Review of: "[Viewpoint] Vaccination campaigns against Covid-19 may promote vaccine hesitancy toward well-established, safe, and effective vaccines"

Kenneth Lundstrom

Potential competing interests: No potential competing interests to declare.

COVID-19 Vaccination Hesitancy: The Real Reasons Behind It!

Kenneth Lundstrom

PanTherapeutics, Lutry, Switzerland

Abstract

The recent COVID-19 pandemic and its handling have obviously received enormous attention bringing out the best and the worst of human thinking and action. Although vaccines against various viral infections have proven successful in saving millions of lives globally, adverse events after mass vaccinations have raised concerns and triggered discussions over vaccine safety. Recently, Dr. Missoni and Dr. Sen called for better transparency from vaccine manufacturers and health authorities as a solution to tackle vaccine hesitancy. Although transparency is much welcome, it is difficult to envision it neither as the cause nor the main solution to reduce vaccine hesitancy. Certainly, the misguided and un-scientific anti-vaccine and anti-system campaigns spreading misinformation and disinformation play a more significant role. Therefore, sharing open, honest, and detailed information about vaccine development and manufacturing, and continuous sound data-based reporting of adverse events present the best ways to reduce vaccine hesitancy related to COVID-19 and emerging future viral infections.

Introduction

Since the outbreak of SARS.CoV-2 in December 2019 and the declaration of its pandemic status by the World Health Organization (WHO) in March 2020 intensive research and development of vaccines against SARS-CoV-2 have taken place applying different approaches including live attenuated vaccines, protein subunit vaccines, viral vector-based vaccines, and nucleic acid-based vaccines [1]. The rapid progress resulted in emergency use authorization (EUA) for vaccines based on mRNA and viral vectors leading to global mass vaccinations to tackle the pandemic [2, 3]. However, the high vaccine demand in an exceptionally short time raised some concerns related to vaccine safety and efficacy. Moreover, claims that untested novel mRNA vaccines are causing serious adverse events even deaths increased the uncertainty and resulted in hesitancy towards vaccinations. Recently, Eduardo Missoni and Kasturi Sen presented their view on hesitancy against promoting COVID-19 vaccines in a recent issue of Qeios [4]. Their message was that lack of transparency and potential conflicts of interest between authorities and the pharmaceutical industry are the main reasons for the mistrust seen among the general public leading to vaccine hesitancy. Although the speed and extent of the COVID-19 vaccine development has been unprecedented the procedure has followed accepted preclinical and clinical

guidelines. As in the case of a fire, where firefighters cannot first ensure that all fire extinction equipment and methods are optimal, we did not have the luxury of thoroughly testing the potential vaccines according to generally accepted timelines. However, it needs to be pointed out that mRNA-based vaccines considered by laymen as novel and dangerous, have been around since the 1990s with plenty of data from studies in animal models [5]. In the context of clinical evaluation, the process was significantly shortened by applying an overlapping strategy of phase I, II, and III clinical trials. Moreover, mass vaccine production was started while results from clinical evaluation were still not yet available [6]. Certainly. improvements are needed related to sharing raw data from clinical studies and from mass vaccination and the communication between governmental organizations, the pharmaceutical industry, and the general public could have been more transparent. However, the viewpoint of the authors is rather simplified, and they have missed a number of relevant factors associated with vaccine hesitancy. Below are described other relevant causes leading to hesitancy in supporting mass vaccinations against SARS-CoV-2.

The Good, The Bad and The Ugly

The human nature is keen to name heroes and villains associated with main global events and the COVID-19 pandemic is no exception. Particularly, in hindsight it is convenient to evaluate and judge who are the good, the bad, and the ugly and question why some drastic decisions such as lockdowns and mandatory vaccinations in some countries were introduced. Undoubtedly objective scientific evidence is overwhelming of the by far superior benefits of the current COVID-19 vaccines compared to their risks, which has been demonstrated in numerous studies and summarized in a recent review on non-communicable diseases (NCDs) and COVID-19 vaccines [7]. However, it is not surprising that adverse events have been reported as more than 13.5 billion COVID-19 vaccine doses have been administered to 70.5% of the world population (Coronavirus (COVID-19) Vaccinations - Our World in Data, https://ourworldindata.org/covid-vaccinations, accessed 5 October 20222). Human history has never seen mass vaccinations on such a scale. Despite that immunization with COVID-19 vaccines has resulted in significantly fewer adverse events and lower death rates than in unvaccinated individuals. Moreover, when evaluating vaccine-related adverse events, pre-existing conditions and comorbidities need to be taken into account [8].

The major points causing vaccine hesitancy according to Missoni and Sen comprise the limited vaccine safety assessments, transparency and potential conflicts of interest, and neglect of side effects [4]. Especially, the last point is quite surprising as a number of studies and reviews on adverse events have been published on NCDs [7], autoimmunity [9], vaccine-induced thrombotic thrombocytopenia (VITT) [10], congenital and genetic disorders [11], myocarditis [12], and in pediatric patients [13].

Moreover, a number of studies have been published on COVID-19 vaccine hesitancy [13-24]. For example, in a search based on publications conducted before July 17, 2021, the acceptance of COVID-19 vaccines showed a broad variation between 12 and 91.4% [14]. Factors affecting vaccine hesitancy included sex, age, race, education level, and income status. In the US, unwillingness to receive COVID-19 vaccines was higher in men and in the Black/American population. Moreover, pregnant and breastfeeding women showed a stronger vaccine hesitancy [14]. In China, the overall prevalence of COVID-19 vaccine hesitancy was only 8.40% for the first-dose vaccination and 8.39% for the booster vaccination based on a national study of 29,925 individuals [15]. Generally, the willingness to receive COVID-19 vaccines was higher among

women, persons with higher education, married individuals, persons in good health, non-smokers, and individuals taking care of their hygiene (washing hands, wearing masks, social distancing, etc.). Moreover, trust in medical doctors and disapproval of conspiracy theories are factors favoring COVID-19 vaccinations. Vaccination hesitancy has also been studied in youth [16]. In a study of 12-15 years old in Arkansas, US 42% showed no hesitancy towards COVID-19 vaccines, 22% were “a little hesitant”, 21% were “somewhat hesitant”, and 15% were “very hesitant” [16]. However, age, gender, race, and parental education did not present any statistical significance. In contrast, a statistically significant correlation between the hours of TV watching and vaccine hesitancy was discovered. In a global meta-analysis of 35 studies in 76,471 healthcare workers, vaccine hesitancy was broad, ranging from 4.3% to 72% [17]. The lowest vaccine hesitancy of 4.3% was recorded in China. In the US, 8-18% of vaccine hesitancy was observed. The largest vaccine hesitancy between 7% and 32.5% was seen in Europe being highest in France and Greece. Moreover, vaccine hesitancy is very high in Africa with 72% recorded in Congo. The meta-analysis also showed that male healthcare workers, persons of older age, and doctoral degree holders were less prone to oppose vaccinations.

A study of 4571 Norwegian adults identified COVID-19 vaccine hesitancy in males, residents in rural areas, and parents with children younger than 18 years of age [18]. Moreover, those who received vaccine-related information from peers, social media, online forums, blogs, and campaigns spreading false information showed a higher degree of vaccine hesitancy. Several studies have underlined the importance of sharing accurate information with the general public, which unfortunately today due to the loud voices of anti-system and anti-vaccine campaigns has demanded enormous resources to counteract misinformation and disinformation [19]. Typically, opponents of COVID-19 vaccinations claim that today COVID-19 cases are more frequent in vaccinated than in unvaccinated individuals and although some studies have indicated that more deaths occur among vaccinated than unvaccinated individuals it is not an indication of vaccine failure, but rather due to the large number of vaccinated individuals (80% in many countries), the delay in booster vaccinations, and many unvaccinated COVID-19 patients have gained immunity (www.kff.org, accessed on October 9, 2023). According to the CDC, unvaccinated individuals are still at much higher risk of death. Moreover, a recent study during the period of August 4 to 31, 2023 from the Washington State Department of Health clearly demonstrated that unvaccinated individuals were between 1.7 and 5 times more likely to be hospitalized with COVID-19 compared to persons who received at least one booster dose of vaccine (www.doh.wa.gov, accessed on October 9, 2023). An online survey of 467 participants confirmed a positive correlation between conspiracy theories and vaccine hesitancy [20]. Moreover, vaccine hesitancy is also prominent among individuals who deny the existence of the SARS-CoV-2 virus and/or COVID-19. According to a national survey in the US individuals who possessed less knowledge of SARS-CoV-2/COVID-19 were more likely to consider the COVID-19 vaccines unsafe and were more likely to believe in COVID-19 vaccine myths and conspiracy theories [21]. Vaccine hesitancy has also been linked to lower education levels, lower income, and living in rural areas [22]. It is therefore essential to understand the psychological factors related to vaccine hesitancy to be able to address, correct, and prevent the spread of false information through clear science-based sharing of facts to avoid putting public health at risk [20]. Hesitancy, resistance, and refusal to vaccinations have also been linked to social determinants of health, convenience, ease of availability and access, clarity of information, trust of authority and healthcare professionals, and sound judgment of benefit versus risk [23, 24].

Finally, as mentioned above the point raised by Missoni and Sen about the importance of the vaccine manufacturers and

health authorities to commit to transparency and information sharing should be taken seriously. However, to put the pandemic situation in the right context, the global emergency was unprecedented and did not allow the luxury of unlimited time to solve all issues. Moreover, hindsight is another thing that has been frequently misused in relation to the COVID-19 pandemic.

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