Preferences for *Clostridioides difficile* Vaccine Attributes Among Adults in the United States

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INTRODUCTION

- *Clostridioides difficile* is a bacterium that can cause *C difficile* infection (CDI), resulting in diarrhea, colitis, and fever, among other symptoms, which have a considerable impact on health-related quality of life, healthcare resource use, and inpatient mortality.[1-4]
- Existing preventative measures can reduce transmission and hospital-acquired CDI[5] but will do little to impact the environmental reservoirs of *C difficile*, whereas vaccination may be a viable way to prevent or mitigate both hospital-acquired and community-acquired CDI.
- Vaccine recommendations in the United States are made using the Evidence to Recommendation framework, which incorporates values and preferences of the target population.
- Vaccines for CDI are in development, but data on preferences to inform potential recommendations are lacking.

OBJECTIVE

- This study assessed willingness to receive a *C difficile* vaccine and how selected vaccine attributes affect hypothetical choices to receive a vaccine to protect against CDI.

METHODS

Study design and sample

- A cross-sectional online survey that included a discrete choice experiment (DCE) was conducted with a commercial survey panel in October–December 2021 among US adults. Important vaccine attributes to vary in the DCE were identified through qualitative interviews and literature.
- Respondents were presented with information about CDI taken from the Centers for Disease Control and Prevention website before completing the DCE.
- Each respondent completed a series of 11 choice tasks, each including 2 hypothetical vaccine profiles with varying levels of each attribute and a no-vaccine opt-out option. An example choice task is shown in **Figure 1**.
- Attributes included in the DCE were vaccine effectiveness, duration of protection, impact on severity of breakthrough infections, dosing schedule, injection site reactions, systemic side effects, and out-of-pocket (OOP) costs (see **Figure 2** for attribute levels).

METHODS (continued)

Figure 1. Example Discrete Choice Experiment Choice Task

Vaccine A	Vaccine B	No Vaccine
65% effective For every 100 people who are vaccinated, **65** will be protected from CDI	**50% effective** For every 100 people who are vaccinated, **50** will be protected from CDI	
Provides protection against CDI for **5 years**	Provides protection against CDI for **15 years**	
The vaccine **reduces symptom severity by about half** if a CDI occurs (symptoms are about half as severe as they would be without the vaccine)	The vaccine **does not reduce symptom severity** if a CDI occurs (symptoms are just as severe as they would be without the vaccine)	
3 doses of the vaccine (taken on 3 separate occasions **over 6 months**)	**2 doses** of the vaccine (taken on 2 separate occasions **over 6 months**)	
Moderate to severe injection site pain that interferes with daily activities	**No** injection site pain	
10% have side effects For every 100 people who are vaccinated, **10** have mild to moderate fatigue, headache, or diarrhea lasting up to 24 hours	**5% have side effects** For every 100 people who are vaccinated, **5** have mild to moderate fatigue, headache, or diarrhea lasting up to 24 hours	
Total OOP cost for vaccine, including all doses, is **$150**	Total OOP cost for vaccine, including all doses, is **$0 (free)**	

CDI=*Clostridioides difficile* infection; OOP=out of pocket.

- Respondents were required to be aged ≥50 years, US residents, and able to read and understand English; to provide informed consent; and to not be participating in a clinical trial for a *C difficile* vaccine.
- Respondent characteristics assessed included sociodemographic characteristics, chronic medical conditions, and use of medications that increase the risk of infection.

Statistical analysis

- Hierarchical Bayesian modeling was used to analyze the choice data and generate preference weights for each level of each attribute.
- Attribute relative importance (RI) was computed by dividing the range of each attribute (preference weight of the most favorable level minus preference weight of the least favorable level) by the sum of the ranges of all attributes and multiplying by 100 to standardize. RI estimates were stratified by age, race, sex, education, and high risk/immunocompromised status.
- Subgroups were compared on RI using the 2-sample *t* test.

RESULTS

Table 1. Sample Characteristics

Characteristic	Respondents (N=1216)
Sex, n (%)	
Male	347 (28.5)
Female	868 (71.4)
Prefer not to answer	1 (0.1)
Age, mean (SD), y	65.7 (8.1)
Age group, n (%), y	
50–64	599 (49.3)
≥65	617 (50.7)
Race, n (%)	
White only	1094 (90.0)
Any other race	116 (9.5)
Prefer not to answer	6 (0.5)
US region, n (%)	
Northeast	249 (20.5)
Midwest	323 (26.6)
South	426 (35.0)
West	218 (17.9)
Education, n (%)	
≤High school degree	314 (25.8)
>High school degree	902 (74.2)
Employment status, n (%)	
Employed/employed on temporary leave of absence	388 (31.9)
Not employed/retired/other	828 (68.1)
Taking medications that lower ability to fight infections, n (%)	
Yes	46 (3.8)
No	1109 (91.2)
Don't know	61 (5.0)
Comorbidities, n (%)*	
Anemia	80 (6.6)
Cancer	119 (9.8)
Chronic kidney disease	38 (3.1)
Chronic liver disease	5 (0.4)
Chronic lung disease	74 (6.1)
Congestive heart failure	39 (3.2)
Diabetes	191 (15.7)
HIV	2 (0.2)
Inflammatory bowel disease	32 (2.6)
Risk status, n (%)†	
Not high risk	796 (65.5)
High risk	420 (34.5)
Immunocompromised status, n (%)‡	
Not immunocompromised	1107 (95.8)
Immunocompromised	48 (4.2)
High risk and/or immunocompromised, n (%)	
No	774 (63.7)
Yes	442 (36.3)

*Respondents could select >1 option.
†High risk defined as self-reported diagnosis of any of the following: anemia, cancer, chronic lung disease, chronic kidney disease, congestive heart failure, diabetes, inflammatory bowel disease, and chronic liver disease.
‡Immunocompromised defined as self-reported diagnosis of HIV and/or self-report of currently taking medications that lower body's ability to fight infection.

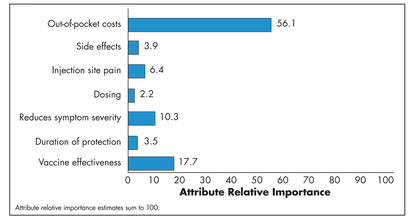
Study sample

- Overall, 1216 adults aged ≥50 years completed the study survey and were included in the analyses.
- In total, 617 participants were aged ≥65 years and 420 could be considered at high risk of CDI.
- Participants were distributed across the 4 US regions, most were women (71%), White (90%), and had more than a high school degree (74%); nearly one-third were currently employed **(Table 1)**.

Vaccine preferences

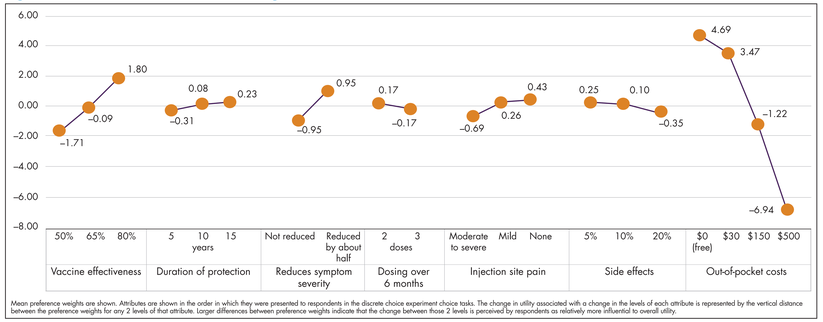
- Across the DCE choice tasks, respondents chose a *C difficile* vaccine 58% of the time vs the opt-out option.
- Attribute-level preference weights are depicted in **Figure 2**.
  - Respondents were most sensitive to OOP costs, and some changes in OOP costs were more influential to vaccine choice than the maximal possible changes in other attributes.
  - Choices indicated respondents were willing to accept a small increase in OOP costs for improvement in effectiveness or severity reduction of breakthrough cases.
  - Changes in duration of protection, dosing, injection site pain, and risk of side effects had relatively little impact on choice.
- The relative importance estimates demonstrate that participants most valued a reduction in OOP costs from $500 to $0 (56.1), followed by an increase in vaccine effectiveness from 50% to 80% (17.7) and a change in symptom severity from none to reduces symptom severity by half (10.3). Decreasing the number of required doses from 3 to 2 was the least important attribute (2.2) in vaccine selection **(Figure 3)**.
- Subgroup analysis found that rank order of the RI estimates was consistent across all subgroups, although some minor differences were observed:
  - Reduction in symptom severity was more important to respondents aged ≥65 years than to those <65 (10.9 vs 9.6, *P*=0.004).
  - Vaccine effectiveness was more important to men than women (19.3 vs 17.1, *P*=0.002), whereas a change in symptom severity was more important to women than men (10.7 vs 9.2, *P*=0.004).
  - Vaccine effectiveness was more important to respondents with >high school degree than to those with ≤high school degree (18.4 vs 16.0, *P*<0.001), whereas a change in OOP costs from $500 to $0 was more important to respondents with ≤high school degree than to those with >high school degree (58.1 vs 55.4, *P*=0.002).
  - No differences in attribute relative importance were observed by race or by high-risk/immunocompromised status.

Figure 3. Attribute Relative Importance Estimates



Attribute relative importance estimates sum to 100.

Figure 2. Attribute-Level Preference Weights



Mean preference weights are shown. Attributes are shown in the order in which they were presented to respondents in the discrete choice experiment choice tasks. The change in utility associated with a change in the levels of each attribute is represented by the vertical distance between the preference weights for any 2 levels of that attribute. Larger differences between preference weights indicate that the change between those 2 levels is perceived by respondents as relatively more influential to overall utility.

LIMITATIONS

- Women were overrepresented in our study. However, the few differences by sex were very small in magnitude, suggesting they are not practically meaningful.
- The DCE cannot accommodate all factors that could potentially influence vaccine preferences or real-world vaccination decisions. Accordingly, stated preferences may not perfectly correspond to actual vaccine choices.
- Sociodemographics and health information were self-reported and could not be confirmed for accuracy, although this limitation was expected to have minimal impact on results, as vaccine preferences are likely to depend on subjective respondent perceptions.

CONCLUSIONS

- **If OOP costs are minimal, US adults' preferences to receive a *C difficile* vaccine are most influenced by vaccine effectiveness and by reduction of the severity of CDI that does occur, while the tested levels of duration of protection, injection site pain, dosing, and side effects had relatively little influence.**
- **Taken together, findings suggest that adults aged ≥50 years are receptive to vaccination against CDI, especially when OOP costs are low. The impact of reducing severity of breakthrough infections on preferences highlights the importance of considering effectiveness against severe outcomes in addition to CDI cases avoided.**

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