



A
QUALITATIVE
STUDY

UNDERSTANDING VIEWS, PERCEPTIONS
AND ATTITUDES TOWARDS ZIKA VIRUS,
AND THE ACCEPTABILITY OF A ZIKA
VIRUS VACCINE AMONG MIGRANT
LATIN AMERICAN WOMEN

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List of abbreviations

ANC	Ante-Natal Care
CDC	Center for Disease Control and Prevention
CHKV	Chikungunya Virus
CNS	Central Nervous System
CZS	Congenital Zika Syndrome
DENV	Dengue Virus
ECDC	European Centre for Disease Prevention and Control
GBS	Guillain-Barré Syndrome
GT	Grounded Theory
HBM	Health Belief Model
HPV	Human Papillomavirus
IDI	In-Depth Interview
IgG	Immunoglobulin G
IgM	Immunoglobulin M
PHEIC	Public Health Emergency of International Concern
RNA	Ribo-Nucleic Acid
RT-PCR	Reverse-Transcriptase Polymerase Chain Reaction
TPP	Target Product Profile
U.S.	United States
WNV	West Nile Virus
WHO	World Health Organization
ZIKV	Zika Virus

Executive summary

Background

The rise of Zika virus (ZIKV), from an almost unknown pathogen to a recognized cause of microcephaly, led to 3.500 children born with birth defects since 2015. In order to guide targeted public health campaigns and to design disease control strategies, qualitative research is necessary to assess ZIKV knowledge and perceptions of populations at risk, namely women of reproductive age. In the next few years a vaccine is expected to be available, and discerning the best messaging to promote vaccination is crucial.

Objectives

To gain understanding on the knowledge, perceptions and attitudes towards ZIKV infection, and to assess the hypothetical willingness to receive a ZIKV vaccine, if this would become eventually available.

Methods

Using Phenomenological and Grounded Theory approaches and through In-Depth Interviews, this study conducted between December 2018 and June 2019 explored the lived experience of 11 migrant Latin American women living in Catalonia, who were followed-up during pregnancy, following a diagnosis of confirmed or probable Zika infection.

Findings

Most participants knew mosquitoes can transmit ZIKV, but only a few mentioned that the virus could be spread from a sexual partner, or how often those infected were symptomatic. All participants identified microcephaly as the only negative Zika outcome. While in areas of ZIKV exposure, precautions taken to avoid infection were dependant on their perceptions of both risk and severity of the infection. Almost all women would agree to vaccination against ZIKV, if available, as the vaccine was perceived to protect their babies.

Conclusions and recommendations

These results help in identifying knowledge gaps and misconceptions on ZIKV and may be useful to inform and design improved community-based preventive interventions related to Zika. Additional efforts are needed on education about ZIKV disease and prevention, as well as information and support during medical follow-up of those infected. Our results will also guide future research and interventions focusing on overcoming vaccination barriers.

1.Introduction and background

Zika Virus and infection

Zika Virus is an encapsulated, spherical particle, RNA virus. It is a vector-borne virus whose natural transmission cycle involves mainly mosquitoes from the *Aedes* genus (*A. aegypti* being the most important), and monkeys, while humans are just occasional hosts (1). It is classified in the family *Flaviviridae*, genus *Flavivirus*, as other mosquito-transmitted and tick transmitted arboviruses that are considered human pathogens: Dengue Virus (DENV), Chikungunya Virus (CHKV), West Nile Virus (WNV), Yellow Fever Virus, and others (2). Although some of the diseases that flaviviruses cause have been known for many years, recent important outbreaks and the relative facility with which some of them have been introduced into new environments highlight their potential impact to human health, concentrating extensive research efforts (2).

In most cases, ZIKV infection causes a self-limited illness with mild symptoms. The most frequently reported symptoms are skin rash, fever, headache, arthralgia, myalgia, non-purulent conjunctivitis referred by the patients as “red eyes”, and lower back pain (3). The incubation period of the infection ranges between 3 and 12 days. Because of the mild nature of the disease, about 80% of ZIKV cases remain unnoticed, posing a challenge to surveillance and case tracking systems. This spectrum of symptoms of ZIKV disease overlaps with those from other arboviral infections such as Dengue and Chikungunya, but maculopapular, immune-mediated skin rash typically predominates as a characteristic for the differential diagnostic of ZIKV infection, even though it is not present in all cases. (4).

ZIKV is also transmitted from mother to foetus during pregnancy, through sexual intercourse, transfusion of blood and blood products, and organ transplantation. Because of its neurotropism –it shows great affinity by brain tissue-(5), ZIKV has been linked to a high incidence of acute neurological conditions such as meningitis, Guillain-Barré Syndrome (GBS) and Congenital Zika Syndrome (CZS) (6).

Historical evolution of an apparently inoffensive virus

Initially identified in 1947 in a rhesus monkey at the Ugandan Zika forest, for 60 years, interest in ZIKV was mainly confined to a few specialised researchers (1). Despite studies showing generalized human exposure in Africa and Asia, Zika fever was not a disease of special concern to humans because only 14 cases had been officially documented globally (5).

But in 2007, for the first time a substantial ZIKV human outbreak was declared in the Micronesian island of Yap located in the western Pacific Ocean (7). Although it was first confused with DENV, confirmatory tests analysing RNA were positive for ZIKV. In fact, this was the first time that cross-reactivity with other flaviviruses was suggested (5).

Mosquito transmission was the only known infection route until 2015, when sexual transmission of ZIKV through semen was proven to be a non-vector route of infection (8).

Disease Control and Prevention (CDC) issued guidelines for the prevention of sexual transmission of ZIKV, applying to all men who had travelled to or resided in areas with active ZIKV transmission and their female or male sex partners (12). The alarming scale of the epidemics and the potential for global transmission of this virus heightened awareness of this emerging disease.

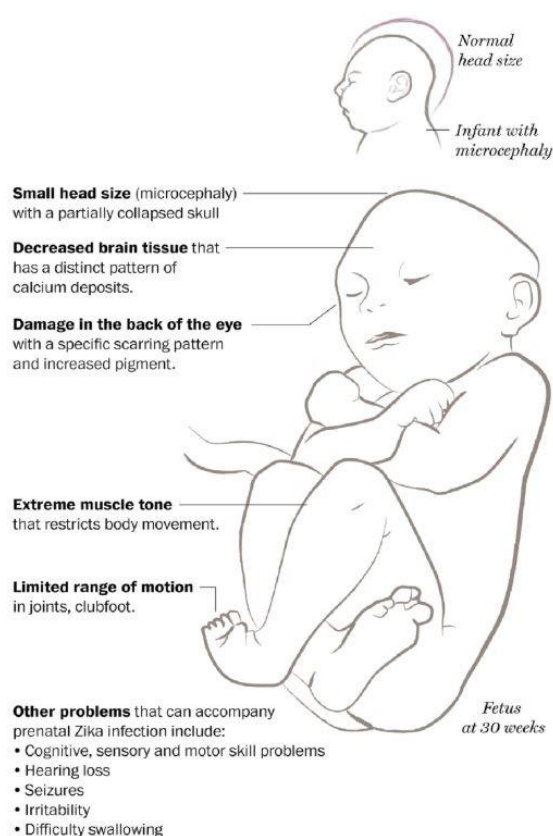
Impact on foetal and infant health: microcephaly and Congenital Zika Syndrome

This epidemic had diverse impacts on population health. Although ZIKV infection often leads to mild or no symptoms, the emergence of ZIKV in America coincided with an abrupt increase in the number of cases of GBS, and to an unexpected peak in the number of newborns with neurological complications and severe congenital malformations such as congenital microcephaly (9).

Although the first reports on the increased occurrence of microcephaly were met with scepticism by some experts (13), several studies evidenced its relationship with ZIKV infection (14). This convinced the Brazilian Ministry of Health (MoH) to declare a national public health emergency in November 2015, followed by the decision by the World Health Organization (WHO) on the 1st February 2016 to declare a Public Health Emergency of International Concern (PHEIC). Alarming enough, during the epidemic phase and until 2018, the total number of microcephaly cases that followed this outbreak was 20 times higher than baseline levels. ZIKV also led a 2-fold to 3-fold increase in the incidence of GBS. Nowadays, the international community is aware that the impact of ZIKV infection is much different from that of other flaviviruses (3).

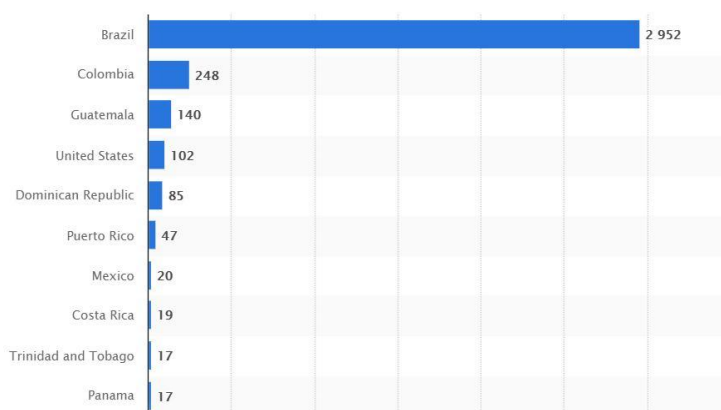
It has been demonstrated that ZIKV crosses the placental barrier and presents tropism by the nervous system (10). For this reason, ZIKV infection in pregnant women can provoke a vast spectrum of consequences, including placental damage, intrauterine growth restriction, microcephaly, miscarriage and foetal death (15). Those were reported in a higher proportion in cases of ZIKV infection during the first trimester of pregnancy, when the virus has greater circulation. Much of the concern regarding the teratogenicity of ZIKV infection has focused on microcephaly. However, there are a variety of brain abnormalities that can be found in fetuses exposed to intrauterine ZIKV infection. In fact, microcephaly is not an outcome but a consequence of several brain lesions with severe intracranial volume loss named “Congenital Zika Virus Syndrome” (10). A recent review concluded that CZS differs from other congenital infections for its five distinct features shown in Figure 2 (16). From the beginning, diagnosing and managing CZS through imaging during pregnancy presented a challenge for health professionals (14).

Figure 2: Clinical features of Congenital Zika Syndrome in newborns.
Source: CDC



During the 2015-2016 epidemics, it is estimated that up to 10% of babies born from mothers infected in the gestational period have any kind of birth defect. Hearing loss and abnormal eye development with important consequences on vision were the most common (3). As per microcephaly, the estimated incidence was estimated in 2.8 per 100.000 live births in Brazil. In total, almost 3.000 newborns only in this country (5). (Figure 3)

Figure 3: Number of confirmed cases of CZS in the Americas as of January 2018. Source: Statista.com

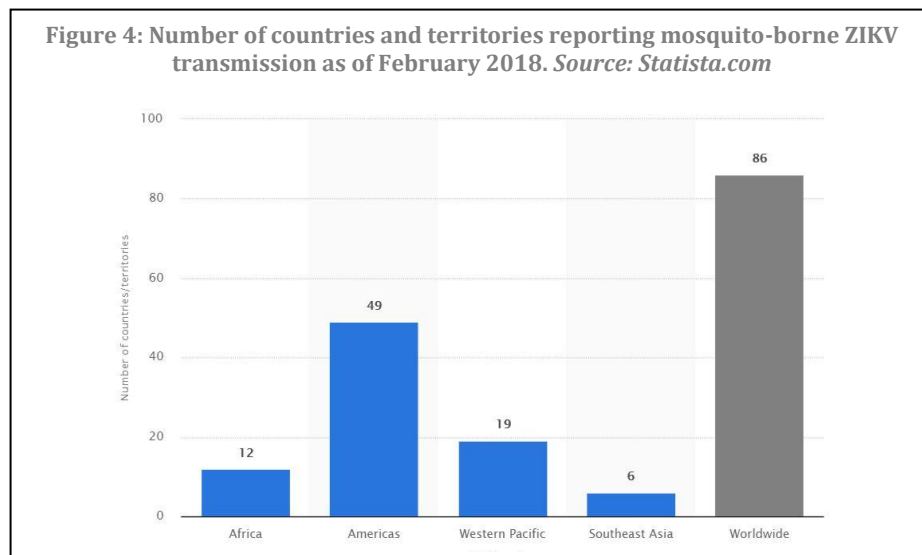


In addition, recent research has suggested that postnatal infection in young children may also lead to neurological problems, and even the appearance of postnatal microcephaly has been described in humans and macaques (17). In the first 2 years of life the brain is still in development and the tropism of ZIKV could have unknown consequences. These findings suggest that our knowledge of the implications of ZIKV infection in babies is incomplete and a question in need of an answer. Long-term developmental defects of children born in the time of Zika are current topics of study (18).

Before the end of 2016, WHO called an end to the PHEIC (19). Most of the affected countries had a substantial decline in the number of cases in 2017, going from a weekly infection rate of more than 25.000 in 2016 to less than 1.000 in May 2017. Birth defects associated with ZIKV also decreased by over 50% (6).

Nevertheless, presently, local cases of ZIKV infection are still being reported in at least Brazil, Colombia, Peru, Bolivia, Mexico, Guatemala, El Salvador, Puerto Rico, Thailand and Singapore. As the European Center for Disease Control and Prevention (ECDC) has noted, the limited ZIKV surveillance capacity in many areas of the world provide us with a significant level of uncertainty about the extent of current local transmission (20). The last statistics on reported ZIKV cases can be seen in Figure 4.

Moreover, the future of Zika disease will be determined by the duration of serological protective immunity after infection, that remains unknown, and the potential effect of the antibodies of other co-circulating flaviviruses (11).



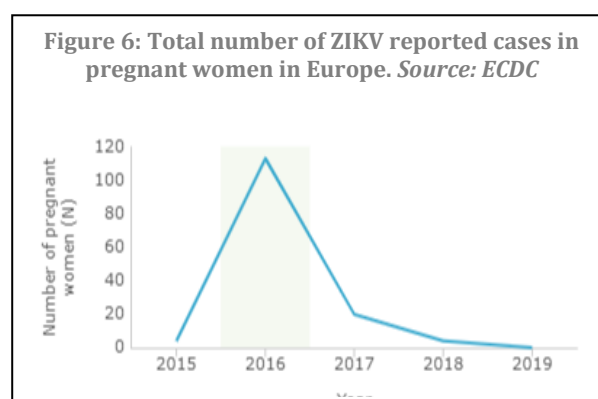
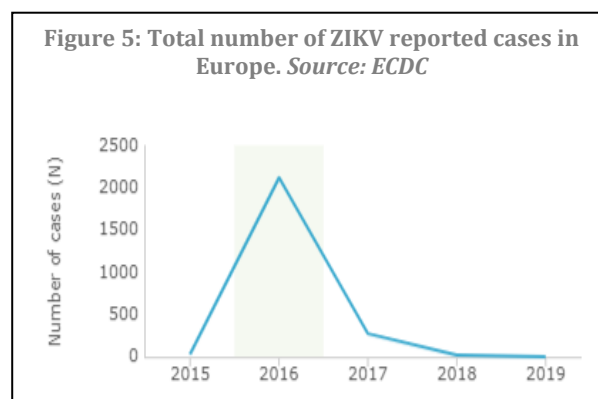
Risk and impact of ZIKV in Europe and Spain

While ZIKV rapidly spread in the Americas, imported cases among travellers and migrants have also been reported in non-endemic countries. An initial risk assessment by the WHO announced that the risk of an outbreak of ZIKV in Europe shall not be underestimated. In some continental parts of the European Union, including Spain, there are two mosquito vectors that have been shown to be competent for ZIKV in laboratory studies: *A.albopictus*

and *A.japonicus*, while the main vector *A.aegypti* is present in the Portuguese island of Madeira (21)(22). Mosquito-borne autochthonous outbreaks of CHKV, DENV and WNV in Europe have already occurred, confirming that this possibility exists (20).

Another reason for concern was that ZIKV RNA can stay in semen for several months in both symptomatic and asymptomatic men, and potentially sexually transmitted (23), although recent modelling studies have shown that sexual transmission wouldn't be enough to sustain an outbreak in such a context (20).

Accordingly, the ECDC quickly implemented epidemiological surveillance of ZIKV infection in 2016, following the PHEIC declaration. Between June 2015 and April 2019, 2,398 confirmed cases of travel-associated ZIKV infection (Figure 5), with 139 confirmed cases among pregnant women (Figure 6), were reported in 22 European countries (20). France reported 48% of the cases, Spain 15% and the UK 9%. In addition, 25 sexual transmission infections from returning travellers to their partners have been reported in 8 European countries, representing 1% of the totality of infections. Spain reported 512 cases of ZIKV infection –almost all coming from the Americas-, among which 86 were pregnant women (24). Finally, from November 2018 until present, still 7 imported cases have been notified in Europe (20).



Prevention of ZIKV in Europe has been challenging given that the vast majority of cases are imported and, apart from travel health clinics, there are limited opportunities to provide prevention advice to target populations. Efforts were done to strengthen travel health advice before peak travel periods, particularly targeting pregnant women and their partners (25).

Ascertainment of Zika cases: a diagnostic challenge

All along the epidemic, access to effective diagnostics was essential to understand its magnitude, but those were not available and its development was greatly delayed by the low access to samples and materials (4).

During the acute phase of the disease the virus can be isolated in blood (up to 7 days after the onset of symptoms), urine (up to 20 days after), semen, vaginal secretion, saliva, cerebrospinal fluid, amniotic fluid, placental tissue, and breast milk (5). An accurate laboratory diagnosis of ZIKV infection requires combining molecular testing to detect this viral RNA, serology, and clinical and epidemiological criteria. Serology interpretation is complex due to extensive cross-reactivity with immunoglobulin M (IgM) and immunoglobulin G (IgG) from other flaviviral infections and previous vaccinations. As almost all countries affected by the epidemic were also endemic for DENV and CHIKV, infected individuals may have high levels of antibodies to multiple flaviviruses that impede conclusive determination of the virus responsible for the most recent infection, since some antibodies persist at detectable levels long after the end of each infection (26). Moreover, DENV and CHIKV present similar symptoms to those from ZIKV infection, so clinical confirmation based on symptoms is challenging. Not to mention the fact that most of the infections are asymptomatic. This is especially an issue for pregnant women for whom proper diagnosis of a ZIKV infection, even if asymptomatic, is crucial (27).

Socio-economic impact of ZIKV

The consequences of the epidemic in the Americas surpassed its epidemiological impacts and suppose a financial burden for affected nations. The United Nations Development Program calculated an economic impact of 7 to 18 billion dollars; 1.2 billion accounting for direct medical and productivity losses (28).

Other social and economic impacts are of a late-arriving and long-lasting nature. Fear struck Brazilian maternities since ZIKV was linked to brain damage in newborns. As most ZIKV cases caused no noticeable symptoms, women had no idea if they had been infected during or around pregnancy, which could have led to increased levels of anxiety and psychological suffering (29).

Presently, thousands of children in Brazil are living with impairments caused by congenital ZIKV infection. Although its long-term consequences are still unknown, it is becoming clear that many of these children will require continuous and specialized care from clinicians and from their caregivers, usually the family. Mothers of babies born with microcephaly suffered from anxiety and depression according to a study in Brazil (29). This impact will be even more pronounced since CZS disproportionately affected poor communities. Deficiency and poverty are elements that interact with one another. This will remain a social sciences study topic as long as those children grow-up.

The gender perspective of ZIKV infection and its consequences

Mothers included in the mentioned Brazilian study (29) were mostly single, with low income and living in rural areas. This was a pattern of the majority of the mothers with babies born with microcephaly in many of the affected countries in Latin America; about 83% of affected babies in Brazil were born from non-white women, whereas only about 50% of the female Brazilian population is non-white (30). The level of information received and related knowledge about the disease, healthcare seeking practices and access to health services was limited in several cases. On the other hand, mothers are, in many cases, the main caregivers of the affected newborns; their physical autonomy, capacity to work, generate income and earn financial autonomy has been severely limited (31).

The structural gender inequalities in Latin America are well documented (32). Women often are not in control of their reproductive decisions. The most affected areas by ZIKV often had limited access to reproductive health services, so antenatal care (ANC), contraception counselling and services -including emergency contraception-, safe abortion, and post-abortion care were out of reach for many (33).

In addition to that, in 2015 many affected countries had restrictive abortion laws, making safe abortion completely illegal or very difficult to access. In most of the countries, the epidemic did not change the voluntary abortion landscape in any relevant way. In Brazil it was the opposite: a law was introduced to increase jail sentences for women seeking abortion “due to microcephaly or other foetal anomaly”(34). In other affected countries, unrealistic official recommendations left the woman solely responsible to avoid infection. For example, in El Salvador and Colombia, countries with high incidence of sexual violence inside and outside the couple, authorities recommended sexual abstinence to women as preventive measure (31). These kinds of policies don't address some of the root causes of ZIKV and instead compromise women's reproductive rights.

Preventive strategies for ZIKV: current landscape

Although the number of ZIKV cases has dropped since 2016, the efforts towards ZIKV treatment drugs and vaccine development remains strong, given the clinical importance of CZS and the potential for outbreaks to be contained through immunization. Re-emerging viruses like ZIKV with potential of creating a new epidemic are a threat in the 21st century where international travel open doors to viral epidemics (35). Those efforts have culminated in a long list of potentially effective drug candidates and a few ongoing clinical trials for ZIKV therapies from which 45 are vaccine candidates (36).

There are numerous challenges that the ZIKV vaccine development process is undergoing, such as the difficulty to find ZIKV-naïve individuals in endemic regions, the low incidence of ZIKV symptoms and sequelae than can make outcomes difficult to determine in clinical trials, and the co-existence of other flaviviruses such as DENV and CHIKV in the same geographical areas, incrementing the possibility that the cross-reactive immunity interferes with ZIKV vaccine efficacy or safety. In fact, increased replication of ZIKV has been reported in human placental tissue in the presence of DENV-specific antibodies. Therefore, ZIKV vaccine trials in DENV-endemic areas should consider the possibility that pre-existing DENV-specific antibodies may induce unpredictable reactions, similar to the

safety issues that recently occurred in the trial of Dengvaxia®, a new DENV vaccine that is currently under investigation for its link with about 600 child deaths in The Philippines (23).

Another topic not exempt of controversy is the inclusion of pregnant women in ongoing clinical trials, once safety has been guaranteed. Even though clinical research with pregnant woman is now considered ethically permissible, there is still reluctance to do it (37). The WHO Target Product Profile (TPP) for ZIKV vaccines identified women of reproductive age as the preferred target group for vaccination, potentially including pregnant women, with the aim to protect the foetus from infection during pregnancy (38). Not admitting pregnant woman in trials makes imperative to demonstrate that immunization is long-lasting, so once administered before pregnancy it would prevent CZS during the pregnancy (23).

Vaccine acceptability and its determinants

Vaccination is one of the most cost-effective ways of avoiding disease associated morbidity and mortality. Even today, about 1.5 million deaths could be averted each year through vaccination. However, evidence suggests that many people are sceptical of the development and approval process of vaccines (39). Extreme media attention, as that received by the ZIKV epidemic, can boost public concern about both the disease and the vaccine. This may increase the likelihood that people will refuse a ZIKV vaccine once it will become available and highlights the importance of exploring people's perceptions and concerns with qualitative research (40).

"Vaccine hesitancy" refers to a situation where people are doubtful about vaccinations or where they choose to refuse immunizations despite the availability of vaccination services. Lack of knowledge about vaccines is usually identified as a cause of vaccine hesitancy and concern about vaccine safety is one of its leading reasons (41). It has already been recognized by the WHO as a Major Public Health Threat for humanity. With a growing vaccine hesitancy movement and the news of Dengvaxia® adverse reactions circulating through media, general vaccine acceptance could be affected in other parts of the world with negative consequences on other vaccination programs (41). Vaccine hesitancy is not only a phenomenon concerning parents; it is also prevalent among other adults and pregnant women, due mainly to similar concerns about safety (42,43).

To achieve high vaccine coverage, clear information needs to reach the public (44). Targeted educational interventions in increasing the acceptability and knowledge of a future ZIKV vaccine could be built from results from preceding anthropological research studying the willingness to accept vaccination, and its reasons. As far as we know, there aren't any studies published assessing the acceptability of a hypothetical ZIKV vaccine in a European context or among previously infected people in a non-endemic region. Considering the potential of ZIKV to become a global threat for a second time, and that the mobility of populations is an important factor for the transmission of the virus, it is crucial to understand if people living in non-endemic areas but with regular contact with them, such as Latin American migrants, would perceive a necessity of getting immunized in the case that this ZIKV vaccine existed.

Public health campaigns and the importance of health promotion and education

Due to the lack of vaccines and treatment for ZIKV, public health experts in the affected countries accentuated non-pharmaceutical interventions to reinforce prevention and with the aim of reducing density of mosquito populations, risk of transmission, and the likelihood of birth defects (45). Successful environmental strategies included insecticide spraying and bed net distributions, whereas recommendations on behavioural strategies (mosquito repellent, minimal skin exposure, or condom use) were also widespread. In addition, clinical strategies were adopted in some places promoting availability of reproductive health services and increased access to ZIKV testing.

In addition, as a consequence of the WHO declaration as a PHEIC, country-specific recommendations were made to pregnant women and women of reproductive age. Those advices included to avoid travelling to affected countries, to use condom with partners returning from affected countries or to delay pregnancy up to 2 years (9).

The introduction of several qualitative and quantitative research studies in the most affected countries helped to better understand community needs and guide public health outreach practices. For example, in 2016, the WHO released a survey of Knowledge, Attitudes and Practices (KAP) specific for Zika (46). KAP surveys allowed to quickly obtaining valuable information in order to tailor interventions to better address people's needs at community level, contributing to the overall public health response to ZIKV. This KAP was adapted and used in several ZIKV affected countries. In addition to KAP, other strategies such as smartphone-based surveys were crucial to inform measures and policies (47).

In other non-endemic settings, similar surveys were performed. Qatar, for example, is a country with chances of hosting a ZIKV outbreak. With a large expatriate community native from ZIKV endemic countries, in 2016 it also had presence of vector species and dozens of daily flights to countries with active transmission. Aware of the risks during the epidemics, the country surveyed migrant population and tried to assess the level of public awareness of risk factors and disease characteristics in order to successfully implement disease preventive programs (48).

Health information, media and risk perception

Nowadays, information on any disease or intervention, including Zika or a future Zika vaccine, can be found in the Internet and social media, not always coming from verified sources. For example, at the same time that ZIKV vaccine pseudo-scientific claims grew up, conspiracy theories about Zika being a bio-weapon, or being spread by the company Monsanto, emerged in the Internet together with the spread of the epidemics information (49).

As a matter of fact, the explosive growth of the Zika virus outbreak catalysed news media coverage, particularly during 2016. News and the media play an important role in the information the public receives during an infectious disease outbreak. Research has shown that the news media serves as an important mediator of risk information by highlighting or downplaying certain messages and influencing the volume of certain

messages about an event (50). This way, news can influence knowledge and perceptions of risk: what people understand about the virus and ways to protect from infection.

With this in mind, there is a well-studied relationship between how risk perceptions and perception of diseases shape behaviour. The Health Belief Model (HBM), for example, proposes that individual behaviour is directly shaped by perceptions of risk. Perceptions of risk and knowledge are linked to the sources of information from which they come from, and consequently people concerned enough about a disease are probably more likely than the average to adopt health behaviours (51).

Zika-Preg study and QUAZIK study

Spain has a dynamic migrant population from Latin America and the Caribbean who frequently travel to their countries of origin to visit friends and relatives (52). In 2018, 816.000 residents in Spain were native from those regions, accounting for the biggest Latin American population in Europe. Among them, Ecuador, Colombia, Bolivia and Dominican Republic, where ZIKV had the most devastating consequences, were the most represented immigrant nationalities (53).

It has been studied that migrants visiting their home countries are less likely than tourists to ask for travel health advice, and therefore to adopt preventive behaviours during their stay, representing an important entry point for ZIKV in Europe (54). With that in mind, surveillance systems in Spain were under alert during the peak of the Zika epidemics. According to the official guidelines issued by the Catalan Public Health Agency in January 2016, all pregnant women who had travelled to high-burden countries during the 8 weeks preceding pregnancy or during pregnancy were referred from their regular ANC visits to reference hospitals and screened for ZIKV, regardless of the presence of symptoms. Screening was also done in case the sexual partner had travelled to endemic areas during the 6 previous months. In Catalonia, two reference hospitals were in charge of ZIKV management: Hospital Clínic and Hospital Vall d'Hebron, both located in Barcelona.

Serological and molecular tests were used to diagnose the infection, but as it has been explained, accurate results were very difficult to obtain. Women were classified as confirmed ZIKV infection when RT-PCR tested positive, or probable ZIKV infection when ZIKV-IgM and/or ZIKV-IgG and ZIKV Plaque-Reduction Neutralization Test (PRNT) were positive (55). A more extensive explanation of the diagnostic algorithm can be seen in Figure 7.

A prospective cohort study, *Zika-Preg*, aimed at studying the clinical and epidemiological characteristics of pregnant women travelling to ZIKV affected areas, the risk of acquisition of ZIKV infection, and the effects on maternal and birth outcomes, was conducted by ISGlobal at the Hospital Clínic of Barcelona and Hospital Sant Joan de Deu (56).

Figure 7: Case definition for ZIKV infection from Spanish guidelines. Source: Marban E. Zika virus infection in pregnant women travelling to endemic areas: Results of a prospective observational surveillance study. Under peer Review. 2018

ZIKV infection	Case definition
Confirmed	Presence of ZIKA RNA in serum or urine by rRT-PCR Positive IgM antibodies against ZIKV confirmed by NT (titer >1/32) and negative IgM antibodies for DENV
Probable	Positive IgG antibodies against ZIKV confirmed by NT and negative IgM antibodies for DENV Positive IgM or IgG antibodies against ZIKV with low titers by NT (titers between 1/152 and 1/32)
Negative	Negative IgM and IgG antibodies against ZIKV Positive IgM or IgG antibodies against ZIKV discarded by NT (titer <1/152)

DENV: Dengue virus; Ig: Immunoglobulin; rRT-PCR: Real-time Reverse Transcriptase Polymerase Chain Reaction; NT: Neutralization Test; ZIKV: Zika virus

Pregnant women referred through the mentioned system were invited to participate in *Zika-Preg*. From January 2016 until December 2017, 195 consenting women were enrolled and followed as exposed, if they had a confirmed (n=4) or probable (n=40) test for ZIKV infection, and as unexposed, if their test was negative (n=151). Women enrolled in *Zika-Preg* were followed-up until delivery on a monthly basis, with the aim of detecting possible abnormalities in the fetus.

In 2019, the *Zika-Preg* study is still ongoing, with the offspring of ZIKV confirmed or probable cases being assessed for neurodevelopment and cognitive capacity during the first 2 years of life. So far, children born to those women had normal developmental assessments at birth.

During *Zika-Preg* follow-up visits, the need of further understanding how those women were living the experience motivated researchers to design an ancillary qualitative study: “A qualitative study on views, perceptions, and attitudes on Zika Virus, and acceptability of a Zika virus vaccine among migrant population and health professionals” (QUAZIK). This way, QUAZIK was born in 2018 with the aim to explore views, perceptions and attitudes regarding ZIKV in migrants from endemic countries, travellers from Europe to affected areas, and health professionals, and the theoretical acceptability of ZIKV vaccination among women participating in *Zika-Preg* with a positive or probable ZIKV infection diagnostic, but not only; QUAZIK study aims to study also their partners and some of the health professionals involved in their care and women never exposed to ZIKV.

This Master Final Project makes part of QUAZIK and will focus on the data collected from the women who travelled to endemic areas during or around pregnancy and had a confirmed or probable ZIKV infection.

2. Problem statement

While there is previous research about the socio-economic impact of ZIKV in the epidemic affected countries, social, economic, cultural and personal consequences of Zika in the affected patients are still to be explored.

Anthropological and qualitative research during outbreaks and in infectious diseases contexts in general are an essential part of effective risk communication and community engagement. They can help understand the social pathways of disease transmission and barriers to health seeking behaviour among the population, and to use socio-cultural approaches for responding effectively to an epidemic such as the ZIKV crisis (57). In this way, this investigation is an ideal opportunity to determine the perceptions of this particular population that might have the potential to influence future decisions on how to communicate diagnosis, preventive measures and an upcoming vaccine, as well as the management of the interventions planned.

ZIKV has not disappeared and it could potentially cause new outbreaks in the future. Previous research has found gaps in ZIKV knowledge regarding infection and preventive measures, both in endemic and non-endemic ZIKV countries (45,58–62). However, no studies have been found assessing patients' knowledge, perceptions and attitudes that would help understand if enough communication about the infection was effectively transmitted by health professionals and what was the perception of risk among Latin-American migrants returning from affected areas.

Equally, understanding vaccine acceptability in our study population is essential to help develop targeted information and vaccine promotion interventions both in their countries of origin and in Spain. From the few studies that have addressed this topic (51,63–66), none of them was done in a European context and with a study population of these characteristics.

3. Research questions

- How do migrant Latin American women in Catalonia that had a probable or confirmed ZIKV infection while pregnant perceive the ZIKV infection?
- Which are the strategies and supports that these women use to cope with the (confirmed/probable) diagnosis?
- What are the barriers and facilitators for the acceptability of a hypothetical ZIKV vaccine among this population?

4. Objectives

The purpose of this study was to expand the scarce previous research on Latin American women's perceptions and attitudes through assessing knowledge about ZIKV, and to study

the relationship between health beliefs about ZIKV and ZIKV vaccine acceptance, including their willingness to become vaccinated against ZIKV. This information is expected to be helpful in understanding barriers and facilitators to healthcare provision as well as a future ZIKV immunization.

The specific objectives of this Master Final Project were:

- To further understand views, attitudes and perceptions towards ZIKV among migrant Latin American women that travelled to endemic areas and had a confirmed or probable ZIKV infection.
- To explore their acceptability of a hypothetical vaccine against ZIKV, and to identify factors associated with interest or refusal in receiving a future Zika virus vaccination among Latin migrant women that already passed the infection.

5. Methodology

Study design

For this study, a qualitative methodology was chosen to investigate how perceptions and beliefs about ZIKV can crucially shape the attitudes and practices of the study population towards healthcare. Qualitative research is in-depth research aiming to understand the experiences and attitudes of people, and why people think, feel, react and behave in the way that they do (67).

The study was based in Phenomenology, a qualitative approach that focuses in studying the structure of various types of lived experience (67). It was the method of choice because our study aimed to understand what an experience meant to a particular group of people; this way, it would be possible to gather detailed descriptions of their personal experience with the ZIKV infection which would be rich in detail, as well as their reflections. Furthermore, Phenomenology is particularly useful for examining topics which are complex and sensitive (67).

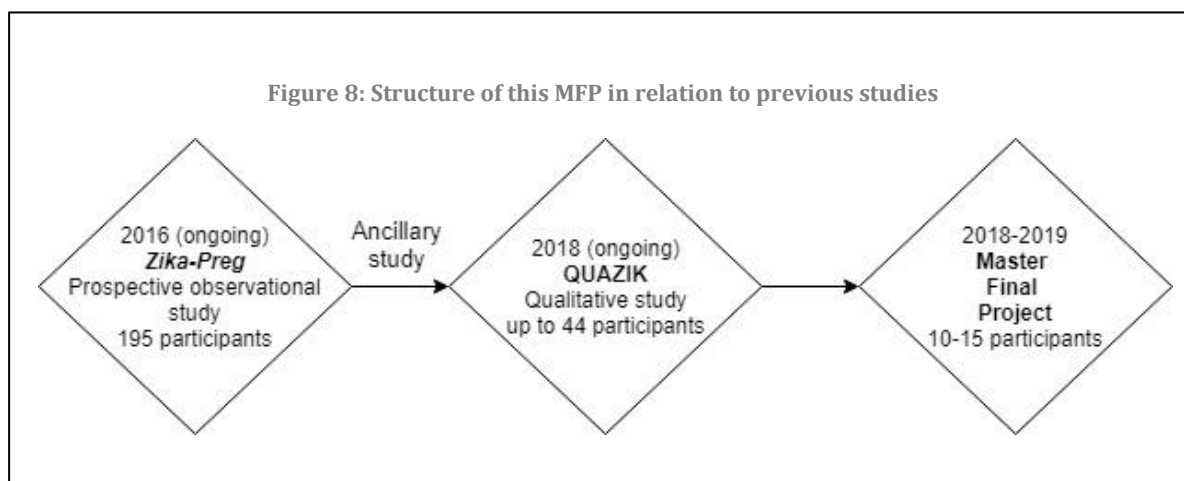
Grounded Theory (GT) approach was also used as a methodological approach and for the data analysis. The research began with no pre-existing hypothesis which allowed a theory to inductively emerge from the data, following a systematic set of data collection and analysis procedures. GT is widely used in qualitative research when no formal theories exist about the subject of study, or when there is no significant previous research. Therefore, the generation of the theory was based on comparative analyses among data collected from different participants, and pre-existing conceptualisations weren't used (68).

Study site and population

The study took place in the region of Catalonia, in Spain, between November 2018 and June 2019. Participants were selected from the cohort of women *Zika-Preg*, and

specifically from those with a diagnosis of confirmed or probable ZIKV infection. These women were exposed to ZIKV at some moment before or during their pregnancies.

This Master Final Project focused on studying the women from *Zika-Preg* among the three target groups that will be surveyed in QUAZIK (Figure 8)



Sampling

For this Master Final Project, a minimum sample size of 10 to 15 participants was defined based on similar studies' experience in reaching saturation (the non-addition of new substantive information after the continuous recruitment of more interviewees). Saturation point could be reached before or after the minimum sample size (69).

Purposive sampling, a preferred method in qualitative research, was used to only enrol those who were information-rich cases related to the phenomenon of interest (women infected with ZIKV during or before pregnancy) (69). Their knowledge, availability, willingness to participate and ability to communicate their experiences were crucial in conducting this study.

The only inclusion criteria for this study were to belong to *Zika-Preg* cohort, be older than 18 years old and willing to talk in detail about their experiences.

Recruitment strategy

Participants were contacted by phone and, if reached, invited to participate. Their contact details were made available to the researchers from the *Zika-Preg* study database. During the phone calls, the purpose of the study was explained in detail and researchers made sure that women understood the confidentiality and anonymity of the data collected, following the assumption that some participants may refuse to feel comfortable if they thought they were going to be interviewed and give feedback to the same team that followed their pregnancies and babies. Equally, this was later explained in person to minimize the risk of desirability bias, right before the signature of the informed consent.

Women that showed interest were asked to propose a preferred location and time for the interview. No compensation was provided to the participants.

Data collection

The data collection for this research started in December 2018 and finalised in April 2019. This data was collected in the form of In-Depth Interviews (IDIs). IDIs are a qualitative research data collection tool that involves conducting intensive individual interviews with a small number of respondents and using open-ended questions. They are useful to gather detailed information about perspectives, thoughts, feelings and behaviours on a particular idea or situation, especially on subjects for which little is known. Given the sensitivity of the topics under study, IDIs were the method of choice, assuming that the participants may feel comfortable and talk more openly than if they were in a group (as in Focus Group Discussions, for example).

For the interviews, a guide was developed, compiling the set of themes that needed to be discussed and explored to answer the research questions (Annex 1). This guide was reviewed as needed, when new themes arose from the already performed interviews; some of those new themes were incorporated to the interview guide when considered relevant.

The interviewees were encouraged to choose an interview setting where they felt comfortable and where the atmosphere would be silent. They were also asked to be - whenever possible- alone with the researcher(s), as to ensure privacy. Consequently, most of the interviews were held at the participant's house, except for those who explicitly expressed to feel more comfortable in a different setting. In the first interviews, a second researcher was present and taking notes, in order to better understand the reactions of the participants and improve the interview guide to ensure best quality of the data. Interviews from 45 to 90 minutes duration were conducted in Spanish, language in which researchers and participants were fluent or native. A digital audio recorder was used to register the interviews. Following each interview, additional field notes were taken, including brief comments on the participant interviewed and on observations made during the interview. All these field notes were used alongside the transcripts throughout analysis.

Data analysis

The audios of the interviews were transcribed using *verbatim* transcription method. This method consists on capturing each verbal sound in an audio recording into a text format, exactly the way it is delivered, including the pauses, non-verbal utterances and even silences. The purpose is not only to record the words or to attempt to capture the meanings and perceptions, but also to record the context in which it happened (67).

Later on, all transcriptions were quality-checked by a second researcher and discrepancies were discussed to ensure integrity of the data.

Data was thematically coded using the software Dedoose®, specialised in qualitative research analysis. The coding was done in agreement between two researchers. This

coding process consisted in the identification of passages of text related to the topics of interest to the research questions and the labelling of those with codes and sub-codes. A specific particularity of GT is that collection and analysis of data occur simultaneously as part of an iterative process and the technique of constant comparison (68). The researcher can only discover what themes to explore next by first coding the initial data and then looking for patterns and relationship between those patterns by which to saturate the emerging codes. Therefore, as more interviews were performed and their transcripts were gradually imported into the Dedoose® project and read meticulously, codes were refined, added or eliminated, depending on their pertinence to the research questions, the already coded data and the emergent data. By grouping text that was coded similarly, themes were constructed and compared and the main conclusions emerged.

Ethical considerations

Acknowledging the sensitivity of the topic under investigation, a special caution was placed in ensuring that all potential participants received comprehensive information on the study, including potential risks and benefits.

Participation in these interviews involved minimal risk. Nevertheless, discomfort could be caused by the recall of the hard situations lived and the emotional stress encountered in the period of the experiences with ZIKV.

The study protocol for QUAZIK study was approved by the ethical committee of the Hospital Clínic of Barcelona (HCB/2016/0250) (Annex 2). Written informed consent was obtained from all participants (Annex 3). All data were managed only by the main researchers and based on unique identification numbers so as to guarantee its confidentiality and the participant's anonymity. All study documents in audio and digital format were protected with a password only known by the researchers. Equally, in the interview transcripts, all names or details that could compromise anonymity were coded, eliminating any possibility of identification of the source.

This Master Final Project complies with the Consolidated Criteria for Reporting Qualitative Research (COREQ) checklist (Annex 4).

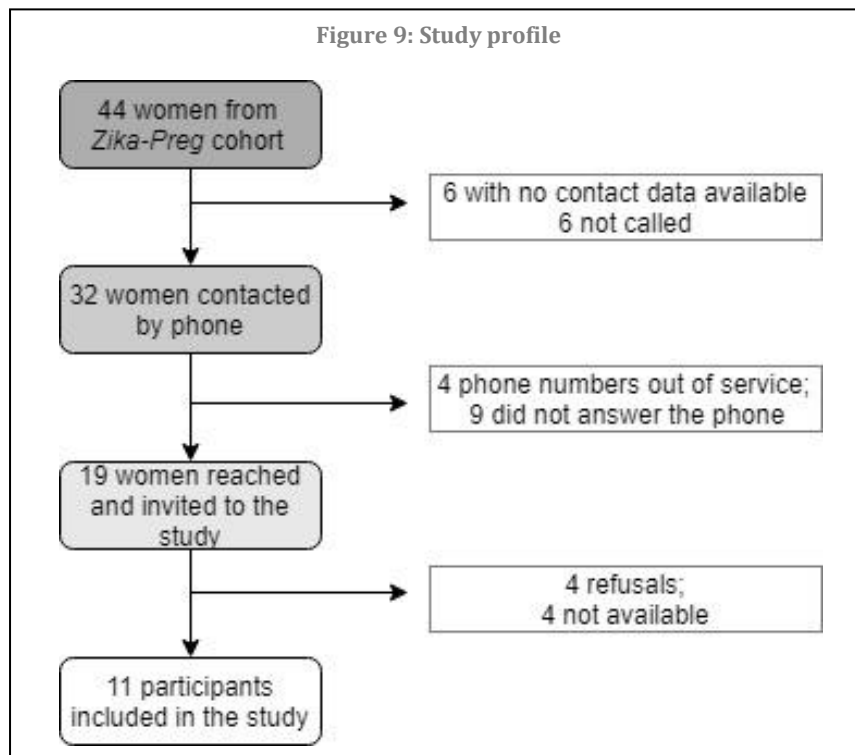
Work plan

Given the qualitative nature of this Master Final Project, it was required that 2 researchers worked together in the data collection, management and analysis. By doing so, integrity and quality of the data was assured. For this purpose, the author of this work was integrated in the QUAZIK research team and collaborated with the study coordinator in all stages of the study performed until this date (June 2019), including development of SOPs data collection tools, the data collection and quality control and data transcription and coding with Dedoose®. QUAZIK study was granted in 2018 and began implementation in November 2018. IDIs with other *Zika-Preg* women, their partners and health professionals are still ongoing.

6. Findings

Of the 44 eligible participants -women from *Zika-Preg* cohort-, 6 did not have a telephone contact available. Among the 38 with a telephone number, 19 of them were contacted and invited to participate, 13 were contacted but not reached and 6 were not called due to time constraints. For those who could not be reached, 4 telephone numbers were no longer in service, and 9 were called several times with no response or with the voicemail as only answer.

Eight contacted women didn't participate in the study, for diverse reasons. Three of them accepted in first place but later canceled the interview appointment. Another woman explained that she was interested but she had no time, and four women refused the proposal. Among those four, one of the women declared not feeling comfortable recalling her experience because of the suffering lived.



The final number of participants enrolled and interviewed was 11 (see Figure 9 for study profile). All of them were women between 22 and 42 years of age living in Catalonia (Spain). Most of them were married (9/11) or in a stable relationship (2/11). The predominant nationalities of the participants were Dominican Republic (4/11) and Honduras (4/11). All the participants had completed, at least, primary education in their home countries, whereas more than half were unemployed (6/11). Six of them declared professing Christian religion. The average time living in Spain was of 9.8 years, with a minimum period being 3 years and the maximum being 18 years. Six women were primigravidae at the time of exposure to ZIKV infection. Of the 11 women, 2 of them

declared that they were pregnant during the interviews. Of note, only one of the women had a confirmed positive test for ZIKV, whereas the others were probable (not confirmed) cases for ZIKV infection.

A summary of their socioeconomic characteristics and data related with ZIKV is shown in Table 1:

Table 1: Socio-economic and baseline characteristics of the study participants.

Age (years)	N	%
<22	0	0
22-28	3	27,3
29-35	6	54,5
36-42	2	18,2
>42	0	0
Level of education	N	%
Primary	1	9,1
Secondary	4	36,4
Profesional training	1	9,1
University incomplete	2	18,2
University completed	2	18,2
Unknown	1	9,1
Occupational status	N	%
Unemployed	6	54,5
Employed	5	45,5
Religion	N	%
Christian	7	63,6
Atheist	1	9,1
Unknown	3	27,3
Marital status	N	%
Single	0	0
De facto relationship	1	9,1
Unmarried but living together	1	9,1
Married	8	72,7
Unknown	1	9,1

Number of children at the time of the interview	N	%
0	0	0
1	6	54,5
2	3	27,3
3	2	18,2
>3	0	0
Country of origin	N	%
Brazil	1	9,1
Colombia	1	9,1
Dominican Republic	4	36,4
Honduras	4	36,4
Venezuela	1	9,1
Time living in Spain (years)	N	%
less than 3	0	0
3 to 10	5	45,5
11 to 16	3	27,3
more than 17	2	18,2
unknown	1	9,1
Country of ZIKV exposure	N	%
Brazil	1	9,1
Colombia	1	9,1
Dominican Republic	4	36,4
Honduras	4	36,4
Venezuela	1	9,1
Parity during diagnose	N	%
Primigravidae	5	45,5
Multigravidae	6	54,5
ZIKV infection	N	%
Confirmed	1	9,1
Probable	10	90,9

To note, the presented quotes from the participants have been translated from Spanish to English by the author of this MFP.

How do women who travelled to ZIKV endemic areas while pregnant and had a probable or confirmed ZIKV infection perceive the ZIKV infection?

General views and perceptions about Zika

During the interviews, all participants were aware that Zika is an infectious disease that can be transmitted. Most of them (6/11) pointed out that it is caused by a virus and said that everyone is susceptible to acquire the infection. While one woman alluded to the possibility of the disease being caused by the spread of an insecticide by the company Monsanto, another confessed that for a long time she questioned the existence of the disease:

“It was on the news and my grandmother said «do you know there is a disease called Zika?». And I said: «and what is that?». She said: «it harms pregnant women’ foetus, causes pain in the bones, pain, fever, red eyes... ». I said: «that is nonsense... Honduras is crazy! (...) you are imagining diseases». Because it [Zika] is a weird name... (Honduras, 33 years old, 12 years in Spain)

It was also said that the disease was only present in some countries: many participants named their home country as endemic, while a few (3/11) also mentioned Brazil as the place where the disease was striking strong. One participant held the view that people living in Spain could also be at risk, because there are mosquitoes in Spain as well.

Transmission and prevention of ZIKV infection

Women were asked about the ways of transmission of ZIKV and preventive strategies against infection.

The majority of respondents (9/11) mentioned mosquito bites as one of the principal routes of infection. Consequently, most of them (7/11) explained that avoiding mosquito bites was a very important measure for prevention. To avoid such bites, using skin repellent and other house insect repellents were the most commonly remarked (6/11), while covering the skin was only named by one participant. A few also reported the use of mosquito bed nets (2/11). Approximately half of the respondents were aware that the same mosquito that transmits ZIKV is also responsible for DENV and CHKV transmission, but nobody mentioned the species of the mosquito that transmits those diseases, nor its diurnal biting habits. One woman claimed that “there is a mosquito called Dengue that gives you fever and can transmit typhus”.

Less than half of the interviewees (5/11) were aware that the infection can be transmitted through sexual contact. In this sense, prevention of sexual transmission of Zika was only discussed by some of the women who brought up this transmission route; almost all of them mentioned “using condoms” as an effective preventative measure (4/11).

Four participants expressed concerns regarding the existence of other possible ways of person to person transmission. They explained that they felt uncertain about them. Two of them mentioned airborne transmission, one named “sweat of an infected person”, while other just said “touching”.

"I don't know if it was my husband [who passed me the infection], since we were sleeping together. Sure, it may be that from the fever itself, as he was sweating, he passed it to me (...). I don't know. I mean, we were touching each other ". (Dominican Republic, 42 years old, 18 years in Spain)

Among other preventative measures alluded to by participants, most of them were in reality vector control methods for mosquito prevention and included: avoiding keeping standing water near the houses to reduce breeding sites (5/11), fumigating (1/11), cutting grass (1/11), and adding "mosquito poison" to water tanks –probably referring to the larvicide pirotaxifen- (1/11). A participant noted that vector control actions were beyond her own personal capacity:

"It is the mosquito, and you can't leave standing water... the water from the dogs, it has to be changed 3 times per day! Because if you don't, the mosquito throws the larvae there and so the mosquito reproduces there. So there [in my home country] people try hard not to leave things around... even in a bottle cap it [the mosquito] can put the eggs... So, you have to be very careful. But, I take care, my neighbour doesn't, there is where it grows! That's it!" (Brazil, 36 years old, 11 years in Spain)

Regarding ZIKV prevention misbeliefs, two participants held the view that maintaining household cleanliness would help to prevent the spread of the infection, while another said that hand washing and face washing were useful ways to avert ZIKV.

Symptoms of ZIKV

Almost all participants correctly and consistently named some of the most common symptoms of ZIKV infection, including fever (7/11) and body pain (6/11). Just a few of them also mentioned headache (2/11) and red eyes (2/11), while skin rash (3/11), the most appealing symptom of ZIKV infection, was mentioned by only one third of the respondents, specifically from those who suffered it. Other symptoms suggested were stomach disorders and oedema. One woman referred to ZIKV symptoms as "flu symptoms", and two respondents said that ZIKV doesn't give any physical presentation. When asked about duration of symptoms, responses varied, ranging from 1 to 4 days.

These symptoms were frequently compared to those of Dengue fever and Chikungunya infection without prompting from the interviewer. In general, it was said that ZIKV symptoms were supposed to be milder. The following quote of one participant typifies the description of the differences:

"(...) but there [in her country] Zika didn't get so much attention because it wasn't as painful as Chikungunya (...). Because there were people (...) that looked like zombies when they got that disease [CKV]. One could see them wandering, shouting because of the fever, with body pain, they couldn't walk... some people had to be carried to the health center (...). Yes, in that time we had Chikungunya but people reacted more like «well, Zika causes a little thing and that's it». (Dominican Republic, 42 years old, 18 years in Spain)

Contrarily, some of the participants declared that when they presented their own symptoms, those were so strong that they didn't think they got ZIKV but DENV or CHIKV. Indeed, a few of them still perceived this:

"I had body pain, fever, well, all that. All that that one gets with dengue, that's why we thought it was... it was dengue. Well, I still think I got dengue. Because with Zika, people said it was severe, but no... [in my case] it wasn't severe at all, and it lasted one or two days..."
(Honduras, 31 years old, 5 years in Spain)

"I woke up one day and told my mother «I can't bare this anymore, I have pain even in my soul», and I laid down... One gets pain in the legs, in the arms, everywhere! (...). It's terrible, it's a horrible time with the virus. But... I thought it was dengue!" (Brazil, 36 years old, 11 years in Spain)

Perceived risk of acquiring Zika

The majority of the respondents repeated during the interviews that they were not aware of the moments and ways in which they acquired their infections. The general belief was that they were bitten by infected mosquitoes although one suspected person-to-person transmission by direct contact with her partner.

Only a few women were using family planning methods during the time of infection and among those, some revealed that they were not using them correctly. As in all participants but one the purpose of their family planning was to avoid a pregnancy and not to avert sexually transmitted infections, the preferred methods within our participants were hormonal contraceptives.

Furthermore, women that got pregnant some time after being in areas of Zika exposure claimed that they were not aware of the risk related to a pregnancy happening up to 3 months after infection. Only one participant was informed of this particularity, but she thought the timeframe of risk was up to 2 months, as official guidelines and recommendations changed some times during the epidemics.

In the view of other participants, they only perceived risk once somebody they were close with got infected. Up to that moment, they didn't start using preventative measures.

"And from that day he [my husband] started having Zika symptoms (...) I promptly bought some repellent and, of course, with my pregnancy (...). Finally, one day after he got all his symptoms, I saw I had skin rash". (Brazil, 36 years old, 11 years in Spain)

The following quote from one of the participants threw more light on the low perception of risk reported by almost all women:

"I could not believe it... After all those years that we have been coming to Brazil and not had any problem... and I only got sick now that I am pregnant" (Brazil, 36 years old, 11 years in Spain)

Perceptions on ZIKV severity

There was almost consensus explaining that ZIKV is only a reason to worry if one is pregnant, since non-pregnant infected people don't suffer any bad consequences from the infection.

"(...) the true problem with Zika is pregnancy, when one is pregnant. It's almost not going to affect me [but the foetus]. Physically the disease is not going to hurt me at all." (Dominican Republic, 42 years old, 18 years in Spain)

Many held the view that a mosquito-borne infection causing birth defects was something "unimaginable" and "astonishing". This is reflected in the quote below:

"(...)what I thought is that it strikes you with... pain and all that but I never imagined that a "zancudo" [mosquito] I mean, something like Zika could lead to a child... born in a bad way. I never, never, never, thought of that" (Honduras, 24 years old, 3 years in Spain)

It was also said by a majority, that the infection can induce different manifestations in each person, or even not have any manifestations. However, one participant confessed that she never believed having the infection since she didn't have any symptom:

"I was surprised [when I got diagnosed], because... (...) as that [ZIKV] gives symptoms... I never had anything, just the normal. I got a lot of mosquito bites, yes, many bites. But wasn't even suspecting that [because of those bites]... until I started to have «deeper» tests done (...). I didn't know I had that [ZIKV], but it is normal, because actually I never had fever, or any discomfort. I never felt anything". (Dominican Republic, 32 years old, 18 years in Spain)

Zika infection treatment and health seeking behavior

When participants shared their understanding of treatment for Zika, most women mentioned that "there is nothing that one can take to cure Zika", thus that there is no treatment for the infection. Despite this, three participants named "paracetamol" and "ibuprofen" as useful remedies for overcoming Zika infection symptoms, specifically fever and pain.

At the same time, different healthcare seeking actions during infection were reported. Two participants went to private health facilities in their home countries and were diagnosed with Zika without a blood test. They said that, also in their countries, they received injections or had "injected a vaccine" from a health professional to relieve pain.

However, the majority of respondents that reported symptoms revealed having used home remedies or self-medication of non-prescribed painkillers, perceiving that their symptoms were controllable. One of them explained that she knew that she had to take that treatment because she was working at a pharmacy in that time and there were several health notifications coming from the Ministry of Health (MoH), while other simply followed her mother's advice. Furthermore, one woman referred taking coconut juice during the infection to keep hydrated and reduce fever, and a local remedy used in her home country (Brazil) with tree leaves whose name the author of this work is not able to

reproduce. She took them “because that is what we people take when we have dengue and fevers”.

Coping with the probable/confirmed diagnostic: resources, strategies and supports

Reactions and emotions following the diagnose

Due to their low perception of risk, the general reaction of all participants when they received a possible Zika diagnose in Catalonia was of “surprise”.

As for the lived experiences regarding their infection around pregnancy, the majority of the women disclosed that they experienced high levels of anxiety due to the uncertainty on the state of their foetuses. Emotion expressions such as “suffering”, “crying”, “fear” and “worrisome” were repeated during all the interviews. Some women expressed feeling “culpability” as if they could have prevented their infections and protected their babies from that risk. In some cases, those emotions would decrease with follow-up visits and positive messages from health professionals, whereas a few participants found this insufficient and searched relief by looking for more information.

Searching information about Zika

In fact, a general comment from many interviewees was that, despite there was available information about ZIKV and its associated risks, only at the moment when they got a Zika diagnose was when they started to get interest and actively look for more information about the infection and mainly, about the fatal consequences on the foetus.

“Because when one doesn’t need something, one does not explore about that, but when you need something... you examine it in depth” (Honduras, 24 years old, 3 years in Spain)

The majority of women confessed that they didn’t actively ask health professionals in detail about what they wanted to know about the infection and consequences, even though they perceived that having enough information would help them cope with anxiety. Contrarily, they said that in those moments their main source of information was the Internet (YouTube and internet forums were mentioned) and most admitted that they thought that the data they accessed had limited reliability. Many participants also relied on television to get informed about Zika. Some of them noticed that sometimes, that information mainly increased their levels of anxiety, due to the type of images and messages found of CZS.

“In Brazil there was this information about children that were being born «with eaten heads». Ah! That was what made me feel bad. I saw this on the internet and TV, yes. A lot of information on Venezuelan TV (...) Children were born like that. [I felt] so bad. You can’t imagine... But my husband used to tell me «why do you torture yourself?». And I said: «I am not torturing myself, but I want to know everything, everything, everything»”. (Venezuela, 33 years old, 10 years in Spain)

Sources of support

On the other hand, all women that had a partner or husband (10/11) at the moment of the presumed infection and pregnancy stated that they were the main source of emotional support. The majority also relied on family members living in Spain or in their home countries and had regular communications with them. On the other hand, a few women decided to hide their risky situation to their relatives in order to not worry them:

“My family, for example, I didn’t mention anything until I was sure that... that I didn’t have anything, that the final results were negative (...). Because this is something serious and I didn’t want my parents to worry about it. (...) I didn’t want to say anything until... until everything was good. Until I knew that everything was going fine” (Dominican Republic, 34 years old, unknown time living in Spain)

Only a couple of participants searched relief in friends and another two found very helpful the support provided by health professionals involved in their follow-up. One woman said that her Christian faith had been crucial to “overcome the harsh times”, because “God had put on her way people who could help her”.

Another way to cope with the situation for many women was to adopt a positive mindset, and to oblige themselves to believe that “in the end, everything was going to be alright”. In order to maintain this good attitude, having trust on their health professionals was told to be essential.

Under those circumstances, only one participant said that she had received psychological assistance through the public social services, as something that she was offered by her general practitioner. In contrast, other participants had thoughts about it but didn’t look or ask for this kind of support.

Thoughts about termination of pregnancy

Almost all participants discussed the topic of “termination of pregnancy” during the interviews, as something of what they had thought, discussed and/or got informed about, at a given moment of their pregnancies. The reason for this was exclusively the concern about the state in which their baby could be born, with a few mentions to the impact on the quality of life of both the child and the family.

“That is what I was struggling more with [during my pregnancy], the disease, that the child would come sick. Because I said: «bringing a... a child like that into the world, I think... my own opinion is that doing that... brings suffering». (...) I always... said so (...). It is mean to say that I am going to terminate a pregnancy but... bringing him to suffer...” (Dominican Republic, 42 years old, 18 years in Spain)

Despite this, only a minority said that they had felt a true desire to end the pregnancy at some point, and there were several comments about the regret that they felt for those thoughts and desires. In fact, most of them perceived that the mere act of thinking of terminating a pregnancy was a bad thing.

Acceptability of a hypothetical ZIKV vaccine among migrant Latin American women living in Catalonia

Participants were inquired about their perceptions about vaccines and about their willingness to receive a vaccine protecting against ZIKV, in the hypothetical situation that this vaccine existed and was available for the general public.

Views and perceptions on a future ZIKV vaccine

All women interviewed were aware of the preventive purpose of vaccines. They mentioned “prevention of health outcomes” and “to avoid bad consequences” as the biggest advantage of having a ZIKV vaccine available. There was unanimity in declarations of the will of keeping their baby’s health safe as the main reason for getting the vaccine, as well as avoiding the psychological stress that they had personally experienced. They felt that immunization in the future would give them, “more peace of mind” or “a sense of security and safety”.

In order to understand if the administration route of the vaccine could be a factor affecting the vaccine acceptance among the participants, they were asked about their preferences. There was no consensus regarding this topic. The majority of the participants said that they would prefer an oral vaccine, whether it would be in the form of tablets or drops. The reason mostly mentioned was fear to needles, but one participant explained that, in her opinion, it would be easier for men to accept to be vaccinated if the vaccine was administered as oral drops:

“Well, ideally [this vaccine] would target everybody because it is also transmitted through sexual intercourse. So that would be, ideally. And since I know that men don’t like needles, then a drop will do it, alright?”(Honduras, 31 years old, 5 years in Spain)

“I prefer oral (...) because I hate needles.”(Venezuela, 33 years old, 10 years in Spain)

Nonetheless, some of the participants preferred injected vaccines. It was said that injected vaccines are more effective since they go directly to the blood, and that it is something that is administered at once so it is less difficult to forget the doses.

“[I prefer] something that reaches. It’s like, I say, if you get an injection, then it reaches better because it goes more directly to blood, isn’t it? (...). I have panic to needles but I prefer it to go directly” (Honduras, 33 years old, 12 years in Spain)

Some others had no predilection about the administration route, and even declared that they wouldn’t want it to be a limitation for them to receive the vaccination, as the most important factor is effectiveness:

“I don’t care [about the administration route]. As long as it will help control the disease, I don’t care if it is drunk, if it is intravenous, whatever.” (Dominican Republic, 42 years old, 18 years in Spain)

“If there is [a vaccine] for Zika? Without hesitating. (...) Even if it [the needle] was long, super long....”(Honduras, 22 years old, 3 years in Spain)

Some of the participants talked about the moment in which they would prefer to be vaccinated. They expressed their desire to get the vaccine as soon as possible, before getting pregnant or in the first months of the gestational period, thinking that this would offer them better protection against negative ZIKV outcomes on their babies.

Regarding who should be vaccinated, the majority of the participants spoke as if the vaccine would be meant for female population only. Only two of the participants said that everybody, and not only women, should get the vaccine. One of them explained that the reason for this is that ZIKV can be transmitted through sexual intercourse.

The other informant defending universal vaccination claimed that mosquitoes are not only in ZIKV endemic regions:

"Well, everybody [should be vaccinated]. Because it's not like... because I come from there [her home country] and you don't, [it doesn't mean that] you can't get Zika. Because here [in Spain] there are mosquitoes too..." (Venezuela, 33 years old, 10 years in Spain)

Barriers and facilitators for ZIKV vaccine acceptance

Almost all participants felt positive about being vaccinated if a ZIKV vaccine was available at any time. They said things like "it's my obligation" and "if I can prevent problems, of course I would like to be vaccinated". Only one informant hesitated. She said that there was no point in getting the vaccine unless she was living in her country (Colombia) or in another endemic area.

The main reason explained for accepting a ZIKV vaccine was the positive, protective effect that this would have in the foetus. For example, one participant felt that given the majority of ZIKV cases in adults are very mild, the benefit of preventing the infection during gestation would have greater outcomes on the baby's health. Other said that she would get the vaccine without any doubt; she suggested that after living the infection during her last gestation "she was aware" of the consequences and this would make her accept the vaccination "with even more conviction".

One of the barriers mentioned by the participants was being pregnant at the time of vaccination. Indeed, the majority of the women interviewed declared that if they were offered the vaccine during pregnancy, they would think twice before accepting. Half of them expressed that the final decision would depend on the presence of ZIKV in their country of residence, whether it is Spain or any other, or on planning to travel to a place with a current outbreak.

Some of the participants also expressed concerns regarding the possible adverse effects of a ZIKV vaccine. It was mentioned that a key determinant to decide whether to get vaccinated or not would be being sure that it wasn't going to affect their pregnancies or cause any harm to their future babies. Things like "if there are no risks", "if it is completely safe for the baby" and "as long as the foetus is fine" were reiterated during the interviews. One participant also suggested that she would trust the recommendations of health professionals regarding vaccination in order to take the decision of being vaccinated.

At the same time, only a few participants claimed that they would accept a ZIKV vaccine during breastfeeding unconditionally. In fact, the majority said that they feared consequences on the quality of the milk or on the health of the baby and that they would need reassurance, but they would feel trust if they were told that the vaccine was safe, not specifying from whom should this message come. Nobody mentioned the possibility of stopping breastfeeding as a measure to counteract these concerns.

Equally important, nobody mentioned the cost of the vaccine as a reason to accept or not to be vaccinated.

7. Discussion

The results of this study represent an important contribution to the scarce available literature exploring knowledge, views and perceptions about ZIKV among Latin American women. At the same time, they provide a novel approach by describing a study population consisting on women that have experienced a confirmed or possible ZIKV infection during or around pregnancy, and specifically migrant women living in a European context where there is no current or past local transmission. It also represents an important contribution to global health by helping to understand if such perceptions and other demographic factors may predict an individual's acceptance of the future ZIKV vaccine. As the published literature on these topics in a Spanish or European context is inexistent, to our knowledge, comparisons with previous studies can't be done but with different study populations. The previously mentioned study in Qatar (48) is an example reflecting the importance of this kind of surveys among non-endemic countries with risk of imported transmission of ZIKV and even a potential for transmission of autochthonous cases, similar situation to that of Spain. In Europe, Spain is the country that reported the highest number of imported cases of ZIKV in pregnant women, followed by France and Belgium.

The background of the participants in this study is varied and complex; some of them were permanently living in the country of exposure to the virus and migrated to Catalonia just before or during pregnancy. Others had been living in Spain for many years and acquired the infection during a visit to their home countries. Therefore, it is difficult to find a pattern linking the information that they received and were exposed to and their actual views, perceptions and attitudes. However, all our participants were attended by the specialized services in the Catalan Public Health System as *Zika-Preg* study participants (56).

The results of this study reflect that although these women with an exposure to ZIKV were in general informed about mosquito-borne transmission of the virus, they frequently didn't know that the virus can be sexually transmitted. To point out, most of those women came from Honduras, a country where a knowledge assessment was performed in 2017 following a health education campaign, with similar results regarding sexual transmission of ZIKV among female population (70). Our findings regarding this particularly low level of knowledge on this key issue are also consistent with results reported in previous qualitative and quantitative surveys; two targeting pregnant women in Martinique (71)

and Virgin Islands (72) in 2017, another one exploring women of childbearing age in Brazil in 2016 (73), and one studying young Latina women in South Florida in 2017 (45).

Besides this, the correlation between knowledge about ZIKV vectors and attitudes on mosquito bite prevention in our results is worth mentioning. As the *Aedes* mosquito is a day biting mosquito, the use of bite protection measures during the day and especially at dawn or dusk would be a more appropriate action to prevent Zika than using mosquito bed nets at night, but none of the women mentioned this fact, as they didn't mention that ZIKV is specifically transmitted by this mosquito species. Few participants used skin repellent to prevent bites and only one used to wear long clothing for this purpose. Moreover, one participant expressed the possibility of the infection being transmitted in Catalonia, possibly referring to local mosquitoes that don't belong to *Aedes* genus. Similar results have been found in previous research targeting residents from Zika endemic regions, where perceived risk of infection was not considered to be different according to the mosquito species (47,74). Comparatively, it has been found that most of the participants didn't know at which moment they acquired the infection, as sometimes mosquito bites can go unnoticeable. In fact, in a study in Rio de Janeiro, only 38% of people with a suspected ZIKV infection remembered getting a mosquito bite (75), being this in good agreement with findings from the participants in our study.

Another important finding is that the majority of women interviewed mentioned only the symptoms that they personally had, and not the symptoms that are typically linked to the infection. For example, skin rash was just reported by 1 out of 11 women and never described as "itchy", although clinical studies have described this differential characteristic in almost all Zika rashes (75). When speaking about the perception of severity of ZIKV infection symptoms, there was a disconnection between the severity of symptoms reported by different participants, in comparison with other co-existing arboviruses such as DENV and CHIKV: some women saw ZIKV symptoms as milder, while others perceived they were more severe. This disparity of the severity of ZIKV symptoms is a fact (75), and as DENV and CHIKV were prevalent at the same time than ZIKV they may have had a masking effect and shaped people's perceptions about ZIKV manifestations. If our participants were asymptomatic during their presumed infections, some of them questioned having ZIKV, and among the symptomatic ones, others also questioned it because their symptoms were less or more severe than expected for ZIKV. No other studies have been found assessing perceptions of Zika symptoms among population that already passed the infection, but other previous research found this same disparity in terms of symptoms perceptions in the general population (59,75,76).

Always regarding preventive practices, knowledge on transmission of infections has been associated with adoption of preventative measures (59). But the existent evidence on the association between knowledge and perceptions and preventative practices against Zika is limited. For example, a study from 2017 in Brazil found that adoption of such practices was significantly associated with knowledge of Zika transmission among women of childbearing age (73). However, the findings of our study are inconclusive on this topic, as several participants were aware of the mosquito transmission and nevertheless they didn't take preventative measures consistently. The same applies in our results for the sexual transmission.

Perhaps what mostly shaped the adoption of preventative behaviour in our population of study was the perception of risk. As mentioned before, HBM suggests that the greater the perceived personal risk is, the more likely individuals are to take preventative measures (45). A study in Florida, where local ZIKV transmission was confirmed in 2016, compared the ZIKV preventative actions taken by inhabitants who perceived themselves to be at risk versus those who did not perceive to be at risk. The percentage of people that took preventative actions was much higher among those who perceived risk of acquiring the infection (77). In another study performed in a rural area of Dominican Republic with ZIKV endemicity in May 2017, women attending health services were surveyed regarding their basic knowledge, attitudes, and perceptions of ZIKV. It was found that only 51% of respondents thought that Zika was an important issue in their community, a relatively low perception of risk. Besides lacking basic knowledge on virus transmission, one third of participants didn't know how to prevent Zika, and over half of women surveyed didn't take any preventative action (47). In our findings, participants reported, in general, a low perception of risk before contracting the presumed infection. Notably, there was no pattern in the differences according to the place where they lived at the time of infection. Certainly, this low perceived risk had concrete implications on how participants dealt with the infection, both with prophylactic and curative actions.

In the past, differences in how people perceive risk of infection have directly impacted the effectiveness (or not) of public health campaigns (39). Several public health campaigns were deployed in the countries of origin of the participants of this study, to raise awareness about the infection and its consequences. Communication specialists and researchers agree that an important element of effective risk and crisis communication is informing about how people can protect themselves and reduce negative consequences of a crisis (50). But the basis of effective public health is not just a matter of information and communication. As some participants disclosed during the interviews, certain populations may have been aware of the risk they were facing but not able to access the suitable preventative tools, such as repellents or contraceptives. In fact, the assessment of the effects of the CDC Zika Prevention program in Puerto Rico (78) showed that, among all the measures taken, the distribution of Zika prevention kits had the greatest effect on the adoption of ZIKV prevention behaviours. Our findings suggest how poverty and lack of access to health services and tools have also been determinant for the control of the infection in endemic countries.

Most of our participants reported frequent stress and anxiety during their pregnancies, due to the uncertainty of the possible outcomes. Then again, all of them but one could not receive a definitive result about their Zika infection status, so they were medically followed-up as "positive". In those situations, receiving social support is essential to positively cope with such difficult moments and it has been demonstrated that it promotes psychological and physiological well-being (79). Evidence suggests that partner support is an established determinant of mental health. Moreover, receiving positive support from a partner during pregnancy has been linked to lower levels of depression and anxiety in healthy pregnant women (80,81). Our findings are consistent with this evidence, as women declared that the main source of relief during the medical follow-up was the support from their husbands and/or boyfriends. Additionally, it is remarkable that,

despite the levels of stress and anxiety reported, our study participants did not actively seek psychological counselling.

In order to deliver proper care to patients, health care providers need to do more than diagnosing and performing procedures. Communication is an essential component in all steps of the process. When it comes to the mental wellbeing of the patient, the need for concise, effective communication about the condition and the prognosis are always present in the health field. On the other hand, a consultation between a patient and a health professional could be the richest source of health information and education; an invaluable opportunity to transmit reliable information serving to counteract possible misbeliefs and pseudo-scientific claims, and alarming information that contribute to the already existing anxiety in this kind of patients (82). This research has shown that having access to sufficient and reliable information was crucial for our study population to live the medical follow-up and the tests that they confronted with a positive attitude. The most relied sources of information were health professionals and the media, with the Internet being the main one.

Therefore, the importance of health information and communication from the media when it comes to shaping our study participants' knowledge and perceptions is suggested in this study. It has been studied how information spread by the media can play a key role in influencing people's opinion, perceptions of disease and risk, in general and particularly for Zika. For example, in an analysis done about the information provided in the U.S. media about ZIKV and travel in 2016 and 2017 (83), almost all news stories mentioned mosquito-borne transmission but just over half mentioned sexual transmission, and they were more likely to talk about ZIKV outcomes than ZIKV symptoms. Moreover, that paper showed that outcomes affecting babies were mentioned more frequently than those affecting adults. Indeed, apart from foetus malformations, women in our study believed that ZIKV had no other major health consequences among adults; GBS and meningitis were never suggested or mentioned explicitly. Other previous studies had similar results on this topic (47,77). The immense media attention grabbed by CZS and the fact that CZS was the biggest concern for these women during their gestations may be some of the reasons for this. Identically, none of the participants could mention the ZIKV endemic countries but their own countries and Brazil, where the infection got the majority of the attention from the media because of the high number of babies born with microcephaly (3).

Because the diagnostic of ZIKV-related anomalies is difficult in the beginning of pregnancy, yet that moment is when abortion may be most accessible, women may decide to end a pregnancy based on their perception of risk. In fact, one study evaluated changes in online abortion demand in Latin American countries with ZIKV transmission, compared to 2010 levels (84). Results showed that in all affected countries there had been an increase of requests for abortion services of minimum 20%, reaching 108% in Brazil and Ecuador or 36% in El Salvador and Costa Rica. The results of those studies may provide an overview into how concerns and warnings about ZIKV may have influenced women's decisions about pregnancy (84). In contrast with that tendency, it would seem that our study participants coped with the diagnostic in a different way, given that, in general, they did not look for information or think seriously about terminating their pregnancies. This could

be due to several reasons, for example, many of them mentioned their strong Christian background as a barrier to think about a voluntary abortion. Other possible explanations could be the restrictive abortion policies in their countries of origin, the unfamiliarity with Spanish abortion legislation, or the high level of trust on the positivity of their medical follow-up that was generally reported, although our available data doesn't allow making conclusions on this sensitive topic.

Given the potential future vulnerability to ZIKV among Latin migrants that visit their countries regularly and the probabilities that a commercial ZIKV vaccine will soon be available, the second part of our study aimed to understand factors affecting vaccine acceptability in our study population, as an important step to help develop targeted information and vaccine promotion interventions. In an era of growing vaccine hesitancy and where some vaccination promotion campaigns are not succeeding as expected (42), research on effective pro-vaccine messaging is needed.

Previous research has studied willingness to get a hypothetical ZIKV vaccine in different target populations (45,51,85). For example, a survey among University students in the U.S. found that most of the participants were willing to receive such vaccination, with no significant differences by gender. Both increased knowledge about ZIKV and access to reliable information on ZIKV were identified as facilitators of willingness to accept a ZIKV vaccine (51,86). However, few studies have explored vaccine acceptability among women in risk of ZIKV exposure (51,85,87), and, to our knowledge, no previous research exists on women that already coped with an infection. This is a novel study assessing the interest in a ZIKV vaccine among this type of population.

According to the HBM theory, people's motivations to use vaccines would be influenced by their judgements about both the vaccine and the outcomes it prevents (86). One of the most notable findings from this study is that the majority of participants intended to receive a ZIKV vaccine. This may be related with an increased perception of risk and severity as a result of going through a presumed infection, as these participants were presumably more aware of the potential consequences on the foetus than other women that didn't live the medical follow-up. Moreover, almost all of our participants are still in childbearing age and declared to be willing to have more children. In another recent study in the U.S., risk perception and concern about acquiring ZIKV infection while travelling to a country with ZIKV incidence was found the only positive predictor of ZIKV vaccine acceptance, that was higher among female participants and specifically among those who were planning a pregnancy (65). On the contrary, knowledge of ZIKV symptoms in adults was a negative predictor of willingness to receive a ZIKV vaccine. This study was conducted in March 2017 when the peak of the epidemic was over, which could have influenced the results somehow (65). This fits well with the findings of our study. The same increased risk perception was also one of the facilitators found in this research, and, in general, the acceptance of a ZIKV vaccine would depend on the willingness of having more children in the future, but it was made clear that participants were not looking for a protective effect for themselves, but for their babies, since they perceived that ZIKV can not harm non-pregnant people.

Although our findings found some gaps in the level of knowledge about ZIKV among our participants, they were all very conscious about CZS and reducing the risk of CZS in a

hypothetical future pregnancy was the major vaccine acceptance facilitator in this study. Moreover, information and recommendations coming from health professionals have been identified as facilitators for the vaccine acceptance in our study, reflecting the high level of trust that these women have on medical teams. Frequent misinformation about vaccines in the media make even more important for health professionals to provide accurate information to their patients in order to increase vaccine acceptability. Studies have shown that when information provided by health professionals is insufficient, people might investigate other sources that may contain misleading information, or information that may be misinterpreted (88). This again helps to highlight the importance of effective health communication coming from health professionals.

On the other hand, our results show that the willingness to accept this hypothetical vaccination during pregnancy is lower than outside pregnancy. Overall, our results are in line with a recent literature review (42) assessing vaccine hesitancy and barriers for vaccination among pregnant women, where it was found that the main concern was regarding the safety of vaccines in pregnancy and their possible negative consequences on the foetus. According to this review, public acceptance of maternal immunization needs to be improved. A recent study in the United States (89) associated a high level of willingness to participate in a Zika vaccine clinical trial among pregnant women to the trust on safety evidence communicated by health professionals. In our study, once again, recommendations from health care workers to receive vaccination during pregnancy were reported to increase positive attitudes about vaccine effectiveness and safety, and, in consequence, to increase vaccination uptake.

Apart from pregnancy, another identified barrier to vaccination among our study population was the feeling of worrisome about needing to stop breastfeeding their babies because of the vaccine. Vaccines developed for maternal immunization often aim to provide passive immunity to the baby through the transfer of antibodies through the milk of the mother (90), so the concern of the participants in our study could be based in the belief that the virus and thus the infection could equally be transmitted through the milk. Similar concerns about the safety of breastfeeding after vaccination have been studied with Influenza vaccine offered to recently pregnant women (91) and therefore, it is a subject of special consideration for the vaccine development process.

Significantly, some participants agreed on the fact that, if available, a ZIKV vaccine should be administered to the whole population, regardless of gender and age. Specifically, this was proposed by women who were previously aware of the sexual transmission of the virus. It is undeniable that the consequences of a congenital Zika infection have repercussion in the whole family unit, even if the 2015 epidemic has proven that women bear the highest burden. The WHO TPP for the development of a ZIKV vaccine put the focus on women of reproductive age as target group for immunization, scaling it up to men and male adolescents if this would become possible in the future. Similar discussions have been going on around Human Papillomavirus (HPV) vaccine, which has the potential to prevent cancer mostly in female population, but not only. While in the beginning this vaccine targeted adolescent girls, a few countries have recently started to vaccinate young boys intending to protect them from anal and oral cancer (92). This measure, not absent of controversy, is also considered an effective strategy to achieve herd immunity with a rapid

decline in the viral load among the population, reducing the incidence of sexually-acquired HPV among both men and women. In the case of ZIKV, where vector transmission doesn't discern between genders, gender-neutral vaccination would probably have a similar or even greater impact in reducing viral loads.

Finally, another interesting finding is that participants in our study did not speak about the cost of a hypothetical ZIKV vaccine as a barrier or facilitator to get the immunization. As this was not a "willingness to pay" study, this topic was not directly investigated during the interviews, but it would be interesting to explore it in future research. The fact that all these women are actually living in Spain, where most of the vaccines are provided for free by the Public Health System (93), could be a possible explanation of these results.

8. Study limitations

There are some limitations related to this research. First, this phenomenological research involved only women who had ZIKV infection, received testing and medical care and therefore they may have been more knowledgeable about the virus and the disease than others. Their perceived susceptibility to the virus may be higher because of this same reason. However, this fact is also one of the main strengths of our study, because this approach provides very rich first-hand information from women exposed to Zika infection, which was found to be a gap in the published literature.

The small sample size, typical of qualitative research, limits generalization to other migrant Latin American women in other settings. However, as mentioned earlier, generalization is not the main purpose in qualitative research, but its inductive findings based on few subjects can be applied to other research settings and contribute to knowledge.

Another limitation was that some women from *Zika-Preg* cohort did not have the opportunity to participate in this study, which probably could have given a more comprehensive view of our questions in research. Nevertheless, purposive sampling assured that only participants willing to talk in detail were enrolled; the number of participants invited who were not willing to talk was trivial, as only one woman refused explicitly.

An additional limitation of this study is that the data used were collected to answer more research questions from QUAZIK study, apart from the questions mentioned in this document. The findings presented are, therefore, preliminary results obtained from a study that is still undergoing.

In addition, given that the acceptance of a ZIKV vaccine was presented and discussed with the participants as a hypothetical scenario -as these vaccines are not yet available-, there is a need to validate these results under real-life conditions if a ZIKV vaccine is accessible in the near future.

Finally, the accuracy of responses may have been compromised by recall bias and social desirability bias. Some of the explored questions might be sensitive and/or difficult to

answer to, and perhaps there is also a “need” to give “politically correct” answers. This is what is called social desirability bias, and it is a typical limitation when conducting IDIs. Triangulating the data with other data gathering methods such as Focus Group Discussions would have contributed to avoiding this bias. However, information gathered during the IDIs was rich and the intimate way in which they were performed was reflected in the language and expressions used by the participants, which was relaxed and casual. As for recall bias, questioning participants about experiences from their past could have implied a reduction in accuracy and volume of the information gathered.

9. Conclusions and recommendations

This study has been conducted with the intention to improve the ways in which ZIKV response and management are guided nationally and regionally in countries with high risk of hosting imported cases, and to contribute to knowledge in ZIKV endemic countries.

Recommendations derived from this study address multiple stakeholder levels. For public health officials and policy makers in endemic countries, it is advisable to design programs that address the social determinants of Zika. Access to individual preventive measures needs to be improved, together with public efforts on water and sanitation advances, to help to fight the spread of ZIKV. Health systems should also get prepared to respond to the specific health needs and rights of women, who bear the highest burden of Zika, by listening to their concerns and engaging them in the policies that affect them.

Knowledge gaps about ZIKV were prevalent amongst migrant Latin American women, even after a medical follow-up with regular visits. In non-endemic countries, it is recommended to use additional methods of information dissemination to raise awareness about Zika in populations at risk (e.g. migrants, international travellers), for example, through travel agencies and airlines that operate in endemic regions. This work has revealed that health communication through the popular media shaped people’s perceptions of risk and severity of ZIKV infection. On a global scale, the engagement of the media and social media could also be a useful tool for health promotion and education, given that our results show that information-seeking behaviour is often sought from those sources.

To counteract related misconceptions on ZIKV, recommendations for the health sector include an emphasis on the provision of improved health education by health professionals to people with risk of infection. The introduction of psychosocial counselling is also recommended to positively contribute to the short-term mental health and quality of life of women with a presumed ZIKV congenital infection, especially given the lack of a confirmatory ZIKV test that could provide a definitive diagnosis and relief uncertainty.

Our results provide evidence from high-risk female population that a future ZIKV vaccine should be offered to women in risk of exposure to ZIKV, during or around an outbreak. A high level of vaccine acceptance among Latin American women who passed a ZIKV infection has been related to an increased knowledge of ZIKV-associated risks and severity, after coping with a presumed infection, due to the exposure to additional information about Zika. To improve ZIKV vaccine acceptance, messages in vaccine promotion interventions should describe the benefits of avoiding severe infection outcomes in newborns, while accentuating vaccine safety for the foetus, and compatibility with breastfeeding. A committed involvement of health professionals in vaccination promotion messages is also recommended. Women of reproductive age in regions affected

by ZIKV constitute the population that will most likely benefit from vaccine introduction, and they should be prioritised in all steps of vaccine evaluation, licensing, and distribution. On a global scale, limiting the spread of future outbreaks and holding back the infection will ideally entail gender-neutral, universal vaccination.

For researchers and academics, there is a need to understand if any herd immunity protects the population of endemic areas, and to develop efficacious diagnostic tests for the diagnosis of Zika. Further collection of data on knowledge, perceptions and attitudes about ZIKV will continue providing valuable information from different study populations. As progress is made towards approving a ZIKV vaccine, it is important to integrate socio-behavioural assessments, as done in this study, to improve communication of benefits and risks of the vaccine and to guide future public health interventions. It is also recommended to stimulate further research about mental health impact during medical follow-up of infected pregnant mothers.

Although the dramatic decrease in the number of Zika and CZS reported cases is a welcome sign, ZIKV control shouldn't cease. It is necessary to improve the ability to anticipate and mitigate the risk of spread of ZIKV and to address its fatal consequences in the future through a continuous and interdisciplinary international response. This would impact positively on public health and in the overall quality of life of people at risk of acquiring Zika, and people coping with the infection.

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12. Annexes

Annex 1: Interview guide for QUAZIK study.

Explored themes related to this Master Final Project are highlighted. The language used was the participant's mother tongue (Spanish).

Usted ha sido invitada a participar en esta entrevista en profundidad porque su opinión es importante para nosotras.

Primero, vamos a hablar de lo que sabe del virus Zika y de su prevención. Después, de la atención médica recibida durante el seguimiento de su embarazo y de su bebé; y finalmente, de la posibilidad de tener nuevas medidas de prevención contra esta enfermedad.

La entrevista va a durar unos 45 ó 60 minutos. Y le recuerdo que si hay alguna pregunta que le incomode, no hace falta que responda, podemos seguir.

Para que conste, hoy es __(fecha)__, a las__(hora)__ y nos encontramos en_ (ciudad y lugar concreto) __.

TEMA	TEMAS A EXPLORAR	NUEVOS CONCEPTOS QUE SURGEN	COMUNICACIÓN NO VERBAL (GESTOS, INTERRUPCIONES, VOZ, etc.)
Historia personal	<ul style="list-style-type: none"> -edad -país -estudios, trabajo -familia -adaptación en España, apoyos -religión 		
Conocimientos del Zika	lo que sabía del Zika? lo que sabe a día de hoy EXPLORAR: <ul style="list-style-type: none"> -síntomas -quién puede infectarse -transmisión -prevención -cómo se enteró de esto y Cuándo -dónde obtuvo la información 		
Gente de tu alrededor	<ul style="list-style-type: none"> -qué sabían? -se sabía cómo prevenirlo? -usaban medidas preventivas? 		
Embarazo	<ul style="list-style-type: none"> -cómo fue? -cuándo: 1ª vez que le hablaron del Zika? -qué pensó? -cómo reaccionó? 		
Resultados de Zika	<ul style="list-style-type: none"> -1ª vez que le hablaron fue cuando le dijeron que podía tenerlo? -obtención de los resultados -momento -tiempo pasado -cómo se sintió durante la espera? -qué le dijo la doctora? -quién había allí? 		

	<ul style="list-style-type: none"> -cómo se sintió? -cómo fue el trato de los profesionales? 		
Discriminación	<ul style="list-style-type: none"> -a quién le contó que podía tener Zika? -cómo se lo contó? -cómo reaccionaron esas personas? -cómo se sintió usted tras su reacción? 		
Seguimiento	<ul style="list-style-type: none"> -cómo fueron las primeras visitas? -qué piensa de todas las visitas? -qué dificultades pudieron surgir? -qué ayudas tuvo? -qué cambiaría de la atención médica? 		
Seguimiento bebé	<ul style="list-style-type: none"> -explícame el seguimiento del bebé -cómo está? -son muchas visitas o pocas? -cómo va al hospital? -es un problema ir hasta allí? -apoyos 		
Relación personal	<ul style="list-style-type: none"> -cómo le afectó? 		
Vida sexual	<ul style="list-style-type: none"> -cómo le afectó? -quién tomaba la iniciativa? -usabais preservativo? -teníais sexo oral o anal? -con preservativo? -cómo se sentía? 		
Interrupción embarazo	<ul style="list-style-type: none"> -alguno de los dos, pensó en algún momento interrumpir el embarazo? -cómo fue la decisión de seguir adelante? 		
Vacuna	<ul style="list-style-type: none"> -se vacunaría? por qué? -embarazada? por qué? -dando el pecho? por qué? -bajo qué circunstancias? 		

	-cómo sería la vacuna ideal?		
Ensayo clínico	-aceptaría participar? por qué?		

Annex 2: Ethical Approval Document

DICTAMEN DEL COMITÉ ÉTICO DE INVESTIGACIÓN CLÍNICA

NEUS RIBA GARCIA, Secretario del **Comité Ético de Investigación Clínica del Hospital Clínic de Barcelona**.

Certifica:

Que este Comité ha evaluado la propuesta del promotor, para que se realice:

Nueva versión protocolo y HIP/CI. Incorporación de un CO-IP.

Protocolo v4.0 15th May 2018 - HIP/CI v01_ 15 Mayo 2018 Nuevo CO-IP P. Efraín Pantoja (ISGlobal)

del estudio:

CÓDIGO: NÚMERO EUDRACT:

TÍTULO: SURVEILLANCE OF ZIKA VIRUS INFECTION IN PREGNANT WOMEN TRAVELLING FROM AFFECTED AREAS

PROMOTOR:

y emite

DICTAMEN FAVORABLE

Y hace constar que:

1º En la reunión celebrada el día 12/07/2018, acta se decidió emitir el informe correspondiente a la enmienda de referencia.

2º El CEIC del Hospital Clínic de Barcelona, tanto en su composición como en sus PNTs, cumple con las normas de BPC (CPMP/ICH/135/95).

3º Listado de miembros:

Mod_5 (V2 de 22/10/13)

Reg.HCB/2016/0250

AC_ESM

Página 1/3

Presidente:

- BEGOÑA GÓMEZ PÉREZ (Farmacéutica Hospitalaria, HCB)

Vicepresidente:

- JOAQUIM FORÉS I VIÑETA (Médico Traumatólogo, HCB)

Secretario:

- NEUS RIBA GARCIA (Médico Farmacólogo Clínico, HCB)

Vocales:

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- VIRGINIA HERNANDEZ GEA (Médico Hepatólogo, HCB)
- NURIA SOLER BLANCO (Farmacéutica Hospitalaria, HCB)

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- MARINA ROVIRA ILLAMOLA (Farmacéutico Atención Primaria, CAP Eixample)
- JOSE LUIS BLANCO ARÉVALO (Médico Medicina Interna, HCB)
- MIRIAM MÉNDEZ GARCÍA (Abogada, HCB)
- MERCÈ VIDAL FLOR (Enfermera, HCB)

Que en el caso de que se evalúe algún proyecto del que un miembro sea investigador/colaborador, éste se ausentará de la reunión durante la discusión del proyecto.

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NEUS -
46540984R

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Barcelona, a 19 de julio de 2018

CIF - G-08431173

Annex 3: Informed Consent for the study participants

DOCUMENTACIÓN DE INFORMACIÓN AL PACIENTE

VIGILANCIA DE LA INFECCIÓN POR VIRUS ZIKA EN MUJERES EMBARAZADAS PROVENIENTES DE ZONAS DE RIESGO: PARTICIPACIÓN EN ENTREVISTA Y/O GRUPOS FOCALES

Como ustedes saben, en la mayoría de hospitales y en particular en el Hospital Clínic, además del trabajo asistencial se lleva a cabo investigación. Esto requiere, entre otras cosas, recoger datos de pacientes para analizarlos y obtener conclusiones que puedan ser útiles para futuros pacientes. Usted participó en el proyecto de vigilancia de infección por el virus Zika en mujeres embarazadas del Instituto de Salud Global de Barcelona (ISGlobal, investigadora principal Dra. Azucena Bardají), realizado en colaboración con el Servicio de Medicina Tropical (Dr. Quim Gascón) y el Servicio de Medicina Materno-Fetal del Hospital Clínic de Barcelona (Dra. Anna Goncé).

El **objetivo** que aquí se presenta pretende avanzar en el **conocimiento, percepción de riesgo y prevención** de los pacientes acerca de la infección por el virus Zika, las **barreras y los facilitadores** que han tenido durante el seguimiento de su embarazo y la infancia de sus bebés. Su participación es voluntaria y quedará confirmada, si así lo decide, con su firma al final de este documento. Este estudio cuenta con la aprobación del comité de Ética del Hospital Clínic.

¿En qué consiste el estudio? Queremos invitarle a una entrevista en profundidad y/o grupo focal. Por comodidad de los grupos de sujetos, los grupos focales se realizarán en el Hospital Sant Joan de Dèu y las entrevistas donde usted decida (Hospital Clínic, Hospital Sant Joan de Dèu, ISGlobal o su propio domicilio).

Ninguna muestra será recogida para esta parte del estudio. No hay ningún riesgo asociado para usted en caso que decida participar .

Los datos serán recogidos mediante dos modalidades:

-Entrevista en profundidad semi-desestructurada: Se desconoce la percepción de las mujeres que han tenido un resultado positivo para virus Zika durante el embarazo respecto a la comunicación del riesgo y su afectación personal durante el embarazo; las barreras que han tenido que afrontar y cuáles han sido los facilitadores durante el seguimiento de su embarazo y de sus bebés. Por ello, se realizará una entrevista considerando la perspectiva antropológica, psicológica y epidemiológica.

-Grupos focales: Le invitamos a participar en grupos focales que nos permitan entender mejor las experiencias comunes entre mujeres que han tenido el mismo diagnóstico. Se realizarán los grupos focales considerando la perspectiva antropológica, psicológica y epidemiológica.

En ambos casos se considerará grabar el audio de las entrevistas y/o grupos focales.

¿Cuáles son los beneficios de participar en este estudio? Si usted decide participar, nos ayudará a comprender el estado de los conocimientos que tiene del virus del Zika, su percepción del riesgo y a describir cómo llevó el embarazo y la crianza de su bebé.

¿Existe algún riesgo por participar en este estudio? Esta parte del estudio de investigación cualitativa (entrevista o grupos focales) por infección del virus del Zika en la gestante **NO conlleva riesgos** para usted ni para su bebé. En cualquier momento usted puede cambiar de opinión y dejar de participar en el estudio.

¿Qué ocurre si se niega a participar en el estudio? Nada. El seguimiento de su familia se realizará siguiendo los protocolos habituales.

Con el objetivo de llevar a cabo este estudio, le invitamos a participar. Para esto y, de acuerdo con las normas bioéticas y la legislación vigente, necesitamos su autorización. Sus datos serán utilizados siempre de forma codificada y absolutamente confidencial, de forma que únicamente miembros autorizados dispondrán de acceso a la información obtenida según el Reglamento (UE) 2016/679 del Parlamento Europeo y del Consejo de 27 de abril de 2016 relativo a la protección de las personas físicas en lo que respecta al tratamiento de datos personales y a la libre circulación de estos datos y por el que se deroga la Directiva 95/46/CE (Reglamento general de protección de datos)*. Asimismo, aunque los resultados obtenidos de la investigación se publiquen en ámbitos científicos, su identidad no será facilitada. Usted podrá disponer en todo momento de toda la información obtenida y ésta se limitará a la mencionada en este texto. Agradecemos su colaboración y estamos a su disposición para contestar cualquier pregunta que quiera realizar.

Su participación es totalmente voluntaria. Puede negarse a participar o retirar su consentimiento en cualquier momento sin tener que explicar los motivos y esto no repercutirá negativamente en su asistencia médica, presente o futura.

Datos de contacto: Dra. Azucena Bardají, ISGlobal, Hospital Clínic- Universitat de Barcelona, teléfono

93-227-54-00 (Extensión 4145) / 93-227-18-51

*Responsable del Tratamiento: Fundación Privada Instituto de Salud Global Barcelona (ISGlobal), CIF: G65341695, Dirección postal: Calle Rosselló, número 132, 6ª de Barcelona (08036). Correo electrónico: lopd@isglobal.org

Delegado de Protección de Datos, contacto: lopd@isglobal.org

De acuerdo a su participación en el proyecto de investigación VIGILANCIA DE LA INFECCIÓN POR VIRUS ZIKA EN MUJERES EMBARAZADAS PROVENIENTES DE ZONAS DE RIESGO, el Responsable del Tratamiento le informa que, en cumplimiento de lo establecido en el Reglamento General de Protección de datos (en adelante RGPD), sus datos de carácter personal serán utilizados, para llevar a cabo la investigación a la que usted ha consentido participar.

Asimismo, es importante informarle que los datos de carácter personal, con el consentimiento que ha otorgado, también serán utilizadas por otros proyectos / investigaciones dentro del área del presente proyecto, o bien en proyectos de investigación en salud global, tanto en enfermedades infecciosas como no-comunicables, y salud ambiental, para estudiar el efecto de los factores ambientales en la salud de las personas.

La comunicación de sus datos se convierte en un requisito necesario contractual para llevar a cabo el proyecto de investigación sin el cual no podría llevarse a cabo, sin perjuicio de que usted en cualquier momento tiene derecho a retirar los consentimientos prestados en cualquier momento, sin que esto afecte la licitud del tratamiento realizado previamente a su retirada.

Los datos proporcionados serán conservados mientras esté en activo el proyecto de investigación o bien los sucesivos proyectos de investigación dentro de la misma área o línea de investigación en los que se traten sus datos de carácter personal, de acuerdo a los criterios que establezca la legislación vigente.

Esta información será utilizada por el Grupo de Investigación encargado de la investigación / es (en particular, el investigador del estudio y sus colaboradores, autoridades sanitarias, y los monitores y auditores del promotor) los cuales estarán sometidos al deber de secreto inherente a su profesión, para comprobar los datos y procedimientos del estudio, pero siempre manteniendo la confidencialidad de los mismos de acuerdo con la legislación vigente. También será transmitida la información a los estamentos oficiales públicos o privados que, por obligación legal o necesidad material, deban acceder a los datos a efectos del correcto desarrollo del proyecto de investigación, de acuerdo a las buenas prácticas

científicas. En ningún caso sus datos de carácter personal serán transferidos a terceros países u organización internacional, fuera de la Unión Europea.

Usted es el responsable de la veracidad y corrección de los datos que nos entrega y tiene la facultad de ejercer los derechos de acceso, rectificación, supresión, limitación del tratamiento, portabilidad y de oposición de sus datos de acuerdo lo dispuesto en la normativa en materia de protección de datos. Para ejercerlos, deberá dirigirse por escrito al Delegado de Protección de Datos a lopd@isglobal.org en cualquier caso se deberá adjuntar una fotocopia de su documento nacional de identificación o bien equivalente.

Por último, además de la posibilidad de ejercer sus derechos, si no está de acuerdo con el tratamiento realizado por la Entidad o considera infringidos sus derechos podrá presentar una reclamación en todo momento ante la Agencia Española de Protección de datos.

Ante la presente información que el Responsable del Tratamiento me ha otorgado, y habiendo entendido esta, ofrezco mi consentimiento al tratamiento de:

- ☐ Mis datos personales para llevar a cabo el proyecto de investigación
- ☐ Mis datos personales para llevar a cabo proyectos de investigación afines al presente o de la misma área de investigación

HOJA DE CONSENTIMIENTO INFORMADO

Título del proyecto:

VIGILANCIA DE LA INFECCIÓN POR VIRUS ZIKA EN MUJERES EMBARAZADAS PROVINIENTES DE ZONAS DE RIESGO: PARTICIPACIÓN EN ENTREVISTA Y/O GRUPOS FOCALES

Yo (nombre y apellidos).....

He decidido participar en:

☐ ENTREVISTA ☐ GRUPO FOCAL ☐ ENTREVISTA Y GRUPO FOCAL

He leído la hoja de información que se me ha entregado.

He podido hacer preguntas sobre el estudio.

He recibido suficiente información sobre el estudio.

He tenido tiempo suficiente para considerar de manera adecuada la participación en el estudio.

Comprendo que mi participación es voluntaria.

Comprendo que puedo retirarme del estudio cuando quiera, sin tener que dar explicaciones y sin que esto repercuta en mis cuidados médicos.

Comprendo que los datos obtenidos serán recogidos y almacenados de manera anónima.

Presto libremente mi conformidad para participar en el estudio.

Lugar, fecha:

Nombre, DNI y firma del participante:
investigador:

Nombre y Firma del personal

EJEMPLAR PARA LA PACIENTE

HOJA DE CONSENTIMIENTO INFORMADO

Título del proyecto:

VIGILANCIA DE LA INFECCIÓN POR VIRUS ZIKA EN MUJERES EMBARAZADAS PROVINIENTES DE
ZONAS DE RIESGO: PARTICIPACIÓN EN ENTREVISTA Y/O GRUPOS FOCALES

Yo (nombre y apellidos).....

He decidido participar en:

☐ ENTREVISTA ☐ GRUPO FOCAL ☐ ENTREVISTA Y
GRUPO FOCAL

He leído la hoja de información que se me ha entregado.

He podido hacer preguntas sobre el estudio.

He recibido suficiente información sobre el estudio.

He tenido tiempo suficiente para considerar de manera adecuada la participación en el estudio.

Comprendo que mi participación es voluntaria.

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Comprendo que los datos obtenidos serán recogidos y almacenados de manera anónima.

Presto libremente mi conformidad para participar en el estudio.

Lugar, fecha:

Nombre, DNI y firma del participante:
investigador:

Nombre y Firma del personal

EJEMPLAR PARA EL PERSONAL INVESTIGADOR

Annex 4: Consolidated Criteria for reporting qualitative studies (COREQ): 32-item checklist (94)

No. Item	Guide questions/description	Answer
Domain 1: Research team and reflexivity		
<i>Personal Characteristics</i>		
1. Interviewer /facilitator	Which author/s conducted the interview or focus group?	Ana Villén and Elena Marbán
2. Credentials	What were the researcher's credentials? E.g. PhD, MD	Researchers' hold both a MsC
3. Occupation	What was their occupation at the time of the study?	Researchers' occupations included doctoral researcher and research assistant.
4. Gender	Was the researcher male or female?	Both researchers are female
5. Experience and training	What experience or training did the researcher have?	Both researchers had at least 3 years experience on global health related work.
<i>Relationship with participants</i>		
6. Relationship established	Was a relationship established prior to study commencement?	The participants were not acquainted to AV but knew EM from previous <i>Zika-Preg</i> study.
7. Participant knowledge of the interviewer	What did the participants know about the researcher? e.g. personal goals, reasons for doing the research	The participants knew that the intent of the study was to understand knowledge, perceptions and attitudes and to explore the acceptability of a hypothetical ZIKV vaccine in order to improve health promotion and delivery services. Interviewees knew that the researchers were affiliated with University of Barcelona and Hospital Clinic.
8. Interviewer characteristics	What characteristics were reported about the interviewer/facilitator? e.g. Bias, assumptions, reasons and interests in the research topic	No biases or previous assumptions were used

Domain 2: study design		
<i>Theoretical framework</i>		
9. Methodological orientation and Theory	What methodological orientation was stated to underpin the study? e.g. grounded theory, discourse analysis, ethnography, phenomenology, content analysis	A phenomenological approach was used with grounded theory for the data analysis
<i>Participant selection</i>		
10. Sampling	How were participants selected? e.g. purposive, convenience, consecutive, snowball	Participants were chosen purposively and by convenience
11. Method of approach	How were participants approached? e.g. face-to-face, telephone, mail, email	Participants were contacted through phone calls
12. Sample size	How many participants were in the study?	11 participants were included in the study
13. Non-participation	How many people refused to participate or dropped out? Reasons?	5 people refused to participate (4 due to lack of time and 1 because she didn't feel comfortable with the interview) and 3 recruited participants dropped out before the interview because they had no time
<i>Setting</i>		
14. Setting of data collection	Where was the data collected? e.g. home, clinic, workplace	Data were collected at the participant's houses or at cafeterias.
15. Presence of non-participants	Was anyone else present besides the participants and researchers?	A few interviews were done in the presence of the children of the participants, who had to take care of them.
16. Description of sample	What are the important characteristics of the sample? e.g. demographic data, date	All participants were women between 22 and 44 years old, living in Catalonia and having participated in <i>Zika-Preg</i> cohort prospective study following a confirmed or probable Zika virus diagnostic.
<i>Data collection</i>		
17. Interview	Were questions, prompts,	There was an interview guide and it was pilot-tested.

guide	guides provided by the authors? Was it pilot tested?	
18. Repeat interviews	Were repeated inter views carried out? If yes, how many?	No
19. Audio/visual recording	Did the research use audio or visual recording to collect the data?	A digital audio recorder was used to collect data
20. Field notes	Were field notes made during and/or after the interview or focus group?	Field notes were taken during and after every interview
21. Duration	What was the duration of the inter views or focus group?	All interviews had a duration of 45 to 90 minutes
22. Data saturation	Was data saturation discussed?	Data saturation was discussed
23. Transcripts returned	Were transcripts returned to participants for comment and/or correction?	Transcripts were not returned to participants
Domain 3: analysis and findings		
<i>Data analysis</i>		
24. Number of data coders	How many data coders coded the data?	Data was coded between 2 researchers
25. Description of the coding tree	Did authors provide a description of the coding tree?	The coding tree was built from the data
26. Derivation of themes	Were themes identified in advance or derived from the data?	Themes were derived from the data
27. Software	What software, if applicable, was used to manage the data?	Dedoose software was used
28. Participant checking	Did participants provide feedback on the findings?	Participants didn't provide any feedback on the findings
<i>Reporting</i>		
29. Quotations presented	Were participant quotations presented to illustrate the themes/findings? Was each quotation identified? e.g.	Quotes were presented with identifiers

	participant number	
30. Data and findings consistent	Was there consistency between the data presented and the findings?	There was consistency between the data presented and the findings
31. Clarity of major themes	Were major themes clearly presented in the findings?	The major themes were clearly presented in the findings
32. Clarity of minor themes	Is there a description of diverse cases or discussion of minor themes?	There is description of diverse cases to some extent