

# Hepatitis B Risks and Immunization Coverage Among American Travelers

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**Background.** Hepatitis B is endemic in much of Asia, Africa, and parts of South America, regions that are increasingly popular destinations for American travelers. The frequency of hepatitis B risks during travel has been examined for Europeans but not Americans. Further, limited data are available to describe the domestic hepatitis B risk factors of American travelers, the proportion vaccinated, and whether immunization activities target travelers at highest risk. We conducted a survey of international travelers to address these issues.

**Methods.** A survey was mailed to 884 American international travelers, of whom 618 (70%) responded. The survey covered demographic and travel characteristics, sources of pretravel health advice, immunization status, and items needed to assess hepatitis B vaccination candidacy. Travel-specific items concerned the most recent trip to a hepatitis B endemic region. Hepatitis B risk during the most recent trip was classified as high, potential, or none based on potential exposure to blood or bodily fluids.

**Results.** Only 31% of respondents visited any health practitioner to obtain pretravel health advice; 13% visited a travel medicine specialist. Totally 45% of respondents reported  $\geq 1$  domestic or travel-related hepatitis B risk, and 8% were at high risk during travel. Risk factors were more common among younger travelers and those with longer travel durations. Travel medicine specialists were more likely than nonspecialists to provide hepatitis B vaccine (40% vs 21%,  $p = 0.01$ ). Travelers with risk factors were no more likely to be vaccinated in specialist or nonspecialist settings. Upon departure, only 19% of all travelers and 30% of travelers with risk factors had received three or more hepatitis B vaccine doses.

**Conclusions.** Most US travelers to hepatitis B endemic regions do not secure pretravel health advice, and most have not received three doses of hepatitis B vaccine. A substantial share are candidates for hepatitis B vaccination based on their domestic activities and/or face hepatitis B risks during travel.

Hepatitis B is endemic in much of Asia, Africa, and parts of South America, regions that are increasingly popular destinations for American travelers. A 1990 study estimated the incidence of overt hepatitis B at 6 per 10,000 travel months in

Asia and 2 per 10,000 travel months in Africa and Latin America.<sup>1</sup> Since most adults infected with hepatitis B remain asymptomatic until and unless chronic infection causes long-term liver damage,<sup>2</sup> infection rates are probably severalfold greater.

The effects of adult hepatitis B infection are considerable. Typical symptoms of acute infection include anorexia, nausea, vomiting, jaundice, and abdominal pain.<sup>3</sup> About 20% of cases are hospitalized, with a twofold greater risk among persons 50 years or older.<sup>4</sup> The risk of acute liver failure is at least 0.7%.<sup>3</sup> Among these patients, most die without liver transplantation.<sup>5</sup> Those receiving a transplant incur significant lifetime medical costs and impaired quality of life.<sup>6,7</sup> Though the probability that hepatitis B will develop into chronic infection

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declines with age,<sup>8</sup> this remains a concern. The risk of chronic infection is 8% among young adults, declining to about 6% among those infected after age 40 years.<sup>9</sup> Persons chronically infected pose significant risks to their household and sexual contacts, and face substantially elevated risks of cirrhosis and hepatocellular carcinoma, significantly reducing life expectancy.<sup>9</sup>

Americans visiting developing countries may be less likely to obtain pretravel health advice than Europeans. Among 404 Americans traveling to developing countries, 36% reported having sought travel health advice.<sup>10</sup> A similar survey of 5,067 Europeans revealed that 52% had sought travel health advice.<sup>11</sup> About 8% of European adults engage in activities placing them at high risk of hepatitis B while traveling, and nearly 67% face some risk.<sup>12</sup> However, the risk factors of American travelers have not been assessed. Further, limited data are available to describe hepatitis B vaccination coverage among US travelers, the characteristics of travelers who obtain versus do not obtain pretravel health advice, and the domestic hepatitis B risk factors of US travelers. We conducted a survey of American travelers to examine these issues.

## Methods

### *Respondent Selection and Recruitment*

The Buyers Choice Survey of America is a mailing list developed from responses to extensive lifestyle surveys. From this listing, we identified 87,000 persons reporting international travel as a leisure activity. Business Travelers at Home is a mailing list of 7.8 million corporate employees, of whom 1.1 million self-identified as international business travelers. Systematic samples were drawn to select 5,000 travelers from each list, who were mailed a letter describing the study. Persons having traveled since January 2000 to regions of high or intermediate hepatitis B endemicity (defined by a map enclosed with the letter) were asked to return a postcard indicating their willingness to complete a confidential survey. A prepaid phone card was offered to persons who returned the postcard and subsequently completed the survey. Survey activities were conducted between October 2004 and January 2005.

### *Entry Criteria and Definition of Index Trip*

The study was limited to persons who (1) had departed the United States for travel to a region of high or intermediate hepatitis B endemicity since

January 2000 and were upon departure (2) age 18 years or older, (3) a citizen or permanent resident of the United States, and (4) not a member of the Armed Forces. Respondents provided general and travel-specific information, with the latter regarding a specific index trip. The index trip was the most recent US departure including an overnight stay in any high or intermediate hepatitis B endemic region.

### *Survey Description*

The survey instrument (available from the corresponding author) was derived from an interview guide used in a similar European study<sup>12</sup> and an adult vaccination screening tool.<sup>13</sup> When possible, items were presented using a "yes/no" format. The survey was divided into sections covering (1) study eligibility, index trip definition, and travel itinerary; (2) respondent demography; (3) domestic hepatitis B risk factors; (4) sources of pretravel health information; (5) hepatitis B vaccination status at the earlier of presenting for pretravel health advice or index trip departure; (6) hepatitis vaccines received as a consequence of pretravel health advice; and (7) activities occurring during the index trip representing possible exposures to blood-borne pathogens. To aid recall, the survey explained differences between hepatitis A vaccine, hepatitis B vaccine, and immune globulin shots.

### *Operational Definitions*

The presence of a domestic hepatitis B risk factor was based on a series of items regarding sex practices, medical conditions, occupation, and other possible exposures (eg, living with a chronic hepatitis B patient).<sup>13</sup> Two definitions of hepatitis B risk during the index trip were defined. Persons suffering an accident or illness requiring invasive medical attention, receiving dental treatment, undergoing skin-perforating cosmetic procedure, or engaging in sex with a previously unknown endemic region native were deemed to be at high risk. Those sharing personal grooming items with an endemic region native, participating in sporting or adventure activities (eg, horseback riding), or undergoing cosmetic practices with a risk of skin perforation (eg, haircut, manicure) were deemed at potential risk. Travelers meeting either definition were considered at any travel risk. To reduce the number of cells with small sample sizes, respondent demography was categorized as age (18–40 years, 41–59 years, >59 years), race/ethnicity (non-Hispanic white, other), marital status (currently married or living with partner, other), and annual income (<\$50,000,

\$50,001–\$100,000, >\$100,000). Travel purpose was defined as visiting friends or relatives (may also include tourism), tourism only, or any purpose other than tourism or visiting friends or relatives (including research, education, missionary or volunteer work, or business). Companionship was dichotomized (with US family, friends, or business associates; alone). Travel duration was categorized based on the number of days spent in hepatitis B endemic regions (<7 days, 7–20 days, >20 days). Hepatitis B vaccination coverage was examined based on the number of doses received prior to departure, whether obtained as a consequence of pretravel health advice or previously.

### Statistical Methods

Associations between respondent characteristics and obtaining pretravel health advice from a health professional were investigated using logistic regression. In regression models, “any pretravel health advice visit” and “pretravel health advice from a travel medicine specialist” each served as dichotomous dependent variables. Adjusted odds ratios were determined for each independent variable, with 95% confidence intervals calculated using the Wald method.<sup>14</sup> Identical methods were used to examine traveler characteristics predicting the presence of (1) a domestic hepatitis B risk factor, (2) high hepatitis B risk during travel, (3) any hepatitis B risk during travel, and (4) either a domestic or travel-related risk factor. Logistic regression was also used to examine factors predicting hepatitis B vaccination of travelers who had received less than three vaccine doses upon presenting for pretravel health advice. The number of hepatitis B vaccine doses obtained prior to departure was assessed by age and risk factor presence. Differences were examined using the chi-square test, and *p* values <0.05 were considered statistically significant.

## Results

### Response Rates

Of the 10,000 letters mailed, 328 were returned as undeliverable and 884 postcards were received, reflecting a 9% response rate. It is impossible to determine the proportion of nonrespondents who were ineligible versus disinterested in participation. Of the 884 surveys mailed, 618 (70%) were returned. There were no significant differences between respondents and nonrespondents with respect to age, gender, US geographic region of residence, or international regions visited on their index trip.

### Respondent Characteristics

A plurality of respondents were aged 41 to 59 years (Table 1). Most described themselves as non-Hispanic whites, were currently married, and had annual incomes exceeding \$50,000. Only 15% traveled without US companions. Most respondents traveled for tourism only, while 18% traveled to visit friends or relatives. The 24% of respondents traveling for other reasons most often cited business, research, or education. A majority of respondents stayed in hepatitis B endemic regions for 7 to 20 days.

### Sources of Pretravel Health Information

Pretravel health information was obtained by 69% of respondents, but only 31% visited a health professional and 13% visited a travel medicine specialist (Table 1). The most frequently cited sources of travel health information were books or the Internet (34%), travel agents (27%), friends or acquaintances (27%), and pharmacists (9%). Travel duration >20 days was most strongly associated with obtaining pretravel health advice from any medical practitioner (odds ratio 5.8, 95% confidence interval 2.7–12.2) or a travel medicine specialist (16.5, 3.5–76.5). Travelers visiting friends or relatives were least likely to obtain pretravel health advice. Other factors independently associated with obtaining pretravel health advice from a specialist were age >59 years, being unmarried, having higher income, and traveling alone. Other factors associated with obtaining pretravel health advice from any medical practitioner were being unmarried and having higher income.

### Hepatitis B Risk Factors

A domestic, travel-related, or either risk was reported by 23, 32, and 45% of respondents, respectively (Table 2). The most frequently reported domestic risk factors were related to occupation (eg, medical or public safety work) or sexual activity (eg, more than one partner during the past 6 months). Eight percent of respondents reported ≥1 high-risk activity during travel, with sexual activity (4% of respondents) and dental treatment (2%) being most common. Of the potential risk activities considered, participation in sporting activities (15% of respondents) and cosmetic practices with a risk of skin perforation (16%) were most commonly reported. Travel duration >20 days was strongly associated with high risk during travel (odds ratio 4.6, 95% confidence interval 1.7–12.6). Other factors independently associated with high risk during travel were male gender, being unmarried, and traveling

**Table 1** Characteristics associated with securing pretravel health advice from medical practitioner

		Any practitioner	Travel medicine specialist
	N (%)	OR (95% CI)	OR (95% CI)
>59 years	150 (24)	1.5 (0.9–2.5)	<b>2.3 (1.1–5.0)</b>
41–59 years	264 (43)	1.2 (0.7–1.9)	1.5 (0.7–3.2)
18–40 years	204 (33)	1.0 (reference)	1.0 (reference)
Female	284 (46)	1.0 (0.7–1.4)	1.2 (0.7–2.0)
Male	334 (54)	1.0 (reference)	1.0 (reference)
Other than non-Hispanic white	516 (84)	1.5 (0.9–2.4)	1.6 (0.8–3.2)
Non-Hispanic white	102 (16)	1.0 (reference)	1.0 (reference)
Currently unmarried	440 (71)	<b>2.0 (1.3–3.1)</b>	<b>2.6 (1.4–4.8)</b>
Currently married*	178 (29)	1.0 (reference)	1.0 (reference)
Annual income >\$100,000	145 (23)	<b>2.2 (1.3–3.8)</b>	<b>4.1 (1.8–9.3)</b>
Annual income \$50,001–\$100,000	252 (41)	<b>2.0 (1.2–3.4)</b>	1.8 (0.8–3.9)
Annual income <\$50,000	221 (36)	1.0 (reference)	1.0 (reference)
Travel alone	92 (15)	1.3 (0.8–2.1)	<b>2.6 (1.4–5.0)</b>
Travel with companions	526 (85)	1.0 (reference)	1.0 (reference)
Travel for other than tourism or visiting friends or relatives	149 (24)	<b>2.4 (1.3–4.4)</b>	<b>2.4 (1.0–5.5)</b>
Travel for tourism only	359 (58)	1.7 (0.9–2.9)	<b>2.8 (1.2–6.7)</b>
Travel to visit friends or relatives (may include tourism)	110 (18)	1.0 (reference)	1.0 (reference)
>20 days travel duration	116 (19)	<b>5.8 (2.7–12.2)</b>	<b>16.5 (3.5–76.5)</b>
7–20 days travel duration	407 (66)	<b>4.0 (2.2–7.5)</b>	<b>9.4 (2.2–39.6)</b>
<7 days travel duration	95 (15)	1.0 (reference)	1.0 (reference)

OR = odds ratio; CI = confidence interval.

\*Includes persons living with unmarried partner. OR adjusted for other listed covariates. Differences  $p < 0.05$  (vs reference group) are depicted in bold type.

alone. The strongest predictor of having any hepatitis B risk factor was age 18 to 40 years (odds ratio 5.8, 95% confidence interval 3.4–9.8). Longer travel duration, race/ethnicity other than non-Hispanic white, male gender, and being unmarried were also independently associated with any hepatitis B risk.

#### Administration of Hepatitis B Vaccine

We identified 149 persons who secured pretravel health advice from a medical practitioner and had not previously received at least three hepatitis B vaccine doses. Among such patients, those presenting to a travel medicine specialist were more likely to receive hepatitis B vaccine (40% vs 21%,  $p = 0.01$ ). However, the presence of a hepatitis risk factor was not associated with being vaccinated. Only 25% of those presenting with a domestic risk factor or subsequently experiencing a travel-related risk were immunized versus 31% of those reporting no hepatitis B risk factor ( $p = 0.45$ ). This lack of association

was present in both specialist ( $p = 0.35$ ) and nonspecialist settings ( $p = 0.90$ ). In logistic regression, the only patient characteristic associated with hepatitis B vaccination was having already begun the vaccination series. Only 23% of travelers with no prior doses received hepatitis B vaccine as a consequence of a pretravel health advice visit versus 43% of those with one or two prior doses ( $p = 0.02$ ). Respondents who obtained travel health information from books or the Internet, travel agents, friends or acquaintances, or pharmacists were neither more nor less likely to receive hepatitis B vaccine at pretravel health advice visit.

#### Immunization Coverage

Upon departure, 29% of respondents had received at least two hepatitis B vaccine doses, while just 19% had received three or more doses (Table 3). Although the presence of hepatitis B risk factors was associated with higher coverage in each age group, most at-risk travelers departed with fewer than three doses, including 62% of persons with a domestic

**Table 2** Characteristics associated with hepatitis B risk factors

	Domestic risk	Any travel risk	High travel risk	Any risk
	23%	32%	8%	45%
% of respondents with risk factor	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
18–40 years	<b>5.9 (3.2–10.9)</b>	<b>3.6 (2.1–6.0)</b>	1.9 (0.8–4.9)	<b>5.8 (3.4–9.8)</b>
41–59 years	<b>2.2 (1.3–3.9)</b>	1.4 (0.9–2.3)	1.2 (0.5–2.6)	<b>1.8 (1.2–2.8)</b>
>59 years	1.0 (reference)	1.0 (reference)	1.0 (reference)	1.0 (reference)
Male	<b>1.7 (1.1–2.6)</b>	<b>1.6 (1.1–2.4)</b>	<b>3.4 (1.7–7.0)</b>	<b>1.5 (1.1–2.2)</b>
Female	1.0 (reference)	1.0 (reference)	1.0 (reference)	1.0 (reference)
Other than non-Hispanic white	<b>2.9 (1.7–4.8)</b>	0.8 (0.5–1.4)	1.0 (0.5–2.4)	<b>2.0 (1.2–3.4)</b>
Non-Hispanic white	1.0 (reference)	1.0 (reference)	1.0 (reference)	1.0 (reference)
Currently unmarried	<b>2.0 (1.2–3.3)</b>	<b>1.8 (1.2–2.8)</b>	<b>2.4 (1.2–5.0)</b>	<b>2.0 (1.3–3.1)</b>
Currently married*	1.0 (reference)	1.0 (reference)	1.0 (reference)	1.0 (reference)
Annual income <\$50,000	<b>0.4 (0.2–0.8)</b>	0.8 (0.5–1.4)	1.2 (0.5–3.0)	0.8 (0.5–1.3)
Annual income \$50,001–\$100,000	0.8 (0.5–1.2)	1.0 (0.6–1.5)	1.1 (0.5–2.5)	1.0 (0.7–1.5)
Annual income >\$100,000	1.0 (reference)	1.0 (reference)	1.0 (reference)	1.0 (reference)
Travel alone	0.8 (0.5–1.4)	0.9 (0.6–1.6)	<b>2.0 (1.0–4.2)</b>	0.7 (0.4–1.2)
Travel with companions	1.0 (reference)	1.0 (reference)	1.0 (reference)	1.0 (reference)
Travel for other than tourism or visiting friends or relatives	1.0 (0.6–1.6)	0.9 (0.6–1.4)	1.4 (0.6–3.2)	0.8 (0.5–1.2)
Travel to visit friends or relatives (may include tourism)	1.1 (0.6–2.0)	1.0 (0.6–1.7)	2.0 (0.8–4.8)	1.0 (0.6–1.7)
Travel for tourism only	1.0 (reference)	1.0 (reference)	1.0 (reference)	1.0 (reference)
>20 days travel duration	1.4 (0.7–2.9)	<b>5.6 (2.9–10.7)</b>	<b>4.6 (1.7–12.6)</b>	<b>4.6 (2.4–8.7)</b>
7–20 days travel duration	0.9 (0.5–1.5)	1.5 (0.9–2.4)	0.7 (0.3–1.7)	1.3 (0.8–2.1)
<7 days travel duration	1.0 (reference)	1.0 (reference)	1.0 (reference)	1.0 (reference)

OR = odds ratio; CI = confidence interval.

\*Includes persons living with unmarried partner. OR adjusted for other listed covariates. Differences  $p < 0.05$  (vs reference group) are depicted in bold type.

risk factor, 73% of those with a travel-related risk factor, and 68% of those at high risk during travel.

## Discussion

In this series of American travelers to hepatitis B endemic areas, 45% reported either a domestic or travel-related hepatitis B risk factor. Most did not obtain pretravel health advice prior to departure,

and of those who did, less than one third reported getting hepatitis B vaccine. We found no evidence that vaccine doses administered at pretravel health advice visits targeted higher risk travelers. Upon departure, 81% of all travelers and 70% of at-risk travelers reported having received fewer than three hepatitis B vaccine doses.

Our findings with respect to the frequency of pretravel health advice and vaccination coverage

**Table 3** Hepatitis B vaccination coverage, by age and risk factor status

	≥2 doses received prior to departure			≥3 doses received prior to departure		
	Any risk factor (%)	No risk factor (%)	<i>p</i> Value	Any risk factor (%)	No risk factor (%)	<i>p</i> Value
All respondents	108/276 (39)	70/342 (20)	0.001	84/276 (30)	35/342 (10)	0.001
Respondents 18–40 years	50/103 (49)	12/46 (26)	0.05	40/103 (39)	9/46 (20)	0.05
Respondents 40–59 years	39/110 (35)	34/154 (22)	0.05	33/110 (30)	18/154 (12)	0.001
Respondents >59 years	19/63 (30)	24/142 (17)	0.05	11/63 (17)	8/142 (6)	0.01

mimic those of a survey conducted among Americans departing for the developing world.<sup>10</sup> To our knowledge, this is the first assessment of hepatitis B risks of American travelers. Similar data indicate that 10 and 64% of European travelers to endemic regions are at high and potential risk, respectively,<sup>12</sup> somewhat higher percentages than we detected. Yet, differences in methods, rather than behaviors, may be responsible for the disparities. Our study considered the most recent trip to a hepatitis B endemic region, while the former study considered all such trips within the past 5 years. We used an anonymous mail survey rather than a telephone interview. While the European study inferred sexual contact from an item referencing a holiday romance, we asked specifically about oral sex or intercourse with a previously unknown person native to the region visited. Few women but 6% of males reported such sexual activity, and 3% of men reported paying for sex.

This study is limited in several respects, including its method of subject recruitment. Only 9% of persons contacted about the study requested a survey. The proportion meeting entry criteria but choosing nonparticipation cannot be determined. Nor can the potential effect of such a selection bias on study results. Nonetheless, the survey response rate was a reasonable 70%, and we found no difference in baseline characteristics between respondents and nonrespondents. A second limitation is our inability to validate traveler-reported vaccination history. This is particularly problematic because Europeans are often unable to differentiate between hepatitis A and B,<sup>12</sup> and there is no reason to expect Americans are more knowledgeable. Our reliance on traveler recall may have led us to overstate or understate immunization coverage. Based on assessments conducted in other settings,<sup>15,16</sup> it is more likely that coverage was overstated. Finally, travelers reported the number of hepatitis B vaccine doses received, not the dates of each dose. Some may have received 0-, 7-, and 21-day doses of an accelerated schedule but not the final dose. This too would have led us to overstate immunization coverage upon departure.

Underimmunized travelers may be responsible for an important share of US hepatitis B cases. Approximately 4.1 million US residents visit Asia (excluding Japan) each year for an average of 16 days.<sup>17</sup> The incidence of overt hepatitis B among travelers is 6 per 10,000 travel months. If only 19% of travelers are fully immunized (as we report) approximately 1,000 overt hepatitis B cases, and perhaps 1,500 asymptomatic infections<sup>2</sup> result

annually. More than 200 hospitalizations and nine deaths would be expected.<sup>4</sup> Further, 150 travelers would become chronically infected,<sup>9</sup> placing them at increased risk of cirrhosis and hepatocellular carcinoma. The number of infections may be lower since our data indicate at-risk travelers more often complete vaccination, some achieve immunity fewer than three doses,<sup>18</sup> and a small share have natural immunity.<sup>19</sup>

The proportion of underimmunized US travelers will decline over time due to increased childhood vaccination activities. Universal infant vaccination and immunization of previously unvaccinated 11- and 12-year-olds were first recommended in 1991 and 1995, respectively.<sup>20</sup> Early childhood coverage now exceeds 90%,<sup>20</sup> but 43% of adolescents had still not received three vaccine doses in 2002.<sup>21</sup> Thus, it may be a decade or more before most young adult travelers can be expected to have vaccine-induced hepatitis B immunity.

Hepatitis B immunization coverage among travelers could be improved through either of two mechanisms—increasing the rate at which travelers obtain pretravel health advice or increasing the rate of hepatitis B vaccination at pretravel health advice visits. Our data indicate that both will need to occur for substantial hepatitis B risk reduction. Totally 82% of the travelers we surveyed were underimmunized when making travel plans. Of these, 71% did not obtain pretravel health advice, 21% obtained pretravel health advice but were not immunized, and 8% were immunized. Thus, doubling the frequency of pretravel health advice visits would only increase the immunization rate to 16%. Despite our finding that partially immunized travelers were more likely to receive hepatitis B vaccine, series completion remains problematic. Reminder systems, including the use of cellular phone text messaging,<sup>22</sup> appear to be effective tools for increasing compliance.

Reasons for low immunization rates among travelers obtaining pretravel health advice may include a lack of awareness by physicians, which may conceivably explain differences between specialists and nonspecialists. Alternatively, it may simply reflect that specialists are more likely to have hepatitis B vaccine available, a predictor of improved coverage in other high-risk populations.<sup>23</sup> Our survey did not consider how often hepatitis B immunization was recommended but declined due to cost concerns, another barrier to improved coverage.<sup>24</sup> While formal economic analysis would be desirable, it seems reasonable that vaccination of US travelers would be acceptably cost-effective. Hepatitis B vaccination

of US college students is cost-effective based on a presumed 3.4% lifetime infection risk beyond age 18 years.<sup>9</sup> Persons who spend substantial time in endemic areas will face an elevated lifetime risk of infection. Thus, other parameters being equal, vaccination of travelers would be even more cost-effective.

In this study, 13% of travelers had a domestic risk factor only, 21% faced travel-related risks only, and 11% had both domestic and travel-related risks. US adults should be evaluated for up to eight vaccines,<sup>25</sup> and it would not be surprising to see a similar risk distribution for many of these vaccine-preventable illnesses. A validated patient-administered self-assessment is available<sup>16</sup> and may significantly reduce the time required to assess risk factors through personal interview. Further, travel clinics typically have vaccines on-site, and patients may be more receptive to immunization because it is seen as an integral part of pretravel health planning. Pretravel health advice visits may thus represent an excellent opportunity to address vaccination needs whether indicated due to travel or other reasons.

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### Conflict of Interests

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