Zika Inquiries Made to the CDC-INFO System, December 2015–September 2017

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We examined Zika-related inquiries to CDC-INFO, the national contact center for the Centers for Disease Control and Prevention, to identify potential communication gaps. The most frequently asked questions related to travel or geographic location of Zika (42% of all inquiries), information about laboratory testing (13%), or acquiring a Zika test (11%).

A rapid increase in Zika virus disease transmission rates throughout Latin America in 2015, followed by transmission in some US states and outbreaks in several US territories, sparked widespread attention (*1*–*3*). We systematically examined Zika-related inquiries to the CDC-INFO system, the national contact center for the Centers for Disease Control and Prevention to determine public concerns and questions about Zika and potential communication gaps. We analyzed inquirer type, inquiry topic, and number of inquiries. In this article, "question" refers to the content of each call/email and "inquiry" to individual calls/emails, regardless of content. Inquiries may include >1 question.

The CDC-INFO Zika dataset contained 32,668 English-language inquiries (calls/emails) about Zika made from December 1, 2015 (when inquiries about Zika began to be tracked), through September 29, 2017 (when CDC's emergency activation for Zika response ended). We analyzed the number of inquiries over time using all database records and information on inquirers and topics using a 10% simple random sample (n = 3,268). After an initial pilot process, 2 study authors coded notes made by operators for information on the types of inquirers and types of questions (*4*) (Appendix, https://wwwnc.cdc.gov/EID/article/26/5/18-1694-App1.pdf).

We grouped inquirers into 3 different categories; however, most did not specify a category affiliation. The first category, the pregnancy group, made up 19% of all inquirers and was composed of pregnant women (10%), women planning to become pregnant and their partners (6%), and partners of pregnant women (3%). The second category, clinicians, made up 14% of all inquirers. (CDC also initiated a separate hotline for clinicians during the Zika response; information from those calls was not included in this data analysis.) The third category, all other inquirers (67%), included family members and parents (8%); public health practitioners, students and educators, politicians and political staff, media, and salespeople (3%); and inquirers who did not specify identity (56%).

The most frequent questions (present in 42% of inquiries) were about travel or geographic location (geolocation) of Zika outbreaks (Table). Approximately 13% of all inquiries included questions seeking factual background information about laboratory testing, including how to obtain results, how to administer tests, how to interpret results, and criteria for testing. Questions about getting tested for Zika were present in 11% of inquiries. Questions related to transmission factors (e.g., incubation, persistence, immunity, semen, mosquitoes) were present in 9% of inquiries. Only 4% of inquiries included questions about health effects and related issues (e.g., potential harm to fetus, self, children) (Table).

Some types of questions were asked more frequently than others by certain groups. For example, the pregnancy group most frequently asked questions about travel or geolocation of the disease (65% of all inquiries from this group), whereas clinicians most frequently sought information about tests (46%) (Appendix Table 1).

Analysis of the number of inquiries over time showed 2 distinct peaks. The first occurred early in the response, with ≈4,000 biweekly inquiries at the peak in late January/early February 2016, when news media coverage of the outbreak increased. The second occurred in late July/early August 2016, after local US transmission was confirmed, with nearly 2,000 biweekly inquiries (Appendix Figure 1). The number of inquiries by date for the 4 most frequently asked questions (about travel or geolocation of Zika, seeking information about tests, seeking to be tested for Zika, and transmission) generally reflected the same overall pattern as all inquiries. One exception was questions about travel/geolocation of the disease, which showed a third, smaller rise in volume in late 2016/early 2017 (Appendix Figure 2). The frequency of

Table. Percentage of inquiries with specific question topics to CDC-INFO, December 1, 2015–September 29, 2017*

Question topic	% Inquiries with question topic, n = 3268
Information gathering	
Transmission: includes persistence, presence in semen, mosquitoes, and immunity	9
Incubation period	<1
Signs and symptoms	2
Outbreak response processes	3
Seeking information about diagnostic tests	13
Seeking information about treatments, countermeasures, vaccines	1
Clinician seeking clinical recommendation/assistance for a patient with Zika	1
Information about risks	
Health effects/issues: includes harm to self, fetus, pregnant woman, or child	4
Health effects: specifically long-term reproductive effects	4
Exposure: mosquito-related or sexual exposure	2
Infection: asking if inquirer could have Zika	1
Safety of protective actions: includes spraying or repellant	<1
Actions	
Protective actions	
What activities should be done to protect from getting Zika	3
Waiting to get pregnant	4
Safe sex practices	1
Insect repellent/preventioning bug bites/mosquito control	3
What action to take following possible exposure	1
Acquiring a Zika test	11
Travel and geolocation	42
Actions for infected persons	<1
Other	
Seeking access to materials/tools	4

*When inquirers asked >1 type of question, each type was counted separately. As a result, total percentage adds up to >100%. CDC-INFO, the national contact center for the Centers for Disease Control and Prevention.

questions about transmission, signs/symptoms, health effects, long term health effects, and insect management was significantly greater early in the outbreak, before local transmission was confirmed in the United States ($p<0.05$ by χ^2 test). Questions about waiting to get pregnant and geolocation were made significantly more often after local transmission occurred ($p<0.05$ by χ^2 test).

Outreach to CDC-INFO might indicate that Zika messages reached intended target populations. Of those who volunteered demographic information, 44% were in the pregnancy group and so might have been made aware of heightened risks and sought more specific information about ways to reduce them. Results show that information needs were most intense at the time the threat emerged, although events during the outbreak, such as news of local transmission cases in the United States or new transmission routes, might also have increased public interest.

Inquiries made to CDC-INFO about Zika might represent potential information gaps from other sources. Inquirers most frequently asked about travel/geolocation of disease and testing, which was already included in CDC messaging and disseminated through various channels. Our findings could indicate that the information previously provided was perceived to be insufficient or difficult to locate or understand or that it was hard to keep up with changes in messaging during the response.

CDC-INFO records are a source of data that has been underanalyzed but that provides critical information about inquiries from the public about active efforts to obtain information from CDC. Our findings may help with future messaging efforts around infectious disease outbreaks by identifying topics of information that should be emphasized to improve public understanding.

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Serologic Detection of Middle East Respiratory Syndrome Coronavirus Functional Antibodies

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We developed and validated 2 species-independent protein-based assays to detect Middle East respiratory syndrome coronavirus functional antibodies that can block virus receptor-binding or sialic acid-attachment. Antibody levels measured in both assays correlated strongly with virus-neutralizing antibody titers, proving their use for serologic confirmatory diagnosis of Middle East respiratory syndrome.

The zoonotic introductions and ongoing outbreaks of Middle East respiratory syndrome (MERS) coronavirus (MERS-CoV) pose a global threat (*1*,*2*) necessitating continuous serosurveillance to monitor virus spread alongside the development of vaccine and antibodies as countermeasures. Both approaches require validated assays to evaluate specific antibody responses. Although MERS-CoV serologic assays have been developed (*2*–*6*), those detecting functional antibodies cannot be applied in all laboratories and can require Biosafety Level 3 (BSL-3) containment. Recombinant protein-based immunoassays are easier to operate and standardize and do not require BSL-3 containment. However, MERS-CoV protein-based assays developed thus far can only detect antibody binding and give no information on antibody functionality. The MERS-CoV spike protein N terminal subunit (S1) contains 2 functional domains: the N-terminal domain ($S1^A$), which binds sialic acid, the viral attachment factor; and the receptor-binding domain (RBD) ($S1^B$), which binds dipeptidyl peptidase 4, the virus receptor (*7*,*8*). Antibodies against those 2 domains can block MERS-CoV infection (*9*). Based on this fundamental knowledge, we developed 2 recombinant protein-based functional assays.

First, we developed an S1-based competitive ELISA, a receptor-binding inhibition assay (RBI), to test for antibodies that block the interaction with dipeptidyl peptidase 4, the viral receptor (Appendix Figure 1, https://wwwnc.cdc.gov/EID/article/26/5/19-0921-App1.pdf). We validated the specificity of the assay for human diagnostics using serum samples from healthy blood donors, PCR-confirmed non–coronavirus-infected patients and non–MERS-CoV–infected patients (cohorts H1–H3) (Appendix Table 1). At a 1/20 dilution, none of the samples from non–MERS-CoV-infected humans showed a ≥50% reduction in signal (RBI_{50}) (Figure, panel A), indicating a high specificity of the assay. MERS-CoV–specific RBI antibodies were detected in all the 90% plaque reduction neutralization assay ($PRNT_{90}$)–positive serum samples of the PCR-confirmed MERS-CoV patients tested (Appendix Table 2, Figure 2). The percentage reduction in signal strongly correlated with neutralizing antibody titers (Figure, panel B). The RBI_{50} assay showed similar sensitivity to the $PRNT_{90}$ assay.

Because the RBI assay is species-independent, we validated its ability to detect RBI antibodies in dromedaries. At a 1/20 dilution, none of the naive dromedary serum samples (*10*) reacted in the assay, whereas all samples from MERS-CoV–infected dromedaries (2) resulted in a >90% reduction in signal (Appendix

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Appendix

Methods

Terminology

The term “question” is used to specify content of each call or email to CDC-INFO while “inquiry” is used as an umbrella term to describe calls or emails to CDC-INFO, regardless of specific content, and may include >1 question.

Sample

The full CDC-INFO Zika dataset contained 32,668 English language inquiries (calls and emails combined) made from December 1, 2015 (when inquiries about Zika began to be tracked) to September 29, 2017 (when the CDC’s emergency activation for Zika response ended). These inquiries were identified using a combination of a keyword search on the term “Zika” and a search on a list of Zika prepared responses identification numbers that operators log when responding to an inquiry. Each inquiry was recorded separately, even if it was made by an individual who had previously contacted CDC-INFO. To evaluate public inquiries about Zika, we analyzed a 10% simple random sample (N = 3,268).

Content Analysis Approach and Measures

The research team reviewed the information gathering process specific to the general public described by Slaughter et al. (*1*) and developed a coding instrument that focused on general health-related information gathering (i.e., questions addressing general knowledge gaps about Zika), questions about Zika-related risks, and questions about potential actions to be taken. Emotional and social themes (e.g., fears/concerns, pressure from family) were considered but were determined to be too difficult to reliably interpret using the notes of CDC-INFO agents.

Five members of the research team piloted the coding instrument on a random sample of 350 inquiries that were not included in the final analytic sample. Piloting was performed to test

the coding instrument, note potential issues, ensure group consensus on the meaning of codes, and revise the instrument. The team iteratively reviewed the instrument after each round of 50 pilot inquiries. The final coding instrument included date of inquiry, type of interaction, type of inquirer, and items related to potential questions about the Zika virus (Appendix Table 2). Type of inquirer was coded from the question text and the self-identification field. If an inquiry included >1 question, each question type was included.

Two members of the team independently coded the first 600 inquiries of the analytic sample to assess interrater reliability for each question on the instrument, coded as a dichotomous (yes/no) variable. Kappa values and percent agreement were then calculated on the final set of coded items (N=22). All coding items (i.e. Zika question topics) had high percent agreement, with the majority showing greater than 99% agreement and the lowest item showing 96% agreement. The majority of coding items had kappa values above 0.80, and all but 1 coding item/grouping had kappa values above 0.69. (*2*) This item, related to misinformation, was found to be too subjective and was excluded from the final analysis (Appendix Table 3). The remainder of the sample (N=2,668) was split evenly between coders, who periodically reviewed difficult-to-interpret questions with 2 research team members to ensure continued agreement.

Data Analysis

Descriptive statistics related to volume and inquiry type (phone call or email) were calculated using the full CDC-INFO Zika dataset. The 10% random sample described above was used for the remainder of the analysis. To evaluate the content of inquiries to CDC-INFO, we calculated the proportion of inquiries in the sample that included each Zika-related question. Chi-squared tests were used to test differences in question frequency before and after local disease transmission was confirmed in the continental United States.

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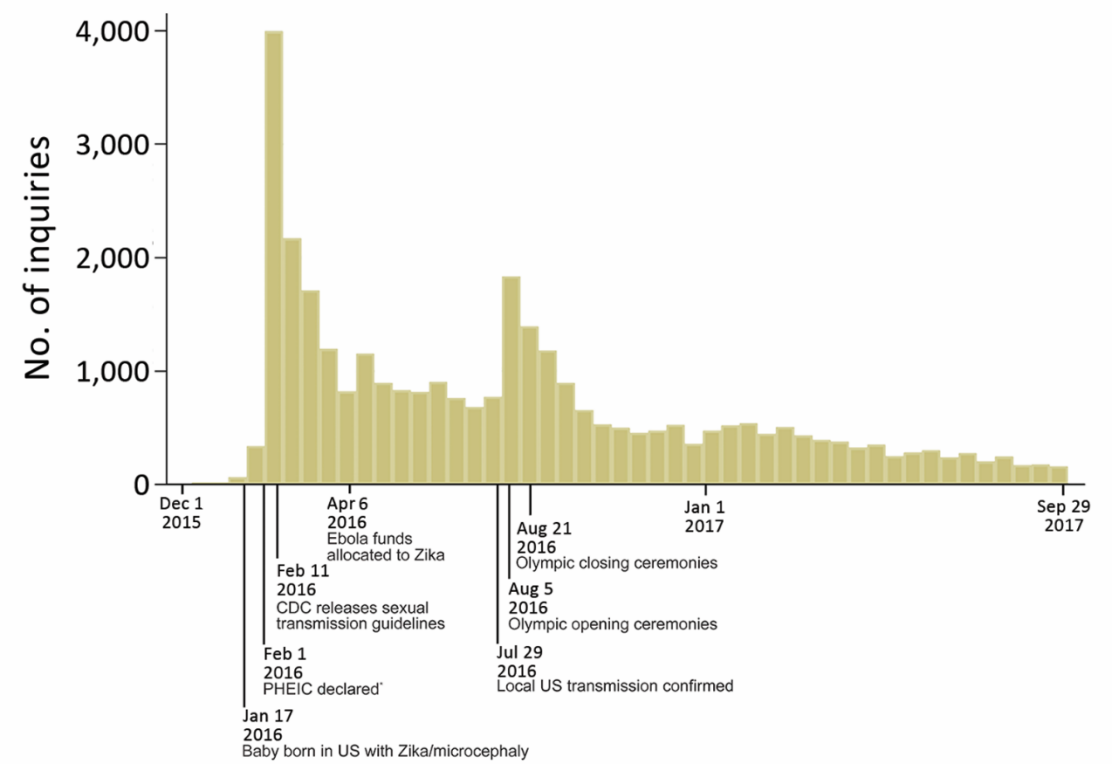
Appendix Table 1. Percentage of inquiries with question topic by three types of inquirers to CDC-INFO, December 1, 2015–September 29, 2017

Question topic	% of pregnancy group* (n=624)	% of clinicians (n=443)	% of all other inquirers (n=2201)
Information gathering			
Transmission (Includes persistence, presence in semen, mosquitoes, and immunity)	6	5	11
Incubation period	<1	<1	<1
Signs and symptoms	<1	<1	3
Outbreak response processes	2	3	3
Seeking information about diagnostic tests	6	46	8
Seeking information about treatments, countermeasures, vaccines	<1	1	2
Clinician seeking clinical recommendation/assistance for a patient with Zika	0	5	0
Information about risks			
Health effects/issues (includes harm to self, fetus, pregnant woman, or child)	3	2	4
Health effects, specifically long-term reproductive effects	<1	1	5
Exposure (mosquito-related or sexual exposure)	3	1	2
Infection (Asking if inquirer could have Zika)	1	0	1
Safety of protective actions (Includes spraying or repellant)	<1	<1	<1
Actions			
Protective actions: what activities should be done to protect from getting Zika	3	0	3
Protective actions: waiting to get pregnant	6	4	3
Protective actions: safe sex practices	2	1	<1
Protective actions: insect repellent/prevention bug bites/mosquito control	2	<1	3
Protective actions: what action to take following possible exposure	1	<1	1
Acquiring a Zika test	14	12	9
Travel and geolocation	65	12	41
Actions for infected persons	0	<1	<1
Other			
Seeking access to materials/tools	<1	9	5

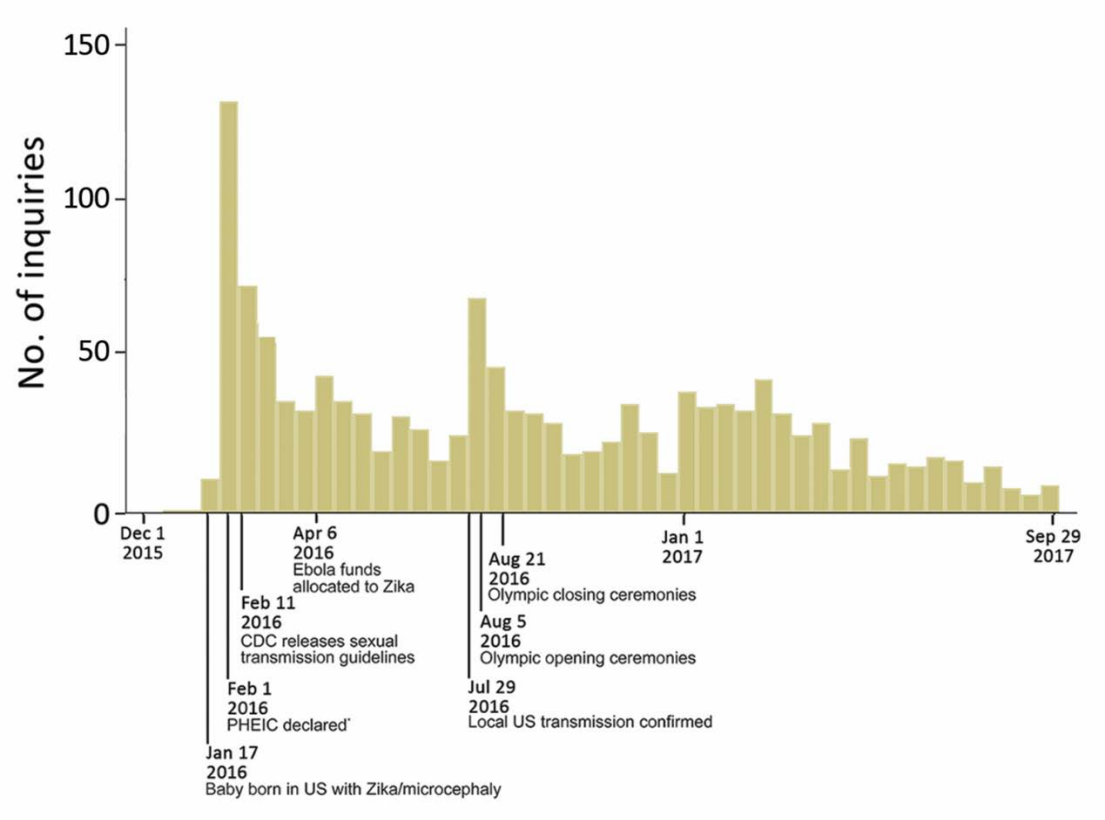
* Inquirers who were pregnant, the partners of pregnant women, or those who were planning on starting a family

Appendix Table 2. Coding topics, percent agreement for coders, and interrater reliability as measured by Kappa Scores

Question topic	% agreement	Kappa
Transmission (Includes persistence, presence in semen, mosquitoes, and immunity)	98.8	0.92
Incubation period	100.0	1.00
Signs and symptoms	100.0	1.00
Outbreak response processes	98.5	0.70
Seeking information about diagnostic tests	97.0	0.85
Seeking information about treatments, countermeasures, vaccines	99.8	0.94
Clinician seeking clinical recommendation/assistance for a patient with Zika	99.7	0.75
Health effects/issues (includes harm to self, fetus, pregnant woman, or child)	97.2	0.74
Health effects, specifically long-term reproductive effects	99.7	0.83
Exposure (mosquito-related or sexual exposure)	99.8	0.80
Infection (asking if inquirer could shave Zika)	99.7	0.80
Safety of protective actions (Includes spraying or repellant)	99.9	0.86
Protective actions: what activities should be done to protect from getting Zika	98.8	0.78
Protective actions: waiting to get pregnant	99.5	0.91
Protective actions: safe sex practices	99.5	0.72
Protective actions: insect repellent/prevention bug bites/mosquito control	99.9	0.89
Protective actions: what action to take following possible exposure	100.0	1.00
Acquiring a Zika test	96.3	0.79
Travel and geolocation	96.0	0.92
Actions for infected persons	100.0	1.00
Seeking access to materials/tools	98.0	0.84
Questions/comment about rumors or misinformation	99.5	0.40



Appendix Figure 1. Number of CDC-INFO Zika inquiries over time December 1, 2015–September 29, 2017. Total inquiries: 32,668. Each bar represents a 14-day period. *PHEIC: Public Health Emergency of International Concern.



Appendix Figure 2. Inquiries to CDC-INFO about travel and geolocation of Zika over time for all inquirers December 1, 2015 – September 29, 2017. Total inquiries: 32,668. Each bar represents a 14-day period. *PHEIC: Public Health Emergency of International Concern.