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# Trust issues in vaccine uptake

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Three major vaccines for the prevention of novel 2019 coronavirus (COVID-19) have been approved for administration to patients in the United States via emergency use authorization [1-3]. These include two mRNA based vaccines, commonly known as the Pfizer (BNT162b2) and Moderna (mRNA-1273) vaccines along with the adenovirus vector based Janssen (Ad26.COV2·S) vaccines. The studies which evaluated the efficacy and safety of these vaccinations were conducted using patient populations of no fewer than 19,000 patients representing all major ethnic and racial groups from across the US. Additionally, enrollment in and progress of the vaccine studies was highly publicized. Despite this attempted demographic balance and the recent FDA approval of the Pfizer vaccine, there remains substantial hesitancy to receiving a COVID-19 vaccine throughout the US population. This hesitancy persists despite concerns about the ability of the US health care system to care for 'surges' of patients who are hospitalized due to acute COVID-19 pneumonia.

There are multiple causes for this lack of facility capacity which results from lack of physical or human infrastructure such ICU beds or clinical staff, but also commonly required and crucial items such as medications and disposable equipment. Supply chain systems both within the US and internationally have demonstrated substantial fragility in the manufacturing of chemicals and pharmaceuticals with resulting disruptions manifested during the COVID-19 pandemic [4]. Crisis standards of care have had to be implemented in various jurisdictions during the pandemic [5]. Additionally, surges in COVID-19 cases not only reduces treatment capacity for those infected with COVID-19, but have been shown to effect the mortality of patients who do not have a COVID-19 yet require hospitalization for another reason [6]. Prevention of COVID-19 infection with vaccination and pathogen hygiene appear to be the primary means to minimize the clinical burden of COVID-19 infection.

The World Health Organization has declared vaccine hesitancy a "major threat" to global health [7]. It is important to note that vaccine hesitancy is not unique to the new COVID-19 vaccines and in fact has been an ongoing concern for many years. The proliferation of social media, a medium which permits the immediate dissemination of uneditorialized content to a worldwide audience, has been credited with facilitating and sustaining the 'anti-vaccine' movement. In the US, political party affiliation, preferred sources of news and underlying state of health have been demonstrated to correlate with the likelihood of intent to be vaccinated for COVID-19 [8]. Additionally, conspiracy

theories pertaining to makeup and intention of the COVID-19 vaccines as well as the origins of the COVID-19 virus itself abound [9].

Cited as an effort to protect both patients and health care professionals, multiple health care facilities have begun requiring vaccination as a condition of employment, even though the Food and Drug Administration (FDA) has only granted an Emergency Use Authorization (EUA) for the Moderna and Janssen vaccines mentioned above [10]. The issuance of the EUA does not imply less diligence on the part of the FDA, but the long-term outcome studies commensurate to a traditional full FDA authorization have not been practically possible given the scope of the COVID-19 pandemic. While many facilities are allowing religious or health related exemptions, most hospital employees will have to either agree to be vaccinated or face termination of employment. Examples where this could be particularly challenging include pregnant women or members of historically marginalized minority communities which have a pre-existing distrust of the health care system. Nonetheless, transmission of COVID-19 from hospital employees to patients is known to occur and vaccination is an important tool to minimize this potential transmission, though transmission of COVID-19 by vaccinated individuals albeit as a much lower frequency [11]. An analogous approach has been taken for the influenza vaccine for many years, though it is fully FDA approved for use in the US. The power of the example of health care practitioners may play role in public acceptance of any of the COVID-19 vaccines; the fact that in some practices and countries, many healthcare team members are unwilling to get vaccinated may further stoke fears in the general population [12].

As multiple variants have emerged increasing the infectivity and immunogenicity of COVID-19 infection, the ramifications of any societal disparities in vaccine adoption are likely to become more pronounced. Potentially, the most effective mechanism to overcome misinformation obtained from rogue news, social media platforms, and antivaccination associates may be personal interactions with trusted friends and neighbors. Additionally, more intentional inclusion of individuals of multiple ethnic, cultural, and political backgrounds may allow penetration into subsections of society less inclined to be vaccinated. Clearly, setting realistic expectations about the potential protective effects of vaccination is also important, as any medical predictions of future COVID-19 trends that do not turn out to be accurate can serve to dissuade confidence in the US public health apparatus. Even with data supporting the administration of COVID-19 vaccines, well informed individuals may have an understandable hesitancy to receiving a vaccine product that has been so rapidly developed and deployed. Indeed, fear in general or various clinical scenarios such as pregnancy, previous negative experience

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with other vaccinations and additional factors may result in an intractable resistance to considering vaccination. In such instances, regular testing should be offered whenever logistically feasible while maintaining patient safety. Finally, it is important for the medical community to prepare to accept the significant possibility that a significant portion of the population may never consent to be being vaccinated; therefore, modeling of future public health plans should take that reality into account.

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