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The Marginal Willingness-to-Pay
for Attributes of a Hypothetical HIV Vaccine

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Abstract

This paper estimates the marginal willingness-to-pay for attributes of a hypothetical HIV vaccine using discrete choice modeling.

We use primary data from 326 respondents from Bangkok and Chiang Mai, Thailand, in 2008-2009, selected using purposive, venue-based sampling across two strata. Participants completed a structured questionnaire and full rank discrete choice modelling task administered using computer-assisted personal interviewing. The choice experiment was used to rank eight hypothetical HIV vaccine scenarios, with each scenario comprising seven attributes (including cost) each of which had two levels. The data were analyzed in two alternative specifications: (1) best-worst; and (2) full-rank, using logit likelihood functions estimated with custom routines in Gauss matrix programming language.

In the full-rank specification, all vaccine attributes are significant predictors of probability of vaccine choice. The biomedical attributes of the hypothetical HIV vaccine (efficacy, absence of VISP, absence of side effects, and duration of effect) are the most important attributes for HIV vaccine choice. On average respondents are more than twice as likely to accept a vaccine with 99% efficacy, than a vaccine with 50% efficacy. This translates to a willingness to pay US$383 more for a high efficacy vaccine compared with the low efficacy vaccine.

Knowledge of the relative importance of determinants of HIV vaccine acceptability is important to ensure the success of future vaccination programs. Future acceptability studies of hypothetical HIV vaccines should use more finely-grained biomedical attributes, and could also improve the external validity of results by including more levels of the cost attribute.

Keywords

HIV vaccine; willingness-to-pay; conjoint analysis; discrete choice; Thailand

JEL Classification

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1. Introduction

A safe, efficacious and accessible prophylactic vaccine for HIV remains elusive despite promising results in some recent trials [1-3]. Nevertheless, with an estimated 2.5 million new HIV infections each year [4], a vaccine is the most promising means of controlling the epidemic. Ongoing research on candidate vaccines will continue to require the support of thousands of volunteers for enrolment in Phase II and Phase III vaccine trials. An increasing focus on implementation science in health care, and recognition of the significant gap between efficacy in clinical trials and effectiveness in the real world in the case of already licensed vaccines (e.g., HBV, HPV), also raises the importance of research that looks beyond clinical trials [5-6]. To date there have been relatively few investigations of the potential uptake of future HIV vaccines, particularly outside the United States [7]. An understanding of the factors associated with vaccine acceptability, particularly within high-risk groups, and the vaccine attributes or characteristics that contribute to acceptability, is important to ensure uptake of a future vaccine.

Vaccine acceptability is a measure of potential users' judgment of the satisfactoriness of the vaccine and their willingness to be vaccinated [7]. In quantitative studies, vaccine acceptability is typically measured as a dichotomous yes/no response to a willingness to be vaccinated question (e.g. see [8-9]), or measured on a Likert scale (e.g. see [10-11]) or as a probability of accepting vaccination (e.g. see [12-13]).

An alternative to investigating vaccine acceptability is to directly consider the willingness-to-pay (henceforth WTP) for it by potential recipients. Few studies have adopted a contingent valuation approach to estimate WTP for hypothetical HIV vaccines (e.g. see [14-16]). This approach involves presenting the respondents with one or a small number of scenarios that include a price for a hypothetical vaccine of given attributes, then adjusting the price in several steps in order to determine the respondent's maximum willingness-to-pay for each vaccine scenario [17]. The advantage of these studies is that they provide a more direct way to estimate the potential demand for a future HIV vaccine, rather than simply the vaccine's acceptability; more work of this type is clearly needed [18].

In most studies of vaccine acceptability, the vaccine-specific attributes determining its acceptability are typically investigated by presenting each survey respondent with a number of different vaccine alternatives, each of which has different attributes. Some studies have presented a limited number of scenarios with few vaccine attributes (e.g. see [19]), but most have used a more complex experimental design involving conjoint value analysis (e.g. see [11,20,21]). In conjoint value analysis, the respondent is presented with a series of cards, each of which describes an alternative hypothetical vaccine on the basis of its attributes. Respondents disclose their preferences by ordering the cards (alternative vaccines) from best to worst. They are then asked to rate the scenario on each card in terms of acceptability, using one of the measures noted above.

To investigate the determinants of vaccine acceptability, most studies then convert the vaccine acceptability variable into either a linear form for ordinary least squares regression analysis (e.g. see [22-23]) or into a dichotomous variable for logistic regression analysis (e.g. see [24]). In either case vaccine acceptability is the dependent variable and respondent characteristics and hypothetical vaccine attributes may be used as explanatory variables (e.g. see [20]). Newman and Logie [7] conducted a systematic review and meta-analysis of HIV vaccine acceptability studies of these and other types, and found that the acceptability of a hypothetical vaccine varied between 37.2 and 94.0 on a 100-point linearised scale, with a weighted mean of 65.6, and that vaccine acceptability was substantially higher for high efficacy versus moderate efficacy vaccines. They also found that effect sizes were largest (and significant) for efficacy, non 'risk group' membership, pragmatic obstacles (e.g. transportation and access to health facilities), and vaccine cost.

The key problem with the linearised or dichotimised vaccine acceptability approach described above is that conventional choice-based conjoint value analysis, as conducted in these studies, does not have a natural mapping into ordinal utility theory and hence into measures of economic welfare change. The analysis implicitly uses vaccine acceptability as an indicator of cardinal utility, which is not necessarily how the respondent interprets acceptability in their decision making process. Furthermore, because in most studies vaccine cost, if included, is effects coded, the opportunity for a more detailed consideration of the marginal willingness-to-pay of different vaccine attributes is lost. This is in spite of the recognition of the advantage of including cost in order to represent preference between attributes in monetary terms [25].

An arguably more appealing approach to assessing end user preferences is provided by interpreting observed choices by means of utility-theoretic frameworks [26-27]. For example, using a random utility model approach, the marginal effects on utility levels of changes in attributes (e.g., efficacy, duration of effect) of hypothetical vaccines can be identified and estimated. This enables researcher to evaluate the acceptability of different vaccine profiles (or combinations of vaccine attributes) in the target population. When one of the attributes evaluated is the cost of the hypothetical vaccine then the trade-off between other attributes and cost can be evaluated in terms of probability of acceptance at any given cost within the range explored [28]. In other words, commonly accepted economic estimates of welfare change (consumer surplus and marginal willingness to pay) for separate vaccine attributes can be identified and estimated from the ranking data when handled as discrete choices between mutually exclusive competing alternatives [29]. A full ranking of seven alternatives can, for example, be interpreted as a sequence of six discrete choices [30]. The first ranked alternative is chosen from seven, the second ranked from six, and so on until the alternative ranked second to the last is selected from two remaining attributes. There exists a vast literature on choice modelling based on random utility theory that can be used to analyse ranking data of this sort [30,31]. The category of models of reference includes the multinomial logit and probit models [32,33] and its very numerous extensions [34]. Among

the major advantages of applying the random utility approach to choice-based conjoint analysis is its efficiency and precision.

In this paper, we adopt the random utility approach to derive estimates of the marginal willingness-to-pay for different attributes of a hypothetical HIV vaccine among men who have sex with men (MSM), male sex workers, and transgender women in Thailand.

2. Methods

Based on preliminary qualitative data collection and previous studies of vaccine acceptability, eight hypothetical HIV vaccine scenarios were constructed. Each scenario featured a bundle of seven dichotomous vaccine attributes: (1) 99% versus 50% efficacy; (2) no versus minor side effects (specifically temporary body aches, skin rash and fevers); (3) 10-year versus one-year duration of protection; (4) vaccine-induced seropositivity (VISP) (wherein vaccinated individuals would subsequently test antibody positive for HIV) or not; (5) administered at private versus public hospitals; (6) high versus low social saturation (the proportion of the population already vaccinated); and (7) vaccine cost of THB100 versus THB2500 (about US$3 versus US$75). Eight scenarios with seven attributes (including cost) were chosen in order to keep the cognitive task manageable for respondents. Formative qualitative research was used to decide on the final attributes and levels for inclusion. A fractional factorial orthogonal design allowing only for main effects was used to develop the eight scenarios, based on a Plackett-Burman design [35]. We note that out-of-pocket costs for medical procedures, including vaccines, are not unusual in Thailand – thus the problem of respondents' misinterpretation of the cost variable [36,37] is less likely to arise, since the respondents should understand the true financial consequence of their choices.

Respondents (aged 18 years or over) were selected using purposive, venue-based sampling [38] across two strata in Bangkok and Chiang Mai cities. The first stratum included gay entertainment venues such as gay strip clubs, movie theatres, massage parlours, and sex motels. The second stratum included community-based organisations providing HIV prevention services to high-risk groups such as MSM, male sex workers, and transgender women. Data were collected from 326 respondents between March 2008 and February 2009 using Computer-Assisted Personal Interviewing [39]. The median age of respondents was 27 years; 67.2% were male, 20.2% female, and 12.6% transgender; 63.2% self-identified as gay or homosexual, 4.3% bisexual, and 32.2% heterosexual. The median monthly income of respondents was THB11,197 (US$345). Further details on data collection are available in Newman et al. [40]. The research was approved by the institutional review boards of UCLA and the University of Toronto, and written informed consent was obtained from all respondents.

Each respondent was first presented with eight laminated cards, one with each vaccine scenario, and asked to rank the eight scenarios, from the 'best' vaccine to the 'worst' vaccine.

The respondents did this by first selecting the vaccine scenario they thought represented the 'best' vaccine, then selecting the vaccine scenario they though represented the 'worst' vaccine. Finally, they were asked to arrange the remaining six scenarios in order between their chosen best and worst scenarios. This procedure leads to a complete rank ordering of the scenarios, as well as a definite procedure by which the respondents arrive at their ranking that can be exploited in the analysis. There was no opt-out option, i.e. respondents were forced to choose their ranking with no alternative option which is not to be vaccinated at all (a 'forced choice' experiment). Our results therefore reflect the probability of a respondent choosing a vaccine scenario in a forced choice rather than the probability of that scenario being acceptable to the respondent. Given that one of the attributes in the conjoint scenarios is cost (price) of the vaccine, we can use this to evaluate the trade-off between other attributes and cost in terms of probability of acceptance at any given cost. Furthermore, because this procedure is a forced choice, methods of estimating monetary valuations remain valid, as noted by Ryan [41].

Rank ordered choice data lend themselves to various alternative specifications. In the first specification, the data were fitted to a multinomial logit likelihood function using only the best and worst choices of each respondent [42]. In this specification, the 'best' alternative is chosen from all eight scenarios, but the 'worst' alternative is chosen from the seven remaining alternatives (i.e. excluding the 'best'). The literature proposing this approach argues that focus on extremes of preference rankings is cognitively less difficult or costly for the respondent and hence the utility functions are less affected by error variance. In the second specification, the data were fitted to a logit likelihood function using the full ranking data provided by the respondents using the rank-exploded logit model [30]. In this second specification, the ranking is interpreted as a sequence of seven discrete choices - the 'best' ranked alternative is chosen from all eight scenarios, the 'worst' is chosen from the remaining seven, the 'second best' is chosen from the remaining six, and so on until the 'fourth best' scenario is selected from two remaining scenarios. This specification follows the procedure that respondents were asked to follow, in first determining the best, then the worst alternative, before ranking the remaining six scenarios. We assume that respondents follow the same procedure (best, worst) throughout. Recent research in alternative utility coding for full-rank choice sets suggests that repeated best is consistent with what a large fraction of respondents appear to be naturally doing in their selection. It also suggests that other ways to code utilities (e.g. repeated worst) produce mostly insignificant differences in estimated value for the utility coefficients [43,44]. In both specifications only vaccine attributes, inclusive of cost, were used as attributes of the systematic component of the utility function. All attribute levels were dummy-coded with the exception of cost.

Finally, we were able to evaluate the trade-off between other attributes and cost in terms of probability of acceptance at any given cost. The marginal willingness-to-pay for each vaccine attribute was estimated by taking the ratio of the estimated coefficient on each vaccine attribute to the estimated coefficient on cost. From these marginal willingness-to-pay

estimates, a mean willingness to pay and associated confidence interval can be estimated for any combination of vaccine attributes.

Two respondents recorded invalid rankings, reducing the final sample size to 324. The marginal effects on utility of the vaccine attributes were estimated using maximum likelihood estimation routines coded in Gauss matrix programming language (Aptech Systems). Marginal effects were converted to odds ratios to aid interpretation.

3. Results

The results from the best-worst specification, in terms of estimated impact on vaccine choice, are presented in Table 1. Efficacy is the vaccine attribute with the greatest marginal effect on choice – on average respondents are more than three times as likely to choose (odds ratio 3.432) a vaccine with 99% efficacy, than a vaccine with 50% efficacy. Absence of moderate side effects more than doubles the probability of choice, while probability of choice is almost doubled by the absence of VISP. Duration and social saturation both significantly increase the probability of choice, but venue for vaccination is statistically insignificant.

Table 1: Factors affecting probability of vaccine choice – best-worst specification

Attribute	Odds Ratio	Estimate	Std. Error	P-value
Efficacy	3.432	1.2332	0.0951	<0.0001***
(Absence of) VISP	1.907	0.6456	0.0853	<0.0001***
(Absence of) Side Effects	2.138	0.7597	0.0862	<0.0001***
Cost	0.226	-1.4857	0.3472	<0.0001***
Social Saturation (Majority)	1.180	0.1658	0.0823	0.0438**
Duration	1.508	0.4105	0.0838	<0.0001***
Venue (Private)	0.983	-0.0168	0.0541	0.7563

*** significant at the 1% level; ** significant at the 5% level; * significant at the 10% level.

The results from the full rank specification are similar, as shown in Table 2. Efficacy has the greatest marginal effect on choice, but in this specification VISP is the second most important attribute. Social saturation and venue for vaccination have small, but statistically significant (although only at the 10% level for venue), effects on vaccine choice.

Table 2: Factors affecting probability of vaccine choice – full rank specification

Attribute	Odds Ratio	Estimate	Std. Error	P-value
Efficacy	2.238	0.8055	0.0487	<0.0001***
(Absence of) VISP	1.933	0.6590	0.0486	<0.0001***
(Absence of) Side Effects	1.506	0.4094	0.0466	<0.0001***
Cost	0.523	-0.6482	0.1926	0.0008***
Social Saturation (Majority)	1.140	0.1311	0.0474	0.0057***
Duration	1.263	0.2334	0.0473	<0.0001***
Venue (Private)	1.081	0.0782	0.0460	0.0895*

*** significant at the 1% level; ** significant at the 5% level; * significant at the 10% level.

The results from both specifications, when converted to marginal willingness-to-pay, are shown in Table 3, along with the 95% confidence interval for the estimates (derived using the Krinsky-Robb procedure [45], with 10,000 replications). These results are similar to those reported in the earlier two tables. Efficacy has the greatest contribution to willingness-to-pay, with respondents on average willing to pay US$244 more for a high (99%) efficacy than low (50%) efficacy vaccine in the best-worst specification, and willing to pay US$383 more for a high efficacy vaccine in the full rank specification. This willingness-to-pay for high efficacy is particularly high, given that the mean monthly income of the sample was US$375 per month.

The average willingness-to-pay for an HIV vaccine with any combination of attributes can also be derived from Table 3. For instance, the willingness-to-pay for the most advantageous (in the eyes of respondents on average) HIV vaccine (i.e. a vaccine with 99% efficacy, no side effects, no VISP, a 10-year duration, where the majority have also been vaccinated, and delivered at a private hospital) is US$1100.50 (with a 95% confidence interval of between US$684.82 and US$2544.18). The willingness-to-pay for a lower cost or less optimal vaccine which might correspond more closely to early vaccine rollout (e.g. 50% efficacy, minor side effects, no VISP, 10-year duration, where the majority have not been vaccinated, and delivered at a private hospital) is US$461.09 (with a 95% confidence interval of between US$281.78 and US$1103.67).

Table 3: Marginal willingness-to-pay for vaccine attributes

Attribute	Best-Worst WTP ($US) (95% C.I.)	Full-Rank WTP ($US) (95% C.I.)
Efficacy	256.11 (167.88–482.61)	382.65 (240.50–900.90)
(Absence of) VISP	134.09 (83.14–252.70)	313.09 (192.80–745.82)
(Absence of) Side Effects	157.78 (98.62–303.14	194.50 (116.21–466.76)
Social Saturation (Majority)	34.44 (1.02–89.03)	62.27 (17.51–172.07)
Duration	85.26 (42.34–179.42)	110.86 (56.52–269.94)
Venue (Private)	-3.49 (-28.64–20.90)	37.14 (-6.17–117.95)

4. Discussion

In general, we found that the biomedical attributes of a hypothetical HIV vaccine (efficacy, absence of VISP, absence of side effects, and duration of effect) were the most important attributes to respondents, in the sense that these were the vaccine attributes that they were willing to pay the most for. Other attributes (social saturation, venue for vaccination) were valued less by respondents. These results are important for consideration prior to the rollout

of any future HIV vaccine. A vaccine with low efficacy, and/or which results in vaccine-induced seropositivity or moderate side effects, would have significantly lower acceptability among high-risk groups, and lead to lower uptake and reduced impact on HIV transmission within the group. However, the vaccine attributes investigated here were necessarily coarse, especially efficacy (99% versus 50%). While we can say that respondents were willing to pay significantly more for 99% efficacy as opposed to 50%, we cannot say whether, for instance, a reduction to 80% efficacy would significantly affect the acceptability of a future HIV vaccine. Future studies should look at more fine-grained efficacy and duration of protection attributes, in order to determine whether small changes in these attributes are important to potential vaccine recipients, particularly as it is unlikely that a vaccine with efficacy of anywhere close to 99% will become available for some time.

The signs on the coefficients for social saturation are interesting, although *a priori* we had no strong expectation for a given sign on the coefficient. The signs on the social saturation coefficients imply that respondents are willing to pay more for (and hence more willing to accept) a vaccine where a majority of the population has already been vaccinated. This contrasts with Heal and Kunreuther [46], who showed that the incentives to be vaccinated reduce as more of the population become vaccinated, because the private benefits of individual vaccination reduce. This 'free-riding' explanation does not appear to hold in our data. This may be because this study is based on stated preference data and not actual vaccination behavior. Alternatively, it may be that people are more likely to get vaccinated because of the perceived benefits to others (altruism), or because the number of people who have already decided to become vaccinated provides a signal that the decision to become vaccinated is a good decision ('bandwagoning') [47]. While altruism is consistent with Theravada Buddhism, the predominant religion in Thailand, we have no way of directly testing whether it is altruism or bandwagoning that is driving the coefficient on social saturation in this data. However, this result is clearly important because social saturation has a small but significant effect on vaccine acceptability. Future studies should consider in more detail whether and through which mechanism or mechanisms social saturation impacts on vaccine acceptability. For example, socio-cultural factors such as communitarian norms or stigma [40,48] should be investigated. If this result proves to be a general result, then it would provide a justification for broad government-subsidized vaccination when a safe, efficacious vaccine becomes available.

In low- and middle-income countries, it is particularly important to consider the impact of cost; an increase from $3 to $75 resulted in nearly 50% lower odds of vaccine acceptability among men and transgender women in Thailand at high risk of HIV exposure. From the perspective of lifetime costs of HIV treatment, estimated at $500,000 [49,50], this suggests that government and privately funded subsidies could have a substantial and cost-effective impact on the epidemic by increasing vaccine uptake. In this context, an actual vaccine priced at the estimated willingness-to-pay for the hypothetically best vaccine, absent cost subsidies, might result in low uptake among high-risk communities, thereby substantially reducing the

effectiveness of the vaccine on a population level. This paper used only two levels of the cost attribute, which were spaced far apart in terms of affordability for respondents. Future studies could improve the external validity of results by including more levels of the cost attribute.

Our analysis using random utility models clearly shows that efficacy is the most important vaccine attribute, both in terms of the probability of vaccine acceptability and in terms of marginal willingness-to-pay. This result is different from those obtained with the same data using conjoint value analysis based on linearised acceptability with ordinary least squares regression (see [40]), where VISP was found to be the most important attribute, followed by efficacy and side effects. The results from our paper (primacy of efficacy) resonate with results from previous studies from North America (e.g. see [11]). While VISP was also found to be an important vaccine attribute in the present analysis, the difference between the two analyses demonstrates a potential for bias when less information about ranking of attributes is used and different assumptions are invoked in the analysis of data. On a substantive level, the importance of VISP might be mitigated with broad educational campaigns delivered in tandem with future vaccines, and may abate once an HIV vaccine achieves broad coverage (such that many of one's peers also test positive due to the vaccine) along with easy access to tests that detect the difference between VISP and actual HIV infection [40].

The discovery of a safe and efficacious HIV vaccine will be a momentous event for global public health. Further evidence that supports bridging the gap between vaccine availability and public utilization [51], such as that reported here, is crucial to the success of future HIV vaccines in reversing the epidemic.

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