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MINI-REVIEW

COVID-19 vaccine hesitancy: Considerations for reluctance and improving vaccine uptake

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ABSTRACT

The emergence of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2; COVID-19) pandemic during the fall of 2019 led to the rapid development of vaccines aimed at curbing viral infection, spread, and its potential eradication. A recent trend is an overall increase in vaccine hesitancy, leading to the World Health Organization citing this as a problem which needs to be addressed. With the development and approval of vaccines for COVID-19, this trend has quickened, leading to potential negative ramifications in the ability controlling COVID-19 spread. Here we describe reported examples in overall vaccine hesitancy prior to the emergence of COVID-19, as well as summarizing recent reports on vaccine hesitancy related to COVID-19 vaccines. Gaining a better understanding of the reasons individuals have, as well as potential methods for decreasing hesitancy in the future, will hopefully lead to a greater percentage of vaccinated individuals and aid in ending the current pandemic.

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Introduction

The emergence of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2; COVID-19) pandemic during the fall of 2019 led to the rapid spread of COVID-19 infections worldwide. The resulting numbers of severe cases and hospitalizations placed massive strain on local, regional, and worldwide health systems. Almost immediately, world leaders in Government and the Health Care Industry called for the rapid development, testing, and implementation of COVID-19 vaccines aimed at curbing viral infection, spread, and potentially its eventual eradication. Although the vaccines have been effective in decreasing infection rates of early strains, along with the morbidity and mortality of more recent variants such as Omicron, they have been met with high levels of hesitancy.

Current COVID-19 vaccine statistics

As of March 14th, 2022, approximately 63.8% of the world population has received at least one dose of a COVID-19 vaccine.[1] This equates to approximately 10.94 billion doses. A general trend is that urban and suburban counties have higher vaccinations than rural counties. The percentages of fully vaccinated individuals are higher based on age, with a higher percentage of older individuals being fully vaccinated (including having received a booster) than younger people. Additionally, the number of vaccine doses administered to upper middle and high income individuals is vastly higher than those in lower-middle and low income brackets.[1] This data follows the trends from early surveys regarding vaccine hesitancy.

In terms of efficacy of the COVID-19 vaccines, the United States Centers for Disease Control and Prevention reports a vaccine efficacy against symptomatic infection of 93.5% against Delta variant, and a 67% vaccine effectiveness against symptomatic infection for the Omicron variant when compared to unvaccinated individuals. In terms of hospitalizations, full vaccination (three doses of mRNA-based vaccine) was 94% effective vs. Delta and 90% effective vs Omicron when compared to non-vaccinated individuals.[2] As of January 1st, 2022, the United States death rate per 100,000 population of fully vaccinated individuals (including boosters) was .45 while the unvaccinated death rate was 12.06.[3] COVID-19 vaccine side effects have also been reported, with very low rates. Anaphylaxis, a severe type of allergic reaction that can occur after any type of vaccination, has occurred in approximately five people per million vaccinated in the United States.[4] Thrombosis with thrombocytopenia syndrome (TTS) after Johnson & Johnson's Janssen (J&J/Janssen) COVID-19 Vaccination was found in 59 cases in more than 18.4 million doses, and only 4 cases have been reported in the 535 million doses of mRNA COVID-19 vaccines as of 3 March 2022.[4] 305 preliminary reports of Guillain-Barré Syndrome have been reported from the 18.4 million J&J/Janssen COVID-19 vaccination, largely in men over age 50 years and older. Myocarditis, inflammation of the heart muscle, and pericarditis, inflammation of the outer lining of the heart, after COVID-19 vaccination, as of 3 March 2022, have been reported in 2,282 individuals, with most cases having been reported after receiving mRNA based vaccines, and most commonly in males under 30 years of age.[4] Finally, out of the 555 million doses, 12,989 preliminary reports of death were reported among people who received a COVID-19 vaccine (.0023%); however these are not specifically tied to the vaccine administration.[4]

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Vaccine hesitancy

Despite the success of vaccines preventing and reducing transmission of a number of pathogenic diseases, such as smallpox and polio,[5–9] hesitancy and resistance toward vaccination is not a new phenomenon.[10–18] Vaccine hesitancy is described as a "delay in acceptance or refusal of vaccines despite availability of vaccination services".[19] A multitude of factors have been identified as contributing to the hesitancy of vaccine uptake, including contextual influences, individual and group influences, as well as vaccine/vaccination-specific issues.[19] Due to this complexity, recognizing and addressing vaccine hesitancy are not always straightforward, as the decision of a person to vaccinate themselves or their child is multifactorial.[15,19,20]

Despite extensive data documenting vaccine safety,[21] recent studies demonstrate that concerns over serious side effects and overall vaccine safety are major factors influencing the uptake of both routine vaccinations and annual influenza vaccinations.[13,22,23] In addition, the fear of needles and/or blood has also been identified as a factor for refusing a vaccine.[23,24] Safety concerns have also been identified due to individuals potentially having an allergic reaction to a vaccine component or prior negative experiences with respect to vaccinations.[23] Vaccine schedules, costs, and reliability also factor into the decision regarding vaccine uptake.[19]

Another common influence on individuals' decisions regarding vaccines was based upon religious thought. While major religious leaders typically support vaccines in principal, another factor influencing vaccine hesitancy is based on personal religious affiliations, with religious and ethical based objections to vaccination dating as far back as the late 1700s.[25] Religious-based vaccine hesitancy has been a noted factor in the outbreak of vaccine-preventable diseases affecting religious communities and settings.[25,26] A recent study found that US clergy from multiple religions have complex attitudes toward vaccines and the promotion of vaccines within their congregations.[26] Concerns over the use of blood components, pharmaceutical excipients of porcine or bovine origin, and cell-culture media or media constituents of fetal origin are all factors associated with religion-based hesitancy.[25,26]

Other contextual influences also must be considered in terms of vaccine hesitancy, including historical, sociocultural, environmental, health system/institutional, economic, and political factors.[19] A common theme of philosophical exemption is rooted in the basis of personal belief. These beliefs are often shaped by the media, government, political leaders and policies, geographical barriers, as well as the perception of the pharmaceutical industry. Philosophical resistance to vaccines and vaccinations has been reported since the first vaccine mandate for smallpox in the 1850s and can reasonably be considered the beginning of the anti-vaccination movement.[12] One of the main reasons for such a movement was due to the mandate requiring the vaccination of children up to fourteen years old. If parents had not abided by such mandates, they were subject to fines and imprisonment, which spurred social unrest.[27]

Hesitancy toward vaccination is profoundly concerning as the emergence of vaccine resistance and antivaccination movements has accompanied the increase in incidence of some communicable diseases.[24] Measles, for example, was once considered eradicated in the US due to vaccination efforts that became available during the 1960s.[28] However, in 2011, a significant increase in cases was reported and was determined to be mainly due to unvaccinated individuals who traveled outside of the US, contracting it while abroad.[12] In addition, measles cases increased considerably again in January 2019 with over 700 cases having been reported, with roughly 70% of those cases in unvaccinated individuals.[29] Examples of vaccine preventable disease outbreaks such as these raises concerns for the safety of public health at large, both in the US and globally.

It is critical to note that being vaccine hesitant and being against vaccinations in general are not the same. Determinants for vaccine refusal and hesitancy include modifying factors, such as age, gender, ethnicity, and other demographic variables, along with individual beliefs such as perceived susceptibility to and severity of the disease, along with the perceived benefits and barriers of vaccination all playing a prominent role.[30,31] Thus, it is imperative to continuously reexamine motives for vaccine hesitancy, especially as new vaccines and vaccine technologies are introduced, in an attempt to reduce vaccine hesitancy for the health of our communities. In this narrative review, our aim was to examine and describe factors influencing COVID-19 vaccine hesitancy, mainly in the context of the United States, with a purpose of providing a summary of information on factors driving COVID-19 vaccine refusal.

Materials and methods

Search strategy

Literature searches were conducted between October 13th, 2021 and November 15th, 2021 to have a more comprehensive understanding of the focused research topic. Published papers in PubMed/Medline that aimed at evaluating COVID-19 vaccine hesitancy and vaccine acceptance were eligible for inclusion. Only studies in English language that met the inclusion criteria were considered in this review. The inclusion criteria were: 1) peer-reviewed published articles indexed in PubMed; 2) the major aim of the study was to evaluate COVID-19 vaccine acceptance or hesitancy; and 3) the publication language was English. Exclusion criteria were 1) unpublished manuscripts; 2) the article did not aim to evaluate COVID-19 vaccine acceptance/hesitancy; and 3) the publication language was not English. Searches were conducted using the following terms: (COVID-19 * vaccine [Title/Abstract]) OR (COVID-19 * vaccine * hesitancy [Title/Abstract]) OR (COVID-19 * vaccine * acceptance [Title/Abstract]) OR (Vaccine * hesitancy [Title/Abstract]). Original studies and reviews focusing on vaccine acceptance, willingness, hesitancy, or intention regarding the COVID-19 vaccine were examined independently by all authors (K.P., K.G., and B.A.C.), followed by a summarizing of the main points from each publication and providing a collective narrative of conclusions.

Hesitancy toward COVID-19 vaccines

Demographic variance

The development of vaccines aimed at preventing COVID-19 infection began with numerous announcements of clinical trial data in November 2020, with federal and regulatory approvals in early December of 2020. In the United States, Operation Warp Speed aimed at delivering more than 300 million doses of COVID-19 vaccines by January 2021. Numerous studies began to examine the acceptance of the novel vaccines in order to determine the likelihood of individuals to become vaccinated.[32–43] Generally, results show that from 50–76% of those surveyed would likely become vaccinated, with approximately 15–30% unsure, and between 7 and 20% reporting they would not become vaccinated.[33,35,41–43] There were numerous demographic factors which seemed to play a role in the acceptance or hesitancy toward vaccination. The older a person is, the more likely they are to uptake the COVID-19 vaccine.[33,40,41] In addition, lower levels of education and/or income were associated with higher rates of hesitancy.[35,40,41] While higher levels of education are reported to decrease vaccine hesitancy, a study surveying medical students found that 23% were unwilling to take the COVID-19 vaccine immediately upon FDA approval; however, 53% of those surveyed did indicate they would take part in a COVID-19 vaccine trial.[37] Ethnicity and race were also listed as a contributing factor, with vaccine hesitancy higher among Blacks and Hispanics.[33,35,36,38,39,41] Additional demographic factors that have been reported to influence COVID-19 vaccine hesitancy include gender, perceived health status and comorbidities, religion, political affiliation, rural vs urban dwelling, and having children at home.[32–43]

It is important to note that the hesitancy toward vaccination is very much dependent upon several unique elements, including spatial-temporal factors, demographic groups and subgroups, as well as in a vaccine-specific context. A recent study investigating the role of health beliefs and prior vaccine hesitancy in US mothers' intentions to vaccinate against COVID-19 found that a mother's previous attitudes toward vaccinations did not fully capture their willingness to accept the COVID-19 vaccine or the perception of COVID-19 threat.[43] A similar study conducted in Italy found that parents of children with high average vaccination rates had a vaccine acceptance rate of just above 26%.[42] These studies highlight the importance of investigating and understanding the variations that likely exist, even across similar populations in regards to vaccine hesitancy now, and in the future.

COVID-19 vaccine safety and efficacy

By far one of the most common reasons among vaccine-hesitant individuals is the perceived safety of the vaccines.[37,44,45] COVID-19 vaccines were the fastest vaccines ever to be developed, and with this comes the connotation of rushed vaccine development and trials, which has led many individuals to become skeptical of the safety of the vaccine. In addition, the novelty of the mRNA-based technology for many of the COVID-19 vaccines has increased these concerns.[44–47] A study by Pogue et al. (2020) found that as the amount of time the COVID-19 vaccines spent in clinical trials increased, the higher likelihood individuals would uptake the vaccine, with the same holding true when asked about their willingness to vaccinate their children.[44] Increased testing and decreased side effects were also associated with an increased likelihood to vaccinate. General vaccine avoidance[45]along with general fears of injections can explain only a fraction of individuals not uptaking a COVID-19 vaccine.[46] Furthermore, the efficacy and length of immunity were also stated to have an influence on vaccine hesitancy, with increases in both the efficacy and immunity (as indicated by the need for boosters) ameliorated some of the fears or hesitancy associated with the vaccine.[44] Several of these studies have also found that the risk of side effects affects the rate of vaccination for COVID-19. While the Centers for Disease Control and the US Food and Drug Administration continuously monitor the safety of the COVID-19 vaccines, the potential of unknown risk(s) surrounding novel vaccines, especially when considering a novel technology such as mRNA based vaccines, are strong determinants toward vaccine hesitancy. Furthermore, the reporting of side effects with differential incidence rates among age groups (such as a higher incidence of TTS and pericarditis in younger individuals,[4] poses the need for further discussion on the risk-benefit balance of the vaccine.

Government and health official mistrust

As reported by Coustasse et al. (2021),[33] many individuals are skeptical about the information provided by the government and health organizations regarding COVID-19 and the new vaccines. Mistrust in the development of vaccines, as well as rates of misinformation have led to an increase in vaccine hesitancy among the general public.[37] Race and ethnicity have been reported to play a fairly significant role in the COVID-19 vaccine hesitancy due to mistrust in the health system in general.[36,38,39,48,49] According to Willis et al.[49] "Distrust of the medical establishment by Black/African Americans is often traced back to the Tuskegee syphilis study, but the distrust is deeply rooted beyond a single incident and is predicated on centuries of racist exploitation by medical researchers and doctors. Racism within the medical establishment is ongoing, and Black/African Americans do not need an extensive knowledge of the history of medical racism to inform their view of vaccines when many only need to consider recent experiences." In addition, it is reported that misinformation and information disputes among higher officials also lead to a higher sense of mistrust among Blacks toward the healthcare system.[39] Additionally, combining the exploitation and prior fears, vaccine mistrust seems far more prominent than vaccine hesitancy among the black population.

Decreasing COVID-19 vaccine hesitancy

While its likely most individuals think of COVID-19 as a global problem, a large number remain hesitant toward vaccines against it. The development of efficacious and safe vaccines is an enormous challenge and doing so quickly amid a pandemic only adds to the issue. Hesitancy toward these vaccines adds unique challenges that must be overcome. It is critical for

health care professionals to provide consistent and accurate messaging to individuals regarding the need and safety of the COVID-19 vaccines.[33] Additionally, governmental and health care officials must provide transparent, steady and dependable information, especially regarding the severity of the pandemic. In regard to vaccine safety, it is important to educate individuals on the function and benefits of vaccines. To do so it is important that governments and health care officials be unified in their message and promotion of the vaccine. Additionally, as it has shown that rural and low-income areas have higher levels of hesitancy, local leaders including religious leaders should promote vaccinations. Furthermore, specific efforts must be made toward racial and ethnic populations to ensure that individuals in highly hesitant groups have access to and trust the information regarding vaccination. Significance must be placed on the overall global, social and community good of vaccination against COVID-19 and the potential deleterious outcomes of remaining unvaccinated.

Conclusions

Vaccines have the potential to prevent disease and death from a number of viruses, including COVID-19. The hesitancy shown toward the COVID-19 vaccines is not a new concept, with a vast and varying number of reasons, and appropriate measures need to be taken to minimize it. The emergence of the highly transmissible variants, including Omicron, has led to an increased number of breakthrough cases among vaccinated individuals. Thus, it is important to continue to investigate individuals' reasons for COVID-19 vaccine hesitancy and find ways to promote vaccine uptake. While the vaccinations may not fully prevent the disease, a lessening of the severity, as well as decreases in the rates of hospitalizations and deaths in fully vaccinated (including boosters) individuals has been shown.[2,3,50,51] As the COVID-19 pandemic continues to place a stranglehold on health care systems, as well as local and global economies, it is crucial to understand the reasons for hesitancy in becoming vaccinated in order to provide critical information and increase vaccination rates worldwide.

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