Perceptibility and the “Choice Experience”: User Sensory Perceptions and Experiences Inform Vaginal Prevention Product Design

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Abstract

The development of pericoital (on demand) vaginal HIV prevention technologies remains a global health priority. Clinical trials to date have been challenged by nonadherence, leading to an inability to demonstrate product efficacy. The work here provides new methodology and results to begin to address this limitation. We created validated scales that allow users to characterize sensory perceptions and experiences when using vaginal gel formulations. In this study, we sought to understand the user sensory perceptions and experiences (USPEs) that characterize the preferred product experience for each participant. Two hundred four women evaluated four semisolid vaginal formulations using the USPE scales at four randomly ordered formulation evaluation visits. Women were asked to select their preferred formulation experience for HIV prevention among the four formulations evaluated. The scale scores on the Sex-associated USPE scales (e.g., *Initial Penetration* and *Leakage*) for each participant's selected formulation were used in a latent class model analysis. Four classes of preferred formulation experiences were identified. Socio-demographic and sexual history variables did not predict class membership; however, four specific scales were significantly related to class: *Initial Penetration*, *Perceived Wetness*, *Messiness*, and *Leakage*. The range of preferred user experiences represented by the scale scores creates a potential target range for product development, such that products that elicit scale scores that fall within the preferred range may be more acceptable, or tolerable, to the population under study. It is recommended that similar analyses should be conducted with other semisolid vaginal formulations, and in other cultures, to determine product property and development targets.

Keywords: perceptibility, adherence, HIV/STI, prevention, dosage forms, product choice

Introduction

THE DEVELOPMENT OF female-initiated, pericoital biomedical prevention products continues to be a priority in efforts to curb sexual transmission of HIV/AIDS.¹ Overall, clinical trials to date have been unable to demonstrate efficacy of potential products (e.g., vaginal gel microbicides).^{2,3} Poor adherence has been implicated as a barrier to determining efficacy; while intent-to-treat analyses have not demonstrated significant efficacy, *post hoc* analyses among high adherers have shown significant reductions in rates of

HIV infections.³⁻⁵ Notably, these studies have found that high levels of participant self-reported acceptability do not necessarily translate to high levels of adherence on biological testing.² Whether these results suggest a lack of concordance between the actual concepts, or the measures used to assess them, remains an empirical question; the current measurement of product acceptability may not reliably and/or validly define or measure product acceptability, or predict patterns of use/nonuse. In both qualitative and quantitative assessments, some clinical trial participants have identified product-related experiences, such as leakage and sensory interference

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with the sexual experience, as potential nuisance factors that may have implications for use patterns.⁶⁻⁸ Indeed, both positive and negative experiences with vaginal products seem to be weighted and prioritized when potential users consider product choices and/or their willingness to use.⁹ While these phenomena likely do not entirely account for the wide range of product use patterns in clinical trials, such experiences are likely critical to initial product adoption and sustained use.

In the study presented here, our primary aim was to develop standardized tools potential users could utilize to evaluate soft, deformable vaginal formulations (hereafter referred to as “gels”) and to better understand the role that users’ sensory perceptions and experiences (USPEs) might play in product acceptability and adherence. We previously demonstrated that product users can perceive and meaningfully report on the sensory perceptions and formulation “behaviors” experienced while using a semisolid vaginal formulation, and created validated scales measuring discrete USPEs (Perceptibility Scales¹⁰). In this study, we present further analyses, demonstrating that preferred formulation experience profiles can be utilized to understand the range of properties that would be the most acceptable to users. Indeed, while this study specifically focuses on vaginal gels, other soft material formulations, once dissolved or melted, (e.g., vaginal capsules, tablets, suppositories, or vaginal films) also possess rheological and other biophysical properties that can be discerned by users and, hence, may benefit from similar evaluation.

We examine patterns of preferred formulation experience using a novel application of Latent Class Modeling (LCM), a data reduction technique that can identify classes of formulation experience, grouping participants who report similar score profiles on USPE scales. By examining scale scores for each participant’s preferred formulation experience, we identify experiences (e.g., how well the formulation lubricated the vagina at initial penetration and how much leakage a user noticed during sex) that are most tolerated and/or preferred among the majority of women. Once classes or groups of similarly preferred experiences are identified, we determine which experiences (characterized by perceptibility scale scores) are the most critical in selecting a prevention product. In addition, group membership then serves as an outcome variable to examine how sociodemographic or other factors may be associated with preferred product characteristics.

Materials and Methods

The current analysis utilizes data from the final stage of a three-stage scale development and validation study (Project LINK). The goals and outcomes of the first two stages of the study have been described elsewhere in detail.¹⁰ In sum, formative qualitative interviews were used to generate a pool of items capturing the range of sensations elicited by various formulation properties, as experienced during use. We did not focus on conventional microbicide acceptability characteristics, such as smell, taste, and packaging¹¹⁻¹⁵; instead, we aimed to assess USPEs and how those USPEs may relate to rheological and other biophysical properties of topical vaginal formulations. Of note, USPE items are designed to capture user perceptions of formulation performance in factual terms. Items do not ask participants to form cognitive judgments or opinions; these are assessed later in the evaluation process.

Specific sets of items (i.e., scales) generated from the qualitative data described the range of USPEs that could be experienced by users during and following formulation application, ambulation, and sexual activity. We then hypothesized potential associations between USPEs and properties of vaginal formulations also associated with drug delivery in the vagina (e.g., spreading within the vagina, leakage from the vagina). In consideration of these relationships, our formulation science team developed four semisolid vaginal formulations that exhibited a range of rheological and other biophysical properties that potential vaginal microbicide gels might possess, including formulations that might be best-suited to pericoital use, as well as high viscosity forms that could be considered for long-lasting daily use regimens. The analyses described here utilize data obtained in the final stage of Project LINK, in which participants experienced each of these four gels and rated them using eight psychometrically derived and validated USPE scales.

Vaginal formulations

For this study, four gel formulations were used that exhibited a range of rheological and other biophysical properties [e.g., specific characteristics of internal gel friction (viscosity) and predicted rates of gel spreading along the vaginal canal]. The study gels comprised ingredients that are generally recognized as safe by the US Food and Drug Administration and used varying proportions of hydroxyethyl cellulose and Carbopol to achieve a range of predicted vaginal spreadability and retention; each was labeled using a color (i.e., orange, yellow, purple, and green) to avoid primacy effects (e.g., 1-2-3-4). Three formulations were designed for this study and did not represent actual candidate microbicide formulations; one (orange) was the “universal placebo” typically used in vaginal microbicide clinical trials.¹⁶

The orange, yellow, and purple gels were designed to spread relatively well along the vaginal canal. The orange and yellow gels were most distinguished from each other by differences in their yield stress properties, with the yellow gel’s higher yield stress making it less likely to spread and leak than the orange gel. The purple gel had a much higher initial (undiluted) viscosity than the orange and yellow gels, but, upon dilution, its viscosity was comparable to that of the yellow gel and significantly less than the green gel. We hypothesized that the orange gel would spread the most, both because of its relatively low viscosity and its relatively absent yield stress. These properties would likely also allow it to be perceived as smooth, relatively to the higher viscosity and yield stress of the yellow gel. While the yellow gel would initially flow more readily relative to the purple gel due to its lower viscosity, the purple gel’s higher viscosity and lower yield stress would ultimately allow it to be more adhesive than the yellow gel. Once diluted, the yellow and purple gels were hypothesized to be more like each other with respect to leakage and area coated than either the orange or green gels (see Morrow *et al.*¹⁰ for a table of selected formulation properties). Participants applied 3.5 ml of the orange, yellow, and purple gels. This is ~0.5 ml less than the 4 ml volume of the tenofovir gels used in some microbicide trials (e.g., CAPRISA004, VOICE, and FACTS trials^{4,17,18}), but is the same volume used in a number of other trials.^{19,20} The green gel was administered at 2 ml and had a higher viscosity,^{21,22} as has been suggested for gels that could be used for daily (coitally independent) use. We expected the green gel to be

relatively unaffected by dilution during the evaluation period and, therefore, flow very little, if at all.

Human subjects

Study procedures were conducted at two urban sites in the northeastern United States. Volunteers were eligible if they were 18–45 years of age, in general good health, and reported vaginal sex with a male sexual partner in the past 12 months. All study procedures were approved by the relevant human subjects' protection review boards. Each participant provided written informed consent before evaluation visits and was compensated for her time after each visit.

We targeted enrollment based on age and number of vaginal births to represent a range of vaginal anatomy/physiology (0, 1, 2+ vaginal deliveries) and age (18–29 and 30–45 years) to better represent the burden of HIV among women of reproductive age.²³ Women over the age of 45 were not studied because we postulated that postmenopausal changes in the vaginal environment may impact the user experiences being studied. We did not exclude women as a function of their familiarity (or lack thereof) with any type of vaginal product, including medications, personal lubricants, and sex toys. Additional sample and recruitment details are reported elsewhere.¹⁰

Procedures

Each participant completed four randomly ordered formulation evaluation sessions, with at least 5–7 days between sessions. At each session, participants had an opportunity to first manipulate the gel in their hands and to evaluate it using a set of *in mano* perceptibility survey items (data not presented here). The participant then inserted the gel into her vagina using a standardized prefilled applicator (HTI Comfort Tip applicator; HTI Plastics, Lincoln, NE) in a private examination room, walked around the room for 2 min, then simulated sexual intercourse for ~4 min with a condom-covered (nonlubricated) artificial phallus.^{24,25} Each participant then completed, through computer-assisted self-interview, USPE items that captured her product use experiences (i.e., application, walking, simulated vaginal–penile sex, hereafter “sexual activity”). In this study, we report on product use experiences related to sexual activity, as measured by a subset of eight USPE scales first presented previously.¹⁰

Measures

Participants completed questionnaires at the outset of the study and at each study visit. Demographics, sexual and reproductive health history, and vaginal product use history were collected at screening and baseline while sexual partner-specific information (e.g., number of partners; HIV, STI, and pregnancy risk perception) and ratings of USPEs were collected at each study visit. Participants rated their experiences on the entire pool of USPE items, including eight perceptibility scales assessing formulation experiences during sexual activity¹⁰: “Sex: Initial Penetration” (perceived smoothness and lubricity at the introitus during first penetration), “Sex: Initial Lubrication” (sensations of coating and lubrication during first few strokes), “Sex: Spreading Behavior” (ease of strokes and formulation spread over time), “Sex: Product Awareness” (sensations of awareness/feeling

the product during sexual activity), “Sex: Perceived Wetness” (sensations of wetness and vaginal coverage by the end of evaluation), “Sex: Stimulating” (perceptions of the product enhancing sexual pleasure), “Sex: Messiness” (sensations of leakage/dripping/messiness from the product over time), and “Sex: Leakage” (sensations of the product near the introitus or having leaked out during and after evaluation). Each USPE scale is composed of three to seven items, and participants are asked to rate their agreement with each item using a series of statements on a five-point Likert scale: (1) do not agree at all, (2) agree a little, (3) agree somewhat, (4) agree a lot, (5) agree completely. At the final visit, after each participant had experienced each of the four study formulations, she was asked to choose which one she would be most willing to use for HIV prevention (i.e., her “preferred gel”).

Analysis

First, we summarized demographic data (Table 1) using means and standard deviations for continuous data, and percentages and *N*s for categorical variables, and calculated mean (and median) scale scores for each formulation (Table 2). For the purpose of this analysis, USPE scale scores were recoded as binary indicators of whether or not the participant scored higher or lower than the population median. Thus, the full data consisted of vectors of binary indicators of USPEs (one for each of the eight scale scores) for each of the four formulations (orange, green, yellow, purple) for each participant. Participants rated their experiences with each of the four study formulations, thus only USPE scale scores for the participants' *preferred* formulation for HIV prevention are included in the current analysis (the data were reduced to one vector of length 8 for each participant corresponding to their USPE scale scores for their preferred product); the scale scores used in the final model represented

TABLE 1. SELECTED DEMOGRAPHICS AND SEXUAL HISTORY VARIABLES

	<i>n</i> (%)
<i>Completed participants</i> (% completed of 221 enrolled)	204 (92.3)
Age	
Range (years)	125 (61.3)
18–29	79 (38.7)
30–45	
Mean (years)	28.9
Vaginal deliveries	
0	137 (67.2)
1	24 (11.8)
2+	43 (21.1)
Ethnicity	
Latina/Hispanic	30 (14.7)
Race (regardless of Latina/Hispanic ethnicity)	
Black/African American	32 (15.7)
Caucasian/White	110 (53.9)
Asian	4 (2)
American Indian or Alaska Native	4 (2)
Other	15 (7.4)
Multiracial	39 (19.1)
Current use of hormonal contraceptives	71 (34.8)
Ever diagnosed with an STD	39 (19.1)

TABLE 2. AVERAGED SCALE ITEM SCORES BY FORMULATION [MEANS, (SDs), AND MEDIANS] FOR THE FULL SAMPLE (N = 204) AND FOR THOSE WHO CHOSE ORANGE (N = 70), YELLOW (N = 51), PURPLE (N = 52), OR GREEN (N = 31) FORMULATIONS

	Orange		Yellow		Purple		Green	
	Full sample (n = 204)	Chose orange (n = 70)	Full sample (n = 204)	Chose yellow (n = 51)	Full sample (n = 204)	Chose purple (n = 52)	Full sample (n = 204)	Chose green (n = 31)
Sex: initial penetration	3.47 (1.11) 3.67	3.81 (0.98) 4.00	2.88 (1.26) 2.67	2.76 (1.20) 2.67	2.84 (1.23) 2.67	2.68 (1.20) 2.33	2.47 (1.14) 2.33	3.09 (1.27) 3.33
Sex: initial lubrication	3.72 (1.03) 3.80	4.04 (0.90) 4.00	3.23 (1.16) 3.40	3.22 (1.11) 3.40	3.29 (1.08) 3.40	3.02 (1.12) 3.00	2.94 (1.22) 3.00	3.49 (1.32) 4.00
Sex: product awareness	2.86 (0.99) 2.86	2.76 (1.01) 2.64	2.68 (0.99) 2.57	2.59 (0.92) 2.43	2.64 (0.96) 2.71	2.74 (0.85) 2.71	2.63 (0.89) 2.57	2.61 (0.92) 2.57
Sex: perceived wetness	3.00 (1.07) 3.00	3.23 (0.98) 3.00	2.53 (1.07) 2.33	2.33 (1.06) 2.00	2.43 (1.07) 2.33	2.32 (1.08) 2.17	2.18 (1.05) 2.00	2.58 (1.09) 2.33
Sex: stimulating	2.60 (1.06) 2.50	2.80 (1.00) 2.67	2.29 (1.08) 2.17	2.07 (1.02) 1.83	2.17 (1.08) 1.83	2.10 (0.96) 2.00	1.84 (0.90) 1.50	2.34 (1.11) 2.00
Sex: messiness	1.89 (0.88) 1.67	1.88 (0.88) 1.67	1.70 (0.68) 1.50	1.61 (0.86) 1.33	1.64 (0.73) 1.50	1.84 (0.74) 1.67	1.56 (0.66) 1.33	1.77 (0.91) 1.50
Sex: perceived leakage	1.89 (0.82) 1.80	1.96 (0.88) 1.80	1.70 (0.70) 1.50	1.61 (0.85) 1.20	1.64 (0.70) 1.40	1.77 (0.68) 1.60	1.57 (0.68) 1.40	1.68 (0.94) 1.40

Averaged scale score range for each scale is 1–5, where 1 = do not agree at all; 2 = agree a little; 3 = agree somewhat; 4 = agree a lot; 5 = agree completely. Mean (regular font); standard deviation (SDs; in parentheses); medians in *italic*.

different formulations for different participants. For example, if a participant selected the orange gel as her preferred formulation for HIV prevention, then *only* her scale scores for the orange gel were entered into the analysis.

Using LCM, we sought to identify patterns of USPEs related to the preferred formulation experience chosen by each participant. LCM is a data reduction technique that maps vectors of responses (USPEs in this case) to classes, which can be thought of as subsets of the population with similar response profiles. Specifically, analysis yields a vector of probabilities for each participant corresponding to the probability that her responses fall into each of the classes. Class probabilities within participant sum to 100% (in other words, data must belong to one class, but the chance of belonging to each class depends on the participant). In turn, these probabilities identified the most likely class to which the participant belonged; participants within a class have similar response profiles for their preferred study gel. That is, a participants' choice of formulation can be viewed as a *choice of a particular product experience*, as captured by the USPE scale scores and resulting class.

We fit a series of LCMs, with number of classes ranging from two to five, and the final model (i.e., number of classes) was chosen to minimize the Bayesian Information Criteria, as lower values are indicative of better model fit. Models were adjusted for the order in which the formulations were used. A multinomial distribution was used to identify the most likely class for each participant based on the posterior probabilities of class membership identified for each participant. Distribution of classes was summarized across participants and compared across formulations using a chi-squared test. Analysis of variance was used to compare between-class differences in participant level characteristics (e.g., number of vaginal deliveries, prior STD infection). Using a multinomial logistic regression model, we sought to identify the strongest predictors of class, adjusting for preferred formulation choice; specifically, which of the USPE scales contributed the most to the class distribution.

All analyses were carried out in R and SAS Version 9.3 software.

Results

Sample characteristics

Two hundred twenty-one (221) women enrolled in the evaluation study and 204 (92.3%) completed all four formulation evaluation sessions, responded to the Sexual Activity USPE scale items, and selected a preferred product for HIV prevention. Participants were on average 28.9 years old, and 32.9% reported having had at least one vaginal delivery. Approximately half (53.9%) reported being White, while 15.7% reported being Black, and 14.7% reported being Hispanic/Latina. Over one-third (35.3%) reported earning less than \$15,000 US per year. A summary of selected demographic and sexual history variables is presented in Table 1. Mean and median scales scores have been summarized for each formulation, both as a function of the full sample and for the subset of participants who chose that formulation, in Table 2.

Preferred formulation analysis

We asked each participant to select which of the four study formulations she would be most willing to use to

FIG. 1. Example of a pattern of USPE scale scores for a single participant ("Participant X") for her preferred (i.e., "Choice") Formulation. 1 = do not agree at all; 2 = agree a little; 3 = agree somewhat; 4 = agree a lot; 5 = agree completely. *Black line* = Participant X's scores for USPE "Sex" scales. USPE, user sensory perceptions and experience.

prevent HIV; 34% ($n=70$) chose the orange product, 26% ($n=52$) chose purple, 25% ($n=51$) chose yellow, and 15% ($n=31$) chose green. Each participant contributed scale scores for each of the eight USPE scales (her individual USPE pattern) for her preferred product. Data used for analysis consisted of 204 such patterns. Figure 1 depicts a single USPE pattern for "Participant X" who endorsed the purple gel as her preferred product. This represents *one* of the 204 patterns that were analyzed and subsequently grouped into latent classes representing distinct patterns of USPEs. It is important to note that, of the 204 USPE patterns, 70 of those patterns represent the scale scores for the orange product (as rated by participants who chose orange as their preferred product), 52 patterns represent the scale scores for the purple product (as rated by those who chose purple), and so on. Analyzing the data in this way enabled us to deter-

mine, out of the four possible formulation-related sensory experiences, which patterns constituted preferred sensory perceptions and experiences (i.e., preferred formulation experiences).

Analyses supported four classes of USPEs (preferred experience profiles): 14% in Class 1, 28% in Class 2, 25% in Class 3, and 33% in Class 4. Averaged mean scale scores for each class, and average trajectories within class, are presented in Figure 2. Note that the *Sex: Spreading Behavior* scale was dropped from the LCM as it did not contribute to identifying distinct classes or patterns of experience between formulations.

The Class 1 pattern of experience appears to represent the least variation in score ranges (i.e., amplitude) across the scales: all averaged scale item scores fall between two and three (agreeing "a little" and agreeing "somewhat"). This

FIG. 2. Product choice experience: averaged USPE scale item scores for each of the four classes for preferred vaginal gel formulations derived from latent class modeling. 1 = do not agree at all; 2 = agree a little; 3 = agree somewhat; 4 = agree a lot; 5 = agree completely. Class 1: *solid black line*. Class 2: *dotted gray line*. Class 3: *dashed black line*. Class 4: *dashed gray line*.

TABLE 3. BETWEEN CLASS DIFFERENCES IN PREFERRED CHOICE MODEL

	Class 1	Class 2	Class 3	Class 4
Age in years (SD)	28.82 (7.5)	29.67 (8.6)	27.72 (7.9)	29.00 (7.7)
Race (% Caucasian)	57.1	42.6	50.0	65.2
Ethnicity (% Non-Hispanic/Non-Latino)	82.1	83.6	84.8	88.4
Income (% >36k)	25.0	25.0	24.4	34.8
Vaginal deliveries (% None)	64.3	62.3	71.7	69.6
Current use of hormonal contraceptive (%)	28.6	27.9	43.5	37.7
History of STD infection (%)	21.4	20.0	17.8	18.8
Partner type (% main)	75.0	85.2	80.4	71.0
Frequency of sex with selected partner, past 12 months (SD)	49.9 (64.0)	78.2 (94.4)	103 (146.8)	60.2 (86.4)
Number of male vaginal sex partners, past 12 months (SD)	1.6 (1.0)	1.9 (1.8)	2.1 (1.7)	1.8 (2.0)

choice experience is characterized by generally low agreement across scale scores: for example, *Initial Penetration* averaged scale item scores of 2.3, the lowest of the four class experience patterns. The Class 1 pattern is also lowest in agreement for *Initial Lubrication* and *Perceived Wetness*. The Class 1 pattern is in a virtual tie with Class 4 with respect to the *Stimulating* scale. Taken as a whole, then, the Class 1 pattern of USPE is characterized by a relatively minimal sensory experience: “a little” to “somewhat” initial lubrication, “some[what]” product awareness, and “a little” messiness, leakage, and stimulation. This experience, chosen by 14% of the sample, appears to be a rather nondescript experience for the user.

The Class 2 pattern of experience represents the highest averaged scale item scores across all four classes, with the exception of *Initial Penetration*, where Class 3 purports a slightly higher score than Class 2. The averaged scale item scores in Class 2 range from lows of 2.4 on *Messiness* and *Leakage* to highs of 3.9 on *Initial Penetration*, 4.3 on *Initial Lubrication*, and 3.8 on *Perceived Wetness*. The Class 2 experience, as a whole, would appear to be the most noticeable experience from a user perspective: higher lubrication, stimulation, and wetness sensations, with “a little” to “some[what]” messiness and leakage.

The Class 3 pattern of experience represents the greatest variation in amplitude of scores across the scales: averaged scale item scores are as high as 4.4 (between “agree a lot” and “agree completely”) and as low as 1.3 (not agreeing “at all” and agreeing “a little”). Class 3 exhibits lower agreement scores than Class 2 for all scales, except the *Initial Penetration* scale (4.4 vs. 3.9), and appears to offer “a lot” of smoothness and lubricity during the *Initial Penetration* and *Initial Lubrication* experiences, a moderate level of agreement for *Perceived Wetness*, *Product Awareness*, and *Stimulating* scales (thus providing an experience that offers some awareness and sense of arousal), and low *Messiness* and *Leakage*.

The Class 4 pattern of experience is characterized by relatively low agreement throughout, mirroring the pattern of Class 2, although at an appreciably lower amplitude. *Initial Penetration* and *Initial Lubrication* have the highest agreement scores for the class, but still only in the “agree somewhat” range. All other scale scores are among the lowest, with the exception of *Perceived Wetness*, which is slightly higher in agreement than Class 1. Class 4 offers the lower “intensity” of agreement with respect to a *Stimulating* experience, similar to Class 1, but with lower *Messiness*, *Product Awareness*, and *Leakage* scores.

Predicting choice experiences

There were no significant between-class differences in sociodemographics, or in prior STD infection or hormonal contraceptive use (Table 3). Thus, it does not appear that demographic indices, as measured here, contribute to differentiating preferential vaginal gel experiences. Results did suggest that some specific USPE scales predicted class membership. The strongest scale score predictor of class membership was the *Initial Penetration* scale, followed by *Leakage*, *Messiness*, and *Perceived Wetness* (p 's < .01). In other words, these four USPE scales contributed most to the differentiation of experience between the classes. This is evident when looking at the distance between the lines in Figure 2 (the amplitude differences between the classes were highest for *Initial Penetration* and smallest for *Product Awareness*).

Discussion

Using USPE scale scores for each participant's chosen formulation for HIV prevention, analyses identified four classes, or patterns, of formulation-elicited sensations and experiences that were most preferred by participants. Members of each class are characterized by similar scores on each of the eight sexual activity USPE scales. Using these analyses, and interpreting the sensory experiences chosen by participants and captured by the representative scale scores and patterns, we have identified a strategy for determining the ranges of experiences discerned by and preferred by potential microbicide users. The notions of “tolerated” and “preferred” are critical here, for two reasons. On one hand, the data presented here captured a “forced choice,” requiring that they choose one of four formulations evaluated. Thus, the chosen formulation may still not be a person's ideal with regard to the “universe” of all possible formulations. However, it is also interesting to note that, when asked following each individual session how likely they were to use the product evaluated in that session in the future, 74%–80% stated that they would probably or definitely use the orange, yellow, or purple formulations, while 62% stated that they would probably or definitely use the green formulation. On the other hand, there are a multitude of sensations to consider over the course of the use experience. Since a single formulation property may impact more than one sensory perception and/or experience at any point in time, it necessitates that users consider the balance and salience of many sensations (illustrated in the LCM profiles) during product use;

effectively, users choose the *combination* of sensory perceptions and product experiences, likely prioritizing those most important and tolerating those less so. There are several ways in which these data can be useful, both to product design and to identification of potential users, once an efficacious product is achieved. We describe these implications below.

First, it is notable that the *Sex: Spreading Behavior* scale did not contribute to the identification of classes of experience across chosen formulations. The scale items can be characterized as an “averaging” of the participant’s sensations of ease of strokes and spreading in the vaginal canal over time. It is likely that such averaging mitigates a level of sensory discernment beyond the threshold of perception for some women. It is equally as likely that other distinct and salient sensations, represented by the other perceptibility scales, were given greater (or clearer) emphasis by the user.

Second, as seen in Figure 2, the choice-product experience patterns represent a range (in amplitude) of sensations and experiences. It is important to remember that the scale scores represent level of agreement to perceptibility items: it is not the case that a higher (or lower) scale score means that a product was “closer to ideal” than does a lower (or higher) scale score. The preferred score on each of the USPE scales falls within a given range, regardless of product. This indicates that, among this group of women, a product that possesses properties that would be rated within this range on our USPE scales would potentially be acceptable to those users (Fig. 3).

For example, on average, women preferred the product that they rated as between 2.3 and 4.4 on the *Initial Penetration* scale. Conversely, scores in the range of 1.0–2.3 and 4.4–5.0 were outside of the preferred score range for the *Initial Penetration* experience. We would expect that a gel that yielded average ratings in these higher or lower outside ranges would be unlikely to be preferred by women in this population, given the choice between these overall product experiences. Of note, although one might expect that a higher score on *Initial Penetration* (indicating ease of penile entry) would be preferred, the preferred range did not extend up to the maximum score of 5.0. We suspect that there are, potentially, two reasons for this. First, gels that yield extremely low or extremely high average scores on any of the scales

may not be preferred due to other rheologically or other biophysically related experiences. For example, a product that was rated 5.0 on the *Initial Penetration* scale might have a relatively low viscosity, but if it also has a low yield/residual stress, it might also exhibit excessive precoital leakage that would have to be weighed against other experiences to determine product choice. Second, as noted above, a high (or low) scale score does not necessarily represent an “ideal”; indeed, a maximum score of 5.0 or a minimum score of 1.0 on the *Initial Penetration* scale may actually illustrate that a product can be *too* lubricating or *too* drying.

To explore this concept further, it is important to consider the range of interpretations possible when a product is evaluated at a given score for a given scale. Specifically, consider the user’s interpretation(s), or meaning(s), that she derives from the sensory experience elicited by a product’s biophysical properties and rheological performance. As an example, the *Product Awareness* scale captures the user’s physical sensations of the presence of the product during sex, in this case, a gel in the vagina. The scale score represents the degree of agreement with statements of formulation awareness: one cannot assume an “ideal score.” For one woman, a scale score of three or four, which indicates that she can feel the gel in her vagina (“somewhat” or “a lot,” respectively), may represent her ability to protect herself and provide comfort in reminding her that she has taken appropriate precautions. For another woman, that same scale score may be a barrier to the “covert” or discreet product use she feels she needs with a given partner. Thus, it is not the absolute value of the scale score *per se*, but both *how* the experience represented therein is interpreted by the user, as well as how that experience is *weighed* by the user against other evaluable sensory experiences with a given formulation.

We hope to use these ranges in preferred experience to inform product development. We could posit, for instance, that the upper and lower limits in average scale scores for the four classes of preferred experience represent a good starting point for improving formulation design. While constrained by the parameters of the formulations evaluated in this study, it is likely that a candidate microbicide formulation would be acceptable to women in this population if it is rated, for instance, between ~ 2.3 and ~ 4.4 on the *Initial Penetration*

FIG. 3. High and low perceptibility (USPE) scale score averages for preferred vaginal gel formulations, with lines representing the potential target range for USPEs of formulations users are willing to use, as defined by participant choice experiences. 1 = do not agree at all; 2 = agree a little; 3 = agree somewhat; 4 = agree a lot; 5 = agree completely.

scale. If a candidate product elicits scores on the *Initial Penetration* scale that are outside of this range, it may not be considered acceptable or optimal by the majority of potential users. In addition, note that those who were categorized into Classes 1 and 4 had similar scores on the *Initial Penetration* scale (2.3 and 2.7, respectively) and those who were categorized into Classes 2 and 3 had similar scores on the scale, as well (3.9 and 4.4, respectively).

This illustrates the fact that it is unlikely that “one size” will fit all when it comes to HIV prevention products. Indeed, it seems likely that at least two products, one that elicits scores between 2.3 and 2.7 and one that elicits scores between 3.9 and 4.4, would be optimal when considering preferred experiences related to initial penetration. Of course, using a single subscale in isolation will likely *not* lead to the most optimized formulation design; it will be important to consider the constellation of preferred scale scores when making such design decisions.

This final point is illustrated by distribution of participants across classes, each of which defines a preferred formulation experience. The utility of identifying such classes in terms of product design is that if we can identify what factors separate the classes from one another and, hence, identify the preferred experiences for women, then we can utilize this information to aid in the design and marketing of formulations that might fit best with what women want and hence might use consistently. In these analyses, the *Initial Penetration* scale was identified as the scale that best articulated a participant’s class membership. Of course, this is within the context of the entire sensory experience and the user’s weighing of options.

The study has several elements that warrant caution when making interpretations and drawing conclusions. The four formulations evaluated in this study are not candidate microbicides. They allowed us to examine USPEs in soft material formulations with a range of rheological and other biophysical properties. While the formulations chosen do approximate the types of products under investigation, and one of them (orange) is the “universal placebo” that has been used in previous microbicide trials, the formulations used in the current study only provide an initial framework for decision-making related to design of actual vaginal formulations that may advance to clinical trials. Indeed, while vaginal gels have been “de-prioritized” in HIV biomedical prevention product development, as alluded to earlier, other HIV prevention products being developed, including suppositories and films, ultimately melt or dissolve into gel-like material that can be evaluated in a similar manner.²⁶ In addition, there is significant work being done in the multipurpose prevention technology field, where topical semisolid formulations are still among those targeted for combination HIV, STI, and/or pregnancy prevention.^{27,28} To standardize the use experience while establishing proof of concept for this work, women used the gel and simulated coitus in a private room. While this kept the external experience similar for each participant, and therefore, optimal for scale development, its potential applicability is an empirical question to be resolved in subsequent studies. The study was conducted with US women at two sites in the Northeast; further validation among both domestic and international potential microbicide users is warranted.

Using a novel application of LCM, we sought to identify preferred USPEs elicited by the rheological and other biophysical properties of vaginal semisolid gel formulations.

This work is an early step toward assisting product developers in designing products that will have the best chance of being used by the largest number of women who are in need of HIV prevention. Future work should determine whether these scales can be used for other semisolid formulations (e.g., films, suppositories), if they can be translated both linguistically and culturally to understand formulation preferences within specific populations and cultures, and if they can be adapted to facilitate the design of rectal, as well as other vaginal, prevention products. Given that the scale items are intended to assess observable experiences, and are intentionally devoid of judgments and evaluations, we expect that our USPE scales could be used in various settings to identify preferred formulation characteristics. While we created and evaluated a set of prototype gels representing a range of properties, it also will be critical to extend this work to actual candidate products to determine if (1) preferred perceptibility ranges can be determined for different cultural contexts and subpopulations, (2) candidate products have USPE profiles that fit within the preferred range for a given population, and (3) preferred formulation experiences are related to willingness to use or actual product use in both clinical trial and real-world contexts.

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