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HIV vaccine acceptability among communities at risk: The impact of vaccine characteristics

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Abstract

HIV vaccines offer the best long-term hope of controlling the AIDS pandemic; yet, the advent of HIV vaccines will not ensure their acceptability. We conducted a cross-sectional survey ($n = 143$), incorporating conjoint analysis, to assess HIV vaccine acceptability among participants recruited using multi-site ($n = 9$), venue-based sampling in Los Angeles. We used a fractional factorial experimental design to construct eight hypothetical HIV vaccines, each with seven dichotomous attributes. The acceptability of each vaccine was assessed individually and then averaged across participants. Next, the impact of each attribute on vaccine acceptability was estimated for each participant using ANOVA and then analyzed across participants. Acceptability of the eight hypothetical HIV vaccines ranged from 33.2 (S.D. 34.9) to 82.2 (S.D. 31.3) on a 0–100 scale; mean = 60.0 (S.D. 21.9). Efficacy had the greatest impact on acceptability (22.7; CI: 18.5–27.1; $p < 0.0001$), followed by cross-clade protection (12.5; CI: 8.7–16.3, $p < 0.0001$), side effects (11.5; CI: 7.4–15.5; $p < 0.0001$), and duration of protection (6.1; CI: 3.2–9.0; $p < .0001$). Route of administration, number of doses and cost were not significant. Low acceptability of “partial efficacy” vaccines may present obstacles to future HIV vaccine dissemination. Educational and social marketing interventions may be necessary to ensure broad HIV vaccine uptake.

Keywords

HIV vaccines; Consumer preference; Latinos; Populations at risk; Conjoint analysis

1. Introduction

The development of safe and efficacious preventive HIV vaccines offers the best long-term hope of controlling the HIV/AIDS pandemic. Over 30 new candidate vaccines are in clinical trials in 19 countries, with numerous products in the preclinical pipeline [1,2]. While the first HIV vaccines to reach phase III clinical trials, AIDSVAX B/B [3] and B/E [4], were found to be inefficacious, these large-scale efforts demonstrate the feasibility of conducting safe and ethical human trials of HIV vaccines [5]. With growing international advocacy [6] and increased leadership and coordination of vaccine development efforts through the new Global

HIV Vaccine Enterprise [7], HIV vaccine research has gained substantial momentum. Nevertheless, the advent of HIV vaccines will not ensure their acceptability.

Consumers may be faced with important trade-offs in deciding whether or not to accept a first generation HIV vaccine. However, little is known about consumer preferences for HIV vaccines or how they will affect the decision to accept a given HIV vaccine. For one, initial HIV vaccines are likely to be only partially efficacious [8,9]. High levels of vaccine uptake among communities at risk for HIV infection will be required to achieve effective reduction of HIV transmission with low to moderate efficacy vaccines [10,11]. Yet a recent WHO-UNAIDS panel of experts estimated future global HIV vaccine uptake at only 38% of the projected need in the case of vaccines with high (>70%) efficacy and only 19% of projected need in the case of vaccines with low to moderate (30–50%) efficacy [12]. Thus, acceptability may be low for “partial efficacy” HIV vaccines.

Low levels of uptake for adult vaccines that are already widely available in the developed world, such as influenza [13,14] and Hepatitis B [14,15], as well as racial/ethnic disparities in vaccine coverage in the US [14,16,17] suggest additional challenges for HIV vaccine acceptability among communities at highest risk for HIV/AIDS. Suboptimal coverage for Hepatitis B vaccination [14,15], in particular, among precisely those groups at elevated risk for HIV infection, indicate difficulties in achieving adequate coverage with future HIV vaccines [18]. Many MSM, for example, do not perceive themselves to be at risk for Hepatitis B [15,19] and lack basic information about HBV vaccines [20], which are related to lower uptake of Hepatitis B vaccines; this may suggest low acceptability for HIV vaccines that are perceived to entail any risk or that offer less than complete protection.

Limited previous investigations suggest that characteristics of future HIV vaccines may influence their acceptability. Higher levels of HIV vaccine acceptability were associated with greater vaccine efficacy [21–23] and lower vaccine costs (although less than for efficacy) among Midwestern adolescents [21,24]. Route of administration and number of doses had little influence on HIV vaccine acceptability [21]. A qualitative study among high-risk communities in Los Angeles suggests that concerns about low to moderate efficacy HIV vaccines and fears of physical side effects may decrease vaccine acceptability [25]. The possible role of other vaccine attributes on acceptability, such as cross-clade protection and duration of protection, both key elements in vaccine effectiveness on an epidemic level [10], have not been studied.

To prepare for the formidable challenges facing the dissemination of future FDA-approved HIV vaccines, we conducted a survey of ethnically diverse persons at risk for HIV infection in a major HIV/AIDS epicenter in the US. The purpose of this study is to investigate HIV vaccine acceptability, and the impact of hypothetical HIV vaccine characteristics on acceptability, among populations at risk for HIV.

2. Materials and methods

2.1. Participants

Participants ($n = 143$) were recruited using multi-site, venue-based sampling [26–28] from three gay community centers ($n = 61$), three needle exchange sites ($n = 55$) and three Latino primary care clinics ($n = 27$) in Los Angeles County. The nine venues were selected based on their serving diverse populations at elevated risk for HIV in LA County. Eligibility criteria at the venues included: at least 18 years of age, not an employee of the recruitment site and ability to read and understand English. Participants were reimbursed \$20 for engaging in a one-time, 60 min interview. Trained interviewers administered the questionnaire using laptop computers programmed with Questionnaire Development System software [29]. The study protocol was

reviewed and approved by the Human Subjects Protection Committees of UCLA and the University of Toronto. All participants gave informed consent.

2.2. Measures

We used conjoint analysis, a multi-attribute, stated preference method, to measure preferences among HIV vaccines with different attribute profiles. As a decompositional approach, in which individuals assess holistic, multi-attribute products, conjoint analysis more closely approximates decisions about actual product acceptability than traditional single item (i.e., compositional) measures [30,31]. Conjoint analysis has been widely applied in economics and market research [30-33] and is gaining popularity in the health domain for assessing consumer acceptability of health services [33-35] and pharmaceuticals [33,36] before the actual products are developed.

Eight hypothetical HIV vaccines that vary across seven dichotomous attributes were constructed using an eight-run Plackett-Burman design [37], a 2^{7-4} fractional factorial experimental design. This design allowed efficient estimation for the main effects of the seven dichotomous attributes with a minimum number of eight hypothetical vaccines, under the assumption that the impact of the factors are additive, that is, there are no interactions among the factors [38]. Although the additivity assumption creates restrictions, we believe it is appropriate to focus on the main effects for our study given its pioneering nature in assessing the acceptability of multi-attribute HIV vaccines. In contrast to a fractional factorial design, a full factorial design in the present study would entail the assessment of 128 different vaccines, which would clearly represent cognitive overload for participants. The fractional factorial design with its assumption of additivity thus enables the estimation of the acceptability of an array of holistic, multi-attribute products, which more closely approximates consumers “real-world” decisions than eliciting preferences for one or two attributes in isolation, in this case, of an HIV vaccine.

The fundamental steps in the implementation of conjoint analysis involve identification of the product characteristics (i.e., attributes of the HIV vaccines), assignment of plausible values or levels to the characteristics (i.e., in this case two for each attribute) and then the creation of scenarios (i.e., HIV vaccines) [35]. In the present study, vaccine attributes included efficacy for susceptibility (95% versus 50%), duration of protection (lifetime versus 10 years), cross-clade (versus single-clade) protection, doses (1 versus 3), route of administration (oral versus injection), physical side effects (none versus minor (temporary body aches, skin rash and fever)) and cost (\$10 versus \$50). We hypothesized, based on previous studies, that greater efficacy [21,23] and lower cost [21,24] would be associated with higher levels of HIV vaccine acceptability. Lifetime (versus 10 year) duration of protection, cross-clade (versus single-clade) protection, one (versus three) dose(s), oral (versus injection) route of administration and no (versus minor) side effects were also expected to be associated with greater HIV vaccine acceptability.

In describing the hypothetical vaccines, we used the term “effective” rather than “efficacious” and “protection against US and international strains of HIV” rather than “cross-clade protection” in order to confer the meaning of vaccine terminology to lay participants. To date, there exists no empirical research to suggest how best to describe these HIV vaccine characteristics to the general public; our descriptions were based on pre-testing of items in 15 focus groups [25,39], as well as public education materials prepared by the AIDS Vaccine Advocacy Coalition [40]. We selected 50% versus 95% efficacy because our focus groups suggested our target populations expected HIV vaccines to be completely efficacious [25]; our objective was to determine the effect of partial (versus complete) efficacy on acceptability. Similarly, the (10 year versus lifetime) range of duration of protection was based on focus

group analyses that suggested a drop off in acceptability if a vaccine did not attain the expected lifetime protection [25].

Participants were asked to rate the hypothetical HIV vaccines, which were presented concurrently in a set of eight laminated cards. The cards were not demarcated with any schema that might suggest a sequence or preference ranking. Two sample hypothetical HIV vaccines are shown in Fig. 1. Participants rated the acceptability of each HIV vaccine on a 5-point Likert scale, from highly likely to highly unlikely to accept the hypothetical vaccine. The ratings were transformed into a 0–100 scale, with “highly likely” scored as 100 and “highly unlikely” scored as 0.

2.3. Data analysis

The acceptability of each hypothetical HIV vaccine is derived by averaging individual vaccine acceptability scores across respondents. For example, the acceptability of vaccine one is the average of 143 respondents’ individual ratings of that vaccine. Next, a one-way analysis of variance (ANOVA) model is applied to fit each respondent’s acceptability scores for the eight hypothetical vaccines; the seven vaccine attributes serve as independent variables in this model. The effect for each vaccine attribute (e.g., efficacy) in the ANOVA model is the impact score of the attribute on vaccine acceptability for the individual respondent. Individual impact scores are then averaged across respondents for each attribute; the average of these individual impact scores for each attribute is the impact of that attribute (e.g., efficacy) on overall HIV vaccine acceptability. Finally, a one-sample *t*-test is used to determine the statistical significance of the impact of each attribute.

3. Results

A total of 747 persons were approached for the overall study of whom 462 (61.8%) agreed to be screened and 281 of these were deemed eligible. Of the 181 ineligible cases, 156 (86.2%) did not speak English fluently (154 of whom spoke only Spanish), 15 (8.3%) were under age 18 and 10 (5.5%) were employed as staff at the agency. Among those screened as eligible, 266 participants (94.7%) were interviewed for the overall study. The response rate for the overall study is therefore, 58.5% ($=61.8\% \times 94.7\%$), based on the AAPOR definition for multi-phase sample designs [41,42]. Among 266 overall study participants, 143 (53.8%) were randomized to the present vaccine acceptability study; the other 123 participants were randomized to a different survey. Since all non-responses occurred prior to randomization, the response rate for the present study is identical to the response rate for the overall study. Sociodemographic characteristics of participants are reported in Table 1.

Acceptability of the eight hypothetical HIV vaccines ranged from 33.2 (S.D. = 34.9) to 82.2 (S.D. = 31.3) on the 0–100 scale. The average acceptability across all eight vaccines was 60.0 (S.D. = 21.9). Table 2 shows the attribute profile for each hypothetical vaccine and its acceptability (across respondents). The vaccine with the highest rated acceptability (vaccine number one) out of the eight vaccines presented had the following attributes: 95% efficacy, 10 years of protection, cross-clade protection, one dose, oral route of administration, no side effects and \$50 cost.

Table 3 shows the impact of each hypothetical HIV vaccine attribute on vaccine acceptability. Efficacy had the greatest impact on acceptability (22.6; CI: 18.5–27.1; $p < 0.0001$), followed by cross-clade protection (12.5; CI: 8.7–16.3, $p < 0.0001$), lack of physical side effects (11.5; CI: 7.4–15.5; $p < 0.0001$) and longer duration of protection (6.1; CI: 3.2–9.0; $p < 0.0001$). Number of doses, route of administration and cost had no significant effect on acceptability.

Based on the acceptability of each vaccine rated by respondents and estimation of the impact factors of each vaccine attribute, we imputed the acceptability of the best and worst possible HIV vaccines. The theoretical best vaccine (see Table 2)—95% efficacy; lifetime protection; protection against multiple HIV subtypes; 1 dose; administered orally; no side effects; and a cost of \$10—would have an overall acceptability of 88.1% (S.D. = 30.0). Alternately, the worst possible vaccine would have an overall acceptability of 31.8% (S.D. = 38.4).

4. Discussion

This is the first published study to quantify the impact of a broad array of vaccine attributes on HIV vaccine acceptability among adults at risk for HIV infection. The primary finding is that the acceptability of future FDA-approved HIV vaccines is far from guaranteed among communities at risk and is likely to be influenced by characteristics of the vaccine. Adults recruited from among high-risk, low socioeconomic and ethnic minority communities reported a wide range of acceptability in response to hypothetical preventive HIV vaccines with different attribute profiles.

The average HIV vaccine acceptability of 60.0 on a 100-point scale across eight hypothetical vaccines is encouraging; overall, respondents were positively predisposed to HIV vaccines. Nevertheless, even as the acceptability (88.1/100) of the best possible vaccine suggests the potential for widespread coverage with an optimal product (e.g., 95% efficacy, cross-clade protection, etc.), first generation HIV vaccines may be more similar to the worst possible vaccine (31.8/100). A previous investigation among college undergraduates reported a similar range of acceptability from 32.8 to 83.4 on a 100-point scale, among hypothetical HIV vaccines with three varying characteristics (efficacy, cost and social saturation) [24], which supports the importance of vaccine characteristics in future HIV vaccine dissemination. The possibility that first generation HIV vaccines may not be acceptable to populations for whom they are developed suggests the need for sociobehavioral interventions to increase the acceptability of safe but imperfect HIV vaccines.

Vaccine efficacy had the greatest impact on acceptability; a decrease in efficacy from 95% to 50% was associated with a 22.6-point decrease (on a 100-point scale; equivalent to dropping from “somewhat likely” to “neutral”) in the acceptability of an HIV vaccine. HIV vaccines that are less than 50% efficacious may meet with limited acceptability among persons at elevated risk for HIV/AIDS, as suggested by the present findings and corroborated by previous investigations [24,25,39]. However, first-generation HIV vaccines are expected to be only partially efficacious. Mathematical modeling of the epidemic suggests that even a 20%–30% efficacy vaccine could have a beneficial effect on an epidemic level, but only with high levels of vaccine uptake [11,43–45]. Therefore, the development of empirically based strategies to optimize the uptake of low to moderate efficacy HIV vaccines may be crucial to the effectiveness of vaccines in controlling the AIDS pandemic.

This is the first investigation to assess the role of cross-clade protection on HIV vaccine acceptability. Cross-clade protection had the second greatest impact on vaccine acceptability in our study sample in Los Angeles, the second largest HIV/AIDS epicenter in the US [46]. The multicultural demographics of Los Angeles, along with the fact that 14% of participants were non-US born, may result in greater concern about cross-clade protection than in other locales. Nevertheless, concern among lay participants in a major urban AIDS epicenter about protection across different viral subtypes suggests that HIV vaccine education and dissemination efforts should address a vaccine’s range of protection. How best to explain cross-clade protection to the general public remains an empirical question. It is also plausible that participants may have conflated efficacy with cross-clade protection, inferring that 95% efficacy for example, refers to all HIV subtypes regardless of clade. However, the independent

impact of cross-clade protection on HIV vaccine acceptability, in addition to that of efficacy, suggests concerns about viral subtypes beyond those that are prevalent in North America.

Participants rated the acceptability of a vaccine with temporary minor physical side effects lower than a vaccine with no projected side effects. Our analysis further suggests that concerns about physical side effects may attain a lower priority than concerns about vaccine efficacy; consumers may tolerate temporary side effects, such as local pain and inflammation at the injection site—the most common side effect of AIDSVAX B/B [47], for example—particularly in return for a higher efficacy vaccine.

The number of doses required and the route of vaccine administration were not significantly associated with HIV vaccine acceptability. This suggests that consumers may be willing to accept a vaccine requiring booster shots (e.g., using a prime-boost strategy [48,49]), even more so in exchange for increased efficacy and duration of protection. It is also possible that the inclusion of number of doses and route of administration in one line on the scenario card, in the interest of presenting vaccine scenarios that were as compact and cognitively manageable as possible, may have contributed to diminishing the impact of each of the attributes. However, the present findings mirror those among Midwestern adolescents [21], suggesting that dose and route of administration may be less important to HIV vaccine acceptability relative to other characteristics.

Unlike studies of adolescents [21,24], cost was not a significant predictor of vaccine acceptability in the present study. While it is possible that adults, even of low socioeconomic status, are less concerned about vaccine cost than adolescents, it may also be the case that the range of cost (i.e., \$10 versus \$50) presented was not sufficient to produce a significant impact on acceptability. A cost differential of \$300 had a significant effect on HIV vaccine acceptability among adolescents [24]. Furthermore, the fact that the most acceptable vaccine cost \$50 versus \$10 is not an indication that respondents prefer to pay more; rather, the most acceptable vaccine scenario in terms of the other six characteristics was only presented at a cost of \$50 due to the fractional factorial design and, overall, cost was not a significant determinant of acceptability. It may be the case that given the trade-offs among the eight hypothetical vaccines, other preferences (e.g., 95% versus 50% efficacy and cross- versus single-clade protection) had a greater impact on vaccine acceptability than a \$40 cost differential. Another plausible explanation for the lack of impact of cost on HIV vaccine acceptability is that participants may have presumed that the vaccine cost would be borne by the federal government or local health authority and thus would not come out of their own pocket. Participants were, in fact, recruited from public, community-based sites (i.e., health clinics providing means-tested, free medical services and free needle exchange sites) that provide free or subsidized health services, rather than private providers.

Limitations to this study include the small sample size and the use of venue-based sampling of participants, which constrain our ability to stratify by ethnicity or gender and limit generalizability of the results to broader communities at risk for HIV/AIDS. We were also unable to translate all study materials into Spanish due to budgetary constraints; thus our findings may not be applicable to Latinos who are not fluent in English, who may have distinct concerns. While we included a substantial proportion of persons recruited from Latino health clinics, this subgroup was also relatively smaller than the gay/lesbian and needle exchange strata. Additionally, we did not screen for individual risk behaviors; we relied on venue-based sampling to identify individuals likely to be at elevated HIV risk. Individual risk, however, may influence HIV vaccine acceptability. Nevertheless, as one of the first studies of the acceptability of multi-attribute HIV vaccines, we aimed to focus on select communities at elevated risk for HIV infection. Additionally, we modeled our recruitment strategy on the methods likely to be employed in the dissemination of HIV vaccines in the future, so the non-

random sampling may not be as strong a limitation. We also recruited from nine high-risk venues across three risk strata to increase the breadth of study participants. High-risk communities in Los Angeles may be different, however, from those in other urban HIV/AIDS epicenters.

It is also important to note that the acceptability of a hypothetical product is not the same as uptake of an actual product. The actual characteristics of future first generation HIV vaccines are a moving target that can only be estimated. Nevertheless, a strength of the present study is in the use of conjoint analysis, a preferred method for assessing the acceptability of hypothetical products [33] with the ability to convert subjective responses into estimated parameters [31]. The purpose of conjoint analysis is not to suggest, however, that consumers will be presented with an array of choices among different first generation HIV vaccines. Similarly, conjoint analysis need not reflect the exact characteristics of a future HIV vaccine to yield meaningful data; the purpose is to present a meaningful range—to consumers—within each vaccine attribute, in order to estimate the likely impact of vaccine attributes on product acceptability [30,35]. Further investigation of the impact of HIV vaccine cost, in particular, is warranted, perhaps using larger monetary differentials and costs that are emphasized as “out of pocket” so as to address this important characteristic. Another vaccine characteristic that may merit investigation in terms of its influence on HIV vaccine acceptability is efficacy for reducing infectiousness or contagiousness: it is possible that initial HIV vaccines may not prevent infection of the host but may substantially reduce infectiousness to others, which would have a beneficial impact on an epidemic level. Finally, beyond characteristics of HIV vaccines themselves, variables such as place of vaccination [50,51], perception of HIV risk [25,39], social saturation [24](i.e., % of population already vaccinated) and co-morbidities such as Hepatitis C [39] may influence HIV vaccine acceptability.

Notwithstanding these limitations, this study suggests that vaccine characteristics, particularly efficacy, may have a significant impact on the acceptability of future HIV vaccines among communities at risk for HIV. Initial HIV vaccines of less than 50% efficacy may be considered for dissemination among high-risk populations in the US [45]; the present findings suggest low levels of acceptability for such low to moderate efficacy HIV vaccines. Low vaccine acceptability coupled with even modest increases in risk behaviors may seriously compromise the effectiveness of low to moderate efficacy vaccines [43,44]. As a result, tailored social marketing and educational interventions designed to address consumer concerns and to facilitate uptake may be vital to the success of HIV vaccines in controlling the AIDS pandemic [50]. It is prudent to prepare now for the complex challenges of future HIV vaccine acceptability; each year of delay in the dissemination of HIV vaccines once available may result in up to 40,000 HIV incident infections in the US. [52] and millions worldwide that could have otherwise been averted.

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This HIV vaccine:

- Is **50% effective** at protecting against HIV infection
- Lasts **10 years**
- Works against **both U.S. and international strains** of HIV
- Is given by a series of **3 injections (shots)**
- Has **no side effects**
- Costs **\$10**

This HIV vaccine:

- Is **95% effective** at protecting against HIV infection
- Lasts **a lifetime**
- Works against **U.S. but not international strains** of HIV
- Is given by **1 injection (shot)**
- Has **no side effects**
- Costs **\$10**

Fig. 1.

Two sample hypothetical HIV vaccines as presented to participants on separate laminated cards.

Table 1Sociodemographic characteristics of participants (*n* = 143)

Characteristics	<i>n</i>	Percent (%)
Age in years (mean = 36.85; median = 36.00)		
18–34	64	44.7
35–49	55	38.6
50+	24	16.7
Race/ethnicity		
Black/African American	31	21.7
Hispanic/Latino	45	31.8
White	55	38.8
API, native American and other	11	7.7
Born in the United States	123	86.1
Gender		
Male	98	68.2
Female	45	31.8
Sexual orientation		
Heterosexual	63	44.1
Gay	56	39.4
Lesbian	11	7.9
Bisexual	12	8.6
Injecting drug user (IDU)	64	44.9
Education		
No high school degree	19	13.6
High school graduate or GED	42	29.6
Some college, AA degree, trade school	49	34.1
Bachelor's degree or more	32	22.7
Annual income (\$)		
0–5000	37	25.8
5001–10000	19	13.6
10001–25000	53	37.1
25000+	34	23.5
Health insurance		
Employer or other private	52	36.4
Medi-cal, medi-care, VA	40	28.0
None	51	35.6

Table 2
Acceptability (mean/S.D.) of hypothetical HIV vaccines with different attributes in order of decreasing acceptability (*n* = 143)

HIV vaccine number ^a	HIV vaccine acceptability mean (S.D.) ^b	Vaccine attributes					
		Efficacy (%)	Duration of protection	Protection (cross-clade)	Doses	Route	Side effects
Best possible ^c	88.1 (30.0)	95	Lifetime	Multiple types	1	Oral	None
1	82.2 (31.8)	95	10 years	Multiple types	1	Oral	None
2	73.3 (37.8)	95	Lifetime	One type	1	Injection	None
3	73.1 (35.0)	95	Lifetime	Multiple types	3	Injection	Minor
4	56.6 (36.1)	95	10 years	One type	3	Oral	Minor
5	55.6 (35.0)	50	10 years	Multiple types	3	Injection	None
6	54.0 (35.6)	50	Lifetime	Multiple types	1	Oral	Minor
7	51.7 (37.7)	50	Lifetime	One type	3	Oral	None
8	33.2 (35.0)	50	10 years	One type	1	Injection	Minor
Worst possible ^c	31.8 (38.4)	50	10 years	One type	3	Injection	Minor

^aHIV vaccine numbers assigned in order of decreasing acceptability, not in order of presentation to participants.
^bAbbreviation: S.D., standard deviation across individuals.
^cBest possible and worst possible vaccine acceptability were imputed statistically based on actual ratings of the eight hypothetical HIV vaccines.

Table 3Impact of HIV vaccine attributes on hypothetical HIV vaccine acceptability ($n = 143$)

HIV vaccine attributes ^a	Impact on vaccine acceptability Mean (S.D.) ^b
Efficacy*	22.6 (27.2)
Cross-clade protection*	12.5 (23.3)
Side-effects*	11.5 (24.6)
Duration of protection*	6.1 (17.5)
Route of administration	2.4 (18.3)
Doses	1.4 (14.1)
Cost	-0.2 (20.3)

* $p < 0.0001$ for the one sample t -tests.

^a Presented in order of decreasing impact of attributes on HIV vaccine acceptability.

^b Abbreviation: S.D., standard deviation across individuals.