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Perspectives

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What factors promote vaccine hesitancy or acceptance during pandemics? A systematic review and thematic analysis

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Summary

Examine the factors that promote vaccine hesitancy or acceptance during pandemics, major epidemics and global outbreaks. A systematic review and thematic analysis of 28 studies on the Influenza A/H1N1 pandemic and the global spread of Ebola Virus Disease. We found seven major factors that promote vaccine hesitancy or acceptance: demographic factors influencing vaccination (ethnicity, age, sex, pregnancy, education, and employment), accessibility and cost, personal responsibility and risk perceptions, precautionary measures taken based on the decision to vaccinate, trust in health authorities and vaccines, the safety and efficacy of a new vaccine, and lack of information or vaccine misinformation. An understanding of participant experiences and perspectives toward vaccines from previous pandemics will greatly inform the development of strategies to address the present situation with the COVID-19 pandemic. We discuss the impact vaccine hesitancy might have for the introduction and effectiveness of a potential COVID-19 vaccine. In particular, we believe that skepticism toward vaccines can still exist when there are no vaccines available, which is contrary to contemporary conceptualizations of vaccine hesitancy. We recommend conducting further research assessing the relationship between the accessibility and cost of vaccines, and vaccine hesitancy.

Key words: vaccine hesitancy, COVID-19, pandemic, epidemic, systematic review

INTRODUCTION

The new year has been marked with the unprecedented spread of COVID-19 which has drastically affected people and healthcare systems globally. The virus has led to increasing death tolls and a plethora of negative health outcomes in patients. The pandemic has become

a catalyst for many scientific advancements including the possible conception of a COVID-19 vaccine. Now more than ever, there is an urgency to research and develop a vaccine against COVID-19. With the genetic sequence of SARS-CoV-2 becoming available, scientists worldwide have urgently developed a vaccine against the disease (Le *et al.*, 2020). A COVID-19 vaccination is invaluable because of its potential to save countless lives around the world and reduce the burden on current healthcare systems.

Vaccination is a cost-effective public health measure which can prevent disease spread and reduce disease burden. Since the creation of the WHO's Expanded Programme of Immunization in 1974 and the Global Alliance for Vaccination and Immunization in 2000, vaccination against infectious diseases has rapidly increased overtime (Greenwood, 2014). Vaccination has led to the successful eradication of two major diseases, smallpox and rinderpest (Morens *et al.*, 2011). Subsequent vaccines have also been developed against rubella, influenza, poliovirus, measles, along with other pathogens. Despite the lifesaving benefits of increased vaccine uptake, vaccine hesitancy and skepticism are still longstanding barriers to the health of individuals (Centers for Disease Control and Prevention, 2019).

Vaccine hesitancy has been shown to have an effect on disease prevention of past pandemics, including Severe Acute Respiratory Syndrome, Influenza A/H1N1, Middle East Respiratory Syndrome, and Ebola Virus Disease (Majid *et al.*, 2020). The refusal to vaccinate or a delay in the acceptance of vaccination despite its availability is termed as vaccine hesitancy (Majid and Ahmad, 2020a). Vaccine hesitancy can be influenced by several factors and these factors vary depending on social values upheld across various populations and are context dependent (Majid and Ahmad, 2020a).

Vaccination is important in preventing the spread of diseases, particularly in vulnerable populations including pregnant women or immunocompromised individuals who are increasingly susceptible to the disease and developing its associated symptoms (Doherty *et al.*, 2016). Moreover, populations who live in areas where resource and financial limitations exist may be unable to support individuals with serious disease outcomes. The potential economic and health impacts of a vaccine preventable disease necessitate research aimed at the development of strategies addressing vaccine hesitancy.

Previous work has identified a number of factors that may encourage vaccine hesitancy. However, to our knowledge, no systematic review or evidence synthesis has explored how these factors promote vaccine hesitancy during pandemics and epidemics. There is a need to understand how vaccine hesitancy increases during pandemics, epidemics, and global outbreaks. These findings may be incredibly important for ensuring the uptake of a COVID-19 vaccine by the general public. The research questions for this investigation were the following: what factors promote vaccine hesitancy or acceptance during the Influenza A/H1N1 pandemic and the global spread of Ebola Virus Disease? What barriers may impede vaccine uptake?

METHODS

Approach

We conducted a systematic review and qualitative thematic analysis to identify the barriers to vaccine hesitancy and acceptance in individuals and communities during pandemics, epidemics, and outbreaks. While we initially focused on new vaccines that were developed in response to six pandemics or global outbreaks in the 21st century (i.e. Severe Acute Respiratory Syndrome, Influenza A/H1N1, Middle East Respiratory Syndrome, Ebola Virus Disease, and COVID-19), we only found studies relevant to the influenza A/H1N1 pandemic and the global spread of Ebola Virus Disease. Therefore, this study only focuses on these two diseases to identify the factors that promote vaccine hesitancy and acceptance.

Searching

We conducted a focused analysis of data from a recently published scoping review of 149 primary studies on how communities and individuals have responded to five pandemics (Majid *et al.*, 2020). While that review focused on the relationship between knowledge, misconceptions, risk perception, and behavior change, the present review elaborates on barriers to vaccine uptake during pandemics, epidemics, and outbreaks such as cost, accessibility, attitudes toward vaccine manufacturers and administrators, and trust in the healthcare system. The original review searched four databases on 7 March 2020: PsychINFO, MEDLINE, Global Health, and Embase. The search strategy is included in Supplementary File 1.

Screening

We conducted initial and full-text screening through Covidence in pairs with verification. We included articles that discussed factors that promoted or discouraged vaccine hesitancy, acceptance, intention, or uptake in relation to the five pandemics or global outbreaks of interest. However, we only found articles related to Influenza A/H1N1 and Ebola Virus Disease. We

excluded articles that were conducted in an educational setting (i.e. school, university and college) because we were most interested in the barriers to vaccination in the general public. We only included primary quantitative, qualitative, and mixed-methods studies; we excluded abstracts, dissertations, theses, and published papers without primary empirical data (Table 1).

Data extraction and analysis

We developed a standard data extraction form to capture the study and methodological characteristics of included studies such as author, year of publication, title, objectives, country, topic, study methodology, data collection method, and the number and type of participants. We conducted descriptive statistics on these characteristics to develop an overall summary of the included literature that enabled us to identify specific trends in the data.

We then conducted qualitative thematic analysis to organize the findings of included studies (Braun and Clarke, 2006). We conducted three stages of analysis: pilot coding of study abstracts, initial coding and extraction of findings, and focused coding of extracted findings. In the first stage, two reviewers analyzed the abstracts of each included article and developed a list of themes, ideas, concepts, and findings. We used this list to formulate a preliminary coding schema that guided how we organized our initial coding.

In initial coding, we used the preliminary coding schema developed during the first stage to create a number of templates that categorized the findings from the results and discussion sections of included studies (Aronson, 1995). We reviewed each study that included data on factors that promoted or discouraged vaccine hesitancy or acceptance and extracted relevant findings into the appropriate template. We focused on how the authors chose to present the findings, rather than our interpretations of the findings. Where possible, we extracted findings verbatim in order to maintain the original meaning.

In focused coding, we reviewed the templates and categorized our findings according to the most salient themes: demographics factors influencing vaccination, accessibility and cost, personal responsibility and risk perceptions, precautionary measures taken based on the decision to vaccinate, trust in health authorities and vaccines, testing the safety and efficacy of a new vaccine, and lack of information and vaccine misinformation. Using constant comparison approach, we also compared our codes across topics, countries, studies and contexts (Boeije, 2002).

RESULTS

Our initial search strategy produced 1007 studies after the removal of 273 duplicates. After the revision of titles and abstracts, 38 full-text records were reviewed, and 28 articles met the inclusion criteria. Out of the 28 articles, 12 (42.9%) studies were conducted in European countries including France, Germany, Italy, Scotland, the Netherlands, Sweden, Poland, Switzerland, and the UK; nine (32.1%) studies were conducted in Canada or the USA; three (10.7%) studies were conducted in African countries including Guinea, Uganda, and Sierra Leone; two (7.1%) studies were conducted in Australia; and three (10.7%) studies were conducted in countries in Asia including China, India, and Saudi Arabia. The characteristics of each study can be found in Supplementary File 1. Figure 1 which shows our screening process.

We identified seven key areas which played an influential role on vaccine hesitancy or acceptance during Influenza A/H1N1 and Ebola Virus Disease: demographic factors influencing vaccination, accessibility and cost, personal responsibility and risk perceptions,

Table 1: Eligibility criteria

Inclusion	Exclusion
• Primary qualitative, quantitative (experimental and observational), or mixed-methods studies • Secondary analyses or evidence syntheses (e.g. reviews) • Articles that discuss any aspect of vaccine hesitancy or factors that promote vaccine acceptance during any 21st century pandemic, epidemic or outbreak (i.e. SARS, H1N1, Ebola, Zika, MERS, and COVID-19) • Published in the 21st century	• Any basic science articles • Abstract only format or conference proceedings, book reviews and commentaries • Theses or dissertations • Any articles published before the 21st century • Any articles published during the 21st century but focused on epidemics or pandemics that occurred before the 21st century (e.g. 1918 Spanish Flu)

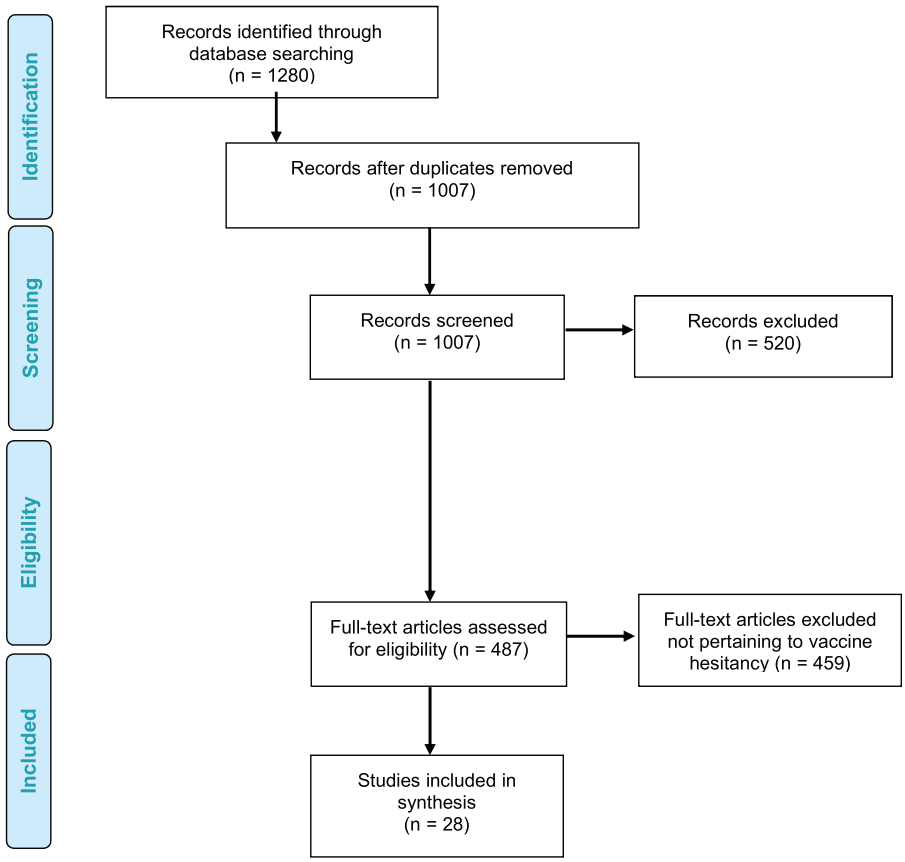

Fig. 1: PRISMA flow diagram. Source: Adapted from Moher *et al.* (Moher et al., 2009).

precautionary measures taken based on the decision to vaccinate, trust in health authorities and vaccines, the safety and efficacy of a new vaccine, and lack of information or vaccine misinformation.

Demographic factors influencing vaccination

Ethnicity. Caucasian and Hispanic populations living in the USA were more willing to vaccinate than Black populations (Mesch and Schwirian, 2015). At the same time, studies in the UK reported that Black people were less willing to vaccinate compared to Asian or Caucasian respondents (Myers and Goodwin, 2011). However, beyond this, we were unable to find major differences in vaccination behavior between other ethnicities or races.

Age. Older populations were the more likely to vaccinate compared to young people in four studies (Ferrante *et al.*, 2011; Myers and Goodwin, 2011; Rönnerstrand, 2013; Mesch and Schwirian, 2015). In Italy, e.g. individuals in the central age group (35–49 years) were less likely to seek vaccination (Ferrante *et al.*, 2011). Individuals who were older were often more concerned about their health because of their higher susceptibility to disease, making these individuals more inclined to vaccinate (Mesch and Schwirian, 2015; Myers and Goodwin, 2011; Rönnerstrand, 2013).

Sex. In terms of sex, both men and women were inclined to vaccinate for different reasons (Hilton and Smith, 2010; Hilyard *et al.*, 2010; Ferrante *et al.*, 2011; Gilles *et al.*, 2011). Males were more likely than females to vaccinate and perceived vaccination as more effective than women (Ferrante *et al.*, 2011; Gilles *et al.*, 2011).

Pregnancy. Women with young children in the UK and the USA were more concerned about vaccinating their children but were significantly less likely than men to express an intention to vaccinate their children (Hilton and Smith, 2010; Hilyard *et al.*, 2010). Pregnant women in the UK and the USA were also found to express concerns over how vaccination may affect their infant, which led them to vaccinate (Hilton and Smith, 2010; SteelFisher *et al.*, 2011; Cassady *et al.*, 2012). In one study from the USA, half the number of pregnant

women vaccinated, which was the highest proportion of vaccination among all demographic groups studied (Cassady *et al.*, 2012). Women with children between the ages of 0 and 6 were more likely to get vaccinated than any other group in Sweden (Börjesson and Enander, 2014). In another study also from the USA, 4 in 10 pregnant women reported that they had received the H1N1 vaccine, and another 8% expected to vaccinate (SteelFisher *et al.*, 2011). Two-thirds (67%) of pregnant women believed the H1N1 vaccine was safe (26% very safe, 41% somewhat safe) for pregnant women to take in the USA (SteelFisher *et al.*, 2011).

On the other hand, studies also showed that pregnant women felt there were mixed messages regarding medication and pregnancy which could hinder vaccine uptake in the UK (Hilton and Smith, 2010). From the same study, three participants mentioned the case of Thalidomide while highlighting the dangers of taking insufficiently tested medical interventions during pregnancy (Hilton and Smith, 2010). During the swine flu pandemic, only 32% of the general population in the UK believed that vaccination was safe for pregnant women (Myers and Goodwin, 2011). Half of the pregnant women subset said that they either did not intend to vaccinate or were unsure (SteelFisher *et al.*, 2011). Hence, pregnant women who were concerned about the safety and efficacy of the vaccine or lacked adequate knowledge were less likely to vaccinate in three studies (Hilton and Smith, 2010; Myers and Goodwin, 2011; SteelFisher *et al.*, 2011).

Education and employment. Level of education and employment were two key demographic factors that influenced individuals to vaccinate in six studies (Hilyard *et al.*, 2010; Myers and Goodwin, 2011; Börjesson and Enander, 2014; Wu *et al.*, 2014; Irwin *et al.*, 2017; Lin *et al.*, 2018). While one study in China demonstrated that the vaccine acceptance rate of 31.4% was independent of sociodemographic factors such as education level (Wu *et al.*, 2014), another study in Sweden reported that social and demographic factors including lower educational level and lower income were all statistically associated with lower vaccination frequencies (Börjesson and Enander, 2014). Individuals that had attained a higher level of education supported proper resource allocation and distribution of vaccines (Hilyard *et al.*, 2010). In addition, participants who had at least a bachelor's degree or were earning an income greater than $50 000 a year were more supportive of prioritizing who should be vaccinated when the vaccine becomes available (Hilyard *et al.*, 2010). In the UK during the H1N1 pandemic, people that were employed were less likely to be vaccinated (Myers and Goodwin, 2011), and another study in the USA found that unemployed individuals were more likely to seek vaccines (Lin *et al.*, 2018). However, during the outbreak of the Ebola Virus Disease in Guinea, higher interest and acceptability of vaccines was seen among men and wealthy or educated people; however, factors including religion and living in a rural or urban setting had no effect on vaccine acceptance (Irwin *et al.*, 2017).

Accessibility and cost

Accessibility and cost of a vaccine were important factors that participants considered before deciding to vaccinate in nine studies (Hilyard *et al.*, 2010; Charania and Tsuji, 2011; Cassady *et al.*, 2012; Hernández-Jover *et al.*, 2012; Walter *et al.*, 2012; Boerner *et al.*, 2013; Wu *et al.*, 2014; Davis *et al.*, 2015; Determann *et al.*, 2016). Most participants from the USA were knowledgeable about where to obtain the vaccine and how to access it for free or at a low-cost (Cassady *et al.*, 2012). The accessibility and speed at which a vaccine became available influenced participants' decision to vaccinate. For example, in Canada, participants who could get a vaccine through primary care clinicians or attended clinics with short line-ups were more likely to vaccinate (Boerner *et al.*, 2013). In order to improve accessibility, Canadian participants in one study suggested that training and deploying more nurses would increase vaccine uptake (Charania and Tsuji, 2011). Participants in the same study found mass immunization clinics to be an effective and accessible strategy to encourage vaccination and suggested increasing the number of these clinics (Charania and Tsuji, 2011). When it came to how the cost of a vaccine influenced vaccination decisions for patients, studies demonstrated a wide range of views. In one study conducted in three European countries (the Netherlands, Poland, and Sweden), the price of a vaccine did not matter for participants as they strongly believed that the benefit of disease prevention far outweighed vaccination costs (Determann *et al.*, 2016). Meanwhile, participants in a study from China suggested that vaccines should be made available for free to prevent disease spread among vulnerable populations (Wu *et al.*, 2014). However, while Polish participants in one study recognized the health benefits of getting vaccinated, they described how the financial undertaking required to provide free vaccination for everyone would not be feasible (Determann *et al.*, 2016).

Participants who refused vaccination reported a number of challenges they faced when accessing vaccines. For example, in Australia and Scotland, participants could not obtain the H1N1 vaccine because hospitals only

administered them to healthcare workers (Davis *et al.*, 2015). Moreover, 5.4% of participants in one study from Australia believed that outbreaks could be managed better if more resources were effectively allocated to vaccine manufacturing and distribution (Hernández-Jover *et al.*, 2012). On the contrary, one study from the USA reported that less than half of the respondents supported setting priorities to determine who would get a limited supply of vaccines (Hilyard *et al.*, 2010). Despite a majority (78%) of participants from one study in Germany reporting that they were sufficiently informed to make a decision on vaccination, vaccination coverage remained low, hindering individuals from accessing available vaccination resources (Walter *et al.*, 2012).

Personal responsibility and risk perceptions

Participants that chose to vaccinate assessed their personal risk based on a variety of factors including: if their perceived risk was high based on past experiences with seasonal influenza; willingness to see a physician; having a family member or friend who was infected with a vaccine preventable disease; the belief that the infection was dangerous; quantitative scientific information on the vaccine including how the infection spreads; the belief that they had an increased risk due to pre-existing health conditions or age; having young children who are more susceptible to infection; having access to radio, television or electricity; having a positive attitude about vaccines; feeling regretful for not vaccinating; and being a community leader (Chanel *et al.*, 2011; Ferrante *et al.*, 2011; Gilles *et al.*, 2011; Myers and Goodwin, 2011; Boerner *et al.*, 2013; Quinn *et al.*, 2013; Börjesson and Enander, 2014; Mesch and Schwirian, 2015; Determann *et al.*, 2016; Irwin *et al.*, 2017). Some cited their reason to vaccinate as a social responsibility that outweighed accessibility barriers such as long wait times (Hilton and Smith, 2010; Boerner *et al.*, 2013). Moreover, individuals who vaccinated emphasized protecting themselves, their community, and at-risk family members to prevent the spread of disease (Boerner *et al.*, 2013; Börjesson and Enander, 2014; Determann *et al.*, 2016).

Personal risk perceptions can hinder vaccine uptake. For example, participants in Sweden and Switzerland with subjectively good health rated vaccination as less effective than participants who reported having poor health (Börjesson and Enander, 2014; Gilles *et al.*, 2011). Similarly, in one study conducted in Canada, 28 of the 31 participants that refused the H1N1 vaccination perceived H1N1 to be of similar risk to seasonal influenza and considered themselves to have good overall health (Boerner *et al.*, 2013). These findings may indicate that people who reported having better health may feel safer and therefore be less inclined to vaccinate. Since they feel healthy, they may not vaccinate and remain a potential source of infection for others around them (Boerner *et al.*, 2013). Participants' willingness to vaccinate was also influenced by their physicians' vaccination decisions (Boerner *et al.*, 2013). If immunization programs against H1N1depended on voluntary adherence, identifying the source of people's motivations to vaccinate and the associated factors may increase vaccine uptake (Ferrante *et al.*, 2011). Having a deeper understanding of how people think and feel toward vaccination, learning about how their perspectives may change overtime, and implementing these findings can enhance the effectiveness of strategies that increase vaccination uptake by the general population.

Precautionary measures taken based on the decision to vaccinate

People who chose to vaccinate were more likely to adopt preventative measures to contain disease spread. In one study, vaccinated persons in Sweden reported higher frequencies of all three recommended behaviors: 81.6% washed their hands more frequently compared to 68.7% of non-vaccinated individuals; 78.8% reported coughing and sneezing into their elbow compared to 69% of non-vaccinated individuals; and 64.9% reported using disinfectants compared to 50% of non-vaccinated individuals (Börjesson and Enander, 2014). Contrarily, a study conducted in India suggested that H1N1 vaccination was perceived to be a lower priority by participants compared to frequent sanitation practices and living an organic and healthy lifestyle (Sundaram *et al.*, 2014).

Trust in health authorities and vaccines

Individuals trust in medical information from health service organizations and their social circle influenced their decision to vaccinate. For example, trust in health authorities was commonly associated with increased patients' willingness to vaccinate in four studies from Canada, France, Sweden, and the USA (Chanel *et al.*, 2011; Boerner *et al.*, 2013; Börjesson and Enander, 2014; Mesch and Schwirian, 2015). In Switzerland, 71% of individuals believed that health service organizations provided accurate knowledge and could be trusted (Bangerter *et al.*, 2012). A one-point increase of trust in health service organizations on a five-point scale made vaccination 2.14 times more likely among participants from Switzerland (Gilles *et al.*, 2011). Some also cited that reluctance to vaccinate was based on their lack of trust in physicians and the vaccine manufacturing

process (Determann *et al.*, 2016). A third of participants in one study from Italy who were affected by a chronic disease and a quarter of youth between ages 18 and 27 years would consent to vaccination if they were actively invited by trusted authorities (Ferrante *et al.*, 2011).

In addition to trusting health service organizations, participants who trusted governments also had a higher perceived efficacy of vaccination (Gilles *et al.*, 2011; Irwin *et al.*, 2017; Lin *et al.*, 2018). Participants often relied on trusted government bodies to introduce vaccines safely and effectively (Hilton and Smith, 2010; Determann *et al.*, 2016). Greater trust in the government's management of the H1N1 pandemic and greater perceived fairness in vaccine distribution was associated with increased support for government actions and intention to vaccinate in the USA (Hilyard *et al.*, 2010). However, when individuals lost trust in government bodies responsible for vaccination, individuals' willingness to vaccinate also decreased. On the other hand, Quinn *et al.* (Quinn *et al.*, 2013) found that trust in government actions was weakly associated with the intention to vaccinate. Instead, participants who decided to vaccinate based their decision on the advice of people they trusted including family and friends (Boerner *et al.*, 2013; Börjesson and Enander, 2014; Determann *et al.*, 2016). In addition, some people chose to vaccinate even if family and friends discouraged them from doing so (Boerner *et al.*, 2013). Although personal networks often have a great influence on an individual's decision to vaccinate, social pressures alone are not sufficient for determining individuals' vaccination decisions (Boerner *et al.*, 2013). Hence, health authorities, governing bodies and personal networks all have a key role in communicating the importance of vaccination to increase vaccination uptake in individuals. Communication thus helps to facilitate an environment for individuals to build trust and have confidence in the information they receive and make informed decisions before they commit to vaccination.

The safety and efficacy of a new vaccine

Some participants were more hesitant and skeptical upon the introduction of a novel vaccine. In Switzerland, 72% of participants believed that the H1N1 vaccine had problematic side-effects and 49% believed that the vaccine was not useful (Bangerter *et al.*, 2012). Similarly, in the UK, individuals in one study were primarily concerned about the speed at which vaccines were developed and whether sufficient testing had been conducted (Hilton and Smith, 2010). Other studies demonstrated that lower trust in health authorities led to increased concerns about the safety of the H1N1 vaccine in the USA (Freimuth *et al.*, 2014; Mesch and Schwirian, 2015). Three studies found that participants reported greater fear and uncertainty surrounding safety, vaccine efficacy and residual long-term side-effects of newer vaccines (Myers and Goodwin, 2011; Cassady *et al.*, 2012; Boerner *et al.*, 2013; Determann *et al.*, 2016). The authors of one study from Canada found that authorities and media outlets often exaggerated the health risks of vaccination (Börjesson and Enander, 2014). This led participants to form a negative view of vaccines that was correlated with lower vaccine uptake (Börjesson and Enander, 2014). Some participants who refused to vaccinate cited that its healthier for the body to clear the virus naturally without taking drugs (Determann *et al.*, 2016). This perception demonstrates that participants perceived vaccination to not be as efficacious as natural immunity, which may decrease one's willingness to vaccinate.

Lack of information and vaccine misinformation

Lack of information and misinformation about vaccination influenced participants decision to vaccinate in seven studies (Raude and Setbon, 2009; Balkhy *et al.*, 2010; Hilton and Smith, 2010; Chanel *et al.*, 2011; Myers and Goodwin, 2011; Boerner *et al.*, 2013; Nyakarahuka *et al.*, 2017). For example, in the UK, participants in one study reported being unsure about the difference between vaccines for swine flu and seasonal flu (Hilton and Smith, 2010). Participants also knew little about how seasonal influenza vaccines worked and wondered whether they would be effective against H1N1 (Hilton and Smith, 2010). Participants suggested that the seasonal flu vaccine must be a safer option because it had been administered for years (Hilton and Smith, 2010). Lacking adequate information surrounding vaccination or encountering contradictory information from different sources can reduce an individual's willingness to vaccinate (Boerner *et al.*, 2013). Although the internet can be a useful resource to spread vital public health information during a pandemic, a lack of clarity and consistency of information may deter people from vaccination (Chanel *et al.*, 2011). For example, in Uganda during the Ebola outbreak, only 11.1% of participants in one study were aware that vaccination was intended to control and prevent the spread of disease (Nyakarahuka *et al.*, 2017). Furthermore, Raude and Setbon (Raude and Setbon, 2009) found that 40% of participants in France believed that vaccination against seasonal influenza would also protect them against

H1N1. In the UK during the H1N1 pandemic, only 53% of participants believed that vaccination would prevent H1N1 (Myers and Goodwin, 2011). People that do not have a comprehensive understanding of how vaccines work are unable to make informed and confident decisions about vaccination. Therefore, it is essential to communicate information regarding vaccination in a clear and accessible manner in order to better educate people and overcome barriers to vaccination.

DISCUSSION

We conducted a systematic review to understand the factors that promote vaccine hesitancy or acceptance during pandemics, epidemics and outbreaks. We examined 28 studies on Influenza A/H1N1 and Ebola Virus Disease and found seven major factors influencing vaccination decisions: demographic factors affecting vaccine acceptance, accessibility and cost of acquiring a vaccine, personal responsibility and risk perception of disease, precautionary measures taken with regard to vaccination, trust in health authorities and vaccines, vaccine safety and efficacy, and lack of information or misinformation about vaccines. These factors can neither be simply interpreted in a causal manner nor independently of one another. Each of these factors plays a crucial role in influencing vaccination decisions during a pandemic, epidemic or outbreak. Moreover, it is much more plausible that several of these factors are working together in a complex and dynamic relationship to influence individuals. We found support for WHO's 3C (confidence, complacency, and convenience) model as representing a number of factors that work together to influence vaccination decision (Larson, 2014). In addition to the WHO model, we further elaborate on other factors that might influence a vaccination decision, including certain demographic factors, and the association between vaccine intention and preventive behaviors. In this section, we reflect on the different factors with respect to the literature on vaccine hesitancy and offer recommendations for planning and policy.

Demographic factors associated with vaccine acceptance

In general, we found that demographic factors positively associated with the intention to not vaccinate included being below the age of 49, being female, and having a lower income and education. Factors that were positively associated with the intention to vaccinate included being pregnant, increased age, male sex and having a higher income (greater than $50 000), and having at least a bachelor's education. Although these were the general trends presented in the data, we also found notable exceptions showing that demographic variables alone cannot determine outcomes of vaccine hesitancy or acceptance. Hence, demographic variables should be examined in a context-dependent manner and viewed as a part of a whole, rather than in a causal or independent manner when referring to vaccination decisions. In the following sections, we discuss how three demographic factors influence vaccine hesitancy or acceptance: age, level of education, and pregnancy.

Age. Older individuals may have a higher likelihood of having chronic diseases and being immunocompromised, which may explain why they may be more likely to vaccinate compared with younger individuals who may believe that they have good overall health (Weinberger, 2018). Older individuals who have pre-existing chronic diseases—especially diseases that put them at a higher risk of mortality from the infection—will perceive a higher susceptibility to the vaccine preventable disease and a greater severity of the infection, providing them with an elevated motivation to vaccinate (Majid *et al.*, 2020). This is in line with the protection motivation theory which suggests that a higher perception of risk is associated with a greater likelihood of compliance with protective health behavior, in this case vaccination (Prentice-Dunn and Rogers, 1986). Older individuals may also be more likely to experience barriers in accessing vaccination, including costs, transportation, and knowledge (Thorpe *et al.*, 2011). These findings coincide with recent research that have found an association between older age and vaccine acceptance (Detoc et al., 2020). Thus, it is crucial that vaccination programs develop strategies tailored to delivering vaccination to older populations, especially if they are known to be a high-risk population.

Level of education. Both education and employment were also two key factors that heavily played a role in influencing vaccine hesitancy. Individuals with at least a bachelor's degree were more inclined to vaccinate because they may spend a greater amount of time understanding disease severity, benefits of vaccination, and deciding whether or not vaccination was in their interest (Hilton and Smith, 2010; Hilyard *et al.*, 2010). According to the theory of planned behavior, behavioral intention is shaped by an individual's beliefs and evaluation regarding the outcomes of a particular preventive action (Ajzen, 1991; Munro *et al.*, 2007). Devoting time into establishing a better understanding of vaccination might contribute to more a positive evaluation about the potential outcomes of vaccination, giving rise to a more favorable attitude toward it and thus, making

individuals with at least a bachelor's degree more likely to vaccinate. Moreover, educated individuals may have an improved understanding of vaccination information as they may be better able to synthesize information from academic research studies to make informed vaccine decisions (Biasio, 2017). On the other hand, some studies have reported that highly educated individuals, including those that had university and college degrees, were more likely to be vaccine-hesitant (Majid and Ahmad, 2020a). We believe that social groups and other external influences that include government and health authorities have a greater impact on individuals' vaccine decision-making process compared with their education level (Senier, 2008; Sobo *et al.*, 2016). According to the theory of planned action, an individual's behavioral intentions are significantly influenced by their normative beliefs and their motivation to act in compliance with these beliefs (Ajzen, 1991; Munro *et al.*, 2007). Individuals may hold certain beliefs regarding whether their family and friends would like for them to vaccinate and they may feel inclined to follow through with these expectations. As such, educated individuals can also express vaccine skepticism if their social circle is predominantly vaccine-hesitant (Majid and Ahmad, 2020a). While we found that higher education generally led to greater intention to vaccinate in the studies reviewed, we identify this as a priority for future research to clarify given the discrepancy with research on previous pandemics and outbreaks. Recent COVID-19 research has also found similar findings (Gagneux-Brunon et al., 2021; Papagiannis et al., 2020), further illustrating the applicability of our research in the context of the COVID-19 pandemic. In particular, vaccine literacy has been found to predict vaccination intention through three factors: country, age, and type of vaccine [(Lorini et al., 2018)—health literacy and vaccination: a systematic review]. However, in line with previous research on the relationship between health literacy and vaccine hesitancy, we find the continued need to further examine the circumstances under which health literacy encourages vaccine uptake. This is especially important as global COVID-19 variant cases continue to rise alongside vaccine availability. There is a need to tailor specific strategies to communicate the importance of vaccination to different groups. Future research is necessary to disentangle the relationship between vaccine hesitancy and education or health literacy level.

Pregnancy. Pregnant women or women who have children were also more likely to vaccinate (Cassady *et al.*, 2012; Börjesson and Enander, 2014). Women may feel a greater sense of responsibility to protect their children because they are more vulnerable. On the other hand, recent research on COVID-19 vaccine hesitancy found that males are less likely to vaccinate because they hold lower risk perceptions and engage in riskier lifestyle behaviors (Grech, 2020). However, some parents may refuse vaccination due to safety concerns over a novel vaccine (Majid and Ahmad, 2020a). Many parents may hold fears of long-term side-effects and express uncertainty whether or not proper testing had been done regarding the safety of vaccines (Majid and Ahmad, 2020a). Parents who lead a 'natural' or 'organic' life may view vaccines as comprising of artificial ingredients that goes against their values (Majid and Ahmad, 2020b). These parents may also believe that it is their primary responsibility to protect their child and may consequently ignore the role of vaccination in protecting the community through herd immunity (Majid and Ahmad, 2020a). However, we emphasize that our general findings on the association between demographic factors and vaccine intention may not be representative of behaviors today, particularly since we analyzed studies from the start of the 21st century, and some research shows that vaccine hesitancy has increased steadily in the past decade (Benecke and DeYoung, 2019).

Accessibility and cost

In terms of accessibility, we found that individuals were more likely to vaccinate if the vaccine was conveniently located, e.g. at mass immunization clinics (Determann *et al.*, 2016). Higher vaccination uptake was also observed in clinics where an efficient system was in place that reduced wait times (Boerner *et al.*, 2013). Lower costs to vaccinate may also increase intention to vaccinate in countries where healthcare is at the expense of consumers (Cassady *et al.*, 2012). Perceived barriers form the strongest dimension of the health behavior model, such that a greater adoption of preventive behavior is noted in the presence of fewer impediments (Janz and Becker, 1984). As such, it seems that vaccine acceptance may be somewhat circumvented if accessibility and cost of vaccination were not barriers to vaccination. However, while some studies explored the relationship between vaccine cost and vaccine uptake, none of the studies explicitly discussed the relationship between access barriers and vaccine hesitancy, skepticism, and confidence in vaccine safety and efficacy. We believe that simply reducing access and cost barriers may not increase vaccine uptake, as decision-makers might expect, unless concerns regarding vaccine safety and efficacy are also addressed. Alternatively, reducing the cost of a vaccine may inadvertently introduce questions about its quality, safety, and efficacy, that further promote

vaccine hesitancy and rejection. There is need for future research to identify how vaccine hesitancy influences access and cost barriers to vaccination, and vice versa.

Risk perceptions and vaccination

We found that participants were more likely to vaccinate when they perceived vaccination as a social responsibility (Hilton and Smith, 2010). Prosocial concern has also been found by recent research on COVID-19 vaccine hesitancy to promote vaccine acceptance (Barello et al., 2020; Bell et al., 2020). Social responsibility to vaccinate may stem from higher risk perceptions pertaining to their personal health and the health of their family and communities (Majid *et al.*, 2020). We found that individuals were more likely to vaccinate if their perceived risk of acquiring disease and perceived disease severity was higher. Previous research demonstrates that risk likelihood, susceptibility, and severity significantly predict vaccination behavior (Brewer *et al.*, 2007). This is in accordance with the health behavior model which posits that a higher perception of disease susceptibility and severity may contribute to a higher motivation to practice behavior that might lower this risk (Janz and Becker, 1984). However, in the case of infectious pandemics or epidemics, we believe that perceived risk of disease does not only include personal risk perception, but also community and family risk perception. For example, individuals who perceived themselves as healthy and at a low risk for acquiring disease may interact with individuals at higher risk for the infection. These individuals may in turn have a higher risk perception and may vaccinate to protect themselves and the people who they frequently interact with. Moreover, participants who vaccinated were also more likely to practice preventative measures against the disease such as hand washing and wearing a mask (Börjesson and Enander, 2014). We believe that with respect to vaccination, the relationship between risk perception and the intention to vaccinate is influenced by individual, family, and community risk perception.

At the same time, we recognize that some individuals who view themselves to be healthy and at a low risk of acquiring disease may be less likely to vaccinate, possibly due to a weaker motivation for taking such action as indicated by the protection motivation theory (Prentice-Dunn and Rogers, 1986). Vaccine acceptance may stem from how well individuals perceive their health to be and whether or not they intrinsically believe that these diseases are a threat to their health (Brewer *et al.*, 2007). For some, information alone on the disease is enough of a reason to persuade them to vaccinate. In contrast, other individuals are less affected by allopathic information, and may be more concerned about the uncertainty of the long-term effects of vaccination on their health (Majid and Ahmad, 2020a). To improve vaccination uptake, decision-makers need to consider how individuals' self-reported health influences vaccine acceptance in the context of pandemics, epidemics, and outbreaks. Public health messages targeted at individuals, families, and communities may be necessary as complementary interventions for improving risk perception and vaccination intention. Since individuals might prioritize different reasons to reject or delay vaccination (Majid and Ahmad, 2020a), different messages may be effective.

Limitations of this study

This review has a few limitations. First, we did not examine studies from all pandemics, epidemics, or outbreaks in the 21st century. We chose five that received the most attention globally and were similar in infectious epidemiology and transmission, and we only found studies on two (Influenza A/H1N1 and Ebola Virus Disease). Examining vaccine hesitancy with respect to other epidemics and outbreaks may provide additional insight on the factors that promote vaccine hesitancy or acceptance. Similarly, we did not examine studies before the 21st century. It would be interesting to analyze whether or not factors that contribute to vaccine hesitancy existed during previous pandemics or global outbreaks. Finally, we found no studies examining vaccine hesitancy and acceptance in the context of COVID-19 at the time we conducted the database search. We know that since that time there have been studies on COVID-19 vaccine hesitancy, and as such, there is a need to dedicate attention to synthesizing this emerging literature and offer important recommendations to the ongoing global crisis. However, while we recognize that attention is necessary to determine how our findings differ in the COVID-19 context, we believe that our recommendations and lessons have important implications for policy planning with regard to future pandemics, epidemics, or global outbreaks.

CONCLUSION

This systematic review examined the factors that promoted vaccine hesitancy and acceptance during pandemics, major epidemics, and global outbreaks. In total, 28 studies were included representing the influenza A/H1N1 pandemic and Ebola Virus Disease. We found seven major factors that promoted vaccine hesitancy and acceptance: demographic factors influencing

vaccination (ethnicity, age, sex, pregnancy, education, and employment), accessibility and cost, personal responsibility and risk perceptions, precautionary measures taken based on the decision to vaccinate, trust in health authorities and vaccines, the safety and efficacy of a new vaccine, and lack of information or vaccine misinformation. While we recognize that the COVID-19 pandemic shares important differences with previous pandemics and outbreaks, we identify multiple similarities that increase the usefulness and applicability of our findings to support current decision-making needs. This is especially the case as global COVID-19 cases rise, while vaccine hesitancy is also rising concurrently. There is an urgent need to consider factors that promote vaccine hesitancy and acceptance to encourage public vaccination, providing communities with the strength to overcome this immense challenge.

SUPPLEMENTARY MATERIAL

Supplementary material is available at *Health Promotion International* online.

CONFLICT OF INTEREST STATEMENT

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