

## Prior Vaccination and Effectiveness of Communication Strategies Used to Describe Infectious Diseases

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We tested the effect of prior vaccination on response to communication strategies in a hypothetical news article about an influenza pandemic. Vaccinated were more likely than nonvaccinated participants to plan future vaccination, and future vaccination intent was greater with certain communication strategies. Using these findings to target communication may increase vaccination rates.

Vaccination rates for influenza remain surprisingly low (1). Despite goals to vaccinate 75% of high-risk Europeans by 2010, <50% had been vaccinated in 2013 (2). The reluctance of at-risk persons to receive vaccinations highlights the challenge of broadly vaccinating the general public.

Improving communication strategies that clinicians and healthcare organizations use to increase vaccination rates is cost-effective (3). Yet randomized trials to improve influenza vaccination rates by improving physicians' communication skills (4) or by using various public health messages (5) have not succeeded. Several studies have examined the effect of various communication strategies to improve vaccination rates for influenza (6–9). However, the greatest predictor of future vaccination is prior vaccination, and these studies assessed participants in aggregate (6). Guided by the Health Belief Model (10), we investigated whether experiences with prior vaccination might affect the effectiveness of certain communication strategies (Appendix, <https://wwwnc.cdc.gov/EID/article/25/4/17-1408-App1.pdf>).

Our study is a secondary analysis of a randomized experiment to test communication strategies and their effects on influenza immunization (6–9). After our study was

deemed exempt from review by the University of Michigan Institutional Review Board, we recruited a stratified random sample of adults from a panel of Internet users through Survey Sampling International (<https://www.surveysampling.com>) (Appendix). We recruited participants from 11 countries: Finland (n = 1,554), Norway (n = 764), Sweden (n = 1,539), Hungary (n = 998), Poland (n = 1,509), Spain (n = 1,604), Italy (n = 1,509), Germany (n = 1,546), the Netherlands (n = 1,938), the United Kingdom (n = 1,762), and the United States (n = 1,787).

Participants read a hypothetical news article that described the spread of influenza in their country. The article directly quoted hypothetical health experts and contained information about the influenza virus, its potential symptoms, and a vaccine in development. Articles were cross-randomized to provide participants with 5 varying communication strategies: 1) graphics (heat map, DOT map, picto-trendline) (6); 2) case severity (severe, typical, both) (9); confident language (scientific certainty, uncertainty, uncertainty with normalizing language) (7); 4) influenza label (H1N3 influenza, horse flu, Yarraman flu) (8); and 5) metaphor use (infectious disease, war, gardening). The Appendix contains more information about communication strategies. Each news article contained all 5 communication strategies. The experiment used a  $3 \times 3 \times 3 \times 3$  between-subjects factorial design in which participants were randomly assigned to each communication strategy. After reading the newspaper article, participants were asked their vaccination status (whether they had received an influenza vaccination within the past 2 years) and intent to get vaccinated in the future (defined by a discrete visual analog scale ranging from 1 [“Definitely would not get a vaccination”] to 7 [“Definitely would get a vaccination”]).

We were interested in the main effect for an individual communication strategy depending on a participant's prior vaccination status. For each communication strategy, we conducted separate ordinal logistic regression models and included an interaction term of prior vaccination and the communication strategy of interest for each model. The dependent variable was intent to get vaccinated. As covariates, we included the participant's age, sex, and marital status and whether the participant was a healthcare worker. We estimated robust SEs with clustering by the participant's country of residence.

Of 20,138 participants, 16,401 (81%) completed the survey; of these, 4,999 (30%) had received an influenza vaccination within the previous 2 years and 11,402 (70%) had not. The average age was 51.4 (SD  $\pm$  16.9) for vaccinated and 44.9 (SD  $\pm$  15.4) for nonvaccinated participants. Approximately 44.6% of vaccinated and 52.1% of nonvaccinated participants were female (Appendix Table 1).

**Table.** Effect of communication strategies on intent for future influenza vaccination, by influenza vaccination status

Strategy	Vaccination over previous 2 y, adjusted odds ratio (95% CI)*				p value for interaction†
	No	p value	Yes	p value	
Graph type					<0.001
Picto-trendline	Referent		Referent		
DOT map	1.1 (0.9–1.2)	0.06	1.0 (0.9–1.1)	0.92	
Heat map	1.1 (1.0–1.2)	0.01	1.1 (0.9–1.2)	0.08	
Case severity					<0.001
Both	Referent		Referent		
Typical	1.0 (0.9–1.1)	0.78	0.9 (0.8–1.0)	0.07	
Severe	1.1 (1.0–1.3)	0.02	1.1 (0.9–1.2)	0.43	
Confident language					<0.001
Uncertainty with normalizing language	Referent		Referent		
Uncertainty	1.0 (0.9–1.1)	0.97	1.1 (0.9–1.2)	0.12	
Scientific certainty	1.2 (1.1–1.3)	<0.001	1.3 (1.1–1.4)	<0.001	
Influenza label					<0.001
Horse	Referent		Referent		
H11N3	1.0 (0.9–1.1)	0.62	1.4 (1.1–1.7)	0.001	
Yarraman	1.1 (1.0–1.2)	0.001	1.2 (1.1–1.4)	0.001	
Metaphor use					<0.001
Infectious disease	Referent		Referent		
War	1.0 (0.9–1.1)	0.78	1.0 (0.9–1.1)	0.60	
Gardening	1.0 (0.9–1.1)	0.75	1.0 (0.9–1.1)	0.41	

\*Multivariable ordinal logistic regression adjusted for participant age, sex, marital status, occupation as healthcare worker, and country of residence.

†Interaction between vaccination status and communication strategy.

Our results showed that previously vaccinated participants were more likely than nonvaccinated participants to plan for future vaccinations (adjusted odds ratio 5.8, 95% CI 4.8–7.0;  $p < 0.001$ ). We found significant interaction effects between prior vaccination and each communication strategy ( $p < 0.001$  for each strategy) (Table; Appendix Table 2). However, this effect varied according to the type of communication strategy. Nonvaccinated participants reported greater intent for future vaccination when heat maps, severe cases, confident language, or exotic influenza labels were used (Table). Vaccinated participants reported greater intent for future vaccination when confident language or scientific/exotic influenza labels were used (Table). The use of metaphors had no effect on either group.

This study should be interpreted in the context of certain limitations. For instance, participants reviewed a hypothetical news article, which may be different than direct communication with a healthcare provider or reading an actual article during a pandemic.

Certain communication strategies, such as use of confident language or an exotic influenza label, were effective regardless of prior vaccination status. Yet use of a scientific influenza label was more effective than use of an exotic influenza label among previously vaccinated participants. Other communication strategies, such as use of heat maps or describing severe cases, were effective among nonvaccinated but not previously vaccinated participants. Vaccination rates for influenza may be improved by targeting healthcare communication based on prior vaccination experiences (11,12).

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## Peripheral Plasma and Semen Cytokine Response to Zika Virus in Humans

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We assessed Zika virus RNA and select cytokine levels in semen, blood, and plasma samples from an infected patient in South America. Viral RNA was detected in semen >2 months after viremia clearance; cytokine profiles differed in semen and plasma. After viremia, Zika virus appears to become compartmentalized in the male reproductive tract.

Before the 2015–2016 outbreak, Zika virus infection had been associated with only mild symptoms. However, the outbreak revealed infection could cause severe clinical manifestations, particularly for fetuses and newborns (1). Furthermore, detection of replicative virus in semen and sexual transmission of the infection resulted in a paradigm shift in Zika virus virology (2,3). Several animal models were developed to study these phenomena, and studies revealed that Zika virus persistence within the male reproductive tract (MRT) results in diminished testosterone and oligospermia (4). However, because of complex ethics considerations, the consequences of infection on the MRT remain poorly understood (5).

To characterize infection in the MRT further, we conducted a longitudinal 6-month study examining Zika virus load and immunologic profile in blood, plasma, and semen in 1 man. The study patient was a 32-year-old immunocompetent white man with an asymptomatic Zika virus infection acquired in South America in January 2016; the control was a healthy 40-year-old white man without risk factors for acute or chronic infection who lived in the same area. We evaluated the concentrations of a select panel of cytokines, including innate immune mediators (interferon [IFN]- $\gamma$ , interleukin [IL]-15, IFN- $\beta$ ); inflammatory factors (IL-6, IL-18, soluble intercellular adhesion molecule 1 [sICAM-1]); chemokines (CC-motif chemokine ligand [CCL] 3, CCL-4, CXC-motif chemokine ligand [CXCL] 1, CXCL-8, CXCL-10); hematopoietic factors (granulocyte colony-stimulating factor [G-CSF], granulocyte-macrophage colony-stimulating factor); the angiogenic factor vascular endothelial growth factor A (VEGF-A); and proteases (matrix metalloproteinase [MMP]-2, MMP-9). We quantified cytokines using ProcartaPlex Multiplex Assay (ebioscience, <https://www.thermofisher.com>).

At admission, the patient had moderate fever, maculopapular rash, myalgia, and arthralgia and recovered within a few days. He was HIV negative; dengue and chikungunya virus infections were ruled out using ELISA Diapro (Diagnostic Bioprobes Srl, <https://www.diapro.it>) and RealStar Dengue and Chikungunya RT-PCR Kit 2.0 (Altona Diagnostics, <https://www.altona-diagnostics.com>). The patient did not experience other genital or urinary tract infections during the study.

Two days after symptom onset, viral RNA was higher in semen ( $1.04 \times 10^5$  copies/mL) than in blood ( $9.4 \times 10^3$  copies/mL); RNA was detectable for up to 100 days in blood

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## Appendix

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## Methods

### Theoretical frameworks

Prior studies have evaluated the effect of certain communication strategies to improve influenza vaccination rates (1–4). Yet, these studies looked at aggregate results among all participants. We hypothesized that people respond differently to messaging, particularly based on their belief system.

Thus, we used the Health Belief Model (HBM) as a theoretical framework for the hypothesis that guided this study (5). HBM was developed as an overarching concept that health behavior is based on personal beliefs about a disease (perceived benefits, perceived barriers, perceived susceptibility, perceived severity), available strategies to mitigate the disease (cues to action, self-efficacy), and modifying variables. We believed that prior vaccination might act on

several layers of the HBM—on perceived benefits, barriers, susceptibility, and severity. In other words, whether or not an individual receives a prior vaccination may be due to their health beliefs, and these health beliefs may affect how they respond to healthcare communication aimed at improving vaccination rates.

### **Study population**

A stratified random sample of adults was recruited by Survey Sampling International (SSI) from a panel of Internet users. Panel members were recruited through various opt-in methods, such as Web sites, Internet banners, e-mails, television advertisements, e-mails, apps, and social media. SSI employs a probability-weighted random process to select panel members.

For this study, quotas were established based on age and gender to ensure that the sample was representative of these characteristics for each country. The sampling algorithm continued to recruit SSI participants until all quotas were achieved. Participants were recruited between February and March 2016. Incomplete surveys were excluded. Upon survey completion, participants were entered into drawings administered by SSI for modest prizes.

Subjects were recruited from Finland, Germany, Hungary, Italy, the Netherlands, Norway, Poland, Spain, Sweden, the United Kingdom, and the United States. Participants received surveys in the primary language of their country of residence. Countries were grouped into six regions for analyses. The regions were defined geographically: North (Finland, Norway, Sweden), East (Hungary, Poland), South (Spain, Italy), West (Germany, the Netherlands), the United Kingdom, and the United States.

### **Survey**

Participants were requested to imagine an epidemic of influenza and then provided with a simulated news article that described the spread of influenza in their country. The article contained direct quotes from hypothetical healthcare experts, as well as information regarding the influenza virus, its potential symptoms, and a vaccine under development. Articles and surveys were translated from English to the country's main language and reviewed with a native speaker from each country.

### **Communication strategies**

Five communication strategies were tested: graphics (1), case severity (4), confident language, influenza labels (3), and metaphor use.

For graphics, articles contained one of three visualizations presenting influenza prevalence (heat map, dot map, or picto-trendline) (1).

For case severity, the average case of influenza was either 1) not discussed, 2) described as mild (moderate fever and cough that is self-limited), or 3) described as severe (high fever, cough, vomiting that generally requires intravenous medication and hospitalization) (4).

For confident language, the article contained quotes from a hypothetical scientific expert, who used language of *scientific certainty* (“Health officials are confident that this outbreak will be a bad one.”), *uncertainty* (“Yet, health officials say it’s still too soon to tell just how bad the outbreak will be.”), or *uncertainty with normalizing language* (“It’s simply too early to predict how severe the flu will be. It might turn out to be mild to moderate like most seasonal flus but could also be more severe than usual.”) (2).

For influenza labels, each article referred to influenza by one of three labels: 1) “H11N3 influenza,” a scientific label; 2) “horse flu,” an animal reservoir label; or 3) “Yarraman flu,” an exotic-sounding label. Yarraman is an aboriginal term for horse (3).

For metaphor use, articles used one of three metaphor styles to describe the spread of the influenza pandemic: 1) infectious disease (using words such as virus and infecting); 2) war (using words such as invading, acts like an army, infiltrate, combat); or 3) gardening (springing up across, grown, acts like a weed) (3).

### **Data quality**

All Survey Sampling International (SSI) participants undergo systematic quality controls before inclusion in any sample. For instance, SSI uses digital fingerprinting to flag duplicate respondents. SSI performs continuous monitoring to assess for inappropriately quick responses or inattention. To confirm location, SSI uses two-factor authentication before reward redemption.

### **Data analysis**

Data management and analysis were performed using Stata 14.2 (StataCorp, College Station, TX). All tests were two-sided with *P* values less than 0.05 considered significant.

## Example of a scenario provided to UK participants

### Intro

Imagine there has been an outbreak of the flu. The following article that you will read describes the current status of the outbreak.

### Scenario

#### PHE Reports H11N3 Influenza Spreading Across the UK

The H11N3 Influenza has been springing up across the United Kingdom. The number of people reported to have H11N3 Influenza has grown recently according to health officials at Public Health England (PHE).

Health officials are confident that this outbreak will be a bad one. “H11N3 Influenza acts like a weed quickly spreading across the UK,” says Dr. Peter Hamilton, the lead expert with the PHE. “We are seeing it spring up and move from city to city with alarming speed.”

“H11N3 Influenza is a severe virus, and people are at risk for serious illness or death,” said Dr. Hamilton. “Although we believe that many people will only have relatively mild to moderate symptoms, we expect to see some severe cases, some of which will lead to death.”

Most of those who have gotten sick have experienced moderate fever with cough and body aches. Symptoms generally go away without medicine. Some extreme cases have required patients seeing a doctor and 1–2 days of hospitalization. These individuals experienced difficulty breathing, sudden dizziness, and severe persistent coughing.

Dr. Hamilton emphasized that the estimates of the symptoms that those with H11N3 will experience are based on the information currently available to health officials.

With a growing number of cases of people getting the virus, Dr. Hamilton promised that the soon to be released vaccine will prevent people from getting H11N3 Influenza. Vaccines eradicate the spread of diseases by using the body’s natural response to prevent us from getting sick. Specifically, the H11N3 Influenza vaccine will create antibodies, which are like the gardeners of the body that identify weeds so the immune system can quickly uproot H11N3 Influenza when it is encountered again.

Dr. Hamilton assured that the vaccine will be safe, effective, and has been tested extensively. “The H11N3 Influenza vaccine uses many of the same elements of vaccines from previous flu seasons and is undergoing standard development and testing. We have every reason to believe the vaccine will be effective, and it’s the best option available right now to protect people against the H11N3 Influenza virus,” said Dr. Hamilton.

“The vaccine is the most effective way we have to prevent the growth of H11N3 Influenza,” he said. Once the vaccine becomes available, Dr. Hamilton urged people to get vaccinated, even if they have questions about their risks of H11N3 Influenza or the effectiveness of the vaccine.

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**Appendix Table 1.** Respondent characteristics by vaccination status

Characteristic	Received vaccination in past two years		All respondents
	No	Yes	
Respondents	11,402 (69.5)	4,999 (30.5)	16,401
Age			
<35	3,354 (29.9)	1,062 (21.7)	4,416 (27.4)
35–50	3,193 (28.4)	1,021 (20.8)	4,214 (26.1)
50–59	1,948 (17.4)	674 (13.8)	2,622 (16.3)
60+	2,733 (24.3)	2,146 (43.8)	4,879 (30.3)
Gender			
Male	5,361 (47.3)	2,718 (54.6)	8,079 (49.4)
Female	5,928 (52.1)	2,217 (44.6)	8,145 (49.8)
Other	87 (0.8)	39 (0.8)	126 (0.8)
Married	6,600 (58.0)	3,350 (67.2)	9,950 (60.8)
Healthcare worker	768 (6.8)	708 (14.3)	1,476 (9.1)
Region			
North	2,726 (23.9)	1,104 (22.1)	3,830 (23.4)
East	2,027 (17.8)	462 (9.2)	2,489 (15.2)
South	2,315 (20.3)	780 (15.6)	3,095 (18.9)
West	2,383 (20.9)	1,074 (21.5)	3,457 (21.1)
UK	1,080 (9.5)	907 (18.1)	1,752 (10.7)
U.S.	871 (7.6)	907 (18.1)	1,778 (10.8)

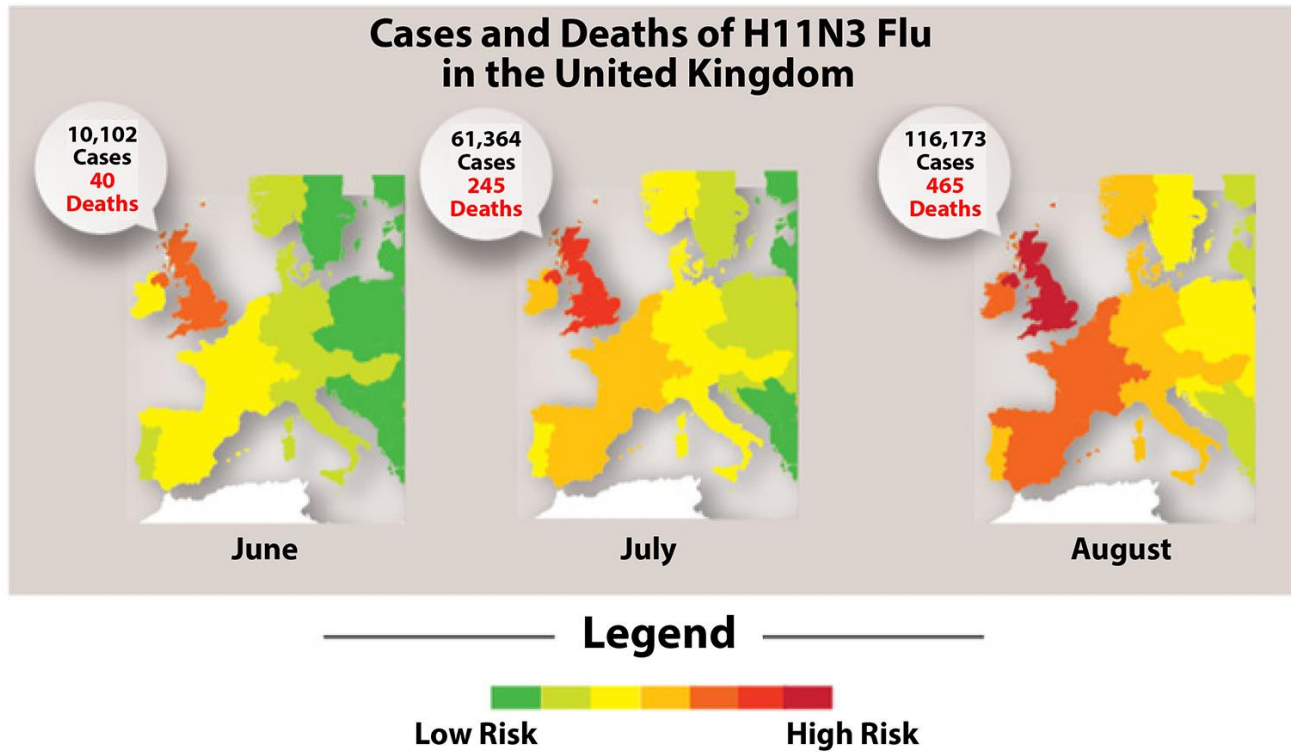
**Appendix Table 2.** Effect of communication strategies on intent to vaccinate with no prior vaccination as the reference category

Strategy	Vaccination over the past two years			
	aOR <sup>a</sup> for “No”*	P for “No”	aOR <sup>b</sup> for “Yes”†	P for row interaction‡
Graphic				
Picto-trendline	Reference	Ref	6.1 (5.0, 7.5)	<0.001
Dot map	1.1 (0.9, 1.2)	0.06	6.2 (5.0, 7.6)	<0.001
Heat map	1.1 (1.0, 1.2)	0.01	6.7 (5.7, 7.9)	<0.001
Case severity				
Both	Reference	Ref	6.4 (5.4, 7.6)	<0.001
Typical	1.0 (0.9, 1.1)	0.78	5.6 (4.6, 6.9)	<0.001
Severe	1.1 (1.0, 1.3)	0.02	6.8 (5.7, 8.1)	<0.001
Confident language				
Uncertainty with normalizing language	Reference	Ref	5.7 (4.7, 7.0)	<0.001
Uncertainty	1.0 (0.9, 1.1)	0.97	6.2 (5.2, 7.3)	<0.001
Scientific certainty	1.2 (1.1, 1.3)	<0.001	7.1 (5.9, 8.6)	<0.001
Influenza label				
Horse flu	Reference	Ref	4.7 (4.1, 5.4)	<0.001
H11N3	1.0 (0.9, 1.1)	0.62	6.5 (5.0, 8.3)	<0.001
Yarraman flu	1.1 (1.0, 1.2)	0.001	5.8 (4.9, 6.9)	<0.001
Metaphor use				
Infectious disease	Reference	Ref	5.9 (4.8, 7.3)	<0.001
War	1.0 (0.9, 1.1)	0.78	5.7 (5.0, 6.5)	<0.001
Gardening	1.0 (0.9, 1.1)	0.75	6.1 (5.2, 7.3)	<0.001

\*Adjusted odds ratio (95% confidence interval). Multivariable ordinal logistic regression adjusted for participant age, gender, marital status, occupation as healthcare worker, and country of residence.

†Reference value for this column is the “No” column.

‡Test of row interactions between vaccination status and the communication strategy.



Appendix Figure. Example of heat map provided to UK participant.