Risk, hope and trust: vaccine confidence and pregnant women

Clarissa Simas Moura

Thesis submitted in accordance with the requirements for the degree of

Doctor of Philosophy

of the

University of London

September 2022

Department of Infectious Disease Epidemiology

Faculty of Epidemiology and Population Health

LONDON SCHOOL OF HYGIENE & TROPICAL MEDICINE

‘No funding received’

(Outside funding received for specific studies in the published papers)

Research group affiliation(s): The Vaccine Confidence Project

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I have read and understood the School's definition of plagiarism and cheating given in the Research Degrees Handbook. I have acknowledged all results and quotations from the published or unpublished work of other people.

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Signed: 

Full name: Clarissa Simas Moura

Date: September 4th, 2022

Acknowledgements

It takes a village, and I'd like to thank mine. First, I'd like to thank Professor Heidi Larson, my mentor and first supervisor, whose unique and ingenious thinking shaped an entire field and fascinated me from day one. Thank you for the learning of a lifetime and for the time to finish this dissertation. I'd also like to thank my second supervisor, Dr Leesa Lin, who was always ready to generously share her wise advice, clarity of thought and unassuming intelligence. Thank you both so much for all your support, friendship, and invaluable input. I will always be grateful and am certain I would not have done this without you.

I'd like to thank my family, in particular my brother Leonardo Simas, and my friends (who all think I know much more than I do). Your love and unwavering faith in what I can achieve is my superpower. Special thanks to Barbara Martinez, who listens when I want to quit but makes sure I keep going; and Fabio Santelli, always lovingly there during dark hours and the climb of many steep mountains, including this one.

I'd also like to acknowledge Dr. Olivier Wouters, whose input pushed this forward in many ways. Thank you for instilling critical thinking and academic rigour, which changed my way of interpreting the world, and for your support during part of my pursue of this PhD.

Finally, I'd like to thank all the women, many of them in dire situations of social vulnerability, who agreed to participate in my studies. Thank you for speaking to me in your homes, hospitals, and research centres, generously sharing experiences and difficulties with trustful openness. It is my hope that more can be done for you which drove all the research I here present.

Abstract

Infectious disease outbreaks can cause severe social disruption and excess mortality while commonly exposing long-standing health inequities and deepening vulnerabilities in populations at risk. For pregnant women, outbreaks, epidemics and pandemics have severe consequences for maternal health, with harrowing effects for infants and mothers-to-be. While optimal immunization is one of the most successful and cost-effective measures to prevent and control infectious disease, vaccination deployment efforts have been hindered by doubtful or refusing publics. In turn, while many diseases can be controlled via immunization, for some diseases there are no vaccines available. In these circumstances, outbreaks can put even more pressure on healthcare systems, leaving populations with incapacitating health consequences. Building confidence in both vaccines and healthcare delivery post-outbreak is an important part of efforts to mitigate the negative health impacts caused by infectious diseases.

In this thesis, I present four qualitative studies and one quantitative study investigating how risk perceptions, hope and trust modulate willingness to accept vaccines and healthcare interventions. First, I investigated how hope and trust influenced the uptake of health interventions in the aftermath of a debilitating Zika outbreak in Brazil. The ability of caregivers to trust healthcare professionals and co-create hope appears to have improved acceptance of recommended treatments for children affected by Zika, despite uncertain outcomes. Second, in a pre-pandemic benchmark study, we mapped trends of vaccine confidence globally, measuring trust in effectiveness and safety of vaccines. This study found important trends in vaccine confidence globally and presented views of safety, effectiveness, and importance of vaccines in 149 countries. In addition, other determinants of vaccine uptake were investigated such as religious compatibility, trust, sociodemographic and information seeking behaviours. Lastly, Brazil, Mexico and Panama were selected for three separate in-depth investigations of views and attitudes towards maternal vaccines. These studies, the first of their kind in the respective countries, explored how attitudes were informed by risk perceptions and multiple dimensions of trust. Results identified important confidence builders among pregnant women, as well as barriers to maternal vaccine uptake which should be accounted for in future policy. My findings contribute to inform strategies and health policy that is sensitive to maternal health and populations affected by outbreaks.

ACRONYMS AND ABBREVIATIONS

CSZ	Congenital Zika Syndrome
COVID-19	Coronavirus Disease 2019
HCP	Healthcare professional
H1N1	Influenza A Virus Subtype H1N1
HIV	Human Immunodeficiency Virus
HPV	Human Papillomavirus
IFF	Fernandes Figueira Institute
Fiocruz	Oswaldo Cruz Foundation
LSHTM	London School of Hygiene & Tropical Medicine
MMR	Measles, Mumps, and Rubella
NPI	Non-Pharmaceutical interventions
SARF	Social Amplification of Risk Framework
UNICEF	United Nations Children's Fund
VCI	Vaccine Confidence Index
VCP	Vaccine Confidence Project
WHO	World Health Organisation
WGM	Wellcome Global Monitor
WIN/GIA	WIN/Gallup International Association

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“Doubt is not a pleasant condition, but certainty is an absurd one”

Voltaire

1. Introduction

While there has been a sharp global decline in deaths attributable to infectious diseases, they continue to account for high morbidity and mortality – particularly in low- and middle- income countries(1). Infectious disease outbreaks can lead to intense social disruption and surplus death, while worsening long-lasting health inequities (2), and intensifying susceptibilities for those at higher risk (3). COVID-19, a prominent case, has overwhelmed most health systems (4) and driven many countries into economic recession (5).

Optimal vaccination coverage within a population can prevent outbreaks and control the spread of infectious diseases. For this reason they are considered one of the most successful and cost-effective public health inventions in history (6), averting epidemics and their multiple negative outcomes (1). Yet in times of global change (i.e. climate, demographics) there is a greater likelihood of the emergence of new pathogens that can spread globally at unprecedented rates (3). Therefore while many diseases can be controlled via immunization, for some – in particular novel viruses - there may be no vaccines available (7). In these circumstances, outbreaks can put even more pressure on healthcare systems, relying on non-pharmaceutical interventions (NPI) and risking debilitating health consequences. Building confidence in healthcare delivery and post-outbreak interventions should be part of larger efforts to mitigate the impacts of infectious disease outbreaks (8). In addition, efforts to build confidence in vaccines and healthcare delivery should aim to reach vulnerable groups, such as pregnant women, who frequently carry the heftiest burden of disease. Pregnancy adds to women's susceptibility to diseases and this groups' particular needs should be addressed in future strategies.

Pregnant women and maternal health in outbreaks

The decrease of maternal and new-born mortality has been a priority worldwide. Infectious disease outbreaks and pandemics can have severe consequences for maternal health, with harrowing effects for infants and pregnant women (9). Evidence from previous epidemics reveal that women are more afflicted than men by negative economic and social effects of infectious disease outbreaks (10). In turn, pregnancy adds to women's vulnerability to negative health effects of disasters and disease (11). The Zika virus outbreak is a notable example of how pregnant women faced significant barriers in the wake of a new pathogen, including inadequate access to healthcare and financial constrains(12).

Globally, maternal immunization programmes have been extremely successful at preventing disease in pregnant women and new-borns (13). Optimal maternal immunization coverage is key for maternal health, and many preventable diseases have been successfully controlled in key regions through immunization (14). Nonetheless concerns about their baby's health and well-being can further amplify apprehensions and attitudes towards maternal vaccines. Barriers to maternal vaccine confidence include rumours (15), issues in access to vaccines (16), and safety concerns (17,18). Strengthening confidence in maternal vaccines is crucial, particularly given women's heightened risk perceptions during pregnancy and intensified information-seeking behaviour, frequently online (7). Yet, views and attitudes in maternal immunization remain understudied in low- and middle- income settings, many of which have high prevalence of infectious diseases.

Confidence in vaccines and healthcare delivery post-outbreak

There are a range of public health strategies aimed at promoting and maintaining health, preventing diseases, and managing existing medical conditions. These efforts encompass a wide spectrum of activities, including but not limited to preventive measures (such as child and maternal immunization programmes); as well as medical treatments and therapies designed to address existing health issues (19).

Despite scientific evidence of safety and efficacy, risk perceptions and trust in vaccines and other public health interventions may vary (20). Even after decades of successful immunisation programs globally, there has been increased scepticism and concerns, impacting acceptance and vaccine confidence (21). Ever since the large-scale introduction of vaccines, there have been sectors of society who have opposed vaccination (22). Vaccine deployment efforts and other outbreak mitigation strategies can be hindered by doubtful or refusing publics (23). Skepticism is not necessarily detrimental to expected public health outcomes. Indeed, a certain amount of skepticism is the basis on which the scientific method itself is constructed. Suspicions and reluctance, however, become problematic when they are disseminated widely to the extent that public health recommendations are subjected to unskilled questioning that challenges and distorts the scientific principles they are founded on (18,19).

Vaccine hesitancy is present in low- and high-income countries alike, with sceptics found in multiple socio, economic, religious, and ethnic groups (26). Hesitancy is both vaccine and

context-specific, varying within countries and groups as well as between vaccines(27,28). Reasons for concerns around vaccines are varied. Determinants of vaccine hesitancy can be contextual (i.e. historic, social, cultural, health systems, or political factors); related to individual and group influences (i.e. personal perceptions or peer influences); or connected to specific issues associated with vaccination (i.e. access to health services, vaccines, and costs associated) (29). Public sentiment around vaccines can fluctuate and confidence in vaccines is known to be volatile: upward and downward trends in confidence can be swayed by virus surges, safety concerns, conflicting information and misinformation around vaccines (30), and contextual factors such as social and political dynamics (31).

Hope, trust, and risk perceptions

There is a multifaceted interaction between risk perceptions, trust and hope within the context of healthcare interventions. Risk perception plays a pivotal role in shaping individual and collective decision-making, particularly in healthcare delivery and the adoption of new medical technologies. The assessment of risk is complex and can diverge from scientific evidence, often influenced by emotional responses, social dynamics, and cultural contexts(32). This is further exacerbated during crises such as vaccine confidence issues or infectious diseases outbreaks, where heightened uncertainty can overshadow rational analysis (33). Understanding how risk perceptions are constructed and communicated becomes essential for effective decision-making and public health interventions.

Perceptions of risk might also be magnified when trust is low. The erosion of trust in experts, institutions, and scientific consensus has introduced new dimensions to the way risks are perceived (34). Trust is critical to acceptance of health interventions, and can make risks appear more manageable, less aversive, in highly uncertain situations(35). The presence of trust, or lack thereof, will guide collaboration needed for adequate healthcare delivery. In turn, hope is intricately entwined with trust. The cultivation of hope in healthcare settings allow trusting relationships to form between healthcare providers and patients(36). Healthcare interventions often necessitate a certain degree of hope, either in terms of the improvement of a given condition or in the protection against diseases. This hope in a prospective future can mobilize healthcare professionals and patients alike, even in the face of daunting risks and uncertainties(37). Preserving space for hope remains profoundly meaningful, as hope emanates from the trust that every conceivable effort will be exerted to enhance one's health (125).

Multiple studies have placed emphasis on pregnant women's trust and confidence in vaccines (17,18,38). Two studies investigated the role of emotions in risk perceptions and trust of maternal immunization among pregnant women (39,40) while another study investigated how emotional regulation can influence decision making around maternal vaccination(41). In turn, the role of hope in the different facets of pregnant women's experience has been studied in other occasions(42–45). However, to the best of my knowledge this is the first study to investigate the intricate dynamics of hope, trust, and risk perceptions and how they will impact acceptance of maternal vaccines and healthcare delivery post-outbreak.

2. Aims and objectives

This thesis examines how risk perceptions, trust, and hope modulate the willingness to accept vaccines and healthcare interventions in outbreak settings. Although maternal immunisation programs and broader healthcare interventions have different strategies, risk perceptions, hope and trust impact acceptance of both. In my thesis I explore these differences and their impact on health outcomes. First, I investigated how hope and trust mediated the uptake of health interventions in the aftermath of a debilitating Zika outbreak in Brazil. My experience with the Zika outbreak in Brazil and its consequences spiked my interest in another important component of outbreak preparedness and response, which is trust and risk perceptions around vaccines. As a result, I co-lead a benchmark study mapping trends of vaccine confidence globally, measuring trust in the safety, effectiveness, and importance of vaccines. This study also measured socio-economic determinants of vaccine confidence as well as religious and ethnic components. Lastly, as the root causes of vaccine hesitancy are context and vaccine specific, Brazil, Mexico and Panama were selected for three separate in-depth investigations of views and attitudes towards maternal vaccines. These studies provide findings that can inform immunisation strategies and health policy aimed at improving maternal and populations health and contribute to preparedness and resilience in the face of disease outbreaks.

2.1. Research questions

Based on my first-authored publications included in my thesis for a PhD by prior publication, the following research questions were investigated:

1) Moving beyond vaccine confidence and investigating the role of emotions in health behaviour: What is the impact of hope and trust in the uptake of health interventions for children affected by Zika?
2) The volatility of risk perceptions and vaccine confidence: What were the global trends and dynamics in vaccine confidence, including safety and efficacy, pre-pandemic?

3) Putting risk and trust in context: How might risk perceptions and trust influence attitudes towards maternal immunization in Mexico, Brazil, and Panama?

2.3 Research aims and tasks

The research questions are addressed via the following five interlinked studies, each with associated methods and findings:

Simas C, Penn-Kekana L, Kuper H et al. (2020). "Hope and trust in times of Zika: the views of caregivers and healthcare workers at the forefront of the epidemic in Brazil." *Health Policy and Planning*, 35(8): 953-961.

Figueiredo A*, **Simas C*** (joint first authors), Karafillakis E, Paterson P, Larson HJ. (2020). "Mapping global trends in vaccine confidence and investigating barriers to vaccine uptake: a large-scale retrospective temporal modelling study." *The Lancet,* 396(10255): 898-908.

Simas C, Paterson P, Lees S, Larson HJ. (2021). " 'From my phone, I could rule the world': Critical engagement with maternal vaccine information, vaccine confidence builders and post-Zika outbreak rumours in Brazil." *Vaccine,* 39(33): *4700-4704.*

Simas C, Larson HJ, Paterson P. (2021). " 'Saint Google, now we have information!': a qualitative study on narratives of trust and attitudes towards maternal vaccination in Mexico City and Toluca." *BMC Public Health,* 21:1170.

Simas C, Larson HJ, Paterson P. (2021). " 'Those who do not vaccinate don't love themselves, or anyone else': a qualitative study of views and attitudes of urban

pregnant women towards maternal immunization in Panama." *BMJ Open*, 11(8) :e044903.

First, in an in-depth qualitative study (46), I investigated how hope and trust facilitated acceptance of healthcare and mediated relationships between healthcare professionals and caregivers of children with debilitating Congenital Zika Syndrome (CZS). In 2015, the World Health Organization (WHO) declared the Zika outbreak in Brazil an international health emergency, with the virus leaving a trail of debilitating consequences in newborns. Congenital Zika Syndrome (CZS) is caused by Zika virus infection during pregnancy and is constituted of an array of diffuse impairments that can affect vision, mobility and cognition(47). In its most extreme, CZS also lead to microcephaly. At the time of the outbreak, not much was known about Zika, and lack of scientific knowledge around the virus and its neurological effects led to great uncertainty(48). The dynamic of contagion was unclear, as well as the extent of damage caused with doubts on life expectancy for children affected as well as extent of damage and impairment. In turn, there was not a clear understanding of the suitability and effectiveness of different treatments proposed. Thus, in the absence of more definite evidence, caregivers and healthcare professionals grappled to identify appropriate care regimens, as well as reliable information and support. Moreover, Zika arrived at a time of social unrest in Brazil, with mass protests emerging due to wavering trust in government and institutions. In addition, long standing inequalities were further exacerbated by Zika, as the group most affected were women of color living in low resource neighborhoods where the mosquito and vector of disease proliferated. Moreover, the continuing social, economic, and political shortcomings in Brazil appeared to be an obstacle for optimal provision of social support and healthcare services that could address the needs of families affected (49).

My study explored the ways in which hope and trust mediated healthcare interactions, relationships, and cooperation between two groups at the forefront of the Zika epidemic: the caregivers of children with CZS and healthcare workers attending to them. The research investigated their trust in public institutions, in the Brazilian health system and government as they were relevant for interactions with healthcare within a wider social context of epidemic.

Second, in a large-scale global study(50), we mapped vaccine confidence across 149 countries between 2015 and 2019. This was a benchmark study and an ecological analyses(51) which deployed the Vaccine Confidence Index (VCI) to explore perceptions of safety, effectiveness and importance of vaccines, and compatibility with religious beliefs. (20) In addition, socio-

economic status and sources of trust were also surveyed. The use of a common metric to quantify confidence, the VCI, allowed for cross-country comparisons of vaccine perceptions. Wavering confidence in immunization has contributed to lower uptake of vaccination globally, leaving entire populations vulnerable to outbreaks of preventable diseases (52–54). This study elucidates ways in which risk perceptions and trust can influence acceptance of vaccines and ultimately impact disease outbreaks.

Reasons for low confidence in vaccines and consequent vaccine hesitancy are often context and vaccine specific (55). While quantification and measurement of vaccine confidence levels provides invaluable information and early signals of changing confidence, in-depth investigations through qualitative research will provide a nuanced understanding of the root causes of distrust and precise drivers of confidence in each setting and of a specific type or set of vaccines. Therefore Brazil(56), Mexico(57), and Panama(58) were selected for three separate in-depth investigations of views and attitudes towards maternal vaccines, to get a more nuanced understanding of drivers of vaccine confidence and acceptance. The three countries were chosen for reasons which allowed comparison of findings: they have all been affected by Zika outbreaks; have previously invested in in national strategies to improve maternal health within its populations (including mass roll out of maternal vaccination); and for their regional and geographical proximity.

While there is a growing body of literature about predictors of maternal immunization globally, this had remained understudied particularly in low- and middle-income countries (59,60). These studies explored, in six different cities (two cities per country), the local confidence builders and barriers to maternal immunization. These studies, each being the first of their type in these respective countries, are in-depth qualitative investigations that provide a thorough and comprehensive analyses into the complex ways maternal vaccine decision making is informed by local perceptions of risk (i.e., risk of vaccines vs risk of disease) and multiple dimensions of trust (i.e., in government, in medical sources, in online information, in family members). The three countries have very different health systems structures as well as social and political configurations. Findings of these investigations contribute to a better understanding of key drivers and barriers of maternal vaccination.

In Brazil (56), a robust National Immunization programme meant that for decades, pregnant women have been offered immunization during their gestational period and beyond. Brazil's

strong health reform that took place in the 70's meant vaccines were widely used and distributed. Yet, despite its successful immunization programmes, uptake of maternal vaccines has varied (61,62). In addition, the emergence of new infectious diseases such as Zika, which directly and severely impacted infants in Brazil, have also affected women's sensitivities to risk and their vulnerability. This study aimed to identify barriers and enablers of maternal immunization in Brazil. Participants were encouraged to discuss their perceptions of the safety, efficacy and importance of vaccines, access to them, exchanges with healthcare professionals, influencers on their decision to vaccinate and their sources of vaccine-related information.

Alongside Brazil and other Latin American countries, Mexico(57) also underwent a healthcare reform aimed at improving access particularly to lower-income populations, which led to the creation of a popular health insurance – or *seguro popular*. Through this popular health insurance, Mexico partially restructured its health systems to provide free pre-natal care and expand maternal immunization services in an attempt to reduce maternal and neonate mortality(63). While there are various reports on this attempt to reduce maternal mortality (64), not much was known about confidence in maternal vaccines among pregnant women in Mexico (65). The study aimed to explore trust, attitudes, and views towards maternal immunization among pregnant Mexican women. We explored their experiences with maternal immunization, and their experience navigating the health systems (both public and private), their information searching habits and influencers in their decision whether or not to vaccinate.

Panama was the last chosen setting for an in-depth investigation(58). Panama, a high income Latin American country, has one of the best immunization programs of the region and estimates that 90% of its population has access to healthcare (66). Panama currently has one of the best immunization programs available in Latin America, and currently offers all recommended vaccines to pregnant women. While there have been qualitative investigations of overall vaccine acceptance in Panama (67,68), not much was known about drivers and possible barriers to maternal vaccination. This study surveyed pregnant women's views and attitudes towards maternal vaccines, exploring their interactions with services, with healthcare professionals, with information (medical and non-medical) and influence of family members and social networks.

3. Core themes

3.1 Uncertainty and health decision-making

Some degree of uncertainty is a feature of all medical technologies and public health interventions (69). While firmly grounded in the best scientific evidence available, vaccines and many other healthcare interventions have risks, albeit minor compared to the vast health benefits. Additionally, much can remain unclear during infectious disease outbreaks: modes of transmission, how to prevent the spread, and whether it will fade or turn into an epidemic or pandemic (70). Besides epidemiological uncertainties, there are information uncertainties (how to identify reliable information and sources), social uncertainties (or how a community and population will act in face of heightened risk) and economic uncertainties, associated with financial insecurities that can come with disease outbreaks (71). All these uncertainties experience by populations affected by outbreaks can influence their willingness to comply with guidelines issued by government and public health officials (71).

Uncertainty can be understood as a dynamic state in which the decision-maker's knowledge of outcomes is unclear, and the perception of one's reduced ability to predict results prompts a discomforting, uneasy sensation (71,72). There are ongoing debates in the literature over how experiencing uncertainty can impact health outcomes(21,69,70,72,73). In the context of ill health and hospitalization, uncertainties about symptoms and outcomes were an indicator of higher stress and anxiety levels (74). Another study showed that lower tolerance to uncertainty was closely associated with decreased willingness to vaccinate (75) and high uncertainty-intolerance during the H1N1 pandemic was linked to increased anxiety and stress (76). In contrast, higher levels of hope have been associated with lower levels of experienced uncertainty among breast cancer survivors (77). As for infectious diseases, higher levels of hope have been protective against anxiety (78) and improved life satisfaction (79) during the COVID-19 outbreak. Hope has also been linked to patients adherence to tuberculosis treatment (80) and to successful support given by midwives to mothers living with HIV (81).

The feeling of uncertainty can be either reduced or escalated by different emotional, cognitive or behavioral reactions – or either by passing of time or change of circumstances (72). When uncertainty cannot be eliminated, the relationship between present action and future outcome gains hold as we anticipate, expect, and speculate about the future (37). It is in the space of yet to come, composed of uncertainties, hopes and fears, that decisions about preventive (vaccines) and curative (health interventions) will take place(37). The act of imagining the future means

to orient one's present actions and decisions, individually and collectively, towards an unknown, uncertain future(37). To anticipate what is to come is to imagine scenarios of an unknown future – in the hope of shaping the future with present action. Anticipation can relieve the anxiety of uncertainty, giving a sense of what should be done. When faced with decision-making regarding one's health, ways that risks and benefits are anticipated might shape decisions and outcomes(37).

Anticipation can also drive a collective response to a sense of danger. To anticipate means to forecast a future based not only on available information, but affective connections to past and future. These anticipatory responses play out into a collective future, one in which negative outcomes can befall a group or community(37). For example, in the case of clinical settings and minorities, negative past experiences with health services could lead to collective anticipation of exclusion from healthcare and collective anticipation that any public health measures would not be truly aimed at improving their community well-being (82,83).

3.2 Risk perceptions and new medical technologies

Risk can be anticipated in different ways and, at times, individual and collective perceptions of risk will not align with available scientific evidence of risk (84).When faced with the risks of engaging with new medical technologies, interpretations of benefits of vaccines and other healthcare interventions outweighing potential harm can waver. In the case of vaccines, although misinformation and rumours can deceive publics and raise concerns, frequently these emotions come from the knowledge that vaccines have risks, even if minor compared to the enormous health benefits. (85). Health risk perceptions, or how an individual or a community perceive and define a health threat, will have a direct impact in health decision-making and consequent outcomes (86). This is heightened in outbreak settings as perceptions of risk can be impacted by emergency outbreak response (15). Pregnant women may be especially prone to emotional distress and heightened risk perceptions during outbreaks and pandemics (87). Anxieties about getting infected (88,89) are compounded with worries about prophylaxis (including vaccines) (88,90,91), disruptions in healthcare services (87), and interference in post and pre-natal care (89). Moreover, pregnant women are more intensely impacted by feelings of uncertainty (89,90,92) and other negative emotional states such as fear, helplessness, uneasiness (88,92).

There are at least three main theoretical perspectives in which risk can be understood and that will drive the conceptualization of risk in my thesis. First, a psychological approach will define emotional and cognitive process will play a role in the formation of risk perceptions, which in turn influence how information is acquired and judgement and assessment of risk for decision making (32,93). Second, the cultural theory of risk in Sociology and Anthropology presumes risk perceptions are determined by an individual's and community's social settings. This perspective considers how socio-cultural context will shape both perceptions of risk and benefits (85,94,95). Finally, among multidisciplinary models the Social Amplification of Risk Framework (SARF) brings together objective assessment of risk with psychological, sociological and cultural perspectives – which, in turn, interact with social and individual components(33).

Emotional and cognitive appraisal of risk: risk as feelings vs. risk as analyses

Slovic et al.(32) highlight two key modes that risk is assessed, one cognitive and one emotional. Risk as analyses refers to a rational, logic evaluation of risk (i.e. taking in consideration all scientific evidence of vaccine safety). This system is normative, relies heavily on rules and rational processes – and therefore is slower, takes more effort and requires conscious control. Risk as feelings refers to a much quicker, intuitive, and emotional response to risk. This experiential system is intuitive, fast, and mostly not available to consciousness. This system relies on images and associations, linked by experience to emotion and affect (a feeling that something is either good or bad). The rational and the experiential system operate in parallel, and each seem to depend on the other for guidance, in a complex interplay between rationality and emotion.

While visceral emotions such as fear certainly play a role within risk as feelings, affect (or a faint whisper of emotion) is what give positive or negative connotations to a stimulus or a situation(32). Affective responses occur quickly, are often the first reactive reaction to stimuli and have implications for how risk is perceived and evaluated, consequently affecting decision making (96). In some circumstances, risk as feelings can outperform risk as analyses (i.e. terrorist threats, crises of vaccine confidence). Events associated with strong feelings can overwhelm us, even in the cases where their likelihood is remote (97). In turn, in times of crises such as illness and outbreaks, anxiety can seep in as imagine futures become blurry and uncertain. Crises of confidence in vaccines have been driven by intense reporting of adverse reactions following immunization. Notable examples are the Dengvaxia vaccine crises in the

Philippines (98), Human Papillomavirus (HPV) vaccine adverse events in Colombia (99), and reported AstraZeneca COVID-19 vaccine risks (100), all circumstances where heightened anxiety eclipsed rational thinking on how the risk of taking a vaccine might be lesser than the risk of vulnerability to disease. Additionally, unknown threats posed by new and emerging infectious disease such as Zika, Ebola and COVID-19, have also demonstrated how heightened uncertainty might lead to an emotional overdrive during risk analyses and refusal of important public health guidelines(101). All these have shown the subjective nature of risk perceptions, and for this reason risk management can be increasingly polarizing and contentious(102).

Socio-cultural construction of risk

Besides cognitive and emotional processes, risk perceptions are also shaped by social dynamics. Slovic (102) argued that whereas danger is real and some fears are physical, risk is socially created. Over the years, different studies have considered the social construction of risk (94,103,104). This approach primarily considers how different systems of knowledge influence individual assessments (15,105). Giddens (95) argued that a society increasingly preoccupied with the future and its safety is one that generates the notion of risk, coining the term *risk society* to describe how modern society attempts to identify and eliminate all risks. The term risk no longer carries its original neutral meaning of statistical probabilities of occurrence of an event, which could be positive or negative. Risk has come to mean danger, or the probability of harm – and any risk is now perceived as negative (85,106).

As a perception of risk or threat is a social process, there are no value-free processes for identifying and responding to risk. What is assessed as risky or potentially harmful depends on the attitudes, values, and beliefs that are considered (85). This, in turn, creates narratives of which risks are acceptable and which are not (107).Therefore people's objections to perceived hazards should not be taken at face value and one must look further to discover what forms of social and political organization are regulating risk perceptions (85). In fact, perhaps physical fears would not menace individuals of a society if they felt confident of justice and social support(85). Past collective experiences of a group, such as dignity denying experiences or historic marginalization, will inevitably lead to different perceptions of what is a risk and what is not. In fact, historical analyses of vaccination views in 19th century England has shown how vaccine debates were closely linked to wider social and political issues (108).

Beck (94) argued that in a risk society era there appears to be increasing public distrust in expert systems as well as corporations, scientific institutions and government (109). The nature of dangers has changed in modern times as major threats to societies are no longer solely in the form of natural hazards. Instead, technological advances brought with them technological and scientific hazards (i.e., pollution, contamination). Concurrently, there is a loss of trust in experts and science's ability to predict and protect people from these hazards. Risks and uncertainties are rife and, concurrently, there is increased erosion of expert consensus and competing knowledge claims of how to best prevent hazards (110). In fact, for every medical technology developed, there is a risk of either harm associated or of innocuous effect. When making a health-related decision, the challenge becomes how to choose the best, safest, most effective course of treatment or prevention in face of eroding trust in institutions, in government, in science.

Narratives and discourses around risk also emerge within public health. In the case of vaccines, risk discourses can shift accountability for low uptake to publics, transferring responsibilities and deflecting political realities that fuel fraught relations between publics, governments, and healthcare providers (111). Therefore risk can also be defined as moral danger when structural determinants of acceptance of health interventions and vaccines are ignored and refusing or hesitant publics are blamed for undesired public health outcomes is placed on (106). In sum, cultural, social and political dimensions of risk perceptions must be central to how we comprehend public attitudes to health interventions from both patients and health officials (15).

Social amplification of risk

Erosion of trust in experts can lead to a mismatch between how risk is considered by experts versus how public assesses the same risk (94). Likewise, social amplification of risk can also lead to differences between experts and laypeople perceptions of nature and seriousness of a risk. The social amplification of risk framework postulates that perceived hazards will interact with psychological, institutional, social, and cultural processes in ways that might amplify or attenuate responses to risk (33,34). Signals about risk, in turn, are processed by individual and social amplification stations: news media, social media, cultural groups, interpersonal networks and even scientists who communicate risks(33). Therefore, risks are amplified or attenuated through these social amplification stations, ranging from individuals to the media. Social amplification can happen in two stages: during initial acquisition of new information and response mechanisms in a group (84). This means that, at times, relatively minor risks or events

can be amplified and elicit substantial impacts in society (84). In fact, previous studies of media coverage around COVID-19 have indicated that media coverage of a particular public health risk (i.e. adverse reactions of a vaccine) can introduce specific attributes to risk which will influence public perceptions and become a forming factor of how risk is viewed (84,112). This is particularly troublesome if message amplified is based on rumours and misinformation. Social media and digital technologies are also key social amplification stations, ones that are particularly responsible for the viral spread of rumours and misinformation, many times increasing risks perceptions over false claims.

3.3 Rumours and health misinformation

Rumours and misinformation also play a part in social amplification of risk. Rumours have been recognized as a health risk to societies and different surveillance systems are in place(113). Rumours are, by definition, unverified pieces of information that are shared withing a group and can be understood as a collective problem solving as people attempt to navigate risk and uncertainties around them (114). In the context of heightened uncertainty of outcomes and information, rumours can flourish as a social attempt to make sense of ambiguity. They can be especially rife in situations where a community or population feel that important decisions impacting their lives are not in their control. In that respect, rumours commonly reflect collective and subjective emotional states and managing rumors should be about understanding emotions that lead to them rather than judgment if they are true or false (115). At times, rumours are depoliticized and taken out of their social context, being discussed solely as an information error(116). Rather, rumours can hibernate and tend to resurface in fertile ground - or in social contexts where broader anxieties about public health interventions are conveyed via rumours(117).

Health misinformation

Health misinformation has been identified as a health risk of pandemic proportions (118). In fact, the World Health Organization (WHO) stated that, alongside the COVID-19 pandemic, it was also battling and 'infodemic'- which has been defined as an excess of information from multiple sources, online and offline (119). Recent studies have been investigating how online misinformation around vaccines might be negatively influencing willingness to vaccinate, with indication of lower intent to vaccinate following exposure (120,121). Consequently, social media companies have come under intense scrutiny and public demand for tighter regulation on online misinformation(21). These companies have subsequently taken action to address or

eliminate denialist speeches from its platforms. However, removal of vaccine misinformation, while a laudable attempt, implies that vaccine hesitancy remains an informational issue, instead of a trust problem(122).

While the importance of health literacy has been acknowledged (123), dominant views focused on debunking misinformation can obscure how concerns and resistance are in fact an indicative of broader mistrust and anxieties(111). Thus, an informational approach runs the risk of depoliticizing rumours and misinformation, placing public ignorance as the key problem to be combated (111). In fact, exposing misinformation will not be enough to change people's mind about vaccines and public health measures as how information is processed is dependent on political, cultural and social values (122).

Undoubtedly social media can be a source of vaccine misinformation, negatively impact decision making as per findings from Panama and Mexico. However while there have been anxieties within public global health regarding heightened health information seeking behaviour, mostly in the context of ongoing online misinformation, findings point that this can be an important element of an informed health decision-making. At the same time, the focus on strengthening moderation of misinformation on platforms often overlooks the role of the individual who is actively engaging with the information, synthesizing information harvested online. How the publics engage with vaccine information has changed considerably in the currently online informational ecosystem(124). Online platforms facilitate a move from the previous reliance on healthcare professionals and traditional broadcast media for information(125). Instead, information about vaccination is readily available, from different online sources, empowering users through immediate, easy access to a wide range of information (126,127). In the case of maternal vaccines, heightened information seeking behavior, especially online, during pregnancy has been a point of concern in public health regarding exposure to misinformation (128,129). However, information gathered will interact with existing beliefs, perceptions and attitudes – as well as trust and mistrust.

3.4 Trust in the context of vaccine acceptance and healthcare delivery

Trust is a key element of human relations, and is central for healthcare systems, which are ultimately relational systems (35). Trust can make risks appear more manageable and less aversive, particularly in highly uncertain situations like disease outbreaks where outcomes are unclear. Trust is based on premises about how another party will act and this anticipation, in

turn, determines whether one is willing to accept the risk and become vulnerable to another person's (or institutional) guidance. To trust is an active choice, a leap of faith (130) taken in times of uncertainty, and one that assumes the trusted party has the trusting individual's best interest at heart (131). The presence of trust, or lack thereof, will likely guide mutual collaboration needed for adequate healthcare provision as well as vaccine uptake. On the other hand, perceptions of risk might be amplified when trust is low.

The significance of trust in patient–provider relationships for healthcare has been acknowledged in the health literature (132). Yet trust is multidimensional, going beyond individual dynamics among healthcare professionals and patients. Trust in both vaccines and healthcare provision is the outcome of a complex interplay of multiple levers of trust. For instance, trust individuals place or not in a system (i.e. political system, health system) is as decisive for establishing the collaboration needed for healthcare delivery. Mistrust in vaccines and health interventions can reflect trust and mistrust in wider social structures, institutions, and actors.

For my thesis, my conceptualization of trust will focus on the following key dimensions of trust as they pertain to vaccines and health interventions: generalized trust (35,133), historical influences on trust (83,134), political/government trust (82), trust in health systems (35), trust in information (131), networks of trust (133) trust in product (i.e. safety and efficacy of vaccines)(54), trust in provider (i.e. healthcare professional) (135), and external levers of trust (131).

Generalised trust is defined as an individual readiness to trust other members of society, particularly in face of a collective problem (35,131,133). This dimension of trust is understood to play a critical part in information streams from health authorities and policy makers to the wider population (35,133). In turn, political or government trust is based on a judgement of trustworthiness of political actors and a government. In circumstances where government and politicians are recognised as trustworthy, populations might be more inclined to comply with recommendations, guidelines and policy (82). This can be another driver of acceptance of health measures in the context of outbreak response when aversive public health measures might be necessary and could potentially be resisted.

Historical interactions with institutions and its actors will also influence trust levels. This is particularly true in case of historical legacies of unfair treatment and exclusion of populations by health and government officials. This can lead to mistrust in healthcare professionals and health systems (83,134). In fact, the lowest levels of trust have been identified among ethnic and religious minorities, which are more frequently stigmatised and consequently marginalised (136,137). Trust in health systems might also be impacted by previous access to those. A health system's past performance will also have an influence on trust building with a given community, especially in cases of historical provision of lower quality and previous exclusion of populations (83,134). The multiple stories of trust and mistrust in institutions based in previous experiences mean that public trust in immunization and respective programs is highly changeable and regionally specific.

Trust in information is another critical lever to healthcare delivery and vaccine uptake. Trust in information is dependent on the belief that the source of the information is trustworthy(131). In addition, trust in information about vaccines depends not only on the trust of information itself, but also the trust in the source of that information. To that end, we considered trust in information as nested within the trust held in the source of that information (131).

Consequently, flow of information and mutual cooperation is strengthened within networks of trust(133), formed when there is enough social capital and mutual trust among members of a group involved in healthcare delivery (medical or non-medical). Concurrently, non-medical sources can be trusted for health information. Notable examples are social circles such as family, friends, religious groups. These can be external influences on trust, all of which can have repercussions for health decision making and outcomes(131).

In the context of vaccine decisions, trust becomes important in helping to make a risk/benefit assessment (131). Besides trust in the wider healthcare system and institutions, essential influencers in the decision to vaccinate are trust in the efficacy and safety of immunization and trust in the healthcare professionals who administer and recommend the vaccine (54,135). In fact, when faced with a decision to vaccinate parents have placed their trust in proximal sources such as doctors rather than more distant ones such as health authorities(138,139); and a key driver of maternal vaccination globally is the recommendation of immunization by a healthcare professional(17,18). Recognizing trust as a complex web of vaccine-related factors can provide valuable insights into the levers of vaccine acceptance, hesitancy or refusal [20].

3.5 Hope and potentiality in clinical settings

Trust is thus a key component of human interactions, and its presence or absence will directly influence reciprocity, cooperation, and optimal communication – and consequently a key driver for healthcare delivery. However much less attention has been given to the role of hope, albeit it is the ability to hope which enable's one capacity to trust (140). Hope is the assessment individuals make of their circumstances and what they can expect for their future (141). To hope is to orient oneself towards a future that is uncertain but desired, and a way of placing present action anticipating expected results (37).

The concept of potentiality is an important aspect of hope. To imagine or see potential is to reflect and consider what does not presently exist – and might never do (142). Nonetheless, potentiality offers a door to change, and a possibility of a different future (37). Potentiality, therefore, can be seen as available for nurturing and direction by individuals, opening the possibility for creation of different realities. The hope for a potential future can fuel present action towards a goal, pushing potential into reality (37). To that end, potentiality can be comprehended as an associate to hope (142).

Medical interventions require a certain amount of hope either in the improvement of a given condition, or protection and prevention against a disease. Hope in a possible future can mobilize healthcare professionals and patients, even with risks and uncertainty – although it requires a trusting relationship between both parts. Even in face of a difficult diagnosis, allowing room for hope is meaningful: hope will result from form the trust that everything possible will be done to improve one's health and condition. Ultimately, hope becomes the crossroad between what is possible and what is probable (141).

However, while hope offer the possibility of a healthier life in face of adversity, what happens when potentiality becomes *impotentia,* or void of potential?(37) Or when the potential of a vaccine is taken over by reports of serious side effects and crises of confidence? Or when a much-anticipated medical treatment is proven ineffective? To hope is also to be reminded of what might not be (i.e. treatment offering no cure) and what might also never be possible (36). This paradox adds to the emotional burden of healthcare professionals as responsibility falls upon them to just give the right amount of hope. How can they support patients finding hope in the absence of cure (36,143,144). Studies have discussed the despair and disruption to

treatment led by lack of hope among patients and their families (145–147). For pregnant women, the threat of loss in face of infectious diseases is compounded by their need to protect their unborn babies(87). Examples from the literature cite feelings of helplessness, responsibility, perceived loss of control and even disengagement even with preventive measures (87,88,90,92). Hope ultimately should be encouraged in a way that is tolerable, despite its abstract promises, and one which can be supported in clinical settings – particularly settings where expensive or even satisfactory care might not be available.

4. Methods

I briefly summarise below the methodology used in each study composing this PhD by prior publication project. I present a short overview of the research approach used in all studies, including sampling, recruitment, and ethics approval.

1.2. **Simas C**, Penn-Kekana L, Kuper H et al. (2020). "Hope and trust in times of Zika: the views of caregivers and healthcare workers at the forefront of the epidemic in Brazil." *Health Policy and Planning,* 35(8): 953-961.

This qualitative study was comprised of ethnographic observation in different spaces in which care and treatment of compromised children took place (hospitals, medical appointments with healthcare professionals, homes of families of children with CZS) and 76 in-depth interviews with caregivers of children with CZS and healthcare workers supporting the long-term care of affected children. Interviews and ethnographic observations were conducted in Recife, Jaboatão dos Guararapes (both cities considered as the epicentres of the outbreak), and Rio de Janeiro, also heavily affected by Zika. In Recife, participants were interviewed at their homes. In Rio de Janeiro, for security reasons participants were interviewed at a reference hospital, the Fernandes Figueira Institute (IFF/Fiocruz). This introduced the possibility of bias as participants interviewed within the hospital setting could be hesitant to openly discuss quality of the care received. Measures were taken to mitigate this, including providing a secluded and confidential space for conducting interviews and reassuring participants that researchers conducting interviews were distinct from the healthcare team. All interviews were digitally recorded, transcribed in Portuguese and later translated into English. To ensure confidentiality, all data were anonymized, and any identifiers were removed. NVivo 11 software (QSR International, Melbourne, Australia) was used to carry a deductive thematic analysis. This

analysis followed a deductive approach guided by the existing literature we reviewed. The interviews were coded according to multiple dimensions of trust. Findings were structured under the two key themes of hope and trust to develop a theory of ways clinical interactions between caregivers and healthcare workers were enabled by these concepts. This study received approval from Research Ethics Committees of the authors' institutes after following all recommended ethical protocols.

1.3. Figueiredo A*, **Simas C*** (joint first authors), Karafillakis E, Paterson P, Larson HJ. (2020). "Mapping global trends in vaccine confidence and investigating barriers to vaccine uptake: a large-scale retrospective temporal modelling study." *The Lancet*, 396(10255): 898-908.

For this sizeable study, we used new and existing VCI surveys datasets totaling nearly 300 000 individuals from 149 countries, looking into confidence in light of socioeconomic factors and levers of trust. One country (Philippines) was surveyed on six separate occasions, while 13 countries were surveyed four times, 28 countries three times, 40 countries twice, and 67 countries only once.Individuals were surveyed for vaccine confidence, through survey statements of their perception on importance, safety and effectiveness of vaccines. Responses were asked on a Likert scale between "strongly agree" to "strongly disagree". In addition, out of the 290 surveys in this study dataset, 144 were collected as part of the 2018 Wellcome Global Monitor (WGM)(148). Besides investigating perceptions of safety, effectiveness and importance of immunization, respondents were questioned on their sources of trust, how they harvested information, and if they had vaccinated their children, if any. In addition, data on demographics (sex, age, and religious beliefs) and socioeconomic status (income and education, including science education) was extracted from the WGM surveys to identify possible barriers to vaccine uptake. Bayesian logistic regression was deployed to investigate the link, in each of the countries surveyed, between vaccine uptake and confidence, trusted sources, information-seeking behaviour, demographics and socioeconomic status. This provided insights into trends around determinants of vaccine uptake across the globe.Vaccine confidence is a critical determinant of vaccine uptake(53). A high level of confidence in trust and safety of vaccines can positively influence vaccine acceptance. Conversely, low confidence in safety of vaccines can contribute to lower uptake rates(20). To the best of my knowledge, this is the largest

global study conducted to date on vaccine confidence, with multiple waves of comparable questions over time. While imperfect, the choice of countries and nationally representative sampling aims to capture as comprehensive picture as possible. Moreover, our recent further update pre- and post-COVID-19 vaccine confidence was published in the 2023 UNICEF State of the World's Children report (149), reflecting the fact that it is being recognized as a reliable measure. While the sample of countries is sizeable and regionally diverse to minimize potential bias, future studies of this magnitude should aim to include countries not yet surveyed.

1.4. **Simas C**, Paterson P, Lees S, Larson HJ**.** (2021). " 'From my phone, I could rule the world': Critical engagement with maternal vaccine information, vaccine confidence builders and post-Zika outbreak rumours in Brazil." *Vaccine,* 39(33): *4700-4704.*

In Brazil, four focus groups (two per location) and twenty in-depth interviews (ten per location) were conducted with pregnant women living in São Paulo (n=30) and Rio de Janeiro (n=30), key urban centers in Brazil. A grounded theory was developed of views and decision-making process of pregnant women. For recruitment, one question was asked to screen participants, assessing their overall willingness to vaccinate when recommended by a healthcare professional (HCP). This was done to purposively sample women with both negative and positive attitudes towards maternal vaccination, aiming to have a balanced sample. We collaborated with WIN-Gallup International Association (WIN/GIA), a well-established global research organization to gain access to a group of participants and purposively recruit pregnant women in Brazil. Furthermore, a trained recruiter went to maternal hospitals, private clinics, healthcare centres offering antenatal care, and other hospitals in both Rio and Sao Paulo to purposively enlist more participants. There was no requirement for an additional chain or snowballing recruitment method. Data were analysed to establish a grounded theory of the attitudes and decision-making towards maternal immunization in Brazil. Findings were organised and coded under themes which emerged when pregnant women were interviewed about different aspects of maternal immunization.

1.5. **Simas C**, Larson HJ, Paterson P**.** (2021). " 'Saint Google, now we have information!': a qualitative study on narratives of trust and attitudes towards maternal vaccination in Mexico City and Toluca." *BMC Public Health,* 21:1170.

Data collection was conducted in Mexico City and Toluca and fifty-four pregnant women at different stages of their pregnancy participated. There were two focus groups per city with eight to ten women each and ten in-depth interviews per location. We partnered with WIN/GIA to recruit pregnant women and collect data in Mexico. We employed purposive sampling to select participants with both positive and negative attitudes toward maternal vaccination, ensuring diversity in terms of age and socioeconomic status. WIN/GIA coordinated with its Mexican subsidiaries to gain access to a pool of potential participants, from which pregnant women were chosen. During screening, participants rated their willingness to follow a doctor's vaccine recommendation on a 1 to 10 scale. Participants were purposively sampled according to their views on maternal vaccination (including both positive and negative), and various ages and socioeconomic status to ensure diversity.

1.6. Study 5: **Simas C**, Larson HJ, Paterson P. (2021). " 'Those who do not vaccinate don't love themselves, or anyone else': a qualitative study of views and attitudes of urban pregnant women towards maternal immunization in Panama." *BMJ Open*, 11(8) :e044903.

Our study surveyed fifty-six pregnant women to investigate views and attitudes towards maternal vaccines. Four focus groups (eight to ten women by group) were conducted and twenty in-depth interviews. In-depth interviews explored individual perceptions and allowed exploration of sensitive topics, while groups investigated shared representations and how different perceptions of maternal vaccines were negotiated among peers. All recruitment was conducted in person. In both Panama City and San Miguelito, a recruiter visited hospitals, healthcare centres offering antenatal care, private clinics, and maternity hospitals to purposively recruit participants. We did not employ a chain or snowballing recruitment approach. For a diverse sample of vaccine attitudes, we assessed participants' willingness to take doctor-recommended vaccines on a 1-10 scale during screening, ensuring a diverse mix of responses in our selection.

Study location selection in Brazil, Mexico, and Panama

We chose study locations in Brazil, Mexico, and Panama based on high population density, diversity, availability of healthcare services and maternal care. Due to recruitment challenges, time constraints, and budget limitations, remote areas were excluded. Populations more distant

from urban centres are likely to have limited access to healthcare and different perceptions. This may introduce bias, impacting maternal vaccine confidence, as later discussed in this thesis and my published work.

Data management and ethics approval in Brazil, Mexico, and Panama

We received approval to conduct secondary data analysis from the London School of Hygiene & Tropical Medicine ethics committee in May 2019 (LSHTM ethics ref.: 17100). For primary data collection, standard industry verbal and written consent was obtained by WIN/GIA. Confidentiality and anonymity were maintained by keeping all data anonymous and excluding any information that could be traced back to participants. All transcripts were stored on secure servers to which only co-investigators cited in ethics approval had access to. All data were analysed using NVivo 11 software (QSR International, Melbourne, Australia).

Deductive approach to data analyses in Mexico and Panama

In both Panama and Mexico a deductive approach was used to develop an initial coding scheme based on research objectives and interviews guides. The initial coding structure was tested on a few transcripts and through an inductive process, and extra codes were derived from deeper interpretation of data and analytical notes. Findings were organised and coded under themes which emerged when pregnant women were interviewed about different aspects of maternal immunization.

5. Main findings

The main findings of the five studies have been organized under three key topics: 1) Hope and trust mediating acceptance of healthcare delivery post-outbreak; 2) Global risk perceptions of vaccine safety, importance and efficacy of vaccines; and 3) Trust, risk perceptions and maternal vaccine confidence in Brazil, Panama, and Mexico.

5.2 . Hope and trust mediating acceptance of healthcare delivery post-outbreak

The Zika epidemic in Brazil cast a shadow of uncertainty on the future of caregivers and children who had been affected by the virus. Treatment of children with CZS usually consisted of heavy routines that include multiple medical appointments, intensive and repetitive

physiotherapy schedules and challenges finding the appropriate medication. In addition, the wide spectrum of CZS impairment makes it difficult to find the most suitable regimen. The lack or existence of hope and trust, in different forms, had significant implications for caregivers' personal investment to treatment and information flow. In consequence, despite individual losses and uncertainty of results, most caregivers remained engaged in arduous care routines, invested in the potential of a less incapacitating future for their children.

Hope enabling generalized trust between caregivers and healthcare workers

The ability to trust and co-create hope between caregivers and healthcare professionals (HCP) may have boosted the acceptance of therapeutic regimens aimed at treating Congenital Zika Syndrome (CSZ). When trust and hope were present in the relationship between caregivers and healthcare professionals, most of the negative emotional and social impacts of CZS appear to have been lessened due to a more open exchange of information, including sharing of emotions and feelings. When hope for their child's recovery was shared, caregivers trusted healthcare workers recommendations even after professionals admitted uncertainty about the outcomes of prescribed interventions.

The healthcare professionals' openness and honesty with caregivers about uncertainty of outcomes, while partaking in their hopes for better futures, helped sustain the 'leap of faith' needed for trust. Caregivers increasingly trusted healthcare professionals who shared their belief in a better future for them and their children – offering hope even in the absence of certainty. Those encounters left a positive impression on caregivers; they were presented with other possibilities opening a potentially different future. Here, the potentiality brought by the idea of other future, allowed hope to grow. In turn, caregivers appeared more enthusiastic and committed to the intense care routine.

Absence of hope and eroding generalized trust between caregivers and healthcare professionals

However, such positive exchanges were not always the case. In contrast, negative interactions between healthcare professionals and caregivers might have led to lower engagement with interventions. Some caregivers interviewed described harrowing experiences of negative communication where healthcare professionals, in face of uncertainty, depicted debilitating futures instead of hopeful ones. The impossibility of potential improvement communicated by certain healthcare professionals had upsetting emotional impacts in caregivers. One mother

described her journey navigating different treatments as one composed of mournful moments when progression of disease, instead of regression, axed the potential for alternative futures to come to fruition.

This mother's experience touches on the complexity of hope in clinical settings, one that brings a challenge to healthcare professionals: when faced with uncertainty of outcomes, what is the right amount of hope that should be given to patients and those attending to them? Should healthcare professionals stimulate hope, which could turn out to be unrealistic, or communicate uncertainty more directly risking ending hopeful optimism and potentially diminishing trust between healthcare professionals and caregivers.

Trust in information in times of scarce evidence and vaccine rumours

Adding to the challenge of administering the right amount of hope, some healthcare professionals wrestled with finding a realistic approach of providing accurate information when they had their own doubts about outcomes. In times of scarce evidence and at times conflicting scientific findings over the Zika virus, caregivers reported receiving dissonant information from different healthcare professionals. This was a driver of mistrust among some caregivers, who sought additional advice and private healthcare services whenever possible. In face of ambiguity, caregivers reported at times preferring to trust HCP who gave them some sense of hope.

The uncertainty of existing information from healthcare professionals and the uncertainty brought by it led to rumours and alternative explanations about what was causing CZS and microcephaly. A usual rumour claimed that microcephaly was caused by expired measles, mumps, and rubella (MMR) vaccines distributed by the government.

External influences on trust and hope in the face of uncertainty around Zika/ Networks of trust and hope

Other external influences impacted trust and hope in face of uncertainty around Zika. Religious beliefs, or God, were commonly cited as an important source of hope, arising from a trust in God and their plans for their life. Often caregivers deferred to their children and their disability as their destiny and mission on earth. This helped manage their own anxieties and difficulties with the children's treatment and impairment. In addition, caregivers found hope and trust among each other, creating networks of trust and support. The information flow among these

networks helped reinforce hope among caregivers. However, the tight bond and easiness of information flow at times led to spread of non-medical advice in terms of medication and courses of treatment.

Political mistrust and hopelessness

There was lower trust in the government (political trust). There was a strong sentiment amid both carers and almost healthcare professionals that Zika's negative impacts were a direct consequence of longstanding social injustices. In addition, mistrust in international researchers and health actors also surfaced in many interviews and during participant observation. Participants questioned whether they were actually the intended beneficiaries of interventions and research agendas, expressing feelings of things being done 'to them' rather than 'for them'.

Generalizability of findings

Results from this qualitative study stem from unique context and social dynamics of a specific setting or population which has implications for applicability beyond the study setting (150). While findings are not strictly generalizable, they provide insights that, when carefully considered, can inform analyses in comparable situations(151).

5.3 Global risk perceptions of vaccine safety, importance and efficacy of vaccines

Views over vaccine safety, importance and efficacy inform global trends in risk perceptions and confidence in immunization. Findings from this study estimate percentages of national population which agree or disagree that vaccines are safe, important and have efficacy – and how perceptions over these three factors interact with each other. In late 2015, Argentina, Bangladesh and Liberia had the highest percentage of respondents who strongly agreed that vaccines are safe. Ethiopia, Argentina, and Bangladesh had the highest estimates of participants who agreed that vaccines are important, whereas Turkey, Morocco and Georgia had the lowest at that time.

Between 2015 and 2019, confidence in vaccine fell across all three factors (vaccine importance, safety, effectiveness) in Indonesia, the Philippines, Pakistan, and South Korea, and for two factors in Afghanistan and Vietnam. Between the same period of 2015 to 2019, vaccine confidence increased across all three elements for France, India, Mexico, Poland, Romania, and Thailand.

In particular, the Philippines had the most significant drop of all countries in all three factors. In 2017, the vaccine maker Sanofi declared that their recently introduced dengue vaccine, Dengvaxia, posed a risk to those who had not previously been exposed to the virus. This has prompted anger and anxieties in the population as almost 850 000 children received the vaccine the previous year. Consequently, the Dengvaxia confidence crises had a spill over effect, eliciting uncertainties that affected confidence and uptake of other routine vaccines recommended by the national immunisation programme. The VCI survey tool has detected a rise in confidence across the country—although confidence is not back to 2015 levels—indicating a possible recovery and highlighting the value of the tool in assessing the effectiveness of national-level policy.

Similarly, in Japan controversies surrounding the HPV vaccination may have amplified risk perceptions around vaccines. Adverse reactions in girls vaccinated against HPV was largely publicized by the media in Japan, exacerbating concerns of side effects of vaccines. As an ambiguous response to the incident, Japan withdrew the proactive recommendation of the HPV vaccination while side effects were being investigated (152). Although no link has been found between the HPV vaccine and side effects, recommendation remained suspended. This study suggests that Japan is one of the countries with the lowest levels of confidence among those surveyed, which might indicate heightened risk perceptions which have been amplified due to HPV vaccine controversy and led to a spill over effect like in the Philippines.

In the EU, between 2018 and 2019 there were decrease in the percentage of respondents agreeing that vaccines are safe in Poland, with increases detected in Finland, France, Ireland, Italy, and the UK. At time, this demonstrated an upward trend in confidence in a continent which had been considered low confidence. This speaks to the volatility of vaccine confidence and risk perceptions, for better and worse.

Out of ten countries that saw decreases in vaccine confidence between 2015 and 2019 (Afghanistan, Azerbaijan, Bosnia and Herzegovina, Georgia, Indonesia, Japan, Malaysia, Nigeria, Pakistan, and Serbia), six had increased concerns over vaccine safety (Afghanistan, Azerbaijan, Indonesia, Nigeria, Pakistan, and Serbia).

Determinants of vaccine confidence

There were significant links between vaccine uptake and sources of trust, vaccine confidence, information-seeking behaviour, socioeconomic status, and demographics. In general, the factors most closely associated with enhanced vaccine uptake were high confidence in vaccines (66 countries); trusting healthcare professionals more than other non-medical sources (i.e. family, friends) for medical and health advice (43 countries); higher levels of science education (35 countries); gender, with women more likely than men to report any child having at least one vaccine (41 countries); age as younger groups were closely associated with increased chances of uptake in 43 countries; and high information-seeking behaviour (18 countries). Religious beliefs and income were less widely associated with uptake; nevertheless, when a link had been found between religion and vaccine uptake, it was usually minority religious groups who were associated with lower probability of acceptance.

Vaccine confidence and vaccine uptake data

Confidence in the safety, importance and efficacy of vaccines are known determinants of vaccine uptake (20,30,53). The main goal of this study was to survey, at scale, spatial-temporal trends in vaccine confidence to anticipate trends in uptake (50). This study brings notable examples of drops in confidence impacting vaccine uptake, as seen in the Philippines and Japan. However, linking in-country vaccine coverage data (including vaccine coverage among pregnant women) to the Vaccine Confidence Index survey falls outside this study's scope. One of the challenges is that the impact of changes in confidence do not immediately translate to increases or declines in vaccine uptake, but the objective of confidence monitoring is to anticipate – and mitigate—potential declines in uptake by addressing drops in confidence before impacting uptake. Future research and public health efforts should further explore these links and investigate maternal vaccine confidence at scale, connecting it to coverage data when possible.

5.4 Trust, risk perceptions and maternal vaccine confidence in Brazil, Panama and Mexico.

Access and trust in maternal health services

There were marked differences in access and trust in public health systems in Brazil, Mexico and Panama. At times, ease or difficulty of access to healthcare appeared to be linked to trust and mistrust in these services. In all three countries, there were reports of a mix use of public and private healthcare services – at times, private services being sought due to lower levels of trust in public health systems.

In Brazil, pregnant women in the study reported good access to both maternal services and immunization. Despite a mix use of private-public services, all vaccines were taken in the public system. Ease of access was cited as a reason to trust the quality of health services. Three key factors were discussed as system confidence builders among the pregnant women: the vaccination card (a booklet used to track vaccines given and received), government mass communication campaigns targeting pregnant women, and recommendation by the healthcare professionals (who were mostly part of the public health system). These key efforts, in place to inform and build trust among pregnant women of the importance of maternal vaccines, were important builders of confidence in the system and consequently stimulated maternal vaccination.

In contrast, study participants in Mexico described barriers to accessing different maternal healthcare services, including immunization with reports of vaccine shortages. Those with financial resources described using private services to ensure adequate care. Due to perceived lower quality of public healthcare services, women discussed higher trust in private healthcare services. Private services were identified to have more control over one's healthcare. Others openly discussed distrust in public healthcare. At times, reposts emerged of dignity-denying experiences in these services – including feeling pushed to vaccinate without being certain or while feeling the need of more information.

In Panama, pregnant women discussed access barriers to maternal immunization, such as availability of immunization and costs associated. They reported a mixed use of private and public maternal services, including for maternal vaccination, with discrepant views over the public health system, and different reasons for choosing one or another (i.e. better quality of private services, choice of doctor). At times, services were seen as satisfactory while others described them as insufficient and difficult to access indicating some fragmentation. Access to maternal vaccines followed a similar pattern, with some participants mentioning paying out-of-pocket for vaccines and difficulty accessing immunization services, key barriers for maternal vaccination in the country.

Trust in government

Differently than in Brazil, pregnant women in Mexico reported mistrust in vaccination campaigns, deeming such efforts were used by the government to change focus from other

political issues. For this reason, participants reported not being willing to take maternal vaccines if offered. However, among vaccine accepting participants, such campaigns could be used to address misinformation around vaccines and 'break the myths' around immunization.

Trust in HCP recommendation of vaccines

In Panama, HCP recommendation to vaccinate was a key driver of maternal immunization. The fact that a healthcare professional recommended a vaccine was perceived as testament to the safety of a vaccine. At times, not much information was offered by HCP, and still their recommendation was enough to convince them to vaccinate. The high reliance on HCP recommendation could backfire and drive women away from vaccination. Many women reported avoiding or not taking vaccines, even if feeling they because their HCP had not recommended them.

In Brazil, HCP are considered a trustworthy source and their recommendation of vaccination is also a key factor for uptake. Among Brazilian women, there was a strong belief that they are the ones best equipped to give this information due to their intense training and formal education (hierarchies of knowledge).

In Mexico, participants reported negative experiences with healthcare professionals, many times resorting to private services to feel safe. When attending public services, many women discussed feeling pushed to vaccinate while still having concerns about the vaccines. In this context, pregnant women felt the responsibility fell upon them to make the right choice.

Trust in external influencers on vaccine decision-making

In Panama, husbands, mothers, and HCPs were involved in women's health decision making. In particular, husbands played a key role. Pregnant women discussed, seeking support from partners. In many circumstances,1 when asked about their own trust in medical advice and information, participants mentioned their husband's views rather than their own. In one case, a husband did not want the woman to vaccinate as he was not comfortable with another man touching her.

In Brazil, pregnant women firmly placed themselves as the key decision makers for their health and vaccination uptake. Ultimately, women discussed relying on themselves to make the better decision on their health. Yet, participants still had conversations with family members and partners about their decisions. Decision-making was also informed by online searches, which

strengthened a sense of ownership and informed decision making (however, among Brazilian study participants, all information harvested online was fact checked with trusted healthcare professionals).

Views on safety risks and effectiveness of maternal vaccines

In the three countries, vaccine safety was commonly discussed considering their effectiveness to protect against infectious diseases active in these regions. Brazil, Mexico, and Panama all have high concentration of endemic diseases, and the risk of vaccinating was commonly contrasted with the risk of not having any protection against multiple viruses. In Brazil, women discussed the large number of viruses present as a reason to vaccinate during pregnancy, to guarantee they were protected against them. Consequently, participants reported vaccinating during pregnancy to feel safe.

Likewise, the high prevalence of infectious diseases in Panama made pregnant women perceive not vaccinating as riskier than having a vaccine (this and the normalizing perception of vaccines). When probed about safety of vaccines, some women associated safety with effectiveness of vaccines. They reported perceiving vaccines as unsafe when they were ineffective. Other participants felt vaccines were more important now they were pregnant.

In Mexico, while there was at times a similar sense of vulnerability to infectious diseases, participants also reported doubts over safety of vaccines. This was true even for some pregnant women who had taken vaccines. Some felt vaccines were useless but decided to have them, and others were openly doubtful about the risks and safety of vaccines. Many were openly mistrustful about vaccines

Vaccine refusal as moral danger

In Brazil, pregnant women were proactive about being vaccinated during pregnancy and this was discussed as a moral responsibility towards their babies. In a setting where they perceived high risk from the infectious diseases circulating, to vaccinate during pregnancy would be to protect their unborn child, and in consequence becoming a good mother through vaccinating. Interestingly, a similar narrative but opposite was present among those who refused vaccination during pregnancy. To these women, not vaccinating was equally a strategy of care if the mother believed the vaccine could injure their babies.

In Panama, maternal vaccines were considered a norm and a routine part of their healthcare during pregnancy. Ultimately, maternal immunization was regarded as a social norm. In a

sense, there is a shared perception that vaccinating during pregnancy is not a choice, that there is no decision to be made – vaccinating is just 'something that you do'. Most of the women reported accepting maternal vaccines and when enquired about what might make a woman choose not to vaccinate during pregnancy, the participants associated such behaviour with maternal negligence. To most in this study, to have maternal vaccines meant being responsible for preventing new-borns from getting hurt. Along these lines, to vaccinate during pregnancy was also mentioned as an act of love towards not only their babies but also the community. The perception that not vaccinating was negligence was true not just for maternal vaccination but also childhood vaccination.

Impact of rumours and misinformation

Despite heightened perception of vulnerability and risk of infectious diseases, and not vaccinating seen as a moral danger, risk perceptions related to safety concerns of vaccines were key drivers of vaccine hesitancy or refusal in the three countries. In Brazil, while most participants felt safer vaccinating and had an overall positive regard for maternal vaccines, there were safety concerns around milder reactions. Even in these cases, participants preferred to risk vaccinating rather than be left unprotected. Nonetheless, among the few pregnant women who were not willing to vaccinate, safety was the main reason. These participants discussed fearing vaccinating during pregnancy could lead to microcephaly. This echoes the experience of maternal health after an outbreak that heavily afflicted pregnant women. There were concerns of Zika being a cover up from a government mistake with expired vaccines; while others mention hearing about this, not knowing if it was true or not – but feeling more hesitant to vaccinate.

In Panama, despite the overall positive regard for maternal immunisation, concerns were recurrently about vaccine safety. Women feared vaccines could be unsafe and lead to miscarriages and to allergic reactions that could be harmful for the foetus. Concerns and doubts over vaccine and their benefits are an important building block of the vaccine decision making process. Yet concerns appear related to deeper mistrust. One participant spoke of Latin American women as guinea pigs used to test vaccines before they are used in high income countries; and another mentioned YouTube videos which affirmed vaccines were made of animal parts, transmitting HIV for those who had taken it.

Information-seeking behaviour and harvesting information online

In Brazil, women commonly harvested and engaged with information online. Online searches about their health were perceived as an important part of their healthcare and decision-making

process while pregnant. Participants discussed feeling empowered, and a sense of self-ownership derived from the power to access information online. Yet, pregnant women showed strong critical thinking when pondering about information harvested online. They discussed concerns about veracity of information and were careful with what was read online.

In Panama, participants reported intense information seeking behaviour regarding overall health. Participants used health apps but did not use group chat technologies to connect with online networks. However, even with high internet usage, women reported checking information with their healthcare professionals. They were pointed as the most trustworthy source of information, and in particular any vaccine related question was directed at them.

In Mexico, participants reported an overall lack of information while being exposed to vaccine misinformation. In this case, they did not cite HCP as their key source of information. Many described trusting what they read online with a direct impact in their decision making. They reported needing to understand more about benefits and associated risks to make up their minds about how necessary vaccinating during pregnancy was. Within this context of low trust and availability of information from medical sources, participants reported high information-seeking online – preferring to use digital platforms instead of consulting healthcare professionals. Many described trusting information harvested online, regardless of sources, which impacted their health decision making. Apps, search engines and social media platforms were all cited as trustworthy sources of health information – including large unregulated Facebook groups, which were described as a main source.

Moreover, women in Brazil and Mexico reported using social media platforms to identify suitable healthcare professionals. In particular, Instagram was perceived as a trustworthy platform to assess if HCP were suitable – this judgement was based usually on number of likes, photos, engagement, etc.

Religious compatibility with maternal vaccination

In the three countries, religious beliefs were not commonly cited as directly associated with a decision to vaccinate or not. However, in Panama, religious beliefs were, at times, used to justify their desire to vaccinate. To them, healthcare professionals had been placed in their lives by God to help them be healthy and free from disease. And while participants of the

study did not see any religious impediment for vaccinating during pregnancy, they cited other traditional and religious cultures in Panama which might see this differently. Panama has a large indigenous community, mostly concentrated in rural areas, and participants of the study mentioned that some indigenous groups were not allowed to vaccinate or did not believe in its benefits.

Generalizability of findings to other countries

While findings are not strictly generalizable, they may be transferrable to other countries with similarities in social, economic, cultural, and political realities. While qualitative research is often context and population specific, researchers aspire to generate insights that can be meaningfully applied in analogous settings. Future qualitative studies should be conducted in further countries to ascertain nuances and determinants of maternal vaccine confidence in other contexts.

6. Discussion

6.2 Research contributions

The five studies included in my thesis have made noteworthy contributions to the field of public health through a better understanding of confidence in vaccines and other healthcare interventions. In face of uncertainty, hope and trust were pivotal to managing risk perceptions. First, the Zika outbreak has left important lessons for policymakers and health officials in Brazil. My study contributed to the discussion on the importance of a trust-based healthcare system between service users and providers (35). My findings indicated that the ability to hope in clinical settings, allowed space for the co-creation of alternative futures, mitigating the stress of uncertainty brought by congenital zika syndrome. In fact, the co-creation of hope between caregivers and healthcare professionals created trustful bonds between the two parts. However, the dynamic was complex as some caregivers appeared to trust healthcare workers who gave unrealistic expectations of therapeutics outcomes, at times nurturing false hope. The challenge lies in administering the right amount of hope in clinical settings, both in terms of treatments and vaccines. Findings of the study also corroborate the idea that trust in clinical settings go beyond patient-provider relationships and include trust in institutions (i.e., governments, health systems), in social actors (i.e., political representatives), and in existing social networks of trust and hope. Source in information was also an important factor, but one heavily anchored in the source of that information. To that end, new digital technologies such as WhatsApp played an

important role in information diffusion, but only in these pre-existing social networks. Moreover, mistrust in international health actors draw attention to the importance of building local and community trust in international health actors. This should be seen as an important component of outbreak and pandemic preparedness as international health emergencies usually draw much research attention and resources. Engaging local communities and building trust should remain a priority in the global health agenda.

Moving specifically into confidence in vaccines, my second paper contributes to a robust understanding of global trends in vaccine confidence and brings important insights on the volatile nature of vaccine confidence. The trust in safety, effectiveness, and importance of vaccines as well as compatibility with religious beliefs, was shown to fluctuate between 2015 and 2019. Findings of the study corroborate the rationale that vaccine confidence and hesitancy are context specific as changes were observed in different settings and at different times. This study indicated how risk perceptions of safety of vaccines can be volatile and rapidly change especially in light of risk that is socially amplified. The study identified rapidly plummeting confidence in the Philippines, albeit with signs of recovery, and findings pointed to Japan having the lowest confidence of all countries surveyed. Risk perceptions have been amplified in both countries due to controversies surrounding the dengue vaccine in the Philippines and HPV vaccine in Japan. Media scandals have the power to shape public risk perceptions and their potential to socially amplify risks have been discussed in the literature - in particular during the COVID-19 pandemic, when big media scandals appeared to have influenced risk perceptions of safety and effectiveness of clinically trialled vaccines(84).

Additionally, different dimensions of trust, socio demographics and information-seeking behaviour were also discussed as important determinants of vaccine confidence. Information-seeking behaviour was pointed as an important determinant of vaccine confidence. Undoubtedly social media can be a source of vaccine misinformation, negatively impact decision making as per findings from Panama and Mexico. However while there have been anxieties within public global health regarding heightened health information seeking behaviour, mostly in the context of ongoing online misinformation, findings point that this can be an important element of an informed health decision-making – and one that will not necessarily be deleterious to desired public health outcomes. This resonates with findings of the following qualitative study looking at maternal vaccines in Brazil, where information seeking behaviour, frequently online, did not necessarily misinform women. Instead, it gave

them a sense of self ownership and control over their health, and they frequently consulted HCP about the information harvested online. The challenge becomes to build trust in the appropriate sources, either institutional or healthcare professionals – or build trust among community leaderships who will inform the rest of a group. This was a pre pandemic study which calls for a follow up study pre pandemic, which could access the global state of vaccine confidence post-pandemic.

The final three qualitative studies composing my thesis contributed to a better, in depth understanding of maternal vaccine confidence in Brazil, Mexico, and Panama – and, as previously mentioned, were the first in these countries. Views and attitudes towards maternal immunization were studied taking in consideration access to maternal vaccines, risk perceptions and levers of trust among pregnant women. Reasons for trust in safety, effectiveness and importance of vaccines was also discussed in more depth as well as impact of information from different sources.

Findings from the three countries point to different health systems configurations and access to vaccine and healthcare during pregnancy. Low access and poor quality at times led to lower trust in systems and vaccines, with Mexico being the most prominent example. Negative experiences with the public health system were compounded by mistrust in government and institutions. In turn, women were the least trustful of maternal immunisation.

HCP recommendations are described in the literature as key drivers, globally, of maternal vaccine acceptance (17,18,153,154). Findings from my studies add nuance to this understanding. However, in Mexico, negative interactions with HCP contributed to lower trust between patient-provider, and vaccine recommendations were not always a driver to vaccinate. This indicates that presence or absence of trust in HCP likely modulates the effectiveness of a HCP recommendation of vaccination. In turn, HCP recommendation of vaccine was a key driver for immunization in Brazil and Panama. However, at the same time, women were highly reliable on their HCP recommendation to have a vaccine in Panama there appeared to be missed opportunities by HCP to recommend the vaccines. In these cases, it was not uncommon for maternal vaccination to be delayed or declined. This was an important system confidence builder in Brazil and a key driver of vaccination. Therefore while Panamanian high reliability in HCP is certainly desirable, other public health efforts such as communication campaigns should be in place to inform population of the needs of maternal vaccines. For example,

findings from Brazil showed that while women relied on their HCP recommendation, they also mentioned mass media communication campaigns as an important driver for their vaccination – and a system confidence builder in maternal immunization. Targeted policy strategies should be in place to ensure most pregnant women are reached.

Given the high concentration of infectious diseases in Latin America, pregnant women in Brazil, Panama and Mexico were hyper aware of their vulnerability to infectious diseases and the threat they posed to them and their babies during pregnancy. In Brazil and Panama, maternal vaccines were mostly seen as the safest, most efficacious way to protect against such diseases. There was hope for a safer, healthier future for them and their babies through maternal vaccines. Due to lower levels of trust in Mexico, many times vaccine safety rumours led women to not take maternal vaccines - and even among women who had the vaccine, there were still doubts. Among the three countries, Mexico was the one with lower levels of trust government, and which was reflected in conspiracy theories shared by participants who believed immunization campaigns were used as smokescreens to mask deeper political issues. Political mistrust led women to believe in rumours of vaccine unsafety more easily, making it more difficult for any government communication campaign to be seen as trustworthy by the public.

Although Mexico was the setting in which rumours appeared to have the most impact in uptake, participants in all countries discussed rumours questioning safety of vaccines. In Brazil, rumours linking microcephaly to vaccines reflect the anxieties that stem from women's experience in a serious outbreak which heavily impacted pregnant women. Albeit the majority was still very confident in vaccines, this rumour was found in two separate studies in Brazil, both conducted at different time. Given the potential of latency of rumours, which can flare given the appropriate fertile ground, this is a point of concern.

Women in the three settings reported high information seeking, particularly online, with very different outcomes for vaccine uptake. In Brazil, a sense of empowerment came from searchers conducted online and information gathered. Yet, women discussed being careful with information gathered online and many times consulted healthcare professionals to confirm veracity. In Panama, women did not share the same feeling of control over their health via online searchers. However they also looked for information online and confirmed with trusted medical sources before following any advice. In Mexico, again probably due to lower levels of trust in general, pregnant women appeared more incline to trust online information and follow

advice. This makes them vulnerable to vaccine misinformation, rife in social media platforms. Findings resonate with the understanding that misinformation is not, in fact, about information – but about trust. The influence of rumours, misinformation, in particular social media, should not be understood within contextual influences. Lower levels of trust could allow rumours and misinformation to be believed and spread. Rumour dynamics is complex and future studies should continue to explore their effects in vaccine confidence and consequent uptake.

In Brazil and Panama, women who refused vaccines during pregnancy were judged as negligent, non-loving mothers. Participants perceived those who did not vaccinate as risk takers not willing to do what it takes to protect their children. In that sense, not vaccinating was as a moral danger. Associating maternal vaccines with protection of them and their babies can be an important driver to vaccinate. However, extending that association to that of bad motherhood if refusing or hesitating vaccination it can lead to stigmatizing of mothers who are doubtful or hesitant about vaccines. The stigma could further alienate these mothers, ultimately pushing them away from vaccines. While the discourse of protecting their child is sensible and constructive, stigmatizing those who choose not to vaccinate or delay vaccination can inhibit important conversations about vaccines and ultimately vaccine uptake.

Finally, there were notable external influencers on pregnant women's trust in vaccines. First, religion and religiosity were discussed in multiple studies composing my thesis. During the Zika outbreak, mothers referred to their children as angels sent by God to be their special mission on earth; in Brazil and Panama, HCP should be trusted also because God had placed them on earth to help people. Globally, religious compatibility was an important determinant of vaccine confidence, and lower trust was observed in religious minorities. These findings point to religion and spirituality as an important component of healthcare and health decision making. Further studies should continue to investigate the roles of narratives and dynamics around religion and spirituality and health outcomes.

Second, family and partners had a level of influence in decisions to vaccinate during pregnancy. In Brazil, participants firmly placed themselves as main decision-makers on their health choices. Nonetheless, after further probing, they admitted discussing options with family members and partners. In Panama the influence was more straightforward as women usually would only make a health decision during pregnancy after consulting their husbands. To that

end, communications of maternal vaccines and future health policy should not target only pregnant women, but also aim to build trust among family members and husbands.

Implications for future research

Findings of these studies point to important areas if exploration for future research. In Brazil, while maternal vaccine confidence was high in the sample, uptake has varied considerably (62). More research is needed in Brazil to understand reasons for low uptake of some maternal vaccines. There are many potential contributors, including possibly unidentified pockets of vaccine hesitancy, supply issues, budgetary pressures and broader access issues (155). Given the reported concerns and rumours over safety of vaccines found future research should aim to examine how this uneasiness might be impacting the decision to vaccinate. It is also possible that there are pockets of vaccine hesitancy in other parts of Brazil (outside Rio de Janeiro and São Paulo), which could help explain low uptake of certain immunizations. Moreover, it is important to investigate regional differences in attitudes towards maternal vaccines, as well as attitudes towards specific vaccines.

In Panama, many participants reported complications when accessing maternal vaccination, pointing to financial and physical barriers which merit further investigation. In addition, future studies of maternal vaccine confidence in Panama should aim to produce evidence that can inform health policy tailored to rural and indigenous populations. Lastly, future investigations in Panama should explore the link between economic, educational, marital, or professional status and willingness to have a maternal vaccine.

A key determinant of low uptake was affiliation to a religious or ethnic minority (50). These findings resonated deeply during the COVID-19 pandemic, were minorities globally resisted the uptake of new vaccines(156–159). Findings from Panama also point to how indigenous minorities, would likely be more mistrusting of vaccines in the sample with not the same access to maternal services and different religious beliefs. The vulnerability to negative health outcomes in minorities has been much discussed in the literature, and the effects of exclusion and marginalization in the trust and acceptance of vaccines and health interventions. Future studies should continue to invest in understanding the social dynamics sustaining inequities and low trust, developing solutions to improve health outcomes of these vulnerable populations.

Lastly, future studies in global trends in vaccine confidence should continue to invest in understanding the social dynamics sustaining inequities and low trust, developing solutions to improve health outcomes of these vulnerable populations. In addition, upcoming studies should aim to map post-pandemic trends in vaccine confidence globally.

6.3. Strengths and weaknesses

The studies presented have a number of strengths and limitations, which are here discussed. First, my study with caregivers and healthcare professionals during the Zika outbreak in Brazil (46) contributed to the important conversation of building trust-based healthcare systems to stimulate cooperation between healthcare professionals and patients. Instead of abstract concepts, my study demonstrated how hope and trust formed relationships that had direct impact in the response to the Zika outbreak. If positive relationships within healthcare are not rebuilt, we risk mistrust and its negative consequences to provision of health and outbreak preparedness. This study has limitations. First, despite many in-depth interviews with caregivers and healthcare professionals, this study was conducted only in two settings in Brazil. Given the country's large geography, population and cultural differences between regions, findings may not be generalizable. Second, although caregivers included were of both genders, women remained the mains caregivers for children affected by Zika, often carrying the burden of care for the child.

Second, my study mapping global trends in vaccine confidence (50) allowed for cross-country comparisons and changes over time. To the best of my knowledge, this was the largest study of global vaccine confidence by time of publication. Although immunisation coverage is routinely registered around the world, there is no similarly robust monitoring system for confidence in vaccines. Our findings emphasise the significance of systematic monitoring that can detect drops in confidence which can prompt interventions and avert more serious confidence crises. The VCI delivers a valuable measurement of confidence levels considering their change in times of disease threats, helping to pinpoint where trust building is needed. Moreover, having a common metric of confidence is crucial for cross-country comparison. This study has limitations to note. First, as not all surveys used had consistent responses, we have made a key assumption that, presented with different options between the extreme categories of "strongly agree" and "strongly disagree" (which are consistent across all surveys), respondents with the strongest sentiment will fall into one of these groups irrespective of additional categories. Second, the Wellcome Global Monitor survey data only permit an

investigation of whether a parent has had any of their children vaccinated against at least one childhood disease. These uptake data are hence not defined on a vaccine-by-vaccine basis, preventing an examination of determinants of vaccine-specific uptake. Moreover, we rely on parental recall being accurate, and patterns of recall error not varying substantially across countries.

Third, my investigations in Brazil, Mexico, and Panama were the first attempt to qualitatively assess views and attitudes of pregnant women in these countries, identifying relevant factors in their decision-making process during pregnancy. Additionally, pregnant women will soon become parents making vaccination decisions for their child, constituting an important target group for policymakers seeking optimal maternal as well as childhood immunization coverage. These investigations identified important system confidence builders, along with possible barriers to maternal vaccine uptake.

In Brazil, the findings encompass system components to ways in which pregnant women reflect upon information received from different sources, including HCPs and internet searches. Many important elements surrounding confidence in maternal immunization in Brazil were identified in this study. A possible barrier to maternal immunization identified was a rumour that blamed vaccines for microcephaly cases, which requires further investigation. In Mexico, my findings highlight the importance of targeted communication, trust-building, and engagement strategies to strengthen confidence in immunization amongst this group given the strong narratives of mistrust discussed by pregnant women. In Panama, my study indicates that there is a high level of positive attitudes towards maternal vaccines among pregnant women in Panama. The willingness to have maternal immunisation was high in the sample studied.

There are limitations to note. First, because they are qualitative investigations, the findings are not generalizable. Instead, the convey experiences and views of participants that may not be captured in quantitative studies. Second, despite a sizable poll of participants, the investigations were conducted in urban centres. In Mexico and Panama, our findings may not reflect the experience of indigenous populations and of those in rural areas which were not included in our sample, as their access to health services are likely to be different. In Panama particularly there is a striking gap in offer of public health services between urban, rural, and indigenous regions; the later experiencing weaker access to maternal immunisation, in addition to lower levels of both vaccine literacy and trust in health services. In Brazil, both cities chosen for this

study are high income settings. Therefore, access to vaccines is not necessarily the same as in other regions that do not have the same financial capacity. Lastly, some participants in Brazil were recruited in health facilities and consequently disposed to use basic health services such as immunization, which might have skewed findings.

The overall strengths of this portfolio are 1) a mixed method approach that includes a large quantitative dataset and in-depth investigations of barriers and drivers of maternal vaccine confidence. This approach embraces the complexity of understanding vaccine confidence, taking in consideration the need to measure it and understand its drivers. 2) By discussing non-pharmaceutical interventions and healthcare delivery post-outbreak, this study offers a holistic view to outbreak preparedness and response, investigating strategies and important social dynamics impacting disease outcomes in cases when vaccines are not available. There are overall limitations to note. Across this thesis all studies were designed, and data collected before the COVID-19 pandemic. This acute global health crises have very likely significantly changed the landscape of risk perceptions of vaccines and healthcare interventions. A new large quantitative study is due to better understand changes in vaccine confidence trends. Moreover, in-depth investigations of maternal vaccine confidence should be replicated in other countries in Latin America to better grasp drivers and barriers to maternal vaccine confidence in the region.

7. Conclusion

Vaccines and post-outbreak health interventions as important cornerstones of outbreak preparedness and mitigation. Yet, they have at times been met with skepticism by the public. This can lead to negative health outcomes, particularly for vulnerable populations such as pregnant women – who commonly suffer a heftier impact of disease. This thesis has provided a comprehensive picture of the complex interplay between risk perceptions, hope and trust – and how they modulate the confidence and subsequent acceptance of vaccines and post-outbreak healthcare interventions. The results reported across this thesis demonstrate the influence of uncertainty, risk, hope and trust on health seeking-behavior and decision making.

In face of uncertainty, the ability to hope and trust may have led to higher uptake of interventions and increased maternal vaccine confidence among pregnant women and mothers affected by infectious diseases. Hope and trust were pivotal determinants in the decision-

making process of pregnant women, particularly when contemplating loss due to infectious diseases. These factors exacerbated risk perceptions, primarily motivated by pregnant women's imperative to nurture and protect their unborn children. Findings also point to the volatility of confidence, commonly driven by emotional responses to risk and danger. Results also indicate the role of the social amplification of risk in informing perceptions, and how trust is multidimensional – and mistrust in different stances can lead to warped risk perceptions, leading to negative health outcomes for a population. Rumours, misinformation and their impacts in health decision making were understood as more closely associated with trust and mistrust instead of a lack of information.

Findings contribute to the literature which shifts from a knowledge-deficit model to a trust building strategy to combat misinformation. In turn, information-seeking behaviour was discussed as an important determinant of vaccine confidence concluding that, in and of itself, heightened information seeking is not necessarily detrimental to vaccine uptake (even if online). Instead, trust in sources of information (i.e., trust in a HCP instead of trust in online sources) appeared to be a greater indicator of the outcomes of heightened information seeking behaviour.

My publications and this thesis contribute to a more nuanced understanding of emotional and attitudinal drivers and barriers of acceptance of vaccines and healthcare post-outbreak. By delving into the complex interplay of trust, hope and risk perceptions, my thesis contributes to a nuanced understanding of how they intersect and impact the acceptance of preventive and therapeutic healthcare offered to pregnant women, emphasizing the importance and novelty of my work. My research contributes to the formulation of health policy that is attentive to the needs of vulnerable populations such as pregnant women, particularly in low- and middle-income countries, who carry the heftiest burden of infectious diseases.

8. References

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