

Using Conjoint Analysis to Measure the Acceptability of Rectal Microbicides Among Men Who Have Sex with Men in Four South American Cities

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Abstract Conjoint Analysis (CJA), a statistical market-based technique that assesses the value consumers place on product characteristics, may be used to predict acceptability of hypothetical products. Rectal Microbicides (RM)—substances that would prevent HIV infection during receptive anal intercourse—will require acceptability data from potential users in multiple settings to inform the development process by providing valuable information on desirable product characteristics and issues surrounding potential barriers to product use. This study applied CJA to explore the acceptability of eight different hypothetical RM among 128 MSM in Lima and Iquitos, Peru; Guayaquil, Ecuador; and Rio de Janeiro, Brazil. Overall RM acceptability was highest in Guayaquil and lowest in Rio. Product effectiveness had the greatest impact on acceptability in all four cities, but the impact of other product characteristics varied by city. This study demonstrates that MSM from the same region but from different cities place different values

on RM characteristics that could impact uptake of an actual RM. Understanding specific consumer preferences is crucial during RM product development, clinical trials and eventual product dissemination.

Keywords HIV · MSM · Rectal microbicides · Acceptability · Conjoint analysis

Resumen El Análisis Conjunto (CJA por sus siglas en inglés) es una técnica estadística de mercadotecnia que sirve para evaluar la valoración que los consumidores otorgan a las características de un producto, y que puede ser usada para predecir la aceptabilidad de productos hipotéticos. Para el desarrollo de microbicidas rectales (MR)—sustancias que podrían prevenir la infección por VIH durante el coito anal receptivo—es necesario contar con datos de aceptabilidad, características deseadas y probables barreras para el empleo de MR por usuarios potenciales, en múltiples escenarios.

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Este estudio aplica CJA para explorar la aceptabilidad de ocho diferentes MR hipotéticos entre 128 HSH en Lima e Iquitos, Perú; Guayaquil, Ecuador; y Río de Janeiro, Brasil. En general, la más alta aceptabilidad se dio en Guayaquil y la más baja en Río. La eficacia del producto tuvo el mayor impacto sobre la aceptabilidad en las cuatro ciudades, pero el impacto de otras características del producto varió por ciudades. Este estudio demuestra que los HSH, aunque son de la misma región, pero de diferentes ciudades, otorgan valores distintos a las características de los MR, lo cual podría afectar el uso de un MR real. Es crucial entender las preferencias específicas de los consumidores durante la investigación, desarrollo y eventual difusión de los MR.

Introduction

The use of antiretrovirals (ARV) is at the forefront of HIV biomedical prevention research with data from four recent studies demonstrating promising results. First, in the CAPRISA 004 trial, a 1% vaginal gel formulation of tenofovir disoproxil fumarate (TDF) inserted vaginally before and after intercourse reduced HIV acquisition by 39% overall among at-risk women [1]. Second, daily oral use of co-formulated emtricitabine/tenofovir disoproxil fumarate (FTC/TDF), a strategy known as PrEP (pre-exposure prophylaxis), showed a 44% overall reduction in HIV acquisition among men who have sex with men (MSM) in the iPrEx trial [2] and, for heterosexual men and women, a 73% overall reduction rate in the Partners PrEP trial [3] and 63% overall reduction rate in the CDC TDF2 trial [4]. The Partners PrEP trial also reported an overall reduction of HIV infection by 62% in a separate arm of the same study that examined the use of TDF alone [3]. A common driver of efficacy in each of these studies was product adherence, with the highest levels of HIV protection seen in subjects most adherent to the drug dosing schedule. In the iPrEx study, for example, subjects who used the drug 90% or more of the time reduced their risk of HIV infection by approximately 73%; however, protection dropped to 21% when drug was used less than 90% of the time [2]. Adherence is mediated by product acceptability which ultimately informs use, [5] and therefore acceptability research plays a key role in product development. As McGowan points out in the case of Rectal Microbicides (RM) (substances which would be applied rectally to prevent or reduce HIV infection) “[they] will only play an important role if the target populations find them acceptable and use them correctly and consistently [6].”

While ARV-based RM are in the early stages of development [7], the field is moving rapidly to prepare not only

for future large-scale clinical trials but also to understand user preferences of RM by implementing acceptability research before actual product efficacy is demonstrated [6]. In the wake of the multiple advances in the ARV-prevention field, great hope is placed on RM which would expand HIV prevention options for persons vulnerable to HIV via anal intercourse. RM acceptability studies, limited mainly to MSM populations in the United States, have examined the use and acceptability of potential RM presentations (e.g., gels [8], suppositories [8], douches [9, 10]). These studies have largely used traditional survey research methods such as focus groups, in-depth interviews, and interval-level scale surveys. Conjoint Analysis (CJA), a market-based research method, offers an alternative approach to measuring user preferences of hypothetical products [11–14]. CJA measures product acceptability by presenting multiple “proxy products” from which the potential consumer chooses. Each of the hypothetical products presented has as a finite set of attributes (e.g., cost, effectiveness, presentation type) that vary in value. Consumers demonstrate product preferences, and therefore the product characteristics most important to them, by completing exercises that force upon them choices (trade-offs) to be made between similar products. This procedure produces a unidimensional interval-level scale of benefit importance based on nominal level choice data (i.e., most important vs. least important). CJA can effectively predict preferences and acceptability of actual products. For example, patients’ HIV treatment medication preferences measured by CJA successfully predicted their actual medication choices [15]. Likewise, CJA is increasingly being used to elicit consumer preferences for a wide range of medical issues, from disease treatment regimens to health care systems [15–25]. While actual use of a product cannot be known until the product in question actually exists, CJA can nonetheless be used to rapidly identify product attributes that may eventually affect product acceptance, and has been applied to the assessment of other developing and hypothetical biomedical HIV treatment and prevention interventions including the characteristics of Highly Active Antiretroviral Therapy (HAART) regimens in predicting adherence [26], and the acceptability of HIV vaccines [27] and PrEP [28]. Based on a theoretical behavioral framework (random utility maximization), CJA has an efficient statistical methodology that allows for the estimation of attribute effects and respondent characteristics with small sample sizes, and allows the model fit to be tested empirically [29, 30].

This pilot study used CJA to explore the acceptability of RM in four South American cities with HIV epidemics concentrated in MSM: Lima and Iquitos, Peru; Guayaquil, Ecuador and Rio de Janeiro, Brazil. The vast majority of HIV infections in South America are among MSM, with transmission occurring during unprotected anal intercourse

(UAI) [31]. A comparison of the HIV prevalence in MSM versus the overall adult (15–49 years of age) HIV prevalence in each of the study cities is demonstrative of the elevated risk of HIV among MSM in the region: Peru’s HIV prevalence in MSM is 12.2% (95% CI 11.7–12.7) vs. 0.61% in the general population, Ecuador’s is 15.1% (95% CI 12.8–17.4) vs. 0.31%, and Brazil’s is 14.4% (95% CI 12.6–16.2) versus 0.58% [32]. With unprotected receptive anal intercourse estimated at 10–20% riskier for HIV infection compared to unprotected vaginal intercourse [33, 34], an effective RM could play an important role in preventing new HIV infections in the region. In Peru, for example, mathematical modelling of the impact of a RM 85% efficacious at preventing HIV infection that is used by 30% of MSM during half of condomless anal sex acts predicts a 17% reduction in incident HIV infections [35]. Using CJA, we constructed hypothetical RM “scenarios”—RM with identical attributes but varying values—to explore MSM’s preferences for RM and their composite attributes among all four cities combined and in each individual city.

Methods

Procedures and Participants

Participants and Setting

MSM were recruited from Lima and Iquitos, Peru, Guayaquil, Ecuador and Rio de Janeiro (Rio), Brazil to participate in two CJA exercises. These cities were selected because of their concentrated HIV epidemics in MSM and the existence of an HIV prevention research infrastructure making them potential strategic partners in future RM clinical trials. A convenience sample of MSM was recruited by peer outreach workers in each city who went to parks, beauty salons, volley-ball courts, community-based organizations, bars, saunas and nightclubs that MSM frequented. The outreach workers were employees at the study sites and worked for various research studies involving MSM. They explained to potential participants that a new study was being conducted to learn about their opinions on products called Rectal Microbicides, which they described as “substances like gels, foams, lubricants or liquids that could be inserted into the rectum before having anal sex in order to reduce the chance of infection with HIV” and that no such product yet existed. If the person was interested in participating, he was referred to the study site and screened for inclusion (at least 18 years of age and reporting sex with another male in the previous 12 months).

A total of 16 groups (4 each in Lima, Iquitos, Guayaquil and Rio) of 8–9 MSM (total $n = 128$) were convened.

Groups were distributed across four different types of MSM: commercial sex workers (hustlers); men who reported being openly gay with friends and family (out of the closet); men who reported not being openly gay (closeted); and male-to-female transgendered persons. We chose this grouping of MSM to ensure that the predominant types of MSM were included in our convenience sample following a previous HIV prevention study in the same cities on the acceptability of circumcision for the prevention of HIV in MSM which used the same sampling procedure [36]. Though RM are currently intended for the receptive partner during anal intercourse, we did not screen for sexual role (insertive vs. receptive) since insertive partners may be involved in the application of the product in their partners and would also have opinions related to the product’s attributes. A similar approach has been used in acceptability studies of vaginal microbicides [37].

Each group met once for approximately 1½ h when the CJA exercises and a sociodemographic survey were conducted. Prior to the CJA exercises, a trained facilitator led the group through a 30-min educational session to ensure a basic understanding of RM, including a detailed explanation of all seven product attributes that would later appear in the CJA exercises. While the educational session was presented in a didactic format, participants could ask questions of the facilitator in order to clarify what RM are, how they would be used, and any questions regarding the attributes to be used in the exercises. The facilitator was instructed to present all information without discussing personal preferences or opinions. To ensure standardization of program content between groups in each of the four cities, a set script was followed which described the RM characteristics that would appear on the CJA scenario cards. Characteristics were put into lay-language with examples to ensure comprehension. For example, the product formulation attribute—gel or liquid—was described as, “Liquid is like water, gel is like toothpaste or shaving gel” and the volume attribute as, “15 ml is about 1 tablespoon while 35 ml is about 2 and a half tablespoons.” Additionally, 40% effectiveness was described as “effective less than half the time,” while 80% effective was described as “effective more than three quarters of the time”; and side effects as “no side effects at all” while “itching, burning, and bloating” were given as examples of some side effects. Next, the CJA portion was administered which took approximately 45 min to complete and was comprised of two different exercises. The two CJA exercises were conducted individually by each participant in order to: (1) measure the acceptability of each of the hypothetical RM scenarios, and (2) to assess the impact of individual characteristics on product acceptability. In the first exercise, participants were presented with eight different, fixed hypothetical RM “scenarios” printed on laminated cards. Each scenario was a description of a

potential RM based on seven different characteristics/attributes. The RM scenario cards were color-coded rather than numbered to avoid introducing a value-bias by having a number appear on the card. Participants compared the eight RM scenarios and then ordered the cards sequentially from 1 (“your most favorite”) to 8 (“your least favorite”). Cards could not be ranked the same in terms of preference; each card required a unique rating. The order of the cards (1–8) was captured on a data recording sheet. Next, participants completed a second exercise measuring their likelihood of accepting each RM scenario using a 5-point Likert-type scale ranging from “1 = highly likely would accept” to “5 = highly unlikely would accept.” This second exercise allowed multiple cards for any response category (i.e., the 8 cards could be placed on any of the 5 points on the scale, and multiple or no cards were allowed on any point on the scale). Finally, a brief demographic questionnaire was administered. Procedures were conducted in Peru and Ecuador by the same Spanish-speaking facilitator and in Brazil (in Portuguese) by a second facilitator, both of whom had extensive experience working with the target population and specific training provided by the investigators on RM research and CJA methodology. An assistant helped the facilitators with data recording and other administrative tasks. Participants were compensated the equivalent of USD 5.00 at the end of the study. Institutional Review Boards at the University of California, Los Angeles, *Impacta Salud y Educación* (for Lima and Iquitos), the *Fundación Ecuatoriana Equidad, Guayaquil, Ecuador* (for Guayaquil) and the *Instituto de Pesquisa Clínica Evandro Chagas—Fundação Oswaldo Cruz* (for Rio) reviewed and approved the study prior to implementation.

Measures

Conjoint Analysis

The cornerstone of CJA is that “consumers” (i.e., target audience) make product choices that are based on the composition of the product’s attributes. Each attribute must have at least two levels and, in order to make the scenarios easy to understand and compare, the number of attributes should be restricted in quantity when presented all at once [38], as was done in this and previous studies [27, 28]. This method, known as Full Profile, differs from other methods that can manage more attributes and values but must be computer administered due to the resulting complexity of the exercise [38]. A fractional factorial design was applied in order to arrive at eight hypothetical RM scenarios with seven dichotomous attributes. Since the integrity of the CJA scenarios depends entirely on its attributes, they must be selected with extreme care so as to be as representative as possible of an actual product. To do this we integrated

input from two teleconferences with a team of four leading experts involved in RM development and acceptability research and consulted published RM reports [7], journals [8, 10, 39] and conference proceedings [40, 41]. When no such information existed specifically from the RM field (e.g., product cost—an important attribute that affects consumer choice but for which no information yet exists), we gathered information from related products currently available. Table 1 presents the seven attributes selected (cost per dosage, effectiveness, side effects, frequency of use, product formulation, dosage/volume, and prescription requirement), their levels (binomial in this study) and the justification for their selection.

Sociodemographics

Sociodemographic information was collected using a brief, self-administered paper and pencil questionnaire. Information collected included race/ethnicity, age, education, employment status, and sexual orientation.

Data Analysis

Sociodemographics

Univariate analyses were used to examine the distribution of the sociodemographic variables for all four cities combined and across each of the individual cities.

Conjoint Analysis

Acceptability of each of the eight hypothetical RM scenarios was derived by averaging individual RM acceptability ratings across respondents. Ratings from the 5-point Likert scale were transformed into a 0–100 scale, whereby “highly likely would accept” = 100 and “highly unlikely would accept” = 0. Next, a one-way analysis of variance (ANOVA) model was applied to fit each respondent’s acceptability ratings across the eight RM scenarios. The 7 RM attributes served as independent variables in the model. The effect for each RM attribute from the ANOVA model is the impact score of the attribute on RM acceptability for the individual respondent. Attributes values were sorted as “preferred” and “non-preferred” in order to arrive at the overall impact score for each attribute which was derived by simple subtraction (impact score = acceptability of preferred RM attribute—acceptability of non-preferred RM attribute). The preferred and non-preferred attribute values were based on published RM acceptability research [9, 39, 42] and advice from experts in the RM field. We then averaged individual impact scores across respondents for each attribute to compute its impact on overall RM acceptability. A one-sample *t*-test was

Table 1 RM scenario attribute and level selection

Attribute	Value 1 preferred	Value 2 non Preferred	Justification for attribute values
1. Cost per application	USD 0.30	USD 5.00	Value 1: approximate cost of a male condom in Peru, Ecuador and Brazil. Lower overall cost Value 2: approximate cost of the contraceptive pill per month in Peru and Ecuador; chosen as an example of a sexual health related product that must be used every day. Higher overall cost
2. Formulation	Gel	Liquid	Value 1: Lubricant use is common among Peruvian MSM during receptive anal intercourse ^a Value 2: Douching is common among US MSM prior to receptive anal intercourse ^b and potentially in Peruvian MSM ^c but may be less practical than a gel
3. Prescription	Available over the counter, without a prescription	By prescription only	Value 1: Would not require engagement with the medical system and may provide more anonymity with regards to product access Value 2: Would require consumers to engage with the medical system (e.g., see a physician) in order to receive a prescription; would necessarily require that the physician know about the consumer's sexual behaviors
4. Frequency of use	Just before sexual intercourse	Daily use regardless of sexual activity	Value 1: The lowest frequency of use that would presumably provide protection Value 2: ARV-based RM may require daily application regardless of sexual behavior in order to confer sufficient levels of drug in the rectal mucosa to prevent HIV infection ^d
5. Effectiveness	80%	40%	Value 1: Considered the highest likely clinical efficacy that a RM may have based on expert opinion Value 2: Considered the lowest likely clinical efficacy a RM could have and still be considered for actual use based on expert opinion
6. Side effects	None	Some (itching, burning, bloating)	Value 1: The ideal RM would have no side effects Value 2: Side effects, if present, would need to be minimal
7. Dosage/volume	15 ml (1 tablespoon)	35 ml (about 2½ tablespoons)	Value 1: Considered the lowest probable product volume that would be needed to confer protection ^e Value 2: Highest tolerable volume of gel that was found acceptable in rectal volume escalation in MSM ^e

^a Kinsler et al. [42]

^b Carballo-Diequez et al. [9]

^c Galea et al. [44]

^d Anton et al. [43]

^e Carballo-Diequez et al. [39]

used to determine the statistical significance of the impact of each attribute on RM acceptability.

Results

Data are presented as an overall aggregate (all cities combined) and by individual city. Demographic information for MSM is presented in Table 2. Table 3 shows the acceptability of all 8 RM scenarios and their attribute profiles and Table 4 shows the impact of each attribute on RM acceptability sorted by “Preferred” versus “Non-preferred” values.

Conjoint Analysis

Overall Acceptability (MSM from all Four Cities Combined)

RM acceptability ranged from 26.02 to 87.30 on the 0–100 point scale with a mean overall acceptability of 50.03 out of 100 across the 8 hypothetical RM. The RM scenario with the highest acceptability, Scenario 1 in Table 3, had the following characteristics: \$0.30 per dose, 80% effectiveness, no side effects, use before sex, gel formulation, 15 ml dosage and prescription required (Table 3).

Effectiveness had the single greatest impact on acceptability across the 7 RM attributes. Participants reported

Table 2 Socio-demographic characteristics of MSM for all four cities combined ($N = 128$); and for each individual city: Lima ($N = 32$), Iquitos ($N = 31$), Guayaquil ($N = 33$), and Rio de Janeiro ($N = 32$)

Characteristics	ALL <i>N</i> (%)	LIM <i>N</i> (%)	IQT <i>N</i> (%)	GYE <i>N</i> (%)	RIO <i>N</i> (%)
Race/ethnicity					
Mestiza	70 (56)	20 (65)	23 (74)	27 (82)	–
White	22 (18)	7 (22)	4 (13)	3 (9)	8 (28)
Indigenous	3 (2)	3 (10)	–	–	–
Black	10 (8)	–	–	–	10 (34)
Mixed race	11 (9)	–	–	–	11 (38)
Other	8 (7)	1 (3)	4 (13)	3 (9)	–
Age					
18–29	96 (79)	21 (75)	26 (87)	30 (91)	18 (62)
30–39	19 (16)	5 (18)	4 (13)	2 (6)	8 (28)
40+	6 (5)	2 (7)	–	1 (3)	3 (10)
Education					
Less than high school	14 (11)	2 (6)	2 (7)	2 (6)	8 (26)
High school	70 (57)	14 (47)	18 (60)	22 (69)	16 (52)
Greater than high school	39 (32)	14 (47)	10 (33)	8 (25)	7 (22)
Employed					
Yes	74 (76)	16 (62)	17 (85)	18 (78)	23 (79)
No	24 (24)	10 (38)	3 (15)	5 (22)	6 (21)
Sexual orientation (self-identified)					
Gay	42 (35)	18 (56)	8 (28)	7 (23)	9 (31)
Bisexual	33 (27)	5 (16)	4 (14)	17 (55)	7 (24)
Transgender	24 (20)	4 (13)	5 (17)	6 (19)	9 (31)
Heterosexual	11 (9)	3 (9)	5 (17)	–	3 (10)
Other	11 (9)	2 (6)	7 (24)	1 (3)	1 (4)

Due to missing data, variables do not sum to total *N*'s

ALL all four cities combined, *LIM* Lima, *IQT* Iquitos, *GYE* Guayaquil, *RIO* Rio de Janeiro

significantly higher RM acceptability with an 80% effectiveness (acceptability = 65.37 on a 0–100 point scale), compared to 40% effectiveness (acceptability = 34.71 on a 0–100 point scale), yielding a net impact score of 30.66 ($P < 0.001$). Side effects had the second greatest impact on RM acceptability. Participants reported significantly higher RM acceptability with no side effects (acceptability = 57.17), compared to using an RM with some side effects (acceptability = 42.98), yielding a net impact score of 14.19 ($P < 0.001$). Frequency of use (preference for using RM before sex vs. daily use), product formulation (preference for gel vs. liquid), cost (preference for an RM costing \$0.30 vs. \$5.00), and need for prescription (preference for prescription needed to obtain an RM vs. purchasing an RM over the counter) also had a significant impact on RM acceptability ($P < 0.001$, $P < 0.001$, $P < 0.001$, and $P < 0.05$, respectively) (Table 4).

Lima

RM acceptability ranged from 25.81 to 83.06 on the 0–100 point scale, with a mean overall acceptability of 46.88 out of 100 across the 8 hypothetical RM scenarios. RM scenario 1 had the highest acceptability (Table 3).

Effectiveness had the single greatest impact on acceptability across the 7 RM attributes (preference for an RM with 80% effectiveness vs. 40% effectiveness) yielding a net impact score of 30.00 ($P < 0.001$). Frequency of use had the second greatest impact on RM acceptability (preference for using RM before sex vs. daily use) yielding a net impact score of 13.00 ($P < 0.05$). Product formulation (gel vs. liquid) and side effects (no side effects vs. some side effects) also had a significant impact on RM acceptability ($P < 0.01$ and $P < 0.01$, respectively) (Table 4).

Iquitos

RM acceptability ranged from 33.33 to 83.06 on the 0–100 point scale, with an overall mean acceptability of 52.50 out of 100 across the 8 hypothetical RM scenarios. RM scenario 1 had the highest acceptability rating (Table 3).

Effectiveness had the greatest impact on acceptability across the 7 RM attributes (preference for a RM with 80% effectiveness vs. 40% effectiveness) yielding a net impact score of 21.30 ($P < 0.001$). Prescription requirement had the second greatest impact on RM acceptability. Participants reported significantly higher RM acceptability with a

Table 3 Comparison of hypothetical RM acceptability scenarios among MSM for all four cities combined ($N = 128$), and for each individual city: Lima ($N = 32$), Iquitos ($N = 31$), Guayaquil ($N = 33$), and Rio de Janeiro ($N = 32$)

RM scenario	RM acceptability mean (SD)*								RM attributes				
	All cities combined ^a	Lima ^b	Iquitos ^c	Guayaquil ^d	Rio ^e	Cost (\$)	Effectiveness (%)	Side effects	Frequency of use	Product formulation	Dosage (ml)	Rx or OTC	
1	87.30 (23.96)	83.06 (26.31)	83.06 (26.92)	92.19 (19.51)	90.83 (20.22)	0.30	80	None	Before sex	Gel	15	Rx	
2	60.77 (33.74)	65.83 (33.40)	62.90 (33.46)	50.00 (34.78)	53.33 (35.19)	5.00	80	Some	Before sex	Gel	35	OTC	
3	58.54 (34.60)	54.03 (33.60)	41.13 (34.49)	60.94 (33.56)	59.48 (34.34)	5.00	80	None	Daily	Liquid	15	OTC	
4	54.64 (35.69)	45.97 (38.78)	71.77 (29.40)	50.78 (28.03)	50.83 (35.04)	0.30	80	Some	Daily	Liquid	35	Rx	
5	42.07 (34.96)	35.48 (34.02)	57.26 (36.63)	78.91 (25.49)	26.67 (31.44)	5.00	40	None	Before sex	Liquid	35	Rx	
6	39.92 (33.42)	32.50 (35.45)	34.68 (29.35)	25.78 (29.43)	40.00 (35.11)	0.30	40	None	Daily	Gel	35	OTC	
7	29.64 (32.10)	31.45 (31.60)	36.29 (33.44)	49.22 (34.48)	25.00 (34.11)	0.30	40	Some	Before sex	Liquid	15	OTC	
8	26.02 (30.05)	25.81 (32.59)	33.33 (31.03)	25.78 (30.11)	18.96 (25.58)	5.00	40	Some	Daily	Gel	15	Rx	

RM rectal microbicide, SD standard deviation, OTC over the counter, Rx prescription

* RM acceptability score is based on a 5 point Likert scale converted to a 0–100 scale

^a Overall RM acceptability among MSM in all four cities combined: 50.03 (12.41); scenario ranking from highest to lowest: 1, 2, 3, 4, 5, 6, 7, 8

^b Overall RM acceptability among MSM in Lima: 46.88 (SD: 13.66); scenario ranking from highest to lowest: 1, 2, 3, 4, 5, 6, 7, 8

^c Overall RM acceptability among MSM in Iquitos: 52.50 (SD: 11.17); scenario ranking from highest to lowest: 1, 4, 2, 5, 3, 7, 6, 8

^d Overall RM acceptability among MSM in Guayaquil: 54.20 (SD: 12.11); scenario ranking from highest to lowest: 1, 5, 3, 4, 2, 7, 6, 8

^e Overall RM acceptability among MSM in Rio: 46.12 (SD: 11.04); scenario ranking from highest to lowest: 1, 3, 2, 4, 6, 5, 7, 8

Table 4 Comparison of impact scores of RM attributes on hypothetical RM acceptability among MSM for all four cities combined, and for each individual city: Lima ($N = 32$), Iquitos ($N = 31$), Guayaquil ($N = 33$), and Rio de Janeiro ($N = 32$)

RM attributes	Attribute values	Acceptability of RM with preferred attribute (mean)				Acceptability of RM with non-preferred attribute (mean)				Overall impact on RM acceptability mean (preferred–non preferred)						
		ALL	LIM	IQT	GYE	RIO	ALL	LIM	IQT	GYE	RIO	ALL	LIM	IQT	GYE	RIO
Cost (\$)	0.30 vs. 5.00	52.87	49.00	56.45	54.29	51.67	46.95	45.58	48.75	54.10	39.66	5.92 [†]	4.42	7.70*	0.19	12.00 [†]
Effectiveness	80 vs. 40	65.37	61.88	61.72	70.51	64.01	34.71	31.88	40.42	37.89	28.23	30.66 [†]	30.00 [†]	21.30 [†]	32.62 [†]	35.78 [†]
Side effects	None vs. some	57.17	51.46	54.03	67.77	54.74	42.98	42.29	51.46	40.63	37.50	14.19 [†]	9.17 [†]	2.57	27.14 [†]	17.24 [†]
Frequency	Before sex vs. daily	54.98	53.33	59.88	57.42	48.96	44.83	40.32	44.79	50.98	42.89	10.15 [†]	13.00*	15.09 [†]	6.44*	6.07
Formulation	Gel vs. liquid	53.51	52.71	52.71	57.03	51.29	46.41	41.04	51.61	51.37	40.95	7.10 [†]	11.67 [†]	1.10	5.66	10.34 [†]
Dosage (ml)	15 vs. 35	50.51	48.59	48.54	55.66	48.92	49.39	45.00	56.65	52.73	42.71	1.12	3.59	-8.11*	2.93	6.20
Rx needed	OTC vs. Rx	47.54	47.29	43.75	53.71	45.04	52.58	46.46	61.67	54.69	47.20	-5.04*	-0.83	-17.92 [†]	-0.98	-2.16

RM rectal microbicide, Rx prescription, OTC over the counter, ALL all four cities combined, LIM Lima, IQT Iquitos, GYE Guayaquil, RIO Rio de Janeiro

* $P < 0.05$, [†] $P < 0.01$, [‡] $P < 0.001$ for the one sample t -tests

prescription needed to purchase a RM (acceptability = 61.67), compared to purchasing an RM OTC (acceptability = 43.75), yielding a net impact score of -17.92 ($P < 0.001$). The negative impact score results from a higher mean acceptability for the non-preferred attribute (prescription needed) than the preferred attribute (over the counter) (i.e., $43.75 - 61.67 = -17.92$). Additionally, dose/volume had a significant impact on RM acceptability (preference for a dosage of 35 ml vs. 15 ml) yielding a net impact score of -8.11 ($P < 0.05$). Frequency of use (preference for using RM before sex vs. daily) and cost (preference for \$0.30 vs. \$5.00) also had a significant impact on RM acceptability ($P < 0.001$ and $P < 0.05$, respectively) (Table 4).

Guayaquil

RM acceptability ranged from 25.78 to 92.19 on the 0–100 point scale, with an overall mean acceptability of 54.20 out of 100 across the 8 hypothetical RM scenarios. RM scenario 1 had the highest acceptability rating (Table 3).

Effectiveness had the greatest impact on acceptability across the 7 RM attributes (preference for an RM with 80% effectiveness vs. 40% effectiveness) yielding a net impact score of 32.62 ($P < 0.001$). Side effects (preference for no side effects vs. some side effects) and frequency of use (preference for using RM before sex vs. every day) also had a significant impact on acceptability ($P < 0.001$ and $P < 0.05$, respectively) (Table 4).

Rio

RM acceptability ranged from 18.96 to 90.83 on the 0–100 point scale, with an overall mean acceptability of 46.12 out of 100 across the 8 hypothetical RM scenarios. RM scenario 1 had the highest acceptability rating (Table 3).

Effectiveness had the greatest impact on acceptability across the 7 RM attributes (preference for a RM with 80% effectiveness vs. 40% effectiveness) yielding a net impact score of 35.78 ($P < 0.001$). Side effects had the second greatest impact on RM acceptability (preference for no side effects vs. some side effects) yielding a net impact score of 17.24 ($P < 0.001$). Cost (preference for an RM costing \$0.30 vs. \$5.00) and product formulation (preference for a gel vs. liquid product) also had a significant impact on acceptability ($P < 0.001$ and $P < 0.01$, respectively) (Table 4).

Discussion

In this heterogeneous convenience sample of MSM from four South American cities we used CJA, a market-based

research method, to assess the acceptability of eight hypothetical RM scenarios composed of identical attributes with dichotomous levels. Acceptability of the best possible RM scenario for all four cities combined and for each of the individual four cities were identical; \$0.30, 80% effective, no side effects, use before sex, gel formulation, 15 ml dosage, and prescription required. These findings suggest the potential for widespread use in our target population of MSM with a product with similar characteristics. Nevertheless, the average acceptability of 50.03 for all four cities combined, 46.88 in Lima, 52.50 in Iquitos, 54.20 in Guayaquil, and 46.12 in Rio (all on the 0–100 scale) across the eight hypothetical RM scenarios may be a more realistic estimate of its probable uptake and indicates that the eventual degree of acceptability of RM is likely to be influenced by the trade-offs made between the specific attributes in our model as well as other product attributes not evaluated in this study, such as social factors, that may also play a role in RM acceptability.

We found that six of the seven attributes (dosage was the exception) significantly impacted RM acceptability in the aggregate findings; however, there were several significant differences in mean impact scores of the different RM attributes between the cities that may impact acceptability of an actual RM. For the Lima MSM, a 40% effectiveness level, presence of side effects, daily product use and a liquid formulation were rated as least acceptable. Thus, actual products with these or similar characteristics may face challenges in uptake by this population. In contrast, the Iquitos MSM rated as least acceptable those hypothetical RM with the higher cost attribute, lower effectiveness, daily use, lower dosage volume, and obtaining the product over the counter. Among the Guayaquil MSM, the attribute levels with the lowest acceptability included low effectiveness, some side effects, and daily product use. Finally, for the Rio MSM, the attribute levels with the lowest acceptability included low effectiveness, some side effects, higher cost, and liquid formulation. First and foremost, this study demonstrates that although this is an MSM population from one region (South America) there are nonetheless variations by city in attribute level preferences that might impact uptake of an actual RM. As in traditional consumer marketing, understanding one's target population and their specific preferences will be crucial during RM product development, clinical trials and eventual product dissemination.

Effectiveness had the greatest impact on acceptability for all four sites with participants significantly more likely to prefer an RM with 80% effectiveness versus 40%. Overall, the 4 RM scenarios with the effectiveness attribute value of 80% were ranked higher than the 4 scenarios with the effectiveness attribute value of 40%, demonstrating that effectiveness “drove” the scenario selection (see Table 1).

While these findings are not surprising, they are interesting in the context of the CAPRISA 004 trial (overall efficacy 39% [1]) and the oral PrEP studies (overall efficacies ranging from 44% in MSM [2] to 73% [3, 4] in heterosexuals) and the widespread public debate regarding what their actual “real world” effectiveness would be if scaled up for HIV prevention use. Would MSM find acceptable an actual RM that was 40% effective? Additionally, what would the tradeoffs need to be with regard to the other product characteristics in order to achieve acceptability at that efficacy level? More importantly, would it be worth bringing to market a product that was 40% effective? Conversely, is an 80% effectiveness level—which implies a higher overall clinical efficacy—a realistic outcome given the concomitant challenges of correct product use and adherence which will surely accompany any RM as it did with the other ARV for prevention studies?

CJA forces trade-offs—the selection of a product based on the inclusion of preferred attributes even when it means accepting some attributes that are less desirable—and can provide unexpected results. In this case it was expected that following product effectiveness, the side effects attribute would rank as the next important for all cities. But while the presence of side effects impacted acceptability in Lima, Guayaquil, and Rio MSM, it did not in Iquitos. We are unaware of any sexual practices or common medical concerns in Iquitos MSM that would make these side effects less important compared to the MSM in the other cities; nonetheless as the smallest and most isolated city in the study, situated deep in the Amazon region, it is plausible that local beliefs, customs or practices regarding these side effects played a role in this outcome. The opposite is also possible: that MSM from larger cities have beliefs or experiences (perhaps shaped by their use of anorectally applied products like lubricants and enemas, likely more accessible in large urban areas) that have shaped preferences such that side effects *are* a salient factor in product acceptance. Further research is needed to understand this result with regards to the type and intensity of side effects that would be required to have this attribute significantly impact (positively or negatively) acceptability and tease out the factors that may cause inter-population preference variability. Additionally, it was thought that cost would rank as an important attribute for all four sites, yet it only impacted acceptability in Iquitos and Rio.

MSM in all cities but Rio significantly preferred a product that was used just before sex rather than on a daily basis regardless of sexual activity, an important finding in light of recent data presented by Anton et al. [43] which demonstrated that a single dose of 1% vaginal tenofovir gel did not inhibit HIV infection in rectal biopsies. If these data are corroborated by future studies and RM are developed that require regular or daily dosing as with the oral PrEP

studies to confer protection regardless of sexual activity, then the issue of product adherence will be especially important to address in future RM studies.

For the Lima and Rio sample, a gel product formulation was preferred over a liquid product. It is possible that MSM from large urban cities (Lima and Rio), each with populations of approximately 10 million inhabitants compared to Iquitos (approximately 379,000) and Guayaquil (approximately 3.3 million) may have greater access to sexual lubricants formulated as gels and so have a greater familiarity with the presentation type. Liquids administered rectally such as enemas and douches and their use by MSM in the study cities is virtually unknown. However, some limited data on rectal douching from MSM in Peru [44] and the US [9] and their implications for RM point to the need for further investigation in this area in South American MSM.

Iquitos MSM stood out with their preference for a RM requiring a prescription (versus purchasing an RM over the counter), and a *higher* dosage volume. Needing a prescription to obtain an RM may indicate that MSM from Iquitos perceive a product prescribed by a physician as being more effective—a “stronger medicine”—than a product not requiring a prescription. Work conducted to understand women’s perceptions of efficacy in a vaginal microbicide study, for example, found that certain personal beliefs of what made the product efficacious were very different from the clinical trial’s scientific aims [45]. Regarding the preference for a higher dose volume, it could be that MSM from Iquitos believe that “more product means greater HIV protection,” or perhaps the use of douches or enemas is already a part of preparing for anal sex among this group and their views on volume were affected by those experiences. It is equally likely that there were other factors driving this finding that are unrelated to personal experiences since dose/volume is arguably a difficult attribute to conceptualize, perhaps even more so when the rectum is the intended destination. Furthermore, even prior experience with rectal products like lubricants or douches/enemas may not provide enough background experience on which to base a volume choice for a RM since their use is likely not “dosed”. These areas warrant further exploration.

There were limitations to our study. First, the small sample size ($n = 128$) and convenience sampling limits the ability to generalize our results to others. While a strength of CJA is that relatively small ($n = 100$) sample sizes can be used to obtain meaningful results, in general, the larger the sample size the greater the ability to generalize the findings. The purpose of this study was to assess various attributes that might impact acceptability of hypothetical RM among MSM populations from four South American cities rather than to generalize our findings to all persons at

risk. Furthermore, a larger overall sample size would permit the investigation of differences between MSM subgroups, where important acceptability differences may be found. For example, the needs (and subsequent acceptability of RM attributes) of a male sex worker may be different than other MSM. Likewise, while we found it important to consider the views of insertive partners (“tops”) in addition to receptive partners (“bottoms”) since both could conceivably be involved in RM use (e.g., in its purchase and application) it is certainly possible that their product acceptability views are different. Also, this convenience sample was not polled on current anal health and habits or product use (e.g., lubricants, enemas, suppositories, etc.) all of which may have influenced their preferences in the CJA exercises. Next, while our use of 7 attributes has been used in other CJA biomedical HIV prevention acceptability studies [27, 28] they were nonetheless limited in number, based on current knowledge when the study was designed, and not inclusive of all possible product attributes and subject to change in a rapidly developing area. Such changes could affect CJA outcomes to actually predict uptake and use. One important factor that could impact RM acceptability involves the type of applicator used for product insertion. This is a recognized area of investigation for vaginal microbicides [46, 47] and is a topic in RM research as well [6]. Ideally, social issues (e.g., perception of HIV risk, HIV testing practices, relationship issues, trust in providers, and stigma/discrimination) [48–50] would be included in the model, as they may also impact RM acceptability. Finally, the 30 min educational session conducted prior to the CJA exercises as well as the CJA exercises themselves that were conducted in a group setting may have introduced biases into participants’ stated preferences.

Conclusion

This study is the first to assess RM acceptability in South America and the first, to our knowledge, to use CJA as a methodology for assessing RM acceptability. While CJA has been used commercially for over 40 years [38] and its use in clinical medicine and the health care delivery field is growing, its application specifically to the biomedical HIV-prevention intervention arena is relatively recent. CJA offers new insight into the characteristics that may affect the acceptability and eventual real-world uptake of any future potential products by presenting them to potential users in ways that that they will eventually be assessed, i.e., as a bundle of attributes which must be considered simultaneously. By presenting hypothetical products in this way, and asking potential users to make choices (trade-offs) between product attributes of differing values, the relative

importance of product characteristics can be quickly established. As RM continue down the developmental pipeline, the CJA models can be refined with the most up-to-date attributes and values, and newer, more complex models can be created to accommodate additional variables and in doing so better predict real-world product acceptability and use.

With ARV-for prevention studies gathering momentum and Phase-I RM studies currently underway, acceptability studies are urgently needed in both U.S. and non-U.S. at-risk populations to keep pace with the clinical findings and will provide valuable information on product characteristics deemed most desirable by a specific target population by shedding light on issues surrounding potential barriers to product use. CJA and other quantitative market-based approaches offer an alternative to the traditional methods for assessing acceptability of hypothetical biomedical HIV prevention interventions. Our study demonstrated that clear differences were observed between similar populations in four different South American cities, and points to the necessity for much deeper exploration of the intended target groups in each environment where RM will be studied or deployed.

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