NIH Public Access
Author Manuscript
Antiviral Res. Author manuscript; available in PMC 2014 March 01.

Published in final edited form as:
Antiviral Res. 2013 March ; 97(3): 280–284. doi:10.1016/j.antiviral.2012.12.024.

Shape of vaginal suppositories affects willingness-to-try and preference

Bangde Li[1,2], **Toral Zaveri**[1,2], **Gregory R. Ziegler**[2], and **John E. Hayes**[1,2,*]

[1]Sensory Evaluation Center, College of Agricultural Sciences, The Pennsylvania State University, University Park, Pennsylvania, USA

[2]Department of Food Science, College of Agricultural Sciences, The Pennsylvania State University, University Park, Pennsylvania, USA

Abstract

HIV and other sexually transmitted infections (STIs) are a global threat to public health that may be countered, in part, by microbicides. A successful microbicide must be both biologically efficacious and highly acceptable to users. Sensory attributes have a direct influence on product acceptability. We created a series of vaginal suppositories appropriate for use as microbicides to investigate the influence of shape on women's *willingness-to-try*. The influence of perceived size and firmness on acceptability was also assessed.

Sexually-active women (n=99) were invited to participate in an evaluation of vaginal suppositories in 5 different shapes including: Bullet, Long Oval, Round Oval, Teardrop and Tampon. The volume (3 ml) and formulation for these 5 prototypes were identical. After manipulating prototypes *ex vivo* (in their hands), participants rated their *willingness-to-try* on a 100-point visual analog scale. The appropriateness of size and firmness were evaluated using 5-point just-about-right (JAR) scales. Each participant evaluated all 5 prototypes individually. Samples were presented in a counterbalanced monadic sequence using a Williams design.

Mean *willingness-to-try* varied by shape, with Bullet and Long Oval receiving significantly higher scores. This was consistent with JAR data for size, as 70 and 65% of women indicated these shapes were `just-about–right', respectively. In contrast, a minority of women endorsed the other 3 shapes as having a size that was `just-about-right'. The proportion of women who felt the firmness was `just-about-right' was uniformly high, irrespective of shape, suggesting prior attempts to optimize the formula were successful. Perceptions of size and firmness were influenced by the physical length and width of the prototypes, in spite of having constant volume. Women showed high *willingness-to-try* when asked to assume they were at risk. These results are relevant for behavioral and formulation scientists working on microbicides, to better understand the influence of sensory attributes on acceptability, as acceptability and compliance ultimately impact effectiveness.

© 2012 Elsevier B.V. All rights reserved

[*]**Corresponding Author:** Dr. John E. Hayes Department of Food Science Pennsylvania State University 220 Food Science Building University Park, PA, 16802, USA jeh40@psu.edu.

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

NIH-PA Author Manuscript
NIH-PA Author Manuscript
NIH-PA Author Manuscript

NIH-PA Author Manuscript

NIH-PA Author Manuscript

NIH-PA Author Manuscript

Keywords

Microbicide; acceptability; consumer behavior; product optimization; sensory perception; just-about-right (JAR) scale

HIV and other sexually transmitted infections (STIs) are a global threat to health; in spite of current prevention efforts, there were 2.7 million new infections world-wide in 2010 (UNAIDS, 2011). Topical microbicides are a promising solution, as they empower women to protect themselves (Morrow et al., 2007; Stone, 2002). More than 50 microbicide candidates are under development (AMD, 2009). A successful microbicide must be biologically efficacious and highly acceptable to users (Elias and Coggins, 2001; Mantell et al., 2005; Severy et al., 2005). Acceptability impacts user adherence to microbicide use and thus real world effectiveness (Abdool Karim et al., 2010; Masse et al., 2009; Nel et al., 2011). User acceptability must be considered along with pharmacokinetics and toxicity if efficacious prototypes from controlled trials are to be effective in the field (Morrow and Hendrix, 2010).

Microbicide acceptability involves myriad factors, including user characteristics, context, and product attributes (Morrow and Hendrix, 2010). At the pre-clinical level, microbicide characteristics are critical for product acceptability (Morrow and Ruiz, 2008); colorless and odorless microbicide gels may be more appealing (Morrow et al., 2003). Lubrication may be a positive feature of microbicides (Whitehead et al., 2006), although sexual pleasure may be reduced due to the messiness from a microbicide gel (Giguere et al., 2012). Perceptual attributes (e.g. ropiness, graininess, slipperiness) that are best quantified with human assessors (Mahan et al., 2011) may also be important. Indeed, sensory attributes may critically influence user acceptability, but their effects have not been well investigated.

In the packaged goods industries, the influence of sensory attributes on acceptability is frequently assessed with just-about-right (JAR) scales (Popper and Kroll, 2005; Rothman and Parker, 2009). A JAR scale is a bipolar instrument with semantic anchors at each end, reflecting appropriateness of a low and high intensity, respectively. The midpoint is labeled `just-about-right', indicating this attribute is at an appropriate level in the product. According to American Society of Testing and Materials guidelines, most researchers use 5 categories (e.g. `much too small', `somewhat too small', `just about right', `somewhat too big', `much too big') (Rothman and Parker, 2009). Hedonic and intensity scales are typically used separately, but JAR scales intentionally combine these two measurements to assess attribute appropriateness (Stone and Sidel, 2004); attribute quality is evaluated relative to a theoretical ideal. JAR scales are popular for product reformulation or optimization (Xiong and Meullenet, 2006) because they are easy to use and generate actionable data. Practically, attempts are made to improve an attribute when more than 20% of the responses are `too-little or `too-much' (Meullenet et al., 2007).

In previous qualitative research, most women (45 of 57) preferred semisoft ovoids over spheres or teardrops, but preferences for size and firmness were less clear (Zaveri et al., 2012). Consequently, we conducted a larger quantitative study on oval prototypes using a factorial design and response surface modeling, identifying an optimum near 3 grams and firmness (G') of 25 kPa (Li et al., 2013). As part of an iterative optimization process, the current study investigated a second generation of suppository shapes at constant physical firmness and volume.

We investigated the effect of shape on *willingness-to-try*, and perceived appropriateness of size (*size*) and firmness (*firmness*). Shapes included Round Oval, Long Oval, Teardrop,

NIH-PA Author Manuscript

NIH-PA Author Manuscript

NIH-PA Author Manuscript

Bullet and Tampon (Figure 1). These names are provided for readability and discussion; they were never used with participants, who referred to samples using random 3-digit codes.

Women (n=99) were recruited as described elsewhere (Li et al., 2013) to evaluate prototypes *ex vivo* (in their hands) at the Sensory Evaluation Center at Penn State. All procedures were approved by the local Institutional Review Board (protocol #36943). Participants reported race and ethnicity using categories in OMB Directive 15. Most were married, college-educated white women; complete demographics are provided in Supplemental Table 1, and vaginal product usage is summarized in Table 1. Of the 99 participants, 37 had participated in our previous microbicide studies.

Participants watched a short video about the product concept in our waiting room, which described how to evaluate a prototype: 1. Take the sample and put it into her non-dominant hand; 2. Gently stroke the sample with the index finger of her dominant hand; 3. Put the sample between her fingers and pinch gently (hand not specified; shown as dominant hand in video); 4. Finally hold the sample between her fingers and imagine she was trying to insert the sample into her vagina (hand not specified or shown). After watching the video, women deciding to participate provided written informed consent before entering individual test booths. Participants were reimbursed for their time.

Women rated *willingness-to-try* using a 100-point visual analog scale. Women were told these products would be used without an applicator. Sample presentation was counterbalanced in a Williams design. To avoid low *willingness-to-try* ratings due to low perceived STI risk, women were asked to assume they might need these products "to prevent potential infections, including Chlamydia, herpes and HIV". Appropriateness of size and firmness were assessed using 5-point categorical just-about-right (JAR) scales. (Here forward, we use *size* and *firmness*, in italics, to refer to appropriateness scores for these attributes). JAR is a global approach; specific contexts (e.g. insertion versus coitus) were not provided. Women ranked the shapes from most to least preferred after all samples had been evaluated. Demographics were collected at the end of the test.

Data were collected using CompusenseFive v5.2 (Guelph, Ontario) and analyzed in JMP v9.0.2 (Cary, NC). Whether shape influenced *willingness-to-try* was tested via ANOVA, with participant as a random effect and shape as a fixed effect. Tukey's Honest Significant Difference was used for post-hoc comparisons. Response distributions within a JAR scale category were compared using the Cochran-Mantel-Haenszel (CMH) test (Rothman and Parker, 2009). Exponential regressions characterized relationships between physical characteristics and percentage of "too-big" and "too-firm" responses using DataGraph v3.0 (Chapel Hill, NC). Ranking was analyzed via Friedman's test; rank-sums were calculated and compared using least-significant-differences (Lawless and Heymann, 2010).

Willingness-to-try values differed by shape ($F_{4, 392}$=6.99, p<0.001); shape explained 67.5% of the variance. Long Oval and Bullet had significantly higher *willingness-to-try* than the other shapes, but were not significantly different from each other (Figure 2). There were no significant differences between Round Oval, Teardrop and Tampon. These data confirm prior qualitative work (Zaveri et al., 2012) quantitatively, and document the differential acceptability of second-generation shapes (Bullet versus Tampon).

All five shapes had mean *willingness-to-try* scores above 50 (the scale midpoint). This indicates our iterative optimization produced generally acceptable prototypes, and suggests participants would be willing to try these microbicides if they were functional and needed. Women have expressed a strong desire to try microbicide gels for preventing STIs whether they were at risk or not (Carballo-Dieguez et al., 2012; Ramjee et al., 2007; Ventuneac et al., 2010). Participants were explicitly informed these prototypes were intended to prevent

NIH-PA Author Manuscript

NIH-PA Author Manuscript

NIH-PA Author Manuscript

transmission of diseases like Chlamydia, herpes and HIV, and that they should evaluate the product assuming they might need such a product to avoid potential `othering', as qualitative interviews (Zaveri, unpublished data) had indicated some women felt they would not need or use these types of products due to low perceived risk.

Regarding *size*, there was large variability in the endorsements of `just-about-right', and the distribution of responses were significantly different (χ^2_8=100.26, $p < 0.001$) across shape (Figure 3, top), in spite of having an identical volume and mass (3 grams). For the Long Oval and Bullet, most participants endorsed just-about-right, consistent with greater *willingness-to-try* scores. Conversely, the Round Oval distribution was skewed toward too small, and the Tampon distribution was skewed toward too big. The Teardrop distribution was not skewed, but was broader than for Long Oval or Bullet, as fewer women thought it was just-about-right. Since all prototypes were the same volume and mass, the effect of shape on *size* was a difference in perception, rather than actual physical size.

To explore this further, we plotted the proportion of participant responses for `too big' against the measured length of the prototype (Figure 4, top). The longer the prototype, the greater the number of women who thought it was `too big' (R^2= 95.1%), suggesting a relationship between perceived size and physical length. (However, panelists did not assess size; instead, they judged the appropriateness of the size, a subtle but important distinction.) Our finding is consistent with work showing that product and container shapes effect volume perception (e.g. taller glasses are perceived as being larger than shorter ones (Raghubir and Krishna, 1999; Wansink and Van Ittersum, 2003)).

Prototype *firmness* appeared appropriate, evidenced by greater than 65% of just-about-right responses. The proportion of just-about-right endorsements should be uniformly high, if our previous optimization (Li et al., 2013) was successful. However, the proportions at the extremes (`too soft' v. `too firm') did vary as a function of shape (χ^2_8=41.59, $p<0.001$). Bullet received the highest proportion of just-about-right endorsements, and most women also reported the Long Oval and Tampon were just-about-right for firmness, though they had slightly broader distributions. Teardrop and Round Oval distributions were skewed toward `too firm'; 29% of women found them too firm, although a majority still felt their *firmness* was just-about-right.

As with *size*, we believe the differing *firmness*, despite a constant formulation, is evidence of a perceptual bias related to the shape. To explore this further, we plotted the proportion of participant responses for `too firm' against the physical width of the prototype (Figure 5, bottom), and as width increased, the proportion of women who thought it was too firm increased (R^2=96.0%). The width of Teardrop was taken at the widest point, as we had informally observed most women grasp it at the larger end (Zaveri, unpublished data). Thus, it seems a thicker cross section appears to make the product seem firmer.

Rankings across the five prototypes were significantly different (χ^2_4=50.02, $p<0.0001$). Bullet and Long Oval had higher Friedman rank-sums than the other three shapes, but their rank-sumswere not significantly different from each other (Supplemental Figure 1). Nor were the remaining shapes different from each other, consistent with the *willingness-to-try* data. Additional insight is gained from the ranking place distributions (Supplemental Table 2). While Tampon rank-sum was not significantly lower than the rank-sums for Round Oval or Teardrop, the Tampon shape was clearly inferior, as it was the last choice for 42% of the respondents. For comparison, Round Oval was the last choice for 29% of the respondents, Tear Drop 22%, and Long Oval and Bullet were 3% each.

In summary, we show that simple changes in the shape of a vaginal suppository influences a woman's *willingness-to-try*. We extend our previous results to a second generation of

NIH-PA Author Manuscript

NIH-PA Author Manuscript

NIH-PA Author Manuscript

prototypes, identifying other shapes that are more preferred by women. One limitation is the use of ex vivo evaluation to measure acceptability; it is quite possible antiviral delivery systems with a high acceptability in the hand may still be unacceptable when used vaginally. However, it is also true that poor ex vivo acceptability may cause failure if women are unwilling to try the microbicide. Thus, ex vivo testing can serve as a rapid, inexpensive screen prior to expensive toxicology studies in animals and clinical trials in humans. Present data indicate Bullet and Long Oval shapes are good candidates for further development. Surprisingly, a familiar shape like Tampon was clearly inferior; our data suggest it might be due to perceived size, although we cannot rule out prior association with menstruation.

We also show that shape strongly influences women's thoughts about the appropriateness of size and firmness, even when volume and formulation are held constant. This is a critical insight that can be leveraged by behavioral and formulation scientists working on microbicides. For example, if a specific volume is required for effective coating and drug delivery, this can be balanced against user perceptions of efficacy (too small) or willingness-to-use (too big) by manipulating the product shape.

Finally, these data support the view that standard sensory science methods for optimizing products can be useful in assessing microbicide acceptability. Our goal here is to adapt existing tools to speed up antiviral microbicide development through the early elimination of delivery systems that are non-starters. While sensory attributes presumably influence acceptability, acceptability and adherence are not synonymous, as acceptability can be defined as factors that potentially influence adherence, within a broader social and cultural context (Mensch et al., 2012). Thus, approaches used here are meant to complement intravaginal testing, and not replace it.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

The authors thank Rebecca Hovingh for help with sample preparation, Rachel Primrose for assistance with data collection, Timothy W. Simpson and the Learning Factory staff at Penn State for making the product moulds, and our study participants for their time and participation. This project was funded by the National Institute Of Allergy And Infectious Diseases grant R21AI094514. This manuscript was completed in partial fulfillment of the requirements for a Doctorate of Philosophy at the Pennsylvania State University by the first author.

References

Abdool Karim Q, Abdool Karim SS, Frohlich JA, Grobler AC, Baxter C, Mansoor LE, Kharsany AB, Sibeko S, Mlisana KP, Omar Z, Gengiah TN, Maarschalk S, Arulappan N, Mlotshwa M, Morris L, Taylor D. Effectiveness and safety of tenofovir gel, an antiretroviral microbicide, for the prevention of HIV infection in women. Science. 2010; 329:1168–1174. [PubMed: 20643915]

AMD. Microbicide Pipeline Summary Report. 2009.

Carballo-Dieguez A, Giguere R, Dolezal C, Chen BA, Kahn J, Zimet G, Mabragana M, Leu CS, McGowan I. “Tell Juliana”: Acceptability of the Candidate Microbicide VivaGel(A (R)) and Two Placebo Gels Among Ethnically Diverse, Sexually Active Young Women Participating in a Phase 1 Microbicide Study. AIDS and behavior. 2012; 16:1761–1774. [PubMed: 21863338]

Elias C, Coggins C. Acceptability research on female-controlled barrier methods to prevent heterosexual transmission of HIV: Where have we been? Where are we going? J Women Health Gen-B. 2001; 10:163–173.

Giguere R, Carballo-Dieguez A, Ventuneac A, Mabragana M, Dolezal C, Chen BA, Kahn JA, Zimet GD, McGowan I. Variations in microbicide gel acceptability among young women in the USA and Puerto Rico. Culture Health & Sexuality. 2012; 14:151–166.

NIH-PA Author Manuscript

NIH-PA Author Manuscript

NIH-PA Author Manuscript

Lawless, HT.; Heymann, H. Sensory evaluation of food principles and practices. 2nd ed.. Springer; New York: 2010. Food science text series

Li B, Zaveri T, Ziegler GR, Hayes JE. User Preferences in a Carrageenan-Based Vaginal Drug Delivery System. PLoS ONE. 2013; 8(1):e54975. doi:10.1371/journal.pone.0054975. [PubMed: 23358688]

Mahan ED, Morrow KM, Hayes JE. Quantitative perceptual differences among over-the-counter vaginal products using a standardized methodology: implications for microbicide development. Contraception. 2011; 84:184–193. [PubMed: 21757061]

Mantell JE, Myer L, Carballo-Dieguez A, Stein Z, Ramjee G, Morar NS, Harrison PF. Microbicide acceptability research: current approaches and future directions. Social Science & Medicine. 2005; 60:319–330. [PubMed: 15522488]

Masse BR, Boily MC, Dimitrov D, Desai K. Efficacy dilution in randomized placebo-controlled vaginal microbicide trials. Emerging themes in epidemiology. 2009; 6:5. [PubMed: 19818138]

Mensch BS, van der Straten A, Katzen LL. Acceptability in microbicide and PrEP trials: current status and a reconceptualization. Curr Opin HIV AIDS. 2012; 7:534–541. [PubMed: 23032737]

Meullenet, J-F.; Xiong, R.; Findlay, C. Analysis of Just About Right Data, Multivariate and Probabilistic Analyses of Sensory Science Problems. Wiley-Blackwell; 2007. p. 207-235.

Morrow K, Rosen R, Richter L, Emans A, Forbes A, Day J, Morar N, Maslankowski L, Profy AT, Kelly C, Karim SSA, Mayer KH. The acceptability of an investigational vaginal microbicide, PRO 2000 gel, among women in a phase I clinical trial. J Womens Health. 2003; 12:655–666.

Morrow KM, Fava JL, Rosen RK, Christensen AL, Vargas S, Barroso C. Willingness to use microbicides varies by race/ethnicity, experience with prevention products, and partner type. Health Psychology. 2007; 26:777–786. [PubMed: 18020851]

Morrow KM, Hendrix C. Clinical evaluation of microbicide formulations. Antiviral research. 2010; 88:S40–S46. [PubMed: 21109067]

Morrow KM, Ruiz MS. Assessing microbicide acceptability: A comprehensive and integrated approach. AIDS and behavior. 2008; 12:272–283. [PubMed: 17592763]

Nel AM, Mitchnick LB, Risha P, Muungo LTM, Norick PM. Acceptability of Vaginal Film, Soft-Gel Capsule, and Tablet as Potential Microbicide Delivery Methods Among African Women. J Womens Health. 2011; 20:1207–1214.

Popper R, Kroll RD. Just-About-Right Scales in Consumer Research. ChemoSense. 2005; 7:3–6.

Raghubir P, Krishna A. Vital dimensions in volume perception: Can the eye fool the stomach? J Marketing Res. 1999; 36:313–326.

Ramjee G, Morar NS, Braunstein S, Friedland B, Jones H, van de Wijgert J. Acceptability of Carraguard, a candidate microbicide and methyl cellulose placebo vaginal gels among HIV-positive women and men in Durban, South Africa. AIDS research and therapy. 2007; 4:20. [PubMed: 17900337]

Rothman L, Parker MJ. Just about Right (Jar) Scales: Design, Usage, Benefits, and Risks. American Society for Testing & Materials. 2009

Severy LJ, Tolley E, Woodsong C, Guest G. A framework for examining the sustained acceptability of microbicides. AIDS and behavior. 2005; 9:121–131. [PubMed: 15812619]

Stone A. Microbicides: a new approach to preventing HIV and other sexually transmitted infections. Nat Rev Drug Discov. 2002; 1:977–985. [PubMed: 12461519]

Stone, H.; Sidel, JL. Sensory Evaluation Practices. Elsevier Academic Press; 2004.

UNAIDS. Epidemic update and health sector progress towards Universal Access. Progress Report 2011. 2011

Ventuneac A, Carballo-Dieguez A, McGowan I, Dennis R, Adler A, Khanukhova E, Price C, Saunders T, Siboliban C, Anton P. Acceptability of UC781 Gel as a Rectal Microbicide Among HIV-Uninfected Women and Men. AIDS and behavior. 2010; 14:618–628. [PubMed: 19757017]

Wansink B, Van Ittersum K. Bottoms up! The influence of elongation on pouring and consumption volume. J Consum Res. 2003; 30:455–463.

NIH-PA Author Manuscript

NIH-PA Author Manuscript

NIH-PA Author Manuscript

Whitehead SJ, Kilmarx PH, Blanchard K, Manopaiboon C, Chaikummao S, Friedland B, Achalapong J, Wankrairoj M, Mock P, Thanprasertsuk S, Tappero JW. Acceptability of Carraguard vaginal gel use among Thai couples. Aids. 2006; 20:2141–2148. [PubMed: 17086053]

Xiong R, Meullenet JF. A PLS dummy variable approach to assess the impact of jar attributes on liking. Food Qual Prefer. 2006; 17:188–198.

Zaveri, T.; Powell, KA.; Li, B.; Hayes, JE.; Ziegler, GR. Improving acceptability of vaginal drug delivery systems by using sensory methods. The Society of Sensory Professionals 3rd Technical and Professional Conference; Jersey City, New Jersey. 2012.

- 99 sexually active women evaluated 5 microbicide prototypes in the laboratory
- Willingness to use and ranked preference both differed as a function of shape
- Even when volume was constant, perceived size varied as a function of length
- Despite constant formulation perceived firmness varied as a function of width
- Two promising candidates were identified for further optimization

NIH-PA Author Manuscript
NIH-PA Author Manuscript
NIH-PA Author Manuscript

NIH-PA Author Manuscript

NIH-PA Author Manuscript

NIH-PA Author Manuscript

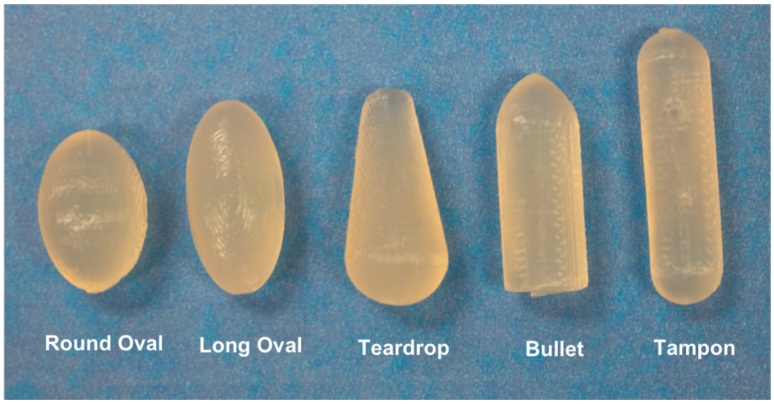

Figure 1.

Second generation microbicide prototypes. Volume is constant at 3mL across all five shapes. Samples were prepared with kappa carrageenan, potassium chloride and water 1 day before evaluation, and stored in 1-oz transparent plastic cups at 16°C with the lids tightly sealed until evaluation.

NIH-PA Author Manuscript

NIH-PA Author Manuscript

NIH-PA Author Manuscript

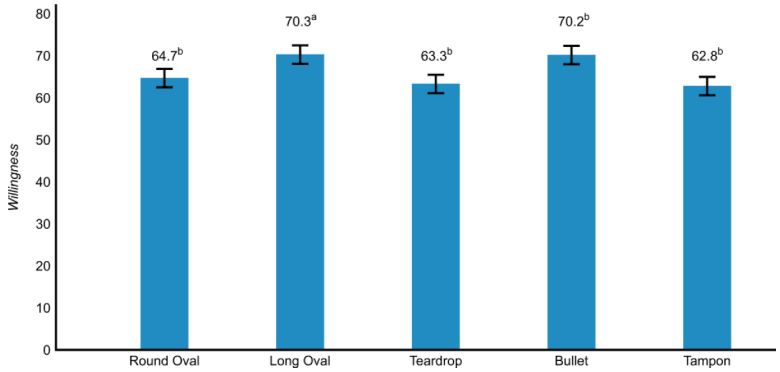

Figure 2.

Effect of Shape on *willingness-to-try*, which was measured on a 100 point visual analog scale. Indented semantic anchors at 10 (`not at all willing') and 90 (`extremely willing') were provided to minimize end avoidance bias. Means with different letters indicate a significant difference at α =0.05 (Tukey's HSD).

NIH-PA Author Manuscript

NIH-PA Author Manuscript

NIH-PA Author Manuscript

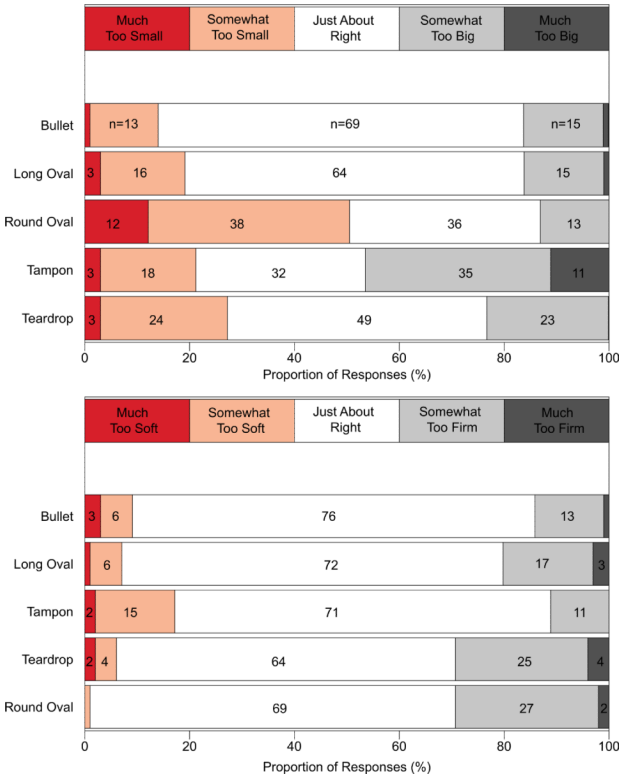

Figure 3.

Distributions of responses for *size* (top) and *firmness* (bottom). X-axis is the proportion of responses for each category on the just-about-right scale for size. Numbers inside the bars are the raw number of participants endorsing that category.

NIH-PA Author Manuscript

NIH-PA Author Manuscript

NIH-PA Author Manuscript

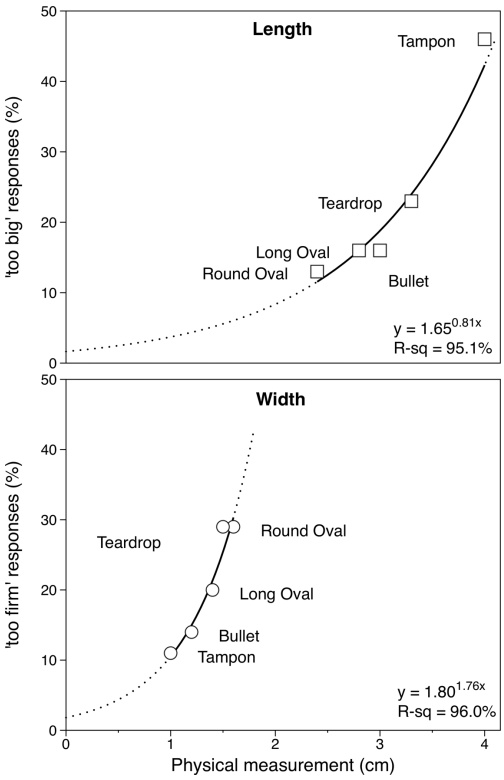

Figure 4.
Relationship between physical measurement and `too big' or `too firm' responses.

NIH-PA Author Manuscript

NIH-PA Author Manuscript

NIH-PA Author Manuscript

Table 1

Product usage

Products	Usage (%)
Menstruation products, such as tampons	64%
Lubrication products such as KY® gels, liquibeads and vitamin-E suppositories	37%
Yeast infection medicines, such as Vagisil® and Monistat®	28%
Douche	8%
Vaginal contraceptive products, such as Nuvaring®	4%
Spermicidal gels and films	2%
Decline to answer	9%