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Pregnant women's perceptions of risks and benefits when considering participation in vaccine trials

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ABSTRACT

Introduction: Despite historical exclusion, there has been recent recognition of the need to address the health of pregnant women in research on vaccines against emerging pathogens. However, pregnant women's views and decision-making processes about vaccine research participation during infectious disease outbreaks remain underexplored. This study aims to examine women's decision-making processes around vaccine research participation during infectious disease outbreaks.
Methods: We conducted qualitative semi-structured in-depth interviews with pregnant and recently pregnant women (n = 13), eliciting their views on four hypothetical Zika Virus vaccine research scenarios and probing their decision-making processes around participation. After recorded interviews were transcribed, thematic analysis was conducted based on a priori and emergent themes.
Results: Most women interviewed were accepting of vaccine research scenarios. Three broad themes—evidence, risk, and trust—characterized women's decision-making processes. Women varied in how different types and levels of evidence impacted their considerations, which risks were most salient to their decision-making processes, and from whom they trusted recommendations about vaccine research participation. Exemplary quotes from each theme are presented, and lessons for vaccine development during the current COVID-19 pandemic and future outbreaks are discussed.
Conclusion: Some pregnant women are accepting of participation in vaccine research during infectious disease outbreaks. Incorporating their priorities into trial design may facilitate their participation and generation of evidence for this important population.

1. Introduction

The current COVID-19 pandemic and the recent Zika epidemic have each highlighted the unique challenges of appropriately caring for pregnant women during infectious disease outbreaks. Although vaccines are one of public health's most powerful defenses against infectious disease, historically pregnant women have been excluded from vaccine research and development. There is expert consensus around the critical need to include pregnant women in vaccine development efforts, and recent guidance offers an ethically sound path forward for the vaccine research agenda [1]. However, pregnant women's decision-making processes about vaccine trial participation are not well understood. Important vaccine trials are planned or ongoing for current and recent outbreaks, including COVID-19 and Zika [2,3] and it is critical to understand pregnant women's motivations for participating in vaccine trials, their perceptions of the risks and benefits of such research participation, as well as their decision-making processes.

In response to the 2015–2016 North and South American Zika Virus epidemic and the Zika Virus vaccines in the development pipeline, we designed a research study that examined pregnant women's willingness to participate in a variety of hypothetical Zika Virus vaccine trials through surveys and in-depth interviews. Survey data, previously reported, indicated that pregnant women are overall willing to participate in vaccine trials [4]. Interview data, reported below, demonstrate the complex and interconnected factors that can influence decision-making in pregnancy and decisions about trial participation, and reveal that nuanced risk–benefit calculations may contribute to final participation decisions. Women's views on participation in Zika Virus vaccine trials offer important lessons for future vaccine development in other disease contexts, including the current global COVID-19 pandemic.

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2. Methods

As part of a mixed-methods study involving a total of 141 participants, we conducted in-depth interviews with 13 women receiving prenatal care at a university hospital. All study materials were approved by the Institutional Review Board at Partners Healthcare (IRB# 2017P000489). English speaking pregnant and postpartum (within one year) women presenting for care at the Massachusetts General Hospital prenatal clinic from May 2017 to August 2017 were eligible. Recruitment was designed around clinic flow and used a non-probabilistic purposive sampling approach. Consistent with qualitative methodology, interviews were conducted until thematic saturation was reached [5]. As study staff availability was limited, a non-response rate was not calculated. Women were offered participation in a survey study or in an interview-based study; participation in both was not allowed. All women provided informed consent prior to study participation. Interviews were conducted in English by a trained interviewer who was not a clinician in a private room in the clinic. Interviews took between 30 minutes and one hour, and participants received $50 cash for their time and to offset the cost of additional parking. During the interview, women were asked whether they would participate in four hypothetical Zika virus vaccine trials [4]. Each scenario was based on a Zika vaccine platform in the development pipeline and included a statement about prior evidence of safety and efficacy where available. The 4 scenarios are described in Fig. 1. In discussing each scenario with interview participants, follow-up questions probed specific risks and benefits, women's shared decision-making with providers or partners, as well as if and how evidence of safety from inadvertent vaccine exposures in pregnancy would change or affect their decisions. Study scenarios were designed to present different levels of vaccine risk for participants, and reflected an effort to communicate scientific information in an accessible, concise manner. Interviews were audio-recorded and recordings of the interviews were transcribed for data analysis.

We developed a codebook from a priori and emergent themes and conducted thematic analysis of the transcripts using NVivo 11. The first three transcripts were double coded, with differences resolved through discussion, to ensure inter-coder reliability. We assigned all participants pseudonyms, and chose quotes exemplifying each theme.

3. Results

The demographic characteristics of our sample were consistent with those of the larger university hospital perinatal population. Two participants self-identified as Black and four as Hispanic, the rest self-identified as White. Nine of thirteen participants reported an education level beyond high school and reported being married (Table 1). Acceptance of participation in at least one scenario was common, with only one woman declining all four scenarios. Among women who accepted at least one scenario, acceptance rates varied between scenarios. While only two women accepted live attenuated virus vaccine trial participation, eight respondents stated they would participate in an inactivated Zika virus vaccine trial and twelve stated they would continue in such a trial if they became inadvertently pregnant. Seven indicated they would participate in a nucleic acid vaccine trial (Table 2). In addition to accepting or declining the trial scenario, participants detailed their decision-making process in response to interviewer prompts. Participants described benefits and risks, and discussed the many complexities that arose as they considered each scenario. Three broad themes characterized women's responses to trial scenarios: evidence, risk, and trust.

3.1. Evidence

Women described varying levels of reassurance or concern related to statements around evidence of vaccine safety. For some women, the fact that the vaccine was shown to be safe in pregnant animals and non-pregnant humans was salient.

> "If it's tested on animals and it's tested on non-pregnant people, what makes me different?"
>
> —Emily

However for others, the lack of evidence specific to pregnant women was more outstanding.

> "If the platform has not been tested in pregnant women that would be concerning to me. I don't know that I would be brave enough to be in the pioneer group."
>
> —Joy

Some participants focused in on one type of evidence, either from pregnant animals or non-pregnant humans, and responses typically depended on whether perceived differences or similarities were more salient. Women who agreed to participate emphasized the similarities between humans and animals.

> "They already tried it in pregnant animals, we are very similar to animals"
>
> —Sarah

However, others emphasized the distinction between humans and animals, and expressed concern that pregnant animal models were being used as a proxy for human pregnancies.

> "Pregnant animals are not the same as pregnant people"
>
> —Vanessa

Similarly, women who expressed a willingness to participate cited similarities between data from pregnant women and non-pregnant people,

> "It would be beneficial to know that it had worked in non-pregnant people. That it was safe, they had no side effects, that seems beneficial"
>
> —Joy

while those declining participation more often emphasized the distinction. In response to interview probes as to whether evidence from inadvertently vaccinated pregnant women would change their responses, many women indicated that it would. Some women expressed a desire to know about efficacy,

> "I don't want to expose my child unless I'm like 100% sure that it's going to work."
>
> —Rachel

while others described specific safety standards they would like to be met prior to participation.

> "I want years and years and years and mountains of research to back something up like that for me personally to participate. . .I wouldn't want to be part of something unless there was just such a wealth of knowledge . . . that I could feel a hundred percent confident that there would not be any risk."
>
> —Courtney

3.2. Risk

Overwhelmingly, women described that their concern was predominantly risk of harm to the fetus or baby, and not to themselves.

Scenario 1: Inactivated Vaccine
You have recently found out you are pregnant, and you are at risk of being infected with Zika virus because of the types of mosquitoes in your neighborhood that are very difficult to avoid. An inactivated, Zika virus vaccine has been tested in a small number of people who are not pregnant and was proven to be safe and effective. Inactivated vaccines contain a part of the virus that has been "killed," bleached, or otherwise deactivated. Pregnant women routinely receive other inactivated vaccines (e.g. flu, TdAP), and this inactivated vaccine uses a mechanism that has been well-tolerated in pregnant women in the past. Researchers are running a trial in which participants receive this inactivated Zika virus vaccine over three separate visits, and are closely monitored over the next year.
Scenario 2: Inactivated Vaccine – 2nd dose after incidental pregnancy
Imagine you are not pregnant. You are at risk of being infected with Zika virus because of the types of mosquitoes in your neighborhood that are very difficult to avoid. You have decided to enroll in a trial of an inactivated vaccine. Inactivated vaccines contain a part of the virus that has been "killed," bleached, or otherwise deactivated. This vaccine requires two doses, spaced seven weeks apart, in order to be protective against Zika Virus. However, the researchers are not including pregnant women in their trial, even though it is believed to be safe in pregnancy. Pregnant women routinely receive other inactivated vaccines (e.g. flu, TdAP), and this inactivated vaccine uses a mechanism that has been well-tolerated in pregnant women in the past. 5 weeks after receiving the first dose, you discover that you are pregnant.
Scenario 3: Live vaccine
You have recently found out you are pregnant, and you are at risk of being infected with Zika virus because of the types of mosquitoes in your neighborhood that are very difficult to avoid. A live vaccine has been tested in pregnant animals and people who are not pregnant and was proven to be safe and effective. Live vaccines contain a weakened version of the virus, which your body recognizes and against which it develops a defense, protecting you against future infection. Live vaccines are generally advised against during pregnancy, even though many pregnant women have received live vaccines and there have never been any problems reported, besides a <1% increased risk of birth defects after the smallpox vaccine. Researchers are doing a research study in which participants receive this Zika Virus vaccine in one dose, and then are closely monitored over the next year.
Scenario 4: Nucleic acid vaccine
Imagine you are pregnant. You are at risk of being infected with Zika virus because of the types of mosquitoes in your neighborhood that are very difficult to avoid. An experimental Zika virus vaccine, which uses Zika DNA (which is not live virus and has no risk of resulting in a Zika infection) has been tested in people who are not pregnant and pregnant animals, and has shown to be safe and effective in both groups. They are running a trial in which participants receive the vaccine over two separate visits, and are closely monitored over the next year. DNA vaccine platforms are believed to be safe during pregnancy, though they have never been tested in any pregnant women.

Fig. 1. Scenario descriptions.

"I'm not as concerned about myself. Honestly, the baby would be my priority"

—Kirsten

Women described different and sometimes conflicting sources of risk. The salient source of risk varied between women; four primary sources women attributed risk to were (1) the vaccine, (2) the virus, (3) pregnancy, and (4) the "unknown unknowns." First, some women focused on risk of harm from the vaccine, particularly the worry that the fetus would be exposed to Zika and harmed because of vaccination:

"They're going to put a part of the Zika virus in me and I'm going to get it, I'm going to pass it to my baby"

—Alyssa

One woman commented that the very exclusion of pregnant women from the trial indicated that there might be potential safety concerns or risks to the vaccine,

"The study wasn't including pregnant women, so there's that little piece in the back of your mind that says 'well why aren't they including pregnant women because if they really felt it

Table 1
Participant Demographics n = 13.

Age	(Mean ± SD)	30.7 (±5.05)
Education	High School Degree or GED	4 (30%)
	At least one year of college	7 (53%)
	Graduate degree	2 (15%)
Marital Status	Married	9 (70%)
Race	White/Caucasian	8 (62%)
	African American/Black	2 (15%)
	Other	3 (23%)
Ethnicity	Hispanic/Latina	4 (31%)
Prior Vaccination (Pregnancy)	TdAP	5 (38%)
	Influenza	8 (62%)

Table 2
Scenario Description and Participation Acceptance.

Scenario 1: Prospective Enrollment Inactivated Zika Virus Vaccine Trial **n = 8**	Scenario 2: Continued Enrollment Inactivated Zika Virus Vaccine Trial after Incident Pregnancy **n = 12**
Scenario 3: Prospective Enrollment Live-attenuated Zika Virus Vaccine Trial **n = 2**	Scenario 4: Prospective Enrollment Nucleic Acid Zika Virus Vaccine Trial **n = 7**

was safe for pregnant women then they might be including pregnant women'"
—Vanessa

The second source of risk raised by some women was the background risk of Zika infection,

"If I don't [get the vaccine] I could end up with the virus anyway"
—Emily

Third, some women pointed more broadly to the background risks of pregnancy and the difficulty of attributing them to a single source:

"Anything you do while you're pregnant is a big risk to take"
—Vanessa

Finally, others spoke of concern due to the unforeseen risks,

"I don't know what the risk could be. And because I don't know what could potentially be the risk, I'd rather not be part of a trial when I'm pregnant"
—Courtney

For some women, these unknown risks were related to the type of platform, raising less concern in the inactivated vaccine scenarios when the vaccines were compared to influenza and TdAP vaccines, and more in the live vaccine scenario,

"[T]he thought of having it live in your body. . .There is so much unknown that I would be uncomfortable"
—Joy

Beyond identifying sources of risk, women described that they would make risk tradeoffs when considering participation in vaccine trials.

"The risks of having a baby born with Zika are so much, are so far greater than the risk of any type of vaccine that they would have developed"
—Chelsea

All women described nuanced risk–benefit calculations, and articulated the ways in which they weighed different risks and benefits. For example, one woman explained,

"I would probably take the chance, even if there's a little risk of birth defects, because I'll still love my baby no matter what and I just want to make sure that I'm safe, and she's safe, for the rest of my pregnancy, because I'm sure if you get Zika, there's more risks"
—Michaela

Other women stated that decision would depend the background risk of Zika infection where they lived.

"If I thought that it was safe and I thought that I was in an area where the risk of getting Zika and having an unhealthy baby was higher than the risk of complications from the vaccine I would get the vaccine. So it's really all about the health of the baby and that risk-reward ratio"
—Vanessa

Finally, women talked about the risk differential between prevention and treatment,

"I would just be too scared to expose myself or my child, or just putting it in my body if it's not something that we know is for sure there—I probably wouldn't do it"
—Rachel

3.3. Trust

A third salient finding from participant responses was the variation in pregnant women's trust of vaccines, research, and the medical establishment in general, as well as the factors described to influence these beliefs. Some women emphasized that they would trust their doctors' opinion when making the decision.

"I'm pretty trustworthy when it comes to the medical field, so if the doctor tells me that it's a good idea, I don't second-guess much"
—Chelsea

However, one woman said that a doctor recommendation would inform but ultimately not change her reticence toward trial participation.

"It would help make it not as bad, but at the end I probably still would be like, 'no'"
—Alyssa

Similarly, some women expressed faith in vaccines generally,

"I take all the vaccines, I don't play with them. . .for somebody else it might be different but I'm a very strong believer in vaccines"
—Lauren

Others described reassurance from comparing an experimental Zika vaccine to routine vaccines:

"If you compare it to a flu shot that everybody gets every year, it definitely doesn't make it sound as scary"
—Chelsea

Another however noted her concerns driven by public hesitance around vaccines, particularly in the face of reports of negative news commentary:

"Sometimes when there's research, and it comes out in the news, or other people talk about it, you think about it a lot more . . . all these negative thoughts like, 'what if, what if.' . . . When

people talk a lot about negatively about these vaccines, it makes you really double think"
—Alyssa

Most women who discussed the research enterprise more generally and the benefits of trials expressed trust and valued evidence generated from trials highly.

"I have diabetes, so I'm pretty sure that … for someone to approve the insulin, they went through this. People weren't sure if it was safe or not. Sometimes you have to do things, even though you're not a hundred percent sure, because it will help you, at the end"
—Sarah

Some women expressed altruistic motivations and the importance of evidence in pregnancy.

"You could provide so much information for pregnant women going forward"
—Jamilah

Several women described a lack of trust related to government recommendations about vaccine trial participation, with several elaborating on reasons for such mistrust:

"The government just wants to look at what they want, and how it's going to better fit their pocket. They're not worried about how it's benefitting me, or my kids, because they don't care if me and kids end up on the street because I got sick and couldn't work because I couldn't get a vaccine"
—Emily

Additionally, one woman described that she would talk to God when making the decision, and trust in her religion to guide her choice.

4. Discussion

As the need to fairly address pregnant women's health needs in vaccine research is increasingly recognized, it is necessary to understand women's attitudes regarding vaccine trial participation during pregnancy. Several other studies examining women's willingness to participate in vaccine trials demonstrate variability in immunization research acceptance between vaccines [6–9]. Specifically for Zika vaccines, acceptance of a hypothetical Zika vaccine during pregnancy in a clinical context ranges from 48% to 94% [10–12]. With regards to acceptance of Zika vaccine trial participation, our previously published quantitative findings demonstrated that 68%, 19%, and 52% of pregnant or postpartum women in the study population were willing to participate in inactivated, live-attenuated, and nucleic acid vaccine platform trials, respectively; and 64% would agree to receive the second experimental dose of an inactivated vaccine platform after falling pregnant [4]. We sought to add to the existing evidence around vaccine trial participation decisions by characterizing the nuances of women's risk reasoning and complex decision-making around Zika vaccine trial participation. We identified three main themes that informed women's decisions about participation in vaccine trials during pregnancy: evidence, risk, and trust. Each theme offers lessons for future trial design, evaluation, and policy.

4.1. Evidence

Critical evidence gaps exist around the use of many medications in pregnancy due to historical exclusion from clinical trials. Consequential gaps also exist around use of vaccines during pregnancy, for which levels of evidence about use, safety, and efficacy in pregnancy vary widely [13–16]. One recent study found that "not enough safety data" and "not enough information to decide" were among the top reasons that women declined to receive recommended vaccines in pregnancy [17]. However, women's perspectives on types and levels of evidence when considering participation in vaccine trials have not been previously characterized. Calls to advance development and ensure uptake of new vaccines in pregnancy emphasize the importance of gathering perspectives of potential research participants to inform research questions and trial designs [18,19]. As new maternal vaccine trials are planned, our finding that women in our study highly valued evidence in general, and pointed to it as a primary motivator of acceptance or decline of participation suggest how the existence of and communication about prior data may be relevant to successful design and recruitment of participants. Our findings emphasize that different types and amounts of data may importantly influence women's views about clinical trial participation during pregnancy. Data from animal models demonstrating immunogenicity and safety will likely be part of the baseline requirement for advancing any vaccine to the clinical setting [20], but some women did not find this reassuring, focusing instead on the differences between humans and other animals. While animal models are a critical first step in vaccine development, they are the floor, and not the ceiling [21]. In line with women's concerns, many researchers have raised concerns about the lack of specificity linking required animal studies to reproductive risk. For example, rats and mice are often used in pregnancy research, but have a different placental structure and shorter gestation [22]. The FDA's 2015 shift from letter categories to risk statements for drugs in pregnancy supports a shift toward qualitative description of animal data in relation to human exposure, with more nuanced distinctions made between drugs based on animal data and other data [23–25].

Women also had varying perspectives on evidence from non-pregnant people. Pathways for maternal immunization research usually include testing in non-pregnant women of reproductive age before testing in pregnancy [20]. In fact, institutional review boards often understand this as a necessary prerequisite to testing in pregnant women [24]. While some women felt reassured by this data, to others, the differences between evidence from pregnant and non-pregnant people were quite salient. Indeed, non-pregnant human data is not sufficient to extrapolate to safety and efficacy in pregnant people. Pregnancy induces physiological changes that alter drug absorption, distribution, metabolism, and excretion, potentially impacting drug safety and efficacy [26,27]. Similarly, physiologic alterations in immune function can potentially impact immune response to vaccines [21]. Historically, vaccine development has established safety in non-pregnant populations then proceeds to market and clinical use, without plans to establish safety or efficacy in pregnancy, despite likely benefit and certain inadvertent exposure [21,28]. Further, the working interpretation of FDA approval for use in adult populations is that the approval extends to healthy pregnant women, despite potential differences in safety and efficacy [20]. Our study results highlight that pursuing pregnancy-specific data in vaccine trials is not only key to ensuring safety and efficacy in pregnancy but important to respecting pregnant women's views and expectations about interventions they may be recommended to receive in clinical settings.

The high value women place on human pregnancy data when deciding about participation points not only to the importance of designing vaccine trials to specifically address the health interests of pregnant women, but also to conducting robust follow-up on women inadvertently vaccinated in the periconception period during vaccine trials or rollouts, and to making a carefully contextualized analysis of these data available in a timely manner. It is critical to characterize the quality and quantity of evidence available, and make clear the limitations of data from inadvertent exposure [29].

Given the potential for a small or false safety signal to derail further investigation or development of a promising vaccine for protecting pregnant women, all communication should include the best available background rates of pregnancy outcomes [29].

Of interest, several women showed the tendency to describe an idealistic but unlikely evidentiary threshold as a prerequisite for participation. Some participants described they would receive the experimental vaccine only if absolute and unequivocal data on safety had been established. Given that the very nature of a trial precludes the possibility that the experimental intervention would have a robust safety and efficacy profile established, this assertion emphasizes that vaccine trial participants should be informed of the range of risks and benefits. The notion that a therapeutic trial could be risk-free may derive from fact that our study was designed to surface initial responses to hypothetical trial scenarios, without a full description of the research process, as the recruitment and consent process would do for a true study.

4.2. Risk

Risk distortions often shape assessment of and communication about medical interventions in pregnancy [30–32] and around vaccines more broadly, which may significantly impact vaccine trial participation decisions during pregnancy [33]. Concerns about risk of harm have been widely cited as a deterrent to vaccine uptake in pregnancy [34,35]. The Health Belief Model, a framework often used to understand vaccine acceptance in pregnancy, describes the perceived risk of the vaccine as one of many inputs into acceptance decision-making [34,36,37]. In this model, another critical input to acceptance decision-making is the perceived risk of non-intervention – and the risks of "doing nothing" are often underestimated [36,38]. Women's responses reflected these two competing sources of risk, and added to evidence suggesting that in pregnancy, risk perception can be deeply subjective and value laden. Consistent with prior studies, we found that women vary in their risk–benefit calculations when it comes to trial participation as well as medical intervention in pregnancy [8,39]. Even among women with the same priorities – fetal health and safety – some decided to participate and others declined based on what they felt to be the greatest threat to their fetus (the vaccine or the virus itself).

When it comes to the inclusion of pregnant women in trials, there is often a concern that tradeoffs must be made between the woman's health and the health of the fetus. Although maternal/fetal interests are interrelated and most often aligned, worry about compromising fetal health remains a primary reason for excluding pregnant women from trials. Our results emphasize that women's decision-making about trial participation is in large part informed by concern for the fetus, and that the tradeoffs that are most salient are between harm to the fetus from intervention versus harm to the fetus from background risk. Few women mentioned risk to themselves, and some more explicitly expressed wishing to distinguish and choose the option that minimized harm to the fetus only.

Women, along with their providers, often need to carefully weigh the relative risks and benefits of intervention and non-intervention, which likely differ between clinical and research settings, as well as non-epidemic and epidemic contexts. Overall, our data offers an understanding about how women consider these risk–benefit calculations in the context of epidemic response research, and demonstrate that such decisions are values-laden and personal.

4.3. Trust

In general, women in this sample expressed trust in doctors and in vaccines more broadly. This is reassuring given the current climate of increasing vaccine hesitancy. Trust in recommendations from providers and public health authorities has been shown to increase vaccine acceptance in pregnancy [34,40–42]. A study of pregnant women's trusted sources of information about vaccination during the H1N1 pandemic found that while some women turned to public health and government authorities, others had mistrust of government sources of information due to misinformation or conspiracy theories [43]. Our previously published quantitative findings suggest women may trust provider recommendation more than government recommendation when considering vaccine trial participation during pregnancy. In the current study, participants were wary of government recommendations about experimental vaccine trials. One participant described the challenges of hearing vaccine hesitancy messaging from others, and articulated that this messaging caused her to have doubts around vaccine use. Her experience again emphasizes the importance of clear and transparent communication around vaccines and pregnancy, and that it is critical to establish vaccine safety with pregnancy specific evidence to support recommendations of use in pregnancy. In terms of trials, women not only trusted that research may be a path for accruing personal benefit, but also as a means to secure societal benefit.

5. Lessons for research

These findings have multiple implications for vaccine trials with pregnant women. Each broad theme offers a unique lesson for trial design, evaluation, and policy, as well as for medicine and public health more broadly:

5.1. Evidence

Collect pregnancy specific evidence in order to be respectful of pregnant women's motivation to participate in vaccine trials. Women interviewed placed highest trust in evidence, a further motivation to collect this data that is distinct from the scientific, policy, public health, and justice reasons for pursuing such information.

5.2. Risk

Women should be provided information that allows them to make risk benefit calculations that are complex, personal, and values-driven, within pre-approved parameters determined by ethics committees. This may include considering ways that consent processes can be adapted to ensure these complexities are understood and that women are supported in their decision-making.

5.3. Trust

In order to facilitate trust and avoid mistrust, get ahead of the curve with evidence. Vaccine hesitancy is a challenge that is broader than maternal immunization, but the research community should anticipate and mitigate future challenges by gathering robust evidence, in order to inform communication around safety with contextualized and appropriate risk statements.

6. Limitations

Our study had several limitations. First, while we achieved in our sample thematic saturation, the sample was relatively homogenous with regards to race, age, education, and general maternal immunization acceptance. It is possible that other themes would be identified across a more diverse population or one with more prevalent vaccine hesitancy. Moreover, the degree

to which such themes are generalizable could be assessed by future quantitative studies. A second limitation is the short length of the scenarios, which reflect our decision to prioritize accessibility and brevity, and summarize the scientific detail that would reflect a trial description and informed consent processes for actual vaccine research trials. As such, while our findings surfaced the range of considerations and priorities that pregnant women may account for when making vaccine trial participation decisions, they should not be used as an indicator whether or not they would actually consent to participate in any given study.

7. Conclusion

Zika vaccines are continuing to be developed, and platforms including inactivated, nucleic acid, and live attenuated vaccines are at varying stages of development [2]. These lessons are also applicable beyond Zika—they extend to the current COVID-19 pandemic where at the time of this manuscript preparation, over 90 candidate vaccines are in the pipeline [3]. As the needs of pregnant women are increasingly addressed in vaccine development efforts to combat emerging epidemic and pandemic threats, these lessons may help the research agenda be more responsive to the priorities of a population it seeks to protect.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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