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Authors: Akamu Ewunkem[1], Uchenna Iloghalu[2], Tiffany Muse[3]

Affiliations: Department of Biological Sciences, Winston Salem State University, 601 S Martin Luther King Jr Dr, Winston-Salem, NC 27110 USA[1], Department of Biology, North Carolina A and T State University, 1601 E Market St, Greensboro, NC 27411 USA[2], Department of Nursing, University of North Carolina at Greensboro, 1400 Spring Garden St, Greensboro, NC 27412 USA[3]

Orcid ids: 0000-0003-3441-9881[1]

Contact e-mail: ewunkemaj@wssu.edu

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COVID 19: Vaccines and Unvaccinated

An Overview of COVID-19 Pandemic: Emphasis on Vaccines and Unvaccinated

Akamu Ewunkem¹ Uchenna Iloghalu² Tiffany Muse³

¹ Department of Biological Sciences, Winston Salem State University, Winston Salem North Carolina, USA

² Department of Biology, North Carolina A and T State University, Greensboro, North Carolina, USA

³ Department of Nursing, University of North Carolina at Greensboro, Greensboro, North Carolina, USA

Correspondent Author: Akamu Jude

Email: ewunkemaj@wssu.edu
judeakamu@gmail.com

**Poster Address: Department of Biological Science
Winston Salem State University**

601 S Martin Luther King Jr Dr, Winston-Salem, NC 27110

Tel: 336-750-2201

Fax: 336-750-3094

Abstract

Since December 2019, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) (causing Coronavirus disease 2019” (COVID-19) has rapidly spread around the world and it is responsible for more than 187 million cases diagnosed and 5 million deaths. Health, education, and economic threats caused governments and institutions to take preventive measures against the spread of the disease. At the city levels the measures include shutdown of businesses such as cinemas and theaters, cancellation of other mass gatherings, school closure, closing workplace. At the individual level preventive and control measures include face masks, frequent hand washing, and getting vaccinated. Various platforms for vaccine development are available with each proven to be relatively safe and highly effective at preventing the infection and serious illness from COVID-19. However, a growing number of peoples around the world are reluctant to receive recommendations or expressing hesitancy. Vaccine hesitancy is defined as the delay in acceptance or refusal of vaccine despite availability of vaccine services. This review is aimed at providing an overview of COVID-19 with more emphasis on vaccines and vaccine hesitancy.

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Introduction

In late December 2019, the novel severe acute respiratory syndrome caused by coronavirus 2 (SARS-CoV-2) that broke out in China has developed into a threat against global health (1). The World Health Organization (WHO) declared the COVID-19 outbreak a public health emergency of international concern and on March 11, 2020, declared COVID-19 outbreak a global pandemic (2). More than 187 million confirmed cases diagnosed with COVID-19 and more than 4 million associated deaths have been counted around the globe by the end of 2021 (3).

As the number of cases of COVID-19 continues to soar globally, the status of the coronavirus outbreak is expeditiously moving from pandemic to endemic partly due to new mutations of the COVID-19 virus (4). Several new COVID-19 variants have surfaced regularly since the pandemic began making much of an impact. Face masks combined with other preventive measures such as frequent handwashing, physical distancing, avoidance of poorly ventilated areas and getting vaccinated can help curb the spread of the virus (5).

Globally, there are more than 125 vaccine candidates and 18 vaccines against COVID-19 approved by at least one country (6). These vaccines have been tested and authorized or approved for use globally to prevent COVID-19. Despite the availability of these vaccines, a high percentage of the public are still unenthusiastic to be immunized, which impedes the attainment of sufficient herd immunity to extinguish the pandemic and to impede the development of variants. Vaccine hesitancy is defined by the World Health Organization (WHO) as delay in acceptance or refusal of vaccination despite availability of vaccination services. This report aims to briefly review COVID-19 and evaluate COVID-19 vaccine hesitancy which will enable health institutions and stake holders have an unequivocal insight into hesitancy

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determinants in both the new world and less developed nations. Understanding vaccine hesitancy will assist global vaccination campaigns since it promotes vaccine acceptance.

The Genesis of COVID-19 and Impact

Coronavirus disease 2019 (COVID-19) is contagious disease caused by the most recently severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) (7-9). Coronavirus 2 was probably circulating undetected about 2 months in advance to the first human cases of COVID-19 in the city of Wuhan, China in December 2019 (10, 11). COVID-19 is known to affect different people in different ways. Infected individuals range from asymptomatic to mild respiratory infections to pneumonia (12). Others may experience a wide range of symptoms from mild symptoms to severe illness. The most common symptoms of COVID-19 are fever, dry cough, fatigue, myalgia, and occasional gastrointestinal disorders (13).

The world Health Organization declared COVID-19 outbreak a Public Health Emergency of International Concern on 30 January 2020 and a pandemic on 11 March 2020 due to more than 80, 000 confirmed cases reported worldwide (14). As of December 30, 2021, authorities in 223 countries and territories have reported more than 285 million cases and 5.42 million deaths, making it one of the deadliest in history (3). The United States, India and Brazil remain the worst-hit countries.

COVID-19 Transmission and Various Variants

Transmission of SARS-CoV-2 occurs primarily through inhalation or ingestions of droplets by coughing, sneezing, and touching infected surfaces (15, 16). The greatest risk of transmission occurs mainly among people who spent at least 10 minutes within 6 feet of each other (17). Preventive measures to reduce transmission include staying at home, wearing face masks, maintaining a distance of at least 6 feet from others, and getting vaccinated (18).

The emergence of viral variants (due to mutations) continues with rapid change and notably higher transmission rates. These variants are known to cause global concern (19)). Currently five major variants have been identified and spread across the world. The earliest variant Alpha (B.1.1.7) was identified in the UK in September 2020. The Alpha variant in comparison with 7 spike protein mutations, was classified as a variant of concern by the CDC in December 2020 (20). The Beta variant (B.1.351) was first identified in South Africa in May 2020 and was known to be associated with an increase in hospitalization and deaths during the second wave in South Africa due to 9 spike protein mutations (21). The Gamma variant (P.1) was first detected in Brazil, and it is known to accumulate 12 spike protein mutations (22, 23). The Delta variant (B.1.617.2) was first detected in India in May 2021 (24). The Delta variant is associated with 17 spike protein mutations causing more severe illness and death (20, 25). The Lambda variant (C.37) was first reported in Peru in December 2020. The Lambda variant which is known to have 19 mutations in the spike protein is spreading in some South American countries (26). There are other variants with a fewer number of spike protein mutations and are shown to cause mild illnesses. These variants include the following: the Eta (B.1.525) variant, first identified in Nigeria in December of 2020; the Epsilon (B.1.427/B.1.429) variant, first identified in the USA in September of 2020 ; the Theta (P.3) variant, first identified in the Philippines in January of 2021; the Kappa (B.1.617.1) variant was, first identified in India in December of 2020; the Iota (B.1.526) variant, first identified in the USA in December of 2020; the Zeta (P.2) variant, first identified in Brazil in January of 2021 (20, 27-32).

The Omicron variant (B.1.1.529) is the notorious newest variant identified in South Africa on 24 November 2021 (33). The omicron has hit hard different nations around the world. The United States of America is the worst hit nation with an average of more than 900,000 new

infections and 2,000 deaths everyday (7). Recent data from Johns Hopkins University showed that 900,832 new covid-19 infections and 2,615 deaths by omicron were registered on January 7, 2022, in the United States of America (7). On November 26, 2021, the WHO declared Omicron a variant of concern. The Omicron variant has a numerous mutation (36 mutations) in the spike protein and has almost exclusively dominated and is more highly transmissible than the Delta variant (B.1.617.2) (34). Omicron also has the potential to escape infection or antibody neutralization by the BNT162b2 messenger RNA vaccine (Pfizer–BioNTech) (34, 35). Yet another strain that combines characteristics of both Delta and Omicron was detected in Cyprus on January 9, 2022, by a Cypriot scientist (36). For being the combination of both Delta and Omicron, this new variant has been named 'Deltacron', Not much is known about this variant. However, it is worthy is note that 'Deltacron' is for the most part detected in hospitalized patients and few cases in vaccinated people.

COVID-19 Prevention

To slow the spread of the ongoing pandemic, COVID-19 governments and WHO took actions and published recommendations pronto. Everyone was admonished to practice "social distancing" measures (approximately 6 feet) and ventilation in confined spaces (37). Social distancing reduces physical interaction between people and reduces the potential cross-transmission of virus-carrying droplets from human respiration (38). Multiple studies provide strong evidence demonstrating that improving ventilation is known to reduce the risk of infection or virus spreading indoors (39-42)). Ventilation and social distancing are not standalone measures. These measures should be implemented as part of a comprehensive package of measures which include the following: avoiding crowds; wearing a face mask, staying at home if sick or having flu-like symptoms; the practice of hand washing at regular interval; coughing or sneezing into a bent elbow, and vaccination. Face masks can protect against both coarser droplet

and finer aerosol transmission (43). Staying at home if unwell is very important because studies have shown that patients infected with SARS-CoV-2 are able to introduce continual shedding of the virus through touching surfaces and coughing within a couple of hours (44-46). Hand washing with soap or the frequent use of hand sanitizer is an effective way to destroy and dislodge many microbes through denaturation (47). The risk of COVID-19 spread also increases where there is large gathering because crowds are a source of transmission in the COVID-19 spread (48). Covering the mouth and nose with a flexed elbow when coughing and sneezing prevent effectively prevent the spread of respiratory germs (49).

Vaccines are one of the most effective ways to limit the spread of COVID-19 infections and has become a beacon for hope for normal life to return (50,51). Vaccines generally are tailored made to a strain and may require years to be developed (52, 53). However, lessons from previous efforts have enabled scientists shortened developmental time which is a remarkable accomplishment (54,55).

Many efforts are directed toward the development of efficacious vaccines against COVID-19 (56)). About 102 candidate vaccines were in clinical development. The World Health Organization (WHO) has approved the 10 vaccines to avert the pandemic. The 10 authorized vaccines were as follows: Novavax: NVX-CoV2373, Serum Institute of India: COVOVAX (Novavax formulation), Moderna: mRNA-1273, Pfizer/BioNTech: BNT162b2, Janssen (Johnson & Johnson): Ad26.COV2. S, Oxford/AstraZeneca: AZD1222, Serum Institute of India: Covishield (Oxford/AstraZeneca formulation), Bharat Biotech: Covaxin, Sinopharm (Beijing): BBIBP-CorV (Vero Cells) and Sinovac: CoronaVac (57,58).

These vaccines were developed based on different technological platforms including traditional platforms (inactivated and live attenuated virus vaccines), and newly established

platforms (replicating and non-replicating viral vector vaccines, nucleic acid (DNA and RNA) vaccines, recombinant subunit vaccines, and peptide-based/virus-like particles vaccines) (59,60). The inactivated vaccines are typically propagated by inactivating the virus through physical and chemical means (61). Inactivated vaccines against COVID-19 are generally safe due to their low incidence of self-reporting adverse reactions and has the capability to induce antibody responses in adults 18–59 years of age (62,63). However, inactivated vaccines are associated with fatigue, muscle pain, headache and/or dizziness (64)). Live attenuated vaccines embodied a weakened (or attenuated) form of the virus that causes a disease (65). Live attenuated vaccines are effective immunization approaches to elicit immune response due to their relatively low productions and delivery costs and their ability to replicate and propagate within host (66). However, there are some concerns regarding adverse effects such as viral shedding into the into the environment, posing a potential risk to the unvaccinated community (67). Other adverse reactions include the presence of attenuated vaccine strains in the nasal cavity, induction of cytokine storm olfactory dysfunction and thrombosis (68,69). Viral vector vaccines utilize modified version of a virus (such as adenoviruses or poxviruses as the vector to deliver the genetic material coding for a viral) different from the virus being targeted to deliver important instructions to cells (70). The remarkable advantage of viral vector vaccines is associated with expression of viral antigens within infected host cells, high gene transduction efficiency, high specificity of genes delivered to target cells, and efficient immune response with increased cellular response (71,72). Despite their efficacy, viral vectors present unavoidable problems that need to be addressed. The most common adverse reactions associated with viral vector vaccines are fever, pneumonia, diarrhea, transient neutropenia and lymphopenia, fatigue, labored breathing, headaches, liver damage, cancer fasting hyperglycemia and neuropathies (73,74). Nucleic Acid (DNA and RNA)-Based

Vaccines are the most recent and cost-effective developments in the biomedical field that provides the cells with a blueprint to construct the protein by host cells to elicit humoral and cell-mediated immunity through production of neutralizing antibodies and cytotoxic T lymphocytes (75,76). The nucleic acid-based vaccines display myriad advantages, such as activation of broad immune responses without replication of the virus, efficient large-scale, low-cost, production and high storage stability (77-79). However, there are some barriers to nucleic acid-based vaccines applications. DNA vaccines low immunogenicity profiles impede the desired clinical application and induces antibody production against DNA. The vaccine has the potential risk of integration into the host genome which may cause cells to become cancerous (80,81). Several laboratories are now testing the virus-like-particles (VLP) platform as a SARS-CoV-2 vaccination approach.

VLPs are exploited as an alternative to traditional vaccines because they utilize a highly purified viral protein antigen (non-infectious) produced in various expression systems such as prokaryotic cells, yeast, insect cell lines, plants, and mammalian cell lines to elicit an immune response (Latham & Galarza, 2001(82-85). VLPs are relatively safe compared to the inactivated or attenuated viruses because a potential incomplete inactivation and reversion of the virus are avoided (53)). Another advantage of these vaccines is their self-adjuvating properties (86). Potential challenges associated with VLPs are risk of genomic integration, difficulty in administration, uncertainty of host cell components and the production of optimal quality, stability, and good immunogenicity at high yield (87).

Plant-based vaccines are one of the available methods in vaccine developments (88)). Plant-based vaccines are generated through the expression of antigenic materials within the plants or algae inducing active immunity or expressing the antibody against coronavirus to provide passive protection. Plant-derived vaccines offer some attractive advantages: they are less

expensive to produce; cause little or no adverse effect on humans; they are environmentally friendly; they are relatively safe and can be used for oral delivery (89,90). However, plant-based vaccines have several challenges which include uncertainty of efficient modifications such as glycosylation, methylation, polymerization, quantity and quality of recombinant proteins, and dosage of vaccines in tissues (91).

Vaccine hesitancy

To bring this pandemic to an end, a large share of the world needs to be immune to the virus. Approximately 11 billion doses can vaccinate 70% of the world's population to achieve herd immunity globally (92). As of January 4, 2022, more than 9.25 billion doses have been administered across 184 countries. About 58.5% of the world population has received at least one dose of an approved vaccine (93). Many governments in the world are relentlessly working to obtain sufficient vaccine supplies and speed up vaccination for the public (30).

Current data suggests that about 27% of people who have received at least one dose of a coronavirus vaccine are from high developed nations, typically from Europe and North America (94). The fastest vaccine rollouts are achieved by high income countries such as Israel, United Arab Emirates, United Kingdom, United States, Bahrain and Chile (95). Two factors affect the differences in vaccination coverage. The first factor is date of vaccination campaigns. For example, United Kingdom and the United States started community vaccination on 8 December 2020 and December 14, 2020, respectively (95). China approved its first COVID-19 vaccines in June 2020 and started administering doses in January 2021 (96). The second factor is the rate of vaccination rollout over time. Vaccination rollout in Israel started in December 2020 and Israel has maintained a consistently high rate of vaccinations over time (97).

COVID-19 vaccines are not distributed equally. Wealthy countries have fully vaccinated about 65% of their populations while in low-income countries, fewer than 3% of people have

been vaccinated (98). Majority of the people in poor countries are not immunized against Covid-19 because they rely on a vaccine-sharing arrangement called Covax. Covax is a WHO-backed program that purchases vaccines for poor nations (99)). As of March 2020, Covax has enabled the shipment of about 2 million doses to 29 countries, marking the beginning of the largest vaccine roll-out in history (100). However, wealthy nations keep purchasing more and more doses. Millions of excess doses soon -to -expire have been given to some poor nations. Unfortunately, poor nations still struggle to get them into people's arms, as they grapple with the potential delivery of the vaccines. Governments in poor nations also may lack the wherewithal to conduct public awareness campaigns and set up more vaccination sites, including the necessary fridges and freezers to store the shots. Misinformation and low case numbers have also left many in poor countries skeptical of the shots. Hordes of people in less developed nations delay or refuse recommended vaccines for themselves or their children (101). Delay response activities by government is also associated with vaccine hesitancy. Not much was done by these governments to debunk theories on social and traditional media that the African continent was "immune" to COVID-19 due to the climatic conditions (102). The cost of vaccines and vaccination is a challenge, as very few are offered free or as part of the national immunization programs (103).

Despite the ready availability of Covid vaccines in wealthy nations, some individuals who are eligible for shots choose not to get them, vaccine hesitancy. Vaccine hesitancy is defined as a delay in acceptance or refusal of vaccines despite availability of vaccination services (104). Vaccine hesitancy entails a mix of cultural, historical influences, gender, socioeconomic, politics, and geographic barriers (104,105). A rise in vaccine hesitancy is linked to loss of trust is associated with social media (106,107). Lack of trust in COVID-19 vaccine safety and distrust in

government or the medical industry are among a long list of factors that also play a role. Hesitant individuals believe that the process for the vaccines was too fast and the institutions that devolved the vaccines are not trustworthy. In the United States pre-existing conditions are the root of the disparities in reference to COVID-19. Blacks are also more likely to suffered from pre-existing conditions (108). Studies have shown that the mortality rate for Blacks is 2.4 times higher than that of whites and about 50,000 African Americans have died from COVID-19 (109). Yet African Americans have nearly the lowest rates of vaccination among any ethnic group for a plethora of reasons. Some African Americans report lower level of trust in the health care system most notably, due to the infamous 40-year-long Tuskegee study, the Henrietta Lacks case and other examples of how Blacks have been treated, and many cases still are treated (110, 111). Vaccine hesitancy in Hispanics like the African Americans was associated with medical mistrust and history of racial discrimination (112). Also, the United States of America is increasingly divided into two starkly different camps: those who refuse to get vaccinated against COVID and those are vaccinated. Political polarization impedes vaccination against COVID-19 vaccine with Republicans became increasingly vaccine hesitant (113).

Among factors contributing to vaccine hesitancy, concerns of side effects associated with COVID-19 vaccines play a major role (114). The vaccines are known to cause deadly unwanted effects. Those who have taken the COVID-19 vaccine have experienced fatigue, muscle pain, blood clots, combinations of thrombosis and thrombocytopenia, bleeding and disseminated intravascular coagulation (115). Health care professionals play a major role in promoting COVID-19 vaccination because they are required to provide information and thus build confidence. A recent peer reviewed survey of health care workers in the US showed that 18% of health care workers did not plan on receiving a COVID-19 vaccine because of concerns over

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adverse effects associated with the vaccines (116). In Europe, thousands of health care workers refused to take COVID-19 vaccine over concern of about side effects (117). In Asia and Pacific Islands less than 5% of the health care workers survey were not willing to take the COVID-19 vaccine (118). In the Middle East, about 60% of participants were hesitant to get the COVID-19 vaccine. The most common reasons for hesitancy were lack of information and fear of side effects (119).

Religious conservatism which includes evangelical and born-again Christianity is positively associated with anti-vaccine attitudes and higher levels of vaccine hesitancy (120, 121). A recent survey showed that about 22% white evangelical Christians say they will not get vaccinated which could be due to conspiratorial, anti-science political views (122). Some evangelicals proclaimed that the Covid-19 vaccine is the “mark of the beast”—a sign of the end times and a symbol of alignment with the Antichrist. (123). This is apocalyptic phrase that comes from the New Testament Book of Revelation (Revelation 13: 16-18). The "mark of the beast signals an allegiance to Satan or those who reject God's memorial of creatorship. This phobia has caused some Christians to request religious exemptions from vaccine mandates (124). The notion of the mark of the beast is also conflated with the believe that Bill Gates uses the vaccine as a pretext to implant microchips into people (125)). Some Christians strongly believe that the solution to crisis on is not based on take behavioral precautions like handwashing, mask-wearing, social distancing, or vaccination but rather to become more religious i.e., attending religious services and the repenting of national sins (121). Also, they assert that the religious belief in God is more superior than any kind of research or learning, as it is unequivocally chronicled in the Old Testament Book of Isaiah, “fear not God will take care of you”.... (Isaiah 42:10).

Many people around the world have turned to natural remedies to fight COVID-19 even as nations begin to roll out vaccine programs. Some adhere to traditional treatments, especially in less developing nations, amid surge in the cases. Proponents of these treatments have been sharing posts and videos questioning the wisdom of vaccinating against the coronavirus., Conspiracy beliefs predicted support for chloroquine as a treatment for COVID-19. Interestingly, none of the conspiracy beliefs referred to the dangers of the vaccines (126). Some consumers are turning to drugs not approved or authorized by WHO such as antimalarials hydroxychloroquine (HCQ) and chloroquine (CQ) which have demonstrated antiviral activity against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) (Yao et al., 2020(127)).

Summary

The coronavirus 2 (SARS-CoV-2) first reported in December 2019 in the Wuhan city of China is continuing to spread around the world, with more than 300 million confirmed cases and more than 4 million deaths. The best preventive measures include wearing face masks, hand washings, avoiding crowd and getting vaccinated. Despite evidence that vaccines are highly effective at preventing both infection and serious illnesses associated with COVID-19, a large segment of the population around the world continues to express hesitancy. We may continue to leave with coronavirus for a longtime as new variants of the virus are expected to occur.

Conflict of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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