMED		RECOVERIES		DEATHS		TESTING		ACTIVE CASES
	Total	Last Week	Total	Last Week	Total	Last Week	Total	Last Week	
Abia	1,338	118	1,212	118	13	1	17,468	517	113
Adamawa	673	42	240	0	28	0	11,464	120	405
Akwa Ibom	1,090	212	574	33	14	4	11,727	1,010	502
Anambra	1,271	378	334	0	19	0	18,336	612	918
Bauchi	1,164	22	1,144	27	17	0	16,064	677	3
Bayelsa	695	26	636	60	24	0	12,410	304	35
Benue	917	69	546	2	21	1	12,771	382	350
Borno	1,085	128	850	76	37	1	17,226	598	198
Cross River	222	27	200	21	12	0	5,331	203	10
Delta	2,396	73	1,744	7	52	0	30,365	1,210	600
Ebonyi	1,540	117	1,269	58	30	0	10,429	307	241
Edo	4,006	212	3,158	112	146	7	28,536	657	702
Ekiti	641	64	494	28	9	0	13,063	610	138
Enugu	1,829	91	1,511	90	21	0	16,984	592	297
FCT	17,824	961	11,474	491	128	2	192,097	5,600	6,222
Gombe	1,802	196	1,541	98	42	0	33,765	686	219
Imo	1,220	104	999	164	19	1	27,054	1,087	202
Jigawa	485	25	402	12	11	0	7,033	201	72
Kaduna	7,818	157	7,505	443	57	0	57,889	2,853	256
Kano	3,314	322	2,841	283	92	13	75,633	2,013	381
Katsina	1,901	37	1,842	112	27	0	33,441	325	32
Kebbi	276	6	257	4	13	0	6,115	38	6
Kogi	5	0	3	0	2	0	3,365	223	0
Kwara	2,158	222	1,575	26	42	1	18,080	1,840	541
Lagos	51,685	2,411	45,249	4,316	343	29	336,297	11,272	6,093
Nasarawa	1,976	166	373	48	13	0	17,076	395	1,590
Niger	847	159	417	0	14	0	15,478	1,075	416
Ogun	3,578	197	3,123	321	45	2	59,575	614	410
Ondo	2,506	206	2,080	80	55	4	18,435	865	371
Osun	1,805	268	1,401	265	33	1	13,839	1,565	371
Oyo	5,905	488	4,160	33	89	4	46,339	1,859	1,656
Plateau	8,297	403	7,904	613	56	3	58,317	1,654	337
Rivers	5,759	483	4,965	481	86	7	123,264	6,215	708
Sokoto	759	11	715	25	26	0	17,657	238	18
Taraba	496	84	379	65	15	0	9,552	421	102
Yobe	250	9	213	14	8	0	7,627	115	29
Zamfara	215	12	195	10	8	0	5,721	97	12
Total	139,748	8,506	113,525	8,536	1,667	81	1,405,823	49,050	24,556

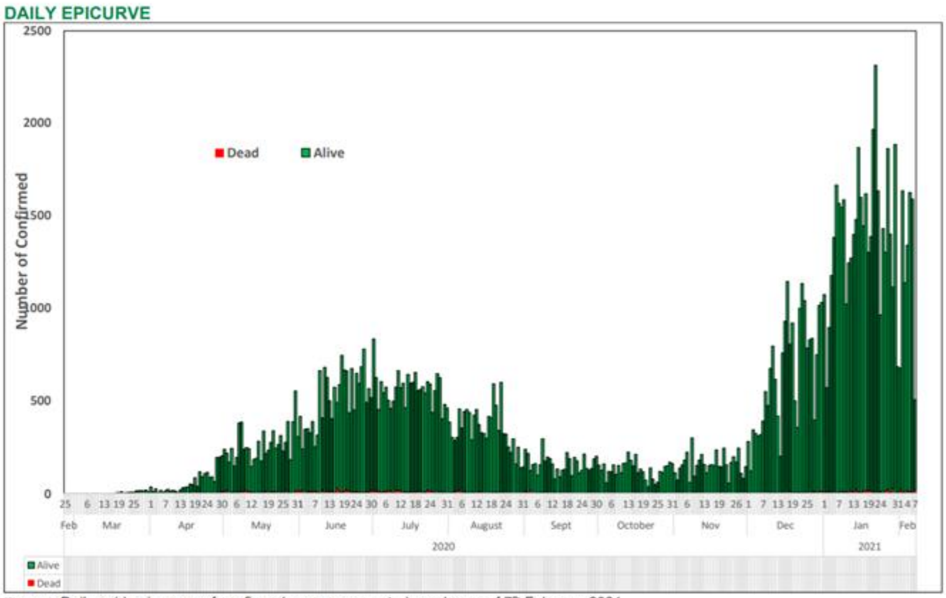
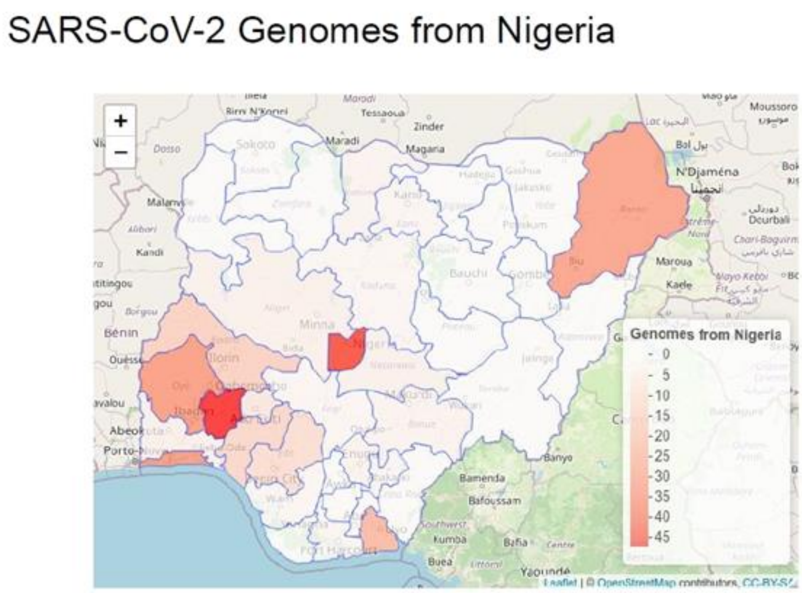


Figure 3: Daily epidemic curve of confirmed cases as reported per day as of 7th February 2021

B. **Which are the prevalent COVID-19 strains in the country by zone? [NPHCDA,NCDC, other reports and plans]/ Genomic history and pattern of mutation.**

Title of Document: Genomic surveillance for COVID-19 in Nigeria.



Type of Document: Nigeria Centre for Disease Control (NCDC)/ African Centre for Genomics of Infectious Diseases (ACEGID)/ Nigerian Institute of Medical Research (NIMR)
Result: The Nigeria Centre for Disease Control (NCDC) in collaboration with the African Centre for Genomics of Infectious Diseases (ACEGID) and the Nigerian Institute of Medical Research (NIMR) have been conducting genomic surveillance for COVID-19 in Nigeria.
As at the 30th of January 2021, 44 different lineages of SARS-CoV-2 have been identified in Nigeria. This indicates multiple introductions of the virus into Nigeria from different parts of the world. The most prevalent of these is the D614G mutation, which is not associated with increased morbidity or mortality.
The B.1.1.7 strain, which was first reported in the UK to be associated with increased transmission has been detected in seven individuals in Nigeria and in five people abroad, with recent travel history out of Nigeria.
It is important to note that about 300 samples only have been sequenced in Nigeria. Although this is being scaled up, it means there may be a higher number of circulating variants. There has not been sufficient sequencing done to provide a break down in the geopolitical zones.

C. Which Coronavirus variants have been identified in previous outbreaks/epidemics in the country? *[NPHCDA,NCDC, other reports and plans]*

Title of Document: Genomic surveillance for COVID-19 in Nigeria.
Type of Document: Nigeria Centre for Disease Control (NCDC) / African Centre for Genomics of Infectious Diseases (ACEGID) / Nigerian Institute of Medical Research (NIMR)

Result: The B.1.1.7 variant, which was first identified in the United Kingdom, has been identified in seven cases in Nigeria. These were identified in cases from Osun (5), Kwara (1) and FCT (1). The NCDC is working with ACEGID, NIMR and other institutions to increase the number of samples sequenced in Nigeria

D. What is the Genomic history of Covid19

Title of Document: Genomic surveillance for COVID-19 in Nigeria.

Type of Document: Nigeria Centre for Disease Control (NCDC) / African Centre for Genomics of Infectious Diseases (ACEGID) / Nigerian Institute of Medical Research (NIMR)

Result: Clinical specimens [specifically saliva, nasopharyngeal and nasal swabs] from suspected COVID-19 cases were passed through confirmatory testing, sequencing and molecular characterization. Viral RNA was extracted using the QiAmp viral RNA mini kit [Qiagen]. RT-qPCR was carried out using the DAAN RT-qPCR assay which confirmed the presence of SARS-CoV-2 viral RNA. Metagenomic sequencing libraries were prepared from total RNA as we previously described and sequenced using the two Illumina MiSeqs in the sequencing platform of ACEGID.

Genome assembly was done at ACEGID using publicly available software [viral-ngs v2.0] implemented on the DNA nexus cloud-based platform. We assembled 24 genomes [18 full and 6 partials].

Representative HCoV whole genome sequences of each of the lineages circulating in Nigeria were obtained from GISAID and aligned with all full genomes from Nigeria so far. The sequences were aligned using MAFFT v7.310 and tree reconstruction using FastTree v2.1.11.

Using Pangolin software [Rambaut et al ., 2020], we assigned the sequences to global SARS-CoV-2 lineages.Sequences from these lineages from Nigeria are clustering with sequences from Asia, Europe, USA, Middle-East, Australia, and other African countries.

D. Has the burden of COVID-19 disease changed following implementation of preventive measures (e.g. lock down) in the targeted states? *[NPHCDA, NCDC, other reports and plans]*

Paper 1

Title of Article/Author/Year/Grade: Easing of lockdown measures in Nigeria: Implications for the healthcare system / Ridwan Lanre Ibrahim, Kazeem Bello Ajide, and Omokanmi Olatunde Julius / 2020 / 5(12)

Type of Article: Observational Study

Link of Article: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7490626/

Objective: We employ the daily situation data on reported cases of COVID-19 to explicate the implications of the lockdown lifting in Nigeria using both qualitative and descriptive statistics. [92]

Result: Considering the aforementioned issues in line with the persistent surge in the cases of COVID-19 virus since the gradual easing of lockdown in the country, one would say without any doubt that the situation will further deteriorate and if care is not taken, might result to a total collapse of the struggling healthcare system. The likely implications on the health indicators in the country may be unimaginable considering the pre-COVID-19 statistics. According to WHO 2019 statistics, Nigeria accounts for 19 percent of the global maternal deaths, which is among the highest. Specifically, the infant mortality is estimated at 19 deaths per 1000 birth and the situation is more alarming at 128 per 1000 births among under age children. In terms of life expectancy, the record stands at 55.4 percent (females), and 53.7 (males) with the average rate standing at 54.4. Intuitively, the ensuing negative effects of the phased lifting of the lockdown could further exacerbate the current state of the various health indicators. [92]

Conclusion: The existing health implications of the COVID-19 cases in the three phases of lockdown are not appealing to Nigeria from all indicators. Every day of the easing phase of the lockdown has witnessed an increasing number of cases. The country is now on an average record of between 500 and 600 cases for most of the reports since mid-June 2020. There are possibilities that these cases may escalate more in future days of phase three. This thus requires the government to go back to the drawing board to put up more plans towards adhering to the WHO outlined prerequisites as exposited in section two above. Until this is done, the future days may likely be more overwhelming for the capacity of the healthcare system contain. [92]

Paper 2
Title of Article/Author/Year/Grade: Estimating the impacts of lockdown on Covid-19 cases in Nigeria / Kazeem Bello Ajide, Ridwan Lanre Ibrahim, and Olorunfemi Yasiru Alimi / 2020
Type of Article: Modelling Study
Link of Article: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7474887/
Objective: The study examines the extent to which lockdown measures impact on COVID-19 confirmed cases in Nigeria. Six indicators of lockdown entailing retail and recreation, grocery and pharmacy, parks, transit stations, workplaces, and residential, are considered. [93]

Result: The results for all the indicators of lockdown variables are statistically significant and negative except for the residential variable. These results consistent with the theoretical *priors,* suggesting the mitigating role of lockdown policies on coronavirus spread. By implication, as people comply with the "stay-at-home" order, and limit their visits to essential places, thus reduce their chances of being infected by COVID-19. Correspondingly, this also tends to reduce human-to-human contact, which is the main transmission channel of COVID-19. Intuitively, a 1% increase in compliance to the stay-at-home order leads to a corresponding reduction by the magnitudes 0.026%, 0.019%, 0.035%, 0.020% and 0.020%. [93]

On the contrary, the impact of residential is positive and statistically relevant. This sounds plausible as people desert essential places of visits, they tend to increase their presence at home. In particular, the majority of infected persons usually have one or more of their family members or close relatives infected. This explains why residential remains a key predicting channel to contacting COVID-19 and such reasons can be advanced as why COVID increases during the lockdown. [93]

Conclusion: This study examines the extent to which lockdown measures impact on COVID-19 confirmed cases in Nigeria. Using the negative binomial regression estimator on the daily situation data, the following results are established. First, retail and recreation, grocery and pharmacy, parks, transit stations, and workplaces are negative and statistically significant across the models. Second, the impact of residential is positive and statistically relevant, thus running contrary to other lockdown measures with negative theoretical *priors*. Lastly, the obtained results are robust to an alternative estimator of Poisson Regression. [93]

Paper 3

Title of Article/Author/Year/Grade: Nigeria's public health response to the COVID-19 pandemic: January to May 2020 / Dan-Nwafor, Chioma, Chinwe Lucia Ochu, Kelly Elimian, John Oladejo, Elsie Ilori, Chukwuma Umeokonkwo, Laura Steinhardt et al. / 2020.
Type of Article: Viewpoint / Commentary
Link of Article: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7696244/
Objective: This is to record the public health response to the COVID-19 pandemic in Nigeria. [94]

Result: Nigeria has, to date, the second-highest number of confirmed COVID-19 cases in Africa, and accounts for 7% of all confirmed cases on the continent. This may be an underestimate of the actual case load given the relatively low testing rate in Nigeria. As of May 31, Nigeria had conducted 63 882 COVID-19 tests, equivalent to 293 tests per million population; in comparison, Ghana had conducted 184 343 (5948 per million population) and South Africa had conducted 488 609 tests (8251 per million population). [94]

Conclusion: Nigeria mounted a swift and aggressive response to COVID-19, leveraging on its existing epidemic preparedness and learning from other parts of the globe where transmission began earlier. The country's initial response included early activation of the national EOC at the NCDC, establishment of the multi-sectoral COVID-19 PTF, and decisive actions to stop international travel and impose a time-limited lockdown in highly affected areas. By rapidly implementing this set of interventions, Nigeria likely slowed down the rate of virus transmission and bought extra time to implement a robust case detection, testing, and treatment centre capacity. However, these efforts, especially testing, needs more private sector involvement to significantly ramp up COVID-19 diagnostic centres across the country. [94]

Paper 4
Title of Article/Author/Year/Grade: Impact of lockdown on COVID-19 prevalence and mortality during 2020 pandemic: observational analysis of 27 countries / Sultan Ayoub Meo, Abdulelah Adnan Abukhalaf, Ali Abdullah Alomar, Faris Jamal AlMutairi, Adnan Mahmood Usmani & David C. Klonoff / 2020 / 6(12).
Type of Article: Observational Study
Link of Article: https://eurjmedres.biomedcentral.com/articles/10.1186/s40001-020-00456-9
Objective: This study aimed to assess the impact of 15 days before, 15 days during, and 15 days after the lockdown on the trends in the prevalence and mortality in 27 countries during COVID-19 pandemic. [95]

Result: The findings showed that 15 days after the lockdown there was a trend toward a decline, but no significant decline in the mean prevalence and mean mortality rate due to the COVID-19 pandemic compared to 15 days before, and 15 days during the lockdown in 27 countries. The mean growth factor for number of cases was 1.18 and for mortality rate was 1.16.

Conclusion: The findings indicate that 15 days after the lockdown, daily cases of COVID-19 and the growth factor of the disease showed a declined trend, but there was no significant decline in the prevalence and mortality.

Paper 5

Title of Article/Author/Year/Grade: Predictive modelling of COVID-19 confirmed cases in Nigeria / Roseline O.Ogundokun, Adewale F.Lukman, Golam B.M.Kibria, Joseph B.Awotunde, Benedita B.Aladeitan / 2020
Type of Article: Modelling Study
Link of Article: https://www.sciencedirect.com/science/article/pii/S2468042720300336

Objective: This study adopted the ordinary least squares estimator to measure the impact of travelling history and contacts on the spread of COVID-19 in Nigeria and made a prediction. [96]

Result: The government made a right decision in enforcing travelling restriction because we observed that travelling history and contacts made increases the chances of people being infected with COVID-19 by 85% and 88% respectively.

Conclusion: This prediction of COVID-19 shows that the government should ensure that most travelling agency should have better precautions and preparations in place before re-opening and should enforce the right policy for the containment of COVID-19.

Paper 6
Title of Article/Author/Year/Grade: Analysis of a mathematical model for COVID-19 population dynamics in Lagos, Nigeria / D.Okuonghae, A.Omame / 2020

Type of Article: Modelling Study.

Link of Article: https://europepmc.org/article/med/32834593

Objective: This work examines the impact of various non-pharmaceutical control measures (government and personal) on the population dynamics of the novel coronavirus disease 2019 (COVID-19) in Lagos, Nigeria, using an appropriately formulated mathematical model. [97]

Result: Numerical simulations of the model show that if at least 55% of the population comply with the social distancing regulation with about 55% of the population effectively making use of face masks while in public, the disease will eventually die out in the population and that, if we can step up the case detection rate for symptomatic individuals to about 0.8 per day, with about 55% of the population complying with the social distancing regulations, it will lead to a great decrease in the incidence (and prevalence) of COVID-19.

Conclusion: To curtail the spread of COVID-19 at the community level, this study recommends, as a matter of urgency, very strict measures to be taken by policy makers and those in authority to identify new cases, through aggressive screening and testing of the population and strict enforcement of the use of facemasks and the social distancing regulations.

Paper 7
Title of Article/Author/Year/Grade: Predicting COVID-19 spread in the face of control measures in West Africa / Hémaho B. Taboe, Kolawolé V. Salako, James M. Tison, Calistus N. Ngonghala and Romain Glèlè Kaka / 2020.

Type of Article: Modelling Study

Link of Article: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7388784/

Objective: Understanding current patterns of the pandemic spread and forecasting its long-term trajectory. [98]

Result: Our results show that timely isolation of symptomatic cases is important in reducing the disease burden in West Africa but not enough as asymptomatic isolation do, although disease elimination is only possible if isolation of infectious symptomatic cases is complemented with another control measure. In particular, if symptomatic humans are identified and isolated within 2 days, i.e., ρs=0.50, then a 45% reduction in the disease transmission rate is required for disease elimination, while if it takes a long time to isolate symptomatic infectious individuals, e.g., within 8 days (i.e., ρs=0.13), a 46% reduction on the disease transmission rate is required to contain the pandemic in West Africa.

Conclusion: Systematic testing on target group, contact tracing and isolation of confirmed disease cases, as well as improvements to the other existing basic public health measures (e.g., social distancing and mask use) in the region, are required to better manage the pandemic. Due to uncertainties and disparities between the economies and health care systems of countries within the region, we conclude that country-level studies are necessary and will provide more insights into disease dynamics and control in the region.

Paper 8

Title of Article/Author/Year/Grade: Association of Country-wide Coronavirus Mortality with Demographics, Testing, Lockdowns, and Public Wearing of Masks / Christopher T. Leffler, Edsel Ing, Joseph D. Lykins, Matthew C. Hogan, Craig A. McKeown, Andrzej Grzybowski / 2020 / 7(12)

Type of Article: Observational Study

Link of Article: https://www.medrxiv.org/content/medrxiv/early/2020/06/16/2020.05.22.20109231.full.pdf

Objective: we assessed the impact of masks on per-capita COVID-19-related mortality, controlling for the aforementioned factors. We hypothesized that in countries where mask use was either an accepted cultural norm or favored by government policies on a national level, the per-capita mortality might be reduced, as compared with countries which did not advocate masks. [99]

Result: In univariate analyses, the prevalence of smoking, per-capita gross domestic product, urbanization, and colder average country temperature were positively associated with coronavirus-related mortality. In a multivariable analysis of 194 countries, the duration of infection in the country, and the proportion of the population 60 years of age or older were positively associated with per-capita mortality, while duration of mask-wearing by the public was negatively associated with mortality. The prevalence of obesity was independently associated with mortality in models which controlled for testing levels or policy. International travel restrictions were independently associated with lower per-capita mortality, but other containment measures and viral testing and tracing policies were not. In countries with cultural norms or government policies supporting public mask-wearing, per-capita coronavirus mortality increased on average by just 8.0% each week, as compared with 54% each week in remaining countries. On multivariable analysis, lockdowns tended to be associated with less mortality ($p=0.43$) and increased per-capita testing with higher reported mortality ($p=0.70$), though neither association was statistically significant.

Conclusion: Societal norms and government policies supporting the wearing of masks by the public, as well as international travel controls, are independently associated with lower per-capita mortality from COVID-19.

Paper 9
Title of Article/Author/Year/Grade: Response strategies for COVID-19 epidemics in African settings: a mathematical modelling study / van Zandvoort, K., C. Jarvis, C. Pearson, N. Davies, R. Ratnayake, T. Russell, A. Kucharski et al. / 2020
Type of Article: Modelling Study
Link of Article: https://europepmc.org/article/pmc/pmc7553800

Objective: We evaluated strategies to reduce SARS-CoV-2 burden in African countries, so as to support decisions that balance minimizing mortality, protecting health services and safeguarding livelihoods. [100]

Result: We predicted median symptomatic attack rates over the first 12 months of 23% (Niger) to 42% (Mauritius), peaking at 2-4 months, if epidemics were unmitigated. Self-isolation while symptomatic had a maximum impact of about 30% on reducing severe cases, while the impact of physical distancing varied widely depending on percent contact reduction and R_0. The effect of shielding high-risk people, e.g. by rehousing them in physical isolation, was sensitive mainly to residual contact with low-risk people, and to a lesser extent to contact among shielded individuals. Mitigation strategies incorporating self-isolation of symptomatic individuals, moderate physical distancing and high uptake of shielding reduced predicted peak bed demand and mortality by around 50%. Lockdowns delayed epidemics by about 3 months. Estimates were sensitive to differences in age-specific social mixing patterns, as published in the literature, and assumptions on transmissibility, infectiousness of asymptomatic cases and risk of severe disease or death by age.

Conclusion: In African settings, as elsewhere, current evidence suggests large COVID-19 epidemics are expected. However, African countries have fewer means to suppress transmission and manage cases. We found that self-isolation of symptomatic persons and general physical distancing are unlikely to avert very large epidemics, unless distancing takes the form of stringent lockdown measures. However, both interventions help to mitigate the epidemic. Shielding of high-risk individuals can reduce health service demand and, even more markedly, mortality if it features high uptake and low contact of shielded and unshielded people, with no increase in contact among shielded people. Strategies combining self-isolation, moderate physical distancing and shielding could achieve substantial reductions in mortality in African countries. Temporary lockdowns, where socioeconomically acceptable, can help gain crucial time for planning and expanding health service capacity.

Paper 10
Title of Article/Author/Year/Grade: Social approaches to COVID-19 pandemic response: effectiveness and practicality in sub-Saharan Africa / Amaechi UA, Sodipo BO, Nnaji CA, Owoyemi A, Omitiran K, Okedo-Alex IN, Eboreime E, Ajumobi O / 2020 / 6(11)

Type of Article: Systematic Review

Link of Article: https://europepmc.org/article/pmc/pmc7704349

Objective: Due to socio-economic and broader peculiarities of SSA countries, social approaches that were effective elsewhere may have limited practicality in these contexts, and if practical; may yield different or even adverse results. We highlighted the effectiveness of these social approaches and their practicality in Sub Saharan Africa. [101]

Result: our review found emerging and varying empirical evidence on the effectiveness of social approaches in the control and mitigation of the COVID-19 pandemic; thus, limiting its applicability in SSA contexts. Nonetheless, our review demonstrates that the effectiveness and practicality of social approaches in SSA contexts will depend on available resources; timing, duration, and intensity of the intervention; and compliance. Weak political coordination, anti-science sentiments, distrust of political leaders and limited implementation of legal frameworks can also affect practicality.

Conclusion: to overcome these challenges, tailoring and adaptation of these measures to different but unique contexts for maximum effectiveness, and investment in social insurance mechanisms, are vital.

E. **Has the epidemiology of COVID-19 disease changed following implementation of preventive measures (e.g. lock down) in the targeted states? [NPHCDA, NCDC, other reports and plans]**

Paper 1

Title of Article/Author/Year/Grade: Estimating the impacts of lockdown on Covid-19 cases in Nigeria / Kazeem Bello Ajide, Ridwan Lanre Ibrahim, and Olorunfemi Yasiru Alimi / 2020
Type of Article: Modelling Study
Link of Article: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7474887/
Objective: The study examines the extent to which lockdown measures impact on COVID-19 confirmed cases in Nigeria. Six indicators of lockdown entailing retail and recreation, grocery and pharmacy, parks, transit stations, workplaces, and residential, are considered. [93]

Result: The results for all the indicators of lockdown variables are statistically significant and negative except for the residential variable. These results consistent with the theoretical *priors,* suggesting the mitigating role of lockdown policies on coronavirus spread. By implication, as people comply with the "stay-at-home" order, and limit their visits to essential places, thus reduce their chances of being infected by COVID-19. Correspondingly, this also tends to reduce human-to-human contact, which is the main transmission channel of COVID-19. Intuitively, a 1% increase in compliance to the stay-at-home order leads to a corresponding reduction by the magnitudes 0.026%, 0.019%, 0.035%, 0.020% and 0.020%. On the contrary, the impact of residential is positive and statistically relevant.

Conclusion: This study examines the extent to which lockdown measures impact on COVID-19 confirmed cases in Nigeria. Using the negative binomial regression estimator on the daily situation data, the following results are established. First, retail and recreation, grocery and pharmacy, parks, transit stations, and workplaces are negative and statistically significant across the models. Second, the impact of residential is positive and statistically relevant, thus running contrary to other lockdown measures with negative theoretical *priors*. Lastly, the obtained results are robust to an alternative estimator of Poisson Regression

Paper 2

Title of Article/Author/Year/Grade: Do as your neighbors do? Assessing the impact of lockdown and reopening on the active COVID-19 cases in Nigeria / Mati, S / 2020

Type of Article: Modelling Study

Link of Article: https://www.sciencedirect.com/science/article/pii/S0277953620308649?via%3Dihub

Objective: his paper employs Autoregressive Integrated Moving Average (ARIMA) modelling and doubling time to assess the effect of lockdown and reopening on the active COVID-19 cases (ACC) based on a sample from 29 February to July 3, 2020. [102]

Result: The estimation is not reported as the coefficient of rt is not significant. Therefore, reopening has neither immediate nor long run effect on the growth rate of the ACC. This might be due to the fact that the reopening sample is small and therefore it is too early to detect its effect on the ACC

Conclusion: This study has examined the "copy-paste" policies of lockdown and reopening to control the spread of COVID-19 in Nigeria. The ARIMA modelling is used to estimate the daily growth rate of the ACC. The lockdown measures have led to the reduction of daily percentage rate of growth of the ACC. Even though the lockdown policy is successful, the big question is whether the benefit of this policy outweighs its cost.

Paper 3

Title of Article/Author/Year/Grade: Early detection of change patterns in COVID-19 incidence and the implementation of public health policies: a multi-national study.

Type of Article: Observational Study

Link of Article: https://europepmc.org/article/pmc/pmc7754913

Objective: The COVID-19 pandemic caused by the novel SARS-CoV-2 coronavirus has drastically altered the global realities. Harnessing national scale data from the COVID-19 pandemic may better inform policy makers in decision making surrounding the reopening of society. We examined country-level, daily confirmed, COVID-19 case data from the World Health Organization (WHO) to better understand the comparative dynamics associated with the ongoing global pandemic at a national scale. [103]

Result: We identified subtle, yet different change points (translated to actual calendar days) by either the mean and variance change point model with small p-values or by a Bayesian online change point algorithm with large posterior probability in the trend of COVID-19 incidences for different countries. We correlated these statistically identified change points with evidence from the literature surrounding these countries' policies regarding opening and closing of their societies to slow the spread of COVID-19. The days when change points were detected were ahead of the actual policy implementation days, and in most of the countries included in this study the decision lagged the change point days too long to prevent potential widespread extension of the pandemic.

Conclusion: Our models describe the behavior of COVID-19 prevalence at a national scale and identify changes in national disease burden as relating to chronological changes in restrictive societal activity. Globally, social distancing measures may have been most effective in smaller countries with single governmental and public health organizational structures.

3.2.2 Clinical characteristics of disease

A. What are signs and symptoms of COVID-19 disease in Nigeria?

Title of Article/Author/Year/Grade: Presenting Symptoms and Predictors of Poor Outcomes Among 2,184 Patients with COVID-19 in Lagos State, Nigeria/Abayomi et al/2021/1

Type of Article: Peer-reviewed, published

Source/Link of Article: PubMed https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7566672/ doi: 10.1016/j.ijid.2020.10.024

Objective: To determine presenting symptoms and predictors of poor outcomes among 2,184 patients with COVID-19 in Lagos State, Nigeria. [104]

Result: The ages of the patients ranged from 4 days to 98 years with a mean of 43.0(16.0) years. Of the patients who presented with symptoms, cough (19.3%) was the most common presenting symptom. This was followed by fever (13.7%) and difficulty in breathing, (10.9%). The most significant clinical predictor of death was the severity of symptoms and signs at presentation. Difficulty in breathing was the most significant symptom predictor of COVID-19 death (OR:19.26 95% CI 10.95-33.88). The case fatality rate was 4.3%.

Conclusion: Primary care physicians and COVID-19 frontline workers should maintain a high index of suspicion and prioritize the care of patients presenting with these symptoms. Community members should be educated on such predictors and ensure that patients with these symptoms seek care early to reduce the risk of deaths associated with COVID-19.

Paper 2

Title of Article/Author/Year/Grade: An update of COVID-19 outbreak in Nigeria/NCDC/2021

Type of Article: Official report Source/Link of Article: https://covid19.ncdc.gov.ng/media/resources/COVID-19_Symptoms_c-2.png

Objective: Communicate to public on what they should suspect as COVID-19 symptoms [105]

Result: Headache, breathing difficulty, runny nose, abdominal pain, sore throat, shivering/chills, body pain, sudden loss of taste and smell, fatigue and tiredness (no specific proportion of occurrences provided)

Conclusion: COVID-19 presents in protean ways. (This source is missing GIT and ocular symptoms of COVID-19).

a. **Are there severe forms of COVID-19 disease? [Systematic Search/WHO website]**

Title of Article/Author/Year/Grade: NATIONAL INTERIM GUIDELINES FOR CLINICAL MANAGEMENT OF COVID-19/NCDC/2021/10

Type of Article: Clinical Management Manual

Source/Link of Article: NCDC website/ https://ncdc.gov.ng/themes/common/docs/protocols/177_1584210847.pdf

Objective: To guide the clinicians at all levels recognize the severe forms of COVID-19 disease [106]

Result: As a respiratory disease the severe forms of COVID-19 could manifest as follow:

Adults: A severe COVID-19 case in an adult is characterized by fever (>38◦ C) or suspected respiratory infection AND one of the following:

● Respiratory rate >30 breaths/minute

● Severe respiratory distress

● SpO2 <90% on room air

Elderly and immunosuppressed patient may present with atypical symptoms. Patients with mild pneumonia may progress to the severe form of the disease and thus require close monitoring

Children: Children with severe COVID-19 infection will typically present with cough or difficulty in breathing AND at least one of the following:

● Central cyanosis or SpO2 <92%

● Severe respiratory distress e.g. grunting

● Very severe chest in-drawing

● Signs of pneumonia with a general danger sign

● Inability to breast feed or drink ● lethargy/unconsciousness/convulsion [106]

Conclusion: Closely monitoring of patients with signs of clinical deterioration such as progressive respiratory failure and sepsis is mandatory and do apply therapeutic as well as appropriate supportive care interventions immediately

B. **What are the long-term complications of COVID-19 disease (Systematic Search/ WHO website)?**

Paper 1

Title of Article/Author/Year/Grade: NATIONAL INTERIM GUIDELINES FOR CLINICAL MANAGEMENT OF COVID-19/NCDC/2021/10

Type of Article: Clinical Management Manual

Source/Link of Article: NCDC website/ https://ncdc.gov.ng/themes/common/docs/protocols/177_1584210847.pdf

Objective: To guide the clinicians at all levels recognize the long-term complications of COVID-19 disease [106]

Result: There are several complications that can arise following infection with COVID-19. Common complications include:

1. Hypoxemic Respiratory Failure (HRF) and Acute Respiratory Distress Syndrome (ARDS)

2. Sepsis and Septic Shock

Conclusion: Worsening respiratory distress is evidenced by failure of response to standard oxygen therapy (continuous increased work of breathing /hypoxaemia despite oxygen delivery via a face mask with reservoir bag). Transfer patient to ICU for further close monitoring and management.

Paper 2

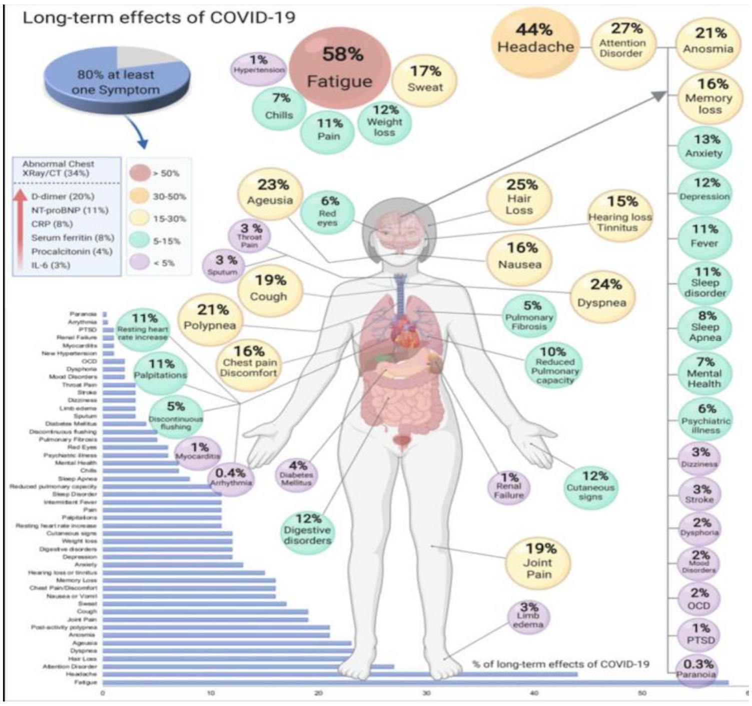
Title of Article/Author/Year/Grade: Lopez-Leon, S., Wegman-Ostrosky, T., Perelman, C., Sepulveda, R., Rebolledo, P. A., Cuapio, A., & Villapol, S. (2021). More than 50 Long-term effects of COVID-19: a systematic review and meta-analysis. Available at SSRN 3769978.

Type of Article: Systematic review

Source/Link of Article: https://europepmc.org/article/med/33532785#free-full-text

Objective: This systematic review and meta-analysis aims to identify studies assessing long-term effects of COVID-19 and estimates the prevalence of each symptom, sign, or laboratory parameter of patients at a post-COVID-19 stage.

Result: The five most common symptoms were fatigue (58%), headache (44%), attention disorder (27%), hair loss (25%), and dyspnea (24%). All meta-analyses showed medium (n=2) to high heterogeneity (n=13). In order to have a better understanding, future studies need to stratify by sex, age, previous comorbidities, severity of COVID-19 (ranging from asymptomatic to severe), and duration of each symptom. [107]



Conclusion: From the clinical perspective, multi-disciplinary teams are crucial to developing preventive measures, rehabilitation techniques, and clinical management strategies with whole-patient perspectives designed to address long COVID-19 care.

Paper 3

Title of Article/Author/Year/Grade: Long term respiratory complications of covid-19/Emily Fraser
Type of Article: Informative Research
Source/Link of Article: https://www.bmj.com/content/370/bmj.m3001
Objective: To assess the long-term effect of COVID-19 on the respiratory system of affected persons
Result: Recently published guidance by the NHS lays out the likely aftercare needs of patients recovering from covid-19 and identifies potential respiratory problems including chronic cough, fibrotic lung disease, bronchiectasis, and pulmonary vascular disease.

Conclusion: Persistent respiratory complications following covid-19 may cause substantial population morbidity, and optimal management remains unclear. Prospective studies are under way to evaluate these complications further and to identify people at greatest risk.

C. **What is the impact of vaccination on individuals who have been previously infected with COVID-19 patients?**

Title/Author/Grade: A cautionary note on recall vaccination in ex-COVID-19 subjects; Riccardo Levi, MSc, Elena Azzolini, MD PhD, Chiara Pozzi, Leonardo Ubaldi, Michele Lagioia, Alberto Mantovani, and Maria Rescigno (2021)/ (8/10).

Link: file:///C:/Users/cfashola/AppData/Local/Temp/2021.02.01.21250923v1.full.pdf

Objective – To understand the impact of the vaccine in individuals previously infected with COVID-19

Result – The data from the studies indicated that the antibody response of ExCOVID patients developed after the first dose of the mRNA-based vaccine depends on the IgG pre-vaccine titer and on the symptoms that they developed during the disorder, with anosmia/dysgeusia and gastrointestinal disorders being the most significantly positively correlated in the LR, while sore throat was negatively correlated because 45% non-COVID individuals reported it. Young subjects had a higher antibody response. The Principal Investigators previously observed that anosmia/dysgeusia were associated with an increase of antibodies over time, independent of vaccination. Thus, one vaccine dose is sufficient to induce a good antibody response in ExCOVID subjects and poses caution for a second dose: over stimulation with high number of antigens could switch-off the immune response due to antigen exhaustion, which occurs in response to several viruses. Alternatively, overactivation of the immune response may drive the development of low-affinity antibodies for SARS-CoV-2 which may foster an antibody dependent enhancement (ADE) reaction when re-exposed to the virus. [108]

Conclusion: These results pose the question whether a second shot in ExCOVID subjects is indeed required and suggest to post-pone it while monitoring antibody response longevity. At a time of vaccine scarcity, these findings may have public health implications.

b. **Which vaccines are most effective against the emerging COVID-19 variants in Nigeria?**

Title/Author/Grade: Interim recommendations for use of the AZD1222 (ChAdOx1-S [recombinant]) vaccine against COVID-19 developed by Oxford University and AstraZeneca

Link: https://apps.who.int/iris/bitstream/handle/10665/339477/WHO-2019-nCoV-vaccines-SAGE-recommendation-AZD1222-2021.1-eng.pdf
Objective – To provide interim guidance to countries on the rollout and administration of COVID-19 vaccines
Method: SAGE applies the principles of evidence-based medicine and has set in place a thorough methodological process for issuing and updating recommendations (2). A detailed description of the methodological processes as they apply to COVID-19 vaccines can be found in the SAGE evidence framework for COVID-19 vaccines (3). This framework contains guidance on considering data emerging from clinical trials in relation to the issuance of vaccine-specific evidence-based recommendations.

Result: SARS-CoV-2 viruses undergo evolution and result in different variants. Some new virus variants may be associated with higher transmissibility, disease severity, risk of reinfection, or a change in antigenic composition resulting in lower vaccine effectiveness.

Preliminary analyses have shown a slightly reduced vaccine effectiveness of AZD1222 against B1.1.1.7 in the V002 trial in the United Kingdom which is associated with only a limited reduction in neutralizing antibody. Preliminary analyses from the Phase 1/2a trial (COV005) in South Africa indicate marked reduction in vaccine effectiveness against mild and moderate disease due to B 1.351 based on a small sample size and substantial loss of neutralizing antibody activity. This study was designed to assess efficacy against disease of any severity, but the small sample size did not allow a specific assessment of vaccine efficacy against severe COVID-19. Indirect evidence is compatible with protection against severe COVID-19; however, this remains to be demonstrated in ongoing clinical trials and post-implementation evaluations.

Conclusion: Despite having an efficacy rate of 63.09% (95% CI 51.81; 71.73) against symptomatic SARS-CoV-2 infection and little evidence showing efficacy against the D614G and B117 strains currently identified in NIgeria, WHO currently recommends the use of AZD1222 vaccine according to the Prioritization Roadmap even if variants are present in a country. Countries are advised to conduct a benefit-risk assessment according to the local epidemiological situation including the extent of circulating virus variants.

These preliminary findings highlight the urgent need for a coordinated approach for surveillance and evaluation of variants and their potential impact on vaccine effectiveness. WHO will continue to monitor the situation; as new data become available, recommendations will be updated accordingly.

D. **What is the medical management of COVID-19 disease? [Systematic search / WHO website/ NCDC website]**

Summary of Medical Management of COVID-19 Disease

S/N	Medication	Pros/Con	Recommended Dose

1	Hydroxychloroquine/chloroquine and azithromycin	Chloroquine and hydroxychloroquine are relatively well tolerated and has been used for ages in patients with systemic lupus erythematosus (SLE) and malaria. However, both agents can cause serious adverse effects (< 10%), like hypoglycemia, retinopathy, psychiatric effects, QTc prolongation. Azithromycin is a commonly used macrolide for respiratory bacterial infections. Gautret et al concluded that combination therapy with azithromycin and hydroxychloroquine cured 100% of patients virologically on day 6 compared to 57.1% in patients treated with hydroxychloroquine only, and 12.5% in the control group (P = 0.001). However, the risk of QT prolongation from these two drugs should be considered, and caution should be taken, especially in cardiac patients, while administering this combination. Moreover, a study among 368 USA veterans found no benefit, rather touted hydroxychloroquine to be more harmful due to its side effect profile.	Hydroxychloroquine dose most used is 400 mg twice daily orally for two doses, then 400 mg daily orally for a total of 5 days. Chloroquine dose suggested by FDA is 1 g on day 1, then 500 mg daily for 4 - 7 days total.

2	Remdesivir	The agent was first discovered in 2015 in the process of finding antimicrobials with activity against RNA viruses. Initially, it was used for Ebola treatment. It has shown promising results in animals' studies with MERS and SARS caused by a coronavirus.	The current dose under investigation is a single 200 mg loading dose, followed by 100 mg daily infusion. Under this EUA, the recommended dosing duration for patients requiring invasive mechanical ventilation and/or ECMO, and for patients not requiring invasive mechanical ventilation and/or ECMO is 10 days and 5 days, respectively.
3	Favipiravir	The safety and efficacy of the drug is not established as of now. Favipiravir is a generic version of brand Avigan used for treating novel influenza infections in Japan. Notable side effects include decreased neutrophil count, diarrhea, increased uric acid levels, elevated transaminases.	Recommended dosing is 2,400 to 3,000 mg loading dose every 12 h for two doses, followed by 1,200 to 1,800 mg twice a day as maintenance dose.
4	Interleukin (IL)-6 pathway inhibitor	Cytokine storm in response to COVID-19 has been found to have devastating consequences in critically ill patients and may facilitate shock and multi-organ failure. IL-6 inhibitors can be helpful by diminishing the effect of an overactive cytokine system. New-onset abdominal symptoms should be monitored as there were reported cases of GI perforation, specifically in patients with a history of diverticulosis. Baseline	Standard dosing for these medications has been used for experimental purposes.

		lipid panel and liver function testing should also be done as these drugs might elevate these parameters significantly.	
5	Lopinavir/ritonavir	Widely and successfully used in HIV management, this combination has been tried in the management of 2019 novel coronavirus (2019-nCoV). This drug has shown some effect in the in vitro model for MERS and SARS treatment.	Commonly studied lopinavir/ritonavir dosing in COVID-19 patients is 400 mg/100 mg twice daily for up to 14 days.
6	Histamine 2 receptor antagonist (H2RA)	Although H2RA is a very commonly used medication that is even available over the counter, no conclusive data are supporting how H2RA helps against COVID-19.	Standard dose to treat gastroesophageal reflux disease.
7	Interferon (IFN) beta	Data obtained from the experiments involving treatment of SARS-CoV and MERS-CoV and ISG's ability to disrupt the IFN signaling pathway would be valuable for selecting IFN-beta as a potential treatment option against SARS-CoV-2.	No specific dose has been validated, especially for COVID-19. The general dosing guideline is being followed.
8	Convalescent plasma (CP)	Cytokine storm in response to COVID-19 has been found to have devastating consequences in critically ill patients and may facilitate shock and multi-organ failure. IL-6 inhibitors can be helpful by diminishing the effect	A preliminary study of five patients with COVID-19 who were severely ill and treated with CP from China was published. All five patients were mechanically ventilated, and one needed ECMO. The donor CP, an apheresis product, had demonstrable immunoglobulin G (IgG) and IgM anti-SARS-CoV-19 antibodies and in vitro virus-

		of an overactive cytokine system.	neutralizing properties. The authors concluded that the CP might have contributed to the recovery, although the patients were also on lopinavir/ritonavir antiviral therapy and IFN
9	Ivermectin	Ivermectin is an inhibitor of the COVID-19 causative virus (SARS-CoV-2) in vitro. A single treatment able to effect ~5000-fold reduction in virus at 48 h in cell culture. Ivermectin is FDA-approved for parasitic infections, and therefore has a potential for repurposing. Ivermectin is widely available, due to its inclusion on the WHO model list of essential medicines. Chaccour et al believe the recent findings regarding ivermectin warrant rapid implementation of controlled clinical trials to assess efficacy against COVID-19. They also raise concerns regarding ivermectin-associated neurotoxicity, particularly in patients with a hyperinflammatory state possible with COVID-19. In addition, drug interactions with potent CYP3A4 inhibitors	Yet to be determined

		(eg, ritonavir) warrant careful consideration of co-administered drugs.	
8	Niclosamide	Niclosamide is thought to disrupt SARS-CoV-2 replication through S-phase kinase-associated protein 2 (SKP2)-inhibition, by preventing autophagy and blocking endocytosis. A proprietary formulation that targets the viral reservoir in the gut to decrease prolonged infection and transmission has been developed, specifically to decrease gut viral load. It is being tested in a phase 2 trial. A phase 2/3 trial is testing safety and the potential to improved outcomes and reduce hospital stay by reducing viral load.	Yet to be determined

Agents Used In COVID-19 Palliative Care	
Prevention and relief of pain or other physical suffering, acute or chronic, related to COVID-19	– Amitriptyline, oral – Bisacodyl (senna), oral – Dexamethasone, oral and injectable – Diazepam, oral and injectable – Diphenhydramine (chlorpheniramine, cyclizine, or dimenhydrinate), oral and injectable – Fluconazole, oral – Fluoxetine, oral – Furosemide, oral and injectable – Haloperidol, oral and injectable – Hyoscine butylbromide, oral and injectable

	– Ibuprofen (naproxen, diclofenac, or meloxicam), oral – Lactulose (sorbitol or polyethylene glycol), oral – Loperamide, oral – Metaclopramide, oral and injectable – Metronidazole, oral, to be crushed for topical use – Morphine, oral immediate release and injectable – Naloxone, injectable – Omeprazole, oral – Ondansetron, oral and injectable – Oxygen – Paracetamol, oral – Petroleum jelly
Prevention and relief of psychological suffering,acute or chronic, related to COVID-19	– Amitriptyline, oral – Dexamethasone, oral and injectable – Diazepam, oral and injectable – Diphenhydramine (chlorpheniramine, cyclizine or dimenhydrinate), oral and injectable – Fluoxetine, oral – Haloperidol, oral and injectable – Lactulose (sorbitol or polyethylene glycol), oral

Phytochemicals used in the Medical Management of COVID-19 [109]

Reference - Renjith, M. R. D., & Sankar, M. SCOPE OF PHYTOCHEMICALS IN THE MANAGEMENT OF COVID-19. *Pharmaceutical Resonance 2020 Vol. 3 - Issue 1.*

Phytochemicals	Mechanism of Action
Flavanoids: Luteolin, apigenin, quercetin, Kaempferol, myricetrin	Interfere with the activation of NRP3 inflammasome
Emodin, anthraquinone	Act by inhibiting the interaction of SARS-CoV S protein with its receptor ACE2 in dose-dependent manner
SAIKOSAPONIN S A,B2,C,D (Triterpene glycosides)	Mode of action possibly involves interference in the early stage of viral replication, such as absorption and penetration of the virus.
Honey	Acts as immunobooster. Honey contains trace amounts of the Bvitamins riboflavin, niacin, folic acid, pantothenic acid and vitamin B6. It also contains ascorbic acid (vitamin C), and the minerals calcium, iron, zinc, potassium, phosphorous, magnesium, selenium, chromium and manganese.

Ginger	Acts as immunobooster. Terpene components of ginger include zingiberene, β-bisabolene, α-farnesene, βsesquiphellandrene, and α-curcumene, while phenolic compounds include gingerol, paradols, and shogaol. These gingerols (23–25%) and shogaol (18–25%) are found in higher quantity than others. Besides these, amino acids, raw fiber, ash, protein, phytosterols, vitamins (e.g., nicotinic acid and vitamin A), and minerals are also present
Turmeric	Acts as immunobooster. Turmeric contains three curcuminoids: curcumin, demethoxycurcumin, and bisdemethoxycurcumin, as well as volatile oils (tumerone, atlantone, and zingiberone), sugars, proteins, and resins.
Garlic	Acts as immunobooster. Sulphur compounds-allicin, alliin, ajoene, allyl propyl disulphide, diallyl trisulphide
Black Pepper	Acts as immunobooster. Alkaloids: Piperine, piperidine, piperanine, piperettine, piperlongumine, lignans,alkyl amides
Onion	Contains flavanoids like quercetin, fructose, quercetin-3-glucoside, isorhamnetin-4-glucoside, xylose, galactose, glucose, mannose, organosulfur compounds, allylsulfides, flavonoids, flavenols, S-alk(en)yl cysteine sulfoxides, cycloalliin, selenium, thiosulfinates, and sulfur and seleno compounds. Acts as immunobooster.

Guidance document 1

Title of Article/Author/Year/Grade: National Interim Guidelines for Clinical Management of COVID-19 / Nigeria Centre for Disease Control / 2020

Link of Article: Clinical Management of COVID-19 - NCDC - Nigeria Centre ...covid19.ncdc.gov.ng › media › files › National_Interi...

Objective: This is an interim guideline developed by the Nigeria Centre for Disease Control to guide health workers in response to cases of COVID-19 in Nigeria. [106]

Guidance document 2

Title of Article/Author/Year/Grade: Clinical Management of COVID-19: Interim Guidance / World Health Organization / 2020

Link of Article: https://www.who.int/publications/i/item/clinical-management-of-covid-19

Objective: This guidance document is intended for clinicians caring for COVID-19 patients during all phases of their disease (i.e., screening to discharge). This update has been expanded to meet the needs of front-line clinicians and promotes a multi-disciplinary approach to care for patients with COVID-19, including those with mild, moderate, severe, and critical disease. [106]

Paper 1

Title of Article/Author/Year/Grade: Medical Management of COVID-19: Evidence and Experience / Bose, S., S. Adapa, N. R. Aeddula, S. Roy, D. Nandikanti, P. M. Vupadhyayula, S. Naramala, V. Gayam, V. Muppidi, and V. M. Konala / 2020 / 6(10)

Type of Article: Literature Review

Link of Article: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7295552/

Objective: In this review article, we seek to collate and provide a summary of treatment strategies for COVID-19 patients with a variable degree of illness and discuss pharmacologic and other therapies intended to be used either as experimental medicine/therapy or as part of supportive care in complicated cases of COVID-19 [110]

Paper 2

Title of Article/Author/Year/Grade: A Multicenter Questionnaire-based Study to Know the Awareness and Medical Treatment Plan of Physicians Involved in the Management of COVID-19 Patients / Maddani, S., S. Chaudhuri, H. Deepa, and V. Amara / 2020 / 6(10)

Type of Article: Qualitative Study

Link of Article: https://europepmc.org/article/pmc/pmc7689132

Objective: As the clinical trials for these drugs are ongoing, we conducted this survey to know the physicians' medical treatment plan for COVID-19 patients.

Result: The majority of the clinicians were aware of the various treatment modalities available for the treatment of COVID-19. Regarding the plan for use of hydroxychloroquine (HCQ), 55% of the total respondents intended to use the drug in combination with azithromycin, even as 62% agreed that there was no clear evidence yet. About 90% of all clinicians, from junior residents to consultants, were monitoring electrocardiogram (ECG) during HCQ therapy; however, there were 10% of physicians who were not practicing ECG monitoring. About 68% of clinicians were aware of the various therapeutic options being tested, like convalescent plasma, lopinavir-ritonavir, and 64% knew about remdesivir. There was divergence regarding the use of steroids in a cytokine storm among the physicians, with only 39% of consultants planning to use steroids whereas about 50% of junior residents and 79% of junior consultants were planning to use the drug. [111]

Conclusion: The majority of the clinicians involved in the management of COVID-19 were aware of the various drug modalities available for treatment. However, more emphasis on the adverse effects and possible drug interactions is required. There is disaccord regarding the use of steroids in cytokine storm in COVID-19 and further guidelines and educational programs should address these issues.

Paper 3
Title of Article/Author/Year/Grade: Evidence Based Management Guideline for the COVID-19 Pandemic-Review article / Nicola, Maria, Niamh O'Neill, Catrin Sohrabi, Mehdi Khan, Maliha Agha, and Riaz Agha / 2020 / 5(10)

Type of Article: Literature Review

Link of Article: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7151371/

Objective: As new findings emerge, there is an urgent need for up-to-date management guidelines. In response to this call, we review what is currently known regarding the management of COVID-19, and offer an evidence-based review of current practice.

Result: Current data has shown that there are an estimated 1,664,384 active cases worldwide, of which 97% (n = 1,623,355) display mild symptoms of the COVID-19 and 3% (n = 41,029) of currently infected patients are seriously (requiring oxygen therapy) or critically unwell (requiring mechanical ventilation). Of the closed cases (n = 834,069), 79% (n = 663,477) of infected individuals have recovered from the disease or have been successfully discharged from hospital. 21% (n = 171,017) of these cases have died of the illness or related complications. As it stands, the 46th WHO situation report estimates the Crude Mortality Ratio of COVID-19 to be between 3 and 4% based on current data. Median time for recovery from the onset of symptoms is approximately 2 weeks in mild cases and 3–6 weeks in severely or critically unwell individuals. [112]

Conclusion: With a peak of 101,736 new cases confirmed on April 3, 2020 alone [[69]], there are fears that these findings could indicate exponential spread of the disease. Implementation and adherence to tighter restrictions of social distancing to suppress and mitigate the spread of COVID-19 will prove to be crucial in the months to come. Up-to-date, evidence-based guidelines for acute management of COVID-19 are imperative to guide clinicians through the rapidly evolving pandemic. As new evidence emerges, it is imperative that current and potential treatment options are frequently re-evaluated in order to offer the best possible care under such unprecedented circumstances.

Paper 4
Title of Article/Author/Year/Grade: Biology of COVID-19 and related viruses: epidemiology, signs, symptoms, diagnosis, and treatment: Considerations for Providing Safe Perioperative and Intensive Care in the Time of Crisis / Kaye, Alan D., Elyse M. Cornett, Kimberley C. Brondeel, Zachary I. Lerner, Haley E. Knight, Abigail Erwin, Karina Charipova et al / 2020 / 4(10)

Type of Article: Literature Review

Link of Article: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7723419/

Objective: We discuss coronavirus disease (COVID-19) biology, pathology, epidemiology, signs and symptoms, diagnosis, treatment, and recent clinical trials involving promising treatments.

Result: With over one million confirmed deaths to date, COVID-19 is the deadliest pandemic of the twenty-first century, matched only in recent history by the influenza pandemics of 1918, 1957–1958, and 1968–1970 and the ongoing HIV/AIDS pandemic. This outbreak will have lasting, widespread socioeconomic effects, including disruption to education, business, and healthcare globally. The need for effective diagnosis and treatment methodologies, grounded in understanding this virus's microbiology and pathophysiology, is clear. [113]

Conclusion: Coronaviruses are a family of enveloped RNA viruses characterized by a large genome and characteristic glycoprotein spikes. Replication of the coronavirus genome is aided by proofreading machinery, unique to coronaviruses, and necessary to maintain their relatively large genome. The process of translation in coronaviruses is unique due to the presence of ribosome frameshifting. Coronaviruses utilize surface glycoproteins to bind to and enter host cells; in SARS-CoV-2, the novel coronavirus responsible for COVID-19, this glycoprotein binds host ACE2 receptor. Coronavirus infection in humans is typically mild and self-limited, confined to the upper respiratory tract, but novel strains of coronavirus can cause severe disease affecting the lungs and other organ systems. Elderly patients and those with comorbidities are particularly susceptible.

Paper 5
Title of Article/Author/Year/Grade: Joint statement on the role of respiratory rehabilitation in the COVID-19 crisis: the Italian position paper / Vitacca, Michele, Mauro Carone, Enrico Maria Clini, Mara Paneroni, Marta Lazzeri, Andrea Lanza, Emilia Privitera et al. / 2020 /
Type of Article: Literature Review

Link of Article: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7316664/
Objective: Be aim was to formulate the more proper and common suggestions to be applied in different hospital settings in offering rehabilitative programs and physiotherapy workforce planning for COVID-19 patients.

Conclusion: The dramatic spread of the current COVID-19 epidemic in Italy has spurred into action also RR specialists (pulmonologists and respiratory therapists), who have been engaged for years in the care of patients with disabilities secondary to respiratory diseases and/or conditions. Their experience acquired in the management of chronic and acute respiratory failure is proving to be a fundamental asset for the management of patients during the COVID-19 epidemic. Hence, it is likely that the reorganization involved in taking care of this scenario will not be a short-term matter. [114]

Paper 6

Title of Article/Author/Year/Grade: Nano-Biomimetic Drug Delivery Vehicles: Potential Approaches for COVID-19 Treatment / Bwalya A. Witika, Pedzisai A. Makoni, Larry L. Mweetwa, Pascal V. Ntemi, Melissa T. R. Chikukwa, Scott K. Matafwali, Chiluba Mwila, Steward Mudenda, Jonathan Katandula, and Roderick B. Walker / 2020 / 5(10)

Type of Article: Literature Review

Link of Article: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7765509/

Objective: In this review, we categorize biomimicry into three types, viz., I, II, and III. These definitions, which are closely adapted to previously described classifications [25], are schematically depicted in using nanospheres as an example and are used in this review as defined vide infra.

Conclusion: The COVID-19 pandemic continues to be a global catastrophe with positive cases rapidly increasing in number throughout the world. Consequently, the development of conventional drugs, medicines, and vaccines, in addition to the use of novel drug delivery technologies, has gained momentum in the fight against this pandemic. State of the art delivery technologies, such as the use of nanospheres/nanocapsules, nanocrystals, liposomes, solid lipid nanoparticles/nano lipid carriers, dendrimers, and nanosponges, based on biomimicry, can be harnessed for targeted delivery of therapeutic compounds to infected individuals for the treatment of COVID-19. However, the expansions of knowledge and understanding of the COVID-19 pandemic are emerging daily, necessitating the use of flexible and agile strategies to curb the ongoing spread of the virus. While researchers continue to seek treatment and/or vaccine development strategies, there is a need to continue to use existing non-pharmacological interventions to prevent the spread of infection, which include but are not limited to regular cleaning and disinfection of surfaces, handwashing and sanitization, physical distancing, wearing a mask, and imposing travel restrictions. [115]

Paper 7

Title of Article/Author/Year/Grade: Pulmonary Rehabilitation in COVID-19 patients: A scoping review of current practice and its application during the pandemic / Siddiq, Md Abu Bakar, Farooq Azam Rathore, Danny Clegg, and Johannes J. Rasker / 2020 / 6(10)

Type of Article: Systematic Review

Link of Article: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7756838/

Objective: In this review, we discuss the role of PR and its recommended strategies in patients with COVID-19 in the light of an extensive review of the literature.

Conclusion: Conducting further research is needed to generate evidence-based methods for effective PR; focusing on optimal dose, duration, intensity and frequency, specifically designed for COVID-19 patients. In conclusion, growing evidence suggest that PR appears to be useful in COVID-19 survivors. [116]

Paper 8

Title of Article/Author/Year/Grade: A Collaborative Multidisciplinary Approach to the Management of Coronavirus Disease 2019 in the Hospital Setting / Razonable, Raymund R., Kelly M. Pennington, Anne M. Meehan, John W. Wilson, Adam T. Froemming, Courtney E. Bennett, Ariela L. Marshall, Abinash Virk, and Eva M. Carmona / 2020 / 5(10)

Type of Article: Review

Link of Article: https://europepmc.org/article/med/32622450

Objective: We provide a concise practical review that summarizes the clinical management of COVID-19 in the hospital setting, including the evaluation of patients, diagnostic testing, treatment strategies, and infection prevention measures.

Conclusion: COVID-19 presents a significant challenge to medical providers worldwide. Management of the disease is mostly supportive care with antipyretics, hydration, and oxygen supplementation, as dictated by clinical need. For patients with moderate to severe COVID-19 that requires hospitalization, medical complications affecting various organ systems are not uncommon and may lead to critical illness and multiple organ failure. Hence, the medical care of patients with COVID-19 is best optimized by the collaboration among various health care providers from different specialties. As illustrated in this management review, clinical expertise in hospital medicine, infectious diseases, clinical microbiology, radiology, pulmonary and critical care medicine, cardiology, hematology, and primary care are essential in ensuring that medical complications are prevented or treated early and aggressively. Finally, when patients are medically ready for hospital discharge, telemedicine will provide proper follow-up and monitoring until the patients have medically recovered from their illness and are ready to be released from home quarantine protocols [117]

Paper 9

Title of Article/Author/Year/Grade: Approaching coronavirus disease 2019: Mechanisms of action of repurposed drugs with potential activity against SARS-CoV-2 / Lisi, L., P. M. Lacal, M. L. Barbaccia, and G. Graziani / 2020 / 5(10)

Type of Article: Review

Link of Article: https://europepmc.org/article/med/32710969

Objective: This review focuses on the molecular mechanisms of action that have provided the scientific rationale for the empirical use and evaluation in clinical trials of structurally different and often functionally unrelated drugs during the SARS-CoV-2 pandemic.

Conclusion: Despite the enormous efforts put on the task of finding a (better) cure for COVID-19 patients by researchers and clinicians, it is clear that the proliferation of small trials, that we have witnessed thus far, is hardly going to answer the fundamental question: would a drug/combination of drugs work and how much better than standard of care would be? Such questions can be answered only by organizing well-designed, randomized, controlled and, hopefully, multicenter clinical trials that would enroll an adequate number of patients in order to get clear-cut responses. These are not trivial aspects to solve, from both a scientific as well as administrative/legal/ethical perspective. The much welcomed, albeit slow, decrease of the number of COVID-19 cases in countries where the infection initially started and the progressive shift of the pandemic's epicenter in other countries/continents highlight the importance of data sharing and international collaboration. However, such meritorious efforts should not distract the medical community and the health system organizations as a whole from other issues that deserve proper attention. Indeed, the battle against SARS-CoV-2 has so much stressed the healthcare systems in most countries, such that too many people with debilitating/severe/chronic diseases not only are at higher risk of getting sick but also have been left to themselves for too long. [118]

Paper 10

Title of Article/Author/Year/Grade: COVID-19 Infection: Implications for Perioperative and Critical Care Physicians / Greenland, John R., Marilyn D. Michelow, Linlin Wang, and Martin J. London / 2020 / 5(10).

Type of Article: Literature Review

Link of Article: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7155909/

Objective: This review provides a comprehensive summary of the evidence currently available to guide management of critically ill patients with COVID-19.

Result: COVID-19 patients have multiple distinct radiologic patterns: diffuse ground glass, reticulation, consolidation suggestive of pneumonitis, diffuse alveolar damage, and organizing pneumonia.[46] In cryptogenic organizing pneumonia, steroid administration has been suggested to prevent progression to hypoxemic respiratory failure in case series. At the same time, the requirement for steroids has been shown to be less relevant for organizing pneumonia with an identified cause, as in COVID-19. Compared with steroids, patients treated with macrolides for mild cryptogenic organizing pneumonia also demonstrated symptom resolution, albeit with higher relapse rates.[98] In case series of COVID-19 patients, steroids and macrolides were commonly used, but we lack data as to their effectiveness. In a retrospective analysis, which could be confounded by indication, steroid therapy was associated with decreased risk of death in patients with ARDS and COVID-19. Specific studies in COVID-19 patients are needed to determine whether corticosteroids or macrolides could be beneficial in a subset of patients, such as those with organizing pneumonia patterns. [119]

Conclusion: In the face of this rapidly emerging global threat, there are several reasons for optimism about future control. As described above, a number of antiviral drugs have shown promise *in vitro*. Even a partially effective antiviral could allow sufficient reduction in viral load so that the immune system can recover and respond to prevent lethal disease. There is even potential that antivirals could be used in chemoprophylaxis to prevent transmission in recently exposed individuals. While resistance to antivirals developed quickly in patients with HIV, studies in coronaviruses suggest this might be less of a problem. Similarly, while HIV readily evades cellular and humoral immunity, sharply limiting vaccination approaches, SARS-CoV infection appeared to induce broad and long-lasting immunity with less evidence of immune escape. Thus, it is likely that as COVID-19 evolves, physicians will have a variety of therapeutic and vaccination options to minimize morbidity and mortality. Until these arrive, anesthesiologists will be called upon to provide supportive care while minimizing the risk of viral transmission to themselves and others.

Paper 11
Title of Article/Author/Year/Grade: COVID-19 medical management including World Health Organization (WHO) suggested management strategies / McFee, R. B / 2020 / 6(10).

Type of Article: Review.

Link of Article: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7455232/

Objective: We recognize that ongoing research, regional variation in treatment experiences, evolving information on new therapeutics, or more optimal approaches to utilizing current interventions continues to be part of the COVID-19 response. It is not a static knowledge base. Additionally, owing to differences in infrastructure, population density, and resources, medical responses to COVID-19, as with other public health threats reflects regional variability in medical care, the following section is an excerpt from the 05/20 World Health Organization Interim Medical Guidance https://www.who.int/publications/i/item/clinical-management-of-covid-19 as general guidance for the purpose of providing basic foundation of approaches to COVID-19. [120]

Paper 12
Title of Article/Author/Year/Grade: From the trenches: inpatient management of coronavirus disease 2019 in pregnancy / Vega, Marisa, Francine Hughes, Peter S. Bernstein, Dena Goffman, Jean-Ju Sheen, Janice J. Aubey, Noelia Zork, and Lisa M. Nathan / 2020 / 5(10)

Type of Article: Literature Review

Link of Article: https://europepmc.org/article/med/32838260

Objective: We offer a guide, focusing on inpatient management, including testing policies, admission criteria, medical management, care for the decompensating patient, and practical tips for inpatient antepartum service management.

Conclusion: The speed of the emergence and spread of COVID-19 around the world has placed an incredible strain on healthcare staff and resources, particularly in the field of obstetrics. The key to responding to this crisis is thoughtful, standardized, and evidence-based care whenever possible. This article contained suggestions for management. However, as more evidence accumulates, guidance will inevitably change. [121]

Paper 13
Title of Article/Author/Year/Grade: Anti-coagulant and anti-platelet therapy in the COVID-19 patient: a best practices quality initiative across a large health system / Watson, R. A., D. M. Johnson, R. N. Dharia, G. J. Merli, and J. U. Doherty / 2020 / 5(10).

Type of Article: Review

Link of Article: https://europepmc.org/article/pmc/pmc7441801

Objective: Our goal is to provide guidance to the utilization of antithrombotic and antiplatelet therapies in patients with known or suspected COVID-19.

Conclusion: COVID-19 has challenged our thinking about the management of critically ill patients. The mechanisms of this disease and its complications continue to be elucidated. That being said the principles of managing these patients are built on the foundations of evidence-based medicine in severely ill patients. There is a narrow therapeutic index between prevention and treatment of venous and arterial thrombosis in these patients and the risk of bleeding. This document can be used to help guide providers to treat cardiovascular patients at high risk during this pandemic (Figure 2). Only by adhering to the principles of practicing what we know and maintaining openness to the greatest challenge of our professional lives. [122]

Paper 14
Title of Article/Author/Year/Grade: Medical management of COVID-19 clinic / Mehta, N., and R. Qiao / 2020 / 5(10)

Type of Article: Review

Link of Article: https://europepmc.org/article/pmc/pmc7718071

Objective: We review the major therapeutic options currently available and look into what the future still holds in order to further our understanding of this mysterious disease.

Conclusion: It has been just under a year since the start of the global pandemic. Although the virus claimed many lives at its onset, the human race has come together to understand how the virus works in order to enlist specific therapeutic targets and even a vaccine against this virus. We still have much more work to do, but as we learn more and research expands, we continue to change the reputation of SARS-CoV-2 from a deadly virus into just another virus. [123]

Paper 15
Title of Article/Author/Year/Grade: Perspectives on Cardiopulmonary Critical Care for Patients With COVID-19: From Members of the American Heart Association Council on Cardiopulmonary, Critical Care, Perioperative and Resuscitation / Maron, Bradley A., Mark T. Gladwin, Sebastien Bonnet, Vinicio De Jesus Perez, Sarah M. Perman, Paul B. Yu, and Fumito Ichinose / 2020

Type of Article: Viewpoint

Link of Article: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7660729/

Paper 16
Title of Article/Author/Year/Grade: Interleukin-1 blockade with high-dose anakinra in patients with COVID-19, acute respiratory distress syndrome, and hyperinflammation: a retrospective cohort study / Cavalli, Giulio, Giacomo De Luca, Corrado Campochiaro, Emanuel Della-Torre, Marco Ripa, Diana Canetti, Chiara Oltolini et al. / 2020 / 9(12)

Type of Article: Cohort Study

Link of Article: https://www.sciencedirect.com/science/article/pii/S2665991320301272

Objective: Our retrospective cohort study is, as far as we know, the first to describe IL-1 blockade with high-dose intravenous anakinra in patients with COVID-19, acute respiratory distress syndrome, and hyperinflammation. [124]

Result: Between March 17 and March 27, 2020, 29 patients received high-dose intravenous anakinra, non-invasive ventilation, and standard treatment. Between March 10 and March 17, 2020, 16 patients received non-invasive ventilation and standard treatment only and comprised the comparison group for this study. A further seven patients received low-dose subcutaneous anakinra in addition to non-invasive ventilation and standard treatment; however, anakinra treatment was interrupted after 7 days because of a paucity of effects on serum C-reactive protein and clinical status. At 21 days, treatment with high-dose anakinra was associated with reductions in serum C-reactive protein and progressive improvements in respiratory function in 21 (72%) of 29 patients; five (17%) patients were on mechanical ventilation and three (10%) died. In the standard treatment group, eight (50%) of 16 patients showed respiratory improvement at 21 days; one (6%) patient was on mechanical ventilation and seven (44%) died. At 21 days, survival was 90% in the high-dose anakinra group and 56% in the standard treatment group (p=0·009). Mechanical ventilation-free survival was 72% in the anakinra group versus 50% in the standard treatment group (p=0·15). Bacteraemia occurred in four (14%) of 29 patients receiving high-dose anakinra and two (13%) of 16 patients receiving standard treatment. Discontinuation of anakinra was not followed by inflammatory relapses.

Conclusion: The uncontrolled nature of our study mandates caution in interpretation of findings, and validation is absolutely required in a controlled setting. A randomised phase 2 clinical trial of intravenous anakinra in COVID-19 is ongoing (NCT04324021). Compared with our study, that trial is assessing lower doses (400 mg/day, approximately half the dose of 10 mg/kg per day in our study) and is not enrolling patients with ARDS. Controlled evidence is awaited, as IL-1 blockade with high-dose intravenous anakinra deserves consideration among anti-inflammatory treatments for COVID-19.

Paper 17
Title of Article/Author/Year/Grade: Systematic review of COVID-19 related myocarditis: Insights on management and outcome / Sawalha, Khalid, Mohammed Abozenah, Anis John Kadado, Ayman Battisha, Mohammad Al-Akchar, Colby Salerno, Jaime Hernandez-Montfort, and Ashequl M. Islam / 2020 / 8(10)

Type of Article: Systematic Review

Link of Article: https://www.sciencedirect.com/science/article/abs/pii/S1553838920304978

Objective: In this paper, we present an extensive systematic review of the reported cases of COVID-19 related myocarditis. We aim to describe the clinical characteristics and management of currently published COVID-19 myocarditis patients. We also aim to investigate the most common presenting features, workup and outcomes in the reported cases to identify a common pattern to aid in the diagnosis and management.

Result: Fourteen records comprising a total of fourteen cases that report myocarditis/myopericarditis secondary to COVID-19 infection were identified. There was a male predominance (58%), with the median age of the cases described being 50.4 years. The majority of patients did not have a previously identified comorbid condition (50%), but of those with a past medical history, hypertension was most prevalent (33%). Electrocardiogram findings were variable, and troponin was elevated in 91% of cases. Echocardiography was performed in 83% of cases reduced function was identified in 60%. Endotracheal intubation was performed in the majority of cases. Glucocorticoids were most commonly used in treatment of myocarditis (58%). Majority of patients survived to discharge (81%) and 85% of those that received steroids survived to discharge.

Conclusion: Guidelines for diagnosis and management of COVID-19 myocarditis have not been established and our knowledge on management is rapidly changing. The use of glucocorticoids and other agents including IL-6 inhibitors, IVIG and colchicine in COVID-19 myocarditis is debatable. In our review, there appears to be favorable outcomes related to myocarditis treated with steroid therapy. However, until larger scale studies are conducted, treatment approaches have to be made on an individualized case-by-case basis. [125]

Paper 18
Title of Article/Author/Year/Grade: Management of COVID-19 patients in Fangcang shelter hospital: clinical practice and effectiveness analysis / Liu, P., H. Zhang, X. Long, W. Wang, D. Zhan, X. Meng, D. Li, L. Wang, and R. Chen / 2020 / 5(12)

Type of Article: Cohort Study

Link of Article: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7675548/

Objective: This paper describes the layout and functioning of a typical Fangcang shelter hospital, Wuhan Dongxihu Fangcang shelter Hospital, where the author has worked, the working mechanism, experience and effectiveness.

Conclusion: In summary, the Fangcang shelter hospital was run successfully with patient management protocol package in situation of limited facilities and medical staff. It was effective and safe in isolating patients, providing basic medical care and identified very early on of potential severe cases. WeChat platform was successfully used to supervise and communicate with COVID-19 patients, which minimised the medical staff's direct contact with patients and avoiding transmission. The experience of Hall C of Wuhan Dongxihu Fangcang shelter Hospital provides a successful example of a working mechanism for the prevention and control of the COVID-19 pandemic worldwide. [126]

Paper 19
Title of Article/Author/Year/Grade: Coronavirus diseases (COVID-19) current status and future perspectives: a narrative review / Di Gennaro, Francesco, Damiano Pizzol, Claudia Marotta, Mario Antunes, Vincenzo Racalbuto, Nicola Veronese, and Lee Smith / 2020 / 5(10)

Type of Article: Review

Link of Article: https://www.mdpi.com/1660-4601/17/8/2690/htm

Objective: This review aims to summarize early findings on the epidemiology, clinical features, diagnosis, management, and prevention of COVID-19.
Result: The data was also indirectly supported by Chin and colleagues that artificially reproduced different environmental conditions in order to study the virus survival capacity. In addition to this

hopeful low impact, if the prevention measures will be implemented, we could register a lower incidence of hygiene-linked diseases that still represent leading causes of death. [127]
Conclusion: This review provides an insight into the COVID-19 current situation and represents a picture of the current state of the art in terms of public health impact, pathophysiology and clinical manifestations, diagnosis, case management, emergency response and preparedness. There is a rapidly growing body of literature on this topic and hopefully it will help in finding an effective vaccine and the best practice for the management and treatment of symptomatic cases. Only once this pandemic ends, one will be able to assess the health, social and economic impact of this global disaster and we should be able to learn lessons especially in terms of public and global health for any future similar pandemics.

Paper 20
Title of Article/Author/Year/Grade: Inpatient obstetric management of COVID-19 / Aubey, Janice, Noelia Zork, and Jean-Ju Sheen / 2020
Type of Article: Descriptive Study
Link of Article: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7373047/
Objective: To describe inpatient management strategies and considerations for pregnant patients with Severe acute respiratory syndrome coronavirus 2 infection.
Result: The novel coronavirus has posed challenges to both obstetric patients and the staff caring for them, due to its variable presentation and current limited knowledge about the disease. Inpatient antepartum, intrapartum and postpartum management can be informed by risk stratification, severity of disease, and gestational age. Careful planning and anticipation of emergent situations can prevent unnecessary exposures to patients and clinical staff. [128]
Conclusion: As new data arises, management recommendations will evolve, thus practitioners must maintain a low threshold for adaptation of their clinical practice during obstetric care for patients with Severe acute respiratory syndrome coronavirus 2 infection.

Paper 21
Title of Article/Author/Year/Grade: Mechanical Thrombectomy of COVID-19 positive acute ischemic stroke patient: a case report and call for preparedness / Mansour, Ossama Yassin, Amer M. Malik, and Italo Linfante / 2020
Type of Article: Case Report
Link of Article: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7512219/
Objective: We report a clinical case of a COVID-19 positive patient presenting to our center with AIS secondary to LVO, treated successfully by MT. We also describe the possible modifications for measures and workflow to deliver appropriate treatment for such patients in the era of the COVID-19 global pandemic.
Conclusion: Intubating such patients in the angiography suite could lead to increasing the exposure to the medical team in the stroke facility. Different protocols could be implemented to decrease such exposure in our case. We recommend intubating the patient before transfer to treating hospital or angiography suite in negative pressure-controlled room in ED or ICU that already had all PPE needed to deal with such cases following COVID-19 protocols. Other protocols for decreasing exposure during intubation may be used like intubating in a negative pressure emergency department room or under cover with video glidescope to avoid direct exposure to the patient's droplets. Additionally, the use of telemedicine in diagnosis and administration of IV thrombolysis may provide the 'social distancing' in stroke practice that could decrease the infection exposure of healthcare workers and should be considered in an AIS management protocol modified to accommodate the recent COVID-19 situation

worldwide. Mechanical thrombectomy was done under GA. Caution should be taken as these patients are more prone to acute respiratory distress syndrome (ARDS) and recommendations for hemodynamics, pulmonary function, and anesthesia drug selection should be considered as in published guidelines. Patients with COVID-19 infection are at increased risk of cerebrovascular diseases and acute ischemic stroke. Mechanical thrombectomy in AIS secondary to LVO in COVID-19 patients is feasible. However, existing stroke protocols should be modified following CDC guidelines for PUI or confirmed COVID-19 cases to deliver effective care for these patients and protect healthcare workers in this field.

Paper 22
Title of Article/Author/Year/Grade: What Should Be Known by a Urologist About the Medical Management of COVID-19's Patients? / Sánchez-González, Á., López-Fando Lavalle, A. Esteban-Fernández, M. Ruiz, V. Hevia, B. Comeche, Sánchez Conde et al. / 2020 / 7(10)
Type of Article: Systematic Review
Link of Article: https://link.springer.com/article/10.1007/s11934-020-00995-y
Objective: It aims to summarize the epidemiological, clinical, diagnostical, and therapeutical characteristics of COVID-19, from a practical perspective, to ease COVID-19 management to non-physician staff.

Result: With 3,759,967 confirmed cases on May 7th, including 259,474 deaths over 215 counties, several systematic reviews have been published about SARS-CoV-2's epidemiology. SARS-CoV-2 has high transmission efficiency, with a basic reproduction range (R0) estimated between 2 and 3 in most studies. The incubation period was estimated to be 4–6 days, ranging from 2 to 11 days after exposure in most cases. In a practical sense, 14 days are considered its upper limit. The transmission was estimated to start 1–3 days before symptoms onset. The risk of transmission from patients with SARS-CoV-2 infection varies by the kind and duration of exposure, use of preventive measures, and individual factors. Infected symptomatic or asymptomatic patients are the source of infection, being respiratory droplets and direct contact with an infected person/surface the most frequent vehicles. It also occurs by long-time exposure to high-virus concentration respiratory aerosols SARS-CoV-2 has been isolated on stool samples, but the feco-oral transmission is not significant. The SARS-CoV-2 yield in urine has not been demonstrated. Not vertical transmission has been demonstrated, although impaired effects have been described in newborns from infected pregnants. Exposure to higher virus concentrations and re-expositions are related to a worse prognosis. The duration of virus transmissibility is uncertain and seems to be related to the severity of illness. Seven days after the clinical onset, the risk of transmission decreases in mild-symptomatic patients, but it may be extended over 24 days in severe cases. [129]

Conclusion: We performed a narrative review of the literature regarding COVID-19, updated to May 8th, 2020, at PubMed and COVID resource platforms of the main scientific editorials. COVID-19, characterized by fever, myalgias, dyspnea, and dry cough, varies widely from asymptomatic infection to death. Arrhythmias and thrombotic events are prevalent. Lymphopenia and inflammatory reactant elevation on laboratory, as well as bilateral and peripheral ground-glass opacities or consolidations on X-Ray, are usually found in its assessment. Little is known about SARS-CoV-2 immunology. To date, no therapy has demonstrated efficacy in COVID-19. Of-level or compassionate-use therapies are prescribed in the context of clinical trials. We should become familiar with specific adverse events and pharmacological interactions.

Paper 23
Title of Article/Author/Year/Grade: SARS-CoV-2–related ARDS in a maintenance hemodialysis patient: case report on tailored approach by daily hemodialysis, noninvasive ventilation, tocilizumab, anxiolytics, and point-of-care ultrasound / Galassi, Andrea, Francesca Casanova, Lidia Gazzola, Rocco Rinaldo, Marco Ceresa, Elena Restelli, Alessia Giorgini et al. / 2020
Type of Article: Case Report
Link of Article: https://europepmc.org/article/pmc/pmc7753751
Objective:
Result: The case supports efficacy of individualized subintensive care, delivered by multidisciplinary team, and the need to allocate health resources for achieving similar goals in the treatment of critically ill COVID-19 MHD patients during second pandemic wave. [130]
Conclusion: Although mortality risk in COVID-19 MHD patients is higher than in general population, MHD should not represent an independent contraindication for admission to subintensive wards. The high rate of ARDS and heart failure, described in COVID-19, requires hospital wards predisposed for noninvasive ventilation also for MHD patients. Eventual preconditioned impaired access to subintensive care for MHD patients during early as unpredictable phase of pandemic emergency should represent a matter of allocating healthcare resources, poorly sustained by clinical and ethical principles up to date. Due to peculiarities of end-stage renal disease (ESRD) concerning prognostic evaluation and fluids management, nephrologist may be included in the acute care team of critically ill COVID-19 dialysis patients admitted to subintensive units.

Paper 24
Title of Article/Author/Year/Grade: A case of novel coronavirus disease 19 in a chronic hemodialysis patient presenting with gastroenteritis and developing severe pulmonary disease / Ferrey, Antoney J., Grace Choi, Ramy M. Hanna, Yongen Chang, Ekamol Tantisattamo, Kaushik Ivaturi, Elisa Park et al. / 2020
Type of Article: Case Report
Link of Article:
Objective: We present a case of COVID-19 in the United States in a long-term dialysis-dependent ESRD patient reported thus far in the 2020 COVID-19 pandemic.
Result:
Conclusion: As the scientific and medical community faces the unknown surge of COVID-19, some of our most vulnerable populations are already gathered for routine treatments in limited space; for example, infusion centers and dialysis centers placing them at great risk for exposure. The importance of rapid use of clinical publication data is paramount to making progress and spreading innovation. We have reported one of the first patients with ESRD undergoing hemodialysis with COVID-19 infection. This scenario presents various epidemiological challenges as far as containing infectious spread in a dialysis unit. This scenario also suggests that home dialysis maybe a protective intervention in the face of such a rapidly infectious pandemic.

Paper 25
Title of Article/Author/Year/Grade: Efficacy and safety of oral corticosteroids and olfactory training in the management of COVID-19-related loss of smell. / Le Bon, Serge-Daniel, Deborah Konopnicki, Nathalie Pisarski, Léa Prunier, Jérôme R. Lechien, and Mihaela Horoi / 2020 / 10(12)
Type of Article: Case Report
Link of Article: https://link.springer.com/article/10.1007/s00405-020-06520-8

Objective: In this pilot study, we investigated the efficacy and the safety of oral corticosteroids and olfactory training as a treatment for patients with persistent olfactory dysfunction as a result of COVID-19.
Result: 72 subjects with documented COVID-19 infection performed the initial olfactory test, on average 5 weeks after losing their sense of smell. Amongst them, 27 (37.5%) patients showed persistent dysosmia and were all included in this study. Nine participants received oral corticosteroids and performed olfactory training (OCS + OT), while 18 performed olfactory training (OT) only. Only participants in the OCS + OT group had significantly improved their olfactory score and did so above the minimal clinically important difference for subjective improvement of smell ($p = 0.007$). Three of the participants who received oral corticosteroids reported minimal and transient side effects.
Conclusion: This pilot study may suggest the combination of a short course of oral corticosteroids and olfactory training is safe and may be beneficial in helping patients with enduring dysosmia recover from olfactory loss due to COVID-19. There is a crucial need for further investigation with larger cohorts to corroborate these findings. [131]

Paper 26
Title of Article/Author/Year/Grade: Low dose radiation therapy as a potential life-saving treatment for COVID-19-induced acute respiratory distress syndrome (ARDS). / Dhawan, Gaurav, Rachna Kapoor, Rajiv Dhawan, Ravinder Singh, Bharat Monga, James Giordano, and Edward J. Calabrese / 2020
Type of Article: Case Report
Link of Article: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7206445/
Objective: To review the effects and putative mechanisms of low dose radiation that may be viable, useful and of value in counter-acting the acute inflammatory state induced by critical stage COVID-19.
Result: Based upon extant empirical findings, we advocate and urge the critical importance of administering a single dose of 0.3–0.5 Gy to patients experiencing pneumonia, ARDS with Cytokine storm, so as to attempt rapid amelioration of the systemic inflammatory cascade, while avoiding unacceptable or adverse long-term effects of RT. [132]
Conclusion: Certainly, we do not endorse the use of RT for all COVID-19 patients; but we do offer its consideration for those patients who are most critical, and for whom other treatments options are unsuccessful or unavailable.

Paper 27
Title of Article/Author/Year/Grade: "A comprehensive strategy for the early treatment of COVID-19 with azithromycin/hydroxychloroquine and/or corticosteroids: Results of a retrospective observational study in the French overseas department of Réunion Island / Dubernet, A., K. Larsen, L. Masse, J. Allyn, E. Foch, L. Bruneau, A. Maillot et al. / 2020 / 4(12)
Type of Article: Cohort Study
Link of Article: https://europepmc.org/article/med/32828896
Objective: This study aimed to evaluate the prognosis of COVID-19 patients in Reunion Island, with a particular focus on the management of patients with hypoxemic pneumonia.
Result: Over the study period, 164 out of 398 patients (41.2%) infected with COVID-19 were admitted to Félix Guyon University Hospital. Of these, 36 (22%) developed hypoxemic pneumonia. Patients with hypoxemic pneumonia were aged 66 [56-77] years, 69% were male and 33% had hypertension. Ten patients (27.8%) were hospitalized in intensive care unit (ICU). Hydroxychloroquine/azithromycin treatment was associated with a lower ICU admission rate (P=0.008). None of the 6 patients treated with corticosteroids were hospitalized in ICU (P=0.16). There were no deaths at follow up (minimum 80 days).

Conclusion: Despite the risk profile of COVID-19 patients with severe hypoxemic pneumonia, the mortality rate of the disease in Reunion Island was 0%. This may be due to the care bundle used in our hospital (early hospitalisation, treatment with hydroxychloroquine/azithromycin and/or corticosteroids, non-invasive respiratory support, etc). [133]

Paper 28

Title of Article/Author/Year/Grade: Low-dose radiotherapy for COVID-19 pneumonia treatment: case report, procedure, and literature review. / Del Castillo, R., D. Martinez, G. J. Sarria, L. Pinillos, B. Garcia, L. Castillo, A. Carhuactocto, F. A. Giordano, and G. R. Sarria / 2020

Type of Article: Case Report

Link of Article: https://europepmc.org/article/med/32816059

Objective: To present the case of a patient treated at our institution, describe the followed biosecurity and disinfection protocol, and review the available evidence regarding this topic published to date.

Conclusion: Radiotherapy arises as a promising option for COVID-19 pneumonia management. Prospective data from a larger cohort of patients are needed to confirm the safety profile and effectiveness of this approach in this specific group of patients

Paper 29

Title of Article/Author/Year/Grade: Coronavirus Disease 2019 (COVID-19) in a Renal Transplant Patient / Chenna, A., V. M. Konala, V. Gayam, S. Naramala, and S. Adapa / 2020

Type of Article: Case Report

Link of Article: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7282362/

Objective: To describe a case of a renal transplant patient who developed COVID-19 and, unfortunately, died from the infection despite all medical management.

Result: There were no reported instances that COVID-19 was spread through organ donation. The detection of SARS-CoV-2 in blood and organs ascertains that transmission through organ donation is a possibility. The transplant societies have issued guidance worldwide on screening the donors and recipients to decrease the spread. Real-time nucleic acid testing (NAT) should be done in deceased and living donors. Taking universal precautions and appropriate personal protective equipment (PPE) should be used to decrease the risk of transmission during organ procurement. The transplant surgeries should be postponed if there is known exposure. The decision to proceed with transplant surgery should be individualized based on the risk and benefits of proceeding with transplantation and the introduction of immunosuppression. The transplant recipients and the care team members should follow the same precautions as the general public in the event of exposure or development of symptoms. [134]

Conclusion: Transplant patients constitute a population more vulnerable to develop COVID-19 because of their immunosuppressed state and higher risk for opportunistic infections. Management includes the modification of immunosuppression with anti-metabolite held in most patients. Prevention is the key, as there is no proven treatment or vaccine available. We advise caution while using high-dose steroids, as it can be associated with delayed viral clearance.

Paper 30

Title of Article/Author/Year/Grade: Experience of N-acetylcysteine airway management in the successful treatment of one case of critical condition with COVID-19: A case report / Liu, Y., M. Wang, G. Luo, X. Qian, C. Wu, Y. Zhang, B. Chen, E. L. Leung, and Y. Tang / 2020

Type of Article: Case Report
Link of Article: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7571913/
Result: The main experience of successful treatment is summarized as follows: Repeated bedside bronchoscopy with a large dose of 10 to 15 g/time of NAC nebulized inhalation solution lavage combined with routine nebulization and sputum suction airway management. Reasonable and invasive respiration support. Reasonable anti-infective treatment. Comprehensive nutritional support, immunotherapy, exceptional medical management and other comprehensive medical investment.
Conclusion: Patients with severe conditions of novel coronavirus pneumonia often encounter bacterial infection in their later illness-stages. They may suffer respiratory failure and refractory hypercapnia that is difficult to improve due to excessive mucus secretion leading to small airway obstruction. This study provided a new insight on the proper treatment severe COVID-19 patients. The use of reasonable antibiotics and symptomatic respiratory support and other treatment, timely artificial airway and repeated bronchoalveolar NAC inhalation solution lavage, expectorant and other airway management are essential for such patients. [135]

Paper 31
Title of Article/Author/Year/Grade: Successful treatment of severe COVID-19 pneumonia and hyperinflammatory syndrome with tocilizumab. / Gentile, Giorgio, Rebecca Davies, Valeria Maria Manfreda, and Zain Ul Abideen / 2020

Type of Article: Case Report

Link of Article: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7798428/

Objective: To assess clinical improvement following administration of intravenous tocilizumab in a rapidly deteriorating patient with severe COVID-19 pneumonia.

Result: Over the following 24 days, SpO_2 drastically improved and the delivered oxygen dose decreased. The patient did not develop any complications from tocilizumab therapy and was discharged home on day 35 after admission once he was able to maintain SpO_2 >92% without supplemental oxygen. [136]

Conclusion: Indeed, under the overwhelming pressure of the urgent need for effective treatments against the COVID-19 pandemic, both studies decided to adopt much broader and somewhat aspecific inclusion criteria (for instance, C reactive protein ≥75 mg/L and oxygen saturation <92% on room air or requiring oxygen in the RECOVERY trial). As pointed out by Furlow,10 this issue might explain the disappointing preliminary results of the COVACTA trial, still unpublished but announced by Hoffmann-La Roche on 29 July 2020, which show that tocilizumab failed to meet its primary endpoint of improved clinical status and to improve mortality, although patients receiving tocilizumab had shorter hospitalisation time compared with the placebo arm. Tocilizumab continues to be evaluated by the RECOVERY trial, which enrolled over 850 patients, almost twice the size of the COVACTA trial, and might confirm or refute the results of COVACTA. Independently from the results of the RECOVERY trial, which suffers from the same limitations as COVACTA (lack of stratification by clinical signs of hyperinflammatory syndrome), we genuinely hope that the current case report could encourage researchers to perform post-hoc analyses of the above studies in due course or, even better, to design new randomised controlled trials which include Hscore as one of the key inclusion criteria.

3.3 Use and costs of health care

A. What are the implications of COVID-19 disease on the primary/secondary/tertiary health care systems in the country? ***[NPHCDA reports and plans]***

Title/ Author/ Grading: 1. Di Bidino R, Cicchetti A. Impact of SARS-CoV-2 on Provided Healthcare. Evidence From the Emergency Phase in Italy. Front Public Health. 2020 Nov 23;8:583583. doi: 10.3389/fpubh.2020.583583. PMID: 33330324; PMCID: PMC7719765.; CASP 6/10 (Pubmed_

Type of study: Systematic review

Summary of study: The SARS-CoV-2 (COVID-19) pandemic led to an emergency scenario within all aspects of health care, determining reduction in resources for the treatment of other diseases. A literature review was conducted to identify published evidence, from 1 March to 1 June 2020, regarding the impact of COVID-19 on the care provided to patients affected by other diseases. The research is limited to the Italian NHS. The aim is to provide a snapshot of the COVID-19 impact on the NHS and collect useful elements to improve Italian response models. Data available for oncology and cardiology are reported. National surveys, retrospective analyses, and single-hospital evidence are available. We summarized evidence, keeping in mind the entire clinical pathway, from clinical need to access to care to outcomes. Since the beginning, the COVID-19 pandemic was associated with a reduced access to inpatient (-48% for IMA) and outpatient services, with a lower volume of elective surgical procedures (in oncology, from 3.8 to 2.6 median number of procedures/week). Telehealth may plays a key role in this, particularly in oncology. While, for cardiology, evidence on health outcome is already available, in terms of increased fatality rates (for STEMI: 13.7 vs. 4.1%). To better understand the impact of COVID-19 on the health of the population, a broader perspective should be taken. Reasons for reduced access to care must be investigated. Patients fears, misleading communication campaigns, re-arranged clinical pathways could had played a role. In addition, impact on other the status of other patients should be mitigated. [137]

Paper 2
Title/ Author/ Grading: Romanelli RJ, Azar KMJ, Sudat S, Hung D, Frosch DL, Pressman AR. The Learning Health System in Crisis: Lessons from the Novel Coronavirus Disease Pandemic. Mayo Clin Proc Innov Qual Outcomes. 2020 Oct 29. doi: 10.1016/j.mayocpiqo.2020.10.004. Epub ahead of print. PMID: 33163894; PMCID: PMC7598312; CASP 6/10(Pubmed)
Type of study: Systematic review

Summary of study: The novel coronavirus disease (COVID-19) pandemic is the gravest public-health crisis that the United States has seen in more than a century. Healthcare delivery systems are the focal point for interfacing with COVID-19; however, many were and remain unprepared for this or similar outbreaks. In this paper, we describe the Learning Health System (LHS) as an ideal organizing principle to inform an evidence-based response to public-health emergencies like COVID-19. We further describe barriers and challenges to the realization of the LHS and propose a call to action for a substantial investment in the LHS, with a focus on public health. Specifically, we advocate for a Learning Health Network that promotes collaboration between health systems, community-based organizations, and government agencies, especially during public health emergencies. We have approached this commentary through the unique lens of researchers embedded within a large, integrated healthcare delivery system, with direct experience working with clinical and operational units in response to the COVID-19 pandemic. [138]

Paper 3

Title/ Author/ Grading: Wijesooriya NR, Mishra V, Brand PLP, Rubin BK. COVID-19 and telehealth, education, and research adaptations. Paediatr Respir Rev. 2020 Sep;35:38-42. doi: 10.1016/j.prrv.2020.06.009. Epub 2020 Jun 18. PMID: 32653468; PMCID: PMC7301824; CASP 6/10 (Pubmed)

Type of study: Systematic review

Summary of results: For decades, there have been government funded services to provide healthcare telephonically to remote sites both on the earth and in the air. This capability has evolved into what we now know as telehealth. The use of telehealth dramatically accelerated as a result of concerns for patient and healthcare provider safety during the SARS-CoV2 pandemic. Similarly, concerns regarding transmission of infection have required medical schools to provide robust, easily accessible virtual education options. At short notice, faculties have had to develop new telehealth focused curriculum components. However, telehealth, online education, and internet enabled research should not be simply a new way to do traditional jobs but rather, an opportunity to take advantage of how technology can best be used to develop new and better ways to provide care, educate health care providers, and support research. [139]

Paper 4

Title/ Author/ Damulak OD, Lugos MD, Ayuba Z, Ma'an VT, Jatau ED, Gaya F, Rumji E. Coronavirus Pandemic: The impact on the regional blood service of a developing country. *Africa Sanguine.* 2020;22(2):11-17. https://dx.doi.org/10.4314/ asan.v22i2.5. CASP 6/10(Pubmed)

Type of study: Retrospective descriptive study- Cohort study

Introduction: COVID-19 pandemic has affected all facets of life, sparing no country or continent. Its impacts on the health care system of nations have been unprecedented, overwhelming in most developed and developing nations.

Aims and objectives: This study sought to determine the impact of the COVID-19 pandemic on the zonal blood service in North-Central Nigeria.

Methods: Registers of the donor clinic and laboratory departments of the North-Central zonal blood service in Jos were reviewed from February to April 2020, for the number of blood drives fixed and carried out, number of people sensitised, number of donors recruited, counselled, deferred, bled and failed bleed. The unit screened for Transfusion Transmissible Infections (TTIs), expired and units returned from hospitals and hospitals that accessed blood were determined and compared with that of the same period in the preceding year. The trend of the TTIs screening outcome of blood units collected during COVID-19 outbreak was also evaluated.

Results: COVID-19 pandemic had both negative and positive impacts on the blood service in North-Central Nigeria. There was reduction in blood drive fixtures, executions, number of donors counselled, donations, number of first-time donors, units screened, hospitals served, and the number of safe units issued. However, repeat donations, failed bleed, crude transfusion transmissible infections rate, returned and expired units increased. The trend of Transfusion Transmissible Infections (TTIs) outcome of units collected during COVID-19 pandemic improved towards safety. [140]

Paper 5

Title/ Author/ COVID-19 Outbreak Situation in Nigeria and the Need for Effective Engagement of Community Health Workers for Epidemic Response/Whenayon Simeon Ajsegri, Olumuyiwa O. Odusanya, Rohina Jishi

Type of study: Case Report

Link: https://jglobalbiosecurity.com/articles/10.31646/gbio.69/

Introduction: The country has continued to experience an increase in the number of cases, which has spread across all 36 states and FCT. While majority of the initial cases were imported, most of the new cases have no travel history or contact with international travelers. This is indicative of ongoing community transmission. Under the current circumstances, the Primary Health Care (PHC) Centres remain the most likely port of call for community members who develop symptoms that could be suggestive of COVID-19. In the face of continued COVID-19 community transmission, the health system may likely become overwhelmed with increased risk of health workers' infection. Considering the fact that most people use the PHC centres, especially those in the rural and hard-to-reach areas, it is important that the staff should be adequately informed and resourced to provide first level care such as screening and referral of patients.

Aims and objectives: The authors describe the current situation of the outbreak and argued the need for effective engagement of community health workers for appropriate responses to COVID-19.

Methods: Review

Results: The continued increase in the number of cases has overwhelmed the human resources for health involved in the various aspects of response activities, particularly contact tracing. Many clinical activities have been reduced or halted in order to control COVID-19 transmission. More so, there have been numerous complaints about the shortages of personal protective equipment and ventilators needed to combat COVID-19. This is further compounded with reported COVID-19 infection among healthcare workers as a result of occupational exposures. Disruption of these health services could lead to reduction in immunization coverage, and increases in morbidity and mortality of infectious diseases as well as maternal, neonatal and childhood health issues. There is a critical shortage of skilled health workforce shortage in sub-Saharan Africa and an effective strategy for the COVID-19 response within the region should involve community health workers (CHWs), especially as flattening of the epidemic curve is hinged on preventive measures.

The government should aim at engaging CHWs in building a resilient health system. This is achievable through a review of their curriculum, current roles and career pathways, especially at this time when the health system has begun to apply the strategy of task-sharing and task- shifting. This will not only make the PHC a reliable healthcare system for major infectious diseases health events, but ensure that the system is better prepared to handle the rising scourge of non-communicable diseases.

Paper 6

Title/ Author/ Collateral damage: the impact of the COVID-19 pandemic on the care of a patient with tuberculous neuroretinitis in Lagos, Nigeria/Temiloluwa Moyosoreoluwa Abikoye (Pan African Medical Journal)

Type of study: Informative research

Link: https://www.panafrican-med-journal.com/content/series/35/2/135/pdf/135.pdf

Field Code Changed

Introduction: The COVID-19 pandemic amplified many preexisting deficiencies of the healthcare delivery system in Nigeria, notably, the infrastructure important for the establishment of effective telemedical services. Most healthcare providers in the country utilize paper medical records and lack electronic patient referral systems [9]; referrals and consultation requests largely rely on the patients being the couriers of the request letters [10] and there is sparse, publicly available information of the contact details for healthcare providers. The combined effects of the reduced accessibility to clinical/laboratory services, insufficient infrastructure for effective telehealth service delivery and the difficulty in facilitating interpractice medical consultations have negatively impacted health care delivery to, and the eventual outcomes of, patients with non-COVID-19-related health problems.

Aims and objectives: This report sought to determine the impact of the COVID-19 pandemic on access to non-COVID-19 related health care needs in Nigeria

Methods: the author followed a case of tuberculous neuroretinitis in Nigeria whose care, and outcome, was impacted by the ongoing pandemic.

Results: This case report highlights the impact of the COVID19 pandemic on the care of a patient with tuberculous neuroretinitis, an unrelated condition which usually has a good outcome. The institution of EMR and electronic referral systems, telehealth services, as well as the provision of mobile healthcare delivery services, will be important, now more than ever, for ensuring accessibility to, and the continuity of, healthcare service delivery in these uncertain times. These important adjustments may help mitigate some of the collateral damages of the COVID-19 pandemic on healthcare as a whole.

a. What is the short- and long-term impact of COVID-19 disease on the healthcare system? *[NPHCDA reports and plans]*

Paper 1
Author/ Title: Zhang J, Lu X, Jin Y, Zheng ZJ. Hospitals' responsibility in response to the threat of infectious disease outbreak in the context of the coronavirus disease 2019 (COVID-19) pandemic: Implications for low- and middle-income countries. Glob Health J. 2020 Dec;4(4):113-117. doi: 10.1016/j.glohj.2020.11.005. Epub 2020 Dec 3. PMID: 33294250; PMCID: PMC7713538; **CASP 6/10v (Pubmed)**
Type of study: Review
Summary of Study: The WHO declared the coronavirus disease 2019 (COVID-19) outbreak as a public health emergency of international concern on January 30, 2020, and then a pandemic on March 11, 2020. COVID-19 affected over 200 countries and territories worldwide, with 25,541,380 confirmed cases and 852,000 deaths associated with COVID-19 globally, as of September 1, 2020.[1] While facing such a public health emergency, hospitals were on the front line to deliver health care and psychological services. The early detection, diagnosis, reporting, isolation, and clinical management of patients during a public health emergency required the extensive involvement of hospitals in all aspects. The response capacity of hospitals directly determined the outcomes of the prevention and control of an outbreak. The COVID-19 pandemic has affected almost all nations and territories regardless of their development level or geographic location, although suitable risk mitigation measures differ between developing and developed countries. In low- and middle-income countries (LMICs), the consequences of the pandemic could be more complicated because incidence and mortality might be associated more with a fragile health care system and shortage of related resources. As evidenced by the situation in Bangladesh, India, Kenya, South Africa, and other LMICs, socioeconomic status (SES) disparity was a major factor in the spread of disease, potentially leading to alarmingly insufficient preparedness and responses in dealing with the COVID-19 pandemic. Conversely, the pandemic might also bring more unpredictable socioeconomic and long-term impacts in LMICs, and those with lower SES fare worse in these situations. This review aimed to summarize the responsibilities of and measures taken by hospitals in combatting the COVID-19 outbreak. Our findings are hoped to provide experiences, as well as lessons and potential implications for LMICs. [141]

Paper 2
Title/ Author; Varanda J, Gonçalves L, Craveiro I. The Unlikely Saviour: Portugal's National Health System and the Initial Impact of the COVID-19 Pandemic? Development (Rome). 2020 Dec 3:1-7. doi: 10.1057/s41301-020-00268-8. Epub ahead of print. PMID: 33288975; PMCID: PMC7710772; Grade: CASP 6/10 (Pubmed)
Type of study: Review
Summary of study: What is the impact of COVID-19 on Portugal's *Serviço Nacional de Saúde* (SNS), the country's national health service? The story, still unfolding, has all the elements of a recipe for disaster: one of the most elderly populations in the world; a weakened SNS, the result of a litany of policies and interventions by the 'Troika' (the European Commission, the European Central Bank and the International Monetary Fund); a health care delivery system focused on non-communicable diseases and long-term care; the growing public distrust in public services, compared to private, hotel-like health care facilities. We are aware that these are still the early days of the epidemic, yet it is safe to say that algorithmic scenarios of doom and gloom have so far been averted. In the past six months of

the pandemic, the level of trust of the Portuguese population in the SNS and its health personnel has significantly improved, while the government has started to provide additional funding and to work for the expansion of the public system. At the very inception of the pandemic, private hospitals practically closed their doors to COVID-19 patients. Unexpectedly a new disease, COVID-19, by definition *the* foe of any health system, has granted the opportunity for a rare consensus amongst different key political and/or corporate actors in a long-called-for reform of the SNS. Social science and humanities, with their analytical tools and theoretical-conceptual frameworks, are mandatory in providing well-funded answers to such riddles and better grasping the reasons for the twist and turns.

Paper 3
Title/ Author: Aggarwal R, Bhatia R, Soni KD, Trikha A. Fast tracking intensive care units and operation rooms during the COVID-19 pandemic in resource limited settings. J Anaesthesiol Clin Pharmacol. 2020 Aug;36(Suppl 1):S7-S14. doi: 10.4103/joacp.JOACP_262_20. Epub 2020 Jul 31. PMID: 33100639; PMCID: PMC7574016 (7/10) Pubmed
Type of study: Review CASP 7/10
Summary of study : The ongoing pandemic of COVID-19 has affected more than 43 million people all over the world with about 280000 deaths worldwide at the time of writing this article The outcome of this pandemic is impossible to predict at the present time as the numbers of both, infected patients and those dying of the disease are increasing on a daily basis. China, Italy, France, Spain, Germany, United Kingdom, and USA are the worst affected countries. All these countries have robust health care systems but despite this there has been a huge shortage of health care facilities especially intensive care beds in these countries. A country like India has different challenges as far as medical care during this pandemic is concerned. The need of the hour is to improve the health care system as a whole. In the present pandemic this involves setting up of patients screening facilities for the disease, enhancing the number of hospital beds, setting up of dedicated high dependency units, intensive care units and operation theatres for COVID positive patients. The present article describes in brief the way this can be done in a short time. [142]

Paper 4
Title / Author: Mazzucchi E, Torricelli FCM, Vicentini FC, Marchini GS, Danilovic A, Batagello CA, Srougi M, Nahas WC. The impact of COVID-19 in medical practice. A review focused on Urology. Int Braz J Urol. 2021 Mar-Apr;47(2):251-262. doi: 10.1590/S1677-5538.IBJU.2020.99.08. PMID: 32840335.
type of study: Systemic review; CASP 8/10
Summary of study: COVID-19 pandemic is a rapidly spreading virus that is changing the World and the way doctors are practicing medicine. The huge number of patients searching for medical care and needing intensive care beds led the health care system to a burnout status especially in places where the care system was already overloaded. In this setting, and also due to the absence of a specific treatment for the disease, health authorities had to opt for recommending or imposing social distancing to relieve the health system and reduce deaths. All other medical specialties non-directly related to the treatment of COVID-19 had to interrupt or strongly reduce their activities in order to give room to seriously ill patients, since no one knows so far the real extent of the virus damage on human body and the consequences of doing non deferrable procedures in this pandemic era. Despite not been a urological disease, the urologist needs to be updated on how to deal with these patients and how to take care of himself and of the medical team he works with. The aim of this article is to review briefly some practical aspects of COVID-19 and its implications in the urological practice in our country.

Paper 5

Title/ Author/ Grade: Gomes CM, Favorito LA, Henriques JVT, Canalini AF, Anzolch KMJ, de Carvalho Fernandes R, Bellucci CHS, Silva CS, Wroclawski ML, Pompeo ACL, de Bessa J Jr. Impact of COVID-19 on clinical practice, income, health and lifestyle behavior of Brazilian urologists. Int Braz J Urol. 2020 Nov-Dec;46(6):1042-1071. doi: 10.1590/S1677-5538.IBJU.2020.99.15. PMID: 32539253; PMCID: PMC752709

Type of Study: Review

Grade: CASP 6/10

Source: Pubmed

Objectives: To evaluate the impact of COVID-19 on clinical practice, income, health and lifestyle behavior of Brazilian urologists during the month of April 2020.

Materials and methods: A 39-question, web-based survey was sent to all urologist members of the Brazilian Society of Urology. We assessed socio-demographic, professional, health and behavior parameters. The primary goal was to evaluate changes in urologists' clinical practice and income after two months of COVID-19. We also looked at geographical differences based on the incidence rates of COVID-19 in different states.

Results: Among 766 urologists who completed the survey, a reduction ≥ 50% of patient visits, elective and emergency surgeries was reported by 83.2%, 89.6% and 54.8%, respectively. An income reduction of ≥ 50% was reported by 54.3%. Measures to reduce costs were implemented by most. Video consultations were performed by 38.7%. Modifications in health and lifestyle included weight gain (32.9%), reduced physical activity (60.0%), increased alcoholic intake (39.9%) and reduced sexual activity (34.9%). Finally, 13.5% of Brazilian urologists were infected with SARS-CoV-2 and about one third required hospitalization. Urologists from the highest COVID-19 incidence states were at a higher risk to have a reduction of patient visits and non-essential surgeries (OR=2.95, 95% CI 1.86 - 4.75; p< 0.0001) and of being infected with SARS-CoV-2 (OR=4.36 95%CI 1.74-10.54, p=0.012).

Conclusions: COVID-19 produced massive disturbances in Brazilian urologists' practice, with major reductions in patient visits and surgical procedures. Distressing consequences were also observed on physicians' income, health and personal lives. These findings are probably applicable to other medical specialties.

Paper 6

Title/Author/ Grading: Iyengar K, Mabrouk A, Jain VK, Venkatesan A, Vaishya R. Learning opportunities from COVID-19 and future effects on health care system. Diabetes Metab Syndr. 2020 Sep-Oct;14(5):943-946. doi: 10.1016/j.dsx.2020.06.036. Epub 2020 Jun 20. PMID: 32599533; PMCID: PMC7305503; CASP 7/10

Type of Study: Review

Source: Pubmed

Abstract

Background and aims: COVID-19 has had a crippling effect on the health care systems around the world with cancellation of elective medical services and disruption of daily life. We would like to highlight the learning opportunities offered by the current pandemic and their implication for a better future health care system.

Methods: We have undertaken a comprehensive review of the current literature to analyse the consequences of COVID-19 on health care system. Using suitable keywords like 'COVID-19', 'telemedicine', 'health care' and 'remote consultations' on the search engines of PubMed, SCOPUS,

Google Scholar and Research Gate in the first week of May we gathered information on various aspects of effect of COVID-19.
Results: There has been a shared drive worldwide to devise strategies to protect people against viral transmission with reinforcement of hand hygiene and infection control principles but also to provide continuity of health care. Virtual and remote technologies have been increasingly used in health care management. [143]
Conclusion: COVID-19 has offered unique learning opportunities for the health care sector. Rationalizing and optimizing available resources with resilience shown on the coronavirus frontline during the crisis are some of most important lessons learnt during the crisis. Importance of personal hygiene and re-enforcement of infection control measures have been acknowledged. Telemedicine revolution will be a vital factor in delivering health care in the future.

<u>Paper 7</u>
Title/ Author/ Grading : Dubey S, Biswas P, Ghosh R, Chatterjee S, Dubey MJ, Chatterjee S, Lahiri D, Lavie CJ. Psychosocial impact of COVID-19. Diabetes Metab Syndr. 2020 Sep-Oct;14(5):779-788. doi: 10.1016/j.dsx.2020.05.035. Epub 2020 May 27. PMID: 32526627; PMCID: PMC7255207; : CASP 7/10; **Pubmed**
Type of Study: Review
Background: Along with its high infectivity and fatality rates, the 2019 Corona Virus Disease (COVID-19) has caused universal psychosocial impact by causing mass hysteria, economic burden and financial losses. Mass fear of COVID-19, termed as "coronaphobia", has generated a plethora of psychiatric manifestations across the different strata of the society. So, this review has been undertaken to define psychosocial impact of COVID-19.
Methods: Pubmed and GoogleScholar are searched with the following key terms- "COVID-19", "SARS-CoV2", "Pandemic", "Psychology", "Psychosocial", "Psychiatry", "marginalized", "telemedicine", "mental health", "quarantine", "infodemic", "social media" and" "internet". Few newspaper reports related to COVID-19 and psychosocial impacts have also been added as per context.
Results: Disease itself multiplied by forced quarantine to combat COVID-19 applied by nationwide lockdowns can produce acute panic, anxiety, obsessive behaviors, hoarding, paranoia, and depression, and post-traumatic stress disorder (PTSD) in the long run. These have been fueled by an "infodemic" spread via different platforms of social media. Outbursts of racism, stigmatization, and xenophobia against particular communities are also being widely reported. Nevertheless, frontline healthcare workers are at higher-risk of contracting the disease as well as experiencing adverse psychological outcomes in form of burnout, anxiety, fear of transmitting infection, feeling of incompatibility, depression, increased substance-dependence, and PTSD. Community-based mitigation programs to combat COVID-19 will disrupt children's usual lifestyle and may cause florid mental distress. The psychosocial aspects of older people, their caregivers, psychiatric patients and marginalized communities are affected by this pandemic in different ways and need special attention. [144]
Conclusion: For better dealing with these psychosocial issues of different strata of the society, psychosocial crisis prevention and intervention models should be urgently developed by the government, health care personnel and other stakeholders. Apt application of internet services, technology and social media to curb both pandemic and infodemic needs to be instigated. Psychosocial preparedness by setting up mental organizations specific for future pandemics is certainly necessary.

<u>Paper 8</u>

Title/ Author/ Grading: Søreide K, Hallet J, Matthews JB, et al. Immediate and long-term impact of the COVID-19 pandemic on delivery of surgical services. *Br J Surg*. 2020;107(10):1250-1261. doi:10.1002/bjs.11670
Type of study: Systemic Review; CASP 6/10; Pubmed/Google scholar [145]
Summary of result: The coronavirus disease 2019 (COVID-19) pandemic has created strong pressure on national health critical care systems. After its initial impact in Asia, the highest case growth is now in the Americas. The South American countries face a strong challenge due to the vulnerabilities of their health systems and the fragile socio-economic conditions of their population. This perspective looks at the impact of COVID-19 in South America and argues that the health critical care systems of these countries are particularly vulnerable due to the underestimation of the number of cases currently confirmed and the strong need for treatment of these patients in intensive care units (ICUs). In particular, Bolivia will need to increase the number of ICU beds 60-fold while Brazil will need to grow 12-fold to meet the growth rates of COVID-19 by the end of July 2020. In this sense, it is argued that national and transnational measures should be taken urgently to face this challenge. Furthermore, it is necessary to perform tests to detect COVID-19 cases earlier to alleviate the need for internment in ICUs.
Surgical services are adapting to mitigate the surge in patients with COVID-19 in need of critical care support. All non-essential elective surgery has been cancelled, or is pending cancellation, in healthcare systems around the globe, impacting millions of patients. The post-pandemic phase will require re-establishment of surgical services, and capacity building to restore normalcy and to appropriately reduce the backlog of cases by priority. A framework for evaluation and a plan to incorporate surgical care into the WHO strategies for national health plans and pandemic mitigation is urgently needed.
In general, there has been inadequate preparedness for COVID-19 pandemic in LMICs as evidenced by the situation in Bangladesh, India, Kenya and South Africa. The socioeconomic status disparity was a major factor in the spread of disease, potentially leading to alarmingly short-term impact of the disease on the health care systems. It is opined that conversely; the pandemic might also bring more unpredictable socioeconomic and long-term impacts in LMICs.
Hospitals are on the front line to deliver health care and psychological services during the pandemic. The early detection, diagnosis, reporting, isolation, and clinical management of patients during a pandemic require the extensive involvement of hospitals in all aspects of patient care. However, private hospitals are reported to have reduced their services at the start of the pandemic and conversely patients were generally avoiding hospitals for fear of infection. It was unexpected that countries like China, Italy, France, Spain, Germany, United Kingdom, and USA with more robust health systems would be the worst affected by the pandemic. There has been a huge shortage of health care facilities especially intensive care beds in these countries.
For many countries like India and indeed Nigeria, it became necessary to set up screening centres for COVID-19 and indeed ICUs outside of health facilities. Brazil for instance will need a 12-fold increase in ICU beds to meet the demand of the pandemic. As for the long-term impact, no one knows for sure the long-term damages to the human body that SARS CoV2 will cause. So, the apprehension may not generate commensurate preparedness. However, what is clear is that the pandemic has exacerbated psychosocial issues across the globe which has short-term, and long-term impact implications.

Health care workers have been particularly affected, by increased exposure to the virus leading to significant HCW morbidity/mortality, along with the economic burden and financial losses that are universal to all. As for private hospitals, a survey of Urologists in Brazil revealed over 50% reduction in outpatient visits and surgical procedures resulting in distressing consequences on physicians' income,

health and personal lives. These findings are applicable to other medical specialties and indeed other professions.
There has also been a reduction in the delivery of surgical services to create access to care for critically ill COVID-19 patients. The re-establishment of surgical services post-COVID-19 pandemic will challenge the surgical capacity across the globe. This will need strategies in the national health plans.
However, it must be acknowledged that COVID-19 has offered unique learning opportunities for the health care sector to maximize the use of the media and in particular the social media, to re-enforce important infection control measures such as hand washing, and in particular for this infection, social distancing and the use of sanitizers. The pandemic has also created the opportunities for telemedicine revolution, which will be a vital factor in delivering health care and capacity building in the health sector in the long-term.

3.4 Alternative measures

a. How effective in terms of incidence, cost are the preventive measures of COVID-19 to the general population as an alternative to vaccination to targeted population? [Systematic Search/WHO website]

Paper 1
Title of Article/Author/Year/Grade: COVID-19 and the economy: an African perspective. / Kanu, Ikechukwu Anthony. / 2020 /
Type of Article: Review
Grade of Article: 7(10)
Link of Article: https://acjol.org/index.php/jassd/article/view/jassd_v3n2_3/290
Objective: While this pandemic affects different dimensions of life and society, this paper is concerned with the economic consequences of the COVID-19 pandemic on the economy of Africa, using the Nigerian economy as a case study.

Result: COVID-19 has led to economic suffering in Nigeria, through loss of jobs and other incomes. As small and medium-sized enterprises are hammered by the lockdown, many workers have lost their jobs while many are working on reduced work schedules. The situation is gradually dragging the Nigerian economy deeper and deeper into recession. It is more challenging for Nigeria as she is still sluggishly grappling with recovery from the 2016 economic recession which was a fall out of global oil price crash and insufficient foreign exchange earnings to meet imports. The financial and corporate sectors in Nigeria are beginning to suffer deterioration. Markets have taken a big hit; financial systems are under stress and banks are likely to see huge pressures on their balance sheets. Private firms are hurt by the collapse in demand. The likelihood of large-scale bankruptcies is rising. [146]

Conclusion: As a way forward, the immediate focus of the nation should be on measures to contain the spread of the disease and to treat the infected. The ability to stop its spread and treat the sick will have very positive consequences on the economy.

Paper 2
Title of Article/Author/Year/Grade: The Socio-Economic Impact of Covid-19 on The Economic Activities of Selected States in Nigeria. / Obi, S. E., Yunusa, T., Ezeogueri-Oyewole, A. N., Sekpe, S. S., Egwemi, E., & Isiaka, A. S. / 2020
Type of Article: Systematic review

Grade of Article: 8(10)
Link of Article: https://ojs.literacyinstitute.org/index.php/ijsei/article/view/10/34
Objectives: We focused on the period from the start of March 2020 when the corona virus began spreading into other states of the federation through May 4th, 2020 when the Federal government relaxed the lockdown policy. Our objective was to examine the socio-economic effect of the lockdown policy on business, transport and service/hospitality industries in three selected metropolis from three states within the period of relaxation.

Result: Findings from data contained in table 1 indicates that cumulative majority of business men and women comprising of traders, retail shops, wholesale of goods, prices of goods and services and customer patronage which greatly affects the economy activities of the study areas vis-à-vis national economy. The statistical effect were; business indebtedness due to perishable goods in the lockdown period (86.6%), change in customer patronage due to COVID-19 lockdown policy (83.3%), effect on supply and sales (100%), inflation of prices of goods (96.7%). This findings shows that the outbreak of COVID-19 pandemic and the consequential lockdown policy significantly affects economic activities which constitutes means of livelihood for millions of unemployed youths and self-employed Nigerians. However, a cursory look at the result reveals the moving average of the pandemic on businesses from perishable products-customer patronage-supply-supply and sales and prices of goods. However, the linear forecast reveals the ongoing effects of the pandemic on business activities; that is, if the lockdown policy is not lifted, they will be disastrous effects on business and might lead to collapse of the economy in the study areas. [147]
Conclusion: The implication of this findings is that, if the lockdown policy continued another economic recession worse than that of 2016 in Nigeria is looming around the corners.

Query: Are vulnerable, hard-to-reach and immigrant populations able to access vaccines administered?

Paper 1
Title of Article/Author/Year/Grade: Delivering Covid-19 Vaccines by Building Community Trust / Cerise, Frederick P., Brett Moran, and Kavita Bhavan / 2020
Type of Article: Commentary
Link of Article: **https://europepmc.org/article/pmc/pmc7793438**
Objective: Black and Hispanic communities have been hard hit by Covid-19, yet they have historical reasons to mistrust health care or defer vaccinations. Here's how Parkland Health is working to rebuild trust in medical systems and health interventions. [148]
Conclusion: Regaining trust in medical systems and health interventions requires a commitment to show up in those underserved communities, listen to their concerns, and include their voices in addressing those concerns with the broader public. We must be intentional in our efforts, employ multiple communication strategies, and make the process easy if we are to successfully get the Covid-19 vaccine to the communities most in need that have been disproportionately impacted by the virus.

Paper 2
Title of Article/Author/Year/Grade: Constructing an ethical framework for priority allocation of pandemic vaccines / Fielding, J., S. G. Sullivan, F. Beard, K. Macartney, J. Williams, A. Dawson, G. L. Gilbert et al. / 2020 / 9(10)

Type of Article: Literature Review
Link of Article: **https://www.sciencedirect.com/science/article/pii/S0264410X20316339**

Objective: We describe a framework for priority vaccine allocation that employed a cross-disciplinary approach, guided by ethical considerations and informed by local risk assessment.

Result: Published and emerging guidance for priority pandemic vaccine distribution differed widely with respect to strategic objectives, specification of target groups, and explicit discussion of ethical considerations and decision-making processes. Flexibility in response was universally emphasised, informed by real-time assessment of the pandemic impact level, and identification of disproportionately affected groups. Model outputs aided identification of vaccine approaches most likely to achieve overarching goals in pandemics of varying transmissibility and severity. Pandemic response aims deemed most relevant for an Australian framework were: creating and maintaining trust, promoting equity, and reducing harmful outcomes. [149]

Conclusion: Once COVID-19 vaccines are available, governments will need to communicate their allocation plans effectively and transparently, among all levels of government responsible for procurement and delivery, health professionals and the public. Suspicion of government decision-making is evident during this pandemic and risks undermining careful planning. This is underscored by a recent global survey of acceptance of a COVID-19 vaccines which identified increased acceptance in nations where respondents had higher levels of trust

Paper 3

Title of Article/Author/Year/Grade: Fair allocation of potential COVID-19 vaccines using an optimization-based strategy / del Carmen Munguía-López, Aurora, and José María Ponce-Ortega / 2020
Type of Article: Modelling Study
Link of Article: **https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7804910/**

Objective: This paper presents an optimization strategy for the allocation of COVID-19 vaccines, when they are available, through different fairness schemes (social welfare, Nash, Rawlsian justice, and social welfare II scheme)

Conclusion: In this work, we presented an optimization formulation for the allocation of potential COVID-19 vaccines through fairness schemes. Distinct parameters to model the distribution of vaccines were considered. Specifically, the case study of Mexico was addressed. We analyzed the allocated vaccines to each state of Mexico given by the allocation schemes (social welfare, Nash, Rawlsian justice, and social welfare II scheme) under different availability scenarios. We observe that the allocation of resources is a complex problem that can result in unfair distributions if it is not addressed properly. Mainly, when several stakeholders (32 states in our case study) are involved, the possible assignations are greater. We also observe that inequalities become critical when resources are scarce. For example, in scenario (b), where the social welfare approaches (standard and II) give preference only to one particular state by depriving the others. Specifically, the first solution obtained by the social welfare approach (standard) tends to favor large stakeholders (greater population) in all scenarios. On the other hand, when the available vaccines are greater, the complexity of the allocation increases since the possible solutions increase as well (such as in scenario (d)). Therefore, it is critical to consider all the possible allocations that the fairness schemes provide to identify the most suitable solution. [150]

Paper 4

Title of Article/Author/Year/Grade: Key populations for early COVID-19 immunization: preliminary guidance for policy / Ismail, Shainoor J., Linlu Zhao, Matthew C. Tunis, Shelley L. Deeks, and Caroline Quach / 2020
Type of Article: Guidance Document
Link of Article: **https://pubmed.ncbi.nlm.nih.gov/33144317/**
Objective: Canada's National Advisory Committee on Immunization (NACI) has developed preliminary recommendations for the efficient, effective and equitable allocation of safe, efficacious Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) vaccine(s) in the context of staggered arrival of vaccines.
Result: Key populations for early vaccination include those at high risk of severe illness and death from COVID-19; those most likely to transmit COVID-19 to those at high risk of severe illness and death from COVID-19 and workers essential to maintaining the COVID-19 response; those contributing to the maintenance of other essential services for the functioning of society; and those whose living or working conditions put them at elevated risk of infection and where infection could have disproportionate consequences, including Indigenous communities. [151]
Conclusion: Existing inequities magnified by this pandemic may be exacerbated with the inequitable allocation of vaccines. Efforts should be made to increase access to immunization services and engage racialized and systemically marginalized populations in immunization program planning. The integration of equity, feasibility and acceptability considerations across all populations is critical for decisions regarding a COVID-19 immunization program.

3.5 Regional and international considerations

c. **What are the existing regional and global recommendations for COVID-19 vaccination? *[Reference handbooks, WHO PP, SAGE or UNICEF website]***
   a. **Does COVID-19 have potential for international spread and pandemics? *[Reference handbooks, WHO PP, SAGE or UNICEF website]***

Paper 1
Title/ AuthorGrading: Michel Bielecki , Dipti Patel , Jochen Hinkelbein , Matthieu Komorowski , John Kester , Shahul Ebrahim , Alfonso J Rodriguez-Morales , Ziad A Memish , Patricia Schlagenhauf (Pubmed; CASP 6/10)

Type of study: Systematic review

Summary of study: Air travel during the COVID-19 pandemic is challenging for travelers, airlines, airports, health authorities, and governments. We reviewed multiple aspects of COVID peri-pandemic air travel, including data on traveler numbers, peri-flight prevention, and testing recommendations and in-flight SARS-CoV-2 transmission, photo-epidemiology of mask use, the pausing of air travel to mass gathering events, and quarantine measures and their effectiveness. Flights are reduced by 43% compared to 2019. Hygiene measures, mask use, and distancing are effective, while temperature screening has been shown to be unreliable. Although the risk of in-flight transmission is considered to be very low, estimated at one case per 27 million travelers, confirmed in-flight cases have been published. Some models exist and predict minimal risk but fail to consider human behavior and airline procedures variations. **Despite aircraft high-efficiency filtering, there is some evidence that passengers within two rows of an index case are at higher risk.** Air travel to mass gatherings should be avoided. Antigen testing is useful but impaired by time lag to results. Widespread application of solutions such as saliva-based, rapid testing or even detection with the help of "sniffer dogs" might be the way forward. The "traffic light system" for traveling, recently introduced by the Council of the European Union is a first step towards normalization of air travel. Quarantine of travelers may delay introduction or re-introduction of the virus, or may delay the peak of transmission, but the effect is small and there is limited evidence. New protocols detailing on-arrival, rapid testing and tracing are indicated to ensure that restricted movement is pragmatically implemented. Guidelines from airlines are non-transparent. Most airlines disinfect their flights and enforce wearing masks and social distancing to a certain degree. A layered approach of non-pharmaceutical interventions, screening and testing procedures, implementation and adherence to distancing, hygiene measures and mask use at airports, in-flight and throughout the entire journey together with pragmatic post-flight testing and tracing are all effective measures that can be implemented. Ongoing research and systematic review are indicated to provide evidence on the utility of preventive measures and to help answer the question "is it safe to fly?". [152]

Paper 2
Title/ Author/ Grading: Mukherjee S, Boral S, Siddiqi H, Mishra A, Meikap BC. Present cum future of SARS-CoV-2 virus and its associated control of virus-laden air pollutants leading to potential environmental threat - A Review. J Environ Chem Eng. 2021 Jan 13:104973. doi: 10.1016/j.jece.2020.104973. Epub ahead of print. PMID: 33462561; PMCID: PMC7805399 (Pubmed Grade: CASP: 7/10)
Type of study: Review
Summary of study: The world is presently infected by the biological fever of COVID-19 caused by SARS-CoV-2 virus. The present study is mainly related to the airborne transmission of novel coronavirus through airway. Similarly, our mother planet is suffering from drastic effects of air pollution. There are sufficient probabilities or evidence proven for contagious virus transmission through polluted airborne pathway in formed aerosol molecules. The pathways and sources of spread are detailed along with the best possible green control technologies or ideas to hinder further transmission. The combined effects of such root causes and unwanted outcomes are similar in nature leading to acute cardiac arrest of our planet. To maintain environmental sustainability, the prior future of such emerging unknown biological hazardous air emissions is to be thoroughly researched. So it is high time to deal with the future of hazardous air pollution and work on its preventive measures. The lifetime of such an airborne virus continues for several hours, thus imposing severe threat even during post-lockdown phase. The world waits eagerly for the development of successful vaccination or medication, but the possible outcome is quite uncertain in terms of equivalent economy distribution and biomedical availability. Thus, risk assessments are to be carried out even during the post-vaccination period with proper environmental surveillance and monitoring. The skilled techniques of disinfection, sanitization, and other viable wayouts are to be modified with time, place, and prevailing climatic conditions, handling the pandemic efficiently. A healthy atmosphere makes the earth a better place to dwell, ensuring its future lifecycle. [153]

Paper 3
Title/ Author/ Grading : Mustapha JO, Abdullahi IN, Ajagbe OOR, Emeribe AU, Fasogbon SA, Onoja SO, Ugwu CE, Umeozuru CM, Ajayi FO, Tanko WN, Omosigho PO, Aliyu AS, Shuwa HA, Nwofe JO, Dangana A, Alaba O, Ghamba PE, Ibrahim Y, Aliyu D, Animasaun OS, Ugboaja NB, Baba Mallam MA, Abubakar SD, Aminu MS, Yahaya H, Oyewusi S. Understanding the implications of SARS-CoV-2 re-infections on immune response milieu, laboratory tests and control measures against COVID-19. Heliyon. 2021 Jan

9;7(1):e05951. doi: 10.1016/j.heliyon.2021.e05951. PMID: 33490695; PMCID: PMC7810769 (Pubmed; CASP 6/10).

Type of study: Systematic review

Summary of study: Several months after the emergence of Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), cases of re-infection after recovery were reported. The extent and duration of protective immunity after SARS-CoV-2 infection is not fully understood. As such, the possibility of re-infection with SARS-CoV-2. Furthermore, cases of re-infection were mainly due to different variants or mutant SARS-CoV-2. Following the fast and pandemic-scale spread of COVID-19, mutations in SARS-CoV-2 have raised new diagnostic challenges which include the redesign of the oligonucleotide sequences used in RT-PCR assays to avoid potential primer-sample mismatches and decrease sensitivities. Since the initial wave of the pandemic, some regions had experienced fresh outbreaks, predisposing people to be susceptible to SARS-CoV-2 re-infection. Hence, this article sought to offer detailed biology of SARS-CoV-2 re-infections and their implications on immune response milieu, diagnostic laboratory tests and control measures against COVID-19. [154]

Paper 4

Title/ Author/ Grading: Patel M, Chaubey AK, Pittman CU Jr, Mlsna T, Mohan D. Coronavirus (SARS-CoV-2) in the environment: Occurrence, persistence, analysis in aquatic systems and possible management. Sci Total Environ. 2020 Oct 2:142698. doi: 10.1016/j.scitotenv.2020.142698. Epub ahead of print. PMID: 33097261; PMCID: PMC7531938; (Pubmed; CASP 6/10)

Type of study: Systematic review

Summary of Study: The year 2020 brought the news of the emergence of a new respiratory disease (COVID-19) from Wuhan, China. The disease is now a global pandemic and is caused by a virus named SARS-CoV-2 by international bodies. Important viral transmission sources include human contact, respiratory droplets and aerosols, and through contact with contaminated objects. However, viral shedding in faeces and urine by COVID-19-afflicted patients raises concerns about SARS-CoV-2 entering aquatic systems. Recently, targeted SARS-CoV-2 genome fragments have been successfully detected in wastewater, sewage sludge and river waters around the world. Wastewater-based epidemiology (WBE) studies can provide early detection and assessment of COVID-19 transmission and the growth of active cases within given wastewater catchment areas. WBE surveillance's ability to detect the growth of cases was demonstrated. Was this science applied throughout the world as this pandemic spread throughout the globe? Wastewater treatment efficacy for SARS-CoV-2 removal and risk assessments associated with treated water are reported. Disinfection strategies using chemical disinfectants, heat and radiation for deactivating and destroying SARS-CoV-2 are explained. Analytical methods of SARS-CoV-2 detection are covered. This review provides a more complete overview of the present status of SARS-CoV-2 and its consequences in aquatic systems. So far, WBE programs have not yet served to provide the early alerts to authorities that they have the potential to achieve. This would be desirable in order to activate broad public health measures at earlier stages of local and regional stages of transmission. [155]

3.6 Economic and operational considerations

3.7 Vaccine related costs and resource use

What is the cost (including operational cost) of administering COVID-19 vaccine per dose to the target population during introduction? ***[NPHCDA reports and plans]***

Title of Article/Author/Year: (UPDATED) Comparing COVID-19 Vaccines: Timelines, Types and Prices / Mark Terry / 2021

Link of Article: https://www.biospace.com/article/comparing-covid-19-vaccines-pfizer-biontech-moderna-astrazeneca-oxford-j-and-j-russia-s-sputnik-v/

Cost of delivering COVID-19 Vaccine in 92 AMC countries, Updated estimates from COVAX Working Group on Delivery Costs / WHO, Gavi & UNICEF / 5th February 2021.

Objective: To compare the COVID-19 Vaccines: Timelines, Types and Prices

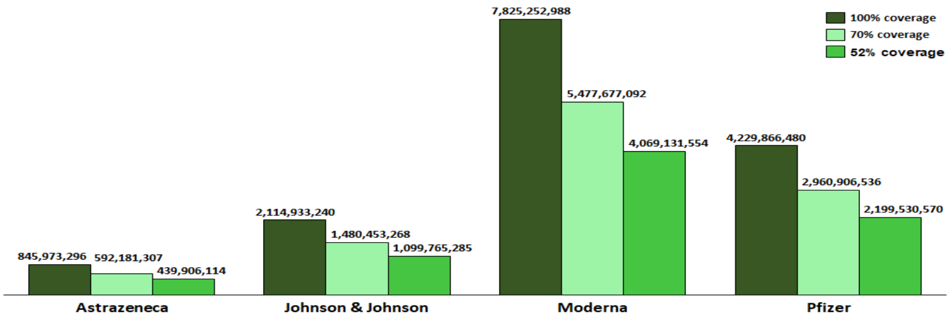
Result: [156, 157]

SN	Vaccine	Type	Doses	Price per dose (USD)	Cost of full vaccination	Total cost (Full vaccination + Operational cost @1.6 per dose
1	Pfizer-BioNTech	mRNA	2, 21 Days Apart	19.5	39	62.4
2	Moderna	mRNA	2, 28 Days Apart	25-$37	50-74	80-118.4
3	AstraZeneca-University of Oxford	Adenovirus-based	2, 28 Days Apart	25-$37	50-74	80-118.4
				4*	14	22.4
5	Sinopharm	Inactivated SARS-CoV-2	2, 21 Days Apart	72.5	145	148.2
6	Russia's Sputnik V Vaccine	Adenovirus-based	2, 21 Days Apart	10	20	32
7	Johnson & Johnson	Adenovirus-based	1	10	20	32
8	Novavax vaccine	Protein subunit	2, 21 Days Apart	16	32	35.2
9	Sinovac Biotech	Inactivated SARS-CoV-2	2, 14 Days Apart	29.75	59.5	95.2
10	CanSino	Ad5-nCoV	1	-	-	-

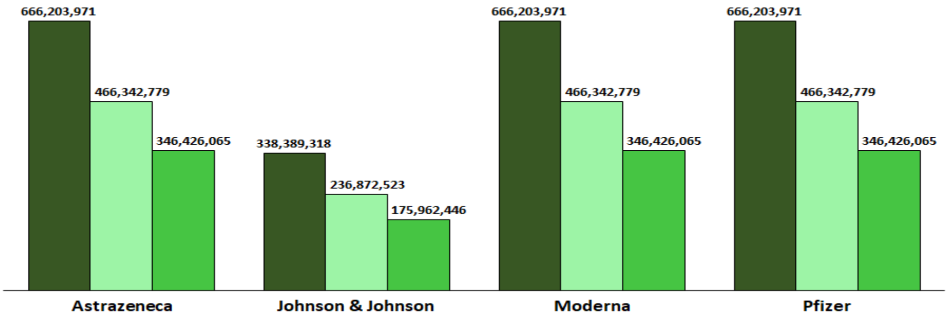
*AstraZeneca has an agreement of $4 with COVAX facility.

**Operational cost for the vaccine delivery program is estimated at $1.6/dose by the COVAX delivery cost working group. It is the estimated unit cost per dose for the outreach strategy. It includes different cost categories needed for vaccine delivery, such as: safety injection devices, PPE for health care workers, cold chain, social mobilization, training, etc. (WHO, UNICEF & Gavi; Costs of delivering COVID-19 vaccine in 92 AMC countries as at 5th February 2021)

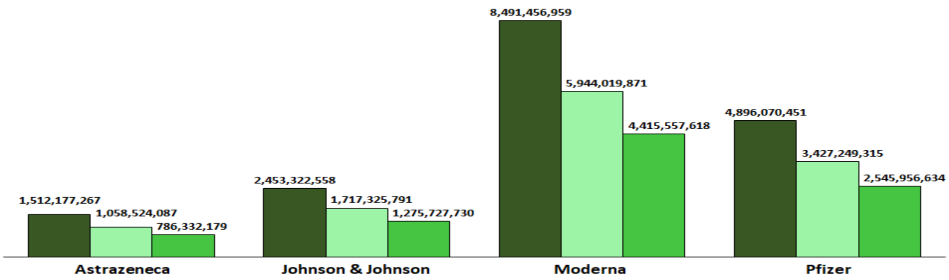
Conclusion: The cost of one dose of COVID-19 vaccine range from $10 to $37. Only two of the COVID-19 vaccines requires a single dose; Johnson & Johnson with efficacy of 66% - 71% depending on the severity of the disease and China's CanSinoBio vaccine with 65.7% - 90% efficacy depending on the severity of the disease.



(Fig above) Estimated vaccination cost in USD for Astrazeneca, Johnson & Johnson, Moderna and Pfizer vaccines by different scenarios of target population



(Fig above) Estimated operational cost in USD per person immunized with 2 doses with Astrazenaca, Moderna and Pfizer (1 for Johnson & Johnson) by different scenarios of target population using estimated operational cost of $3.15 per person vaccinated with 2 doses and $1.6 for one dose

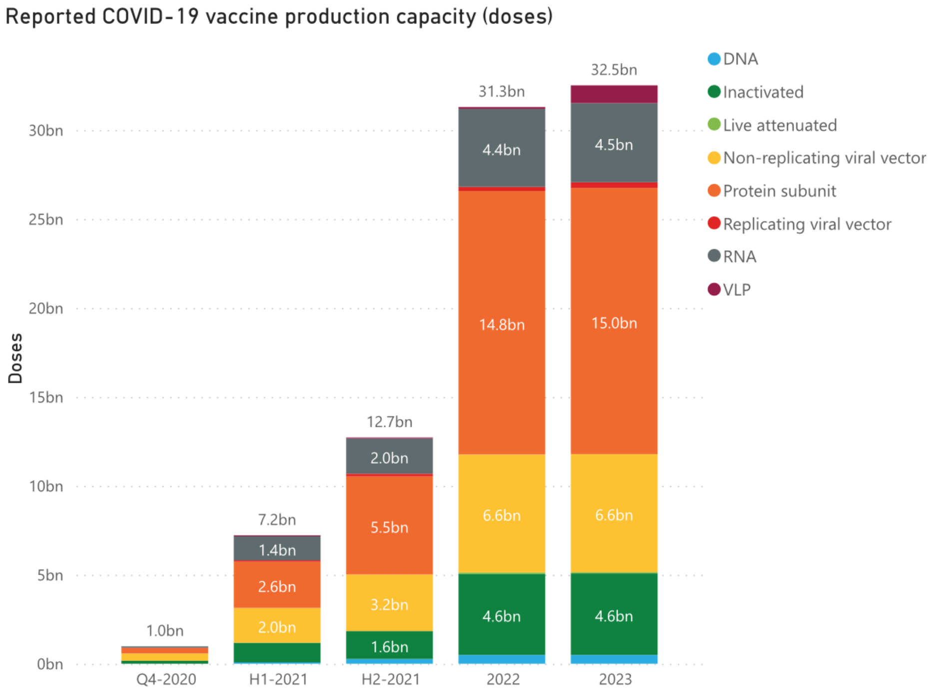


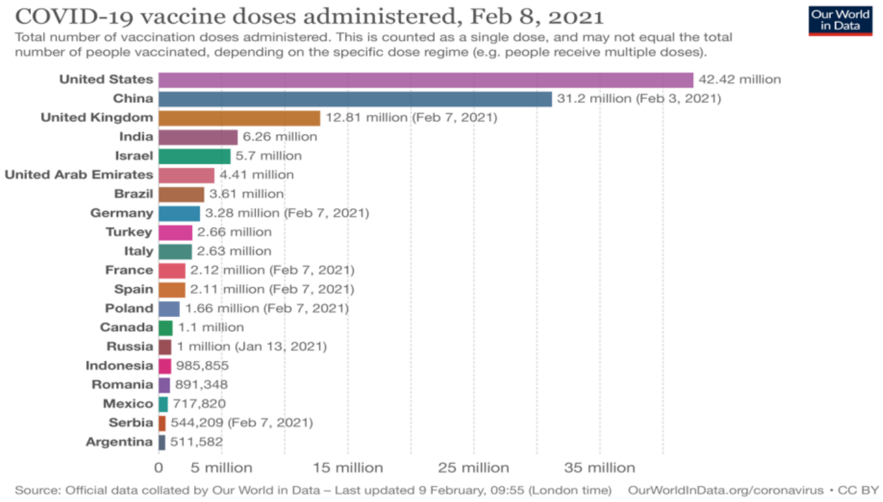
(Fig above) Estimated vaccination + operational cost in USD for Astrazeneca, Johnson & Johnson, Moderna and Pfizer vaccines by different scenarios of target population

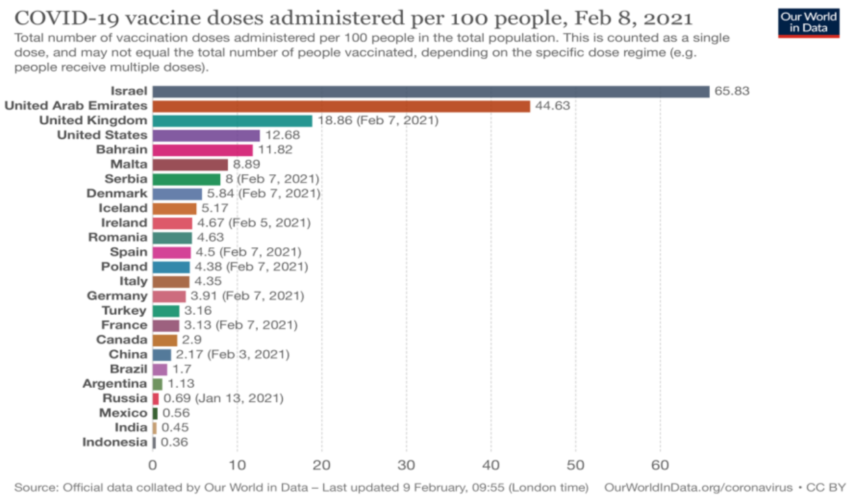
3.8 Vaccine availability

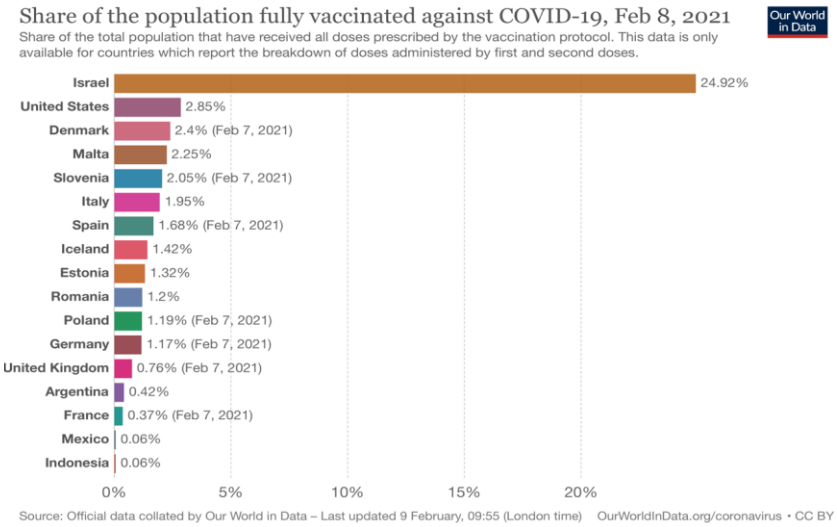
A. What is the global availability of COVID-19 vaccines? ***[Reference handbooks, WHO PP, SAGE or UNICEF website]***

Reported COVID-19 vaccine production capacity in doses. Source: UNICEF, 2020. [158]
Link to source: https://www.unicef.org/supply/covid-19-vaccine-market-dashboard




COVID-19 vaccine doses administered, Feb 8, 2021
Total number of vaccination doses administered. This is counted as a single dose, and may not equal the total number of people vaccinated, depending on the specific dose regime (e.g. people receive multiple doses).
Our World in Data
United States 42.42 million
China 31.2 million (Feb 3, 2021)
United Kingdom 12.81 million (Feb 7, 2021)
India 6.26 million
Israel 5.7 million
United Arab Emirates 4.41 million
Brazil 3.61 million
Germany 3.28 million (Feb 7, 2021)
Turkey 2.66 million
Italy 2.63 million
France 2.12 million (Feb 7, 2021)
Spain 2.11 million (Feb 7, 2021)
Poland 1.66 million (Feb 7, 2021)
Canada 1.1 million
Russia 1 million (Jan 13, 2021)
Indonesia 985,855
Romania 891,348
Mexico 717,820
Serbia 544,209 (Feb 7, 2021)
Argentina 511,582
0 5 million 15 million 25 million 35 million
Source: Official data collated by Our World in Data – Last updated 9 February, 09:55 (London time) OurWorldInData.org/coronavirus • CC BY


COVID-19 vaccine doses administered per 100 people, Feb 8, 2021
Total number of vaccination doses administered per 100 people in the total population. This is counted as a single dose, and may not equal the total number of people vaccinated, depending on the specific dose regime (e.g. people receive multiple doses).
Our World in Data
Israel 65.83
United Arab Emirates 44.63
United Kingdom 18.86 (Feb 7, 2021)
United States 12.68
Bahrain 11.82
Malta 8.89
Serbia 8 (Feb 7, 2021)
Denmark 5.84 (Feb 7, 2021)
Iceland 5.17
Ireland 4.67 (Feb 5, 2021)
Romania 4.63
Spain 4.5 (Feb 7, 2021)
Poland 4.38 (Feb 7, 2021)
Italy 4.35
Germany 3.91 (Feb 7, 2021)
Turkey 3.16
France 3.13 (Feb 7, 2021)
Canada 2.9
China 2.17 (Feb 3, 2021)
Brazil 1.7
Argentina 1.13
Russia 0.69 (Jan 13, 2021)
Mexico 0.56
India 0.45
Indonesia 0.36
0 10 20 30 40 50 60
Source: Official data collated by Our World in Data – Last updated 9 February, 09:55 (London time) OurWorldInData.org/coronavirus • CC BY



3.9 Vaccine affordability

a. What is the annual and medium-term fiscal implications to the government of introducing COVID-19 vaccines into immunization program? *(NPHCDA Plan and Report)*

Title of Article/Author/Year: Estimated cost of COVID-19 vaccines procurement, operations and vaccine delivery/ NPHCDA/2021
Type of Article: NPHCDA reports
Link of Article: Not available
Objective: To estimate the cost of delivering COVID-19 vaccines across Nigeria in 2021 and 2022.
Results:

S/N	Activity	Cost Elements	2021 Cost [NGN]	2022 Cost [NGN]	Remarks
1	Vaccines Procurement Cost				
a	Gavi funding (20%)	42,298,665	-	-	Gavi has committed to fully fund the vaccines procurement for 20% of the total Nigeria population through COVAX facility
b	Federal Government of Nigeria funding (20% in 2021 & 30% in 2022)	42,298,665	130,618,277,520	168,193,553,983	
	Sub-total		130,618,277,520	168,193,553,983	
2	Vaccines Delivery Cost to Every Ward (Operational Cost)				
a	Federal Government of Nigeria funding (100% of the needs)	84,597,330	26,123,655,504	20,082,812,323	In 2021 and 2022, FGoN to fully fun 100% of the operation cost for vaccine introduction
	Sub-total		26,123,655,504	20,082,812,323	
3	Ensuring Availability of PHCs and Health workers to deliver vaccines	Per PHC			
a	Primary Healthcare (PHC) Renovation (5PHCs/LGA)	26,650,000	103,135,500,000	103,135,500,000	PHC renovation includes infrastructural upgrade, accomodation and equipments (Total of 3,870 PHCs)
b	Human Resources for Health(Salaries and capacity building)	27,810,000	107,624,700,000	107,624,700,000	Based on Ward Health System (WHS) basic staffing standard multiplied by average salaries (8 Clinical, 10 non-clinical, plus partly covering LGA staff) and Capacity Building Annually
	Sub-total		210,760,200,000	210,760,200,000	
	Grand Total		367,502,133,024	399,036,566,306	

The country made cost estimation analysis based on the following assumptions: 211,493,324 Total Population (2021); 216,783,381 Total Population (2022); $8 Cost of full dose ($4/dose) in 2021; $6.7 Cost of full dose ($3.35/dose) due to expected potential slight decline in global price in 2022; $0.8 Operational cost per person (50% of the required) 5 LGA (774).

Conclusion: The National Primary Health Care Development Agency (NPHCDA) has estimated approximately N367.5 billion and N399 billion in 2021 and 2022 respectively for COVID-19 vaccine procurement, operations and vaccine delivery to vaccinate cumulatively 70% of the population.

What is the estimated price of COVID-19 vaccine obtained through the COVAX facility? *[NPHCDA reports and plans]*
Title of Article/Author/Year: 1. Here's how the top 3 coronavirus vaccines compare when it comes to efficacy, cost, and more / Isabella Jibilian ; Pfizer and Biontech reach agreement with COVAX for advance purchase of vaccine to help combat COVID-19
Link of Article: https://africa.businessinsider.com/science/heres-how-the-top-3-coronavirus-vaccines-compare-when-it-comes-to-efficacy-cost-and/dx5yxyk; https://www.pfizer.com/news/press-release/press-release-detail/pfizer-and-biontech-reach-agreement-covax-advance-purchase
Objective: To compare how the top 3 coronavirus vaccines compare when it comes to efficacy, cost, distribution, storage, efficacy, and approval.
Result: The frontrunners for COVID-19 vaccines are from Pfizer and BioNTech, Moderna and AstraZeneca, and Oxford University. AstraZeneca's vaccine is the cheapest of the three leading COVID-19 vaccines and has pledged not to make a profit from the vaccine during the pandemic. Based on the company's contract with the US government, one dose of AstraZeneca's vaccine costs about $4. AstraZeneca and Pfizer/BioNTech vaccine have already struck a deal with COVAX, a global initiative to distribute COVID-19 vaccines equitably, including to low-income nations. [159, 160]

Estimated Cost of vaccination, AMC-92 [157]

Cost Component	Cost $ / dose	Comments
Vaccine price per dose and ancillary equipment (unit cost) *	$7	Please note that for AMC92 (cost-sharing), as of 11 December*, Gavi has guided countries to use $7 cost per single dose (inclusive of freight, devices, and procurement and delivery costs). Gavi has not provided the breakdown of such costs.

International delivery, insurance, and procurement fee costs	$0.60 to $0.89	Freight costs will vary primarily based upon vaccine manufacturer location, weight and volume, shipping conditions, and destination. Inclusive of logistics and procurement costs to port-of-entry.
Number of doses/schedules	2	Gavi indicates two dose regimens for budgeting purposes although some potential vaccine candidates may only require one dose.
Sub-total (Total cost per two doses)	$15.20 - $15.79	Using the $7 price for preliminary planning/budgeting purpose.
Vaccine delivery program cost***	$1.6	Estimate from working group on in-country vaccine programme delivery
A. Sub-total .(Total cost per complete immunization)	$18.4 to $18.99	

*Source: COVAX Facility: AMC 92 Q&A Session; Thursday, 10th December and Friday, 11th December 2020 presentation. UPDATED with information from *"WHO, UNICEF & Gavi; Costs of delivering COVID-19 vaccine in 92 AMC countries as of 5th February 2021"*

** The vaccine delivery programme cost of $1.**6** is an estimate made by the COVAX delivery cost working group. It is the estimated unit cost per dose for the outreach strategy. It includes different cost categories needed for vaccine delivery, such as: safety injection devices, PPE for health care workers, cold chain, social mobilization, training, etc.

Conclusion: AstraZeneca and Pfizer/BioNTech vaccine have reached an agreement with COVAX. One dose of AstraZeneca vaccine costs about $4 through COVAX facility but the financial terms of the agreement for Pfizer/BioNTech was not disclosed.

C. What is the estimated price of COVID-19 vaccine obtained directly from the manufacturers? *[NPHCDA reports and plans]*

Title of Article/Author/Year: Here's how the top 3 coronavirus vaccines compare when it comes to efficacy, cost, and more / Isabella Jibilian

Link of Article:

https://africa.businessinsider.com/science/heres-how-the-top-3-coronavirus-vaccines-compare-when-it-comes-to-efficacy-cost-and/dx5yxyk
https://www.biospace.com/article/comparing-covid-19-vaccines-pfizer-biontech-moderna-astrazeneca-oxford-j-and-j-russia-s-sputnik-v/

Objective: To compare how the top 3 coronavirus vaccines compare when it comes to efficacy, cost, distribution, storage, efficacy, and approval.

Result: The Pfizer-BioNTech vaccine costs about $20 per dose, Moderna's costs $25 to $37 per dose while the AstraZeneca's jab costs about $4 per dose (based on agreement with US Government) and $7 per dose through COVAX AMC. [159, 160]

Conclusion: The AstraZeneca vaccine is the cheapest of the three leading COVID-19 vaccines approved for use.

3.9.1 Socio-economic and social impact of disease

A. What is the out-of-pocket expenditure to family and patient? [Systematic Search/WHO website]

Paper 1
Title of Article/Author/Year: Aribisala, A., & Olufolarin, O. Economic Impact of COVID-19 Lock Down on Small Medium Enterprise (Smes) in Lagos State. *International Journal on Integrated Education*, *3*(7), 62-68.
Type of Article: Peer-reviewed
Link of Article: DOI: 10.31149/ijie.v3i7.490
Objective: To assess the economic impact of COVID-19 lockdown on Small Medium Enterprise (Smes) in Lagos state
Result: The COVID-19 pandemic affected borrowers' capacity to service loans which impaired banks' soundness and stability. Also, there were oil demand shocks which reflected in sharp decline in oil price. The lockdown limited people's ability to travel and led to a fall in the demand for aviation fuel and automobile fuel which affected Nigeria's net oil revenue and by extension, Nigeria's foreign reserve. The supply chain industry was severely affected because of Nigeria is heavily dependent on importation. All these affected the national macroeconomy, revision of the national and state's budget and the Nigeria stock market. [161]
Conclusion: The effect of the COVID-19 pandemic on economy has led to some level of economic hardships and employees under SMEs lost their jobs and sources of livelihood. The study concluded that adequate measures are needed from the government to cushion the negative effect of COVID-19 on the economy.

Paper 2
Title of Article/Author/Year: El-Khatib, Z., Otu, A., Neogi, U., & Yaya, S. (2020). The Association between Out-of-Pocket Expenditure and COVID-19 Mortality Globally. *Journal of Epidemiology and Global Health*, *10*(3), 192.
Type of Article: Peer-reviewed
Link of Article: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7509105/

Objective: Estimation and association between out-of-pocket expenditure and COVID-19
Result: The positive association of COVID-19 mortality with out-of-pocket expenditure underscores the challenges of COVID-19 mitigation in resource-limited countries. As with other infectious diseases (e.g. HIV, malaria, Tuberculosis), the COVID-19 is a disease of social inequalities as it exposes the growing gap between the rich and the rest more profoundly than any previous crisis. [162]
Conclusion: COVID-19 management comes at a cost that is associated with the mortality of the disease in literature

Paper 3
Title of Article/Author/Year: Wapner, J. (2020). Covid-19: Medical expenses leave many Americans deep in debt. *bmj*, *370*.
Type of Article: Peer-reviewed
Link of Article: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7509105/
Objective: Cost implications of COVID-19 and catastrophic health expenditure
Result:
It is hard for people to determine the cost of a test before they take it. Of 102 hospitals included in a study by the Kaiser Family Foundation, only 78 had posted their prices for covid-19 diagnostic tests. Among the two largest hospitals in each US state the list price ranged from $20 to $850 (the final, negotiated price may be lower than the list price). Someone without insurance may pay the list price or less: there is no standard approach for uninsured patients. [162]
Conclusion: Lack of standard approach to COVID-19 testing and treatment especially for the uninsured can lead to devastating health expenditure for patients and families

B. What is the evidence for the impacts in terms of economic welfare (e.g., as measured by GDP growth) and economic security (e.g., as measured by number of people living in poverty) of different vaccination targeting approaches across country income groups (high, middle, low)?

Title of Article/Author/Year: COVID-19 vaccination and prioritization strategies in the EU/EEA European Centre for Disease Prevention and Control (ECDC) / 2020
Type of Article: Technical report

Link of Article: https://www.ecdc.europa.eu/sites/default/files/documents/COVID-19-vaccination-and-prioritisation-strategies.pdf

Objective: The objectives of the report are to show how the aim of vaccination strategy should be informed by the characteristics of the vaccines available and; how the prioritization of certain population groups may help achieve the objective of the vaccination strategy. [163]

Result: Target population 1 - Vaccination of people at risk of severe outcomes. This group can be divided into people at risk of severe outcomes due to older age (≥60 ≥70 or ≥80 years) and people at risk of severe outcomes due to preconditions. The risk of COVID-19 hospitalization, ICU admission, and death increase steeply after the age of 60 years. In terms of preventing death, vaccination of the oldest (≥80 years) individuals is the most efficient use of a vaccine. However, given that they have a shorter life expectancy, the most efficient choice in terms of the life-years saved is to vaccinate people ≥ 60 years and over. Targeting individuals with preconditions known to be associated with the increased risk of severe COVID-19 disease may be an efficient approach to reducing hospital admissions, ICU admissions, and mortality. However, singling out all individuals with relevant underlying health conditions may be challenging or controversial.

Target population 2 – Vaccination of health workers. The term "healthcare worker" describes a large and diverse group of people. Prioritization should focus on healthcare workers who are most exposed to SARS-CoV-2, those most at risk of transmitting the disease to vulnerable individuals, and all patient-facing staff in healthcare facilities, whether or not they are clinically trained. The effectiveness and efficiency in terms of life-years gained is dependent on whether the vaccine protects against infection and onward transmission. The higher the degree of protection against infection, the larger the indirect effect, making a healthcare worker vaccination programme increasingly more effective and more efficient.

Target population 3 – Vaccination of adults 18 – 59 years old. It is unlikely that this approach will be part of a COVID-19 strategy in the initial phase when supply is more limited. If the vaccine prevents COVID-19 disease but does not prevent infection, and thereby transmission, it may lead to a reduction in the number of people who are self-isolating. As a result, the level of community transmission may increase, leading to a higher number of confirmed cases, hospital and ICU admissions, and deaths. Vaccination among 18 – 59 may lead to a decrease in deaths in younger adults, but an increase in older adults due to increased background transmission. Vaccinating all adults aged 18-59 years with a vaccine effective in preventing transmission is a potential approach for reducing viral circulation and reaching disease control. However, it is not the most rapid, effective, or ethical way of reducing hospitalizations and deaths in groups at increased medical risk of severe COVID-19.

Target population 4 – Universal vaccination (everyone aged 18 years and over). Universal vaccination could be considered the most equal approach given that enough vaccine doses are available for everyone who can get vaccinated. Unfortunately, this is unlikely to be the case for several months following the introduction of COVID-19 vaccines into the market.

Conclusion: There is evidence in support of prioritization of the target population to receive COVID-19 vaccines. The benefits from vaccination in terms of the number of life-years gained is dependent on the life expectancy of the target population, the effectiveness of the vaccine to prevent infection and disease transmission, the quantity of the vaccines available and the availability of the vaccines to cover the target population and achieve herd immunity. [163]

B. What is the disability-related to productivity lost? [Systematic Search/WHO website]

Title of Article: Impact of the Burden of COVID-19 in Italy: Results of Disability-Adjusted Life Years (DALYs) and Productivity Loss/ Mario Cesare Nurchis, Domenico Pascucci, Martina Sapienza, Leonardo Villani, Floriana D'Ambrosio et al / Published: 13 June 2020
Link: https://www.mdpi.com/742362:
Type of Study: Observational study
Objective of Study: This study aims to assess the socio-economic burden of COVID-19 pandemic in Italy through the estimation of Disability-Adjusted Life Years (DALYs) and productivity loss. The observational study was based on data from official governmental sources collected since the inception of epidemic until 28 April 2020.

Result: The findings of the current study show that productivity loss was largely due to premature mortality. Indeed, the number of deaths is ten times higher in 60–69 working age class than in the 40–49 one. As a consequence, the oldest age class has the highest impact although the number of productive years of life lost is lower than that of the younger age classes. This is translated into a total lost productivity of almost EUR 143 million for the 60–69 age group which represents 0.08% of the national GDP. Even though the lost productivity due to absenteeism is lower than the one due to premature mortality, its impact is significant both at the individual and societal level. In other words, suffering from COVID-19 leads to an average individual loss among working age classes of approximately EUR 915 and a societal loss of roughly EUR 100 million. [164]

Conclusion: The new coronavirus emergency is threatening societies at their core, affecting the lives and livelihoods of millions of people worldwide with devastating impacts on social and economic aspects. Indeed, in Italy in the first quarter of 2020 the excess deaths are 25,354, of which 54% are COVID-19 diagnosed deaths (13,710). The characterization of the Burden of Disease with DALYs and the Productivity Loss metrics is essential to provide support to allow the central government to be accountable for the financing and allocation of resources aimed at the planning of health policies designed to prevent emergency events of such magnitude.

a. **Is there stigma from COVID or its complications in the country? [Systematic Search/WHO website]**

Type of Article: Peer-reviewed

Link of Article: **https://doi.org/10.3390/healthcare8020168**

Objective: The article examined how social determinants of health and stigma are linked to COVID-19 onset, treatment, and outcomes

Result: Stigma in the context of health is the negative association between a person or group of people who share certain characteristics and specific diseases. In COVID-19 cases in Africa, protective measures such as wearing a face mask, being tested, or the belief of coming in contact with an infected person, have led to people being ostracized, harassed, and isolated from others. Also, healthcare workers are not spared from physical exhaustion and poor mental health outcomes as a function of stigma associated with treating COVID-19 cases.

Conclusion: There is no published evidence of stigma from COVID-19 or its complications in Nigeria. However, insights can be gleaned from this global study that report stigma to population taking precautions and frontline healthcare workers treating COVID-19 patients.

3.10 Economic impact on immunization programme

a) **What are the reductions in healthcare costs if COVID is eliminated in the country?**

Paper 1
Title of Article/Author: Projected healthcare resource needs for an effective response to COVID-19 in 73 low-income and middle-income countries: a modelling study

Link: https://www.thelancet.com/journals/langlo/article/PIIS2214-109X(20)30383-1/fulltext

Type of Article: Modelling study

Objective: To assess the impact of COVID-19 elimination on health care costs

Result: The total cost estimate for the COVID-19 response in the status quo scenario was US$52·45 billion over 4 weeks, at $8·60 per capita. For the decreased or increased transmission scenarios, the totals were $33·08 billion and $61·92 billion, respectively. Costs would triple under the status quo and increased transmission scenarios at 12 weeks. The costs of the decreased transmission scenario over 12 weeks was equivalent to the cost of the status quo scenario at 4 weeks. By percentage of the overall cost, case management (54%), maintaining essential services (21%), rapid response and case investigation (14%), and infection prevention and control (9%) were the main cost drivers. [165]

Conclusion: An early and rapid response will not only mitigate future COVID-19 costs, but more importantly, it will be able to mitigate future COVID-19 costs because of a lower number of COVID-19 infections, and a corresponding lower number of deaths and long-term consequences among survivors. A strong pillar 9 response on maintaining essential health services can also potentially decrease the number of deaths indirectly caused by COVID-19. Social and economic disruptions can also be shortened.

Paper 2
Title of Article/Author: Cost-effectiveness of intensive care for hospitalized COVID-19 patients: experience from South Africa

Link: https://bmchealthservres.biomedcentral.com/articles/10.1186/s12913-021-06081-4

Type of Article: Modelling Study

Objective: To assess the cost-effectiveness of intensive care management for admitted COVID-19 patients across the public and private health systems in South Africa

Result: A cost per admission of ZAR 75,127 (N1.9M) was estimated for inpatient management of severe and critical COVID-19 patients in general wards (GWs) as opposed to ZAR 103,030 in GW + ICU (N2.6M). DALYs were 1.48 and 1.10 in GW versus GW + ICU, respectively. The ratio of difference in costs and health outcomes between the two management strategies produced an incremental cost effectiveness ratio of ZAR 73,091 (N1.85M) per DALY averted, a value above the cost-effectiveness threshold of ZAR 38,465 (N973,933).

Conclusion: Results indicated that purchasing ICU capacity from the private sector during COVID-19 surges may not be a cost-effective investment.

a) **What are the potential health gains if COVID-19 vaccines are introduced in the immunization programme?**

Paper 1
Title of Article/Author: Benefits of Getting a COVID-19 Vaccine

Link:https://www.cdc.gov/coronavirus/2019-ncov/vaccines/vaccine-benefits.html?CDC_AA_refVal=https%3A%2F%2Fwww.cdc.gov%2Fcoronavirus%2F2019-ncov%2Fvaccines%2Fabout-vaccines%2Fvaccine-benefits.html

Type of Article: Grey Literature

Objective: To relay the benefits of getting vaccinated with the COVID-19 vaccine

Result: All COVID-19 vaccines that are in development, or that have been developed, are being carefully evaluated in clinical trials and will be authorized or approved only if they make it substantially less likely you'll get COVID-19. Getting COVID-19 may offer some natural protection, known as immunity. Current evidence suggests that reinfection with the virus that causes COVID-19 is uncommon in the 90 days after initial infection. However, experts don't know for sure how long this protection lasts, and the risk of severe illness and death from COVID-19 far outweighs any benefits of natural immunity. COVID-19 vaccination will help protect you by creating an antibody (immune system) response without having to experience sickness.

Conclusion: Experts continue to conduct more studies about the effect of COVID-19 vaccination on severity of illness from COVID-19, as well as its ability to keep people from spreading the virus that causes COVID-19.

Paper 2
Title of Article/Author: The Need for Novel Approaches in Assessing the Value of COVID-19 Vaccines

Link: https://ajph.aphapublications.org/doi/full/10.2105/AJPH.2020.306066

Type of Article: Informative Research

Objective: To assess different factors that will inform the value of COVID-19 vaccines

Result: A societal perspective considers socioeconomic implications beyond clinical outcomes and costs, to capture additional benefits and contextual considerations.[5] These relate to burden of disease (e.g., disease severity and unmet need), equity (distribution of health benefits in the population, e.g., in terms of age, sex, gender, health status, and welfare), innovation (e.g., mechanism of action, spillover effects enabling further product development), indirect costs (e.g., absenteeism, presenteeism, early retirement), public health benefits, financial risk benefits, and fear of contagion benefits; the latter three value aspects are specific to prophylactic interventions such as COVID-19 vaccines, capturing broader societal benefits for the entire population at risk.

Conclusion: Novel approaches are needed to measure the value of COVID-19 vaccines for development, reimbursement, and pricing decisions. Resource allocation in vaccine development should be conducted with WHO Target Product Profiles as guidelines while considering the potential trade-offs among candidates when ideal Target Product Profile levels cannot be reached. For reimbursement and pricing, the value of any COVID-19 vaccine extends beyond health outcomes and costs, encompassing wider societal benefits that ideally need to be evaluated with public preferences to inform access policies and maximum vaccine prices. Only in this way can the evaluation processes capture, rigorously and transparently, what matters most to the relevant experts and societies as a whole.

C) **What is the cost benefit to the country of introducing COVID-19 vaccines into immunization program vs. Preventive measures?**

Paper 1
Title of Article/Author: The Joint Impact of COVID-19 Vaccination and Non-Pharmaceutical Interventions on infections, Hospitalizations, and Mortality; An Agent-Based Simulation

Link: https://www.medrxiv.org/content/10.1101/2020.12.30.20248888v2

Type of Article: Modeling Study

Objective: To simulate the comparative and joint impact of COVID-19 vaccine efficacy and coverage with and without non-pharmaceutical interventions (NPIs) on total infections, hospitalizations, and deaths

Result: In the worst-case vaccination scenario (50% efficacy and 25% coverage), 2,231,134 new SARS-CoV-2 infections occurred with NPIs removed and 799,949 infections with NPIs maintained. In contrast, in the best-case scenario (90% efficacy and 75% coverage), there were 450,575 new infections with NPIs maintained and 527,409 with NPIs removed. When NPIs were removed, lower efficacy (50%) and higher coverage (75%) reduced infection risk by a greater magnitude than higher efficacy (90%) and lower coverage (25%) compared to the worst-case scenario (absolute risk reduction 13% and 8%, respectively). [166]

Conclusion: Simulation results suggest that premature lifting of NPIs while vaccines are distributed may result in substantial increases in infections, hospitalizations, and deaths. Furthermore, as NPIs are removed, higher vaccination coverage with less efficacious vaccines can contribute to a larger reduction in risk of SARS-CoV-2 infection compared to more efficacious vaccines at lower coverage. Findings highlight the need for well-resourced and coordinated efforts to achieve high vaccine coverage and continued adherence to NPIs before many pre-pandemic activities can be resumed.

Paper 2
Title of Article/Author: Impact of Vaccines: Health, Economic, and Social Perspective

Link: https://www.frontiersin.org/articles/10.3389/fmicb.2020.01526/full

Type of Article: Informative Research

Objective: To assess the impact of vaccines on health care costs

Result: Vaccines are estimated to prevent almost six million deaths/year and to save 386 million life years and 96 million disability-adjusted life years (DALYs) globally. **The returns on investment in vaccines, given their increasing provision through Gavi, have been estimated at 12–18, but this is likely an underestimate. The monetary advantages of vaccination programs are important** both to industrialized nations, such as the United States which obtains a net economic benefit of $69 billion, but also **in 94 LMIC where investment of $34 billion, resulted in savings of $586 billion from the direct illness costs.**

Conclusion: The impact of vaccines is broad and far-reaching, though not consistently quantifiable, analyzed or communicated. Traditionally, the perceived benefits of vaccination were to reduce morbidity and mortality from infections, and those remain the drivers for the innovation of new vaccines, in particular in preparation for outbreaks or against infections that afflict the most disadvantaged in society. However, **an increasing appreciation for the economic and social effects of vaccines is being included in the development and assessment of vaccine programs, potentially realizing a greater benefit to society.**

Paper 3
Title of Article/Author: Impact of the Burden of COVID-19 in Italy: Results of Disability-Adjusted Life Years (DALYs) and Productivity Loss

Link: https://www.mdpi.com/1660-4601/17/12/4233

Type of Article: Observational Study

Objective: To assess the socio-economic burden of COVID_19 pandemic in Italy through the estimation of DALYs and productivity loss

Result: On 28 April 2020, the total population at risk of infection was 60,359,546 and the number of SARS-CoV-2 cases were 199,470 while the number of deaths was 25,215. Total years of life lost (YLL) totaled 81,718 in males and 39,096 in females while total years lived with disability (YLD) equaled 302 in males and 333 in females. **The total cost of lost productivity due to absenteeism from work was around EUR 100 million for all the working age classes and the total cost of lost productivity due to COVID-19 premature mortality for all the working age classes was around EUR 300 million and its impact on the national GDP was estimated to be 0.17%**

Conclusion: The suffering from COVID-19 leads to an average individual loss among working age classes of approximately EUR 915 and a societal loss of roughly EUR 100 million. **Burden of Disease with DALYs and the Productivity Loss metrics is essential to provide support to allow the central government to be accountable for the financing and allocation of resources aimed at the planning of health policies** designed to prevent emergency events of such magnitude.

D) What is the cost effectiveness to the country of introducing COVID-19 vaccines into immunization programs vs. Preventive measures?

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Type of Article: Modeling Study

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Conclusion: Simulation results suggest that premature lifting of NPIs while vaccines are distributed may result in substantial increases in infections, hospitalizations, and deaths. Furthermore, as NPIs are removed, higher vaccination coverage with less efficacious vaccines can contribute to a larger reduction in risk of SARS-CoV-2 infection compared to more efficacious vaccines at lower coverage. Findings highlight the need for well-resourced and coordinated efforts to achieve high vaccine coverage and continued adherence to NPIs before many pre-pandemic activities can be resumed.

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Type of Article: Informative Research

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Conclusion: The impact of vaccines is broad and far-reaching, though not consistently quantifiable, analyzed or communicated. Traditionally, the perceived benefits of vaccination were to reduce morbidity and mortality from infections, and those remain the drivers for the innovation of new vaccines, in particular in preparation for outbreaks or against infections that afflict the most disadvantaged in society. However, **an increasing appreciation for the economic and social effects of vaccines is being included in the development and assessment of vaccine programs, potentially realizing a greater benefit to society.**

Paper 3

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Type of Article: Observational Study

Objective: To assess the socio-economic burden of COVID_19 pandemic in Italy through the estimation of DALYs and productivity loss

Result: On 28 April 2020, the total population at risk of infection was 60,359,546 and the number of SARS-CoV-2 cases were 199,470 while the number of deaths was 25,215. Total years of life lost (YLL) totaled 81,718 in males and 39,096 in females while total years lived with disability (YLD) equaled 302 in males and 333 in females. **The total cost of lost productivity due to absenteeism from work was around EUR 100 million for all the working age classes and the total cost of lost productivity due to COVID-19 premature mortality for all the working age classes was around EUR 300 million and its impact on the national GDP was estimated to be 0.17%**

Conclusion: Suffering from COVID-19 leads to an average individual loss among working age classes of approximately EUR 915 and a societal loss of roughly EUR 100 million. **Burden of Disease with DALYs and the Productivity Loss metrics is essential to provide support to allow the central government to be accountable for the financing and allocation of resources aimed at the planning of health policies** designed to prevent emergency events of such magnitude.

Cost implications gap analysis for CCE needed to introduce AstraZeneca, Johnson & Johnson, Moderna and Pfizer vaccines considering current RI and NVIs:

C. **What is the impact on the health budget of targeted (priority groups) versus comprehensive COVID-19 vaccine introduction?**

Title of Article/Author: Guidance on Developing a National Deployment and Vaccination Plan for COVID-19 Vaccines

Link: file:///C:/Users/fpg8/Downloads/WHO-2019-nCoV-Vaccine_deployment-2020.1-eng.pdf

Type of Article: Grey Literature

Objective: Provide guidance to countries to prepare a realistic budget to enable COVID-19 vaccine deployment and vaccination

Result: The NDVP needs to be costed to inform what additional resources are required to implement the plan, with a costing of COVID-19 vaccine-specific interventions and a costing of shared costs with existing health system delivery mechanisms (e.g. PPE for health workers will serve more than immunization activities). It is therefore recommended that the MoH work with the health planning department (in this case, NPHCDA), while costing the deployment plan. This coordination can help to identify existing health system functions (i.e. supply chains, facilities, health workers, data systems, other inputs) that can be leveraged to deploy COVID-19 vaccination.

It is important to evaluate immediate needs and short-term needs that will sustain and position them within longer term investment frameworks. Part of the budget will need to be sustainably funded over the longer term and these budget items need to be identified. For example, when budgeting for training, short-term training can focus on COVID-19 vaccine deployment, which should then be gradually done in conjunction with the national immunization strategy and the health system strategic plan. This coordination can make sure training efforts mutually benefit from system strengthening and system financing.

Conclusion: The budget planning and considerations should align and bear in mind the different phases of vaccine allocation to the country and identified target population, as well as be led by national health experts or NITAGs in wide consultation with stakeholders. The short-term budget should consider the initial allocation that covers the first 3% of the national population (health workers) and the next 17% of the population (older people and those with underlying health conditions). The medium-term budget should consider the incremental shipments to cover beyond the initial 20% (the additional priority populations). The 36-month budgetary horizon is practical as it is compliant with Ministry of Finance (MoF) medium-term budgetary and expenditure exercises.

It is important to plan and budget COVID-19 vaccine introduction while maintaining the budget for ongoing immunization activities (i.e. routine immunization under COVID-19). The estimated cost should include additional costs specific to COVID-19 vaccines, as well as an approximate estimate of ongoing routine immunization and health system costs that will be used for the deployment.

f) **How does pregnancy affect the severity of COVID -19 outcomes?**

Paper 1
Title of Article/Author/Year/Grade: Update: Characteristics of Symptomatic Women of Reproductive Age with Laboratory-Confirmed SARS-CoV-2 Infection by Pregnancy Status - United States, January 22-October 3, 2020 / Zambrano, L. D., S. Ellington, P. Strid, R. R. Galang, T. Oduyebo, V. T. Tong, K. R. Woodworth et al. / 2020

Type of Article: Epidemiological report

Link of Article: https://europepmc.org/article/pmc/pmc7643892

Objective: This report provides updated information about symptomatic women of reproductive age (15-44 years) with laboratory-confirmed infection with SARS-CoV-2, the virus that causes COVID-19. During January 22-October 3, CDC received reports through national COVID-19 case surveillance or through the National Notifiable Diseases Surveillance System (NNDSS) of 1,300,938 women aged 15-44 years with laboratory results indicative of acute infection with SARS-CoV-2. Data on pregnancy status were available for 461,825 (35.5%) women with laboratory-confirmed infection, 409,462 (88.7%) of whom were symptomatic.

Result: Although the absolute risks for severe COVID-19–associated outcomes among women were low, pregnant women were at significantly higher risk for severe outcomes compared with nonpregnant women. This finding might be related to physiologic changes in pregnancy, including increased heart rate and oxygen consumption, decreased lung capacity, a shift away from cell-mediated immunity, and increased risk for thromboembolic disease. [167]

Conclusion: Understanding the risk posed by SARS-CoV-2 infection in pregnant women can inform clinical practice, risk communication, and medical countermeasure allocation. Pregnant women should be informed of their risk for severe COVID-19–associated illness and the warning signs of severe COVID-19. To minimize the risk for acquiring SARS-CoV-2 infection, pregnant women should limit unnecessary interactions with persons who might have been exposed to or are infected with SARS-CoV-2, including those within their household, as much as possible. When going out or interacting with others, pregnant women should wear a mask, social distance, avoid persons who are not wearing a mask, and frequently wash their hands.

Paper 2
Title of Article/Author/Year/Grade: Coronavirus disease 2019 pregnancy outcomes in a racially and ethnically diverse population / Grechukhina, O., V. Greenberg, L. S. Lundsberg, U. Deshmukh, J. Cate, H. S. Lipkind, K. H. Campbell, C. M. Pettker, K. S. Kohari, and U. M. Reddy / 2020

Type of Article: Case Series

Link of Article: https://europepmc.org/articles/pmc7539936/bin/mmc1.docx

Objective: Our study aimed to describe the clinical course of coronavirus disease 2019, effect of comorbidities on disease severity, laboratory trends, and pregnancy outcomes of symptomatic and asymptomatic Severe acute respiratory syndrome coronavirus 2–positive pregnant women.

Result: Of the 1567 tested pregnant and postpartum women between March 3, 2020, and May 11, 2020, 9% (n=141) had a positive Severe acute respiratory syndrome coronavirus 2 result. Hispanic women were overrepresented in the Severe acute respiratory syndrome coronavirus 2–positive group (n=61; 43.8%). In addition, Hispanic ethnicity was associated with a higher rate of moderate and severe diseases than non-Hispanic (18% [11/61] vs 3.8% [3/78], respectively; odds ratio, 5.5; 95% confidence interval, 1.46–20.7; *P*=.01). Of note, 44 women (31.2%) were asymptomatic, 37 of whom (26.2%) were diagnosed on universal screening upon admission for delivery. Moreover, 59% (n=83) were diagnosed before delivery, 36% (n=51) upon presentation for childbirth, and 5% (n=7) after delivery. Severe disease was diagnosed in 6 cases (4.3%), and there was 1 maternal death. Obese women were more likely to develop moderate and severe diseases than nonobese women (16.4% [9/55] vs 3.8% [3/79]; odds ratio, 4.96; 95% confidence interval, 1.28–19.25; *P*=.02). Hypertensive disorders of pregnancy were diagnosed in 22.3% of women (17/77) who delivered after 20 weeks' gestation. Higher levels of C-reactive protein during antepartum coronavirus disease 2019–related admission was more common in women with worse clinical course; however, this association did not reach statistical significance.

Conclusion: Coronavirus disease 2019 in pregnancy may result in severe disease and death. Hispanic women were more likely to receive a positive test result for Severe acute respiratory syndrome 2 than other ethnic groups. Obesity and Hispanic ethnicity represent risk factors for moderate and severe diseases.

Paper 3
Title of Article/Author/Year/Grade: Can immunity during pregnancy influence SARS-CoV-2 infection? – A systematic review / Ana Luísa Areia and Anabela Mota-Pinto / 2020 / 10(10)

Type of Article: Systematic Review

Link of Article: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7566758/

Objective: Ascertain the immunological differences in immune cells of pregnant women that may influence SARS-CoV-2 infection.
Result: The literature search yielded 162 studies, of which 11 were considered appropriate for selection. Only four were used in this systematic review. Our research showed that pregnant women with COVID-19 only differ from other pregnant women in their lower WBC count. The proportion of reduced lymphocyte cases is similar in both groups, as is the case of C-reactive protein levels.

Conclusion: In line with previous coronavirus infections, severe maternal morbidity and perinatal death with COVID-19 infection were more likely to be expected in pregnancy. Our research showed that pregnant women with COVID-19 in terms of immunity only differ from other pregnant women in their lower WBC count.

Paper 4
Title of Article/Author/Year/Grade: Considerations for Obstetric Care during the COVID-19 Pandemic / Dotters-Katz SK, Hughes BL / 2020 / 9(10)

Type of Article: Review

Link of Article: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7356077/

Objective: This review will discuss what is known about the virus as it relates to pregnancy and then consider management considerations based on these data.

Result: After delivery, consideration of mother/infant separation, to minimize risk of transmission to the neonate is recommended by the CDC. 43 The neonate can be cared for by a family member, wearing appropriate PPE. In cases where separation is declined or there are capacity constraints, a physical barrier should be placed in the room, and the bassinet should be more than 6 feet from the mother. 43 The mother should also don a face mask and wash her hands prior to breastfeeding. In cases where separation is selected, pumping and receipt of bottled maternal breast milk is the recommended feeding method in these cases. Pump parts should all be washed with soap and water, and the pump itself disinfected according to manufacturer instructions. When possible, patients with COVID-19 or PUI should have their own designated breast pump during admission.

Conclusion: The highly contagious nature and more severe infection phenotypes than other similar respiratory infections, along with rapid rate of spread have left many health systems overwhelmed with critically ill patients and understaffed due to quarantined and infected health care workers. Though, based on limited data, COVID-19 does not appear to be associated with worse outcomes in pregnant women than in the general population, many challenges still exist for the obstetric care provider. With social distancing as the best protective mechanism, prenatal care spacing and increased telehealth prenatal visits, are recommended to keep patients and providers safe. Infected, but otherwise low-risk pregnant women with mild disease do not need clinical assessment, and may be tested based on local practices.

Paper 5
Title of Article/Author/Year/Grade: A snapshot of the Covid-19 pandemic among pregnant women in France / Kayem, G., V. Alessandrini, E. Azria, J. Blanc, C. Bohec, M. Bornes, F. Bretelle et al. / 2020 / 8(12).

Type of Article: Cohort Study

Link of Article: https://europepmc.org/article/pmc/pmc7270811

Objective: To describe the course over time of Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection in French women from the beginning of the pandemic until mid-April, the risk profile of women with respiratory complications, and short-term pregnancy outcomes.

Result: Active cases of COVID-19 increased exponentially during March 1-31, 2020; the numbers fell during April 1-14, after lockdown was imposed on March 17. The shape of the curve of active critical COVID-19 mirrored that of all active cases. By April 14, among the 617 pregnant women with COVID-19, 93 women (15.1 %; 95 %CI 12.3-18.1) had required oxygen therapy and 35 others (5.7 %; 95 %CI 4.0-7.8) had had a critical form of COVID-19. The severity of the disease was associated with age older than 35 years and obesity, as well as preexisting diabetes, previous preeclampsia, and gestational hypertension or preeclampsia. One woman with critical COVID-19 died (0.2 %; 95 %CI 0-0.9). Among the women who gave birth, rates of preterm birth in women with non-severe, oxygen-requiring, and critical COVID-19 were 13/123 (10.6 %), 14/29 (48.3 %), and 23/29 (79.3 %) before 37 weeks and 3/123 (2.4 %), 4/29 (13.8 %), and 14/29 (48.3 %) before 32 weeks, respectively. One neonate (0.5 %; 95 %CI 0.01-2.9) in the critical group died from prematurity.

Conclusion: COVID-19 can be responsible for significant rates of severe acute, potentially deadly, respiratory distress syndromes. The most vulnerable pregnant women, those with comorbidities, may benefit particularly from prevention measures such as a lockdown.

Paper 6
Title of Article/Author/Year/Grade: What immunological and hormonal protective factors lower the risk of COVID-19 related deaths in pregnant women? / Berhan Y / 2020 / 5(10)

Type of Article: Review

Link of Article: https://europepmc.org/article/pmc/pmc7368414

Objective: This review provides an insight into how the hormonal and immunological changes in pregnancy potentially reduce SARS-CoV-2-mediated inflammatory response.

Result: As exaggerated chemokine directed immunologic response can be diseases conditions in non-pregnant women (autoimmune disease, chronic inflammatory disease, allergic reaction, atherosclerosis, cancer, and the like), unilateral suppressed Th-1 immunity during pregnancy is an advantage for the fetus's intrauterine survival and symptom free life of the mother from the majority of the autoimmune diseases and less severe disease of COVID-19 in most of pregnant women. Therefore, what looks in common for autoimmune disease and COVID-19 is the less risk of severity during pregnancy, probably due to similar immune modulating action of the pregnancy.

Conclusion: The author surmises that pregnant women's risk of having severe COVID-19 very early in gestation (before the Th-2 immunity and placental hormones take control) and in the postpartum period may not be different from the non-pregnant population. Given the limited data on this aspect, and the immunological and hormonal destabilization during postpartum period as transiting from pregnancy to non-pregnancy state, the severity of and mortality due to COVID-19 may be higher than the pregnancy period.

Paper 7
Title of Article/Author/Year/Grade: COVID-19 in pregnancy and the puerperium: A review for emergency physicians / Boushra MN, Koyfman A, Long B / 2020 / 10(10)

Type of Article: Narrative Review

Link of Article: https://europepmc.org/article/pmc/pmc7605788
Objective: This article discusses the clinical manifestations of COVID-19 in pregnant patients, the effects of pregnancy on the course of COVID-19 disease, and the impact of COVID-19 on pregnancy outcomes.

Result: The physiological and mechanical changes associated with pregnancy increase maternal susceptibility to infections and complicate intubation and mechanical ventilation. The most common symptoms of COVID-19 in pregnant patients are cough and fever, although many infected individuals are asymptomatic. The majority of pregnant women diagnosed with COVID-19 disease have a mild course of illness and will recover without needing to deliver, but the risks of critical illness and need for mechanical ventilation are increased compared to the general population. Risk factors for death and severe disease include obesity, diabetes, and maternal age > 40 years. Women in their third trimester have the highest risk for critical illness, intensive care unit admission, and need for mechanical ventilation. Adverse fetal outcomes of maternal COVID-19 infection include increased risk of miscarriage, prematurity, and fetal growth restriction. Vertical transmission of SARS-CoV-2 is possible but has not been conclusively proven.

Conclusion: COVID-19 is a potentially deadly infection, but data are limited concerning the pregnant population. Pregnant patients appear to present similarly to the general population, with fever and cough being the most reported symptoms in studies. Knowledge of these presentations and outcomes can assist clinicians caring for these patients.

Paper 8
Title of Article/Author/Year/Grade: Clinical course of novel COVID-19 infection in pregnant women / Shmakov, R. G., A. Prikhodko, E. Polushkina, E. Shmakova, A. Pyregov, V. Bychenko, T. V. Priputnevich et al. / 2020 / 8(12).

Type of Article: Cohort Study.

Link of Article: https://europepmc.org/article/pmc/pmc7711745

Objective: Evaluation of clinical course of COVID-19 during pregnancy and maternal and perinatal outcomes of this pregnancy.

Result: 15 (22.7%) women were asymptomatic, 25 (38%) had mild disease, while moderate and severe forms were detected in 20 (30.2%) and 6 (9.1%) cases, respectively. Additional oxygenation was required in 6 (9%) cases: 4 (6%) received CPAP therapy and 2 (3%) - mechanical ventilation. Main clinical symptoms were cough (51.5%), anosmia (34.9%), and hyperthermia (33.3%). Laboratory changes included increased levels of lactate dehydrogenase (LDH), creatinine, d-dimer, and C-reactive protein (CRP), anemia, and leukopenia. All pregnant women received low molecular weight heparin and interferon alfa-2b according to the National clinical recommendations. Antimicrobial drugs included Amoxicillin/Clavulanic acid (46%) and macrolides (28%) or carbapenems in severe cases of disease. Spontaneous abortion was reported in 6.1% of cases. Eight preterm (19%) and 34 term deliveries (81%) occurred. The mean weight of neonates was (3283 ± 477) g, 1- and 5-min Apgar score was (7.8 ± 0.6) and (8.7 ± 0.5), respectively. No cases of neonatal COVID-19 infection were reported.

Conclusion: Mostly, the manifestations of COVID-19 were mild. However, 9% of cases were severe, and could contribute to preterm delivery or maternal morbidity. Main predictors of severe COVID-19 course in pregnant women were a decrease in the levels of erythrocytes and lymphocytes and increase in the levels of alanine aminotransferase and CRP. Elimination of the virus in pregnant women required more time due to altered immunity. No evidence of vertical transmission during pregnancy and delivery was found. However, the possibility of this cannot be excluded.
Paper 9
Title of Article/Author/Year/Grade: Immunity and coagulation and fibrinolytic processes may reduce the risk of severe illness in pregnant women with coronavirus disease 2019 / Zhong, Y., Y. Cao, X. Zhong, Z. Peng, S. Jiang, T. Tang, H. Chen et al. / 2020 / 7(12)

Type of Article: Cohort Study

Link of Article: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7578241/
Objective: This study aimed to determine the key factors associated with the deterioration of patients with coronavirus disease 2019 and the differentiating clinical characteristics of pregnant women with coronavirus disease 2019 to interfere with the progression of coronavirus disease 2019.

Result: For the total patient population, the lymphocyte, $CD3^+$, $CD4^+$, $CD8^+$, $CD19^+$, and $CD16^+CD56^+$ cell counts were significantly lower, and white blood cell count, neutrophil count, and neutrophil-to-lymphocyte ratio were higher in those with severe or critical illness than those with mild or moderate illness ($P<.001$). The plasma levels of interleukin-6, interleukin-10, and interleukin-6-to-interleukin-10 ratio were significantly increased in patients with critical illness compared with patients with mild, moderate, and severe illnesses (P<.001). The above immunologic coclusters achieved an area under the receiver operating characteristic curve of 0.801 (95% confidence interval, 0.764-0.838), and its combined model with the coagulation and fibrinolysis indices (prothrombin time, D-dimer) achieved an area under the receiver operating characteristic curve of 0.815 (95% confidence interval, 0.779-0.851) using the random forest regression model to predict severe or critical illness. For pregnant women with coronavirus disease 2019, none had preexisting diseases. Compared with nonpregnant women with mild or moderate coronavirus disease 2019, pregnant women with coronavirus disease 2019 displayed increased white blood cell count, neutrophil count, neutrophil-to-lymphocyte ratio, and levels of D-dimer and fibrinogen, along with decreased lymphocyte and interleukin-4 levels (P<.05). Although they presented similar changes of immunologic markers of lymphocyte; white blood cell count; neutrophil-to-lymphocyte ratio; $CD3^+$, $CD4^+$, $CD8^+$, and $CD16^+CD56^+$ cell counts; and interleukin-6-to-interleukin-10 ratio, compared with nonpregnant women with severe or critical coronavirus disease 2019, none of the pregnant women with coronavirus disease 2019 deteriorated into severe or critical illness. There was no significant difference in white blood cell count, lymphocyte count, neutrophil count, neutrophil-to-lymphocyte ratio, immunologic markers, or coagulation and fibrinolysis markers between pregnant women with coronavirus disease 2019 and pregnant women without coronavirus disease 2019. As for the discrepancy of pathophysiological features between pregnant women with coronavirus disease 2019 and nonpregnant women with severe or critical coronavirus disease 2019, the immunologic markers achieved an area under the receiver operating characteristic curve of 0.875 (95% confidence interval, 0.773-0.977), and its combined model with coagulation and fibrinolysis indices achieved an area under the receiver operating characteristic curve of 0.931 (95% confidence interval, 0.850-1.000).

Conclusion: Immune dysregulation was identified as a crucial feature of patients with coronavirus disease 2019, which developed severe or critical illness, and pregnant women with coronavirus disease 2019 presented with similar immune responses but rarer incidences of severe or critical illness. Immune dysregulation is related to the risks of deterioration into severe or critical illness. The specific coagulation and fibrinolysis systems of pregnancy may reduce the risk of pregnant women with coronavirus disease 2019 without preexisting disease from developing severe illness.

Paper 10
Title of Article/Author/Year/Grade: The clinical course of COVID in pregnancy / Sbaa Syeda,∗ Caitlin Baptiste, Noelle Breslin, Cynthia Gyamfi-Bannerman, and Russell Miller / 2020 / 9(10)
Type of Article: Literature Review

Link of Article: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7373055/

Objective: The objective of this study is to review the literature and describe clinical presentations among pregnant women afflicted with COVID-19.

Result: COVID-19 infection results in both pulmonary and extra-pulmonary manifestations. While the multi-organ involvement of this disease entity has been cited extensively in the literature, there is limited data confirming these findings in the obstetric population. Herein, we reviewed the presentation of this disease per organ system, as well as special considerations that must be undertaken among pregnant patients. Future studies assessing specific findings in the obstetric population will allow clinicians to gain a better understanding of the progression of this disease and develop guidelines for system-based treatment as this pandemic continues to unfold. [168]

Paper 11
Title of Article/Author/Year/Grade: Comprehensive analysis of COVID-19 during pregnancy / Moore, K., and M. Suthar / 2020 / 10(10)

Type of Article: Literature Review

Link of Article: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7759124/

Objective: We highlight recent studies exploring the role of the maternal antibody response to SARS-CoV-2 during pregnancy and the passive transfer of maternal antibodies from mothers with COVID-19 to fetus.

Result: Herein, we provided an overview of the knowledge currently available about COVID-19 during pregnancy. Evidence of SARS-CoV-2 has been detected in the placenta of COVID-19 positive mothers, yet experimental studies are needed to determine if this is indicative of infectious virus capable of replication in the placenta. Additionally, larger studies characterizing neonates born from mothers with COVID-19 would provide more clarity on the frequency of SARS-CoV-2 vertical transmission. SARS-CoV-2 specific IgG has been detected in neonates born to mothers with COVID-19. We offered suggestions for future studies involving the impact of antibodies in COVID-19 pregnancies, such as characterization of maternal antibodies transplacentally transferred and investigation into a possible role of antibody mediated vertical transmission.

Paper 12
Title of Article/Author/Year/Grade: A critical review of the pathophysiology of thrombotic complications and clinical practice recommendations for thromboprophylaxis in pregnant patients with COVID-19 / D'Souza, R., I. Malhamé, L. Teshler, G. Acharya, B. J. Hunt, and C. McLintock / 2020 / 7(10)

Type of Article: Literature Review

Link of Article: https://europepmc.org/article/med/32678949

Objective: There is currently no evidence to recommend the use of intermediate or therapeutic doses of LMWH in thromboprophylaxis, which may increase bleeding risk without reducing thrombotic risk in pregnant patients with COVID-19. Likewise, there is no evidence to comment on the role of low-dose aspirin in thromboprophylaxis or of anti-cytokine and antiviral agents in preventing immunothrombosis. These unanswered questions are being studied within the context of clinical trials.

Result: Although clinical trials aimed at evaluating the optimal type, dose and frequency for antithrombotic therapy among patients with COVID-19 are ongoing worldwide, pregnant women have been excluded from several of these trials. The lack of information on therapeutic agents in pregnancy resulting from restricting the access of pregnant women to clinical trials may lead to a number of untoward outcomes, including the administration of unproven therapies, the denial or delay in administration of potentially effective medications, and over- or undertreatment due to lack of information on pregnancy-specific pharmacokinetics. This potentially exposes women to harm and highlights the importance of gathering data on the safety and effectiveness of antithrombotic therapies for COVID-19 in pregnancy

3.11 Health policy and programmatic issues

3.11.1 Feasibility

a. **What is the evidence that this intervention is accessible to priority groups for vaccination (e.g. health workers, older adults, individuals with co-morbidities, etc.) and to providers?**

Paper 1

Title of Article/Authors/Year/Grading: Global, regional, and national estimates of target population sizes for covid-19 vaccination: descriptive study/Wei Wang et al/2020/11
Type of Article: Descriptive Study
Link to the Article: https://doi.org/10.1136/bmj.m4704
Objective: To provide global, regional, and national estimates of target population sizes for coronavirus disease 2019 (covid-19) vaccination to inform country specific immunization strategies on a global scale.
Results: Target population sizes for covid-19 vaccination vary markedly by vaccination goal and geographical region. Differences in demographic structure, presence of underlying conditions, and number of essential workers lead to highly variable estimates of target populations at regional and country levels. In particular, Europe has the highest share of essential workers (63.0 million, 8.9%) and people with underlying conditions (265.9 million, 37.4%); these two categories are essential in maintaining societal functions and reducing severe covid-19, respectively. In contrast, South East Asia has the highest share of healthy adults (777.5 million, 58.9%), a key target for reducing community transmission. Vaccine hesitancy will probably impact future covid-19 vaccination programmes; based on a literature review, 68.4% (95% confidence interval 64.2% to 72.6%) of the global population is willing to receive covid-19 vaccination. Therefore, the adult population willing to be vaccinated is estimated at 3.7 billion (95% confidence interval 3.2 to 4.1 billion). [88]
Conclusion: The distribution of target groups at country and regional levels highlights the importance of designing an equitable and efficient plan for vaccine prioritization and allocation. Each country should evaluate different strategies and allocation schemes based on local epidemiology, underlying population health, projections of available vaccine doses, and preference for vaccination strategies that favor direct or indirect benefits.

Paper 2

Title of Article/Author/Year/Grade: Multivalue ethical framework for fair global allocation of a COVID-19 vaccine/Yangz Liu, Sanjan Salwi and Brian C Drolet/2020/
Type of Article: Descriptive Study
Link of the Article: https://www.ncbi.nlm.nih.gov/pubmed/32532826
Objective: To analyze four allocation paradigms: ability to develop or purchase; reciprocity; ability to implement; and distributive justice, and synthesizes their ethical considerations to develop an allocation model to fit the COVID-19 pandemic.
Result: Given the inevitable demand for the COVID-19 vaccine and the high burden of disease already placed on many countries, there is a need for an equitable global framework for vaccine distribution.2 Without advanced planning and thoughtful execution, pre-existing health and socioeconomic disparities will only be exacerbated by this pandemic. It seems inevitable that high-income countries

will obtain and use the bulk of vaccines, while lower income countries are in far greater need. Planning for distribution must begin as the vaccine is being developed so that a paradigm is ready when distribution begins. Otherwise, the framework loses efficacy as national interests for developed states favor perpetuation of existing international disparities as seen in the influenza pandemic.10 Although it is difficult to correct for already existing international disparities in healthcare resources, a vaccine for COVID-19 does not yet exist to fall into this trap. Although no single ethical principle can guide vaccine allocation, some consideration must be made for utilitarian considerations, which prioritize saving the most lives or life years.9 13 14 Vaccine deployment is inherently a resource-intensive endeavor that requires specialized transportation, trained personnel for administration and an intact public health infrastructure for identifying need and surveillance.15 Thus, to maximize vaccine benefits and reduce waste due to improper utilization, allocation frameworks should consider a country's ability to vaccinate.

However, this approach will bias against countries that do not have the resources and infrastructure for successful vaccine deployment. Therefore, before allocating based on this principle, all reasonable efforts should be taken to redistribute human and supply chain resources to alleviate these inherent inequalities. Otherwise, disparities are perpetuated (and amplified) by a utilitarian approach to allocation, as low-income countries with poor health outcomes have less access to preventative treatment. After the acute pandemic response, interpandemic years should focus on building up resources in low-income countries.

Conclusion: Given the inevitable demand for the COVID-19 vaccine and the high burden of disease already placed on many countries, there is a need for an equitable global framework for vaccine distribution.2 Without advanced planning and thoughtful execution, pre-existing health and socioeconomic disparities will only be exacerbated by this pandemic. It seems inevitable that high-income countries will obtain and use the bulk of vaccines, while lower income countries are in far greater need. Planning for distribution must begin as the vaccine is being developed so that a paradigm is ready when distribution begins. Otherwise, the framework loses efficacy as national interests for developed states favour perpetuation of existing international disparities as seen in the influenza pandemic.10 Although it is difficult to correct for already existing international disparities in healthcare resources, a vaccine for COVID-19 does not yet exist to fall into this trap.

3.12 Vaccine registration and regulation

A. What is the NRA (e.g. NAFDAC) requirements for registering COVID-19 vaccines in the country for use?

Title of Article/Author/Year: Guidance on Regulatory Preparedness for Licensing or Access to COVID-19 Vaccines / National Agency for Food & Drug Administration & Control (NAFDAC) / 2020
Type of Article: Grey Literature
Link of Article:
https://www.nafdac.gov.ng/wp-content/uploads/Files/Resources/Guidelines/DRUG_GUIDELINES/Guidance-document-on-Covid-19-vaccine-preparedness-finalized.pdf

Objective: This guidance aimed to prepare and put in place a regulatory process for COVID-19 vaccines in advance of vaccines that are being developed for that purpose.
Result: Depending on the pandemic phase and the source of the vaccine, the following regulatory approach could be followed:

Full review – a standard review process to authorize a product licensure that can include a fast-track review. This would require evaluation of the documentation of product quality and of the results of nonclinical and clinical studies to demonstrate safety and efficacy in the target population. During the post-pandemic phase, NAFDAC may conduct a full COVID-19 vaccine dossier review to ensure familiarity with the characteristics of such vaccines.
Fast-track review of basic documentation – a fast-track review process based on basic available information for emergency authorization. Available documents to review include evidence of quality (certificate of analysis or lot release) and good manufacturing practices (GMP) compliance (GMP certificate); CTD Module-2 quality, nonclinical and clinical overviews.
Reliance – a process to review the marketing authorization report/ decision issued by an NRA with WHO ML 3 and above or WHO prequalification. Available documentation required includes a certificate of responsible NRA's marketing authorization decision. Assessment reports of the responsible NRA.
Recognition – recognition of the marketing authorization decision of another NRA or WHO prequalification without further evaluation. Available documentation required includes the certificate of the responsible NRA's marketing authorization decision or WHO prequalification assessment report.

Conclusion: NAFDAC has a published guidelines and approach for the licensing the COVID-19 use in Nigeria. [169]

REGULATORY REVIEW PATHWAYS FOR PROCESSING COVID-19 VACCINES WITH REQUIRED DOCUMENTS, AND TIMELINES

REVIEW PATHWAY	ELIGIBLE VACCINE SOURCE	REQUIRED DOCUMENTS		PROCESS STEPS & TIMELINE (working days)					TIMELINE FOR COMPLETION (days)
				STEP 1 Screening of Application Documents	STEP 3 Issuance of Import permit	STEP 3 Dossier/ AR Review / Laboratory Analysis	STEP 4 Deliberations by NACVB	STEP 5 Issuance of MA or one-off Import permit	
Full review	Not previously registered	Module 1-5		2	2	110	4	2	120
Fast-track review of basic documentation	Other NRAs	-Module 1 -Assessment reports of the responsible NRA -Evidence of quality (certificate of analysis or lot release) and GMP compliance (GMP certificate) -CTD Module-2 quality, nonclinical and clinical overviews		2	2	30	2	2	38
Reliance	NRA-ML3 & above	*Govt Procurement / UNA supply* -Certificate of the responsible NRA's marketing authorization decision OR WHO prequalification/EUL assessment report -Proposed Product label	*Application for MA by Local Agent* -Module 1 -Certificate of the responsible NRA's marketing authorization decision or WHO prequalification/EUL assessment report	2	N/A	10	2	2	16
Recognition	WHO-prequalified /EUL	Same as obtainable under Reliance		2	N/A	10	2	2	16

3.13 Impact on Resources

a. **Is there adequate human, technical and financial resources for distribution of COVID-19 vaccine if introduced into the immunization?**

Source:

1. National Covid-19 Deployment and Vaccination Plan, Nigeria
    - NPHCDA Document Year: 2021
2. Nigeria Health Workforce Profile as Of December 2012
    - Federal Ministry of health document Year 2013

Result: Yes, Nigeria has adequate Human, technical and financial resources for the distribution of COVID-19 vaccine if introduced into the immunization programme.

Human resource estimates show that Nigeria has over 60,000 qualified health workforces with adequate technical capacity already providing routine immunization. In addition, Technical workforce exist at National, zonal, State and Local Government that continue to coordinate and provide managerial support for routine immunization and the introduction of new vaccines. The same structures and personnel have supported various new vaccine introduction (MenA, measles 2nd dose, and campaigns (Polio, yellow fever, measles and MenA campaigns) in the last two to three years. The National Covid-19 Deployment and Vaccination Plan, Nigeria 2021 do not indicate a gap in human resource capacity gap and in the event of a gap provides a pathway of filling this gap. There are sufficient immunization supply chain personnel having experience with dealing with the shipments that come with dry ice at both national and sub-national levels. The Nigeria Health Workforce Profile as Of December 2012 clearly shows that there are adequate number of health workers licensed to give injections and can be rapidly deployed with minimal orientation to provide support if required.

Nigeria has adequate capacity for storage and distribution of the COVID 19 vaccines through its cold chain infrastructure at National, States, LGAs and facilities. Distribution will follow established contractual arrangements. Gaps identified in the Q3 Cold chain Equipment inventory update have been addressed and the country has the volumetric capacity to accommodate the Cold chain space required for vaccines to be stored between -25°C to + 8°C. There is Ultra Cold Chain (UCC)capacity of 2,080 litres from the newly installed freezers at national level to store the expected 100,000 doses (about 500litres) of the COVID-19 mRNA vaccine. Nigeria will vaccinate 70% of its population, 40% in 2021 and 30% in 2022. The COVAX facility will provide 20% of the vaccines while the country has budgeted funds to purchase the remaining 50% including all operational costs.

3.13.1 Ability to evaluate

a. **What is the evidence of a reliable and sustainable surveillance system for COVID-19 in the country?**

Title of Document: Surveillance Outbreak Response Management & Analysis System (SORMAS)
Type of Document: Nigeria Centre for Disease Control (NCDC)

Result: The Nigeria Centre for Disease Control coordinates the surveillance of infectious diseases in Nigeria, including for COVID-19. This is done using the Surveillance Outbreak Response Management & Analysis System (SORMAS). SORMAS is an open-source two-tier management system for case monitoring (surveillance), laboratory data management, contact tracing and disease detection to prevent and manage outbreaks that may occur.
The Government of Nigeria adopted SORMAS as the national tool for digital case-based surveillance in 2016. Since then, it has been used for reporting of epidemic prone diseases including cholera, Lassa fever, monkeypox among others.

Before the COVID-19 pandemic, SORMAS had already been deployed in 22 states (448 local government areas (LGAs)) in Nigeria. Given the need for an integrated tool to be used in all states in reporting COVID-19 data, SORMAS has been deployed and is being used in all 36 states and the Federal Capital Territory, as well as 774 LGAs. The data collected through SORMAS is hosted at the NCDC Headquarters in a secure server.

Through data from SORMAS, NCDC has published daily and weekly situation reports on COVID-19, provided data for modeling and decision making by the Presidential Task Force on COVID-19 among other outputs. Furthermore, SORMAS is used for data entry by personnel at various including health facilities in communities, testing laboratories, treatment centres, State Ministry of Health and NCDC.
To ensure effective use of SORMAS, NCDC has deployed State Surveillance Officers who work with the State Epidemiologist in every state. The support provided by these officers include quality assurance of data, training of data staff at state and LGA-level among others. The NCDC also provides supplementary data bundles to states for the effective use of SORMAS.

The SORMAS Team at NCDC includes epidemiologists, data officers and IT developers, who can quickly introduce iterations for the tool based on the country's needs. This can be adapted for vaccine pharmacovigilance and would ensure integration with the existing national surveillance system for COVID-19 and other infectious diseases.

b. Does the immunization program have the capacity to conduct AEFI monitoring of COVID-19 vaccines administered to the target population?

Title of Article/Author/Year: COVID-19 Vaccines: Safety Surveillance Manual / WHO / 2020
Type of Article: Technical report
Link of Article:
https://www.who.int/vaccine_safety/committee/Module_Establishing_surveillance_systems.pdf?ua=1
Objective: This is the module to establish surveillance systems in countries using COVID-19 vaccines.

Result: To prepare for the COVID-19 vaccine introduction, countries are required to establish AEFI surveillance systems to address several key challenges specific to the COVID-19 pandemic. COVID-19 immunization programmes will likely focus on adult populations initially. Therefore, it will be important to ensure that the surveillance systems are capable of capturing AEFIs in adults. Surveillance systems will need to be able to accommodate the large numbers of AEFIs/AESI reports expected because of the large proportion of the population who will be validated. All countries should define specific protocols for investigating deaths following COVID-19 vaccination.

Conclusion: There is a dearth of data on the capacity of the immunization program to conduct AEFI for COVID-19. However, presented above are excerpts from the WHO safety surveillance manual on COVID-19.

A. Is the immunization program able to adequately measure coverage and utilization for COVID-19 vaccines administered to the target population?

Title of Article/Author/Year: WHO and UNICEF estimates of national infant immunization coverage: methods and processes / Anthony Burton / 2009
Type of Article: Narrative review articles
Link of Article: https://www.who.int/bulletin/volumes/87/7/08-053819/en/
Objective: This article described the WHO and UNICEF's methods and processes of estimating national infant immunization coverage.
Result: The key data sources identified were administrative data and household surveys. Administrative data based on reports from service providers report the number of vaccinations administered during a given period to the LGA who review and report to the next level of data management. Meanwhile, surveys are common sources of immunization coverage data. The three main household survey sources are the Expanded Programme on Immunization (EPI) cluster survey, the UNICEF Multiple Indicators Cluster Survey (MICS), and the Demographic Health Survey (DHS). Both administrative and survey data sources have merits and demerits. While administrative data provide more timely information and are useful for places where surveys may not be practical, survey data allow for estimating immunization coverage even if the size of the target population is unknown and they also include vaccinations given by the private sector. [170]
Conclusion: The immunization program in Nigeria has mechanisms in place for both administrative and survey data that the COVID-19 vaccine supplementary immunization activity can leverage to measure the vaccine's coverage and utilization.

3.13.2 Acceptability

A) What is the evidence that the COVID-19 vaccine is acceptable to stakeholders (ethically, financially, programmatically, etc.)? [Systematic Search/WHO website]

Paper 1
Link: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7605960/

Type of study - Cross-sectional study.
Title/ Author/ Grading: Acceptability of Vaccination Against COVID-19 Among Healthcare Workers in the Democratic Republic of the Congo; Michel Kabamba Nzaji, Leon Kabamba Ngombe, and Elisabeth Mukamba Musenga (2020) 8/10
Result - In the study, 613 HCWs participated and completed the questionnaire, including 312 (50.9%) men and .301 (49.1%) women, most of them were over 25 years. All of the healthcare workers were very much aware of the COVID-19 virus and its impact on human lives. After questionnaires were administered to the HCWs and the survey was analyzed, only 27.7% of HCWs said that they would get vaccinated if the COVID-19 vaccine was available.
In this survey, only 28% of the participants said that they would get a vaccine against COVID-19, if and when one becomes available. The willingness of Congolese healthcare workers to be vaccinated against COVID-19 virus is very low when compared with a comparable study done in

France which found that 77.6% of participants "probably agreed" to get vaccinated against COVID-19. Healthcare workers may have developed vaccine hesitancy due to misinformation's on new media which include rumors on black race extermination through vaccination. This can influence their decision to get vaccinated and promote the vaccine to their patients.

Older HCWs accepted to get vaccinated. This may be due to the notion that older adults and people with serious comorbidities are particularly vulnerable to worse outcomes from COVID-19 can create considerable fear amongst the elderly.

Healthcare worker recommendations play an influential role in their patients' vaccination behavior. They serve as an important source of information for the general public and their consultation can also be a key factor in patients' decision to be vaccinated or not. [171]

Conclusion: To increase vaccine acceptance against COVID-19, it is pertinent that there is increased education on the benefits of the vaccine among HCWs. This is crucial because health professionals' attitudes about vaccines are an important determinant of demand generation and increasing vaccine uptake via recommendation to patients by them.

For acceptability of vaccination against COVID-19 among others education among HCWs is crucial because health professionals' attitudes about vaccines are an important determinant of their own vaccine uptake and their likelihood of recommending the vaccine to their patients. Additionally, more men agreed to become vaccinated than women.

Paper 2

Link: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7498238/?report=reader

Study type – Cross-sectional study

Title/ Author/ Grading - Intention to participate in a COVID-19 vaccine clinical trial and to get vaccinated against COVID-19 in France during the pandemic; Maëlle Detoc, Sébastien Bruel, [...], and Amandine Gagneux-Brunon (2020) 8/10

Result: During the study period, 3656 people opened the weblinks for the online survey, 3259 (89.1%) people answered the online questionnaire. Demographic characteristics indicated that women accounted for 67.4% of the respondents. Seven hundred and eighty-seven (24.1%) respondents reported a chronic medical condition. Vaccine hesitancy was observed in 1150 respondents (35.3% 95% CI 33.6–36.9%). Two thousand four hundred-thirty-four (74.7% 95% CI 73.2–76.2%) respondents had fears about COVID-19; 2124 (65.2% 95% CI 63.6–66.8%) respondents considered themselves at risk for COVID-19 vaccine.

2512 participants (77.6%, 95% CI 76.2–79.0%) will certainly or probably be willing to get vaccinated against COVID-19. Among the 1063 men, 883 (83.1% 95% CI 80.8–85.3%) are COVID-19 vaccine acceptors, 1629 women among the 2196 respondents (74.2% 95% CI 72.3–76.0%) are COVID-19 vaccine acceptors ($p < 0.005$). The proportion of vaccine hesitant respondents who would probably be willing to get vaccinated against COVID-19 vaccine were 61.9% (95% CI 59.1–64.7%) during the current pandemics. The proportion of healthcare workers willing to get vaccinated was 81.5%, and this proportion was 73.7% in non-healthcare workers.

Conclusion: From the online survey, we observed that nearly three quarters of the respondents would accept COVID—19 vaccine. It was also observed that women accounted for the vast majority of our study respondents, indicating that in real settings, COVID-19 vaccine acceptance could be greater amongst women. Older individuals are more prone to get vaccinated in both studies, this is probably due to a greater perceived risk of getting infected and developing a severe disease in older people.

Paper 3

Link: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7573523/

Title/ Author: A global survey of potential acceptance of a COVID-19 vaccine, Lazarus et.al.,2020
Type of study: Cross sectional study
Result: Participants of the online survey were from 19 countries and 13,426 individuals were randomly selected and most of them have been classified as countries with COVID-19 burden. To ensure regional representation, we selected the next most affected country from regions not represented on the top 35 list: Brazil, Canada, China, Ecuador, France, Germany, India, Italy, Mexico, Nigeria, Poland, Russia, Singapore, South Africa, South Korea, Spain, Sweden, the United Kingdom and the United States.

From these numbers, 71.5% responded that they would take a vaccine if it were proven safe and effective, and 48.1% said that they would get vaccinated if their employer recommended. Countries where acceptance exceeded 80% tended to be Asian nations with strong trust in central governments. A relatively high tendency toward acceptance in middle-income countries, such as Brazil, India and South Africa, was also observed. Countries with low trust in their government such as Russia had low acceptance rate. 65% of Nigerians accepted to take the COVID-19 vaccine, one's its available.

Older people were more likely to report that they would take a vaccine, whereas respondents 25–54 and 55–64 years of age were more likely to accept an employer's vaccine recommendation. Men in this study were less likely than women to accept vaccines in general or their employer's recommendation to get vaccinated; however, this association was not strong. Those with a higher income were most likely to accept a vaccine than those with a lower income.

However, high heterogeneity was observed in responses between countries. Reporting willingness to take the vaccine might not be a good predictor of acceptance as vaccine decisions are multifactorial and can change over time.

Conclusions: Future vaccine communication strategies should consider the level of health, scientific and general literacy in subpopulations, identify locally trusted sources of information and go beyond simply pronouncing that vaccines are safe and effective. Strategies to build vaccine literacy and acceptance should directly address community-specific concerns or misconceptions, address historic issues breeding distrust and be sensitive to religious or philosophical beliefs. [172]

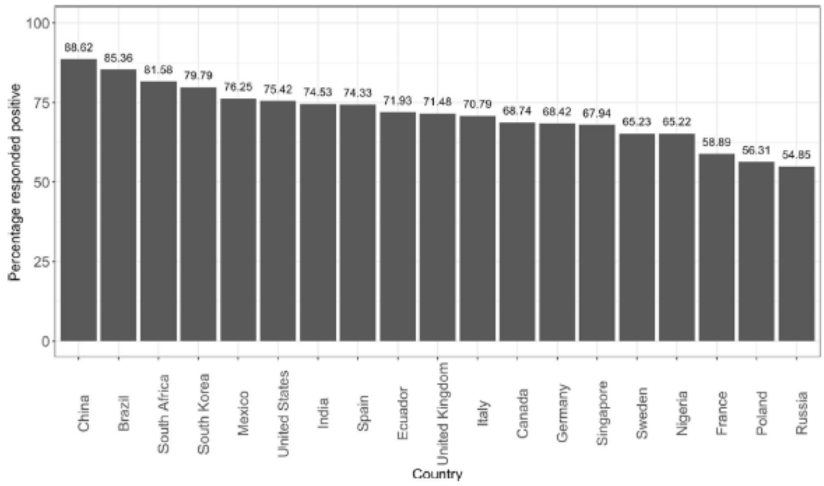


Figure 1 shows the result of participants from different countries providing responses to the question "If a COVID-19 vaccine is available, safe and effective, I will take it"

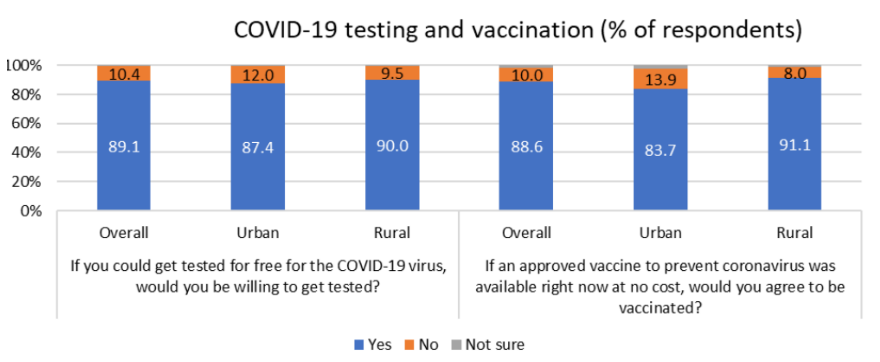
Paper 4

Link: http://documents1.worldbank.org/curated/en/816351608277794350/pdf/Impact-of-COVID-19-on-Nigerian-Households-Sixth-Round-Results.pdf

Title/ Author : The National Bureau of Statistics: World Bank report, 2020

Objective - The National Bureau of Statistics (NBS), with support from the World Bank, launched the COVID-19 National Longitudinal Phone Survey (NLPS); a monthly survey of a nationally representative sample of 1,950 households to monitor the socioeconomic impact of the pandemic and other shocks. The first round (baseline) of the survey was conducted in April/May 2020, during which a federally mandated lockdown was in full effect. The government began lifting restrictions in June and by the time the sixth round was conducted between October 9-24, 2020, there were minimal restrictions on movement within the country.

Result: The vast majority of respondents reported that they were willing to get tested for and vaccinated against COVID-19, if such services were free. Almost 90% of respondents answered "Yes" when asked "If you could get tested for free for the COVID-19 virus, would you be willing to get tested?". Additionally, 89% of respondents answered "Yes" when asked "If an approved vaccine to prevent coronavirus was available right now at no cost, would you agree to be vaccinated?". Respondents in urban areas are more skeptical towards a possible vaccine against the COVID-19 virus: 14% of urban respondents would not agree to be vaccinated (even at no cost) compared to 8% in rural areas. Out of those who would not agree to be vaccinated, 32% indicate that the main reason is because they do not think it would be safe, and 31% say they do not consider them-selves to be sufficiently at risk of contracting COVID-19.



Paper 5
Title/Author/Year/Grading: Acceptability of a COVID-19 vaccine among adults in the United States: How many people would get vaccinated? /2020/Paul L. Reiter et al/10

Type of Article: Descriptive study

Link of Article: https://dx.doi.org/10.1016%2Fj.

Objective: Coronavirus disease 2019 (COVID-19) was declared a pandemic in March 2020. Several prophylactic vaccines against COVID-19 are currently in development, yet little is known about people's acceptability of a COVID-19 vaccine.
Result: Overall, 69% of participants were willing to get a COVID-19 vaccine. Participants were more likely to be willing to get vaccinated if they thought their healthcare provider would recommend vaccination (RR = 1.73, 95% CI: 1.49–2.02) or if they were moderate (RR = 1.09, 95% CI: 1.02–1.16) or liberal (RR = 1.14, 95% CI: 1.07–1.22) in their political leaning. Participants were also more likely to be willing to get vaccinated if they reported higher levels of perceived likelihood getting a COVID-19 infection in the future (RR = 1.05, 95% CI: 1.01–1.09), perceived severity of COVID-19 infection (RR = 1.08, 95% CI: 1.04–1.11), or perceived effectiveness of a COVID-19 vaccine (RR = 1.46, 95% CI: 1.40–1.52). Participants were less likely to be willing to get vaccinated if they were non-Latinx black (RR = 0.81, 95% CI: 0.74–0.90) or reported a higher level of perceived potential vaccine harms (RR = 0.95, 95% CI: 0.92–0.98).
Conclusion: Many adults are willing to get a COVID-19 vaccine, though acceptability should be monitored as vaccine development continues. Our findings can help guide future efforts to increase COVID-19 vaccine acceptability (and uptake if a vaccine becomes available).

E) Are vulnerable, hard-to-reach and immigrant populations able to access vaccines administered?

Paper 1
Title of Article/Author/Year/Grade: Delivering Covid-19 Vaccines by Building Community Trust / Cerise, Frederick P., Brett Moran, and Kavita Bhavan / 2020.
Type of Article: Commentary

Link of Article: **https://europepmc.org/article/pmc/pmc7793438**

Objective: Black and Hispanic communities have been hard hit by Covid-19, yet they have historical reasons to mistrust health care or defer vaccinations. Here's how Parkland Health is working to rebuild trust in medical systems and health interventions.

Conclusion: Regaining trust in medical systems and health interventions requires a commitment to show up in those underserved communities, listen to their concerns, and include their voices in addressing those concerns with the broader public. We must be intentional in our efforts, employ multiple communication strategies, and make the process easy if we are to successfully get the Covid-19 vaccine to the communities most in need that have been disproportionately impacted by the virus.

Paper 2
Title of Article/Author/Year/Grade: Constructing an ethical framework for priority allocation of pandemic vaccines / Fielding, J., S. G. Sullivan, F. Beard, K. Macartney, J. Williams, A. Dawson, G. L. Gilbert et al. / 2020 / 9(10)
Type of Article: Literature Review
Link of Article: **https://www.sciencedirect.com/science/article/pii/S0264410X20316339**
Objective: We describe a framework for priority vaccine allocation that employed a cross-disciplinary approach, guided by ethical considerations and informed by local risk assessment.
Result: Published and emerging guidance for priority pandemic vaccine distribution differed widely with respect to strategic objectives, specification of target groups, and explicit discussion of ethical considerations and decision-making processes. Flexibility in response was universally emphasized, informed by real-time assessment of the pandemic impact level, and identification of disproportionately affected groups. Model outputs aided identification of vaccine approaches most likely to achieve overarching goals in pandemics of varying transmissibility and severity. Pandemic response aims deemed most relevant for an Australian framework were: creating and maintaining trust, promoting equity, and reducing harmful outcomes. [149]
Conclusion: Once COVID-19 vaccines are available, governments will need to communicate their allocation plans effectively and transparently, among all levels of government responsible for procurement and delivery, health professionals and the public. Suspicion of government decision-making is evident during this pandemic and risks undermining careful planning. This is underscored by a recent global survey of acceptance of a COVID-19 vaccine which identified increased acceptance in nations where respondents had higher levels of trust

Paper 3
Title of Article/Author/Year/Grade: Fair allocation of potential COVID-19 vaccines using an optimization-based strategy / del Carmen Munguía-López, Aurora, and José María Ponce-Ortega / 2020
Type of Article: Modelling Study
Link of Article: **https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7804910/**
Objective: This paper presents an optimization strategy for the allocation of COVID-19 vaccines, when they are available, through different fairness schemes (social welfare, Nash, Rawlsian justice, and social welfare II scheme)
Conclusion: In this work, we presented an optimization formulation for the allocation of potential COVID-19 vaccines through fairness schemes. Distinct parameters to model the distribution of

vaccines were considered. Specifically, the case study of Mexico was addressed. We analyzed the allocated vaccines to each state of Mexico given by the allocation schemes (social welfare, Nash, Rawlsian justice, and social welfare II scheme) under different availability scenarios. We observe that the allocation of resources is a complex problem that can result in unfair distributions if it is not addressed properly. Mainly, when several stakeholders (32 states in our case study) are involved, the possible assignations are greater. We also observe that inequalities become critical when resources are scarce. For example, in scenario (b), where the social welfare approaches (standard and II) give preference only to one particular state by depriving the others. Specifically, the first solution obtained by the social welfare approach (standard) tends to favor large stakeholders (greater population) in all scenarios. On the other hand, when the available vaccines are greater, the complexity of the allocation increases since the possible solutions increase as well (such as in scenario (d)). Therefore, it is critical to consider all the possible allocations that the fairness schemes provide to identify the most suitable solution.

Paper 4
Title of Article/Author/Year/Grade: Key populations for early COVID-19 immunization: preliminary guidance for policy / Ismail, Shainoor J., Linlu Zhao, Matthew C. Tunis, Shelley L. Deeks, and Caroline Quach / 2020
Type of Article: Guidance Document
Link of Article: **https://pubmed.ncbi.nlm.nih.gov/33144317/**
Objective: Canada's National Advisory Committee on Immunization (NACI) has developed preliminary recommendations for the efficient, effective and equitable allocation of safe, efficacious Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) vaccine(s) in the context of staggered arrival of vaccines.

Result: Key populations for early vaccination include those at high risk of severe illness and death from COVID-19; those most likely to transmit COVID-19 to those at high risk of severe illness and death from COVID-19 and workers essential to maintaining the COVID-19 response; those contributing to the maintenance of other essential services for the functioning of society; and those whose living or working conditions put them at elevated risk of infection and where infection could have disproportionate consequences, including Indigenous communities.

Conclusion: Existing inequities magnified by this pandemic may be exacerbated with the inequitable allocation of vaccines. Efforts should be made to increase access to immunization services and engage racialized and systemically marginalized populations in immunization program planning. The integration of equity, feasibility and acceptability considerations across all populations is critical for decisions regarding a COVID-19 immunization program.

3.13.3 Equity

a. **What is the evidence that COVID-19 is more common in certain disadvantaged groups or is there evidence that the severity of COVID-19 is greater in people from specific groups or with a comorbidity? [Systematic Search/WHO website]**

Paper 1

Title of Article/Author/Year/Grade: COVID-19 and cardiovascular disease: from basic mechanisms to clinical perspectives. / Nishiga, M., Wang, D. W., Han, Y., Lewis, D. B., & Wu, J. C. / 2020 / 7(10)

Type of Article: Systematic review

Link of Article: https://www.nature.com/articles/s41569-020-0413-9
Objective: We summarize the current understanding of COVID-19 from basic mechanisms to clinical perspectives, focusing on the interaction between COVID-19 and the cardiovascular system. By combining our knowledge of the biological features of the virus with clinical findings, we can improve our understanding of the potential mechanisms underlying COVID-19, paving the way towards the development of preventative and therapeutic solutions.

Result: The interaction between the viral spike (S) protein and angiotensin-converting enzyme 2, which triggers entry of the virus into host cells, is likely to be involved in the cardiovascular manifestations of COVID-19. The presence of underlying cardiovascular comorbidities in patients with COVID-19 is associated with high mortality. COVID-19 can cause cardiovascular disorders, including myocardial injury, arrhythmias, acute coronary syndrome and venous thromboembolism. Several medications used for the treatment of COVID-19 have uncertain safety and efficacy profiles.

Conclusion: Given that numerous studies have demonstrated that SARS-CoV-2 shares many biological features with SARS-CoV, our knowledge of the pathophysiological mechanisms underlying SARS can be used to understand the disease processes involved in COVID-19. Mechanistically, the interaction between the S protein and ACE2 is likely to have a central role in disease pathogenesis, especially in cardiovascular manifestations of this disease, and this interaction is a potential target for the prevention and treatment of COVID-19.

Paper 2
Title of Article/Author/Year/Grade: COVID-19 and the kidney: from epidemiology to clinical practice. / Gagliardi, I., Patella, G., Michael, A., Serra, R., Provenzano, M., & Andreucci, M.
/ 2020 / 9(10)

Type of Article: Systematic review

Link of Article: https://doi.org/10.3390/jcm9082506

Objective: Attention is focused on the epidemiology, etiology and pathophysiological mechanisms of kidney damage, histopathology, clinical features in nephropathic patients (CKD, hemodialysis, peritoneal dialysis, AKI, transplantation) and prevention and containment strategies.

Result: The renal damage observed in COVID-19 patients is the result of complex mechanisms induced directly and indirectly by SARS-CoV-2 that predispose to the development of renal dysfunction. Further studies are needed to better understand the pathophysiological mechanisms of kidney injury, to develop new therapeutic strategies able to limit and/or prevent kidney damage, and to improve the prognosis of COVID-19 patients.

Conclusion: Most of the deceased patients had pre-existing comorbidities; over 20% had chronic kidney disease (CKD). Furthermore, although SARS-CoV-2 infection is characterized mainly by diffuse alveolar damage and acute respiratory failure, acute kidney injury (AKI) has developed in a high percentage of cases. As AKI has been shown to be associated with worse prognosis, we believe that the impact of SARS-CoV-2 on the kidney should be investigated.

Paper 3
Title of Article/Author/Year/Grade: Higher mortality of COVID-19 in males: sex differences in immune response and cardiovascular comorbidities. / Bienvenu, L. A., Noonan, J., Wang, X., & Peter, K. / 2020 / 7(10)
Type of Article: Rapid review
Link of Article: https://academic.oup.com/cardiovascres/article/116/14/2197/5924554?login=true
Objective: We present preclinical evidence identifying the influence of biological sex on the expression and regulation of angiotensin-converting enzyme 2 (ACE2), which is the main receptor used by SARS-CoV-2 to enter cells.
Result: Male patients with COVID-19 are more symptomatic and exhibit increased disease severity, higher complication rates, and ultimately higher mortality. Potential sexual dimorphism in the expression of ACE2, as the docking site used by SARS-CoV-2 to enter cells, has attracted significant attention. Nevertheless, preclinical evidence that ACE2 expression is regulated in a sex-dependent manner has not yet been validated in humans and, although initially postulated, no clinically relevant influence of medication such as ACE-I has yet been documented. However, as a most fascinating area, sexual dimorphism in the genetic and hormonal regulation of the immune response may hold the answer to the bias seen towards male mortality. Differences in inflammatory responses to viral infections between the sexes alongside different inflammatory/immune statuses associated with cardiovascular comorbidities, such as obesity, hypertension, and age, offer potential explanations for the worse outcomes in men with COVID-19.
Conclusion: Further research into sex differences in COVID-19 is necessary; we, and others, argue that both preclinical and clinical studies should include sex as a variable and, where possible, present datasets stratified by sex. The significant bias towards male deaths in COVID-19 and the clear interaction with CVD highlights a poorly understood biological phenomenon that is difficult to investigate, but it also provides a unique opportunity to better understand and treat SARS-CoV-2 infections.

Paper 4
Title of Article/Author/Year/Grade: SARS-CoV-2 disease severity and diabetes: why the connection and what is to be done? /
Type of Article: Systematic review
Link of Article: https://immunityageing.biomedcentral.com/articles/10.1186/s12979-020-00192-y
Objective: In this review we summarize what we think may be the factors driving this pattern between diabetes, aging and poor outcomes in respiratory infections. We also review therapeutic considerations and strategies for treatment of COVID-19 in diabetic patients, and how the additional challenge of this co-morbidity requires attention to glucose homeostasis so as to achieve the best outcomes possible for patients.

Result: Even though a disturbance in immune response may explain the higher risk of infection and worse outcome of diabetic patients with influenza, the relationship between diabetes and respiratory infections caused by the coronaviruses MERS-CoV, SARS-CoV and SARS-CoV-2 may be more complicated. The first step in the process of viral infection is the attachment of the virus to its targeted cells. There are seven known human coronaviruses, all capable of infecting cells in the respiratory system: HCoV-OC43 and HCoV-229E were first described in the 1960s, and are thought to cause the common cold; SARS-CoV, identified in 2003; HCoV-NL63 and HCoV-HKU1 in 2004, associated with weak respiratory infections; MERS-CoV, described in 2012; and now SARS-CoV-2, responsible for the ongoing COVID-19 pandemic.

Conclusion: Individuals with diabetes are at increased risk for infections and, once acquired, generally get more severe infections, and have much greater increase in mortality, compared to non-diabetic patients. This is certainly proving the rule with SARS-CoV-2. It also transpires that 2 coronavirus co-receptors, ACE2 and DPP4, are well-established actors within metabolic and inflammatory pathways, and renal and cardiovascular physiology, and have been front and center in diabetes and metabolic research: ACE2 is a co-receptor for SARS-CoV-2 while DPP4 is a co-receptor for MERS-CoV. The medical and economic consequences of the SARS-CoV-2 epidemic require ongoing and real-time adaptation of protocols and standard medical procedures to deliver diabetes care, and bring SARS-CoV-2 under control so as to lower morbidity and mortality for all, including people who have diabetes and the elderly while the human population waits with breath that is bated for a vaccine.

Paper 5
Title of Article/Author/Year/Grade: Comorbidities, clinical signs and symptoms, laboratory findings, imaging features, treatment strategies, and outcomes in adult and pediatric patients with COVID-19: A systematic review and meta-analysis. / Jutzeler, Catherine R., Lucie Bourguignon, Caroline V. Weis, Bobo Tong, Cyrus Wong, Bastian Rieck, Hans Pargger et al. / 2020 / 9(10)
Type of Article: Systematic review
Link of Article: https://www.sciencedirect.com/science/article/pii/S1477893920303215
Objective: Our aim was to gather all available information regarding comorbidities, clinical signs and symptoms, outcomes, laboratory findings, imaging features, and treatments in patients with coronavirus disease 2019 (COVID-19).
Result: 148 studies met the inclusion criteria for the systematic review and meta-analysis with 12'149 patients (5'739 female) and a median age of 47.0 [35.0–64.6] years. 617 patients died from COVID-19 and its complication. 297 patients were reported as asymptomatic. Older age (SMD: 1.25 [0.78–1.72]; $p < 0.001$), being male (RR = 1.32 [1.13–1.54], $p = 0.005$) and pre-existing comorbidity (RR = 1.69 [1.48–1.94]; $p < 0.001$) were identified as risk factors of in-hospital mortality. The heterogeneity between studies varied substantially (I^2; range: 1.5–98.2%). Publication bias was only found in eight studies (Egger's test: $p < 0.05$).
Conclusion: Our meta-analyses revealed important risk factors that are associated with severity and mortality of COVID-19.

Paper 6
Title of Article/Author/Year/Grade: Immunosenescence and inflammaging: Risk factors of severe covid-19 in older people. / Pietrobon, A. J., Teixeira, F. M. E., & Sato, M. N. / 2020 / 7(10)
Type of Article: Systematic Review
Link of Article: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7656138/
Objective: In this article, we discuss the main mechanisms involved in immunosenescence and their possible correlations with the susceptibility of individuals of advanced age to SARS-CoV-2 infection and the more severe conditions of the disease.
Result: Changes due to aging are also present in the adaptive immune response and are associated with the functional impairment of T and B lymphocytes (153). The sum of these changes renders old people vulnerable to new emerging infectious diseases, as recently observed with SARS-CoV-2. The

most prominent factor involves a decrease in the number of naïve cells because of thymic involution (154), an increase in memory/exhausted T cells and a reduction in B cell progenitors in the bone marrow (155). Consequently, these changes reflect the cumulative effect of previous and persistent infections in older individuals.

Conclusion: Considering the clinical findings obtained thus far concerning SARS-CoV-2 infection and reports of diseases of a similar etiology, it is evident that the immunosenescence process, particularly the increased production of inflammatory cytokines resulting from inflammaging, plays a role in determining the prognosis of COVID-19 in old individuals. From an immunological perspective, the peculiarities of the immune system of older individuals may contribute to both the deficiency of effector mechanisms essential to fighting viral pathogens and the exacerbated inflammatory response, which can accelerate and intensify lung tissue damage. However, despite the strong evidence presented here, tests that accurately demonstrate the association between immunosenescence and the severity of COVID-19 are essential for assisting the search for treatments and the development of vaccines for this most affected age group.

Paper 7

Title of Article/Author/Year/Grade: The Impact of SARS-CoV-2 on the Most Common Comorbidities–A Retrospective Study on 814 COVID-19 Deaths in Romania. / Barbu, Madalina Gabriela, Richard James Thompson, Dana Claudia Thompson, Dragos Cretoiu, and Nicolae Suciu. / 2020 / 8(12)

Type of Article: Cohort study

Link of Article: https://doi.org/10.3389/fmed.2020.567199

Objective: To assess the impact of SARS-CoV-2 on the most prevalent comorbidities, among people who died of COVID-19 in Romania.

Result: The study sample consisted of 61.4% males and 38.6% females; the mean age was 68.2 y; 90.9% of deaths occurred in people 50+ years. The mean number of pre-existing conditions was 2.73 (SD = 1.521), with 97.4% of the patients having at least one. The most prevalent comorbidities were hypertension (43.1%), diabetes (33.2%), and coronary heart disease (26.0%). The calculated relative risk of death due to COVID-19 was divided into 3 risk categories: high impact comorbidities (RR > 3) included diabetes RR = 6.426 (95% CI, 4.965–8.318), chronic renal disease RR = 4.338 (95% CI, 3.556–5.292) and hypertension RR=3.261 (95% CI, 2.687–3.958). The medium impact (RR = 2–3) group comprised chronic pulmonary disease RR = 2.615 (95% CI, 2.061–3.319) and chronic liver disease RR = 1.577 (95% CI, 1.183–2.104) and the low impact group (RR<2) –coronary heart disease RR = 0.664 (95% CI, 0.581–0.758), cancer RR = 0.515 (95% CI, 0.416–0.637) and stroke RR = 0.468 (95% CI, 0.370–0.593).

Conclusion: In the studied sample, SARS-CoV-2 had a greater impact on people with diabetes, chronic renal disease and hypertension and a lesser impact on those with coronary heart disease, cancer and stroke. Therefore, future policies in Romania should focus on shielding people in the high-risk group and prioritizing them for vaccination, whilst encouraging those in the low-risk group to continue seeking treatment for their underlying diseases.

Paper 8

Title of Article/Author/Year/Grade: The impact of obesity on severe disease and mortality in people with SARS-CoV-2: A systematic review and meta-analysis. / Seidu, Samuel, Clare Gillies, Francesco

Zaccardi, Setor K. Kunutsor, Jamie Hartmann-Boyce, Thomas Yates, Awadhesh Kumar Singh, Melanie J. Davies, and Kamlesh Khunti. / 2020 / 8(12)

Type of Article: Cohort study

Link of Article: https://doi.org/10.1002/edm2.176

Objective: This study was designed to include all observational studies (prospective cohort, retrospective, nested case-control and case-control), clinical studies, nonrandomized controlled trials (RCTs) and RCTs reporting a relationship between obesity and the clinical outcomes in patients with COVID-19.

Result: Eight retrospective cohort studies and one cohort prospective cohort study with data on of 4,920 patients with COVID-19 were eligible. Comparing BMI ≥ 25 vs <25 kg/m², the RRs (95% CIs) of severe illness and mortality were 2.35 (1.43-3.86) and 3.52 (1.32-9.42), respectively. In a pooled analysis of three studies, the RR (95% CI) of severe illness comparing BMI > 35 vs <25 kg/m² was 7.04 (2.72-18.20). High levels of statistical heterogeneity were partly explained by age; BMI ≥ 25 kg/m² was associated with an increased risk of severe illness in older age groups (≥60 years), whereas the association was weaker in younger age groups (<60 years).

Conclusion: Excess adiposity is a risk factor for severe disease and mortality in people with SARS-CoV-2 infection. This was particularly pronounced in people 60 and older. The increased risk of worse outcomes from SARS-CoV-2 infection in people with excess adiposity should be taken into account when considering individual and population risks and when deciding on which groups to target for public health messaging on prevention and detection measures.

Paper 9
Title of Article/Author/Year/Grade: Impact of Diabetes in Patients Diagnosed With COVID-19 / Abu-Farha, M., F. Al-Mulla, T. Thanaraj, S. Kavalakatt, H. Ali, Abdul Ghani, and J. Abubaker / 2020 / 8(10)
Type of Article: Rapid Review

Link of Article: https://europepmc.org/article/pmc/pmc7736089

Objective: Explore the current and evolving insights pertinent to the metabolic impact of coronavirus infections with special attention to the main pathways and mechanisms that are linked to the pathophysiology and treatment of diabetes.

Result: Several classes of anti-obesity and anti-diabetes medications (such as metformin, 5-Aminoimidazole-4-carboxamide ribonucleotide (AICAR), and PPARγ agonists) are known to modulate the immune system and result in improved insulin sensitivity. Hence, further investigations are warranted to address their use alone or in combination with other antiviral/immunomodulatory drugs in the treatment of COVID-19. Moreover, GLP-1R agonists and DPP4 inhibitors are known to mediate anti-inflammatory effects in human patients, while controlling glucose levels in hospitalized patients (124) Nevertheless, there is no convincing evidence advocating the use of these drugs as replacements for insulin in severely ill COVID-19 patients. The fast-growing medical information pertaining to the COVID-19 pandemic entails continuing scrutiny to assess the practical use, risks, and advantages of these anti-hyperglycemic drugs and any other associated medications generally used to treat diabetic people, who are at higher risk of coronavirus infections.

Conclusion: Evidence implies that obesity and diabetes are leading risk factors that affect the severity of disease caused by coronaviruses infections, such as COVID-19. Among patients infected with the SARS-CoV-2, history has shown that diabetes and hyperglycemia are independent predictors for mortality and morbidity, and that glycemic control might improve patient prognosis. The risk seen among people with diabetes may be due to insulin resistance, inflammation, or hypercoagulation, or owed to underlying obesity, which may lead to adverse outcome.

Paper 10
Title of Article/Author/Year/Grade: Coronavirus disease 2019 (COVID-19) outcomes in HIV/AIDS patients: a systematic review / TJ Cooper, BL Woodward, S Alom and A Harky / 2020 / 9(10)

Type of Article: Systematic Review

Link of Article: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7405326/

Objective: The aim of the study was to systematically review current studies reporting on clinical outcomes in people living with HIV (PLHIV) infected with Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).

Result: Two hundred and eighty-five articles were identified after duplicates had been removed. After screening, eight studies were analysed, totalling 70 HIV-infected patients (57 without AIDS and 13 with AIDS). Three themes were identified: (1) controlled HIV infection does not appear to result in poorer COVID-19 outcomes, (2) more data are needed to determine COVID-19 outcomes in patients with AIDS and (3) HIV-infected patients presenting with COVID-19 symptoms should be investigated for superinfections. [173]

Conclusion: Our findings suggest that PLHIV with well-controlled disease are not at risk of poorer COVID-19 disease outcomes than the general population. It is not clear whether those with poorly controlled HIV disease and AIDS have poorer outcomes. Superimposed bacterial pneumonia may be a risk factor for more severe COVID-19 but further research is urgently needed to elucidate whether PLHIV are more at risk than the general population.

Paper 11
Title of Article/Author/Year/Grade: Impact of obesity on COVID-19 patients / Yu, Wanqi, Kristen E. Rohli, Shujuan Yang, and Peng Jia / 2020 / 8(10)

Type of Article: Systematic Review

Link of Article: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7690270/

Objective: This review focuses on the impact of obesity on patients with COVID-19. We comprehensively analyzed the various mechanisms of obesity affecting the severity of the disease. In addition, on the basis of the vulnerability of people with obesity during the COVID-19 epidemic, we summarized both individual-level and hospital-level prevention and management measures for COVID-19 patients with obesity and discussed the impact of isolation on people with obesity.

Result: Patients with obesity who have been exposed to COVID-19 patients or high-risk areas for COVID-19 infection, especially those who have subsequently developed suspected symptoms for COVID-19 (e.g., cold, coughing, runny nose, fever), should go to a medical institution for virus testing as soon as possible[92]; those having mild symptoms can be consulted at home through telemedicine and should be self-isolated for 14 days after their symptoms disappear. COVID-19 patients with obesity aged over 60 should be referred to a hospital as soon as possible. Patients with other basic or chronic diseases (e.g., diabetes, hypertension, heart diseases) should seek medical attention urgently. During the treatment, they should continue to strictly comply with appropriate control of blood glucose, blood pressure, and blood lipids; appropriate hypoglycemic, hypotensive, and lipid-lowering regiments should be continued during the treatment.[93] Inflammatory response indicators (IL-6, TNF-α, CRP) and immune response indicators (immunoglobulin, CD4+, CD8+) should be monitored during treatment to prevent "cytokine storms" in a timely manner. When treating individuals with obesity, the feasibility of operations and appropriate tools should be considered in advance to avoid delay in treatment.

Conclusion: Based on the characteristics of people with obesity, we suggest that individuals with obesity should not only follow the general preventive measures and health guidance but should also pay more attention to the control of other underlying diseases. Patients should seek the help of medical staff as soon as possible after being infected with the virus. The treatment of basic diseases should be considered in the treatment process, and the condition indicators should be closely monitored to alleviate the prognosis. In addition, we also recommend the use of telemedicine for obesity training and education.

Paper 12
Title of Article/Author/Year/Grade: Obesity and COVID-19: what makes obese host so vulnerable? / Mohammad, S., R. Aziz, S. Al Mahri, S. S. Malik, E. Haji, A. H. Khan, T. S. Khatlani, and A. Bouchama / 2020 / 7(10)

Type of Article: Rapid Review

Link of Article: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7779330/

Objective: We review the published data related to obesity and overweight to assess the possible risk and outcome in Covid-19 patients based on their body weight. Besides, we explore how the obese host provides a unique microenvironment for disease pathogenesis, resulting in increased severity of the disease and poor outcome.

Result: It is plausible to suggest that acute inflammation arising from COVID-19, may amplify existing chronic inflammation secondary to obesity and lead to more severe disease phenotype and poorer outcomes. A similar hypothesis was proposed in a recent paper by Paul MacDaragh Ryan and Noel M. Caplice [77]. The authors suggested that obese subjects have higher levels of various inflammatory signals and, are more likely to overreact to coronavirus infection. Zhang et al. analyzed 16 retrospective studies and found that inflammatory markers were positively correlated with the severity of COVID-19.

Conclusion: Obesity is a huge healthcare concern because it is associated with several chronic diseases including type 2 diabetes, heart diseases, stroke, and certain types of cancers. Obesity significantly reduces the quality of life and is one of the leading causes of death, worldwide. Recent evidence has shown that obesity weakens the immune system and therefore, making the host vulnerable to infectious diseases. Indeed, Obesity has emerged as a strong risk factor for severe disease in the current pandemic disease, COVID-19. Several independent studies have demonstrated that obese subjects with COVID-19 have a higher risk of severe disease, hospitalization, and increased probability of death.

Paper 13
Title of Article/Author/Year/Grade: Is Sex a Determinant of COVID-19 Infection? Truth or Myth? / Groban, Leanne, Hao Wang, Xuming Sun, Sarfaraz Ahmad, and Carlos M. Ferrario / 2020 / 7(10)

Type of Article: Rapid Review

Link of Article: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7449867/

Objective: Angiotensin-converting enzyme 2 (ACE2), a specific high-affinity angiotensin II-hydrolytic enzyme, is the vector that facilitates cellular entry of SARS-CoV-1 and the novel SARS-CoV-2 coronavirus. SARS-CoV-2, which crossed species barriers to infect humans, is highly contagious and associated with high lethality due to multi-organ failure, mostly in older patients with other co-morbidities.

Result: Accumulating clinical evidence demonstrates that the intensity of the infection and its complications are more prominent in men. It has been postulated that potential functional modulation of ACE2 by estrogen may explain the sex difference in morbidity and mortality.

Conclusion: We review here the evidence regarding the role of estrogenic hormones in ACE2 expression and regulation, with the intent of bringing to the forefront potential mechanisms that may explain sex differences in SARS-CoV-2 infection and COVID-19 outcomes, assist in management of COVID-19, and uncover new therapeutic strategies.

Paper 14
Title of Article/Author/Year/Grade: COVID-19 in cancer patients: clinical characteristics and outcome—an analysis of the LEOSS registry / Rüthrich, Maria Madeleine, C. Giessen-Jung, S. Borgmann, A. Y. Classen, S. Dolff, B. Grüner, F. Hanses et al. / 2020 / 9(12)

Type of Article: Cohort Study

Link of Article: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7648543/

Objective: We present an analysis of cancer patients from the LEOSS (Lean European Open Survey on SARS-CoV-2 Infected Patients) registry to determine whether cancer patients are at higher risk.

Result: In total, 435 cancer patients were included in our analysis. Commonest age category was 76–85 years (36.5%), and 40.5% were female. Solid tumors were seen in 59% and lymphoma and leukemia in 17.5% and 11% of patients. Of these, 54% had an active malignancy, and 22% had recently received anti-cancer treatments. At detection of SARS-CoV-2, the majority (62.5%) presented with mild symptoms. Progression to severe COVID-19 was seen in 55% and ICU admission in 27.5%. COVID-19-related mortality rate was 22.5%. Male sex, advanced age, and active malignancy were associated with higher death rates. Comparing cancer and non-cancer patients, age distribution and comorbidity differed significantly, as did mortality (14% vs 22.5%, *p* value < 0.001). After adjustments for other risk factors, mortality was comparable.

Conclusion: Comparing cancer and non-cancer patients, outcome of COVID-19 was comparable after adjusting for age, sex, and comorbidity. However, our results emphasize that cancer patients as a group are at higher risk due to advanced age and pre-existing conditions.

Paper 15
Title of Article/Author/Year/Grade: Pregnant women with severe or critical coronavirus disease 2019 have increased composite morbidity compared with nonpregnant matched controls / DeBolt, Chelsea A., Angela Bianco, Meghana A. Limaye, Jenna Silverstein, Christina A. Penfield, Ashley S. Roman, Henri M. Rosenberg et al. / 2020 / 10(12)

Type of Article: Cohort Study

Link of Article: https://pubmed.ncbi.nlm.nih.gov/33221292/

Objective: We aimed to describe the outcomes of severe and critical cases of coronavirus disease 2019 in pregnant vs nonpregnant, reproductive-aged women.

Result: A total of 38 pregnant women with Severe acute respiratory syndrome coronavirus 2 polymerase chain reaction-confirmed infections were admitted to 5 institutions specifically for coronavirus disease 2019, 29 (76.3%) meeting the criteria for severe disease status and 9 (23.7%) meeting the criteria for critical disease status. The mean age and body mass index were markedly higher in the nonpregnant control group. The nonpregnant cohort also had an increased frequency of preexisting medical comorbidities, including diabetes, hypertension, and coronary artery disease. The pregnant women were more likely to experience the primary outcome when compared with the nonpregnant control group (34.2% vs 14.9%; P=.03; adjusted odds ratio, 4.6; 95% confidence interval, 1.2-18.2). The pregnant patients experienced higher rates of intensive care unit admission (39.5% vs 17.0%; P<.01; adjusted odds ratio, 5.2; 95% confidence interval, 1.5-17.5). Among the pregnant women who underwent delivery, 72.7% occurred through cesarean delivery and the mean gestational age at delivery was 33.8±5.5 weeks in patients with severe disease status and 35±3.5 weeks in patients with critical coronavirus disease 2019 status.

Conclusion: Pregnant women with severe and critical coronavirus disease 2019 are at an increased risk for certain morbidities when compared with nonpregnant controls. Despite the higher comorbidities of diabetes and hypertension in the nonpregnant controls, the pregnant cases were at an increased risk for composite morbidity, intubation, mechanical ventilation, and intensive care unit admission. These findings suggest that pregnancy may be associated with a worse outcome in women with severe and critical cases of coronavirus disease 2019. Our study suggests that similar to other viral infections such as Severe acute respiratory syndrome coronavirus and Middle East respiratory syndrome coronavirus, pregnant women may be at risk for greater morbidity and disease severity.

Paper 16

Title of Article/Author/Year/Grade: Association of diabetes and hypertension with disease severity in covid-19 patients: A systematic literature review and exploratory meta-analysis / Parveen, Rizwana, Nouroz Sehar, Ram Bajpai, and Nidhi Bharal Agarwal / 2020 / 9(10)

Type of Article: Systematic Review

Link of Article: https://europepmc.org/article/pmc/pmc7332452

Objective: The aim of the meta-analysis was to assess the association of diabetes and hypertension with severity of disease.

Result: Diabetes was lower in the survivors (OR: 0.56; 95%CI: 0.35-0.90; p = 0.017; I^2: 0.0%) and non-severe (OR: 1.66; 95%CI: 1.20-2.30; p = 0.002; I^2: 0.0%) patients. No association of diabetes was found with ICU care. Hypertension was positively associated with death (OR: 0.49; 95%CI: 0.34-0.73; p<0.001; I^2: 0.0%), ICU care (OR: 0.42; 95%CI: 0.22-0.81; p = 0.009; I^2: 0.0%) and severity (OR: 2.69; 95%CI: 1.27-5.73; p = 0.01; I^2: 52.4%).

Conclusion: Our findings suggest that diabetes and hypertension have a negative effect on health status of COVID-19 patients. However, large prevalence studies demonstrating the consequences of comorbid diabetes and hypertension are urgently needed to understand the magnitude of these vexatious comorbidities.

Paper 17

Title of Article/Author/Year/Grade: Diabetes Mellitus is Associated with Severe Infection and Mortality in Patients with COVID-19: A Systematic Review and Meta-analysis / Shang, Luxiang, Mengjiao Shao, Qilong Guo, Jia Shi, Yang Zhao, Jiasuoer Xiaokereti, and Baopeng Tang. / 2020 / 9(10)

Type of Article: Systematic Review

Link of Article: https://europepmc.org/articles/pmc7413048/bin/mmc1.docx

Objective: We aimed to assess whether diabetes mellitus (DM) would increase the risk of severe infection and death in patients with COVID-19.

Result: A total of 76 studies involving 31,067 patients with COVID-19 were included in our meta-analysis. COVID-19 patients with DM had higher severe infection and case-mortality rates compared with those without DM (21.4 vs. 10.6% and 28.5 vs. 13.3%, respectively, all *p* <0.01). COVID-19 patients with DM were at significantly elevated risk of severe infection (*OR* = 2.38, 95% CI: 2.05–2.78, *p* <0.001) and mortality (*OR* = 2.21, 95% CI: 1.83–2.66, *p* <0.001).

Conclusion: DM is associated with increased risk of severe infection and higher mortality in patients with COVID-19. Our study suggests that clinicians should pay more attention to the monitoring and treatment of COVID-19 patients with DM.

Paper 18

Title of Article/Author/Year/Grade: Clinical outcomes and immunologic characteristics of Covid-19 in people with HIV / Ho, H. E., M. J. Peluso, C. Margus, Matias Lopes JP, C. He, M. M. Gaisa, G. Osorio, J. A. Aberg, and M. P. Mullen / 2020 / 10(12)

Type of Article: Cohort Study

Link of Article: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7337732/

Objective: We performed a retrospective study of coronavirus disease 2019 (COVID-19) in people with human immunodeficiency virus (PWH). PWH with COVID-19 demonstrated severe lymphopenia and decreased $CD4^{+}$ T cell counts. Levels of inflammatory markers, including C-reactive protein, fibrinogen, D-dimer, interleukin 6, interleukin 8, and tumor necrosis factor α were commonly elevated.

Result: These findings suggest that PWH remain at risk for severe manifestations of COVID-19 despite antiretroviral therapy and that those with increased markers of inflammation and immune dysregulation are at risk for worse outcomes. This analysis reveals that a subset of PWH develop severe COVID-19 associated with a profound inflammatory response. Prospective studies with carefully matched control groups to identify determinants of severe COVID-19 in PWH will be crucial to understanding the biological mechanisms and clinical impact of SARS-CoV-2 coinfection in this population. [174]

Conclusion: These findings indicate that PWH, particularly those with prolonged duration of HIV infection and medical comorbidities, remain at risk for severe manifestations of COVID-19 despite suppressive ART and immune reconstitution. Substantial inflammation and immune dysregulation occurred in a subset of individuals who experienced poor outcomes. Additional work is needed to determine whether and how the pathophysiology of COVID-19 in PWH differs from that in the general population.

b. What is the evidence that strategies have been developed to reduce the risk of discrimination in access to the vaccines? [Systematic Search/WHO website]

Source of evidence / Year:

National Covid-19 Deployment and Vaccination Plan, Nigeria

- NPHCDA Document Year:2021.

Who-2019-Ncov-Sage_Framework-Allocation_And_Prioritization

- WHO Document Year: 2020

-Who Sage Roadmap for Prioritizing Uses of Covid-19 Vaccines in the Context of Limited Supply

- WHO Document Year: 2020

Result: Strategies currently employed to reduce risk of discrimination include the following:

1. The definition and selection of the target groups were identified adhering to the principles as outlined in the WHO vaccine allocation framework and prioritization roadmap as well as using the COVID-19 disease burden data from the NCDC.
2. The microplanning process for the COVID-19 vaccine introduction will identify all individuals, groups, and location where they reside. Human, material, and financial resource needs will be identified, and gaps addressed to avoid discrimination and issues of emanating from equity gaps.
3. To reach the most vulnerable amongst the prioritized groups, vaccine delivery has been fashioned to have special teams that are responsible to provide vaccination to identified hard to reach, conflict and security compromised areas and populations with other special needs.

3.13.4 Social Consideration

c. Are there potential social, cultural and legal implications of administering vaccine only to this target population? [Systematic Search/WHO website]

Title of Article/Author/Year: Economic and Behavioral Influencers of Vaccination and Antimicrobial Use / Wagner, C. E., Prentice, J. A., Saad-Roy, C. M., Yang, L., Grenfell, B. T., Levin, S. A., & Laxminarayan, R. / 2020

Type of Article: Systematic review Link of Article: https://doi.org/10.3389/fpubh.2020.614113

Objective: Review of drivers shaping the use of vaccines and antibiotics in the context of three factors: individual incentives, risk perceptions, and social norms and group dynamics.

Result: People form risk perceptions using heuristics rather than reflective thinking. For example, mass vaccination successfully reduces the population-level prevalence of an infectious disease, knowledge of the disease also declines over time, leading to underestimations of its severity.

Also, the tendency for individuals to feel more responsible for a negative outcome when it is due to their action rather than inaction increases the general tendency to avoid risks associated with even very rare events. Therefore, when the possible adverse effects of a vaccine are known, even if the chances of them occurring are very low, individuals tend to be more cautious about actively getting vaccinated compared to the potentially riskier inaction of doing nothing. [175]

Conclusion: Key findings from this article relative to COVID-19 is the possibility of underestimation of the risk of a disease because of herd immunity and overestimation of the risk of adverse events from vaccination. This underscores the importance of aggressive public campaigns and rigorous vaccine testing to maintain public trust.

A. What is the evidence that proposed vaccine use recommendations are consistent with the 6 core principles as outlined in the "WHO SAGE Values Framework for the

Allocation and Prioritization of COVID-19 Vaccination"? [Systematic Search/WHO website]

Name of Document used to answer the query/ Year:

1. National Covid-19 Deployment and Vaccination Plan, Nigeria
   - NPHCDA Document Year:2021**.**
2. Who-2019-Ncov-Sage_Framework-Allocation_And_Prioritization
   - WHO Document Year: 2020
3. Who Sage Roadmap for Prioritizing Uses of Covid-19 Vaccines In The Context Of Limited Supply
   - WHO Document Year: 2020

Result: The planned deployment and vaccination plan as captured in the National Covid-19 Deployment and Vaccination Plan, Nigeria 2021 is consistent with all the principles as outlined in the WHO SAGE Values Framework for the Allocation and Prioritization of COVID-19 Vaccination". The principles have been clearly considered and applied to the Nigeria context. This is t ensure equitable distribution of vaccines to the most vulnerable while prioritizing the continuation of essential health services and providing equal opportunity to all based on available scientific evidence and transparency.

Human Wellbeing and Reciprocity: In order to protect the continuing functioning of essential services, including health services, the healthcare workers, support staff alongside contingencies (Point of Entry workers, Rapid Response Teams, contact tracing teams, COVID-19 vaccination teams etc) have been prioritized for vaccination in the Phase 1. This also ensures that vaccine is first offered to those who by their occupation bear exceptional risks in order to protect them and vulnerable individuals they come in contact with.

Equal Respect: The Nigeria deployment plan ensures that equal opportunity is provided for all individuals and groups who qualify under prioritization criteria. Estimates based on population figures of individuals within groups have been collated and vaccine will be deployed based transparent allocation to ensure equal opportunities to individuals in spite of are of residence within the country.

Global Equity: This has been ensured by the allocation of vaccines to 20% of countries populations through the COVAX facility.

National Equity: To achieve national equity, All States and LGAS have been included in the prioritization plan for vaccine deployment. The design of the delivery strategy includes fixed post located at designated Health facilities, temporary fixed post teams located at strategic areas within the communities and special teams for other areas not covered by fixed post and temporary fixed post teams. The special teams have mobile capability and are designed to provide vaccination in hard-to-reach areas, security compromised areas and other identified populations with special needs. In this way national equity will be achieved and the most vulnerable groups will be vaccinated.

Legitimacy: The prioritization process for the Nigeria deployment plan has been conducted in a very transparent manner using available information and scientific principles. Demographic data obtained from the National Population Commission, epidemiologic data on COVID-19 epidemiology in Nigeria from the Nigeria Centre for Disease Control, guidelines from the WHO documents, from the National Primary Health Care Development Agency/Federal Ministry of health amongst others have been key to making reproducible decisions on prioritization and allocation. A broad stakeholder base is involved in making these key decisions, they include Government officials at National and State level; officials from other ministries other than the ministry of health such as the national Orientation agency, Nigeria Television Authority; officials from the Nigeria medical association and other medical associations; partners including WHO, UNICEF, World Bank, GAVI, CDC, AFENET, BMGF, CHAI, Sydani, SOLINA and DCL/IVAC.

4 Discussions

Fernando et al in a randomized double-blind clinical trial revealed that two-dose regimen of Pfizer-BioNTech mRNA vaccine, BNT162b2, conferred 95% protection against COVID-19 in persons 16 years of age or older. Safety over a median of 2 months was similar to that of other viral vaccines and characterized by short-term, mild-to-moderate pain at the injection site, fatigue, and headache. The frequency of any severe systemic event after the first dose was 0.9% or less. Severe systemic events were reported in less than 2% of vaccine recipients after either dose, except for fatigue (in 3.8%) and headache (in 2.0%) after the second dose. The incidence of serious adverse events was low and was similar in the vaccine and placebo groups.

Similarly, Lindsey et al in a randomized double-blind clinical trial of the second mRNA derived vaccine, Moderna vaccine, mRNA 1273, also demonstrated a safe profile and 94.1% efficacy in persons 18 years and above. Vaccine recipients had higher rates of local reactions (e.g., pain, erythema, swelling) and systemic reactions (e.g., headache, fatigue, myalgia) than placebo recipients. Most reactions were mild to moderate and resolved over 1–3 days. There were higher adverse events, in the mRNA-1273 group (8.2%), than in the placebo group (4.5%). The incidence of treatment-related severe adverse events was higher in the mRNA-1273 group (71 participants [0.5%]) than in the placebo group (28 participants [0.2%]). The relative incidence of these adverse events according to vaccine group was not affected by age.

Voysey et al in a pooled information from double blind RCT at four sites revealed that AstraZeneca-Oxford Vaccine (ChAdOx1 nCoV-19 vaccine) has good safety profile with serious adverse events and adverse events of special interest balanced across the study arms. Serious adverse events occurred in 168 participants, 79 of whom received ChAdOx1 nCoV-19 and 89 of whom received MenACWY or saline control. There were 175 events (84 in the ChAdOx1 nCoV-19 group and 91 in the control group), three of which were considered possibly related to either the experimental or a control vaccine.

Local and systemic reactogenicity of ChAdOx1 nCoV-19 are less both in intensity and number in older adults, with lower doses, and after the second dose. There were three cases of transverse myelitis initially reported as suspected unexpected serious adverse reactions, with two in the ChAdOx1 nCoV-19 vaccine study arm, triggering a study pause for careful review in each case. Independent clinical review of these cases has indicated that one in the experimental group and one in the control group are unlikely to be related to study interventions, but a relationship remained possible in the third case. Careful monitoring of safety, including neurological events, continues in the trials.

Zhang et al conducted RCT on the inactivated vaccine, CoronaVac by Sinovac Life Sciences, Beijing, China. The study groups were relatively small, 743 participants received at least one dose of investigational product (n=143 for phase 1 and n=600 for phase 2; safety population). Two doses of CoronaVac at different concentrations and using different dosing schedules were well tolerated and moderately immunogenic in healthy adults aged 18–59 years. The incidence of adverse reactions in the 3 µg and 6 µg groups were similar, indicating no dose-related safety concerns but more long-term follow-up is needed. Furthermore, most adverse reactions were mild, with the most common symptom being injection-site pain, which is in accordance with previous findings for another inactivated COVID-19 vaccine from Sinopharm (Beijing China).

Xia et al conducted a double-blind placebo-controlled phase I and II clinical trial on Sinopharm's inactivated SARS-CoV-2 vaccine, BBIBP-Cor. It is safe and well tolerated at all tested doses in two age groups. Humoral responses against SARS-CoV-2 were induced in all vaccine recipients on day 42. Two-dose immunisation with 4 µg vaccine on days 0 and 21 or days 0 and 28 achieved higher neutralising antibody titres than the single 8 µg dose, or 4 µg dose on days 0 and 14.

Contraindications to administration of either of the mRNA COVID-19 vaccines are severe allergic reaction (e.g., anaphylaxis) after a previous dose of an mRNA COVID-19 vaccine or to any of its components. This includes immediate allergic reaction of any severity to a previous dose of an mRNA COVID-19 vaccine or any of its components (including polyethylene glycol [PEG]), or immediate allergic reaction of any severity to polysorbate (due to potential cross-reactive hypersensitivity with the vaccine ingredient PEG). Individuals with an immediate allergic reaction to the first dose of an mRNA vaccine should not receive additional doses of either of the mRNA COVID-19 vaccines.

The interim recommendations for use of the Pfizer-BioNTech COVID-19 vaccine, BNT162b2, under Emergency Use Listing/WHO/2020/10 is based on SAGE applying the principles of evidence-based medicine to set in place a thorough methodological process for issuing or updating recommendations on the use of COVID-19 candidate vaccines. Specifically, for COVID-19 vaccines, a detailed description of the methodological processes can be found in the SAGE evidence framework for COVID-19 vaccines. This framework is intended to offer guidance for considering data emerging from clinical trials in support of issuing vaccine-specific evidence-based recommendations.

There is lack of data on the safety and efficacy of mRNA COVID-19 vaccines administered simultaneously with other vaccines, therefore the vaccine series should routinely be administered alone, with a minimum interval of 14 days before or after administration with any other vaccine. However, mRNA COVID-19 and other vaccines may be administered within a shorter period in situations where the benefits of vaccination are deemed to outweigh the potential unknown risks of vaccine coadministration (e.g., tetanus toxoid-containing vaccination as part of wound management, measles or hepatitis A vaccination during an outbreak) or to avoid barriers or delays to mRNA COVID-19 vaccination (e.g., in long-term care facility residents or healthcare personnel who received influenza or other vaccinations prior to/upon admission or onboarding). If mRNA COVID-19 vaccines are administered within 14 days of another vaccine, doses do not need to be repeated for either vaccine. Likewise, the AstraZeneca-Oxford vaccine does not have safety information on co-administration with other vaccines.

The durability of the antibody responses to SARS-CoV-2 remains unknown. However, previous longitudinal studies of patients with SARS-CoV infection reported substantial waning of neutralizing antibody titres between 1 year and 2 years after infection. This is consistent with classical studies showing a relatively rapid waning of antibodies to the seasonal coronavirus 229. There are currently no immune correlates of protection for SARS-CoV-2 or other human coronaviruses. Thus, it is unclear what titre of neutralizing antibodies is sufficient to confer protection against infection. Establishing such correlates will be essential to guide the development of effective COVID-19 vaccines.

There is limited data on the immunological response to COVID-19 vaccines by certain groups that include, pregnant women, lactating women, children and adolescents, people living with HIV, the immune-compromised, people previously vaccinated and people with previous history of SARS CoV2 infection.

Herd immunity is estimated to be between 60-80% of the world population. Target population sizes for covid-19 vaccination vary markedly by vaccination goal and geographical region. The differences in demographic structure, presence of underlying conditions, and number of essential workers lead to highly variable estimates of target populations at regional and country levels.

Presentation of the various vaccines is critical to the logistics of handling the vaccines and the administration of the vaccines to individuals. For instance, Pfizer-BioNTech Vaccine, Moderna Vaccine, AstraZeneca-Oxford Vaccine and Sinovac Vaccine require -70 oC, - 25 ^{o}C to -15 ^{oC}, and 2-8 ^{o}C respectively. The impact of vaccine presentation on programmatic issues could challenge the infrastructural capacity and affordability of the vaccine. For this reason, the requirement of ultra-cold chain for mRNA vaccines is a major consideration for procurement. Nigeria has acquired 3 Ultra cold chain equipment to cater for antigen between -60^{o}C to -80^{o}C.

With exception of Pfizer-BioNTech vaccine which is a two-dose regimen administered 21 days apart the frontline vaccines for EUL consideration are mostly two-dose vaccines delivered at 28 days interval except for AstraZeneca-Oxford vaccine that has shown improved sero-conversion when the dose 2 is administered 8 to 12 weeks after the dose 1, and the Janssen Pharmaceutical vaccine (*Johnson and Johnson vaccine*) that has shown significant sero-conversion after one dose vaccination. All the vaccines are administered intramuscularly, therefore requiring skilled health care worker to administer the vaccine. When *Johnson and Johnson vaccine* becomes available, it has an added advantage for resource constrained countries like Nigeria because of the storage requirement of regular refrigeration at +2ºC - +8ºC and the convenience and cost-effectiveness of a single dose administration. However, the capacity for production to meet the demands should be an anticipated challenge. It is therefore prudent that Nigeria begins negotiation with Janssen Pharmaceutical company, makers of this vaccine, in anticipation of a global rush for this vaccine. The Sputnik-V vaccine, a two- vector adenovirus vaccine, is presented in a lyophilised form that also stores at +2 - +8º C. The safety profile and efficacy at 91.4% are competitive with other vaccines.

The vials of Pfizer-BioNTech COVID-19 vaccines contain 6 doses of 0.3ml per dose. It is important to ensure that vaccinators are aware of this dose which is different from the dose of 0.5ml for many of the other vaccines and therefore flags a potential for vaccine administration error. The clinical trials have been in individuals 16 years old and older. The dose and schedule of administration are as published by the manufacturer and are based on optimal interval to stimulate sero-conversion.

Nigeria has, to date, the second-highest number of confirmed COVID-19 cases in Africa, and accounts for 7% of all confirmed cases on the continent. This may be an underestimate of the actual case load given the relatively low testing rate in Nigeria. As of May 31 2020, Nigeria had conducted 63 882 COVID-19 tests, equivalent to 293 tests per million population; in comparison, Ghana which had conducted 184 343 (5948 per million population) and South Africa had conducted 488 609 tests (8251 per million population).

In a study by Dan-Nwafor et al, reports that Nigeria mounted a swift and aggressive response to COVID-19, leveraging on its existing epidemic preparedness and learning from other parts of the globe where transmission began earlier. The country's initial response included early activation of the national EOC at the NCDC, establishment of the multi-sectoral COVID-19 Presidential Task Force (PTF), and decisive actions to stop international travel and impose a time-limited lockdown in highly affected areas. By rapidly implementing this set of interventions, Nigeria likely slowed down the rate of virus transmission and bought extra time to implement a robust case detection, testing, and enhanced capacity of treatment centres. However, these efforts, especially testing, needs more private sector involvement to significantly ramp up COVID-19 diagnostic centres across the country.

Systematic testing of target groups, contact tracing and isolation of confirmed disease cases, as well as improvements to the other existing basic public health measures (e.g., social distancing, hand washing and use of face mask) in the region, are required to better manage the pandemic. Due to uncertainties and disparities between the economies and health care systems of countries within the region, we conclude that country-level studies are necessary and will provide more insights into disease dynamics and control in the region.

Hémaho et al in a modelling study posited that systematic testing of target group, contact tracing and isolation of confirmed disease cases, as well as improvements to the other existing basic public health measures (e.g., social distancing, hand washing and use of face mask) in the region, are required to better manage the pandemic. Due to uncertainties and disparities between the economies and health care systems of countries within the region, they also concluded that country-level studies are necessary and will provide more insights into disease dynamics and control in the region. Amaechi et al concluded that due to socio-economic and broader peculiarities of Sub-Saharan African countries, social approaches that were effective elsewhere may have limited practicality in these contexts, and if implemented, they may yield different or even adverse results, and therefore to overcome these challenges, tailoring and adaptation of these measures to the different but unique contexts for maximum effectiveness, and investment in social insurance mechanisms, are vital.

Coughlin et al used models to describe the behaviour of COVID-19 prevalence at a national scale and to identify changes in national disease burden as relating to chronological changes in restrictive societal activity. They revealed that globally, social distancing measures may have been most effective in smaller countries with single governmental and public health organizational structures.
The presentations of COVID-19 in Nigeria were similar to other regions of the world; the ages of the patients ranged from 4 days to 98 years with a mean of 43.0(16.0) years. Of the patients who presented with symptoms, cough (19.3%) was the most common presenting symptom. This was followed by fever (13.7%) and difficulty in breathing, (10.9%). The most significant clinical predictor of death was the severity of symptoms and signs at presentation. Difficulty in breathing was the most significant symptom predictor of COVID-19 death (OR:19.26 95% CI 10.95-33.88). The case fatality rate was 4.3%. Primary care physicians and COVID-19 frontline workers should maintain a high index of suspicion and prioritize the care of patients presenting with these symptoms. Community members should be educated on such predictors and ensure that patients with these symptoms seek care early to reduce the risk of deaths associated with COVID-19.

A severe COVID-19 case in an adult, as stated in the Clinical Management Manual published by NCDC is characterized by fever (>38◦C) or suspected respiratory infection and one of respiratory rate >30 breaths/minute or severe respiratory distress or SpO_2 <90% on room air. The elderly and immunosuppressed patient may present with atypical symptoms. Patients with mild pneumonia may progress to the severe form of the disease and thus require close monitoring

Children with severe COVID-19 infection will typically present with cough or difficulty in breathing and at least one or more of the following: cyanosis or SpO_2 <92%, severe respiratory distress such as grunting, very severe chest in-drawing, signs of pneumonia with a general danger sign and inability to breast feed or drink, lethargy or unconsciousness or convulsion. Common complications include Hypoxemic Respiratory Failure (HRF) and Acute Respiratory Distress Syndrome (ARDS), sepsis and septic shock. Worsening respiratory distress is evidenced by failure of response to standard oxygen therapy (continuous increased work of breathing /hypoxemia despite oxygen delivery via a face mask with reservoir bag). Such a patient should be transferred to the ICU for further close monitoring and management.

A compendium of pharmaceutical treatment strategies for COVID-19 patients with a variable degree of illness and other therapies continue to generate global debate because currently, there is no cure for COVID-19 disease. A study indicated a broad awareness by clinicians of the various pharmaceutical agents being used but also indicated less awareness of drug interactions. A series of antiviral drugs that include remdesivir, Lopinavir and Ritonavir (some protease inhibitor drugs used in HIV management) are still being evaluated without significant evidence of their impact on the course of COVID-19 disease. Also, ivermectin, a known anti-parasitic drug is being projected as an effective anti-SARS CoV2 drug. This is also being evaluated through clinical trials in several regions across the globe that include, USA, Australia and Nigeria. Hydroxychloroquine was also initially identified as an effective drug in the management of the disease, but the consensus of the various articles is that the concern about the cardiovascular toxicity of the drug outweighs the possibility of minimal benefit. Drugs that boost immune status such as Zinc, vitamin C and vitamin D have become integral part of the management of the disease. However, there is a need to determine the effect of ingesting high doses of lipid soluble vitamins over a long period of time, given the existing caution about use of high doses of such vitamins.
Up-to-date, evidence-based guidelines for acute management of COVID-19 are imperative to guide clinicians through the rapidly evolving pandemic. As new evidence emerges, it is imperative that current and potential treatment options are frequently re-evaluated in order to offer the best possible care under such unprecedented circumstances.

While researchers continue to seek treatment and/or vaccine development strategies, there is a need to continue to use existing non-pharmaceutical interventions to prevent the spread of infection, which include but are not limited to regular cleaning and disinfection of surfaces, handwashing and sanitization, physical distancing, wearing a face mask, and imposing travel restrictions.

The management of COVID-19 disease is mostly supportive care with antipyretics, hydration, and oxygen supplementation, as dictated by clinical need. For patients with moderate to severe COVID-19 that require hospitalization, medical complications affecting various organ systems are not uncommon and may lead to critical illness and multiple organ failure. Hence, the medical care of patients with COVID-19 is best optimized by the collaboration among various health care providers from different specialties that include clinical expertise in hospital medicine, infectious diseases, clinical microbiology, radiology, pulmonary and critical care medicine, cardiology, haematology, and primary care. These are essential in ensuring that medical complications are prevented or treated early and aggressively.

There is a rapidly growing body of literature on this topic and hopefully it will help in finding an effective vaccine and the best practice for the management and treatment of symptomatic cases. Only when this pandemic ends, that one will be able to assess the health, social and economic impact of this global disaster and we should be able to learn lessons especially in terms of public and global health for any future similar pandemics

COVID-19 pandemic impacted all arms of the health care delivery system, primary, secondary and tertiary. A study of the Italian National Health Service during this pandemic by di Bidino et al revealed that it was associated with a reduced access to inpatient and outpatient services, with a lower volume of elective surgical procedure. In a study of the North-Central zonal blood service in Jos, Damulak et al revealed that there was reduction in blood drive fixtures, number of donors counselled, units screened, hospitals served, and the number of safe units issued. They also observed decline in number of donations, first-time donors repeat donations. But failed bleed, crude transfusion transmissible infections rate, and return expired units increased.

The pandemic has also increased the utilization of telehealth. Romanelli et al alerted to the crisis in learning health during this pandemic and researchers embedded within a large, integrated healthcare delivery system, with direct experience working with clinical and operational units in response to the COVID-19 pandemic, advocated for a Learning Health Network that promotes collaboration between health systems, community-based organizations, and government agencies, especially during public health emergencies as a necessary intervention to improve the healthcare delivery system. Similarly, concerns regarding transmission of infection have required medical schools to provide robust, easily accessible virtual education options, by development of new telehealth focused curriculum components within a short period.

The short-term impact of the COVID-19 disease, declared by WHO on March 11, 2020 as a pandemic, on the healthcare system, has placed hospitals in the fore front of the early detection, diagnosis, reporting, isolation, and clinical management of patients. This required the extensive involvement of hospitals in all aspects of health care delivery and psychological services, a similar situation in almost all nations and territories regardless of their development level or geographic location, although mitigation measures differ between developing and developed countries. There is well founded anticipation that the pandemic will have long term impact on healthcare systems.

Veranda et al in describing Portugal national health service, one of the most elderly population in the world, alerted that the impact of the pandemic is just unfolding and that it has all the elements of a recipe for disaster. They highlighted the weakened National Health Service, the result of a litany of policies and interventions by the 'Troika' (the European Commission, the European Central Bank and the International Monetary Fund); a health care delivery system focused on non-communicable diseases and long-term care; the growing public distrust in public services, compared to private hotel-like health care facilities. They noted that the pandemic has stimulated increased government spending on health care delivery, and this may avert the doom.

Aggarwal et al highlighted that China, Italy, France, Spain, Germany, United Kingdom, and USA are the worst affected countries, and these countries have robust health care systems but despite this there has been a huge shortage of health care facilities especially intensive care beds in these countries. India has different challenges as far as medical care during this pandemic is concerned. The need of the hour is to improve the health care system as a whole by setting up patients screening facilities, enhancing the number of hospital beds, setting up of dedicated high dependency units, intensive care units and operation theatres for COVID-19 positive patients.

COVID-19 produced massive disturbances in Brazilian urologists' practice, with major reductions in patient visits and surgical procedures. Distressing consequences were also observed on physicians' income, health and personal lives. These findings are probably applicable to other medical specialties.

There have been various psychosocial issues caused by the pandemic that will require psychosocial crisis prevention and intervention models to be urgently developed by the government, health care personnel and other stakeholders.

Kanu in his paper on COVID-19 and the economy: an African perspective, used Nigeria as a case study to highlight that COVID-19 has led to economic suffering in Nigeria, through loss of jobs and other incomes. As small and medium-sized enterprises are hammered by the lockdown, many workers have lost their jobs while many are working on reduced work schedules. He stated that the situation is gradually dragging the Nigerian economy deeper into recession. It is more challenging for Nigeria as she is still sluggishly grappling with recovery from the 2016 economic recession which was a fall out of global oil price crash and insufficient foreign exchange earnings to meet imports. The financial and corporate sectors in Nigeria are beginning to suffer deterioration. Markets have taken a big hit; financial systems are under stress and banks are likely to see huge pressures on their balance sheets. Private firms are hurt by the collapse in demand. This negative impact on the economy was also revealed in the study by Obi et al on the "The Socio-Economic Impact of Covid-19 on The Economic Activities of Selected States in Nigeria". In this study, they determined that the implication of their findings is that, if the lockdown policy continued another economic recession worse than that of 2016 in Nigeria is looming around the corners.

Governments will need to communicate their allocation plans effectively and transparently, aid the procurement and delivery of the vaccines to maintain the public trust, health professionals and the public when vaccine is available. Suspicion of government decision-making is evident during this pandemic and risks undermining careful planning. This is underscored by a recent global survey of acceptance of COVID-19 vaccines which identified increased acceptance in nations where respondents had higher levels of trust of their government.

Existing inequities have magnified the impact of this pandemic and this may be exacerbated by the inequitable allocation of vaccines. Canada's National Advisory Committee on Immunization (NACI) has developed preliminary recommendations for the efficient, effective and equitable allocation of safe, efficacious COVID-19 vaccines in the context of staggered arrival of vaccines. The Committee noted that efforts should be made to increase access to immunization services and engage racialized and systemically marginalized populations in immunization programme planning as well as ensuring the integration of equity, feasibility and acceptability considerations across all populations. There is evidence in support of the prioritization of the target population to receive COVID-19 vaccines. The benefits of the vaccines on the population in terms of the number of life-years gained is dependent on the life expectancy of the target population, the effectiveness of the vaccine in preventing infection and disease transmission, and the quantity of the vaccines available to cover the population to achieve herd immunity and these are critical for decisions regarding a COVID-19 immunization programme.

COVAX Facility AMC 92 Q&A Session of 10th and 11th December 2020 projected the estimate of US$7 per dose of vaccine. There is also the addition of international delivery, insurance, and procurement fee costs of US$$0.60 to $0.89 per dose; and each vaccinee requires 2 doses. Therefore, the cost of administering 2 doses vaccine to each individual is US$15.20 - $15.79. There is also the vaccine delivery programme cost of US$1.74 per dose, an estimate made by the COVAX delivery cost working group. Therefore, the total cost of immunizing an individual is $18.68 to $19.27. So far, the manufacturers of both Pfizer-BioNTech and AstraZeneca-Oxford have reached an agreement with COVAX facility. AstraZeneca-Oxford vaccine for US$7 per dose. The details of Pfizer agreement are not yet known.

A modelling study by Edejer et al, revealed that the sizeable costs of a COVID-19 response in the health sector will escalate, particularly if transmission increases. Instituting early and comprehensive measures to limit the further spread of the virus will conserve resources and sustain the response.

Vaccine availability is a topical issue as countries scrambled to have access to the vaccine that they invested in its production, placed orders or already started administering to their citizens.

5 Proposed Recommendation (s)/Options

1. **The first question posed to NGI-TAG is "Should the COVID-19 vaccines be introduced for use among targeted Nigerian populace?"**

NGI-TAG recommends that safe and efficacious COVID-19 vaccines should urgently be introduced into the country because there is an ongoing "second wave" of SARS CoV2 transmission in the country with a current surge in community transmission that is more than twice the peak of the first wave. The increasing need for hospitalization of cases of the disease is a major challenge for the fragile health system. In less than one year, the global community of researchers have produced various safe and efficacious vaccines in an unprecedented time. The introduction of the COVID-19 vaccine would reduce the severity of the disease and the high disease burden. The COVID-19 vaccine should complement non-pharmaceutical interventions for optimal control of the pandemic.

2. **The second question to NGI-TAG is "If so, which COVID-19 vaccines should the country introduce?"**

To date, only three vaccines, the Pfizer-BioNTech, Moderna and AstraZeneca-Oxford vaccines have been authorized by the WHO into the Emergency Use Listing (EUL). Based on the NGI-TAG ranking of the available COVID 19 vaccines on their safety, efficacy, cold chain requirements, cost per dose, global availability, and WHO EUL status, the NGI-TAG recommends that in the interim, FMoH and NPHCDA should **introduce Pfizer-BioNTech and/or Moderna and/or AstraZeneca-Oxford vaccines in Nigeria**. Given the global supply update on the limited number of doses of COVID-19 vaccines, the NGI-TAG recommends that **the three vaccines** stated can be introduced **concurrently**.

The recommended schedule for the vaccines are:
Pfizer-BioNTech vaccine – 2 doses at 21-day interval
Moderna vaccine – 2 doses at 28-day interval
AstraZeneca-Oxford vaccine – 2 doses at 4 – 12-week intervals, as longer intervals have been associated with better seroconversion.

The NGI-TAG takes special notice of pipeline vaccines with sufficient evidence of safety and efficacy that have received approval for use by respective National Regulatory Authorities (NRAs) of other countries such as Sputnik-V, Novavax and CoronaVac. Also of notice is the *Johnson and Johnson* vaccine still under evaluation, with a profile well suited for LMICs in terms of single dose efficacy and cold chain requirement. The NGI-TAG will closely monitor emerging evidence from independent reviews of these vaccines by Nigeria NRA (NAFDAC), African Vaccine Regulatory Forum (AVAREF), WHO, and other sources with a view to rapidly updating its recommendations.

3. **The third question posed to NGI-TAG IS "What groups should be prioritized to receive the vaccines first?"**

NGI-TAG recommendation on the prioritization of the target populations to receive COVID-19 vaccine is based on the epidemiology of the disease in Nigeria. The considerations include the most vulnerable to severe morbidity and mortality from the disease, and those who are inevitably exposed to the virus in the line of their essential public duties. Therefore NGI-TAG prioritization of vaccination is the following order:

1. COVID-19 health care frontline workers
2. Frontline health care workers
3. Individuals 50 years old and above
4. Individuals 16 years old and above with co-morbidities such as diabetes, hypertension, and Obesity
5. Frontline workers in other essential social services - the police, airport workers
6. Individuals living in IDP Camps
7. Other individuals 16 years and older

Pregnant women who are at high risk of exposure such as frontline workers and those living with co-morbidities should consult their health care provider to determine if the benefit of getting the vaccine outweighs the risk.

4. This pandemic has brought to the fore the painful loss of vaccine production capability of the country. Nigeria was previously involved in local vaccine production, specifically, the country produced yellow fever vaccine between 1949 to 1991 [37]. Nations are in a rush to acquire enough doses of vaccines for their citizens. The wealthy nations of the world have a clear advantage especially because the vaccines are being manufactured in their countries. Some countries participated in vaccine trials and this gave them an advantage to access the vaccines. The vaccines produced by some countries may not have achieved EUA, but the global community is advocating for a liberal sharing of research data and technology transfer so that more manufacturers can quickly become capable of augmenting the global vaccine demands. So, only countries with existing vaccine production capability will be in positions to leverage into the global vaccine production economy. Therefore, NGI-TAG strongly recommends that Nigeria should urgently invest hugely in local vaccine production.

5. With the on-going pandemic, it is expedient for the FMoH to engage stakeholders and relevant industries to strengthen research and development, and medical innovations. NGI-TAG therefore recommends a scale up of government support in these areas especially in the area of Immunology, vaccinology and related fields, phytopharmacology, virology, ecology and

medical interventions through capacity building, establishment of standardized laboratories, clinical trial centres, adequate planning of financial budget lines and release of funds at the appropriate time.

6 Annexes

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