

EXPLORING THE CONTEXTUAL DETERMINANTS OF VACCINE  
ACCEPTABILITY

EXPLORING THE CONTEXTUAL DETERMINANTS OF VACCINE  
ACCEPTABILITY: AN IN-DEPTH LITERATURE REVIEW

By

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TITLE: Exploring the Contextual Determinants of Vaccine Acceptability: An In-Depth Literature Review

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## **Lay Abstract**

The contextual determinants of vaccine acceptability have been seemingly under-researched relative to other individual-level factors. As a result, this thesis aims to explore and develop a greater understanding of the contextual determinants of vaccine acceptability and their evolution over time and across different global contexts. To achieve this objective, an in-depth literature review of 139 identified articles was conducted in an effort to explore and identify themes related to the contextual determinant of vaccine acceptability. Ultimately, through this review 32 themes across the seven contextual determinant categories were identified and discussed. These findings helped elucidate the complex and fundamental role that contextual determinants have in shaping demand for vaccines.

## **Abstract**

**Background:** Poor demand for vaccines has long been recognized as a threat to the realization of public and global health objectives. Consequently, over time a range of interventions have been researched, proposed, and implemented in an attempt to improve the acceptability of vaccines and overcome vaccine resistance. However, much of the contemporary research concentrates disproportionately on individual-level determinants as viable targets for interventions. This disparate focus on individual-level factors has seemingly been at the expense of research into fundamental contextual influences. As a result, the primary aim of this thesis is to explore and develop a greater understanding of the contextual determinants of vaccine acceptability and their evolution over time and across different global contexts. Furthermore, emerging themes will be analyzed in an effort to explore how different contextual determinants work together or separately to influence vaccine acceptability. **Methodology:** The methodological approach adopted for this thesis concentrated on enabling and conducting an in-depth literature review of the contextual determinants of vaccine acceptability. To begin, a concept analysis was conducted to inform the design, focus, and implementation of a literature review. Subsequently, an in-depth literature review of research derived from the Global Health database was conducted using relevant papers published between 1910 and 2022. Data related to publication and content characteristics were extracted to support the analysis process and discussion. Ultimately themes related to the seven contextual determinants categories were identified, extracted, and analyzed. **Results:** Through the final analysis, 32, often interrelated themes were identified across the seven contextual determinant categories. The determinant category of *Politics & Policy* was found to be relevant in

70.5% (n=98) of articles included in this literature review. *Religious, Social & Cultural* determinants were relevant in 53.24% (n=74) of articles, followed by *Communication & Media Environment* at 43.16% (n=60), *Influential Leaders* at 41.37% (n=58), *History & Historical Factors* at 38.13% (n=53), *Pharmaceutical Influences* at 24.46% (n=34), and *Geographic Influences* at 18.7% (n=26). **Conclusion:** The acceptability of vaccines is undoubtedly influenced by the broader factors that shape the contexts in which vaccines are delivered. Additionally, these contextual determinants are likely to interact with, or influence the many commonly referenced putative individual-level determinants of vaccine acceptability. As a result, the complex nature of any relevant contextual determinants should be considered in the design of efforts aimed at promoting or improving demand for vaccines.

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## **List of Abbreviations**

WHO – World Health Organisation

VH - Vaccine Hesitancy

VA - Vaccine Acceptability

WG – (SAGE) Working Group

SEP – Smallpox Eradication Programme

EPI – Expanded Programme on Immunization

UCI – Universal Childhood Immunization Initiative

GAVI – Global Alliance for Vaccines and Immunization

DICT – Digital Information and Communication Technology

HIV – Human Immunodeficiency Virus

AIDS – Acquired Immunodeficiency Syndrome

HBV – Hepatitis B Virus

HPV – Human Papillomavirus

MMR – Measles, Mumps, and Rubella

DTaP – Diphtheria, Tetanus, and Pertussis

OPV – Oral Polio Vaccine

QCA – Qualitative Comparative Analysis

CC – Cabcodes

ID – Identifiers

HW – Heading Words

NCEE – National Commission on Excellence in Education

LRS – London Royal Society

## **Declaration of Academic Achievement**

The following is a declaration that the content of the research in this document has been completed by Noah Smith and recognizes the contributions of Christy Gombay and Laura Banfield in both the research process and completion of the thesis.

## Introduction

Over time, vaccines have proven to be some of the most effective means of shielding populations from the burdens of disease. Due to their impact and cost-efficacy, vaccines have become an indispensable part of public and global health efforts. However, universal access to these vital tools of preventative and protective medicine has consistently been frustrated by supply-side hurdles, leading historically to issues of global inequities and enduring burdens of immunizable disease. As governments, health agencies, and various organizations work to address these supply-side exigencies, ensuring that requisite public demand for vaccines exists becomes an increasingly important consideration. Unfortunately, public demand for vaccines has historically been challenged by what has come to be widely known as 'vaccine hesitancy'. As much of the literature suggests, vaccine hesitancy has reduced vaccination uptake, undermined coverage goals, and contributed to the re-emergence of immunizable disease (Hussain et al., 2018; Hussain et al., 2016; Iammarino & O'Rourke, 2018; Ullah et al., 2016).

Vaccine hesitancy continues to be a contentious and poorly defined concept despite being named one of the WHO's ten greatest contemporary threats to global health (WHO, 2019). There appears to be a prevailing lack of consensus on vaccine hesitancy's causes. Many of these differences seem to stem from a fundamental lack of agreement on what constitutes vaccine hesitancy. This issue continues to be exacerbated by the imprecise use of the term in the media and everyday conversation (Bedford et al., 2017). Nonetheless, several interventions have been proposed and implemented to address vaccine hesitancy. Many of these are predicated on targeting specific determinants related to different and



sometimes competing schools of thought. This level of disagreement is perhaps understandable in light of vaccine hesitancy's recent conceptual origins, and the recent surge in interest the subject has received, likely motivated by the COVID-19 pandemic. However, as the field grows, new, more precise concepts and theories will undoubtedly emerge and strengthen the collective understanding of vaccine hesitancy.

Through the early stages of the research process, it became evident that much of the existing literature in global health focused on individual-level determinants of vaccine acceptability, hesitancy, and other related concepts. However, as Taylor (2009) argued, vaccine campaigns, like other disease eradication efforts, cannot be delivered in a vacuum. As such, a narrow focus on individual-level determinants appeared to overlook many of the broader factors that shape the contexts in which vaccine programs are delivered and, consequently, act on or influence individual-level determinants. The primary motivation for this research was to explore the apparent lack of such a contextual understanding. Accordingly, this thesis centered around two primary aims. The first is the desire to explore and develop a greater understanding of the contextual determinants of vaccine acceptability and their evolution over time and across different global contexts. The second is to understand better how various contextual determinants work together or separately to influence vaccine acceptability. To achieve these objectives, a concept analysis and an in-depth literature review were conducted to explore the following primary and secondary research questions:

1. How have the contextual determinants of vaccine acceptability manifested and evolved over time and across different global contexts?

- a. How have vaccine-related policies evolved over time or interacted with vaccine acceptability?
- b. How do different contextual determinants interact to influence vaccine acceptability?

This thesis is organized into seven distinct chapters. The first background chapter introduces the reader to vaccination programmers and some of the hurdles these efforts face in realizing vaccine coverage goals. The chapter subsequently discusses vaccine uptake and its relevance to global health before introducing vaccine resistance, acceptability, and several related contemporary perspectives. The second chapter focused on the methodological approach used for this thesis. At the outset of the chapter, the process and steps taken to arrive at a final methodology are explained and reasoned. Following an overview of these early deliberations, the chosen methodological approach is explained in detail. The third chapter consists of a concept analysis of vaccine hesitancy. This chapter looks at the relatively short conceptual and terminological history of vaccine hesitancy before describing a series of prominent conceptual models used to explain the phenomena. Through this concept analysis, several relevant conceptual and practical challenges are identified. The chapter concludes with a discussion of how these challenges influenced and refined the research focus of this thesis. The fourth chapter describes several vital concepts and theories used to guide the research process, analysis, and discussion. Perhaps most importantly, this chapter includes sections on the guiding conceptual foundation used for this thesis and descriptions of essential terms. The fifth chapter focuses on the results of the literature review. Much of the chapter is spent summarizing the thematic findings in the

results. The sixth chapter discusses key findings related to the research questions and aims of the thesis. This chapter includes discussions on historical continuities and discontinuities, complex causality, limitations, and more. Finally, the concluding chapter, chapter seven, provides a brief summary of the thesis, its goals, and some key takeaways.

# 1 Background

Vaccines are widely regarded as some of the most impactful and effective tools available for reducing global burdens of disease. The life-saving promise of vaccines has been recognized since the first smallpox vaccine was developed at the turn of the 17th century. Over the past two centuries, new vaccines have been developed to protect against more than two dozen diseases. The WHO now suggests that immunizations prevent an estimated 2-3 million deaths each year (Toor et al., 2021). Furthermore, forward-looking models project that between 2000 and 2030, vaccines for 10 of the most prevalent preventable diseases will avert 97 million deaths across 112 countries (Toor et al., 2021). It is perhaps of little surprise, then, that immunizations continue to be considered a cornerstone of public and global health efforts.

Consequently, over time, vast amounts of time and resources have been allocated to the creation and distribution of new vaccines. In addition to their life-saving value, vaccines are understood to be some of the most cost-effective means of preserving and promoting human health. This health-preserving and economic value are now reflected in many policies and health agendas established across the globe. Thanks to remarkable advances in biomedicine, new vaccines continue to be developed for many of the world's most burdensome diseases. Should immunization development efforts for diseases such as HIV-1, Tuberculosis, and Malaria prove successful, it is foreseeable that the delivery of these tools will become increasingly affixed to public and global health campaigns.

## 1.1 A Brief History of Immunization Campaigns

In 1966 the World Health Organization (WHO) began emphasizing the importance of eradicating smallpox in endemic regions of some African and Asian nations (Henderson, 1987). At the time, an estimated 10-15 million cases of smallpox were occurring each year. The WHO launched the *Smallpox Eradication Programme* (SEP) in 1967 to facilitate the types of “mass vaccination” campaigns that had successfully eradicated smallpox in North America and many parts of Europe (Henderson, 1987). However, the WHO quickly adapted its strategy to include improved disease surveillance and outbreak containment strategies alongside vaccination efforts. Additionally, the creation of new freeze-dried vaccines and the bifurcated needle allowed for more widespread and efficient vaccination campaigns in rural and urban areas (Henderson, 1987). Furthermore, this WHO program trained staff and supported other national vaccination programs, such as India’s 1975 *Operation Smallpox Zero* (Lahariya, 2014), to ensure that campaigns could effectively adapt to the heterogeneity of the contexts in which they operated.

In 1974 the WHO launched the *Expanded Programme on Immunization* (EPI) to improve global coverage of routine vaccinations in children (Cherian & Mantel, 2020). One original objective of the EPI was to ensure that by 1990, every child on earth had access to vaccinations for poliomyelitis, measles, tuberculosis, tetanus, pertussis, and diphtheria. As a result of the EPI’s slow progress, the United Nations International Emergency Children’s Fund and WHO collaborated to launch the *Universal Childhood Immunization Initiative* (UCI) (Cherian & Mantel, 2020). The collaboration led to substantial increases in global DTP3 vaccine coverage. Through the EPI, the WHO established guidelines from

which nations worldwide could model their respective national vaccination programs. The early success of these programs gave rise to the creation of new, more ambitious efforts targeting eradicating, eliminating, and controlling diseases such as polio, measles, rubella, neonatal tetanus, hepatitis B, and Japanese encephalitis (Cherian & Mantel, 2020).

Despite mean decreases in global vaccine coverage, many groups or regions worldwide are still poorly vaccinated. GAVI was founded in 2000 to address immunization barriers related to costs in some of the world's poorest countries (Cherian & Mantel, 2020). GAVI provides support to eligible nations that are working to introduce new vaccination campaigns or improve national health systems. Through GAVI, many of the world's poorest countries have been able to offer more significant numbers of vaccines to cover a broader range of diseases. Since the establishment of the SEP, EPI, UCI, and GAVI, many developing nations have achieved substantial increases in vaccination coverage, some even exceeding that of high-income countries.

## **1.2 Vaccine Uptake & Global Health**

Since they were first introduced, vaccines have consistently ushered in dramatic reductions in deaths from diseases such as smallpox, polio, measles, pertussis, and, more recently, COVID-19. In fact, recent mathematical modeling suggests that COVID-19 vaccines prevented nearly 14.5 million deaths between December 2020 and December 2021 (Watson et al., 2022). However, Watson et al. (2022) estimate that if the 40% first-year vaccine coverage goal set by the WHO had been achieved across low-income countries, 111% more deaths could have been prevented. These estimates underscore the need to achieve universal vaccine coverage in the Global South, not only for the sake of

reducing the impacts of COVID-19, but for reducing the inequitable health burden of all immunizable diseases. Today, equitable and comprehensive immunization coverage rates are at the foundation of many global health goals and development agendas, such as some of the Sustainable Development Goals established by the United Nations in 2015.

The need to achieve and maintain high levels of vaccine coverage has been consistently emphasized by researchers and global health advocates alike. The health-promoting impact of vaccines can be destabilized when vaccine coverage is below what is needed to achieve herd immunity. While vaccine equity and under-allocation issues undoubtedly contribute to poor health outcomes in the Global South, a different global phenomenon has, for centuries, undermined the realization of health agendas and has consequently contributed to the spread and re-emergence of controlled diseases in the Global South and North alike. Achieving vaccine coverage targets depends on more than suitable supplies and effective campaign logistics. Public willingness to accept and receive vaccines can serve as a significant barrier to sufficient levels of uptake. While there is unquestionably a need to continue bolstering global efforts to distribute and deliver vaccines, there is also now just as much of a need to work to address what is widely believed to be the burgeoning challenge of vaccine hesitancy. In fact, as mentioned before, in 2019, the WHO declared vaccine hesitancy to be one of ten threats to global health (WHO, 2019).

### **1.3 A Brief History of Vaccine Resistance & Acceptability**

Historical literature and case studies from the late 1700s and early 1800s describe the burgeoning challenge of public resistance that emerged alongside the earliest vaccines

(Holmberg et al., 2017; Kaufman, 1967). In the decades following Edward Jenner's 1796 smallpox breakthrough, countries around the world began to vaccinate their respective population for what was, at the time, one of the world's most deadly diseases (Wolfe & Sharp, 2002). Following Jenner's breakthrough, it would take nearly two centuries for smallpox to be declared eradicated. Over that course of time, dozens of new vaccines for infectious diseases would be developed and delivered, albeit many times inequitably, to populations in need.

Despite the evidenced efficacy of vaccines, many public health efforts to increase uptake have consistently been frustrated by low levels of acceptability and public resistance (Hussain et al., 2018; Hussain et al., 2016; Iammarino & O'Rourke, 2018; Ullah et al., 2016). Even with global improvements in vaccine accessibility and affordability, surveillance programs, and national immunization strategies, immunization coverage remains suboptimal in many regions of the world (Cherian & Mantel, 2020). Cost, access, awareness, and regional health infrastructure are all barriers to increased global vaccination coverage. However, these factors are not the only obstacles in the way of achieving global immunization targets. Low vaccine acceptability and resistance continue to affect coverage in nations around the world. These adverse impacts have garnered a substantial amount of attention over the decades leading up to, and during the COVID-19 pandemic (Mian & Khan, 2020). While resistance and acceptability are not the only barriers to realizing target vaccine coverage goals, they have consistently led to suboptimal levels of immunizations and immunizable disease outbreaks. This rejection, opposition, or reluctance to receiving vaccinations has come to be commonly known as 'vaccine hesitancy'. The section below



will introduce some common perspectives on vaccine hesitancy, acceptability, and resistance, and interventions aimed at improving vaccine uptake.

## **1.4 Contemporary Perspectives**

Despite its extensive history, the urgent need to address vaccine hesitancy, and its related concepts, appear to have only become agenda-setting issues in recent decades. As a result, a considerable amount of effort is now being focused on researching the nature and causes of vaccine hesitancy and the most effective means of responding to this public health threat. Despite the recent growth in attention, the domain remains relatively disjointed, with several prevalent and sometimes competing fundamental theories and intervention proposals. The following sections provide a non-exhaustive summary of some contemporary perspectives on vaccine hesitancy and interventions intended to address it.

Due to its more recent conceptual origins and the prevalence of competing perspectives, the term ‘vaccine hesitancy’ remains poorly defined. In an effort to establish greater conceptual clarity, a concept analysis is conducted in a subsequent chapter in order to interrogate the etymology of ‘vaccine hesitancy’. While vaccine hesitancy, resistance, and acceptability will all be used in this chapter to introduce important contemporary perspectives, for reasons explained in the concept analysis, throughout subsequent chapters the term ‘vaccine acceptability’ will be used as the principal descriptive concept and the use of ‘vaccine hesitancy’ will be avoided.

### **1.4.1 Information Deficits**

Contemporary interventions aimed at addressing vaccine hesitancy have focused predominantly on overcoming what many believe are information deficits within target

populations (McClure et al., 2017). Several authors have suggested that interventions directed at overcoming information deficits frame vaccine hesitancy as an issue of "science versus ignorance" (Goldenberg, 2016). Ignorance, in this sense, can be understood several different ways. While often used as a pejorative term to describe a willful disregard for factual information, ignorance may also describe an involuntary lack of scientific literacy.

Concerns expressed by the U.S. National Commission on Excellence in Education (NCEE) in 1983 and the London Royal Society (LRS) in 1985 appear to have spurred contemporary discussion on the troubling disconnect between science and public understanding (Goldenberg, 2016). At the root of these concerns was the notion that a lack of scientific understanding could impair the public's ability to make informed decisions regarding scientifically grounded policies. In the 1985 *Bodmer Report*, the authors of the LRS stated:

*“Science and technology play a major role in most aspects of our daily lives both at home and at work. Our industry and thus our national prosperity depend on them. Almost all public policy issues have scientific or technological implications. Everybody, therefore, needs some understanding of science, its accomplishments and its limitations.”*

While the report draws attention to the broader economic implications of a general lack of scientific understanding, it also makes specific mention of the personal health consequences that can emanate from scientific illiteracy, stating:

*“An understanding of science is also important for the individual in his or her private life. Personal decision, for example about diet, smoking, vaccination, screening programmes or safety in the home and at work, should all be helped by some understanding of underlying science. Greater familiarity with the nature and the findings of science will also help the individual to resist pseudo-scientific information. An uninformed public is very vulnerable to misleading ideas on, for example, diet or alternative medicine. An enhanced ability to sift the plausible from the implausible should be one of the benefits from better public understanding of science.”*

Today, the concerns voiced by researchers at the LRS are frequently echoed by researchers and decision-makers working on vaccine hesitancy and related issues. Consequently, many common interventions mirror the calls-to-action outlined in the *Bodmer Report*, which includes bolstering formal scientific education, leveraging mass media to promulgate accurate scientific information and improve public perceptions of science, and bridging the gap between the scientific community and the general public to support efforts to improve scientific literacy.

Drawing from the work of Dr. Paul Offit, Goldenberg (2016) describes how specific knowledge-focused interventions can be categorized as either negative or positive strategies. This delineation also appears to be very much related to the nature of the ignorance that the intervention is designed to treat. As alluded to previously, scientific illiteracy may be the product of an involuntary or uncontrollable lack of understanding stemming from factors such as poor scientific education or even difficulty grasping sophisticated concepts. Positive strategies are often leveraged to address these knowledge deficits as a corrective means to overcome what is presumed to be a misunderstanding of the science (Goldenberg, 2016). In practice, these strategies often aim to communicate pro-vaccine information and recommendations to the public that are grounded in scientific research and evidence. The crux of the effort is to nurture a supportive public perception of vaccines backed by a shared and authoritative scientific consensus.

Conversely, *negative* strategies are used to counter and refute the misinformation and disinformation that emerges from vaccine-resistant groups and organizations. Many of these efforts aim to undermine the credibility of the science used to support oppositional

messaging and the authority of the sources who promulgate such information. In recent years, examples of negative strategies have included ‘fact-checking’ vaccine-related information on social media platforms and, in some cases, censoring misleading information altogether.

While deficit-based interventions have historically been popular, not all information deficits revolve around a lack of understanding or knowledge. A suboptimal level of awareness of a vaccine or vaccine campaign can also affect uptake levels, given that some may not be cognizant of the fact that a vaccine is available to them or someone they know. Just as researchers have advocated for the promulgation of information grounded in scientific consensus to improve general understanding, others have advocated for the more effective dissemination of practical information related to the “who, where, and when one should be vaccinated” (Dubé et al., 2013), with the goal of spreading awareness.

Despite the popularity of interventions directed at information deficits, many researchers have criticized strategies grounded in this school of thought. In fact, some have gone as far as to suggest that public awareness and education campaigns risk reinforcing oppositional views amongst certain groups (McClure et al., 2017). Furthermore, Dubé et al. (2013) write, “studies have shown that parents who choose to vaccinate their children generally have limited knowledge of vaccination and vaccine-preventable diseases compared with parents who refuse to vaccinate.” The implications of these findings might be that treating vaccine non-compliance as an information deficit issue may be an oversimplified or misguided strategy. Even the way in which information deficit theories have historically been framed has led researchers to question derived strategies. The

assumption that more or better information will enable individuals to overcome their hesitancy toward vaccines treats the general public as passive, ignorant actors (Goldberg, 2016). In doing so, strategies of this nature often ignore the “contextual nature of scientific knowledge” (Goldberg, 2016) and how social, political, and cultural factors affect how individuals engage with and understand science.

### **1.4.2 Religion, Culture & Traditional Practices**

As mentioned in the preceding section, several different contextual factors influence how individuals and groups interact with or interpret scientific information. As a result, these contextual factors are widely considered to be principal sources of vaccine hesitancy and resistance. Of the many context influences cited in the literature, religious and cultural factors appear to be two of the more commonly referenced.

Religious affiliation and related beliefs have often been found to dissuade or prohibit adherents from being vaccinated. While few religious canons explicitly forbid the receipt of vaccines, many have been interpreted in such a way that precludes some devotees from accepting a vaccine. Some of this religious opposition stems from restrictions over the consumption of ingredients or materials sometimes contained in vaccines. For example, some resistance to vaccines amongst Hindus has been attributed to the use of bovine constituents in immunizations (Wombwell et al., 2015). In other cases, resistance towards vaccines can be traced back to religiously influenced fundamental understandings of disease and how it is to be managed.

Local religious and cultural leaders are known to influence the health decision-making of community members and followers (Cooper et al., 2008; Hussain et al., 2016;

Lahariya, 2014; Siddiqui et al., 2013). In fact, some of the most vigorous opponents to early vaccines were traditional leaders and healers whose authority or livelihood was threatened by these medical innovations. Some early smallpox vaccination efforts in India were frustrated by the opposition led by traditional healers. When smallpox vaccines began to arrive in the country, variolation was a prevalent and lucrative practice for many (Lahariya, 2014). As efforts were made to supplant the practice in favour of vaccination, many practitioners of variolation were at risk of losing a primary source of income. Consequently, many opposed vaccines and instead turned to spreading rumours about vaccines and refuting their efficacy.

However, fundamental beliefs at odds with vaccination efforts also extend beyond science, traditional practices, and perceptions of disease. Customs engrained in religious doctrine, cultural practice, and traditions have all been found to influence social hierarchies and power structures within families and communities. Limited decision-making power or deference to recognized family decision-makers can also act as barriers to the receipt of vaccines. Furthermore, cultural, religious, or traditional leader intransigence can hinder vaccine uptake in the communities under their authority.

Leveraging the influence and decision-making power of these influential figureheads is widely understood to be vital to the success of vaccination campaigns. Garnering support from religious, cultural, and traditional leaders can help persuade communities and followers to accept vaccines. Moreover, these leaders can often act as gateways into target communities. Consequently, collaborative support is thought to allow for the creation of more culturally- or religiously-sensitive vaccine campaigns. Strategies

of this nature thus appear to overcome some of the criticisms levied against the aforementioned information deficit strategies.

Unfortunately, in cases where there is a failure to engender vaccine support from vocal religious, cultural, and traditional leaders, vaccination efforts can be severely compromised. Over time, resistance from religious opponents led to the creation of special religious and ideological exemptions to vaccine requirements. In fact, intense opposition from religious leaders towards early compulsory mandates in the United Kingdom led to the creation of the world's first exemption clause and the coining of the term “conscientious objector” (Wolfe & Sharp, 2002). Since then, exemption clauses have proliferated across the globe, speaking to the ongoing struggle between democratic politics, public health, and religious rights.

### **1.4.3 Policies & Mandates**

Despite recent calls for the depoliticization of science and public health, the two fields are, and have long been, inextricably linked. In fact, the history of compulsory vaccination laws dates back to the early 1800s in nations such as the United States and the United Kingdom (Malone & Hinman, 2007). Shortly after their earliest implementation, and even until today, compulsory laws and targeted vaccine policies have been a prominent fixture of vaccination campaigns. Consequently, over time, these policy levers and others like them have been some of the most powerful tools that decision-makers can use to promote and compel compliance with vaccination efforts (Bardosh et al., 2022).

Over time, studies have consistently shown vaccine policies and mandates to be effective means of improving uptake and vaccination coverage (Abrevaya & Mulligan,

2011; Gravagna et al., 2020; Mello et al., 2022; Perkins et al., 2016; Willis et al., 2022). In general, the policy tools that decision-makers have at their disposal can be broadly categorized as being either incentive-based or disincentive-based. These distinct approaches leverage a range of different approaches to either persuade or compel adherence to vaccine schedules and programmes (Dubé et al., 2022). The persuasive, incentive-based approaches aim to encourage vaccine uptake through financial rewards, cash lotteries, investments, and in-kind payments (Savulescu et al., 2021). Alternatively, disincentive-based approaches employ fines, social restrictions, employment conditions, and the suspension or withholding of state benefits in order to compel adherence (Dubé et al., 2022; Savulescu et al., 2021).

Despite their evidence efficacy, these political tools have long been criticized and vigorously opposed. Much of the opposition has historically emerged from political and religious opponents who see compulsory laws as an infringement on basic, fundamental, and inalienable rights (Malone & Hinman, 2007). Furthermore, biomedical principles have been used to interrogate the use of incentive- and disincentive-based policy measures. The provision of cash and other in-kind payments introduces ethical concerns related to undue inducement (Dubé et al., 2022). Furthermore, the use of broad, coercive vaccine mandates and restrictions as disincentives has been questioned based on proportionality (Lewandowsky et al., 2022). At the core of this debate is a utilitarian question of whether a “greater restriction of liberty may provide greater public-health benefits” (Savulescu et al., 2021). These debates relate to the aforementioned historical rights-based concerns voiced by opponents of compulsory vaccine laws. As mentioned before, these forms of



resistance to early compulsory laws eventually led to the creation of special clauses which allow for exemptions from compulsory vaccine mandates on religious or ideological grounds (Malone & Hinman, 2007).

Nonetheless, many authors have suggested that even if mandates are successful in compelling and persuading compliance with vaccination schedules, they do so at the risk of sustainable current and future public adherence (Bardosh et al., 2022; Lewandowsky et al., 2022; Schwartz, 2009; Sprengholz et al., 2021). Like many of the other proposed interventions discussed above, these political levers seem to, in many cases, miss the mark in terms of addressing the root of hesitancy, low acceptability, and resistance. Furthermore, in a number of instances, vaccine policies and compulsory mandates have been shown to reinforce oppositional stances. Unlike information deficit-based strategies, which appear to overlook crucial aspects vital to addressing the issue, vaccine mandates often ignore them altogether in favour of swift policy remedies. Put differently, instead of working to nurture public cooperation and trust, compulsory laws compel or persuade compliance, potentially at the expense of future cooperation and trust (Bardosh et al., 2022; Schwartz, 2009).

## **2 Methodology**

### **2.1 Early Deliberations**

From the outset of the planning process for this thesis, a primary focus has been to explore themes that pervade the history of vaccine acceptability across the globe, with the goal of extracting lessons from the past that can be applied to contemporary debates on the issue. It became apparent during early exploratory work that much of the research on vaccine hesitancy and acceptability focused primarily on the characteristics and decisions of individuals. Put another way, much of the existing literature positioned people and their decisions as the primary focus of study. Consequently, not as much attention appeared to have been given to the essential contexts, systems, and processes that operate around and act on people.

While the desired general research focus has been, for the most part, clear, the methodological approach most conducive to its actualization has required a considerable amount of deliberation. Much of these early deliberations were focused on identifying a principal research method that would allow for a qualitative and historical exploration of the evolution of vaccine acceptability, with an emphasis on global processes and contexts. As a result, several different methodologies were considered and explored throughout the early stages of the research process.

#### **2.1.1 A Global History Methodology**

Following the development of an initial set of research questions, a Global History methodology was the first approach considered and explored. Shestova (2013) describes

the subject of global history as “the global socio-historical processes considered from the perspective of the natural world changes.” Global history, as a method of inquiry and analysis, allows for the production of an account inclusive of the many different causalities which have interacted over time to shape a global phenomenon or event of interest. As a result, the methodology has often been described as a study of the “processes of long duration (*long durée*)” (Shestova, 2013). Unlike world history’s focus on “linear and broad narrative(s) around convergence” (Birn, 2020), which are often organized around nation-states, global history allows for the focus to be shifted away from civilizations as primary units of inquiry and to consider transnational phenomena with nuances and causes that cannot be described through “macro processes alone” (Conrad, 2016).

While nations, individuals, and civilizations are undoubtedly part of any global history, they are not the singular (or primary) actors in it. Vaccine acceptability and resistance, as global human phenomena, cannot be fully understood through the isolated lens of any single nation, region, or related unit of measure. The plurality of attitudes towards vaccines stems from a confluence of origins. Furthermore, some common events could elicit dissimilar outcomes depending on the contextually defined conditions that preceded them. While the use of “micro-perspectives” (Conrad, 2016) from varying contexts can be valuable tools for evaluating global phenomena such as this, an inquiry into global history requires these perspectives to be inclusive of both internal and external influences and the different interactions between them.

A focus on the global evolution of vaccine acceptability, analyzed entirely through a biomedical lens, risks perpetuating a Eurocentric, “West versus the rest” (Birn, 2020)

bias, through which a diversity of meaningful perspectives could be devalued or ignored. While it is critical to include non-western perspectives, histories, and voices, incorporating these diverse perspectives cannot be at the expense of any others, including those of the West (Conrad, 2016). The development and spread of vaccines are inextricably related to Euro-American histories and the global diffusion of biomedical paradigms. As such, the global influence and integration of western biomedical models and vaccines cannot be ignored if a representative historical account is to be produced. Alternatively, non-western means of disease control and medical models existed long before vaccines and, in many cases, competed with vaccines. Consequently, the interaction and integration of different perspectives must be considered.

To garner a more complete global historical understanding of vaccine acceptability and resistance, the goal should not be a substitution of one centrism or historical account for another. Instead, the objective should be to understand how these different histories have coalesced or influenced one another while recognizing “the role of uneven power” (Birn, 2020). In line with this goal, global history would allow for an inquiry and analysis that is more reflexive of the many different centrisms that, when considered alone, have been hallmarks of many world history endeavors (Conrad, 2016).

A methodology of this nature would allow for a more comprehensive and inclusive perspective of how many relevant drivers of global changes have influenced vaccine acceptability and resistance. Through this method, it is possible to explore the effects and outcomes of integrating an expanding global biomedical network from the West with the many “alternative” medical networks in other spatialities. Furthermore, the dynamic

influence of other technological, political, economic, cultural, and biological drivers of global change can be considered and represented (Conrad, 2016). As a result, a global historical account of the evolution of vaccine acceptability and resistance and its plurality of causes could be created.

Exploring the Global History methodological approach helped shape and refine the ultimate vision for this thesis. However, after careful deliberation, it became clear that the approach would not be a suitable method to use to move forward. The approach, as Conrad (2016) explains, is undoubtedly well-suited for studying global processes of “integration,” “exchanges and connections,” and the “global reality in a specific period.” However, when looking at the evolution of vaccine acceptability, the *local* appears to be often just as important as the *global*. Consequently, an approach not partial to either local or global processes would instead be required. Nonetheless, there was still a desire to identify a method that would support an exploration of areas of interest motivated by early work with the global history approach. Specifically, the way in which common global factors shape context-specific vaccine attitudes differently was identified as one area that, if possible, would be worth carrying forward.

### **2.1.2 Qualitative Comparative Analysis**

Based on the desire to explore and better understand processes and phenomena between different global contexts, the use of a comparative method appeared to be a promising approach for this thesis. Specifically, comparative research methods focused on individualizing or variation-finding comparisons were explored (Adiyia & Ashton, 2017). Individualizing comparisons were investigated due to the emphasis placed on using “a

small number of cases in order to grasp the peculiarities of each case” (Tilly, 1984). In theory, a method of this nature would allow for an exploration and comparison of relevant cases over different time periods. Thus, individualizing comparisons could capture the historical themes that are integral to the objectives of this thesis. Comparative methods rooted in variation-finding were also explored due to the focus placed on comparing “numerous forms of a single phenomenon to discover logical differences among instances and establish a standard of variation in the character or intensity of that phenomenon” (Adiyia & Ashton, 2017). A method of this nature appeared to be well-suited to compare different instances of low vaccine acceptability or resistance over time and across different global contexts.

Eventually, the decision was made to attempt to move forward with a social science-based approach called a Qualitative Comparative Analysis (QCA). QCA is a set theory methodology used for researching and analyzing complex causality using contemporary and historical case studies (Ragin, 2014). This mixed-methods approach, first developed by Charles Ragin, is helpful in analyzing social and political change, amongst others. QCA is predicated on two foundational assumptions. The first assumption is “that one factor is rarely sufficient to produce change.” The second assumption is that “different combinations of factors can produce the same result” (Delve, n.d.). Put differently, QCA is based on the notion that outcomes are not often fully understood using a single causal explanation. Additionally, there could be a range of different complex combinations of causes that each lead to similar or dissimilar outcomes. These foundational assumptions appeared to

position QCA as a practical means of researching and analyzing the evolution of vaccine acceptability and resistance and the heterogeneity of related origins and influences.

Using a small-to-intermediate number of cases, QCA helps analyze many different causal “recipes” (Hanckel et al., 2021) that can all lead towards or away from an outcome of interest. These causal combinations can include different groupings of both necessary and sufficient conditions (Ragin, 2014). Thus, adopting a QCA for this thesis appeared to be a suitable approach to revealing the many, often contextually defined factors influencing vaccine acceptability across different places and times. To this end, various instances of vaccine resistance and low acceptability were to be explored comparatively in an effort to determine how tensions and interactions between alternate and sometimes competing perspectives could have influenced attitudes towards vaccines in different historical and contemporary cases. Therefore, a qualitative comparative analysis could have helped elucidate the evolution of vaccine acceptability and resistance, and its plurality of potential causes might have been described.

Existing literature on the use of QCA suggests that, in general, researchers should use between 10-50 cases in their comparative analyses (Kane et al., 2014). However, the methodology requires no absolute maximum (or minimum) number of cases. A smaller number of chosen cases may allow for a more detailed account of each respective case but may also limit or miss some relevant factors that could be considered in the analysis. Alternatively, a large number of cases could result in a less comprehensive understanding and contextualization of each chosen case. As a result, the researcher needs to balance these

considerations, amongst others, when deciding on the number of cases to compare (Kane et al., 2014).

Many authors have described QCA as an iterative process (Kane et al., 2014; Pattyn et al., 2019; Simister & Scholz, 2017). While, in general, the method follows six sequential stages it is likely that as research progresses, new insights would require modifications to be made to theories and models developed in previous stages. Nonetheless, the first step in conducting a QCA is identifying an outcome of interest and developing a research question around it. Subsequently, a theory or conceptual model should be adopted or developed that consists of factors that are presumed to have an influence over the outcome of interest. This theory can then eventually be used to help explain the ultimate findings of the analysis.

In an effort to establish a grounding theory of this nature, exploratory research would be conducted to identify a well-defined outcome of interest related to the phenomena of vaccine acceptability. Additionally, many of the explanatory factors and variables used in the final analysis, also known in the method as ‘conditions’, could have been identified at this stage. However, it quickly became apparent through the research that a well-defined or specific outcome would be challenging to delineate. Furthermore, there seemed to be a paucity of precise information on relevant conditions related to this thesis's desired contextual research focus. These challenges appeared to stem from a considerable lack of conceptual clarity and consistency on topics such as vaccine hesitancy, resistance, acceptability, or the theories used to explain their causes. Without a clearer understanding of the phenomena, it would be challenging to determine when an outcome or condition related to vaccine acceptability is present in a case, or when it is not. Consequently, despite



the promise of QCA, it was difficult to justify moving forward with a methodology predicated on a precisely defined outcome when one could not easily be delineated.

### **2.1.3 Final Deliberations**

After working through the aforementioned methodological challenges, it became clear that a more thorough understanding of vaccine acceptability and its related concepts needed to be firmly established and described before any alternate analytical approach could be pursued. Since early in the planning process, there has been an emphasis placed on using historical themes as a cornerstone of this thesis. Thus, it was crucial to refocus efforts on developing a greater understanding of how different conceptualizations of vaccine acceptability and resistance had evolved before any proper analysis of the phenomena itself could be conducted. Consequently, several other methodological approaches were explored. Three additional methods considered for this thesis were a narrative review, scoping review, and a rapid review (Arskey & O'Malley, 2005; Dobbins, 2017; Xiao & Watson, 2019). The final methodological approach chosen for this thesis is discussed and summarized in subsequent sections of this chapter.

## **2.2 Methodological Overview**

Ultimately, the methodological approach adopted for this thesis centered around enabling and conducting an in-depth literature review of the contextual determinants of vaccine acceptability. Overall, the methodological approach can be broken down into three distinct stages. First, at the project's outset, an exploratory research stage was undertaken to better understand prevailing contemporary perspectives on the subject of interest. It was through this stage of research that much of the deliberations mentioned above occurred. In

addition to guiding the methodological deliberations, this exploratory research stage also allowed for the identification of key concepts and knowledge gaps that would be crucial to explore before moving forward with a core research methodology. The second stage consisted of a concept analysis which focused on establishing a greater conceptual and terminological clarity on the topic of ‘vaccine hesitancy’. Information gathered through this concept analysis would be used to support the structure and design of the subsequent in-depth literature review stage and final discussion.

### **2.2.1 Rationale**

After much deliberation, an in-depth literature review, with elements drawn from a thematic synthesis and framework synthesis, was chosen as the core methodological approach for this thesis. In their 2019 publication, Xiao & Watson (2019) describe how the stand-alone literature reviews “attempt to make sense of a body of existing literature through the aggregation, interpretation, explanation, or integration of existing research.” Accordingly, stand-alone literature reviews can be broadly grouped into four categories: “describe, test, extend, and critique” (Xiao & Watson, 2019). For the purposes of this thesis, only the types of reviews focused on ‘describing’ or ‘extending’ were found to be relevant. Descriptive reviews are detailed as being focused on examining “the state of the literature as it pertains to a specific research question, topical area, or concept” (Xiao & Watson, 2019). These descriptive reviews are not meant to “expand upon the literature, but rather provide an account of the state of the literature at the time of the review” (Xiao & Watson, 2019). Conversely, extending reviews go “beyond a summary of the data” and attempt “to build upon the literature to create new, high-order constructs” (Xiao & Watson, 2019).

Concerning this thesis, the second broad approach focused on ‘extending’ emerged as the more relevant approach. Given that existing gaps in the literature constrained the use of other aforementioned methodologies, incorporating elements of a thematic synthesis to synthesize evidence into analytical themes and generate “third order constructs” (Xiao & Watson, 2019) appeared to be valuable and well-suited for extending the understanding of the contextual determinants of vaccine acceptability and its related concepts. Furthermore, given that a guiding conceptual framework will be identified through the concept analysis (see Appendix E) stage, elements of a framework synthesis could also be integrated into the review. As Xiao & Watson (2019) explain, following the review process, the guiding conceptual model can be modified using evidence that has been collected. In the case of this thesis, analytical themes identified through the review can therefore be used to extend upon the original adopted framework.

An emphasis on ‘extending’ appears to be well-aligned with the exploratory and analytical aims of this thesis, which are to develop a deeper understanding of the contextual determinants of vaccine acceptability, their evolution over time and across different global contexts, and their interactional effects. As a result, an in-depth literature review, with elements of thematic and framework syntheses, will be used as the core methodology for this thesis, supported by earlier exploratory research.

## **2.3 Exploratory Research**

During this thesis's initial planning and proposal stage, exploratory research was undertaken to develop a greater understanding of the diverse and often discordant historical and emerging perspectives on the determinants of vaccine uptake, acceptance, hesitancy,

and other related concepts. This early stage of research was largely unstructured and generally involved the manual exploration of databases and resources such as Google Scholar, Dimensions Analytics, MEDLINE, and more. While much of the exploratory research focused on concepts related to the topic of interest, time was also spent exploring and identifying research methodologies that could be applied to the remainder of this thesis.

## **2.4 Concept Analysis**

Despite the overwhelming use of the newly developed term “vaccine hesitancy” in contemporary research and the recent surge in interest on the subject, the term remains relatively ambiguous. Consequently, to establish greater conceptual clarity regarding ‘vaccine hesitancy’ and its many interrelated topics, a limited search of two databases (Global Health and MEDLINE) was conducted. Articles and reviews were manually searched for explicit definitions of VH, conceptual models, and disclosed search strategies. Relevant references included in sourced publications were extracted and reviewed to ensure greater saturation. Some derived resources included grey literature, conference notes, and supplementary materials. A concept analysis was conducted following a detailed search and exploratory review of the literature. Subsequently, a list of key search terms more commensurate to the timescale of interest was created, drawing inspiration from prior search strategies (see Appendix D) and other relevant terms identified during the conceptual analysis. Furthermore, a guiding conceptual model was identified through this stage of the research process (see Appendix E).

## **2.5 Literature Review**

### **2.5.1 Information Sources**

While the concept of vaccine hesitancy is relatively new, discourse on its conceptual predecessors dates back much further. Given the desire to explore and capture these historical themes, the information had to be sourced from resources that had available more historical literature. Consequently, searches were conducted through Ovid using the Global Health database, which includes international material dating back to 1910. Searches were also conducted using the Health Systems Evidence and OECD iLibrary. However, no relevant publications were identified using these sources.

### **2.5.2 Search Terms**

Bayliss & Beyer (2015) stress the importance of “choosing the right vocabulary” when designing a search strategy to ensure that “all relevant materials are retrieved.” In many cases, a number of different synonymous terms can be used to describe a subject of interest. Furthermore, over time, the vocabulary used to describe a subject of interest may have evolved. Consequently, it is important to ensure that this terminological evolution is accounted for when identifying relevant search terms (Bayliss & Beyer, 2015; Xiao & Watson, 2019). To this end, the work conducted through exploratory research and concept analysis helped establish an expansive terminological key that was used to guide and structure the subsequent search strategy. The final set of search terms and the primary sources from which terms were derived can be found in Appendix D.

### 2.5.3 Search Strategy

Relevant search terms previously identified were organized into four thematic groups to structure the search queries (see Table 1). The resulting sets of search terms were categorized under the following headings: A) Intervention, B) Action, Behaviour, or Psychological State, C) Disease, and D) Determinant. Given the variability in terms used and the number of relevant synonyms, truncations were used to expand the scope of the search to ensure greater saturation. Each respective set included a string of related search terms connected by *OR* functions. Subsequently, all four sets were put together into a query using *AND* functions, ultimately giving the search a structure of A + B + C + D. While search queries were, in some cases, modified for specific databases, the full search strategy took the following general form: (*vaccin\* OR imuniz\* OR immunis\* OR inoculat\**) *AND* (*Accept\* OR Intent\* OR Hesita\* OR Attitude OR Sentiment OR Reluct\* OR Willing\* OR Demand OR Confiden\* OR Resist\* OR Refus\* OR Concern OR Reject\* OR Skepti\* OR Scepti\* OR Recepti\* OR Adhere\* OR Oppos\* OR Uptake OR Belie\* OR Doubt OR Fear OR Mistrust OR Trust OR Distrust OR Object\* OR Choice OR Decision*) *AND* (*COVID-19 OR Polio OR Small pox OR Smallpox OR HPV OR Human Papilloma Virus OR MMR OR Measles OR Mumps OR Rubella*) *AND* (*Context\* OR Mandate OR Compulsory OR Policy OR Politic\* OR Policies OR Media OR Influen\* OR Leader OR Lobby OR Lobbies OR Industr\* OR Pharma\* OR History OR Historical OR Religi\* OR Cultur\* OR Factor OR Root OR Caus\* OR Determinant OR Gatekeep*).

Interventions	Actions, Behaviours & Sentiments	Diseases	Determinants
A	B	C	D
Vaccin* Immunis* Immuniz* Incoulat*	Accept* Intent* Hesita* Attitude Sentiment Reluct* Willing* Demand Confiden* Resist* Refus* Concern Reject* Skepti* Scepti* Recepti* Adhere* Oppos* Uptake Belie* Doubt Fear Mistrust Trust Distrust Object* Choice Decision	COVID-19 Polio Small pox Smallpox HPV Human Papilloma Virus MMR Measles Mumps Rubella	Context* Mandate Compulsory Policy Politic* Media Influenc* Leader Lobby Lobbies Policies Industr* Pharma* History Historical Religi* Cultur* Factor Root Caus* Determinant Gatekeep

Table 1: Search terms and search structure

### 2.5.4 Eligibility Criteria

Studies using quantitative, qualitative, and mixed-methods approaches were eligible for inclusion in this literature review. However, quantitative studies focused only on levels or incidence of hesitancy, resistance, and acceptability, or without reference to contextual determinants, were excluded. Given this study's emphasis on historical continuities and discontinuities, no limits were placed on publication dates. All publication types except for full books were eligible for inclusion. However, single chapters from books

were eligible for inclusion. The exclusion of books was related to practical time and resource limitations. Concerning data collection methods, no exclusion criteria were established.

Furthermore, no restrictions were applied based on study populations or location. Publications were excluded if they focused solely on individual-level or vaccine/vaccination-specific determinants without mention of contextual determinants. Publications related to the development of new or prospective study designs were also not eligible for inclusion. Only studies published in, or translated into English were deemed eligible. A full list of eligibility criteria can be found in Table 2 below.

Category	Specified Criteria
Inclusion	<ul style="list-style-type: none"> <li>• Published or accessible in English</li> <li>• No restriction on data collection methods</li> <li>• No publication year limits</li> <li>• All formats other than books, but including single chapters or sections</li> <li>• No restrictions on study populations</li> <li>• No restrictions on location of study</li> <li>• Inclusive of quantitative, qualitative, and mixed-method approaches</li> <li>• Publications that include discussion/mention of contextual determinants and factors related to contextual determinant categories</li> <li>• Publications related to HPV, Polio, Smallpox, MMR, COVID-19, or general commentary were eligible for inclusion.</li> </ul>
Exclusion	<ul style="list-style-type: none"> <li>• Publication in book or novel format</li> <li>• Studies focused on <i>only</i> individual-level or vaccine/vaccination-specific determinants <i>without</i> mention of contextual determinants</li> <li>• Publication focused only on quantitative outcomes/levels <i>without</i> mention of contextual determinants</li> <li>• Studies in languages other than English</li> <li>• Publication focused on only proposed or prospective study designs</li> <li>• Publications focused primarily on diseases other than HPV, Polio, Smallpox, MMR, or COVID-19</li> </ul>

Table 2: Inclusion and exclusion criteria



### 2.5.5 Study Selection

Once collected, full-text references were imported into an AirTable database, where a four-stage filtration process was undertaken to establish a final data set. Once imported, the datasets were screened for duplicates based on title, abstract, unique identifiers, and DOI. Second, given the large number of publications retrieved in the search, it was essential to efficiently identify and eliminate any publications unrelated to the subject and topic of interest. Thus, publications were filtered and screened based on CABICODES (CC), Identifiers (ID), and Heading Words (HW) (see Table 3). Third, following the initial filtration step, titles and abstracts were manually screened using the established eligibility criteria. Any publications missing abstracts were retained for full-text review. The complete files of all remaining publications were then procured for the final full-text screening stage. Publications were once again screened using the established eligibility criteria. All publications remaining were then selected for inclusion in the final review. Through the review, articles were assigned a numerical rating between 1, 2, and 3 based on their relevance to the research focus and search questions. A rating of 1 denoted an article with an indirect mention of a case or example related to a contextual determinant. A rating of 2 denoted an article with a direct or indirect discourse on one or more contextual determinants as a subordinate part of a broader, primary discussion. A rating of 3 was given to any articles with a primary emphasis on contextual determinants of interest. While all articles in the final dataset could have been included in subsequent stages of the literature review, only entries with a rating of 3 were advanced due to practical time and resource limitations.

Label	Excluded Codes, Words, or Identifiers
-------	---------------------------------------

Cabicodes (CC)	<ul style="list-style-type: none"> <li>• FF005 (Field Crops)</li> <li>• VV055 (Human Immunology and Allergology)</li> <li>• VV730 (Pharmacology)</li> <li>• VV400 (Animal Models of Human Disease)</li> <li>• VV450 (Animal and In Vitro Models for Pharmaceuticals)</li> <li>• ZZ360 (Molecular Biology and Molecular Genetics)</li> <li>• ZZ395 (Genetics and Molecular Biology of Microorganisms)</li> </ul>
Identifiers (ID)	<ul style="list-style-type: none"> <li>• Phytochemicals</li> <li>• Extraction</li> <li>• Alkaloids</li> <li>• Solvents</li> <li>• Laboratory</li> <li>• Immune response</li> <li>• Inflammation</li> <li>• Clinical aspects</li> <li>• Ligands</li> <li>• Biochemistry</li> <li>• Genetics</li> <li>• Genotype</li> <li>• Antibod*</li> </ul>
Heading Words (HW)	<ul style="list-style-type: none"> <li>• Etiology</li> <li>• Variant</li> <li>• Cell</li> <li>• Antigens</li> <li>• Adverse</li> </ul>

*Table 3: List of excluded Cabicodes (CC), Identifiers (ID), and Heading Words (HW)*

### 2.5.6 Data Charting Process

Search results were first exported as spreadsheets for preliminary data cleaning. Given the large number of results returned by the search and export limitations, several separate spreadsheets had to be downloaded individually. Subsequently, these files were cleaned to eliminate any data points that would not be used in the filtration, selection, or data extraction stages. After cleaning the data in Excel, each spreadsheet was imported into a single, custom AirTable database, where all further data management was to take place.

AirTable was chosen as the primary tool for data management due to its dynamic and highly customizable feature set. The program allowed for data screening, extraction,

synthesis, data summary, and thematic organization to take place in one centralized database. Furthermore, the program's filter functionality meant that no records needed to be deleted. Instead, filtered and excluded entries were merely hidden during the screening process. Once a final set of entries had been developed for full-text analysis, files were downloaded and attached to the respective article entries in the AirTable base, which allowed for virtual access.

#### *2.5.6.1 Data Items*

- Continent
- Country/Countries
- Study/Publication Purpose
- Study Disease
- Publication Type
- Publication Year
- Period of Study
- Relevant Contextual Determinants

#### **2.5.7 Data Extraction and Synthesis**

A complete reading of all selected articles was conducted to extract relevant data and synthesize information. Extracted data related to the nature and design of studies included information on geographic focus, study population, publication type, disease of study, time period of focus, and relevant contextual determinants. Study results were synthesized to extract themes and key findings relevant to the research questions guiding this literature review. Theme-specific findings related to each article's contextual determinant were summarized and inputted into the AirTable base under the respective

determinant categories. Where applicable, quotes and illustrative case studies were also extracted and inputted. Articles were sorted based on geographic focus and subsequently classified based on thematic relevance.

### **2.5.8 Collating, Summarizing, and Reporting the Results**

Following the data extraction process, extracted information was sorted based on contextual determinant categories. Subsequently, the collated information within each contextual determinant category was analyzed to extract and identify common themes. Once overarching themes had been identified, thematic tags were assigned to specific pieces of relevant extracted information in different entries. This iterative process required multiple readings of the extracted information to ensure that themes and information were correctly and consistently labeled. In many cases, chosen thematic labels were derived from commonly referenced concepts in the literature. Otherwise, new descriptive labels were developed and assigned during the analysis process. It is important to note that few articles included in the final database focused solely on one contextual determinant or contained information on only one theme. Instead, most articles featured information and discussion on a wide range of individual but often interrelated themes.

Consequently, articles in the database are tagged using two or more contextual determinants and a range of themes more often than not. Nonetheless, after tagging articles and extracting data based on contextual determinants and related themes, all data relevant to each thematic tag was organized into respective documents from which descriptive summaries were produced. Finally, articles in the database were grouped based on continent(s) and arranged in chronological order.

### **3 Concept Analysis (Vaccine Hesitancy)**

#### **3.1 Preface**

For nearly two decades, the term vaccine hesitancy has been used to explain the dilemma of poor vaccine uptake and its many putative determinants. Perhaps unsurprisingly, global events in recent years have prompted a surge in interest and discussion around the notion of vaccine hesitancy. However, this burgeoning interest has also elucidated the many conceptual challenges researchers and groups have attempted to reconcile since the term first emerged in 1994 (Bedford, 2017).

Today, when discussing issues related to vaccine coverage and the success (or lack thereof) of immunization campaigns success, VH dominates. Despite its ubiquity, VH has been applied inconsistently to various dissimilar issues, phenomena, and explanations. Consequently, the term has taken on many different, often contextually defined meanings. Such a lack of consistency presents an issue conceptually for its value as a descriptive term and practically for the issues its ambiguity creates for researchers and health professionals. This conceptual challenge is also exacerbated by the colloquial use of the term by news media and across other platforms (Bedford et al., 2017). Before progressing further through the remainder of this paper, we need to establish a consistent and unambiguous conceptual foundation of the subject matter to be discussed. To this end, the conceptual analysis presented in the following section will aim to dispel any relevant ambiguities and describe in detail any essential terms that are to be used.

## 3.2 Towards a Definition

The term “hesitancy” appears to have first been used in the context of vaccines in 1986 by author David K. Sarver. In part one of his publication, Sarver briefly discusses emerging concerns related to the safety of the Hepatitis B Virus (HBV) vaccine. Given that donor plasma was used as a material in the HBV vaccine, some began to question whether acquired immune deficiency syndrome (AIDS) could be transmitted through AIDS-infected donor plasma to the recipient of a vaccine. While Sarver made it clear that there had been no evidence to corroborate these claims, these concerns, and other factors prompted the search for new manufacturing methods, including synthetic biology, that would eliminate the need for human plasma donations.

*“Because of concern regarding HBV vaccine safety, **hesitancy** in its being accepted for general use because of AIDS, and potential problems in maintaining a sufficient supply of plasma to serve as the source for HBsAg, methods are being developed for the manufacture of a recombinant DNA vaccine.” (Sarver, 1986)*

In 1994, hesitancy and its related variations<sup>1</sup> began to be used to “describe physicians’ reluctance to prescribe a vaccine” (Bedford, 2017). However, only after 2006 would VH begin to disseminate more broadly within the published literature. At this point, ‘hesitation’ was used predominantly in the contexts of parental decision-making and the resulting delays in childhood immunizations (Luthy et al., 2009), as well as vaccine attitudes amongst active US military members (Riddle et al., 2008).

*“The lower country immunization rates may be related to the alarming state-wide trend of an increased number of parents who **hesitate** in having their children receive immunizations in a timely manner” (Green & Lee, 2006)*

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<sup>1</sup> Variations of hesitancy also include ‘hesitate’, ‘hesitant’, and ‘hesitation’

*“A disconnect exists between the belief the immunizations are important and the **hesitancy** to receive them.” (Riddle et al., 2008)*

Soon thereafter, the use of VH became much more widespread in discussions of vaccine uptake/non-uptake. However, it would not be until 2012, when the WHO established the SAGE Working Group on Vaccine Hesitancy, that a more focused effort was devoted to defining and conceptualizing vaccine hesitancy. The Working Group (WG) was charged with a number of responsibilities related to defining vaccine hesitancy, scoping the issue, modeling the putative determinants of VH, and suggesting indicators suited for monitoring the prevalence of VH across different global contexts. In 2012, the WG chose the following incipient definition of VH to build from:

*“Vaccine attitudes can be seen on a continuum, ranging from total acceptance to complete refusal. Vaccine hesitant individuals are a heterogenous group in the middle of this continuum. Vaccine hesitant individuals may refuse some vaccines, but agree to others; delay vaccines or accept vaccines but are unsure in doing so.”*

While valuable as a starting point, the WG concluded that this inaugural definition failed to define “the scope nor provide any concept of the many factors that influence hesitancy” (SAGE Working Group, 2014). Eventually, the WG arrived at the following revised definition of VH:

*“Vaccine hesitancy refers to delay in acceptance or refusal of vaccines despite availability of vaccination services. Vaccine hesitancy is complex and context specific, varying across time, place and vaccines. It is influenced by factors such as complacency convenience and confidence.”*

In the years following the publication of the WG’s definition, various alternates and variations have appeared throughout the literature. Despite the new array of proposed meanings, none have been as influential as the definition produced by the WG.

Consequently, even in instances where authors propose substitutes, their alternate definitions often borrow fundamental concepts from the WG's.

For example, Li et al. (2021) defined VH as “the behavioural and psychological concerns that cause people who are able to access vaccination to avoid doing so, either at all or in a timely manner.” The same authors provide an alternative definition that describes VA as “the dynamic and challenging period of indecision around accepting a vaccination.” Similarly, Debendra Nath et al. (2022) offered an alternate, but similar definition for VH, describing it as “the reluctance or unwillingness to get vaccinated or unwillingness to administer vaccines to one's children against an infectious disease, even if the vaccine is proven to be safe and effective, and the service is accessible to uptake the vaccine.”

### **3.3 Conceptual Models & Iterations**

Despite its recent popularity, the term VH and many proposed definitions have been criticized for both practical and conceptual deficiencies. In 2015, Paretti-Watel et al. argued that VH appeared to be more of a 'catch-all' term used to describe a broad and often dissimilar range of phenomena. To create a definition inclusive of the heterogeneity of VH, researchers appear to have produced an ambiguous concept that is interpreted and applied inconsistently across formal and informal contexts. While the aforementioned definitions and uses of VH are valuable in beginning to understand the scope of its meaning, their often concise nature sacrifices essential nuances that are integral to a more complete understanding of VH. For greater clarity on what different authors mean when using the term VH, it is important to examine the conceptual foundations from which many influential definitions have emerged.



Prior to the efforts of the SAGE Working Group on Vaccine Hesitancy, discussions of vaccine uptake/non-uptake were often centred around distinguishing those who had not been vaccinated from those who had. However, as noted by many authors, framing the issue as a matter of acceptance versus rejection could be reductionist or a mischaracterization of its complex, heterogeneous nature. While individual decisions and relatedly demand play a role in vaccine coverage, attributing poor vaccine uptake to demand-side considerations overlooks many broader, supply-side factors that could influence rates of vaccinations. Insufficient supplies, poor logistics, and prohibitive costs can act as supply-side barriers preventing even the most accepting individuals from receiving their vaccines.

Consequently, VH, a term that since 1986 has been used predominantly to describe behaviors, decision-making, and psychological states, was not suited for use as an umbrella concept to describe vaccine non-uptake. In an effort to "depolarize" (McClure et al., 2017) the topic, the WG moved to conceptualize VH in a way that could be distinguished from the aforementioned supply-side factors, stating:

*“The scope of vaccine hesitancy does not apply to situations where vaccine uptake is low because of poor availability e.g. lack of vaccine (stock outs), lack of offer or access to vaccines, unacceptable travel/distances to reach immunization clinics, poor vaccine program communication, etc.”*

To illustrate the critical consideration, the WG described how high rates of VH can lead to low demand, but the inverse might not be accurate. Due to supply-side issues not considered in the scope of VH, low rates of hesitancy are not sufficient to produce high levels of demand. Therefore, the group determined that for hesitancy to exist, vaccines must

be available. Given the notable variation in supply-side exigencies between immunization campaigns and programs, vaccination coverage rates should not be considered indicators of VH levels in a given area. In recent years, this fundamental concept of prerequisite access has led to derivate definitions. In a 2021 publication, Lan et al. (2021) define VH as “the behavioural and psychological concerns that cause people who can access vaccination to avoid doing so, either at all or in a timely manner.” The same authors provide an alternative definition that describes VH as “the dynamic and challenging period of indecision around accepting a vaccination.” Both descriptions explicitly and implicitly frame access to vaccines as a precondition.

Furthermore, by conceptualizing VH as a behaviour that results from an individual’s decision-making process, the working group also needed to produce a definition that was inclusive of the many potential states between outright acceptance of vaccines and absolute refusal. Receiving a vaccine does not preclude an individual from being vaccine hesitant. Similarly, hesitancy, which seems to imply a degree of uncertainty or indecision, might not be the most accurate (or meaningful) way to describe those individuals who, for whatever reason, are steadfast in their rejection of immunizations.

These considerations led to VH being detailed in a manner that moved away from a dichotomous uptake/no-uptake understanding to one that encompasses a broader range of behaviours and psychological states that can exist between those two ends. For example, in her 2014 publication, Larson, a contributing member of the WG, illustrated this essential view by stating:

*“These ‘hesitant’ individuals may refuse some vaccines, but agree to others, delay vaccines, or accept vaccines but are unsure of doing so.”*

Many other authors have developed similar definitions predicated on the notion of VH as a continuum. For example, Schmid et al. (2017) state that “vaccine hesitancy described acceptance of vaccines on a continuum between demand and no demand ranging from accepting all vaccines to accepting no vaccines.” According to these definitions, which seem to characterize VA as an amalgamating term used to neatly describe fundamentally atypical phenomena, hesitancy is not a means through which absolutes should be described. This is to say that vaccination status, or uptake, should not be used to separate those who are hesitant from those who are not.

### **3.3.1 3Cs Model**

In its effort to define VH, the SAGE WG assessed several conceptual models to illustrate its various interrelated complexities. One of the evaluated models was the “Confidence, Complacency, Convenience Model of Vaccine Hesitancy”, or 3C’s for short. The 3Cs model was first proposed in 2011 by the WHO Euro Vaccine Communications Work Group and had already been in use by immunization managers. The 3C’s model was chosen and adapted to suit the WG’s focus on defining VH (MacDonald et al., 2019). Each of the model’s three categories describes one broad dimension that influences vaccine-related decision-making and behavior.

*Confidence* accounts for one’s trust in vaccines, the safety of the vaccines, the medical system and individuals tasked with delivering them, and the individuals charged with making vaccine-related policies.

*Complacency* is used to describe the influences of urgency, such as the perceived risk of immunizable disease and competing health priorities. Due to the overwhelming success of many vaccines in eradicating or attenuating the prevalence of some diseases, many individuals have come to perceive the threat of these well-managed diseases as being low. Such a perception can contribute to vaccine apathy when individuals either no longer see vaccines as a necessary means of risk mitigation or interpret the risks of vaccines as more significant than the immunizable disease. Consequently, vaccines have previously been described as “victims of their own success” (Schwartz, 2009).

*Convenience* describes important supply- and demand-side determinants. Availability, affordability, and general accessibility are some mediators of convenience. Furthermore, the WG described how health literacy, comfort, and cultural context could all affect the broad determinant of convenience.

### **3.3.2 4Cs Model**

In a December 2018 publication, Betsch et al. proposed an extension of the 3Cs conceptual model that added a fourth category they referred to as ‘calculation’. Calculation, based on the authors' description, refers to ones “engagement in extensive information searching” and, subsequently, the “motivation of thinking about and questioning vaccination” (Betsch et al., 2018). As argued by the authors, the constituent elements of the 3C’s model are predicated on concepts shared within psychological theories of human behaviour, including the Health Belief Model and the Theory of Planned Behaviour.

### 3.3.3 5C Scale

In their endeavor to establish a means to measure and monitor different "psychological antecedents of vaccination", Betsch et al. (2018) also established the 5C Scale. Building upon the conceptual foundations of other models, the researchers worked to integrate established theories of psychology and human behaviour to design a scale that could help better explain the "psychological underpinnings of vaccine uptake." The five categories that comprise this 5C scale are confidence, constraints, complacency, calculation, and collective responsibility.

In a similar fashion to the 3C and 4C models mentioned above, Betsch et al. (2018) based the antecedent of confidence around trust in vaccines, the health system, and policymakers. Complacency was thought to exist when the "perceived risks of vaccine-preventable diseases are low, and vaccination is not deemed a necessary prevention action." *Calculation* was defined as an "individual's engagement in extension information searching" and the action of engaging in personal risk calculations.

The researcher's final design of the 5C scale deviated slightly from previously established models in its inclusion and conceptualization of the *Constraints* and *Collective-Responsibility* categories. The constraints category was used to describe "structural and psychological barriers" such as access to a vaccine or a lack of self-control (Betsch et al., 2018). These barriers were shown to exert a strong influence over personal vaccine intention. The researchers defined *collective responsibility* as "the willingness to protect others by one's own vaccination by means of herd immunity." Collective responsibility

affects vaccine uptake differently depending on factors such as empathy, collectivist perspectives, and communal orientation.

While the 5C scale is valuable in so far as it can elucidate psychological and behavioural factors that influence individual vaccine decision-making, the scale is not designed to evaluate systems-level considerations. Nonetheless, those macro-level factors can and do influence the 5C's identified by Betsch et al. (2018).

### **3.3.4 5A Taxonomy**

In an attempt to better understand the roots of low vaccine uptake, Thomson et al. (2015) developed a pragmatic taxonomy made up of 5 causal categories. The authors titled the model the *5A Taxonomy* after its five constituent dimensions of access, affordability, awareness, acceptance, and activation. Most other models appear to attribute vaccine uptake levels to a confluence of common individual behavioural, social, and supply-side determinants. Conversely, Thomson et al. (2015) included a broader range of intervention-specific factors, labeled *Activation*, such as reminders, prompts, and policies, that were found to motivate or “nudge” individuals toward receiving a vaccine. Including some intervention-specific determinants in the final taxonomy helped slightly distinguish it from other previously proposed conceptual models.

Along with concise categorical definitions, the authors also identified an initial series of constituent factors that made up the broad determinant categories. Access, defined as “the ability of individuals to be reached by, or to reach, recommended vaccines” (Thomson et al., 2015), included determinants such as place of birth, location of vaccination, contact with healthcare systems, and convenience of access. Affordability,

which was defined as “the ability of individuals to afford vaccinations, both in terms of financial and non-financial costs (e.g., time)”, included financial incentives and time costs. Awareness, which was defined as “the degree to which individuals have knowledge of the need for, and availability of, recommended vaccines and their objective benefits and risks”, was found to be influenced by factors such as knowledge of vaccines and related schedules, availability of relevant information, and consideration of vaccination. Activation, which the authors defined as “the degree to which individuals are nudged towards vaccination uptake,” included prompts, reminders, and workplace policies (Thomson et al., 2015).

Acceptance, which was defined as “the degree to which individuals accept, question, or refuse vaccination”, was found to be the most commonly researched categorical determinant in the literature. The identified constituent determinants were separated into the four sub-categories of vaccine-specific factors, disease-specific factors, individual characteristics, and social contexts. Vaccine-specific factors included perceptions of vaccine safety and efficacy and attitude valence. Disease-specific factors included individual perceptions of vulnerability and severity of the disease(s) specific vaccines target. Individual characteristics influencing acceptance were health beliefs, omission bias, trust, and past behaviour. Finally, determinants related to social contexts included social responsibility, peer influence, and the influence of healthcare workers (Thomson et al., 2015).

### **3.3.5 Vaccine Determinants Matrix**

In addition to the 3C’s model, the SAGE WG proposed a more detailed “Determinants of Vaccine Hesitancy Matrix” to describe the various interrelated and

complex determinants of VH (SAGE Working Group, 2014). The matrix comprises contextual influences, individual and group influences, and vaccine/vaccination-specific issues. The matrix shares some of its constituent determinants from the aforementioned 3C and 4C conceptual models. The contextual determinants category was defined as the “influences arising due to historic, socio-cultural, environmental, health system/institutional, economic or political factors” (SAGE Working Group, 2014). Related determinants include geographic barriers, perceptions of the pharmaceutical industry, historical events and influences, influential leaders, and the communication and media environment. The WG described the individual and group determinants category as the “influences arising from personal perception of the vaccine or influences of the social/peer environment” (SAGE Working Group, 2014). Some cited determinants include personal or peer experience with vaccinations, knowledge, and awareness of vaccines, health beliefs and attitudes, and perceptions of related risks and benefits. Finally, the WG included the vaccine/vaccination-specific issues to include and elaborate upon many of the determinants covered by its complacency categories in the 3C model. Some of the cited determinants include the mode of administration, the design of vaccination programmes, related costs, reliability of vaccine supply, and more.

### **3.4 Working Interpretation of Vaccine Hesitancy**

Since WHO/SAGE formally worked to investigate and define VH in 2014, many researchers have debated and challenged proposed conceptualizations of the phenomenon. Some common discussions concern whether VH should be understood through a behavioural or psychological lens. Nonetheless, as discussed above, a number of different



models and scales predicated on behavioural and psychological understandings of VH have been developed. Regardless of the school of thought, each model works to demonstrate the heterogeneity of VH. In doing so, the models illustrate how VH cannot be reduced to a single standardized archetype. The limited number of factors that make up each conceptual model is meant to help categorize major behavioural or psychological influences that can lead to varying manifestations of VH. However, specific combinations of influences are not uniformly related to (non)vaccination outcomes. Consequently, VH is generally understood not to be an appropriate way of describing one side of the vaccinated/unvaccinated dichotomy.

Another common feature of many conceptualizations is that VH falls along a continuum between absolute acceptance and absolute refusal. While the VH continuum is a useful theoretical tool for capturing the breadth of the phenomenon, it appears to lead to ambiguity and imprecision in practice. As mentioned before, VH is characterizable by its heterogeneity of manifestations. Despite being a valuable means of depicting what VH *is not*, the continuum fails to elucidate, in a precise way, what VH, in its various forms, *is or can be*. Consequently, while many now acknowledge VH as a state of indecision between uptake and refusal, the space between is far less well-characterized. Nonetheless, some researchers have proposed classification systems for the various degrees of VH (See Appendix F). However, as with formal VH definitions, a consensus has yet to be reached.

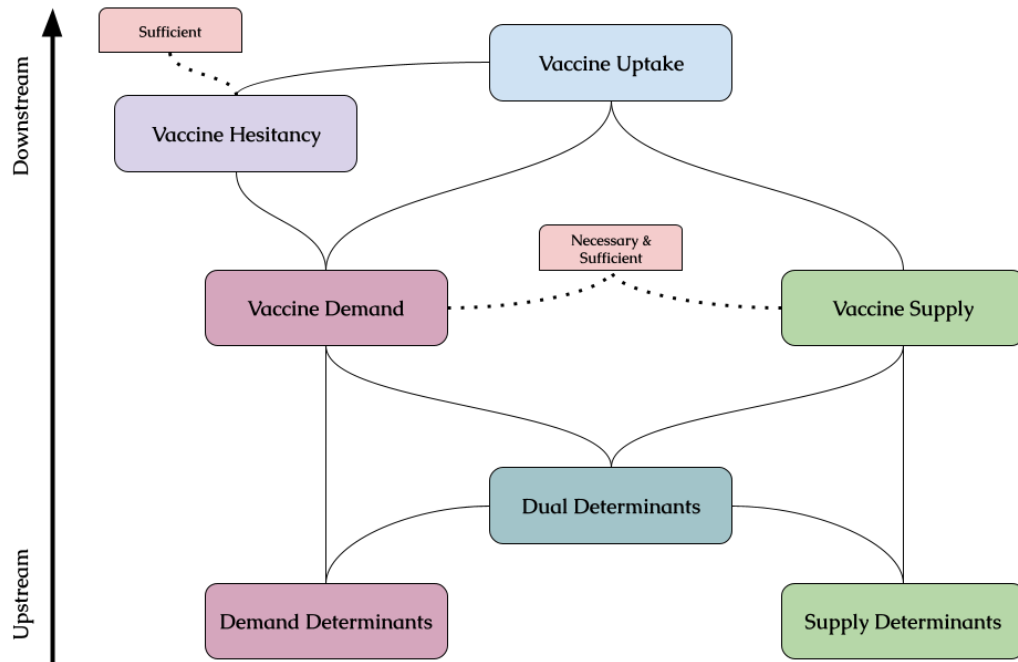
Many researchers have taken to developing conceptual models and scales as a means through which VH's central factors of influence can be identified, assessed,

measured, or monitored. These conceptual models generally feature small sets of factors, many of which have been derived from existing psychological and behavioural theories. These respective factors are assumed to be the elements that influence where one might fall along the VH continuum. Regardless of related conceptual underpinnings, each of the identified factors is influenced by a range of determinants that, under some other models, can also be categorized. However, these often interrelated determinants do not always lead to regular or predictable outcomes. In fact, several determinants have been found to exert opposite or unexpected effects on previously identified factors, and, ultimately, VH. For example, in some cases, higher levels of education have been shown to lead to greater levels of vaccine hesitancy (MacDonald, 2015).

Should the complex and irregular nature of the determinants be misunderstood, or the relationship determinants have with factors be taken for granted, derived interventions risk lacking meaningful impact on the behaviours, or states of mind they target. Nonetheless, the integral nature of these determinants makes them the primary unit in the present conceptualization of VH. When formulating interventions meant to address problematic VH, different combinations of these primary determinants are targeted in an attempt to influence the expression of one or more of the aforementioned factors.

For the purposes of this thesis, a working conceptualization of vaccine hesitancy has been created based on the information and theories outlined above. A brief description and visualization of this conceptualization are outlined below.

*Vaccine hesitancy is the unique, down-stream behavioural/psychological product of influencing factors that are shaped by up-stream contextually-defined primary determinants.*



*Figure 1: Illustrative conceptualization of vaccine hesitancy, demand determinants, and supply determinants*

Category	Related Terms & Concepts
<b>Downstream</b>	
The dichotomous actions mediated by higher-level states and influences.	Acceptance Refusal Uptake Non-Uptake Anti/Pro-Vaccination
<b>Midstream</b>	
The intermediate behavioural and psychological states that are influenced by combinations of upstream determinants and effects.	Intentions Confidence Attitudes Hesitancy

Upstream	
The direct individual, group, and overall effects of upstream determinants of vaccine demand.	Trust Fear Concerns Doubt Beliefs Perceptions

Table 4: Terminological conceptualization

## 3.5 Relevant Conceptual Issues

### 3.5.1 Ambiguity

As illustrated above, the conceptualization of VH continues to evolve. Consequently, the term remains relatively ambiguous and is applied inconsistently inside and outside academia. The models used to explain the categorical determinants of VH, some of which were explored above, are often based on different and inconsistent conceptual underpinnings. Nonetheless, many rely on similar and sometimes overlapping concepts to explain and predict VH. While some definitions of VH have come to be more widely accepted, the scope and meaning of the term remain contentious and fragmented. For example, the definition of VH developed by the WG has been criticized for its predominantly behavioural focus. As some authors have pointed out, VH can be understood from a psychological perspective as a “state of indecision.”

An innumerable amount of combinations of beliefs, perceptions, and attitudes fall between the boundaries of vaccine acceptance and refusal. Despite frequent references to the ‘continuum’ of VH, the term continues to lack the specificity needed to identify where individuals or groups fall along that range. As such, the amalgamation, reduction, and generalization of such a broad and complex phenomenon have seemingly turned VH into a

somewhat nebulous concept. To effectively explore and describe the determinants of vaccine demand, antecedent factors and the related influences need to be well-defined.

### 3.5.2 Continuity

The recent growth in attention given to issues of vaccine hesitancy can be visualized by Figure 2 below. Given that the focus of this research effort will be on historical-contextual trends and themes that predate the origin of VH as a concept, a set of search terms and descriptive terms more commensurate to the timescale will need to be established. As a result, further research cannot proceed without consideration for the etymology of terms such as ‘vaccine hesitancy’, ‘vaccine acceptance’, ‘vaccine resistance’, and more. Fortunately, a number of prior reviews have provided detailed overviews of fundamental and related search terms that will help guide the ensuing search strategy and help establish a greater level of continuity (see Appendix A)

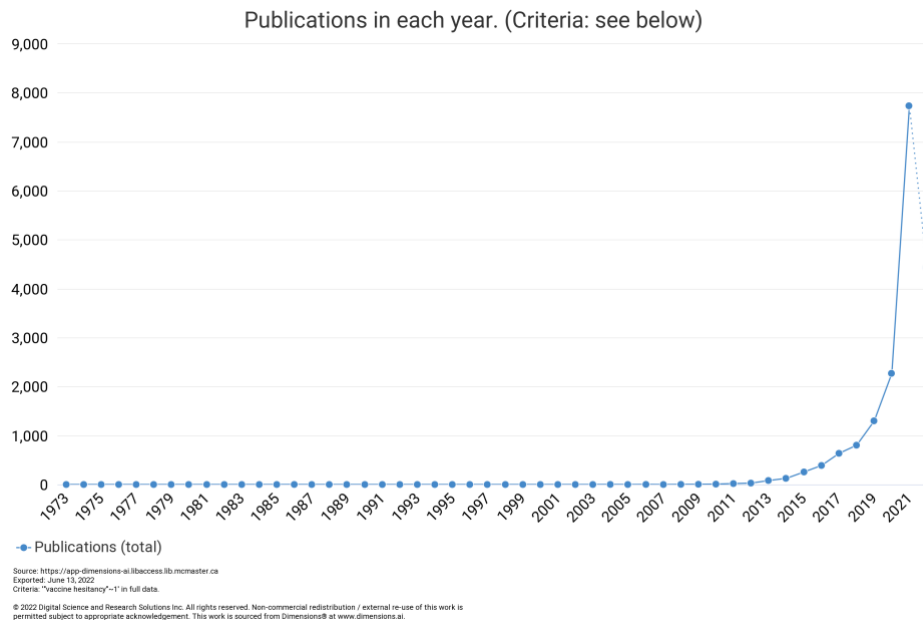
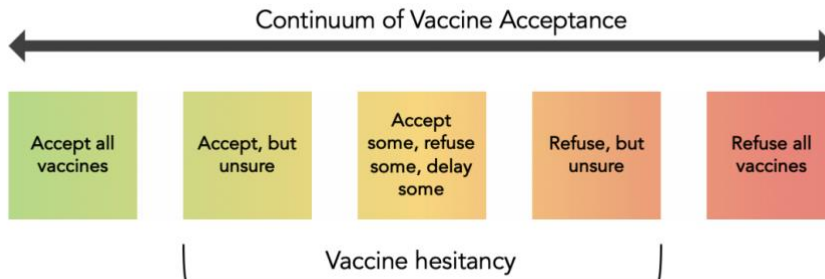


Figure 2: Publications in each year that include the term "vaccine hesitancy"

### 3.5.3 Incompatibility

Instead of focusing on the way in which different putative behavioural and psychological factors influence patterns in decision-making, this thesis will look to identify the contextually-defined determinants that mediate those previously identified influential factors. Put another way, the focus of this research endeavour will be to step back from the individual- and behavioral-focused discourse of vaccine hesitancy. In doing so, emphasis will be put on how different antecedent contextual determinants shape and have shaped broader trends in beliefs and attitudes toward vaccines and not on how beliefs and attitudes affect individual decision-making. Furthermore, as illustrated by Figure 3 below, vaccine hesitancy is often conceptualized as the indefinite state that falls between two categorical ends. However, the broad focus of this thesis requires the absolute ends of the continuum to be considered as well. Therefore, vaccine hesitancy is not a suitable primary descriptor for this research endeavor. Consequently, an alternative, more suitable set of terms will be outlined in a subsequent section.



*Figure 3: Continuum of Vaccine Acceptance from Johns Hopkins (2020)*

### 3.6 Final Conceptualization & Research Focus

Vaccine hesitancy has emerged as an issue of global health due to its relationship with vaccine uptake, immunization coverage, and, consequently, burdens of immunizable disease. Today, VH is widely regarded as a significant barrier to achieving target immunization objectives and global health agendas. Consequently, in 2019 the WHO declared that VH was one of the top 10 greatest threats to global health (WHO, 2019). These goals mentioned above, which are contingent on vaccine uptake, *can* be the product of (non)prevalent VH. While VH is *sufficient* for poor vaccine uptake, it is not a *necessary* condition. Supply-side constraints or barriers such as vaccine stock, distribution, and cost can all lead to suboptimal levels of vaccine coverage in target areas. In fact, these supply-side exigencies are *necessary* conditions that must be satisfied to achieve target immunization goals and high vaccine uptake levels. Even in the complete absence of VH, supply-side constraints can and have led to insufficient vaccine coverage.

While VH undoubtedly contributes to suboptimal vaccine coverage, the relationship between VH and vaccine outcomes is not definite. As noted in the literature, some hesitant individuals may nevertheless choose to receive their vaccine in spite of any negative concerns, doubts, perceptions, or beliefs. Thus, while levels of VH may be a useful barometer for gauging the *potential* of suboptimal vaccine outcomes, it should not be used as an ultimate predictor of uptake. Even in instances where VH is thought to be prevalent, supply-side exigencies might still contribute more to poor levels of immunization coverage.

VH is undoubtedly a problem that *can* and *does* lead to poor uptake. However, addressing it is not straightforward due to its heterogeneity. Not all interventions work to overcome all instances of VH as a result of unique combinations of underlying determinants. As mentioned in preceding sections, many contemporary interventions prioritize and target only specific subsets of vaccine hesitancy's putative determinants. Furthermore, some proposed determinants of VH have been shown to have an inverse relationship with VH outcomes depending on the context where individuals or groups reside. For example, many researchers have treated VH as an issue caused by poor health literacy, awareness, and other related knowledge deficits. Interventions focused on improving knowledge and awareness, have been shown to be effective in some contexts. However, in others, they have been suggested to reinforce opposing beliefs and resistance towards vaccines (Dubé et al., 2015).

Psychological and behavioural concepts have dominated the discourse on VH. While perhaps unsurprising due to the WHO/SAGE Groups' explicit focus on behaviour as the basis for VH, this conceptual emphasis has strongly influenced research on VH and, consequently, proposed interventions. Many proposed and actioned interventions appear to relate strongly to individual and group-level determinants. However, due to the heterogeneity of hesitant groups, interventions may only be effective in targeting small-group subsets with similar characteristic influences. The prioritization of individual-level factors such as knowledge, awareness, and risk perceptions might come at the cost of overlooking other integral antecedent contextual determinants that shape attitudes towards vaccines and acceptability at a broader population level.



Suppose vaccine uptake is accepted to be a downstream effect of all antecedent influences. In that case, VH might be best understood as a broadly defined intermediary point between upstream determinants of vaccine supply and demand and downstream vaccine outcomes. However, VH, as a *sufficient* condition, only encompasses an ambiguous segment of the overarching *necessary* condition of vaccine demand. Given that vaccine uptake is contingent on there being a demand for vaccines, macro-level drivers of confidence, favourable attitudes, trust, and receptiveness seem all to be important considerations, not just for levels of hesitancy but for the acceptability of vaccines overall.

Some authors have suggested that many of the fundamental theories of vaccine acceptance, which underpin public and global health efforts, have evolved since the successes of polio and smallpox campaigns (Taylor, 2009). As a result, there may be a need to revisit some of the broader assumptions upon which contemporary immunization campaigns and programmes are constructed. In other words, before developing specific interventions for VH group subsets, there is perhaps a need to step back and ensure that many of the more broadly applicable determinants are being considered and addressed.

## **4 Key Concepts & Theories**

### **4.1 Supply vs Demand**

Reducing the global burden of immunizable disease has been given a great deal of political attention, especially as it relates to the Global South. Consequently, global stakeholders have enshrined international and domestic health targets to affirm and support the commitment to attenuating these disease burdens. Vaccines have long been touted as one of the more cost-effective and impactful means of achieving widespread reductions in immunizable diseases. As a result, many related public and global health efforts emphasize the need to achieve high immunization coverage rates within target populations.

The success (or failure) of global immunization efforts is predicated on several interrelated determinants. Borrowing from fundamental economic models, the relationship between supply and demand is an uncomplicated and illustrative means of describing what is needed to achieve target immunization goals (Taylor, 2009). On the supply side, there is a crucial need to ensure that the requisite amounts of effective vaccines reach targeted populations. While intuitive, supply-side constraints have historically contributed to the inequitable distribution of global vaccine coverage and, consequently, disparate burdens of immunizable disease. Barriers related to, amongst other things, costs, distribution, and proximal production capacity have all contributed to insufficient levels of global vaccine accessibility. However, overcoming these supply constraints has also brought about a range of proposed and actioned political, economic, and scientific innovations.

As Taylor (2009) explained, the failure of prior disease immunization programmes has been often, and sometimes erroneously, attributed to financial, scientific, or administrative shortcomings. These explanations treat disease eradication as being largely contingent on the sufficient allocation of resources. An underlying assumption thus appears to be that increased funding for scientific research, programme development, and logistics are primary solutions to lackluster results.

However, if contemporary efforts to immunize the global population against COVID-19 have revealed anything, it is that a near ‘limitless’ allocation of human and financial resources to a single disease may not be the panacea some might have hoped. Even in instances where supply-side exigencies have been satisfied, demand-side influences can still hinder the achievement of immunization targets (van Heemskerken et al., 2022). As Taylor (2009) states, “(disease) eradication relies on absolute commitment among all engaged parties.” Without considering the plurality of contextually defined demand-side factors that mediate the acceptability of, and compliance with an immunization programme, efforts will and have struggled to achieve targeted goals. Unfortunately, research efforts into potential solutions to address the heterogeneity of demand-side difficulties have not benefited, to the same degree as the previously identified supply-side exigencies, from vast human and financial investments.

## **4.2 Acute vs Chronic**

Vaccine hesitancy and a lack of acceptability or confidence have generally been treated as acute issues. This is to say that proposed interventions seem to follow a pattern of targeting individual-level determinants of the phenomena. However, the heterogeneity

of VH often makes targeted interventions of this nature ineffectual in specific subsets of the VH spectrum. For example, while education initiatives have been touted as effective means of overcoming knowledge deficit drivers of VH, some evidence suggests that these targeted education campaigns reinforce antithetical beliefs in some groups while aiding in attenuating doubt in others. Additionally, while policy measures such as “vaccine passports” may aid in motivating complacent or apathetic subsets of the VH population, for others, these policy levers only strengthen oppositional stances and push individuals further to the extremes.

History has demonstrated that resistance and hesitancy to vaccines have existed for as long as technology. Despite the predictable presence of low vaccine acceptability during routine and mass immunization campaigns, many decision-makers have failed to take the pre-emptive, forward-looking steps needed to cultivate population-level receptiveness to vaccines. Instead, “short-term reactive policies” are favoured over “long-term proactive policies” (Khalid et al., 2022). Reactive interventions targeting suboptimal vaccine acceptability treat the heterogenous phenomena as an acute issue and are often tailored to small and specific groups. However, some researchers have suggested that treating low vaccine acceptability as a chronic issue might allow for a greater proactive focus on many of the antecedent determinants that shape vaccine-related sentiments and receptiveness on a population level. Such an effort would foreseeably require a greater emphasis placed on macro-level levers and influences as opposed to the individual-level factors that have dominated much of the ongoing discourse.

### 4.3 Guiding Conceptual Foundation

For the purposes of this thesis, the term “vaccine hesitancy” will be avoided. Instead, a supplementary set of more precise terms will be defined and used to explain specific outcomes and effects of particular determinants. Despite avoiding the use of the ambiguous term VH, elements from some of the models previously used to support its conceptualization will help guide the focus of this thesis. Specifically, the determinants matrix developed by the SAGE Working Group will serve as a conceptual foundation (See Appendix E). Given that this thesis focuses on trends and themes related to demand-side determinants, the WG’s conceptual model (which excludes supply-side factors) is a well-suited basis for inquiry.

The VH Determinants Matrix developed by the SAGE WG was inspired, in part, by a 2011 conceptual model of vaccine hesitancy developed by researchers at Sherbrooke University. This predecessor to the WG’s matrix, titled the *Determinants of Vaccine Hesitancy Model from Canada*, illustrated a comprehensive array of influences, factors, and contexts that make up the roots of vaccine hesitancy. However, due to its complexity, the WG felt that the Canadian model would be impractical for use in the field (SAGE Working Group, 2014). Instead, in consultation with several immunization managers, the WG moved to design its matrix using a systems approach that organized determinants into three overarching groups. As illustrated in the figure above, the WG matrix grouped determinants into the categories of *contextual influences*, *individual/social influences*, and *vaccine and vaccination-specific issues*.

Of the three determinant categories that make up the WG determinant matrix, contextual influences appear to have received the least attention. These categorized determinants, defined as “influences arising due to historic, socio-cultural, environmental, health system/institutional, economic or political factors” (SAGE Working Group, 2014), include many macro-level elements that might be fundamental to understanding the dynamic history of vaccine acceptability on a population level.

<b>Contextual Influences</b>	Influences arising due to historic, socio-cultural, environmental, health system/institutional, economic, or political factors
<b>Communication and Media Environment</b>	Media and social media can create a negative or positive vaccine sentiment and can provide a platform for lobbies and key opinion leaders to influence others; social media allows users to freely voice opinions and experiences and it can facilitate the organization social networks for or against vaccines
<b>Influential leaders, gatekeepers and anti- or pro-vaccination lobbies</b>	Community leaders and influencers, including religious leaders in some settings, celebrities in others, can all have a significant influence on vaccine acceptancy or hesitancy
<b>Historical influences</b>	Historic influences such as the negative experience of the Trovan trial in Nigeria can undermine public trust and influence vaccine acceptance, as it did for polio, especially when combined with pressures of influential leaders and media. A community’s experience isn’t necessarily limited to vaccination but may affect it
<b>Religion, culture, gender, and socioeconomic factors</b>	A few examples of the interplay of religious/cultural influences include: <ul style="list-style-type: none"> <li>- Some religious leader prohibit vaccines</li> <li>- Some cultures do not want men vaccinating children</li> <li>- Some cultures value boys over girls and fathers don’t allow children to be vaccinated</li> </ul>
<b>Politics and policies (mandates)</b>	Vaccine mandates can provoke vaccine hesitancy not necessarily because of safety or other concerns, but due to resistance to the notion of forced vaccination

<b>Geographic barriers</b>	A population can have general confidence in a vaccine and health service, and be motivated to receive a vaccine but hesitate as the health center is too far away or access is difficult
<b>Pharmaceutical industry</b>	Industry may be distrusted and influence vaccine hesitancy when perceived as driven only by financial motives and not in public health interest; This can extend to distrust in government when perceived that they are also being pushed by industry and not transparent

*Table 5: Overview and description of the contextual determinants of vaccine hesitancy from the SAGE Working Group (2014)*

## 4.4 Terminology

Issues of ambiguity and continuity make the use of the term VH challenging. Furthermore, based on the interpretation discussed above, VH does not appear to be a suitable conceptual basis for the focus of this thesis. Instead, a series of related terms will be classified and defined below in order to establish a more precise terminological and conceptual foundation to move forward with. However, it is essential to note that the terms and definitions listed below are not being proposed as substitutes for terms used more commonly in the literature.

### 4.4.1 Vaccine Acceptability

This thesis will use acceptability to describe prevailing public attitudes toward vaccines and vaccine-related programmes, campaigns, and policies. Acceptability can be used to describe receptiveness towards vaccines and related efforts. Similarly to vaccine hesitancy, vaccine acceptability may be understood as falling on a continuum ranging from low acceptance, oppositional attitudes, and refusal to high levels of acceptance and supportive attitudes. This conceptualization of vaccine acceptability draws inspiration from the adapted *Vaccine Acceptance Spectrum* identified in a publication by Li et al. (2022).



Fig 1 | Vaccine acceptance spectrum. From: Leask, J. (2015, May 12). Improving communication about vaccination, adapted from Julie Leask's online blog [5].

*Figure 4: Vaccine Acceptance Spectrum from Li et al. (2022)*

#### 4.4.2 Vaccine Resistance

Vaccine resistance will be used to describe opposition to vaccines, public dissent towards vaccine campaigns, and intentional non-compliance with vaccine-related policies or laws. Vaccine resistance should not be conflated with low acceptability. Instead, it is meant to be used to describe intentional, opportunistic, and strategic medical dissent and opposition towards vaccines or vaccine programmes, campaigns, and policies.

#### 4.4.3 Vaccine Demand

For this thesis, vaccine demand will refer to the prevailing level of demand for a vaccine. Once again, this term should not be conflated with vaccine acceptability. Instead, it describes a population who desire, are willing, and are supportive of receiving vaccinations. However, as discussed in the preceding section, the presence of demand for vaccines may not result in vaccine uptake when supply-side exigencies are not met. Consequently, vaccine demand should, for the purposes of this thesis, can be understood as the antithetical counterpart to vaccine resistance.



#### **4.4.4 Vaccine Uptake**

Vaccine uptake will be used in this thesis to describe the receipt of vaccines. In some instances, it can be used synonymously with vaccine coverage. Low vaccine uptake may be understood as the result of low vaccine acceptability or high levels of vaccine resistance. Conversely, high vaccine uptake may be understood to result from high levels of vaccine acceptability and low levels of vaccine resistance. Vaccine uptake is the final downstream result of vaccine demand, influenced by acceptability, resistance, and vaccine supply.

## **5 Results (Literature Review)**

### **5.1 Extent of the Literature**

AirTable was used to perform all data screening and extraction stages. Subsequent to the May 2022 database search, 13,604 complete references were imported into the AirTable database. Using an internal script, the database was searched for duplicate records based on common titles, abstracts, DOI, and source links. Following the search, 55 duplicate articles were removed. Next, the remaining articles were screened and flagged for exclusion based on Identifiers (ID), Cabicodes (CC), and Heading Words (HW). It is worth noting that through this initial screening process, several articles were flagged for meeting more than one of the exclusion criteria mentioned above. In total, 4,804 were excluded during this first screening stage. This total consisted of 581 articles flagged for exclusion based on ID, 2,915 based on CC, and 2,267 based on HW. A total of 8,745 articles were subsequently screened for eligibility based on titles and abstracts using the relevant criteria. Ultimately, 8,210 articles were excluded, leaving 535 articles available for full-text analysis. A total of 5 articles could not be accessed for full-text analysis. After retrieving and importing all files into the AirTable database, individual articles were assessed for eligibility. Following the full-text analysis, 221 articles were deemed ineligible for inclusion. The remaining articles were categorized based using a relevance rating. Only articles with the highest relevance rating were to be included in this literature review. Consequently, a further 165 articles were excluded, leaving 139 articles eligible for final inclusion in the review.

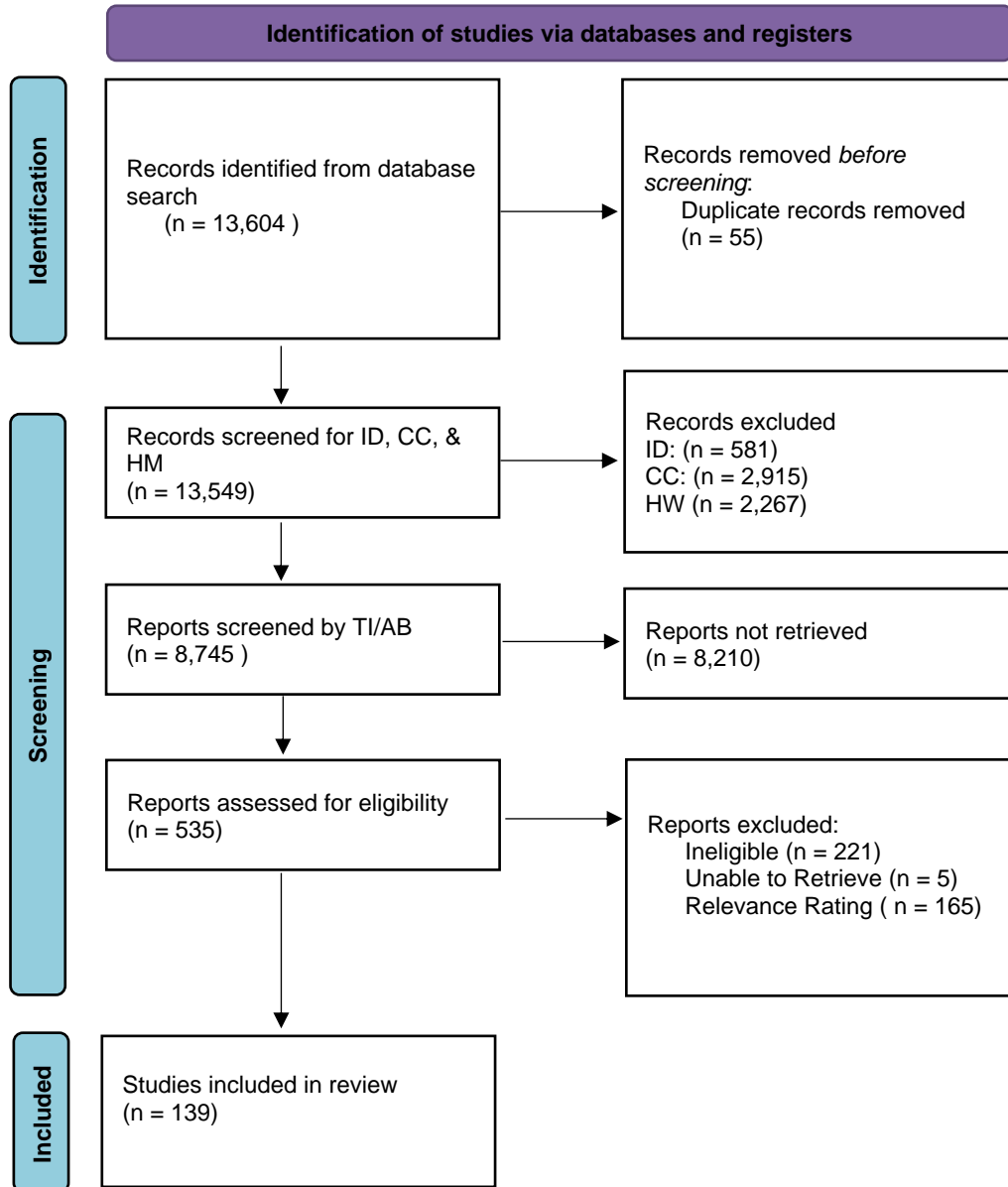


Figure 5: Flow Diagram

## 5.2 Nature of the Literature

Characteristic	Number of Studies
<b>Publication Year</b>	
2022	12
2021	29
2020	11
2019	8

2018	6
2017	5
2016	9
2015	8
2014	3
2013	4
2012	4
2011	6
2010	5
2009	5
2008	1
2007	4
2006	3
2005	1
2004	1
2003	2
2001	1
2000	1
1995	1
1972	1
1971	1
1968	2
1948	1
1941	1
1937	1
1936	1
1934	1

Table 6: Characteristics of the publications included in the literature review

<b>Table 7: Characteristics of Publication Content</b>	
Characteristic	Number of Studies (n=)
<b><i>Continent of Study</i></b>	
North America	33
South America	4
Europe	22
Africa	27
Asia	21
Oceania	1
Global	31
<b><i>Disease of Study</i></b>	
COVID-19	40
HPV	23
Measles, Mumps, Rubella	30
Polio	45
Smallpox	23
<b><i>Period of Study</i></b>	

1800-1850	5
1851-1900	6
1901-1950	13
1951-2000	22
2000-2022	78
General	38
<b><i>Contextual Determinants</i></b>	
Politics & Policy	98
Cultural, Social & Religious Factors	74
History & Historical Factors	53
Communication & Media Environment	60
Influential Leaders	58
Pharmaceutical Influences	34
Geographic Influences	26

*Table 7: Characteristics of the content included in the literature review*

### 5.2.1 Publication Year

The overall ascending distribution of publications appears to reflect the trend mentioned in the preceding section regarding the burgeoning interest in ‘vaccine hesitancy’ over the past two decades. The majority (~93%) of studies included in this literature review were published after 2000. However, 52 of the 139 (~37%) studies included in the literature review were published over the three years between 2020 and 2022. This also appears to reflect an apparent surge in the attention given to vaccine acceptability, hesitancy, and other related concepts throughout the COVID-19 pandemic.

### 5.2.2 Geographic Focus

The final dataset featured publications with a predominantly balanced geographic focus, with the notable exception of Oceania (n = 1) and South America (n = 4). Studies focused on North America (n = 33) accounted for 23.7% of the dataset, followed by Globally-focused studies at 22.3% (n = 31), Asia at 19.4% (n = 27), Europe at 15.8% (n = 22), and Africa at 15.1% (n = 21). However, the dataset appeared to be less balanced with

respect to constituent countries included or discussed in articles. The United States, Pakistan, Nigeria, and India were the most frequently mentioned nations, perhaps due to the exemplary instances of vaccine resistance and low acceptability that have historically occurred in these nations.

### **5.2.3 Period of Study**

While publication dates were skewed towards the previous two decades, the temporal focus of the publications included was more evenly distributed. In fact, only 48.1% of the articles focused on events over the previous two decades. Roughly 52% of included articles contained a general temporal focus or studied periods between 1800 and 2000. Nonetheless, the bulk of vaccine acceptability and resistance research certainly appears to have focused on events over the previous two decades. This finding once again seems to reflect a recent growth in attention to vaccine acceptability, resistance, and other related concepts in light of the COVID-19 pandemic.

### **5.2.4 Disease of Study**

Five immunizable diseases were selected for inclusion in this study due to their successive temporal distribution, from the earliest periods of interest up until current times. While topics related to polio and polio vaccines were the most prevalent over time, COVID-19 has garnered a disparately large amount of attention in the literature relative to its more recent date of origin. Once again, this reflects the recent burgeoning interest in vaccine resistance and acceptability stemming from the COVID-19 pandemic. Interestingly, in North America, there appears to be an upward trend over time in terms of disease-specific references to vaccine acceptability and resistance. While this could be an artifact in the

database and not an accurate representation of actual temporal trends, it may also reflect the growth in interest or prevalence of more contemporary vaccine resistance and low acceptability in North America. Nonetheless, in other instances, the primary immunizable disease of issue in certain continents is evident. For example, the challenge of resistance towards polio vaccines in Pakistan and Nigeria is represented in the graph below.

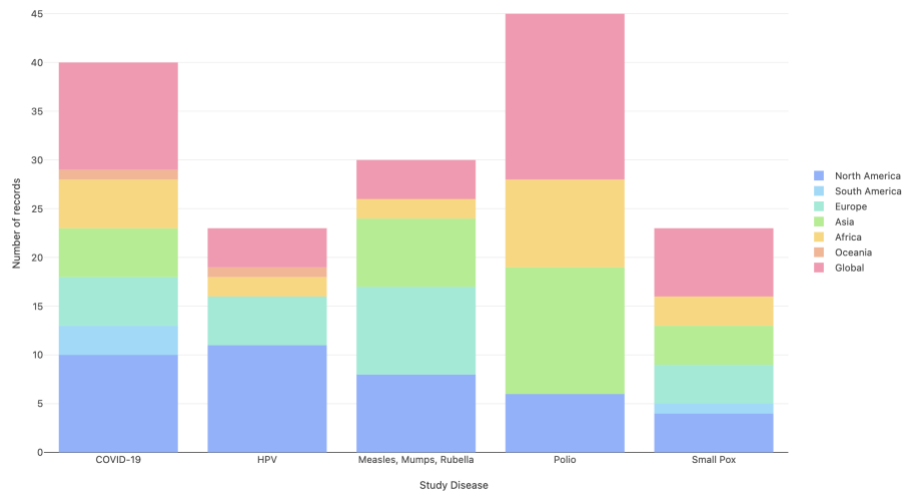


Figure 6: Distribution of publications based on continent and immunizable diseases

### 5.3 Contextual Determinants

Based on the results of this review, Politics & Policy appears to have been one of, if not the most relevant contextual determinant over time. Of the 139 articles selected for this review, 98 (70.5%) included information related to political and policy themes. Politics & Policy was the most relevant contextual determinants in articles with a Global, North American, European, and South American focus (see Appendix C). As a result, themes related to vaccine mandates, partisanship, government performance, and more all dominated the literature. In articles focused on Asia and Africa, Religious, Social &

Cultural contextual determinants were the primary concern. Overall, this determinant category was relevant in 53.24% (n=74) of all articles included in this literature review. The contextual determinants of Communication & Media Environment, Influential Leaders, and History & Historical Factors were, on the whole, relatively balanced, appearing in 43.16% (n=60), 41.73% (n=58), and 38.13% (n=53) of included articles respectively. Pharmaceutical Influences and Geographic Influences, while vital and interesting determinants, appeared in only 24.46% (n=34) and 18.7% (n=26) of articles, respectively. The difference in the distribution of contextual determinants based on geographic focus may reflect disparities in the primary vaccine-related challenges various countries face. Alternatively, this distribution may also be the product of differences in research areas of focus between continents and countries. Nonetheless, Figure 7 and 8 below provide an overview of the distribution of findings that emerged through this literature review.

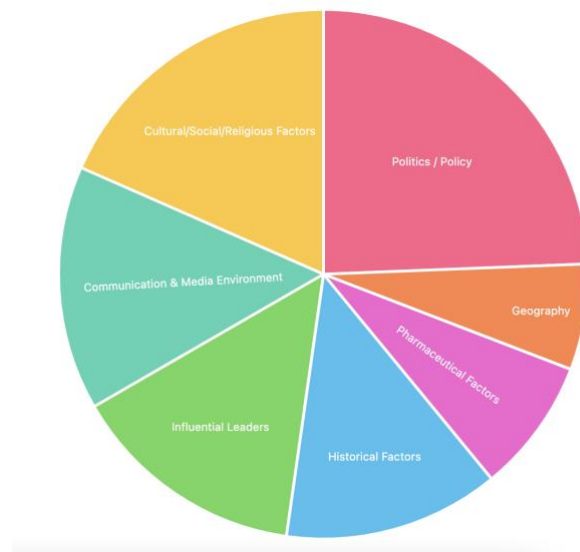




Figure 7: Distribution of contextual determinants across publications included in the literature review

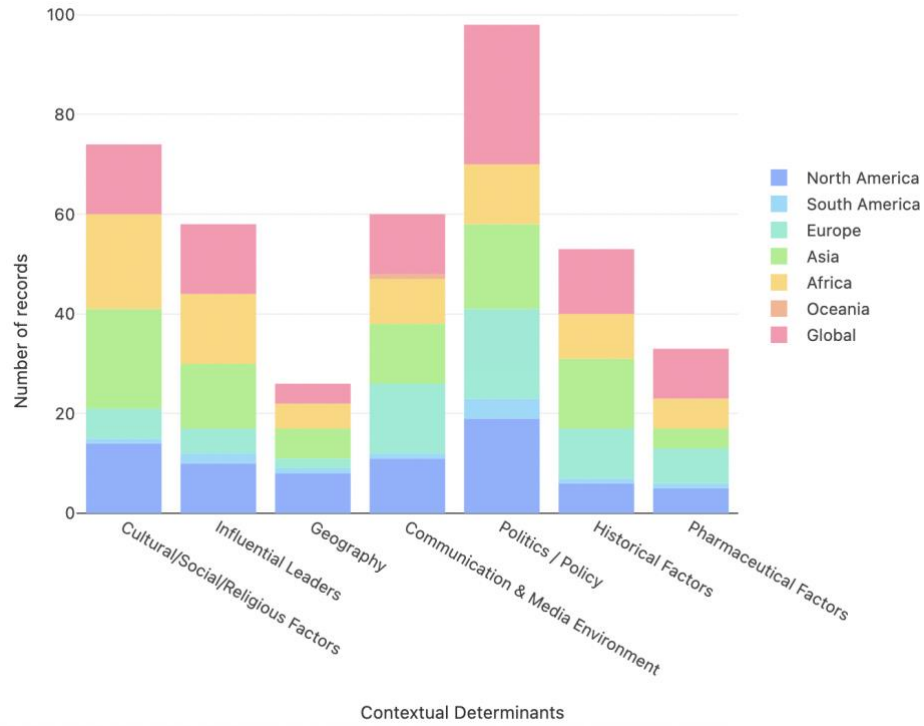


Figure 8: Distribution of contextual determinants between continents across publications included in the literature review

## 5.4 Themes

### 5.4.1 Summary of Findings

The findings, categorized based on relevant contextual determinants, were analyzed to extract consistent and important themes from the literature that have appeared over time, throughout various disease outbreaks, and across different global contexts. This analysis was initially guided by descriptions of the seven contextual determinants that have previously appeared in the literature. However, the scope of these definitions was quickly exceeded through the analysis. In the end, 32 often interrelated themes were identified

across the seven guiding contextual determinants. These findings are summarized in the tables and descriptions of thematic findings below.

<b>Contextual Determinants &amp; Themes</b>	<b>Number of Relevant Studies (n=)</b>
<b>Politics &amp; Policy</b>	
Partisanship & Polarization	21
Distrust & Skepticism	26
State-Society Relations	23
Mandates & Policies	26
Government Performance	22
Geopolitics & Conflict	23
<b>Religious, Social &amp; Cultural Factors</b>	
Religion & Culture	49
Social Contexts	10
Traditional Practices	14
Gender Dynamics	9
<b>History &amp; Historical Factors</b>	
Evolving State & Social Contexts	20
Colonial Legacies	18
Medical Experimentation	10
Evolution of Policies & Mandates	12
Political & Geopolitics Events	13
<b>Communication &amp; Media Environment</b>	
Health Misinformation & Disinformation	22
Evolving Media Sources	24
Rumors & Conspiracy Theories	13
Inconsistent Messaging	9
Media Representation & Tone	13
<b>Influential Leaders</b>	
Political Leaders	24
Religious Leaders	27
Community Leaders	17
Medical Professionals	9
Traditional Medical Leaders	10
<b>Pharmaceutical Influences</b>	
Industry Interests & Lobbying	12
Disruptive Biomedicine	7
Corruption & Distrust	17
Location of Origin	7
<b>Geographic Influences</b>	
Geographic Clustering	8
Cultural, Political & Religious Divides	10
Rural-Urban Divides	11

*Table 8: Number of articles related to each identified theme based on contextual determinant categories*

## **5.4.2 Politics & Policy**

Themes related to the *Politics & Policy* contextual determinant category were identified in 70.5% (n=98) of the articles included in this literature review. The following six themes emerged through the thematic analysis: *Partisanship & Polarization* (n=21), *Distrust & Skepticism* (n=26), *State-Society Relations* (n=23), *Mandates & Policies* (n=26), *Government Performance* (n=22), and *Geopolitics & Conflict* (n=23).

### **5.4.2.1 Partisanship & Polarization**

Several studies revealed that trends in vaccine acceptability could be traced along political party lines. In particular, partisanship in the United States was found to be a common and significant predictor of vaccine attitudes, with Republicans being less accepting of vaccines compared to their Democrat counterparts (Lee & Huang, 2022; Lin et al., 2020). While Ward et al. (2020) described partisanship as “an important determinant of attitudes towards future vaccines” in France, their findings also suggest vaccine acceptability was lowest amongst groups who did not align or identify with any political party. Alshurman et al. (2021) found that on a global level, “political conservatives were less likely to get vaccinated than liberals.” This might mean that even in instances where an affiliation with a specific political leaning is not a significant predictor of vaccine acceptability, tensions between fundamental political leanings or ideologies might still substantially influence attitudes towards vaccines.

Some have suggested that vaccines, and the public health policies that support their delivery, have increasingly become “the subject of a political game” (Walkowiak et al.,

2022). The politicization of vaccines and related public health efforts has consequently allowed political opposition parties to garner public support by way of challenging “the establishment and the prevailing narrative” (Walkowiak et al., 2022), even if it means undermining the health of constituents. To this end, opposition groups sometimes work hard to polarize the issue and undermine the public’s trust and support for governmental decision-making. Consequently, attitudes toward vaccines and their acceptability stand to be affected by the nature of the polarized political context in which they are being delivered (Baumgaertner et al., 2018; Gagneux-Brunon et al., 2022; Gollust et al., 2010; Latkin et al., 2020)

However, the politicization of vaccines is a tool also leveraged by groups and communities not necessarily affiliated with any formal political organization or party. As suggested by Yeun (2022), the refusal of vaccines may be a manifestation of political defiance against the government, motivated by other co-founding factors. In Nigeria, some regard public opposition to polio eradication campaigns in the early 2000s as a means through which the “disapproval of the policies of the Southern-led federal government that had just been elected” could be expressed (Njeru et al., 2016). The visibility given to disease eradication initiatives, such as the polio vaccination campaigns in Nigeria, has made them attractive targets of anti-government efforts in contexts characterized by political turmoil (Closser et al., 2016).

#### *5.4.2.2 Distrust & Skepticism*

Low levels of trust in standing governments and public health authorities can undermine the compliance with and impact of public health efforts and, consequently, the

acceptability of vaccines (Lee & Huang, 2022; Yuen, 2022). In fact, throughout the COVID-19 pandemic, low levels of trust in the government were found to be associated with more vigorous opposition to compulsory vaccination policies (Gagneux-Brunon et al., 2022). In England, low trust in the state was found to be associated with MMR vaccine non-compliance (Cassell et al., 2006). A prevailing level of distrust towards the government might make the general population more skeptical of vaccine-related information being provided by the government and its affiliated organizations (Biswas et al., 2019; Latkin et al., 2020).

However, in the case of COVID-19 vaccines, the political context in which vaccines were approved was found to have a significant impact on overall public trust in the vaccines and, consequently, acceptability (Bokemper et al., 2021). This influential political context is undoubtedly impacted by many confounding factors that reach across various contextual determinants. The opaque relationship between the pharmaceutical industry, politicians, and political parties has often undermined public trust in this way.

As Boas et al. (2016) suggested, fostering trust in the system has been integral to successful vaccination campaigns. Unfortunately, a lack of political and regulatory transparency can undermine this trust's stability. A lack of transparency, coupled with implementing of punitive policies for non-compliance, can undoubtedly undermine the trust in, and acceptability of, vaccines and vaccination campaigns. However, requisite levels of public trust may not be easily cultivated, especially in political contexts where distrust and skepticism are the products of damaging historical events and influences. As recently witnessed in Nigeria, pervasive levels of distrust towards the government can lead

the general public to believe that their government is overstating the severity of a disease outbreak or using it for their financial gain (Perveen et al., 2019; Wonodi et al., 2022).

#### *5.4.2.3 State-Society Relations*

Vaccination campaigns are and have historically been inherently political public health endeavors. The structure and design of these campaigns have varied over time and across different global contexts. Taylor (2009) described how early vaccination programmes were predicated on top-down political governance structures. However, in many cases, over time, these programmes evolved to incorporate more bottom-up structures, motivated by growing societal demands for personal autonomy, inalienable rights, individual responsibility, community ownership, and greater involvement in decision-making.

This evolution in state-society relations has long been on display in the United States, where “for more than two centuries, debates about vaccination have been shaped by broader American values of self-reliance and independence” and “the deeply ingrained belief that Americans should take responsibility for their own health” (Lanzarotta & Ramos, 2018). Similarly, in England, parental choice has emerged as a consistent theme in debates on MMR vaccine policies (Cassell et al., 2006). However, the degree of influence that a society can exert over the decisions made by the state is strongly mediated by the political contexts in which they find themselves. In cases where state-society power dynamics have remained characteristically imbalanced, community trust may be undermined (Neel et al., 2021). As Kakalia & Karrar (2016) suggest, “in a wider

estrangement from the state, and removal from democratic decision-making, vaccine refusal can be classified as a form of everyday resistance.”

Widespread resistance to vaccines and vaccination campaigns may be a manifestation of society's exclusion from political participation (Taylor, 2015). The inflexible nature of many top-down vaccine policies meant that community involvement and engagement were often underutilized or ignored during development and implementation (Bhattacharya & Dasgupta, 2011). Consequently, many campaigns of this nature have historically failed to adapt to the contextually-defined “social, political, and economic conditions” (Bhattacharya & Dasgupta, 2011) in which they are being deployed. Beyond provoking a desire for changes to state-society relations, top-down vaccination programmes, incongruent with local contexts, may therefore motivate high levels of resistance and diplomatic friction, as opposed to the high levels of acceptability and ownership that are now shown to be crucial to campaign success (Nasiru et al., 2012).

Unfortunately, tensions in state-society relations have also influenced how governments and decision-makers view and deal with non-compliers. As Kieslich (2018) states, “it is difficult to argue that current anti-vaccination groupings are perceived by policymakers and the public health community as anything other than a societal force that needs to be contained .”As noted by many authors, the result has often been a counterproductive and divisive “normalization of the use of stigma in dealing with anti-vaccine sentiment” (Bardosh et al., 2022).

#### *5.4.2.4 Mandates & Policies*

Mandates and strong compulsory immunization policies have long been shown to be effective means of enforcing vaccine compliance (Franco et al., 2019; Landriean, 1972; Walkowiak et al., 2021). However, opposition to compulsory vaccine laws has been a consistent theme since the first mandates of this nature were implemented in the United States and many European countries during the early 1800s. As Rich (2011) describes, the United States, one of the world's earliest adopters of such laws, “has a long history of antagonism to compulsory smallpox vaccination” and vaccines more broadly. US resistance to vaccine mandates has even been characterized as a “vigorous tradition of medical dissent” (Rich, 2011). Many authors have reported that amongst some groups, punitive and compulsory vaccine policies may serve to reinforce or strengthen existing oppositional views (Bardos et al., 2022; Gollust et al., 2010; Khan et al., 2019; Vamos et al., 2008).

The United States has historically not been alone in its experience of opposition to compulsory laws. In fact, many now argue that implementing vaccine mandates, while in some cases can be effective at increasing vaccine coverage, is detrimental to the trust-building integral to the long-term success of public health interventions predicated on the delivery of vaccines. This argument centres around the notion that compulsion serves as a temporary remedy to a more fundamental issue and, in many cases, impairs the acceptability of future vaccines and policies (Bardosh et al., 2022). Vaccine workers operating in Pakistan have reported that punitive or forceful vaccine policies lead to more



significant levels of resistance, more hostility, and a sense of hatred towards subsequent vaccination campaigns (Khan et al., 2019).

#### *5.4.2.5 Government Performance*

In many cases, vaccines are being delivered by or in partnership with domestic governments. Consequently, societal satisfaction with government performance appears to have a strong influence over the acceptability of vaccines and the programmes and policies designed to deliver them. Prior government errors, state-led disenfranchisement, and marginalization caused by political actions can all substantially affect vaccine acceptability (Ward et al., 2020). Put another way, “vulnerability and marginalization influences people to oppose a public health initiative that is visibly driven by the state” (Kakalia & Karrar, 2016), especially when the state has been the primary driver of disenfranchisement.

Such dissatisfaction with government performance has been particularly apparent in Nigeria, where some predominantly-Muslim regions felt that the government had neglected their communities' development. As Hussain (2015) illustrates, this sense of marginalization “has been known as a general cause of resistance, as people refused vaccination due to perceived misalignment of government priorities: failure to provide basic infrastructure while compelling individuals to vaccinate.” It appears that compliance with vaccination programs, in this case, polio eradication efforts, have been leveraged as a bargaining tool by communities to further their interests.

If communities lack trust in their domestic healthcare system due to poor performance, underfunding, and inadequate services, it is likely that they might also lack trust in the vaccines being delivered through it. Yahya (2007) states that “part of the

suspicion surrounding the polio campaign undoubtedly stems from a perfectly understandable failure on the part of local people to understand why such disproportionate resources are being devoted to it.” In contexts burdened by weak and underfunded healthcare systems, locals may question why other essential health services are being overlooked for the sake of vaccination campaigns (Closser et al., 2016; Yahya, 2007). The same can be said for government performance more broadly. One respondent in Pakistan iterated these concerns, saying, “why should we trust our government which never bring us requirement of our living like sugar and flour, and which is unable to employ us, yet had endless resolve and resources for the polio vaccination campaign. What is so special about it?” (Khan et al., 2019).

#### *5.4.2.6 Geopolitics & Conflict*

Throughout the literature, domestic and global political dynamics have consistently appeared as contextual themes that affect the acceptability of vaccines. On a domestic level, war and conflict have demonstrated their ability to act as disruptors to vaccination programmes and attenuate the demand for vaccines. While many conflict-derived challenges emerge through disruption to supply-side factors, other relevant demand-side determinants have also been mentioned. Recently, ongoing political tensions and conflict between Hong Kong, its citizens, and China, negatively affected the acceptability of vaccines amongst groups who felt that China was exerting too strong of a political influence over Hong Kong’s policies (Yuen, 2022). Political conflict also emerged in Nigeria in 2003 when alleged electoral fraud helped a new president come to power. Following the election, many from the northern part of the country challenged the decision and ultimately lost.

Many authors suggest that this civil-political turmoil was one of many contextual drivers of the polio vaccination boycott that would subsequently occur (Ghinai et al., 2013; Kaufmann & Feldbaum, 2009; Kennedy, 2016).

While domestic political conflicts undeniably have an impact on the demand for vaccines, geopolitical dynamics and tensions have seemingly been one of the most significant drivers of low acceptability. Namely, Western military intervention in the Middle East has historically motivated a substantial distrust in vaccination campaigns due to their purported link to the West. For example, polio vaccination campaigns have been banned in areas of Pakistan controlled by militant factions due to the belief that they were being used as a pretense to collect intelligence that could use for targeting drone strikes (Mushtaq et al., 2015; Kennedy, 2017).

The effects of geopolitical conflicts in the Middle East have seemingly spilled over into distant nations such as Nigeria, where many interpreted US intervention in the Middle East as a conflict between the West and Islam (Ghinai et al., 2013; Yahya, 2007). One respondent echoed this perspective held by many in Nigeria, saying, “If America is fighting people in the Middle East, the conclusion is that they are fighting Muslims” (Murphy, 2004). Resistance to vaccination campaigns in the region has consequently been tied to the prevailing anti-Western sentiments or the belief that domestic vaccine programs were Western plots (Ghiani et al., 2013; Kaufmann & Feldbaum, 2009). Interestingly, Kaufmann & Feldbaum (2009) suggested that Saudi Arabia’s implementation of WHO polio vaccination recommendations helped quell fears surrounding polio immunization efforts in Nigeria.

Vaccine nationalism appears to have impacted equitable supplies of vaccines and the population's perceptions of the vaccines when they arrive. Yahya (2007) described how the complex and interwoven nature of geopolitical dynamics could shape the acceptability of vaccines, stating, “it is glaring to see how Western medical science in the form of an international health campaign has the potential to lose its cloak of neutrality, acquiring significant political and cultural meaning reflective of a global political climate.” This quote speaks to the relevance of geopolitics and the influences of increasingly globalized processes on vaccine acceptability. In fact, some respondents in Sub-Saharan Africa have previously voiced vaccine-related concerns that appear to have emerged from global power structures, events, or dynamics. As Deignan et al. (2021) describe, these respondents expressed that they felt HPV vaccines were “just a government-supported initiative for population control of Africans or that Africa was receiving ‘second-tier’ or ‘left over’ vaccines from first world countries.”

### **5.4.3 Religious, Social & Cultural Factors**

Themes related to the *Religious, Social, and Cultural Factors* contextual determinant category were identified in 53.24% (n=74) of the articles included in this literature review. The following four primary themes emerged through the thematic analysis: *Religion & Culture* (n=49), *Social Contexts* (n=10), *Traditional Practices* (n=14), and *Gender Dynamics* (n=9).

#### **5.4.3.1 Religion & Culture**

In 1968, Mendelsohn (1968) described the relationship between culture and perspectives on health, stating, “people react to issues of health in symbolic ways and

symbols are merely culturally derived meaning that we personally attach to objects, relationships, and ideas.” Since then, many authors have highlighted how cultural factors have acted on and influenced the acceptability of vaccines over time and across different contexts. Religious factors have also been found to exert a significant influence on the acceptability of vaccines. In many cases, these cultural and religious themes share a substantial level of overlap. As Serquina-Ramiro et al. (2001) explain, “culture, traditions, and social norms, including traditional beliefs, the influence of traditional healers, and religious expectations also play key roles in immunization acceptance.”

Culturally- and religiously defined understandings and meanings of disease have been shown to affect vaccine acceptability (Ghinai et al., Harpan et al., 2021; Hossain et al., 2021; 2013; Pop, 2015; Sabahelzain et al., 2019; Vamos et al., 2008; Wonodi et al., 2022; Yahya, 2007). For example, Yahya (2007) explains how definitions of polio in Hausa culture have come to conflicted with biomedical definitions, resulting in “clashes of perspective” and “worries about polio vaccines.” These tensions appear to stem from the spiritual understanding of Shan-Inna, the Hausa name for polio, held in the Hausa culture (Yahya, 2007). In some instances, religious beliefs that diseases are of divine origin or religious fatalism have been found to affect vaccine acceptability. Hossain (2021) found that fatalistic views such as “beliefs that ‘everything is in the hands of Allah,’ and [a] sense of inability of avoiding death when it is the will of Allah” could contribute to low vaccine acceptability amongst some Muslim populations. More recently, Wonodio et al. (2022) reported that some Christians had interpreted the COVID-19 pandemic through a religious lens, believing that it was “a sign of the end times, a fulfillment of the scriptures, a result

of God's anger, a punishment for politicians from God, a plan of the devil, and a plot of the Anti-Christ." These views, sometimes promulgated by religious leaders, can contribute to low vaccine acceptability.

One more common theme identified in the literature was the religious and cultural origin of low acceptability and resistance towards the HPV vaccine (Colgrove et al., 2010; Haas et al., 2009; Kasstan, 2021; Redd et al., 2022; Vamos et al., 2008). As Kasstan (2021) explains, much of this resistance centres around the fact that "the HPV vaccine has been associated with sexual behaviour which is stigmatized in some social/cultural environments." Consequently, in some cases, "religious parents believe that the vaccine could increase their children's sexual behaviours" (Redd et al., 2022). Therefore, the fear that HPV vaccines might "undermine shared values" (Vamos et al., 2008) has historically led to low vaccine acceptability and resistance issues.

In the past, the contents of vaccines have sometimes been used as grounds for objection amongst religious followers of Judaism, Hinduism, Islam, and some denominations of Christianity (Grabenstein, 2013; Wombwell et al., 2015). Despite an apparent lack of explicit prohibitions outlined in religious scriptures, some shared interpretations of religious texts have led to low levels of vaccine acceptability and significant resistance. For example, as Lahariya (2014) describes, historical resistance towards smallpox vaccines emerged amongst Hindus in India "on the pretext of vaccine coming from a cow, which is considered a sacred animal." Porcine ingredients used in some vaccines, deemed 'haram' in Islam, have also previously been a source of religious resistance (Hossain et al., 2021; Kakalia & Karrar, 2016; Kasstan, 2021; Uthman et al.,

2021; Wombwell et al., 2015). Finally, as Grabensetin (2013) explained, some Christian denominations have historically “expressed concerns about the use of aborted fetal cell lines used to manufacture some types of vaccine.” These concerns purportedly stem from cell lines “drawn from tissue obtained from two abortions that took place in the 1960s and 1970s” (Nhamo & Sibanda, 2021).

While “antipathy towards vaccinations is not a universal feature of faith-based organizations” (Levin et al., 2022), the religious makeup of many regions of the world, for any number of reasons, has historically been associated with lower levels of vaccine uptake and more prevalent levels of resistance (Akmatov et al., 2007; Doan & Kirkpatrick, 2013; Franco et al., 2019; Hossain et al., 2021; Warraich, 2009). Consequently, strong religious and cultural resistance to vaccines and vaccine-related policies have historically contributed to the establishment of conscientious and religious exemptions to compulsory vaccine laws in some countries (Colgrove et al., 2016; Rich, 2011).

#### *5.4.3.2 Social Contexts*

Social contexts and prevailing societal attitudes have historically been found to affect vaccine acceptability and the acceptability of vaccine-related policies. Spicher & Weiss (2019) explain how social contexts with more collectivist attitudes often had superior vaccine uptake and greater levels of acceptability. However, Weber (2010) describes how in Great Britain, “there is an increasingly strong emphasis on individual choice and involvement in decision-making in the healthcare system.” Such a shift towards more individualist attitudes appears to undermine the type of “solidarity and social responsibility” (Boas et al., 2016) characteristic of collectivist contexts and integral to the

success of collective public health campaigns. Kieslich (2018) describes the struggle between individual and collective needs, stating that “balancing parental autonomy and the autonomy over one’s own body with public interests such as maintaining or achieving herd immunity will always be subject to a degree of contestation and deliberation in liberal democracies.”

Estep & Greenberg (2020) describe how specific regions might “attract groups of individuals who carry more individualistic perceptions that are tied to vaccine refusal.” However, there may also be a substantial variability between nations regarding these prevailing attitudes, which could help explain the international difference in vaccine acceptability. For example, Walkowiak et al. (2022) characterize Poland “family society” wherein people lack generalized trust towards others outside their immediate family circles. This lack of trust undermines efforts, like vaccination campaigns, that are predicated on collective action.

#### *5.4.3.3 Traditional Practices*

As briefly mentioned, religious and culturally derived understandings of disease have long been found to influence the acceptability of vaccines. However, as many authors have noted, traditional medical practices are also critical contextual determinants to consider (Basharat et al., 2017; Challenor, 1971; Closser et al., 2016; Davidovitch & Greenberg, 2007; Ghinai et al., 2013; Imperato & Traore, 1968; Lahariya, 2014; Leonard, 2011; Soumonni, 2012; Yahya, 2007) For example, Challenor (1971) provides a historical account of how the complex polytheistic religion found in the Kingdom of Dahomey influenced the prevailing spiritual understandings of smallpox, how it was to be treated and



consequently undermined local acceptability of vaccines. As Challenor (1971) describes, during early smallpox vaccination efforts in regions Dahomey, resistance towards vaccines “occurred when the villagers themselves ... opposed vaccination because the smallpox outbreak in their village was viewed as a social of supernatural stigma and not as a medical phenomenon where vaccination or any other medical practice could furnish a meaningful approach”. Furthermore, specific individuals in many villages, described as ‘fetisheurs’, were solely responsible for the care of individuals affected by smallpox. However, tensions reportedly arose when that traditional role was challenged by the introduction of vaccines (Challenor, 1971). Similar instances of resistance stemming from traditional practices and belief systems have previously been described by Imperato & Traore (1968) among the Songhai of Mali. Several authors have described how traditional beliefs and practices such as these have often been in conflict with biomedical paradigms (Basharate et al., 2017; Davidovitch & Greenberg, 2007; Leonard, 2011; Soumonni, 2012; Yahya, 2007). Resistance to vaccines and low acceptability thus appears to be a consequence of these fundamental tensions.

#### *5.4.3.4 Gender Dynamics*

Local gender dynamics were referenced in several articles as important determinants of vaccine acceptability. In particular, in Zambia, Kenya, Tanzania, and Zimbabwe, gender dynamics were found to influence vaccine-related decision-making, with women needing permission from their husbands to be vaccinated or have their children vaccinated (Deignan et al., 2021). One respondent was quoted saying, “[there is] the cultural background that a woman should seek permission from her husband, whether she

should take her daughter for the vaccines ... so those are cultural issues that will always be there” (Deignan et al., 2021). Furthermore, as Grabenstein (2013) explains, “given that many religions hold beliefs about sexual propriety, there are some objections based on the pathogen route of exposure.” In some cases, HPV vaccines for younger women are rejected due to the prevailing belief that they will encourage or enable “premature sexual relations” (Grabenstein, 2013). Finally, some authors referenced challenges in reaching female target populations in some areas as a result of gender dynamics (Kahn et al., 2019). These challenges were made worse when vaccination teams consisted exclusively of men (Hussain et al., 2016).

#### **5.4.4 History & Historical Factors**

Themes related to the *History & Historical Factors* contextual determinant category were identified in 38.13% (n=53) of the articles included in this literature review. The following five primary themes emerged through the thematic analysis: *Evolving State-Society Relations* (n=20), *Colonial Legacies* (n=18), *Medical Experimentation* (n=10), *Evolution of Policies & Mandates* (n=12), and *Political & Geopolitical Events* (n=13).

##### **5.4.4.1 Evolving State & Social Contexts**

Using the Cold War and the dissolution of the Soviet Union in 1991 as relevant case studies, many authors illustrate how political and social change of this nature can affect the acceptability, resistance, and demand for vaccines (Akmatov et al., 2007; Bazylevych, 2011; Pop, 2015; Taylor, 2009; Walkowiak et al., 2021). In their article, Akmatov et al. (2007) suggest that as a country “goes through a transition from one political system to another, the main determinants of vaccination coverage may also go through a major

transition.” From a political point of view, Bazylevych (2011) describes how “socialist ideology placed public health well before that of the individual.” Consequently, comprehensive immunization campaigns were often a priority “of the Soviet state because they fit well with the ideology that valued the group over the individual and promised a cheap way to secure the health of the labor force” (Bazylevych, 2011).

Furthermore, as Taylor (2009) suggests, militarized and authoritarian Cold War-era smallpox eradication efforts in the former Soviet Union and the United States appear to have been influenced by the competitive geopolitical climate of the time. However, following the dissolution of the Soviet Union, evolving political and social contexts may have contributed to a renegotiation “of biomedical authority” (Bazylevych, 2011) through which individuals advocated for personal rights and liberties. Consequently, resistance to vaccines may represent the expression of individual choice in a population that historically lacked such a level of medical autonomy. As Taylor (2009) explains, “while early vaccine programs were predicated on top-down political structures, as time progressed, this transitioned into a desire for more bottom-up approaches on the back of inalienable rights, rights to non-compliance, and greater challenges with enforcement as a result.”

Despite a period of significant political, economic, and social transition, historical legacies may continue to exert an influence over contemporary vaccine acceptability. In Romania, for example, Pop (2015) recounts how “traumatic experiences from the totalitarian Socialist era” have contributed to contemporary resistance to HPV vaccination efforts amongst women who had previously experienced “state-driven intrusion into their sexuality and reproduction.” Walkowiak et al. (2021) draw attention to the widespread and

enduring impact of this political history, stating, “even after three decades, the Former Iron Curtain is still visible on the map of Europe, with former eastern countries clearly underperforming in their ability to convince their population to receive the COVID-19 vaccine”. However, former-Soviet states are not the only areas in which political and social change has been suggested to have affected the acceptability of vaccines. Laurent-Ledru et al. (2011) describe how “there has been an evolution in healthcare away from a disease centered approach toward a patient centered approach.” As a result, healthcare in many countries has shifted towards being what some authors describe as “less paternalistic” (Boas et al., 2016). Individuals seem to demand more of a voice in healthcare decision-making, and power has shifted away “from the medical profession to the laity” (Laurent-Ledru et al., 2011). Consequently, balancing public health and individual rights appears to have become more challenging to navigate. As Taylor (2009) eludes, the increasingly tough competition between collective health and individual rights may “reflect in the success of vaccination programs.”

#### *5.4.4.2 Colonial Legacies*

Discourse on the lasting impacts of colonial legacies on vaccine acceptability, resistance, and demand was prevalent in the literature. Harrison & Wu (2020) describe how “in the nineteenth and twentieth centuries, ... vaccination campaigns were a tool of colonial and military enterprises seeking to sanitize bodies that were viewed as a threat to the security of privileged classes, an occupying army, or economic interests”. Before the Second World War, ‘health’ was generally understood to be an absence of disease (Davidovitch & Greenberg, 2007). For colonial states, maintaining the health of both

occupied and occupying populations was necessary in order to successfully develop regions and achieve economic interests (Davidovitch & Greenberg, 2007; Harrison & Wu, 2020). Consequently, for colonial states, vaccines appeared to be the most cost-effective means of improving the health of populations living in occupied regions.

As some authors have iterated, the means adopted by colonial governments to achieve health goals were often intrusive, coercive, and met with strong resistance from local populations (Closser et al., 2016; Hussain et al., 2015; Peckham, 2018; Seytre, 2022; Soumonni, 2012). As Davidovitch & Greenberg (2007) explain, “the civilizing power of medicine and public health was a crucial part of the colonial regimes, and within this scheme, vaccinations had an advantageous position. However, this was not a simple and uncontested process”. In the nineteenth century British India, the colonial state established the 1880 *Vaccination Act* as a means to enforce vaccination against smallpox. However, these efforts often faced resistance from local populations based on political, religious, and cultural tensions (Peckham, 2018). Religious resistance to colonial vaccination efforts also emerged during the French colonization of Algeria, where smallpox vaccines were often “rumoured to be a tool of forced Christianization” (Seytre, 2022). Conflict and resistance towards smallpox vaccination efforts occurred in West Africa during the colonization of Dahomey. As Soumonni (2012) describes, the French colonial administration often targeted the nation’s pre-existing “traditional healing systems” and beliefs; ultimately, “its harassment of the so-called fetish priests and other coercive measures turned out to be counterproductive.”

The effects and legacies of colonialism, stemming from broader political actions, also appear to influence contemporary vaccine acceptability and resistance. Kennedy (2016) describes how “many post-colonial states are still unable to rule without the aid/support of foreign governments. Fringe and extremist groups might represent some of the more disenfranchised segments of these populations and are consequently resistant to government interventions”. In Canada, colonial policies have historically had a disparately negative effect on the health and well-being of the nation’s indigenous populations (Henderson et al., 2018; Mosby & Swidrovich, 2021). Mosby & Swidrovich (2021) state that today, “the prioritization of Indigenous population in the receipt of vaccines often raises questions” due to the historical effects of colonialism and the residential school system.

#### *5.4.4.3 Medical Experimentation*

Lin et al. (2020) describe how today, “much of minorities hesitancy towards vaccines and medical research stems from histories of abuses and experimentations.” Many researchers have noted how certain groups have historically fallen victim to medical malpractice as well as harmful or unethical medical experimentation (Biswas et al., 2019; Closser et al., 2016; Ghinai et al., 2013; Khan et al., 2021; Lin et al., 2020; Mendoza et al., 2021; Mosby & Swidrovich, 2021; Njeru et al., 2016; Whittacker et al., 2019; Yahya, 2007). The enduring effects of these events are now suggested to manifest in the form of low vaccine acceptability and vaccine resistance, and many historical examples have been cited in the literature. In 1996, for example, the pharmaceutical giant Pfizer conducted a clinical trial in Nigeria on Trovan, a new antibiotic, that resulted in the deaths of a number

of children (Ghinai et al., 2013; Njeru et al., 2016). The company was alleged to have conducted the trial “without licence, ethical approval or informed consent” (Ghinai et al., 2013). The outcomes of this trial are believed to have contributed to Nigeria's eventual boycott of the oral polio vaccine in 2003 (Closser et al., 2016; Whittacker et al., 2019). In the United States, the legacies of the Tuskegee syphilis experiments are believed to contribute to contemporary suspicion of pharmaceutical companies and, consequently, poor vaccine acceptability amongst black Americans (Biswas et al., 2019; Khan et al., 2021). Other examples of the legacies of medical experimentation include the Dengvaxia controversy in the Philippines (Mendoz et al., 2021) and a 12-year-long clinical trial of the BCG vaccine that was conducted on Indigenous people in Canada (Mosby & Swidrovich, 2021).

#### *5.4.4.4 Evolution of Policies & Mandates*

Vaccine-related policies and mandates have taken many forms since they were first introduced in the early 1800s (Bifulco et al., 2022; Colgrove et al., 2016; Fowler, 1941; Lahariya, 2014). Before the spread of the earliest smallpox vaccine, its predecessor, variolation, had long been practiced in many parts of the world. However, these practices would quickly become the target of some of the earliest vaccine laws. In the years following the introduction of smallpox vaccines, some nations chose to outlaw the practice of variolation to promote vaccines as the primary means of proactive care (Lahariya, 2014; Stewart & Delvin, 2006).

In addition to these policies aimed at supplanting traditional practices, governments also began establishing compulsory vaccine laws and mandates early in the 19th century.

For example, in 1821, mandatory smallpox vaccination was introduced into the Kingdom of the Two Sicilies by Ferdinand I (Bifulco et al., 2022). Additionally, in 1853, the government of England and Wales introduced a compulsory vaccination law with the establishment of its *Vaccination Act* (Stewart & Delvin, 2006). Over time, many other nations would follow suit in implementing various compulsory laws and mandates. However, widespread and fierce resistance to these policies and laws would lead to the creation of conscientious objection and other exemption clauses at the turn of the 20th century in nations such as the United Kingdom and the United States (Colgrove et al., 2016; Stewart & Delvin, 2006).

The resistance to paternalistic and top-down government-led policies has long been an important force in shaping vaccine policies and mandates. Contemporary top-down policies and coercive mandates have continued to experience significant levels of resistance, similar to their historical predecessors (Walkowiak et al., 2021). As Boas et al. (2016) describe, these government-led policies “often stand at odds with our contemporary zeitgeist of individualism.” Consequently, when it comes to laws and mandates that govern health, “people do not lightly offer themselves (or their immune systems) to governments, even when its authority is legitimate” (Leonard, 2011).

#### *5.4.4.5 Political & Geopolitical Events*

Domestic and international political events appear to have an enduring impact on the acceptability of vaccines and, in some cases, the emergence of vaccine resistance. Perhaps the most commonly referenced example of this phenomenon was the fallout stemming from a 2011 CIA-led fake vaccination campaign in Northern Pakistan (Akil &



Amad, 2016; Hussain et al., 2016; Kennedy, 2017; Khan & Qazi, 2013; Mushtaq et al., 2015; Peckham, 2018; Perveen et al., 2019). The campaign was conducted in Abbottabad, where the US intelligence agency believed Osama Bin Laden had been hiding. The CIA sought to collect DNA from the children of Bin Laden in order to confirm his location (Mushtaq et al., 2015; Kennedy, 2017). Mushtaq et al. (2015) described the events' consequences, stating “such a political move under the guise of vaccination not only created distrust among a society already resistant to health-care campaigns but also affected the morale of campaigners themselves.” Following the publicization of this campaign, militant groups in some areas of Northern Pakistan instituted a ban on polio vaccination efforts which was said to have put 250,000 children at risk (Khan & Qazi, 2013).

#### **5.4.5 Communication & Media Environment**

Themes related to the *Communication & Media Environment* contextual determinant category were identified in 43.32% (n=60) of the articles included in this literature review. The following five primary themes emerged through the thematic analysis: *Misinformation & Disinformation* (n=22), *Evolving Media Sources* (n=24), *Rumours & Conspiracy Theories* (n=13), *Inconsistent & Mixed Messaging* (n=9), and *Media Representations & Tone* (n=13).

##### **5.4.5.1 Health Misinformation & Disinformation**

Information promulgated through media channels has long been recognized as having an influence over the health decisions of those who consume it. Consequently, the content of that information can affect the demand for vaccines. Vaccine-related misinformation and disinformation shared over social media have consistently been cited

as primary drivers of poor vaccine acceptability (Clemente-Suarez et al., 2022; Biswas et al., 2019; Tamysetty et al., 2022; Wiyeh et al., 2019). The refuted association between MMR vaccines and Autism, first described by Andrew Wakefield and colleagues, represents perhaps the most notorious example of this phenomenon and the enduring damage it can have. In 1998, the now-disgraced UK physician published a case series in *The Lancet* in which a temporal association between the MMR vaccine and Autism was purportedly identified (Schmitt et al., 2003). The flawed report, which included 12 case studies, was quickly disproven and retracted by *The Lancet* (Richwine et al., 2019). However, extensive media and news coverage of the disinformation induced damaging levels of parental anxiety and severely undermined the acceptability of the MMR vaccines, ultimately leading to detrimental declines in vaccine uptake both inside and outside of the United Kingdom (Burgess et al., 2006; Schmitt et al., 2013; Stewart & Delvin, 2006; Richwine et al., 2019).

Schmitt et al. (2013) noted that the MMR vaccine is not the first or last vaccine to be associated with adverse disorders and diseases. Other often spurious or questionable associations have included Guillain-Barré syndrome, lupus erythematosus, multiple sclerosis, Crohn's disease, and more. Despite many of the claims being quickly refuted, the deleterious effects caused by their dissemination endure long after claims are disproven (Richwine et al., 2019). False or misleading information can drastically undermine vaccine confidence and the “scientific press” (Schmitt et al., 2003). However, correcting these misconceptions is often challenging, if not futile. David Elliman described the fragile relationship between vaccines and public trust, stating, “it is much easier to create doubt

and damage a vaccine’s reputation than it is to restore it” (Burgess et al., 2006). Widely circulated false claims of this nature have previously undermined vaccine acceptability and led to the reemergence of previous controlled immunizable diseases (Stewart & Delvin, 2006).

Suspicion stemming from vaccine-related misinformation has been noted as “a significant barrier to achieving the GPEI’s goals” (Hussain et al., 2016) for polio eradication. It is perhaps unsurprisingly, then, that nation-states and ideological groups leverage the influence of vaccine-related misinformation and disinformation to undermine the acceptability of vaccines in adversarial regions deliberately. For example, it has been suggested that disinformation and misinformation campaigns sponsored by the Russian government are being used to erode vaccine acceptability in the West and promote the nation's domestic vaccine business (Gawel et al., 2021). Furthermore, other authors have suggested that Islamist insurgent groups in areas such as Pakistan have spread misinformation about vaccine efficacy and safety in an effort to frustrate vaccination campaigns in certain regions (Hussain et al., 2016; Kennedy et al., 2015).

In regions with less regulated and organized media environments, the challenge of misinformation and disinformation often appears to be intractable (Khan et al., 2021). Without well-established sources of credible vaccine-related information, misinformation and disinformation are challenging to monitor and refute. However, even in regions with more established and regulated media environments, the growing reliance on the internet and social media as a source of health information has “accelerated” the spread of false or misleading materials (Clemente-Suarez et al., 2022). Biswas et al. (2019) found that

“widespread misinformation communicated through social media was responsible for degrading vaccine acceptance rates” across the globe. Vaccine-resistant groups actively spread misleading or false information on social media platforms such as Facebook (Biswas et al., 2019; Wiyeh et al., 2019). These unreliable sources of online information often focused on erroneous claims of adverse effects, have consistently been found to impact perceptions of vaccines and undermine vaccine acceptability (Biswas et al., 2019; Khan et al., 2021; Tamysetty et al., 2022).

#### *5.4.5.2 Evolving Media Sources*

In a recent publication, Clemente-Suarez et al. (2022) suggest that an evolving media landscape, led by technological advancement and digitization, has contributed to the proliferation of misinformation and disinformation. The authors state that “in many ways, the promulgation of mis and disinformation has accelerated thanks to the speed of the internet and the digitization of media.” While false rumors and information are characteristic of past pandemics and vaccine campaigns, the contemporary difference appears to be the speed and reach of modern information networks and media sources (Clemente-Suarez et al., 2022; Kieslich, 2018; Rich, 2011; Seytre, 2022).

Before the widespread digitization of media and information networks, newspapers, medical journals, radio, television, and word of mouth were all primary sources of information and debates regarding vaccines and related policies (Lanzarotta & Ramos, 2018; Seytre, 2022). For example, early opponents of smallpox vaccine mandates voiced their opposition in newspapers, spreading claims that smallpox vaccinations lacked efficacy or transmitted syphilis to the recipient (Sater, 2003). While influential, the

influence of these media sources was previously limited geographically. However, as Rich (2011) notes, the increasingly globally connected and digitized media landscape has allowed vaccine-resistant groups to “meet, organize, and disseminate information on previously unfeasible scales, leading to what Anna Kata views as a recent ‘re-emergence of anti-vaccination sentiments’.” Through the internet and social media, small groups of vaccine-resistant individuals have been able efficiently “harness the power of the press” (Howard-West, 2007) to achieve “a disproportionate voice in public discussions on vaccination” (Laurent-Ledru et al., 2011).

Vaccine acceptability, mediated by the information presented on the internet and social media channels, thus appears to be an increasingly transnational challenge (Kieslich, 2018). Nonetheless, in many regions of the world, traditional media sources such as radio and television are still suggested to be essential and seemingly reputable sources of vaccine-related information (Bhuiya et al., 1995; Hilton et al., 2010; Osur et al., 2022; Wonodi et al., 2022). In fact, some authors found that exposure to vaccine-related information from these sources can lead to increased demand for vaccines (Bhuiya et al., 1995; Osur et al., 2022). Conversely, it has been found that individuals who are exposed to or rely on online vaccine-related information often have lower levels of vaccine acceptability (Alyward & Heymann, 2005; Hossain et al., 2021; Khan et al., 2021; Osur et al., 2022; Tamysetty et al., 2022).

#### *5.4.5.3 Rumors & Conspiracy Theories*

In a similar fashion to health misinformation and disinformation, rumors and conspiracy theories have been found to adversely affect vaccine acceptability, spur vaccine

resistance, and reduce vaccine demand. In fact, Alyward & Heymann (2005) described how in 2004, the promulgation of vaccine rumors and conspiracy theories “led to the reinfection of 13 previously polio-free countries and the largest polio epidemic in Africa in recent years”. Many prevalent conspiracy theories and rumors in countries such as Nigeria, Pakistan, and Afghanistan appear to reflect geopolitical and religious tensions. Common themes include the notion that vaccination programmes are Western-led efforts to sterilize Muslim populations, that vaccines are designed to depopulate certain regions, or that vaccines have been intentionally contaminated with other diseases such as HIV (Hussain et al., 2016; Hussain et al., 2015; Nasir et al., 2014; Kennedy, 2016). In regions of Nigeria and Pakistan, these conspiracy theories have previously led regional leaders to suspend polio vaccination programmes (Nasir et al., 2014). However, other more common COVID-19-related conspiracy theories have been reported recently in both the Global North and South. These include claims that vaccines “were propelled by the devil” (Nhamo & Sibanda, 2021), that the virus itself was of man-made origin, or that the disease and vaccines were biological weapons (Wonodi et al., 2022).

#### *5.4.5.4 Inconsistent Messaging*

Confusing, mixed, or shifting messaging on vaccines and vaccine-related policies can undermine public confidence and trust in messaging sources (Bardosh et al., 2022; Vamos et al., 2008). Some authors have reported the negative impact of inconsistent messaging on the acceptability of vaccines (Bardosh et al., 2022; Biswas et al., 2019; Lazarus et al., 2020; Vamos et al., 2008). In a global study, Biswas et al. (2019) found that “inconsistent messages from health organizations lead to hesitation in making decisions

about vaccination.” Furthermore, the authors also noted that “inconsistent risk messages regarding COVID-19 reduced the intention of vaccine uptake”. These findings echo a similar notion forwarded by Penta & Baban (2014). The authors suggest that a “lack of clear and transparent vaccine-related information” could increase suspicion towards vaccines and ultimately undermine their acceptability. Therefore, Lazarus et al. (2020) recommend the use of “clear and consistent messaging” to foster a higher level of vaccine acceptability. Large deviations in government messaging or policy justification can undermine trust and lead to public controversy. For example, prior to the introduction of vaccines in France, President Emmanuel Macron declared that vaccines would not become compulsory in the country. However, soon after, the government instituted a mandatory COVID-19 vaccination policy (Gagneux-Brunon et al., 2022). Inconsistent messaging, policy deviations, and resulting controversy can undermine public confidence and vaccine acceptability (Gollust et al., 2010; Lazarus et al., 2020).

#### *5.4.5.5 Media Representation & Tones*

Given the substantial influence traditional media outlets have historically held, the tone and representation of vaccine-related messages and stories have been shown to affect vaccine acceptability (Bazylevych, 2011; Bhattacharya & Dasgupta, 2011; Burgess et al., 2006; Gollust et al., 2010; Mason & Donnelly, 2000; Schmitt et al., 2003). One apparent and damaging feature of media messaging is its propensity to appeal to famous vaccine-related controversies, anxieties, and concerns (Bazylevych, 2011; Gollust et al., 2010; Schmitt et al., 2003). For example, Bazylevych (2011) explains how in Ukraine, “media attention to population anxieties, alleged side effects of the vaccines, and finally a death

popularly linked to such side effects” led to the termination of an MMR vaccination campaign in 2008. While the timely dissemination of vaccine-related information is undoubtedly an essential function of the media, Gollust et al. (2010) suggest that in some cases, “journalistic practices might contribute to the sensationalization” of already controversial health debates.

Many studies have found that media articles published on topics of vaccines are often negative in tone (Das et al., 2021; Gollust et al., 2010; Penta & Baban, 2014; Sacerdote et al., 2020). Negatively toned articles have previously been found to provide less disease- or vaccine-related information and contain more inaccuracies (Penta & Baban, 2014). Unfortunately, a number have studies have found a prevailing rate of negative media reporting on vaccines in countries such as the United States, Romania, and India (Das et al., 2021; Penta & Baban, 2014; Sacerdote et al., 2020). For example, Sacerdote et al. (2020) describe how during the COVID-19 pandemic, positive developments and reporting on vaccines received less attention from US media outlets compared to controversial topics such as the use of hydroxychloroquine.

While negative tones can undoubtedly undermine the acceptability of vaccines, in the case of MMR, Penta & Baban (2014) also suggest that “even ‘balanced’ media reporting (presenting claims both for/against an autism-vaccine link) negatively influenced judgments of risk and vaccination intentions.” For example, Burgess et al. (2006) described how balanced reporting on the Andrew Wakefield controversy led to stories that “pitched parents against medical experts.” This more adversarial framing seemingly came at the expense of an emphasis on expert medical opinions. Consequently, it appears that media



representation and tone can influence consumer emotions and perceptions and the quality of information that consumers receive.

#### **5.4.6 Influential Leaders**

Themes related to the *Influential Leaders* contextual determinant category were identified in 42.65% (n=58) of the articles included in this literature review. The following five primary themes emerged through the thematic analysis: *Political Leaders* (n=24), *Religious Leaders* (n=27), *Community Leaders* (n=17), *Medical Professionals* (n=9), and *Alternative Medical Influencers* (n=10).

##### **5.4.6.1 Political Leaders**

Socio-political contexts have been found to exert a strong influence over the acceptability of vaccines. As such, the political leaders who help shape these contexts have the capacity to persuade public perceptions and trust in vaccinations (Baumgaertner et al., 2018). Many authors have suggested that the expression of doubt, skepticism, or opposition to vaccines or vaccination campaigns by influential political figures can be highly damaging to acceptability and demand (Alshuran et al., 2021; Bokemper et al., 2021; Kennedy, 2017; Perveen et al., 2019; Spicher & Weiss, 2019; Wonodi et al., 2022). For example, the ex-Tanzanian president John Magufuli described the vaccines as “dangerous for our health” (Wonodi et al., 2022). A Chief Justice in South Africa claimed in a public prayer that COVID-19 vaccines were “propelled by the devil” (Nhamo & Sibanda, 2021). Furthermore, an influential militant leader in Pakistan criticized the polio vaccinations as “a conspiracy of the Jews and Christians to stunt the population growth of Muslims” (Kennedy, 2017). Comments such as these, coming from influential political figureheads,

have been shown to adversely affect the success of vaccination efforts by sowing distrust and undermining levels of acceptability.

The increasingly politicized and polarized nature of public health and vaccines leaves them susceptible to the influences of political leaders. Consequently, political endorsements have been found to increase vaccine acceptability, even amongst groups that traditionally have more oppositional attitudes (Bokemper et al., 2021; Deignan et al., 2021; Lee & Huang, 2022). In Zambia, cervical cancer advocacy and awareness efforts on the part of the first lady we found to positively impact the acceptability of HPV vaccines (Deignan et al., 2021). Conversely, the expression of doubt, uncertainty, or unrealistic goals regarding vaccine development and related policies might also serve to undermine public trust (Spicher & Weiss, 2019). Near the outset of the COVID-19 pandemic, then-President Donald Trump’s claim that “vaccines would be delivered ‘within weeks’” (Lin et al., 2020) was purported to have stoked fears about rushed development. Additionally, the perpetuation of conspiracy theories and disinformation by political figures has also been shown to damage the general acceptability of vaccines (Alshurman et al., 2021; Perveen et al., 2019).

#### *5.4.6.2 Religious Leaders*

Religious leaders have consistently been credited with their ability to influence popular perceptions and attitudes toward vaccines. Consequently, their engagement in community vaccination efforts is often regarded as being integral to campaign success (Nasir et al., 2014). One respondent in a study by Khan et al. (2019) describes the impact of religious authority, stating, “it is better to persuade one religious scholar rather than the

persuasion of hundreds in a locality. Religious scholars will convince people to feed the vaccines”. In fact, the 2003 Nigerian polio vaccine boycott was resolved, in part, with the help of influential Islamic scholars (Whittaker et al., 2019).

Like other leaders, however, the authority and influence held by religious leaders have also been used to undermine vaccine campaigns and acceptability. As a study by Perveen et al. (2019) described, many religious leaders use various religious interpretations to dissuade followers from receiving vaccines. In Pakistan, for example, religious and political groups have previously issued Fatwas against polio vaccinations (Warraich, 2009). Vaccine opponents in Canada and the United States commonly include church groups, clergy, and religious figureheads (Haas et al., 2009). In 2003, Muslim leaders in Northern Nigeria called for a complete boycott of polio vaccine campaigns, which halted vaccination efforts in some of the country’s northern states (Njeru et al., 2022).

One unique challenge that religious leaders pose to the success of vaccination efforts is that their appeals to deep-rooted cultural and religious beliefs are difficult to counter using scientific evidence (Wonodi et al., 2022). Furthermore, in different contexts, these beliefs are protected as inalienable human rights, and to compel vaccination in these cases may constitute a violation or infringement of those rights. Consequently, in many nations, resistance from religious leaders has led to the creation of special exemptions to vaccine laws (Colgrove et al., 2016).

#### *5.4.6.3 Community Leaders*

Baumgaertner et al. (2018) describe how influential individuals exert a substantial level of influence over the world views of those who view them as trustworthy. Over time,

local community leaders and influential figures such as village chiefs, business people, teachers, and celebrities have been shown to have the capacity to shape attitudes towards vaccines. Often, guidance is sought from these leaders and groups due to their purported impartiality (Lazarus et al., 2020). For example, Osur et al. (2022) reported how in Kenya, many individuals who intended not to receive a vaccine were found to have been obtaining vaccine-related information from meetings with local chiefs. The perpetuation of misinformation or disinformation by community leaders drastically undermines vaccine acceptability due to these individuals' authority and reputation. Consequently, authors have previously found the local spread of false rumours related to vaccines to be one of the more substantial barriers to eradication efforts (Alyward & Heymann, 2005). However, it is worth pointing out that the spread of false or misleading information by community leaders, such as teachers, who are involved in vaccine efforts might also be the product of improper training (Deignan et al., 2021). Nonetheless, community leaders have consistently been cited as critical determinants of vaccine acceptability in low- and middle-income countries (Mshelia et al., 2020).

It is logical, then, that campaign organizers have, over time, emphasized the involvement of these local leaders in promoting vaccine acceptability. The influence of community leaders was even leveraged during the establishment of colonial “Village Health Leagues” in British India. Prasada (1937) explains how “each village should preferably have its own health league” that includes a chairman who “should preferably be an influential person commanding the respect of the inhabitants” and a secretary who “may be an educated young man or schoolteacher resident in the village.” The historical emphasis

on community leaders appears to have been carried forward through time. Today, as Johnson & Goronga (2020) explained, infectious disease control responses such as vaccination campaigns “must be done with communities, and not done to communities.” As a result, the mobilization of community leaders and non-medical individuals is still suggested to be an important aspect of successful vaccination efforts (Deignan et al., 2021; Johnson & Goronga, 2020; Nasir et al., 2014).

#### *5.4.6.4 Medical Professionals*

In a global study, Rozek et al. (2021) found that “trust in medical professionals as experts and leaders was strong across all studied countries.” As a result, national medical associations and advocacy groups are integral to shaping debates and perceptions of vaccines and vaccination policy (Haas et al., 2009). For example, the Canadian Women’s Health Network and New Zealand Women’s Health Action organization expressed doubts over proposed HPV vaccine programs. Some of these concerns stemmed from a lack of safety and efficacy data on the vaccine in specific groups and the “hurried introduction” of proposed efforts (Haas et al., 2009). Regardless of merit, expressions of concern from reputable medical professionals and organizations are probable causes of distrust and mediators of acceptability.

Between 1960-1976 in the United States, a public debate emerged regarding the discontinuation of routine smallpox vaccination efforts. However, as Rich (2011) describes, “the 1960s and 70s campaign to discontinue smallpox vaccination originated from within the biomedical community itself, an internal push that accomplished its aim without upsetting the hegemony of biomedicine”. During that time, prominent medical

professionals expressed their objection not based on “a broader political or philosophical principle, but only on the basis of the vaccine’s biomedical danger to the general U.S. population, which due to unique historical circumstances they felt now outweighed its biomedical benefit” (Rich, 2011). The largely depoliticized biomedical justifications used by many medical experts may help explain why trust in medical professionals was found to be higher than trust in political leaders (Rozek, 2021).

However, medical professionals have also “played central roles in previous vaccination rumour episodes” (Ghinai et al., 2013). For example, the now disproven relationship between the MMR vaccine and autism described by disgraced UK physician Andrew Wakefield led to dramatic decreases in vaccine acceptability, coverage, and lasting global effects (Ghinai et al., 2013; Triggler, 2010). Furthermore, influential Nigerian physician Dr. Datti Ahmed’s claim that the oral polio vaccine contained ‘anti-fertility substances’ was suggested to impact vaccine acceptability (Ghinai et al., 2013).

#### *5.4.6.5 Traditional Medical Leaders*

Many authors have described the high level of influence that traditional healers have historically exerted in their communities. Due to the “fundamental position within the local social fabric” (Davidovitch & Greenberg, 2007) traditional healers have held, vaccine campaign organizers have often described and leveraged the vital role they play in motivating vaccine acceptability (Serquin-Ramiro et al., 2001). While collaborating with these traditional leaders can undoubtedly support the realization of vaccination campaign targets, their influence cuts both ways.

The opposition led by traditional healers has previously been documented during smallpox vaccine rollouts in countries such as India, Nigeria, Dahomey (present-day Benin), and more (Challenor, 1971; Davidovitch & Greenberg, 2007; Lahariya, 2014; Soumonni, 2012). As Challenor (1971) described, traditional leaders in West Africa were strongly resistant to smallpox eradication efforts as it “represented a threat to their standing in the community.” While some of this influential resistance appears to stem from self-interest or financial motives (Lanzarotta & Ramos, 2018; Soumonni, 2012), other intentions undoubtedly include the desire to preserve longstanding traditional and cultural practices being disrupted by Western biomedicine.

#### **5.4.7 Pharmaceutical Influences**

Themes related to the *Pharmaceutical Influences* contextual determinant category were identified in 24.46% (n=34) of the articles included in this literature review. The following four primary themes emerged through the thematic analysis: *Industry Interests & Lobbying* (n=12), *Disruptive Biomedical Innovation* (n=7), *Corruption & Distrust* (n=17), and *Manufacturing Location* (n=7).

##### **5.4.7.1 Industry Interests & Lobbying**

Across the globe, the acceptability of vaccines was found to be influenced by the actions taken by vaccine developers and prevailing perspectives on the pharmaceutical industry and company interests. As described by Haas et al. (2009), actors in the pharmaceutical industry have historically used lobbying to engage with and persuade decision-makers in an effort to have treatments approved, subsidized, and in some cases, integrated into vaccine mandates. While lobbying efforts take shape differently across

varying contexts, these practices have raised concerns and potentially undermined support for vaccines or vaccination policies.

For example, in the United States, the pharmaceutical giant Merck previously engaged in lobbying efforts in an attempt to have HPV vaccine regulations implemented by legislators (Mello et al., 2012). The company was compelled to end its lobbying efforts after it was revealed that Merck had financially supported a political campaign, and concerns started to emerge that the company had been working hard to have school mandates instituted. Similar concerns have emerged across Canada and Germany, where many in the public began to believe that companies like Merck, Sharp, and Dohme were attempting to influence politicians to establish a subsidy for their vaccines (Haas et al., 2009). Events such as these have led some to question how many vaccine mandates have been influenced by lobbying from the pharmaceutical industry and may contribute to low vaccine acceptability (Mello et al., 2012; Haas et al., 2009).

Today, many anti-vaccination websites prominently feature concerns about pharmaceutical industry interests (Penta & Baban, 2014). Relatedly, the for-profit interests of many pharmaceutical companies have reportedly led some to believe that pursuing financial gains might supersede public health interests (Dinga et al., 2021). Prevailing beliefs such as these, whether they are founded or not, can partly explain a lack of trust that many in the public have towards the pharmaceutical industry (Alshurman et al., 2021; Dinga et al., 2021; Mello et al., 2012). However, these doubts are not only restricted to oppositional groups. In fact, similar sentiments were echoed by healthcare providers in Ukraine. As Bazylevych (2011) explains, “many providers associated vaccination



campaigns with the ruthlessness of the open market, which triggered the appetites of those in power to accept kickbacks from pharmaceutical companies instead of paying attention to strict quality standards.”

#### *5.4.7.2 Disruptive Biomedicine*

Biomedicine has long conflicted with alternative and more traditional forms of medicine. From the earliest smallpox vaccines, these tensions have impacted the acceptability of vaccines. Before the introduction of smallpox vaccinations, variolation practices had been used as a primary defense against smallpox in many parts of the world. In fact, inoculation was, in many cases, and primary source of income for physicians in countries like the United States. Consequently, vaccines, as a risk to their livelihoods, were vehemently opposed by many (Lanzarotta & Ramos, 2018). In the US, these tensions played out publicly, with debates appearing in both popular media and medical journals (Lanzarotta & Ramos, 2018). The disruptive impact that vaccines was mirrored in Victorian England when the nation’s first vaccination act banned the act of variolation and, as a consequence, “incited resistance from heterodox medical practitioners who were forced out of business” (Weber, 2010)

The introduction of vaccines, as an extension of Western biomedicine, has been characteristically disruptive to traditional, “unorthodox” medical practices in many regions of the world. In India, for example, the arrival of vaccines and eventual outlawing of variolation spurred significant opposition from *Tikadaars*, who, at the time, were involved in the practice of variolation against smallpox. However, even after the practice had been outlawed, *Tikadaars* continued to variolate individuals until the mid-Twentieth century

(Lahariya, 2014). Resistance to the disruptive power of vaccines has also been documented in areas such as Palestine, Nigeria, and the Kingdom of Dahomey (present-day Benin). This resistance is believed to be motivated in many cases by the threat vaccines pose to traditional medical practices and the standing of traditional healers in communities (Challenor, 1971; Davidovitch & Greenberg, 2007; Soumonni, 2012; Yahya, 2007).

#### *5.4.7.3 Corruption & Distrust*

Opponents of vaccines and non-compliers have often been found to lack trust in pharmaceutical companies, the drug development process, or the regulatory environment. While surely connected to the concerns mentioned above regarding lobbying efforts, this distrust also appears to stem from more fundamental doubts regarding corruption and a lack of transparency (Cassell et al., 2006; Dinga et al., 2021; Hobson-West, 2007; Mello et al., 2012; Nhamo & Sibanda, 2021; Perveen et al., 2019; Wonodi et al., 2022).

Recently, regulatory aberrations such as accelerated vaccine development and emergency use authorizations have stoked these concerns in individuals across the globe (Lin et al., 2020). Whether valid or not, the ‘expedited’ development timelines in some cases led to a lack of trust in regulatory oversight and drug development (Bardosh et al., 2022). The speed at which COVID-19 vaccines were brought to market play into concerns and arguments echoed by opposition groups put forward in the early 2000s. As Hobson-West (2007) described, many groups “make the argument that we do not know the effects of vaccination because of insufficient safety trials, both pre- and post-license.” These concerns are amplified by a purported lack of transparency from drug developers and

regulators, leading to distrust and the notion of corruption (Nhamo & Sibanda, 2021; Wiyeh et al., 2019)

It is probable that external political and historical contextual factors have shaped pre-existing views of the pharmaceutical industry. Nonetheless, notions of corruption and distrust in the industry have led some to believe that “companies would send the suboptimal stock of vaccines to Africa” (Dinga et al., 2021) and that vaccines were being used for corrupt profiteering or foreign dominance (Pop, 2015; Wonodi et al., 2022). Put together, these themes have the capacity to undermine the acceptability of vaccines and related public health programmes.

#### *5.4.7.4 Location of Origin*

The location in which vaccines are developed and manufactured has been shown to have a heterogenous influence over the acceptability of vaccines depending on the context in which they are being delivered. While this theme is undoubtedly tied in with other political and cultural determinants, it has become clear that individuals in various contexts are more or less receptive to vaccines depending on their country of origin. In the United States, respondents were generally more accepting of vaccines developed and manufactured domestically compared to a vaccine developed in China (Alshurman et al., 2021). Conversely, studies examining vaccine acceptability in Pakistan found that Western-made vaccines were less desirable (Hossain et al., 2021; Perveen et al., 2019). Finally, Bazylevych (2011) found that in Ukraine, some believed that vaccines “manufactured in India or other ‘Third World’ countries cannot possibly be of good quality, but are instead unsanitary.”

### 5.4.8 Geographic Influences

Themes related to the *Geographic Influences* contextual determinant category were identified in 18.7% (n=26) of the articles included in this literature review. The following three primary themes emerged through the thematic analysis: *Geographical Clustering* (n=8), *Cultural, Religious, and Political Divides* (n=10), and *Rural-Urban Divide* (n=11).

#### 5.4.8.1 Geographic Clustering

Many publications highlighted the way in which vaccine acceptability and resistance seem to cluster geographically (Estep & Greenberg, Gollust et al., 2010; 2020; Richwine et al., 2019; Smith et al., 2004; Uthman et al., 2021). These geographic “pockets of homogeneity” (Estep & Greenberg, 2020) sometimes appear to manifest by way of characteristically low levels of vaccine uptake, measured by localized vaccine coverage (Tesfahun et al., 2019). However, researchers have often identified geographical clustering of individuals claiming special exemptions to vaccine laws on medical, religious, or philosophical grounds (Gollust et al., 2010; Richwine et al., 2019; Smith et al., 2004).

However, the nature and origin of this phenomenon appear to be poorly understood. As Estep & Greenberg (2020) describe, it is unclear whether “it is the areas that attract a homogenous group of people, of the people who influence the decision making of the area through social pressure.” Gollust et al. (2010) explain that one explanation for geographic clustering may be the influence of local media and leaders. If true, this may mean that prevailing norms in “lifestyle enclaves” can strongly influence the vaccine-related decisions made by individuals in that area through conformity and other reinforcing social

processes (Estep & Greenberg, 2020; Tesfahun et al., 2019). Alternatively, certain groups may be drawn to specific geographic locations where their individual preferences are shared and are not subject to the same level of stigmatization (Estep & Greenberg, 2020). Nonetheless, a geographic cluster is undoubtedly the result of interactions between multiple contextual and individual determinants.

#### *5.4.8.2 Cultural, Political & Religious Divides*

Cultural, political, and religious geographic divides have been found to influence vaccine acceptability, demand, and resistance substantially. In the United States, attitudes toward vaccines and vaccination rates were found to vary across geographical regions (Guntuku et al., 2021; Lee & Huang, 2022; Smith et al., 2004). In some cases, localized political leaning, republican-dominant areas, was linked lower vaccine acceptability (Lee & Huang, 2022). Furthermore, in the United States, specific religious hubs, especially Evangelical-dominant areas, were found to have a disproportionately lower level of vaccination uptake compared to other regions (Guntuku et al., 2021).

Political and religious geographic divides affecting vaccine acceptability, demand, and resistance have also been identified in countries such as India, Pakistan, and Nigeria. As explained by Hussain et al. (2015), much of the religious and political divides in India can be traced back to the 1947 partition of British India, through which Pakistan was established “as a ‘Muslim homeland’, and India as a secular, but ‘Hindu-majority’ state.” Muslims who remained in India assembled into segregated neighborhoods that would become characteristically underdeveloped over time. As a consequence, pockets of low

vaccine acceptability and resistance now appear along political and religious divides in some of these underdeveloped Muslim areas (Hussain et al., 2015).

Similarly, as Njeru et al. (2016) note, political divides and tensions between Northern and Southern Nigeria contributed to vaccine resistance and a vaccine boycott in the Northern part of the country in 2003. Much of the resistance is suggested to stem from the government's decision to make Sharia law unconstitutional in the country. At the time, a number of states in Northern Nigeria practiced Sharia law (Ghinai et al., 2013). It would be in these states where the polio vaccination boycotts would subsequently occur, leading many to suggest religious and political divides between the North and South as a primary driver of vaccine resistance and low acceptability in the regions (Ghinai et al., 2013; Njeru et al., 2016; Yahya, 2007)

#### *5.4.8.3 Rural-Urban Divides*

A number of researchers have found disparities in vaccine uptake between urban and rural communities (Fernandez et al., 2011; Grundy & Biggs, 2019; Mushtaq et al., 2015; Olivera et al., 2021; Pop, 2015). In 1936, Collins noted that “as measured by vaccination histories, cities are considerably better vaccinated than the small towns and rural areas.” However, seldom has rurality alone been found to be an accurate predictor of vaccine acceptability. Instead, this variability has been suggested to be the product of interactions between rurality and other socioeconomic or demographic factors (Fernandez et al., 2011; Olivera et al., 2021). However, other authors have noted that some remote, rural communities often lack experience poor healthcare delivery (Hussain et al., 2016; Yahya, 2007). While healthcare service inequities of this nature may not have the most

decisive *direct* impact on vaccine acceptability and demand, as noted in preceding sections, they may influence demand and acceptability indirectly.

## **6 Discussion**

### **6.1 Historical Continuities**

One primary goal of this study was to explore, from a historical perspective, the continuities present in the determinants of vaccine acceptability across different global contexts. In the end, published literature dating back to the late 1930s was included and analyzed. While the breadth of analyzed publications spanned only the last century, many of the constituent publications in the file database focused on a period of study dating back to the late 1700s and early 1800s. As such, the depth of articles included in this study helped elucidate many historical themes and continuities, three of which will be discussed below.

#### **6.1.1 Trust**

This study has revealed the inextricable link between trust and acceptability. Through the research and analysis process, it became apparent that most, if not all, contextual determinants interact with and influence, either directly or indirectly, trust toward vaccines and vaccine-related policies. In one way or another, vaccine acceptability, resistance, demand, and uptake all appear to be profoundly impacted by prevailing levels of trust. Simply put, determinants found to have a negative impact on trust, such as colonial legacies, medical experiments, marginalization, corruption, and poor government performance, also appear to have a deleterious impact on the acceptability of vaccines.

While the relationship between trust and vaccine acceptability appears straightforward, cultivating and sustaining that trust has proven to be an onerous task. Many of these challenges seem to stem from the fact that vaccine acceptability, as a product of trust, has historically been affected by more than just vaccine-related factors. Many indirect



determinants and events that define the broader contexts in which vaccines are delivered affect trust and, consequently, vaccine acceptability to an equal or greater extent. Moreover, contemporary levels of trust have often been found to be the outcome of events and influences with protracted origins.

The enduring impacts of government actions and vaccine-related policies were consistently referenced throughout the literature. Legacies of government neglect towards healthcare, state-led marginalization, legacies of medical experimentation, and political corruption all appear to impact contemporary vaccine acceptability due to the damaging effects these factors have had on public trust. Furthermore, government-imposed vaccine mandates and policies have been found to undermine current levels of trust and reinforce or exacerbate preexisting distrust and resistance toward vaccines. Suppose a government has historically given its people little reason to trust in its decision-making. In that case, it is not surprising that suspicion, defiance, and rejection may hinder compliance with vaccine-related policies. When these low levels of acceptability and compliance are addressed through coercive measures, the already tenuous relationship between a nation's government and its citizens might very well be strained further.

Vaccines and vaccine-related programmes have long been regarded as tools of colonization due to the emphasis placed on widespread vaccination in the health strategies of many colonial states. Despite their efficacy, colonial vaccination efforts in these contexts were, in many cases, highly disruptive. Coercive measures were consistently reported and often found to target prevailing traditional health practices and beliefs. Moreover, given the low cost and high impact of vaccines, colonial states appear to have improved the health of

colonies without the need for more extensive development of healthcare infrastructure and systems. As Kennedy (2016) suggests, many post-colonial nations now struggle to sustain or develop healthcare systems without foreign support.

Consequently, it would appear that the disruptive legacies of a colonial past continue to endure. As many authors have described, these historical effects more than likely influence public trust towards governments and healthcare programmes and consequently undermine the acceptability of vaccines. These legacies are significant to consider in light of how involved many ex-colonial states are in the design, delivery, and implementation of vaccine programmes.

Trust, as a significant mediator of vaccine acceptability, must be cultivated over time. As a product of historical precedent, a lack of trust will not be rectified without a commitment to and consideration of its historical determinants. While these historical roots must undoubtedly influence the design of restorative efforts, forward-looking considerations are of similar importance. Consequently, the enduring effects that contemporary measures might have on future levels of trust should also be a key consideration in the design of vaccine-related campaigns and policies today. However, as some authors have pointed out, interventions aimed at improving the acceptability of vaccines have often been based on a mischaracterization or simplified account of what has led to prevailing attitudes. As discussed in preceding chapters, treating low vaccine acceptability as an acute issue ignores the complex and vital interplay of historical effects and legacies that have shaped contemporary contexts. Given the apparent importance of trust in promoting vaccine acceptability, addressing chronic levels of low trust emerging

from these historical contexts requires a commitment to more comprehensive and permanent remedial efforts that many acute interventions fail to attain.

### **6.1.2 Power Dynamics**

Over time, general levels of vaccine acceptability have consistently appeared to be the product of struggles for power in decision-making between the state and society. Some authors have pointed out that top-down decision-making structures and policies have often been met with widespread resistance. These tensions have manifested in opposition to compulsory vaccine laws stemming from concerns over individual rights, medical autonomy, and disagreements over limits to the scope of the state's power. It appears, then, that in many cases, a desire for greater levels of decision-making power has been a fundamental demand of individuals and groups. Paternalistic policies and vaccine-related efforts, which ostensibly treat recipients of vaccines as passive actors, often do not satisfy this widespread desire. Consequently, vaccine resistance and low levels of acceptability have been shown to emerge regularly from political contexts with tenuous state-society power dynamics.

Additionally, socially- and culturally-defined power dynamics appear to exert a strong influence over the contexts in which vaccines are delivered and their acceptability. As many authors have pointed out, tensions between local leaders of wide varieties and vaccine programmes have consistently led to poor local vaccine acceptability and suboptimal delivery outcomes. A lack of consideration for these contextually defined power dynamics may result in vaccine programmes being at odds with local authority structures. Disregarded gender dynamics and the need for approval and support from

community leaders represent two broadly referenced examples of how contextually defined power dynamics can hinder or bolster vaccine acceptability. Contextual considerations such as these have and continue to impact prevailing vaccine acceptability levels and vaccine programs' success.

### **6.1.3 A Victim of Circumstance**

Over time, vaccines have consistently appeared to be at the mercy of prevailing social and political contexts. Many authors have suggested that poor vaccine acceptability and resistance can often be interpreted as manifestations of political and social strife. Resistance towards vaccines and non-compliance with vaccination programmes may be used as a strategic means through which social and political objectives are negotiated. In some of these cases, vaccines become victims of prevailing political and social contexts and are leveraged in an attempt to achieve specific objectives. The visibility of vaccination programmes has also been said to make non-compliance a low-cost and high-impact means of expressing political and social dissatisfaction or dissent. Consequently, throughout the history of vaccines, medical dissent in the form of vaccine resistance has often been attributed to public political opposition and dissatisfaction.

However, the political leverage provided by strategic resistance to vaccines and vaccination policies has also historically been employed by influential leaders. Some authors writing on early vaccine resistance describe how leaders of different varieties intentionally undermined the public acceptability of vaccines and led a resistance against vaccination efforts to achieve desired ends. For example, Sater (2003) described how in the mid-1880s, “partisan politics” and “not scientific issues” led to the rejection of proposed

smallpox vaccination mandates in Chile. Today, contentious and polarized political contexts continue to allow leaders to leverage vaccines as a tool for divisive and oppositional politics, turning health and vaccine-related decisions into polarizing topics that play out along party and ideological lines.

Unfortunately, polarized political contexts exert a strong influence over whom opposing groups recognize as credible or trustworthy. As a result, vaccine acceptability has often appeared to be heavily influenced by a source of vaccine-related information instead of the merit of the information alone. The promulgation of false, misleading, or inflammatory information by opportunistic influential leaders has been characteristic of oppositional vaccine discourse throughout history.

## **6.2 Historical Discontinuities**

While an evaluation of historical continuities was an important aim of this study, to develop a greater understanding of how contextual determinants had evolved over time, historical discontinuities were explored and analyzed. Two primary themes related to these historical discontinuities will be discussed below.

### **6.2.1 Transformative Effects of Technology**

Authors writing on early instances of vaccine resistance frequently describe how debates between opponents and proponents often took place within the margins of newspapers and academic journals. Perspectives on vaccines and vaccine-related policies, whether scientific or philosophical, were argued for and against using what were, at the time, some of the more influential forms of public communication. However, the reach of earlier forms of media was spatially limited due to the need for physical distribution or

limits on technology. As time progressed, more far-reaching communication technologies were developed, opening new channels through which information could pass, and debates could occur.

Specifically, the global connectivity facilitated by the internet has established channels of communication that are, in most cases, no longer spatially limited to the same degree as their traditional processors. Consequently, pre-existing access barriers have been reduced, allowing a more significant number of people to interact with and consume media. As a result, what were once localized vaccine debates are now disseminated by an increasingly global audience. The advent of new digitized social platforms also allows like-minded individuals, who were at one point limited by geography, to coalesce and create homogenous groups through which perceptions and opinions can be influenced or reinforced.

In the past, individuals and groups were more often not involved in creating media or information they consumed. The non-participatory nature of this media context shifted with the advent of digitized forms of communication and media towards a paradigm predicated on greater levels of participation. The public, who were once primarily consumers of media, have been empowered through the internet to be producers. As a result, the evolution of communication and media has contributed to a more accessible media environment in terms of its widespread availability and creation.

It appears then that the evolution and digitization of communication technologies have transformed one of the contextual environments through which the acceptability of vaccines is shaped. This transformation has introduced new, more connected forms of

communication as well as created new opportunities for more participatory forms of communication. As a result, individuals and groups are now, more than ever, able to create, promulgate, and disseminate information, irrespective of its veracity. Furthermore, geographically localized pockets of homogenous groups can connect virtually to amplify the reach and influence of their messaging. These effects can, and have, contributed to what seems to be a burgeoning challenge of vaccine-related misinformation and disinformation and, as a consequence, challenges with vaccine acceptability.

### **6.2.2 Political & Social Evolution**

This study helped identify many essential overarching political and social themes that have, over time, influenced levels of vaccine acceptability. However, these themes contain significant historical levels of social and political variability. As Akmatov et al. (2007) mentioned, a contextual evolution resulting from the transformation of political systems is likely to introduce new determinants of vaccine acceptability. In this study, examples and descriptions of political and social evolutions consistently illustrated how distinct and evolving contexts shape vaccine acceptability in unique ways.

On a fundamental level, the foundation and structure of political systems or governments are essential considerations. The underlying political system strongly influences the relationship between the state and society. While more liberal political systems have historically struggled to balance individual rights and liberties with public health objectives, more authoritarian and socialist structures have, in many cases, not contended with the same tensions. However, as evidenced by the sentiments towards vaccination campaigns held by many in post-Soviet nations, legacies of coercive public

health campaigns may endure and undermine vaccine acceptability even after a political transition has occurred.

Geopolitics has introduced new influences that have been shown to affect vaccine acceptability. Resistance towards vaccines has become increasingly connected to geopolitical tensions, conflicts, and power dynamics. As a result, the once primarily domestic political roots of resistance and low acceptability appear to now transcend national borders.

Disparate social contexts are also suggested to influence vaccine acceptability in different ways. For example, primarily collectivist societies appear to have greater levels of vaccine acceptability than those societies in which individualism is the prevailing norm. These different effects are likely a consequence of contrasting political and social solidarity levels. Nonetheless, it is crucial to recognize the influence political systems and context have on shaping societal attitudes such as those mentioned above.

However, as mentioned in the preceding section, technological transformation increasingly influences social evolution. In contrast to centuries past, social norms are now shaped by virtual interactions, social networks, and communities, in addition to more traditional localized influences. As a result, both local and online social contexts can now exert an influence over the acceptability of vaccines and vaccine-related policies.

This technological transformation has also contributed to a significant evolution in healthcare paradigms away from predominantly paternalistic models of care. As numerous authors have suggested, the power dynamics between patients, their care providers, public health decision-makers, and citizens have been dramatically altered. As a result, individuals



and patients now have an increasing appetite for medical autonomy and decision-making power over choices that affect their health. At the same time, evidence in the literature suggests that vaccination decisions are becoming increasingly informed by information sourced from online and social media outlets. The availability of this information has created a social and political context in which traditional sources of medical information, such as healthcare providers, seem to possess less authority or influence. The effects of this digital transformation, coupled with the aforementioned shift away from paternalistic models of care, have dramatically altered the contexts through which levels of vaccine acceptability are influenced.

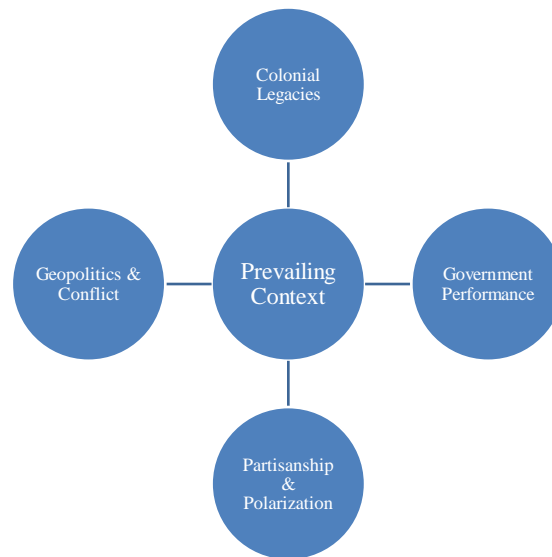
### **6.3 Complex Causality**

Another primary goal of this thesis, and the original motivation for considering the use of a QCA, was to explore how different combinations of contextual determinants can interreact to produce similar or dissimilar outcomes. Unfortunately, causal combinations of determinants could not be evaluated using the same degree of analytic rigor that a QCA might have supported. Nonetheless, the results of the literature review did elucidate how complex and interwoven many of the contextual determinants are. While 32 themes were eventually identified across the seven contextual determinant categories, many, if not all, of the respective themes overlap, varying degrees, with other themes within and across the contextual determinant categories. Based on this high level of overlap, it would appear that few, if any, of the contextual determinants and related themes work alone to influence vaccine acceptability. Put differently, the thematic overlap suggests that vaccine acceptability, demand, resistance, and uptake are the products of different combinations of

contextual determinants. This thesis's results have shown that this complex causality has varied over time and across different global contexts. Two hypothetical examples will be presented below in an effort to illustrate the nature of this complex causality and how it can lead to contexts conducive to poor levels of vaccine acceptability. These examples have been conceptualized based on themes and events identified in the literature review.

### 6.3.1 Illustrative Examples

#### 6.3.1.1 Example 1



*Figure 9: First illustrative example of complex causality*

As some authors have pointed out, colonialism has often been found to have had a significant destabilizing effect on occupied nations. Many of these effects have been found to endure long after colonial states gained independence. Consequently, several post-colonial nations have struggled to develop or maintain domestic healthcare and health infrastructure. Furthermore, in some cases, after separating from colonial states and regaining sovereignty, nations were left divided along political, ethnic, and religious lines.

In addition to creating a political context vulnerable to significant civil conflict and corruption, colonial legacies have undermined many governments' ability to perform. These effects and resulting divides have also been shown to lead to general neglect or underdevelopment of parts of countries. As mentioned in the literature, underdevelopment, government neglect, poor government performance, and a resulting sense of disenfranchisement have damaged vaccine acceptability. What is more, is that many post-colonial states have historically been reliant on foreign support in order to improve domestic healthcare services and deliver vaccines. This reliance introduces other geopolitical dimensions which can and have undermined vaccine acceptability directly and indirectly.

### 6.3.1.2 Example 2

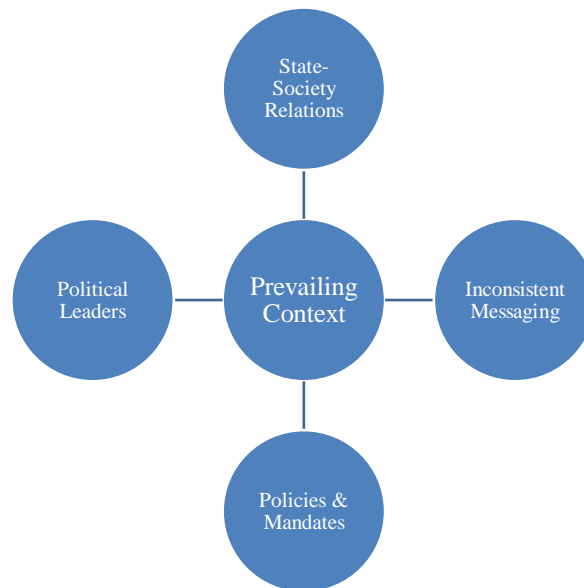


Figure 10: Second illustrative example of complex causality

Changes in social and political dynamics stemming from evolutions in the relationships between the state and society have often been suggested to impact vaccine acceptability. The commonly referenced desired shift away from top-down public health governance in favor of more bottom-up, participatory paradigms appears to have made enforcing coercive and compulsory vaccine requirements more tenuous. Since individuals in many societies desire more power in health decisions that affect them, paternalistic campaigns and recommendations seem to have become more of a challenge to implement or enforce. Resistance to top-down policies, motivated by these issues, has been frequently cited in the literature. However, these contentious issues can and have been exploited by political leaders looking to undermine opponents or garner more political support. This opportunistic and strategic politicization of vaccines enables more polarized and inconsistent messaging from influential leaders. As a consequence, confidence in government decisions and recommendations may be undermined, which in turn affects the acceptability of vaccines.

### **6.3.2 Implications & Added Considerations**

As the examples above hopefully illustrate, many different combinations of determinates and factors can interreact to create complex contexts in which vaccine acceptability is undermined. Overlooking this causal complexity when designing vaccination campaigns or interventions targeting vaccine acceptability risks undermining the support for, the impact of, and ultimately the success of these efforts. As the literature has shown, interventions and campaigns that do not consider such a level of causal complexity might also lead to unintended future vaccine acceptability reductions. It would

appear as though, in many cases, that low vaccine acceptability is a symptom of a more complex set of contextual circumstances which emanate out of historical factors and continue to be shaped by contemporary determinants. In this way, vaccine acceptability might be better understood and approached as a chronic condition that needs routine care rather than an acute issue, treated through patchwork policies and interventions.

## **6.4 Limitations**

### **6.4.1 Practical Limitations**

Some of the more notable limitations of this thesis stem from relevant practical and resource constraints. First, given that this thesis had no other collaborators, the breadth and depth of literature included in the literature review were limited by time considerations and the independent capacity to review a substantial body of literature. As a result, materials were sourced from only one primary database. While the search conducted on the Global Health database returned a considerable number of relevant results, procuring literature from additional databases could likely have added to the depth and breadth of the review and, consequently, the quality of the results and findings. Furthermore, only roughly half (n=139) of the publications that met the final overall eligibility criteria (n=304) were used for the analysis. Omitting this portion of the final dataset was once again motivated by practical and time-related limitations resulting from the independent nature of this thesis. While the final list of included articles was sufficient to facilitate a broad and detailed overview of the field of study, the inclusion of the additional publications would have undoubtedly enriched the literature review.

### **6.4.2 Subjectivity**

Another limitation of this thesis relates to the degree of subjectivity that was likely introduced into the review and discussion in the absence of additional study collaborators. Many of the model reviews, guidelines, and recommendations used to inform this thesis's methodological approach featured or suggested using more than one collaborator when conducting a literature review. In many cases, using two or more reviewers can help ensure a high level of rigor through disagreements, deliberations, and revisions during the research, screening, and analysis stages. While many steps were taken in this thesis to support the production of a rigorous and high-quality study, the lack of collaborators is an important limitation nonetheless. Given the lack of collaborators, the final analysis was guided by a single point of view. Consequently, it may be more strongly influenced by a degree of subjectivity that would otherwise be reduced in more collaborative efforts.

### **6.4.3 Scope**

As mentioned in the preceding section on casual complexity, it is evident that several different combinations of intersecting contextual determinants work together to influence vaccine acceptability, demand, and resistance. However, this thesis did not explore a range of relevant and likely intersecting individual-level and vaccine-specific determinants. As a result, one notable limitation that should be mentioned pertains to the intentionally limited scope of reviewed literature. The findings of this thesis and the resulting discussion explore only one, albeit complex, part of vaccine acceptability. Consequently, any results or implications should be interpreted within the limits of the scope of this research and with the importance of other determinant categories in mind.

## **6.5 Future Directions**

While this thesis focuses on contextual determinants of vaccine acceptability, other determinant categories are essential to consider. As a result, it may be valuable to conduct similar research efforts on the other two determinant categories outlined in the Determinants Matrix. Furthermore, given the emphasis placed on causal complexity and the intersections of multiple determinants, it would be valuable to explore how determinants across categories interact to influence levels of vaccine acceptability.

## **6.6 Contributions to the Field**

To my knowledge, no other study has attempted to explore the historical themes and trends related to the various contextual determinants of vaccine acceptability. As a result, this thesis contributes to the literature by beginning to map and describe this growing field of study. Additionally, it attempts to expand discussions of vaccine acceptability from a predominantly individual level of focus to one more inclusive of contextual factors integral to explaining its various manifestations. Doing so provides a conceptual basis from which future, more directed research may take place.

## 7 Conclusion

Vaccine acceptability plays an essential role in influencing prevailing levels of demand for vaccines. Suboptimal demand for vaccines has long been identified as a threat to the realization of global health agendas. Consequently, improving levels of vaccine acceptability is an important issue with significant implications for global health. Accordingly, this thesis sought to develop a deeper understanding of the contextual determinants of vaccine acceptability.

Through an in-depth global health literature review, 32, often interrelated themes across seven contextual determinant categories were identified and explored. These findings helped elucidate how the acceptability of vaccines is inextricably linked to broader factors, beyond individual determinants, that shape overarching contexts in which vaccines are delivered. These results suggest that contextual determinants, given their demonstrable influence, ought to be central considerations in policies, programmes, and efforts aimed at improving the acceptability of vaccines.

Historical continuities and discontinuities were explored in the discussion chapter to illustrate how the contextual determinants of vaccine acceptability had evolved over time and across different global contexts. Over time, vaccine acceptability has consistently been a product of, amongst others, broader political, social, cultural, and historical circumstances. Consequently, prevailing levels of trust and power dynamics between the public, institutions, and governments have continually had notable effects on vaccine acceptability. However, the literature also revealed how social, political, and technological



evolution has served to both improve and undermine vaccine acceptability differently over time and across different global contexts.

Relationships between contextual determinants were examined to reveal how interactions between various determinants can, over time, lead to poor levels of vaccine acceptability. As suggested in the closing part of the discussion chapter, this complex causality exemplifies the need to treat vaccine acceptability as a chronic condition that demands routine care. Treating low vaccine acceptability as an acute issue overlooks the crucial impact that historical effects and legacies have had on molding relevant and influential contemporary contexts. Establishing contexts conducive to sustaining high vaccine acceptability requires time, careful consideration of the retrospective impacts of historical determinants, and an understanding of how contemporary determinants can shape contexts and acceptability moving forward.

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## A Search Terms & Sources

Search Terms	Variations	Primary Source(s)
<b>Action / Behaviour / Psychological State</b>		
Accept*	Accept, Acceptance, Accepting, Acceptability	(Cella et al., 2020; Larson et al., 2014; Schmid et al., 2017)
Intent*	Intent, Intentions	(Cella et al., 2020; Larson et al., 2014; Schmid et al., 2017)
Hesita*	Hesitant, Hesitate, Hesitancy	(Cella et al., 2020; Larson et al., 2014; Schmid et al., 2017)
Sentiment		(Nindrea et al., 2022)
Reluct*	Reluctant, Reluctance	(Martin, 2022; Prem, 2022)
Willing*	Willing, Willingness	(Nadarzynski, 2021)
Demand		(Schmid et al., 2017)
Confiden*	Confident, Confidence	(Cella et al., 2020; Larson et al., 2014)
Resist*	Resist, Resistance, Resistant	(Martin, 2022; Prem, 2022)
Refus*	Refuse, Refusal, Refuser	(Cella et al., 2020; Larson et al., 2014; Schmid et al., 2017)
Concern		(Cella et al., 2020; Larson et al., 2014; Schmid et al., 2017)
Reject*	Reject, Rejection, Rejector	(Cella et al., 2020; Larson et al., 2014)
Skepti*	Skeptical, Skepticism, Skeptic	(Cella et al., 2020)
Scepti*	Sceptical, Scepticism, Sceptic	(Cella et al., 2020)
Recepti*	Receptive, Reception, Receptivity, Receptive	(Farah, 2021)
Adhere*	Adhere, Adherence	(Cella et al., 2020)
Oppos*	Oppose, Opposition	(Larson et al., 2014; Schmid et al., 2017)
Uptake		(Cella et al., 2020; Larson et al., 2014)
Belie*	Belief, Beliefs, Believe	(Cella et al., 2020; Larson et al., 2014)
Doubt		(Cella et al., 2020; Larson et al., 2014; Schmid et al., 2017)
Fear		(Larson et al., 2014; Schmid et al., 2017)
Mistrust		(Larson et al., 2014; Schmid et al., 2017)
Trust		(Cella et al., 2020; Larson et al., 2014; Schmid et al., 2017)
Distrust		(Larson et al., 2014; Schmid et al., 2017)
Object*	Object, Objection, Objector	(Larson et al., 2014; Schmid et al., 2017)
Choice		(Cella et al., 2020; Larson et al., 2014; Schmid et al., 2017)

Decision		(Larson et al., 2014)
<b>Determinant</b>		
Context*	Context, Contextual	(Bedford et al., 2014)
Mandate		(Larson et al., 2014)
Compulsory		(Larson et al., 2014)
Policy		(Schmid et al., 2017)
Politic*	Political, Politics	(Schmid et al., 2017)
Policies		(Schmid et al., 2017)
Media		(Bedford et al., 2014)
Influenc*	Influence, Influential, Influencer	(Larson et al., 2014)
Leader		(Larson et al., 2014)
Lobby		(Larson et al., 2014)
Lobbies		(Larson et al., 2014)
Industr*	Industry, Industrial, Industries	(Larson et al., 2014)
Pharma*	Pharma, Pharmaceutical	(Larson et al., 2014)
History		(Larson et al., 2014)
Historical		(Larson et al., 2014)
Religi*	Religion, Religious, Religiosity	(Larson et al., 2014)
Cultur*	Culture, Cultural	(Larson et al., 2014)
Factor		
Root		
Caus*	Cause, Causal	(Larson et al., 2014)
Determinant		(Schmid et al., 2017)
Gatekeep		(Larson et al., 2014)



## B References By Theme

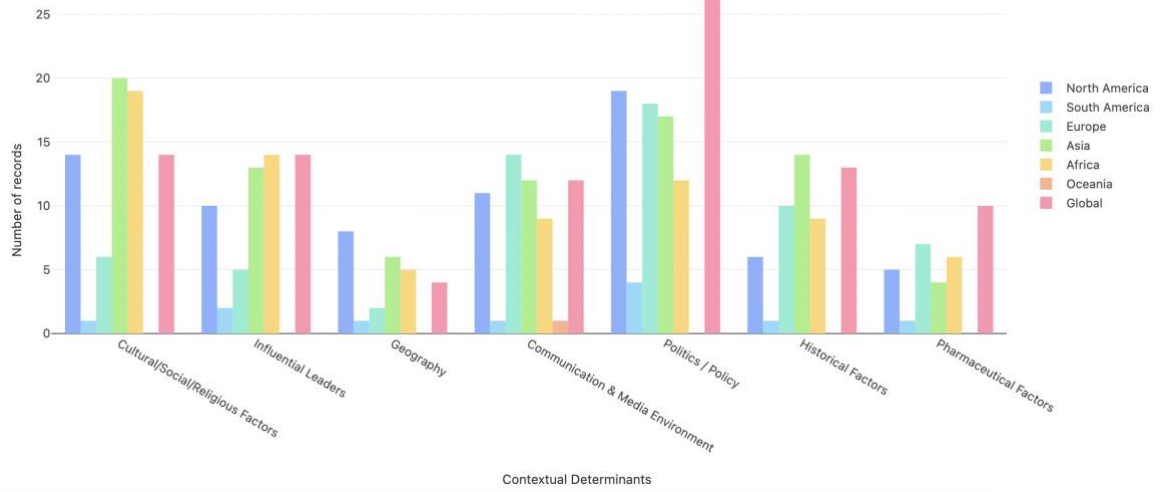
Theme	References
<b>Politics &amp; Policy</b>	
Partisanship & Polarization (n=21)	(Albrecht, 2022; Alshurman et al., 2021; Bardosh et al., 2022; Baumgaertner et al., 2018; Clemente-Suarez et al., 2022; Closser et al., 2016; Doan & Kirkpatrick, 2013; Gagneux-Brunon et al., 2022; Ghinai et al., 2013; Gollust et al., 2010; Kennedy et al., 2015; Latkin et al., 2020; Lee & Huang., 2022; Lin et al., 2020; Njeru et al., 2016; Perveen et al., 2019; Sater, 2003; Walkowiak et al., 2022; Ward et al., 2020; Whittacker et al., 2019; Yuen, 2022)
Distrust & Skepticism (n=26)	(Akil & Ahmad, 2016; Albrecht, 2022; Bazylevych, 2011; Biswas et al., 2019 Boas et al., 2016; Bokemper et al., 2021; Cassell et al., 2006; Colgrove et al., 2010; Deignan et al., 2021; Gagneux-Brunon et al., 2022; Hussain et al., 2015; Kennedy, 2017; Khan et al., 2019; Khan et al., 2021; Lanzarotta & Ramos, 2018; Latkin et al., 2020; Lee & Huang., 2022; Mendoza et al., 2021; Nasiru et al., 2012; Nhamo & Sibanda, 2021; Njeru et al., 2016; Perveen et al., 2019; Rozek et al., 2021; Schwartz, 2010; Wonodi et al., 2022; Yuen, 2022)
State-Society Relations (n=23)	(Akil & Ahmad, 2016; Bhattacharya & Dasgupta, 2011; Boas et al., 2016; Cassell et al., 2006; Closser et al., 2016; Colgrove et al., 2010; Colgrove et al., 2016; Davidovitch & Greenberg, 2007; Ghinai et al., 2013; Kakalia & Karrar, 2016; Kasstan, 2021; Khan et al., 2019; Kieslich, 2018; Lanzarotta & Ramos, 2018; Leonard, 2011; Nasiru et al., 2012; Neel et al., 2021; Prasada, 1937; Spicher & Weiss, 2019; Taylor, 2009; Taylor, 2015; Walkowiak et al., 2022; Yuen, 2022)
Mandates & Policies (n=26)	(Bardosh et al., 2022; Bifulco et al., 2022; Colgrove et al., 2010; Colgrove et al., 2016; Copeman et al., 1934; Franco et al., 2019; Gollust et al., 2010; Grzybowski et al., 2017; Haas et al., 2009; Hobson-West, 2007; Hussain et al., 2016; Johnson & Goronga, 2020; Khan et al., 2019; Kieslich, 2018; Landriouan, 1972; Lazarus et al., 2020; Millard, 1948; Rich, 2011; Richwine et al., 2019; Schmitt et al., 2003) (Spicher & Weiss, 2019; Stewart & Delvin, 2006; Vamos et al., 2008; Walkowiak et al., 2021; Weber, 2010; Weiss & Esparza, 2015)
Government Performance (n=22)	(Bazylevych, 2011; Boas et al., 2016; Chaturvedi et al., 2009; Closser et al., 2016; Deignan et al., 2021; Guarino et al., 2017; Hussain et al., 2015; Hussain et al., 2016; Kakalia & Karrar, 2016; Kaufmann & Feldbaum, 2009; Khan et al., 2019; Leonard, 2011; Neel et al., 2021; Olivera et al., 2021; Osur et al., 2022; Sater, 2003; Seytre, 2022; Taylor, 2009; Taylor, 2015; Toffolutti et al., 2019; Ward et al., 2020; Yahya, 2007)
Geopolitics & Conflict (n=23)	(Akil & Ahmad, 2016; Bajpai & Saraya, 2012; Binga, 2016; Deignan et al., 2021; Gawel et al., 2021; Ghinai et al., 2013; Grundy & Biggs, 2019; Guarino et al., 2017; Harrison & Wu, 2020; Hussain et al., 2016; Kaufmann

	& Feldbaum, 2009; Kennedy, 2016; Khan & Qazi, 2013; Khan et al., 2019; Mushtaq et al., 2015; Nasir et al., 2014; Peckham, 2018; Sater, 2003; Seytre, 2022; Taylor, 2009; Whittacker et al., 2019; Yahya, 2007; Yuen, 2022)
<b>History &amp; Historical Factors</b>	
Evolving State & Social Contexts (n=20)	(Akmatov et al., 2007; Bajpai & Saraya, 2012; Bazylevych, 2011; Boas et al., 2016; Ghinai et al., 2013; Harrison & Wu, 2020; Johnson & Goronga, 2020; Kaufmann & Feldbaum, 2009; Laurent-Ledru et al., 2011; Leonard, 2011; Neel et al., 2021; Pop, 2015; Prasada, 1937; Rich, 2011; Sater, 2003; Taylor, 2009; Toffolutti et al., 2019; Walkowiak et al., 2021; Yahya, 2007; Yuen, 2022)
Colonial Legacies (n=18)	(Akmatov et al., 2007; Bajpai & Saraya, 2012; Bazylevych, 2011; Closser et al., 2016; Davidovitch & Greenberg, 2007; Harrison & Wu, 2020; Henderson et al., 2018; Hussain et al., 2015; Kennedy, 2016; Mosby & Swidrovich, 2021; Peckham, 2018; Prasada, 1937; Sater, 2003; Seytre, 2022; Soumonni, 2012; Toffolutti et al., 2019; Walkowiak et al., 2021; Yahya, 2007)
Medical Experimentation (n=10)	(Biswas et al., 2019; Closser et al., 2016; Ghinai et al., 2013; Khan et al., 2021; Lin et al., 2020; Mendoza et al., 2021; Mosby & Swidrovich, 2021; Njeru et al., 2016; Whittacker et al., 2019; Yahya, 2007)
Evolution of Policies & Mandates (n=12)	(Bifulco et al., 2022; Boas et al., 2016; Colgrove et al., 2016; Davidovitch & Greenberg, 2007; Fowler, 1941; Hussain et al., 2015; Lahariya, 2014; Leonard, 2011; Sater, 2003; Stewart & Delvin, 2006; Walkowiak et al., 2021; Weiss & Esparza, 2015)
Political & Geopolitical Events (n=13)	(Akil & Ahmad, 2016; Hussain et al., 2016; Kaufmann & Feldbaum, 2009; Kennedy et al., 2015; Kennedy, 2017; Khan & Qazi, 2013; Leonard, 2011; Mendoza et al., 2021; Mushtaq et al., 2015; Njeru et al., 2016; Peckham, 2018; Perveen et al., 2019; Whittacker et al., 2019)
<b>Geographical Influences</b>	
Geographical Clustering (n=8)	(Estep & Greenberg, 2020; Gollust et al., 2010; Guarino et al., 2017; Landriano, 1972; Richwine et al., 2019; Smith et al., 2004; Tesfahun et al., 2019; Uthman et al., 2021)
Cultural, Political & Religious Divides (n=10)	(Bhuiya et al., 1995; Ghinai et al., 2013; Guntuku et al., 2021; Hussain et al., 2015; Lee & Huang., 2022; Mushtaq et al., 2015; Njeru et al., 2016; Serquina-Ramiro et al., 2001; Smith et al., 2004; Yahya, 2007)
Rural-Urban Divide (n=11)	(Bhuiya et al., 1995; Collins, 1936; Fernandez et al., 2011; Grundy & Biggs, 2019; Guntuku et al., 2021; Hussain et al., 2016; Mushtaq et al., 2015; Olivera et al., 2021; Pop, 2015; Serquina-Ramiro et al., 2001; Yahya, 2007)
<b>Religious, Social &amp; Cultural Factors</b>	
Religion & Culture (n=49)	(Akil & Ahmad, 2016; Akmatov et al., 2007; Bhattacharya & Dasgupta, 2011; Biswas et al., 2019; Challenor, 1971; Chaturvedi et al., 2009; Colgrove et al., 2010; Colgrove et al., 2016; Davidovitch & Greenberg, 2007; Doan & Kirkpatrick, 2013; Estep & Greenberg, 2020; Franco et al., 2019; Ghinai et al., 2013; Grabenstein, 2013; Grzybowski et al., 2017; Haas et al., 2009; Harpan et al., 2021; Henderson et al., 2018; Hossain et al.,

	2021; Hussain et al., 2016; Johnson & Goronga, 2020; Kakalia & Karrar, 2016; Kasstan, 2021; Kennedy, 2017; Khan & Qazi, 2013; Khan et al., 2019; Lahariya, 2014; Levin et al., 2022; Mendelsohn, 1968; Nasir et al., 2014; Nhamo & Sibanda, 2021; Olivera et al., 2021; Osur et al., 2022; Peckham, 2018; Perveen et al., 2019; Pop, 2015; Redd et al., 2022; Rich, 2011; Sabahelzain et al., 2019; Serquina-Ramiro et al., 2001; Seytre, 2022; Soumonni, 2012; Uthman et al., 2021; Vamos et al., 2008; Warraich, 2009; Weber, 2010; Wombwell et al., 2015; Wonodi et al., 2022; Yahya, 2007)
Social Contexts (n=10)	(Boas et al., 2016; Deignan et al., 2021; Estep & Greenberg, 2020; Johnson & Goronga, 2020; Kieslich, 2018; Mendelsohn, 1968; Spicher & Weiss, 2019; Taylor, 2009; Walkowiak et al., 2022; Weber, 2010)
Traditional Practices (n=14)	(Basharat et al., 2017; Challenor, 1971; Closser et al., 2016; Davidovitch & Greenberg, 2007; Ghinai et al., 2013; Grabenstein, 2013; Hossain et al., 2021; Imperato & Traore, 1968; Lahariya, 2014; Leonard, 2011; Mshelia et al., 2020; Soumonni, 2012; Wombwell et al., 2015; Yahya, 2007)
Gender Dynamics (n=9)	(Akmatov et al., 2007; Alshurman et al., 2021; Deignan et al., 2021; Grabenstein, 2013; Hussain et al., 2016; Khan et al., 2019; Serquina-Ramiro et al., 2001; Tamysetty et al., 2022; Wombwell et al., 2015)
<b>Pharmaceutical Influences</b>	
Industry Interests & Lobbying (n=12)	(Alshurman et al., 2021; Bardosh et al., 2022; Bazylevych, 2011; Colgrove et al., 2010; Dinga et al., 2021; Doan & Kirkpatrick, 2013; Haas et al., 2009; Lin et al., 2020; Mello et al., 2012; Nhamo & Sibanda, 2021; Penta & Baban, 2014; Schwartz, 2010)
Disruptive Biomedicine (n=7)	(Challenor, 1971; Davidovitch & Greenberg, 2007; Lahariya, 2014; Lanzarotta & Ramos, 2018; Soumonni, 2012; Weber, 2010; Yahya, 2007)
Corruption & Distrust (n=17)	(Alshurman et al., 2021; Bazylevych, 2011; Cassell et al., 2006; Closser et al., 2016; Colgrove et al., 2010; Dinga et al., 2021; Ghinai et al., 2013; Hobson-West, 2007; Kasstan, 2021; Mello et al., 2012; Mendoza et al., 2021; Nhamo & Sibanda, 2021; Perveen et al., 2019; Pop, 2015; Whittacker et al., 2019; Wiyeh et al., 2019; Wonodi et al., 2022)
Location of Origin (n=7)	(Alshurman et al., 2021; Bazylevych, 2011; Dinga et al., 2021; Gramacho & Turgeon, 2021; Hossain et al., 2021; Osur et al., 2022; Perveen et al., 2019)
<b>Influential Leaders</b>	
Political Leaders (n=24)	(Alshurman et al., 2021; Baumgaertner et al., 2018; Bokemper et al., 2021; Burgess et al., 2006; Clemente-Suarez et al., 2022; Deignan et al., 2021; Ghinai et al., 2013; Hussain et al., 2015; Hussain et al., 2016; Johnson & Goronga, 2020; Kaufmann & Feldbaum, 2009; Kennedy et al., 2015; Kennedy, 2016; Kennedy, 2017; Lee & Huang., 2022; Lin et al., 2020; Mushtaq et al., 2015; Nhamo & Sibanda, 2021; Perveen et al., 2019; Sater, 2003; Spicher & Weiss, 2019; Warraich, 2009; Wonodi et al., 2022; Zucker et al., 2015)
Religious Leaders (n=27)	(Baumgaertner et al., 2018; Binga, 2016; Colgrove et al., 2016; Deignan et al., 2021; Franco et al., 2019; Gawel et al., 2021; Ghinai et al., 2013; Haas et al., 2009; Hussain et al., 2016; Johnson & Goronga, 2020; Kasstan, 2021;

	Kaufmann & Feldbaum, 2009; Kennedy, 2016; Kennedy, 2017; Khan et al., 2019; Lahariya, 2014; Mushtaq et al., 2015; Nasir et al., 2014; Nasiru et al., 2012; Njeru et al., 2016; Olivera et al., 2021; Perveen et al., 2019; Serquina-Ramiro et al., 2001; Soumonni, 2012; Warraich, 2009; Whittacker et al., 2019; Wonodi et al., 2022)
Community Leaders (n=17)	(Alyward & Heymann, 2005; Baumgaertner et al., 2018; Binga, 2016; Davidovitch & Greenberg, 2007; Deignan et al., 2021; Gollust et al., 2010; Imperato & Traore, 1968; Johnson & Goronga, 2020; Lahariya, 2014; Lazarus et al., 2020; Leonard, 2011; Mshelia et al., 2020; Nasir et al., 2014; Nasiru et al., 2012; Osur et al., 2022; Prasada, 1937; Serquina-Ramiro et al., 2001)
Medical Professionals (n=9)	(Baumgaertner et al., 2018; Deignan et al., 2021; Ghinai et al., 2013; Haas et al., 2009; Lanzarotta & Ramos, 2018; Laurent-Ledru et al., 2011; Rich, 2011; Rozek et al., 2021; Yuen, 2022)
Traditional Medical Leaders (n=10)	(Baumgaertner et al., 2018; Cassell et al., 2006; Challenor, 1971; Davidovitch & Greenberg, 2007; Gawel et al., 2021; Imperato & Traore, 1968; Lahariya, 2014; Lanzarotta & Ramos, 2018; Serquina-Ramiro et al., 2001; Soumonni, 2012)
<b>Communication &amp; Media Environment</b>	
Health Misinformation & Disinformation (n=22)	(Alshurman et al., 2021; Alyward & Heymann, 2005; Aquino et al., 2017; Bazylevych, 2011; Bhattacharya & Dasgupta, 2011; Biswas et al., 2019; Burgess et al., 2006; Clemente-Suarez et al., 2022; Gawel et al., 2021; Hussain et al., 2016; Kakalia & Karrar, 2016; Kennedy et al., 2015; Khan et al., 2021; Kieslich, 2018; Nhamo & Sibanda, 2021; Perveen et al., 2019; Richwine et al., 2019; Schmitt et al., 2003; Stewart & Delvin, 2006; Tamysetty et al., 2022; Wiyeh et al., 2019; Wonodi et al., 2022)
Evolving Media Sources (n=24)	(Alyward & Heymann, 2005; Bhuiya et al., 1995; Biswas et al., 2019; Clemente-Suarez et al., 2022; Das et al., 2021; Deignan et al., 2021; Gawel et al., 2021; Hilton et al., 2010; Hobson-West, 2007; Hossain et al., 2021; Khan et al., 2019; Khan et al., 2021; Kieslich, 2018; Lanzarotta & Ramos, 2018; Latkin et al., 2020; Laurent-Ledru et al., 2011; Nasiru et al., 2012; Osur et al., 2022; Rich, 2011; Sater, 2003; Seytre, 2022; Tamysetty et al., 2022; Wiyeh et al., 2019; Wonodi et al., 2022)
Rumours & Conspiracy Theories (n=13)	(Alyward & Heymann, 2005; Bazylevych, 2011; Bhattacharya & Dasgupta, 2011; Hussain et al., 2015; Kaufmann & Feldbaum, 2009; Kennedy, 2016; Khan et al., 2021; Nasir et al., 2014; Nhamo & Sibanda, 2021; Seytre, 2022; Tamysetty et al., 2022; Uthman et al., 2021; Wonodi et al., 2022)
Inconsistent Messaging (n=9)	(Bardosh et al., 2022; Biswas et al., 2019; Deignan et al., 2021; Gagneux-Brunon et al., 2022; Gollust et al., 2010; Khan et al., 2019; Lazarus et al., 2020; Penta & Baban, 2014; Vamos et al., 2008)
Media Representation & Tone (n=13)	(Bazylevych, 2011; Court et al., 2021; Das et al., 2021; Gollust et al., 2010; Hilton et al., 2010; Laurent-Ledru et al., 2011; Mason & Donnelly, 2000; Penta & Baban, 2014; Sacerdote et al., 2020; Sater, 2003; Schmitt et al., 2003; Stewart & Delvin, 2006; Zucker et al., 2015)

## C Contextual Determinants & Themes



## D Search Strategy Examples

**Table 1**  
Keywords used in search strategy for literature review on vaccine hesitancy.

vaccin*		anxiety attitude*	doubt* distrust	trust mistrust	intent*	dilemma*
immunis*	AND	awareness	dropout*	Perception*	controvers*,	objector*
		behavi*r	exemption*	refus*	misconception*	Uptake
		belief*	fear*	Rejection	misinformation	barrier*
		criticis*	hesitanc*	rumo*r	opposition	choice*
immuniz*		accept*	concern*	compulsory	delay	mandatory
		confidence	decision making	anti-vaccin*	knowledge	
					parent* con*	

(Larson et al., 2014)

**Table 1. Keywords used for the literature search.**

	AND		AND	knowledge	misconception*	misinformation	promoter*	barrier*
influenza*		vaccin*		behavior	delay	criticis*	controvers*	anxi*
seasonal influenza*		immuniz*		behavior	choice*	doubt*	oppos*	confidence
pandemic influenza*		Immunis*		uptake	hesitan*	exemption*	dilemma*	trust
H5N1		Inoculat*		intervention*	demand	rejection*	objector*	distrust
H1N1		prevention and control		increas*	accept*	rumor	determinant*	mistrust
flu				decreas*	refus*	rumour	attitude*	awareness
				dropout*	denial*	mandatory	belief*	fear*
				decision making	concern*	anti-vaccin*	emotion*	perception*
				campaign*	recommend*	polic*	intent*	compulsory

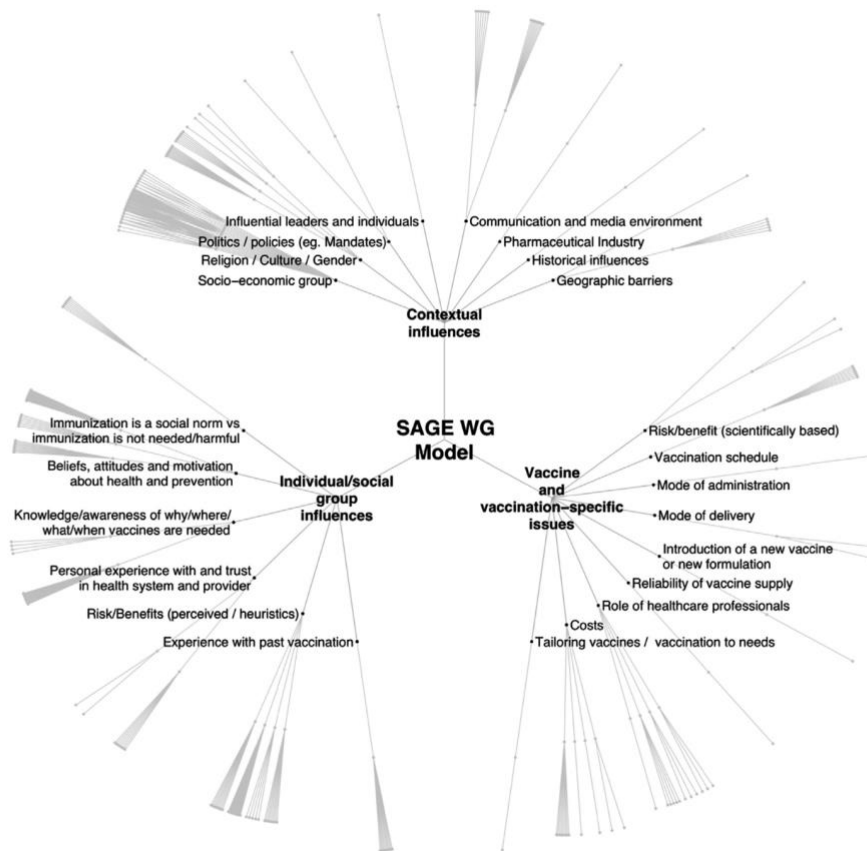
Note: Truncation was removed when a MeSH/CINAHL or Emtree term matched the concept. When databases provided thesaurus services (e.g. Medline MeSH; Cinahl CINAHL; Embase Emtree) keywords were exploded. This means that in these databases certain search terms possessed synonyms (e.g. in Medline the so-called MeSH-Terms for decision-making were Choice Behavior, Negotiating, Uncertainty, Consensus, Dissent and Disputes, Avoidance Learning Decision Making). Upon searching for "decision-making" all specific subterms were automatically entered in the search.

(Schmid et al., 2017)

- *Vaccin\* OR Immuni\**
- AND
- *HPV OR human papilloma\**
- AND
- *West Africa\* Or Gambia OR Nigeria OR Benin OR Ghana OR Burkina Faso OR Guinea OR Senegal OR Guinea-Bissau OR Sierra Leone OR Cape Verde OR Liberia OR Mali OR Togo OR Mauritania OR Cote d'Ivoire OR Ivory Coast OR Niger*
- AND
- *Attitude\* OR aware\* OR access OR predictor\* OR factor\* OR determinant\* OR refus\* OR hesitan\* OR accept\**

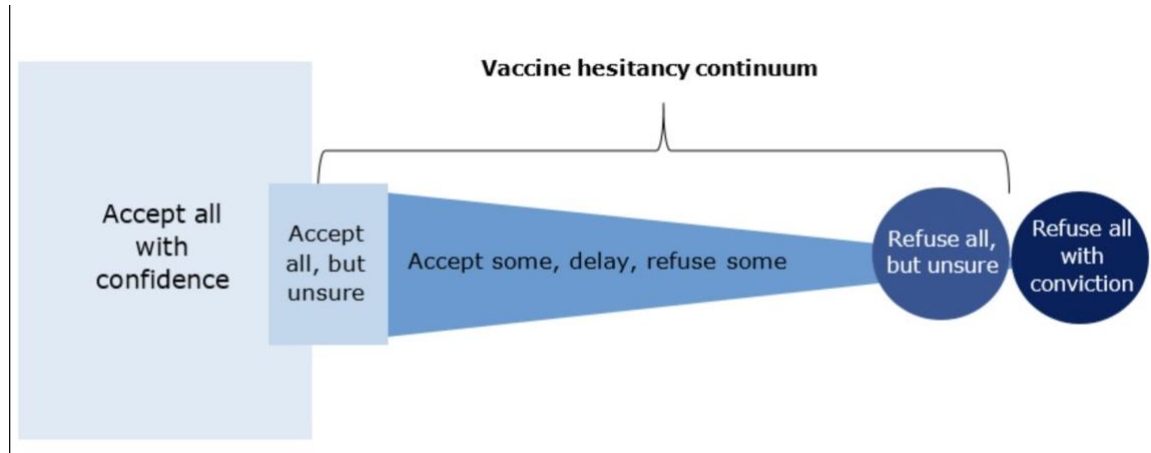
(Wilson., 2021)

## E SAGE Working Group – Determinants Matrix

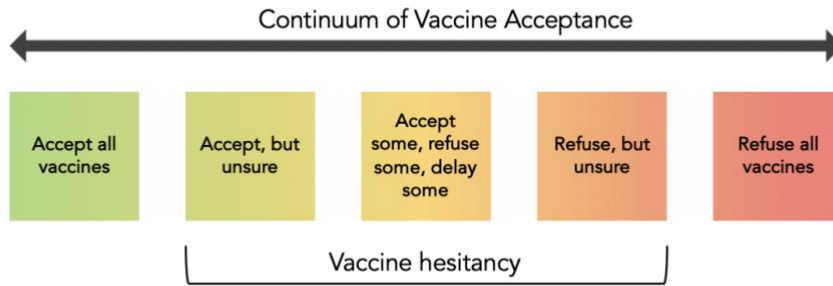


(Larson et al. 2014)

## F Conceptual Models



(Government of Canada, 2021)



*Continuum of Vaccine Acceptance from Johns Hopkins (2020)*