Vaccine Administration Decision Making: The Case of Yellow Fever Vaccine

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Background. Providers must counsel travelers to yellow fever (YF)—endemic areas, although risk estimates of disease and vaccine serious adverse events (SAEs) may be imprecise. The impact of risk information and patients’ requests for participation in vaccine decisions on providers’ recommendations is unknown.

Methods. Vaccine providers were surveyed regarding decisions for 4 patient scenarios before and after being presented information about risk of YF disease vs vaccine SAEs. Participants’ theoretical attitudes were compared with actual responses to scenarios in which patients wanted to share vaccine decisions. Analyses were done by using χ² tests with significance level of .05.

Results. Forty-six percent of respondents made appropriate initial YF vaccine administration decisions for a pregnant woman, 73% for an immunosuppressed man, and 49% for an 8-month-old infant. After receiving scenario-specific information, 20%, 54%, and 23% of respondents respectively who initially responded incorrectly changed to a more appropriate decision. Thirty-one percent of participants made consistently appropriate decisions. Among participants who made ≥1 incorrect decision, 35.7% made no decision changes after receiving information. In the scenario in which either a decision to withhold or to administer vaccine was acceptable, 19% of respondents refused a patient’s request for vaccine.

Conclusions. Targeted information is necessary but insufficient to change the process of vaccine administration decision making. Providers need additional education to enable them to apply evidence, overcome cognitive decision-making errors, and involve patients in vaccine decisions.

Yellow fever (YF), a viral hemorrhagic fever, is caused by a flavivirus transmitted by the bite of an infected mosquito. The disease is endemic in sub-Saharan Africa and tropical South America [1]. The majority of humans infected with YF virus are asymptomatic or have clinically inapparent infection. However, when YF disease occurs, symptoms can range from mild febrile illness to hemorrhagic fever with multiorgan involvement. In severe cases with hepatic and renal involvement, the mortality rate is 20%–50% [1]. Because no specific treatment is available for YF, prevention is paramount and is best accomplished by mosquito bite avoidance and vaccination.

Vaccination of travelers to YF-endemic areas is an essential strategy to prevent disease in individuals and to prevent the importation of YF virus to nonendemic areas that are ecologically suitable for YF virus transmission. The Centers for Disease Control and Prevention (CDC) and World Health Organization recommend YF vaccination for travelers to countries with risk for YF. Nine cases of YF in unvaccinated travelers from the United States and Europe were reported from 1970 to 2002 [2]. In addition, some countries require proof of YF vaccination or a medical waiver for travelers arriving from YF-endemic countries [2].
An extremely effective live-attenuated 17D YF vaccine (17D) has been available since 1936, but potentially fatal serious adverse events (SAEs) infrequently follow vaccination. The most significant SAEs are YF vaccine–associated viscerotropic disease (YEL-AVD) and YF vaccine–associated neurologic disease (YEL-AND). YEL-AVD, first reported in 2001, is acute multiorgan dysfunction or failure after YF vaccination [1, 3]. It resembles wild-type YF disease, with manifestations that can include fever, jaundice, hepatitis, renal failure, thrombocytopenia, and bleeding dyscrasias. The incidence of YEL-AVD is approximately 0.4 per 100,000 doses of vaccine administered, and the case-fatality ratio is 65% [4, 5]. YEL-AND manifestations include meningoencephalitis, Guillain–Barré syndrome, and acute disseminated encephalomyelitis. Its estimated incidence is 0.8 per 100,000 doses administered [5]. Although the majority of patients recover, 2 reports of fatal YEL-AND have been published [6, 7].

Reported risk factors for YEL-AVD are advanced age and history of thymus disease [5, 8, 9]. Four of the first 23 reported cases of YEL-AVD occurred in persons with a history of thymectomy for thymoma [9]. Reported rates of YEL-AVD are 1 and 2.3 per 100,000 doses in persons 60–69 and ≥70 years of age, respectively, 2.5–6 times the overall rate [5]. Similarly, the reported rates of YEL-AND are 1.6 and 2.3 per 100,000 doses in persons 60–69 and ≥70 years of age, respectively, 2–3 times the overall rate [5].

YF vaccine is contraindicated in several situations: allergy to YF vaccine components, age <6 months, symptomatic human immunodeficiency virus (HIV) infection or CD4 T-lymphocyte count <200 cells/mm³, thymus disorder associated with abnormal immune cell function, primary immunodeficiency, malignant neoplasm, organ transplantation, and immunosuppressive or immunomodulatory therapy (including radiation) [4]. Precautions to its use include age 6–8 months, age ≥60 years, asymptomatic HIV infection and CD4 T-lymphocyte count of 200–499 cells/mm³, pregnancy, and breast-feeding [4].

Several studies have demonstrated that the proportion of women vaccinated during pregnancy who develop YF virus antibodies is variable and could be related to the trimester in which they were vaccinated [10, 11]. HIV infection has also been associated with a reduced immunologic response to YF vaccine [12, 13]. Consequently, serologic testing after YF vaccination to document an adequate immune response has been suggested for pregnant patients and those with asymptomatic HIV infection [4].

Healthcare providers need to balance the risk of SAEs associated with the vaccine and benefits of YF vaccination for each patient. However, the risk of SAEs for a given patient and YF disease for a given location is not always known. To address the geographic risk of YF, the World Health Organization, the CDC, and independent experts systematically reviewed countries with risk of YF virus transmission and updated their YF vaccine recommendations [14]. These risk estimates, however, are imprecise and are extrapolated from serosurveys in some endemic areas and may not reflect current risk in all areas. Although practice patterns may differ from those in the United States, a survey of YF vaccination practices in England found that a majority of YF vaccine providers reported the need for provider training and resources on travel health–related topics [15].

Proponents of evidence-based medicine and guidelines have noted the challenge of enhancing providers’ uptake and application of evidence to practice, even when recommendations are available for specific healthcare decisions [16]. Researchers have noted that clinician characteristics (eg, knowledge, attitudes, motivation), characteristics of the evidence (eg, its strength and complexity), and system characteristics (eg, tools, technology, organizational characteristics, environment) may affect whether information is translated into practice [17]. Providers must also apply the evidence to individual patients, communicate that evidence in ways the patient can understand, make recommendations, and reach agreement with the patient about what she or he is able and willing to do [18]. Educational efforts to enhance provider decision making, communication, and shared, informed decision making with travelers regarding vaccine administration must take all these factors into consideration.

The primary objectives of this study were to assess the effects of provider education about traveler- and destination-specific YF disease risk and vaccine SAEs. We investigated the appropriateness of providers’ initial vaccine administration decisions and whether they changed their decisions after receiving case scenario-specific information. A secondary goal of the study was to compare providers’ theoretical attitudes with their actual responses when asked to share a vaccine decision with patients.

METHODS

We reviewed YF vaccine-related questions on a listserv for members of the International Society of Travel Medicine (ISTM) over a 6-month period to identify content areas that were the subject of recurrent questions and discussion. Members from 43 countries participate in this unmoderated online discussion forum. We created 4 case scenarios based on their most frequently asked questions (Table 1). Although the case scenarios in this survey were designed to include a range of interpretations, we defined preferable or “appropriate” responses for each scenario based on destination-specific disease risk and traveler-specific likelihood of vaccine SAEs. Our decisions were informed by scientific evidence and expert opinion, including members of the Advisory Committee on Immunization Practices YF vaccine working group. In 2 case scenarios, we inserted continuations that involved a hypothetical conflict between the provider’s YF vaccine recommendation and the traveler’s preference.
An online link to the survey was e-mailed to clinicians in the CDC YF vaccine registry of providers, and United States–based members of ISTM, and the American Committee on Clinical Tropical Medicine and Travelers’ Health. After viewing each scenario, survey participants selected a yes-or-no vaccine administration choice through a software “forcing function,” before proceeding to the next screen. They then viewed a screen presenting estimated risk from YF disease and vaccine for the described destination and patient. The next screen rerequested a vaccine decision given the information presented. Two cases presented hypothetical challenges in which participants were asked to assume they decided against vaccination, but a traveler who understood the risks, benefits, and alternatives to YF vaccination insisted on receiving it. The following screen again rerequested a vaccine decision.

Data were analyzed by using χ² tests and a significance level of .05. Analyses were performed by using SAS software (version 9.3; SAS Institute). This study was reviewed and determined to be exempt by institutional review boards at Boston Medical Center, and Mount Auburn Hospital and by the CDC Human Research Protection Office review.

**RESULTS**

Of 3400 providers to whom an email was sent, 832 activated the survey link, 772 of whom indicated they discuss YF vaccine with travelers and were therefore eligible to complete the survey. Of 772 participants, 599 (78%) finished the 4 case scenarios; 514 (67%) completed additional demographic questions at the end of the survey. During the year before taking the survey, 483 of 514 respondents (94%) reported accessing information about YF vaccine side effects and contraindications; 491 of 514 (96%) reported accessing information about YF disease incidence in a particular country (data not shown).

**Variables Associated With Appropriate Decisions**

We examined respondent characteristics associated with consistently arriving at correct vaccine administration decisions.
We found a significant association between providers’ age and whether they arrived at ≥1 incorrect decisions ($P = .04$). Although no age group arrived at correct decisions with any consistency, those in the >66-year age group were more likely than the others to arrive at ≥1 incorrect decision.

Provider Responses to Informed Patients’ Hypothetical Preferences
Most providers (692/772; 90%) expressed a hypothetical preference to share decisions with patients about whether to administer YF vaccine. When providers were challenged by a patient who desired the vaccine, 155 of 625 (25%) would not administer YF vaccine to the pregnant traveler (case 1), and 117 of 612 (19%) would not administer it to the elderly traveler (case 2). Of these, 136 of 155 (88%) for case 1 and 104 of 117 (89%) for case 2 had previously expressed a theoretical preference for sharing vaccine decisions with patients.

DISCUSSION
The 4 case scenarios in this survey represent common challenges for providers who must assess risk and communicate vaccine administration recommendations to travelers. Providers must address each traveler’s risk of disease and vaccine SAEs. We found that providers may make inappropriate vaccine administration decisions, that providing case-specific information alone may not change providers’ decisions, and that theoretical preferences for sharing decisions with patients do not necessarily correlate with how providers made decisions in specific cases.

In 2 cases, a small proportion of participants in this study changed an initial inappropriate vaccine administration decision to a more appropriate one after receiving case-specific information (case 1, 20%; case 4, 23%). The appropriate decision was most clear for the patient taking an immunosuppressive medication who was traveling to a country in which the risk of contracting YF has been historically extremely low (case 3). The proportion of providers who retained an inappropriate decision to vaccinate this traveler despite receiving information was surprisingly high (46%), particularly because a decision to administer vaccine in this case might have had adverse clinical consequences for a patient for whom a live virus vaccine was contraindicated.

The scenario in which the largest proportion of participants changed a decision after receiving information was the case of the 72-year-old traveler. This case represents “clinical equipoise,” a situation in which “there is no consensus within the expert clinical community about the comparative merits of the alternatives” [19]. Such circumstances are ideal opportunities for shared informed decision making and
A small proportion (19%) of participants, however, did not drop-off in participation over the course of the survey, the completion rate of case scenarios was 78%. The authors accede to the informed traveler’s request for vaccine in the hypothetical continuation of this scenario. Concerns about risk of the vaccine superseded participants’ theoretical preferences for shared decision making.

The cases of the pregnant traveler and the 8-month-old infant represent situations in which guidance based on expert opinion is available, but there are relatively few authoritative studies to help providers tailor recommendations for particular patients. Providers’ responses to these 2 cases were similar (46% and 49% made appropriate initial decisions in the case of the pregnant traveler and 8-month-old infant, respectively; 20% and 23% changed to an appropriate decision after reading additional information).

The way information is described or “framed” can influence decisions and may partially explain why few providers chose to change some vaccine administration decisions after receiving information. In all case scenarios, the small absolute risks of illness or death due to YF disease were compared with those of vaccine-associated SAEs per 100 000 travelers. The numbers involved in expressing absolute risk, or the risk of an event occurring, are usually small. Relative risks, which compare 2 groups, often involve larger numbers than absolute risks. When disease risk is framed in terms of absolute risk, patients’ uptake of screening and treatment recommendations is lower than when risk is explained in terms of relative risk [21].

Providers may have been influenced by anchoring effects, or the way in which information provided at the outset inhibits the cognitive adjustments that occur in response to subsequent information. People tend to make decisions based on subjective first impressions, which can be difficult to change despite provision of data [22]. Our survey format may have elicited anchoring and premature closure of decision making by compelling participants to make a vaccine decision before receiving information [23].

By providing traveler-specific information, we compelled providers to make contextualized decisions based on the value they ascribed to risk of an act of commission (vaccine administration) compared with the value they ascribed to risk of an act of omission (withholding vaccine). Kahneman and Tversky’s research demonstrated that adverse consequences from action produce more intense regret than inaction [24]. Omission bias (preference for errors arising from inaction over errors arising from action), as well as weighing vaccine risks more heavily than disease risks, has been demonstrated among parents who decide not to vaccinate their children against influenza [25]. Omission bias has also been shown to influence influenza vaccination decisions in adults [26].

Although our study is limited by the survey response rate and drop-off in participation over the course of the survey, the completion rate of case scenarios was 78%. The authors

<table>
<thead>
<tr>
<th>Variable</th>
<th>Arrived at All Correct Decisions, No. (%) (n = 184)</th>
<th>Arrived at ≥1 Incorrect Decision, No. (%) (n = 415)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Profession</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nurse or nurse practitioner</td>
<td>55 (30.2)</td>
<td>127 (69.8)</td>
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<td>263 (69.0)</td>
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<td>5 (33.3)</td>
<td>10 (66.7)</td>
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<tr>
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<td>6 (35.3)</td>
<td>11 (64.7)</td>
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<tr>
<td>Other</td>
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<td>3 (100.0)</td>
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<td>Experience practicing travel medicine, years</td>
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<td>≤5</td>
<td>61 (37.2)</td>
<td>103 (62.8)</td>
<td>.06</td>
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<td>6–10</td>
<td>36 (25.7)</td>
<td>74 (74.3)</td>
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<td>11–20</td>
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<td>&gt;20</td>
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<td>84 (75.7)</td>
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<td>273 (68.4)</td>
<td>.37</td>
</tr>
<tr>
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<td>83 (72.8)</td>
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<td>152 (72.4)</td>
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<td>204 (67.3)</td>
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<td>Travelers seen per week for pretravel consultation, mean, No.</td>
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<td>1–10</td>
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<td>291 (69.0)</td>
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<td>10 (55.6)</td>
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<tr>
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<td>175 (68.9)</td>
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<td>59</td>
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<tr>
<td>Age, years</td>
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<td>&lt;30</td>
<td>2 (28.6)</td>
<td>5 (71.4)</td>
<td>.04</td>
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<td>31–50</td>
<td>49 (27.7)</td>
<td>128 (72.3)</td>
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<tr>
<td>51–65</td>
<td>101 (34.1)</td>
<td>192 (65.5)</td>
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<tr>
<td>≥66</td>
<td>5 (13.9)</td>
<td>31 (86.1)</td>
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<tr>
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<td>27</td>
<td>59</td>
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</table>

Abbreviations, ASTMH, American Society of Tropical Medicine and Hygiene; ISTM, International Society of Travel Medicine.

* Analyses were done using χ² tests, with a significance level of .05.
defined an appropriate vaccine administration decision for each case based on published studies and expert opinion and guidelines. However, the evidence provided in the survey, and that which is generally available to travel medicine providers regarding YF disease risk and vaccine SAEs, may have been insufficient to persuade participants to agree with these standards. Therefore, participants’ perceptions about the quality of the evidence may have influenced their decision making. However, this reflects the situation faced by providers in the majority of clinical decisions. Future qualitative studies are needed to explore what factors cause providers to change or retain their decisions.

**Educational Implications**

The findings of this study suggests that providing information in the absence of supplementary educational strategies, while necessary, may be insufficient to change the process of providers’ decision making and therefore patient care. Despite calls for clinical decisions to be based on timely, up-to-date information, significant barriers to this goal remain, not the least of which is the lack of relevant evidence for most clinical decisions. Training tools and educational resources have recently become available online to educate providers about YF disease, epidemiology, vaccine, and pretravel consultation [27]. Multifaceted educational interventions and resources will probably be necessary to help vaccine providers access and apply available evidence and practice recommendations to individual patients’ circumstances. Such resources currently include print and web-based material and continuing education courses. Interactive case-based formats with questions and immediate computerized feedback, webinars, and facilitated discussion groups could supplement available resources. Furthermore, clinicians need to learn about cognitive errors due to framing, anchoring, and omission bias when making decisions. Educational programs should encourage systematic approaches to the processing of information in the presence of uncertainty, which requires “effortful thinking” to adjust risk perception rather than heuristic-based automatic thinking [23, 28].

Another important component of clinician education relates to communication. Clinicians need to adjust recommendations according to a patient’s preferences and medical history. This requires effective communication skills to elicit patients’ information needs and concerns, tailor information to a patient’s ability to comprehend risk information, address concerns, respond to questions, and reach agreement about vaccine decisions based on informed choices [18]. Competent demonstration of these skills is rare, and improving these skills should be a consideration of professional education programs [29].

Patient decision aids are tools that can be used to enhance the decision-making process. These aids have been shown to improve patients’ knowledge of options and understanding of outcome probabilities, increase involvement in decision making, and decrease decisional conflict [30]. A decision aid has recently been developed to help healthcare workers considering influenza immunization, but such tools are lacking for other vaccines [31].

To implement evidence-based, informed, shared decision making, the healthcare community should develop educational resources, communication skills training, and decision-support systems that enable providers to apply evidence to practice and overcome cognitive errors in decision making. Additional resources are also needed to enhance patients’ knowledge and facilitate their participation in vaccine decisions. Providers would benefit from communication skills training to help them explain risk clearly and to reach decisions that reflect patients’ informed choices.

**Supplementary Data**

Supplementary materials are available at Clinical Infectious Diseases online (http://cid.oxfordjournals.org). Supplementary materials consist of data provided by the author that are published to benefit the reader. The posted materials are not copyrighted. The contents of all supplementary data are the sole responsibility of the authors. Questions or messages regarding errors should be addressed to the author.

**Notes**

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**Disclaimer.** The study design, collection, analysis and interpretation of data, writing the report, and decision to submit the paper were solely the responsibility of the authors. The findings and conclusions of this report do not necessarily represent the official position of the Centers for Disease Control and Prevention (CDC).

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All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

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