#329

Choosing Prevention: The Case for Involving Users in Early Microbicide Development

Kate Morrow, PhD,

Shira Dunsiger, PhD, Joseph L Fava, PhD, Rochelle K Rosen, PhD,

Sara E Vargas, PhD, Julia G Shaw, MPH, & the Project LINK Study Team

ACKNOWLEDGEMENTS

NIH Microbicide Innovation Program
Project LINK **PI: Morrow**
NIH/NIMH R21/R33 MH80591 & CONRAD/USAID PPA-09-0223
Rochelle K Rosen, Joseph Fava, E Milu Kojic, Shira Dunsiger *The Miriam Hospital/Alpert Medical School of Brown University*
David Katz and the Biomedical Engineering Team *Duke University*
Patrick Kiser and the Bioengineering Team *University of Utah*
The Project LINK Study Team: SE Vargas, C Barroso, M Higgins, J Wallace, J van den Berg, L Thompson, D Bregman, C Colleran, A Panameno, JG Shaw; *FCHC team:* L Salomon, K Mayer, D Perry, L Panther, C Covahey, D Dang, M Gelman, V Frontiero
Donations of Study Products and Materials from: *CONRAD, HTI Plastics, Good for Her, Rip n Roll*

The Miriam Hospital
A Lifespan Partner

BROWN
Alpert Medical School

Duke
UNIVERSITY

THE UNIVERSITY OF UTAH

NATIONAL INSTITUTES OF HEALTH

CONRAD
Leaders in Reproductive Health and HIV Prevention

GOALS

- Make the case for a user-centered approach to product development in HIV prevention
- Introduce a new element of understanding factors related to acceptability and adherence:
  - "**Perceptibility**"
- Provide initial data in support of integrating **perceptibility** into biomedical prevention technology development

THE THINKING…

- Microbicides – or any biomedical prevention products – need to be used to be effective
- **Effectiveness** is dependent on both biologic efficacy and user behavior
- Biologic **efficacy** is dependent on drug(s)… and - drug delivery to, and retention in, target tissues
- **Drug delivery** – with respect to vaginal and/or rectal products - is dependent on rheological and other biophysical properties of drug delivery systems
  - Formulations: e.g., gels, films, etc

What's a "rheological or other biophysical property"?...
Viscosity, yield stress at various shear rates, viscoelasticity…
the "feel" and "flow" of semi-solid formulations.

What *if* it turns out that formulation properties (like the ones that govern drug delivery) also govern user behavior…?

- A *non*-optimized user experience will ultimately negate an optimized drug and its delivery (or lack thereof)
- Need to balance optimization of drug delivery with optimization of the user experience

THE EXPLORATION… PERCEPTIBILITY

- **Perceptibility**: The objective measurement of user sensory perceptions and experiences (USPE) of formulation and/or device characteristics and their performance during use
- Distinct from conventional “acceptability” and “tolerability”
  - But… perhaps a precursor to <u>both</u>

MEASURING *WHAT…?*

- Sensations of form, pressure, distortion, slip, texture, etc…:
  - "Feel": lubricity, smooth, tacky, dry, slick, oily, sticky, wet, moist, thick/thin, liquidy, drippy, stringy… etc.
  - Pressure and Movement: physical awareness, fullness, "foreign object," messiness, leakage
  - Changes in USPE over time: during application/insertion, during ambulation, at initial penetration, early intercourse, end of intercourse, "average" over time
    - Changes in viscosity, pressure, temperature, and feel

Arch Sex Behav
DOI 10.1007/s10508-013-0235-5

ORIGINAL PAPER

User-Identified Gel Characteristics: A Qualitative Exploration of Perceived Product Efficacy of Topical Vaginal Microbicides

Kathleen M. Morrow · Kristen Underhill · Jacob J. van de
Sara Vargas · Rochelle K. Rosen · David F. Katz

Project LINK

AIDS Behav
DOI 10.1007/s10461-013-0652-4

ORIGINAL PAPER

Project MIST

"Set it and Forget it": Women's Perceptions and Opinions of Long-Acting Topical Vaginal Gels

Jacob J. van den Berg · Rochelle K. Rosen · Dana E. Bregman · Lara A. Thompson · Kathleen M. Jensen · Patrick F. Kiser · David F. Katz · Karen Buckheit · Robert W. Buckheit Jr. · Kathleen M. Morrow

AIDS RESEARCH AND HUMAN RETROVIRUSES
Volume 30, Number 1, 2014

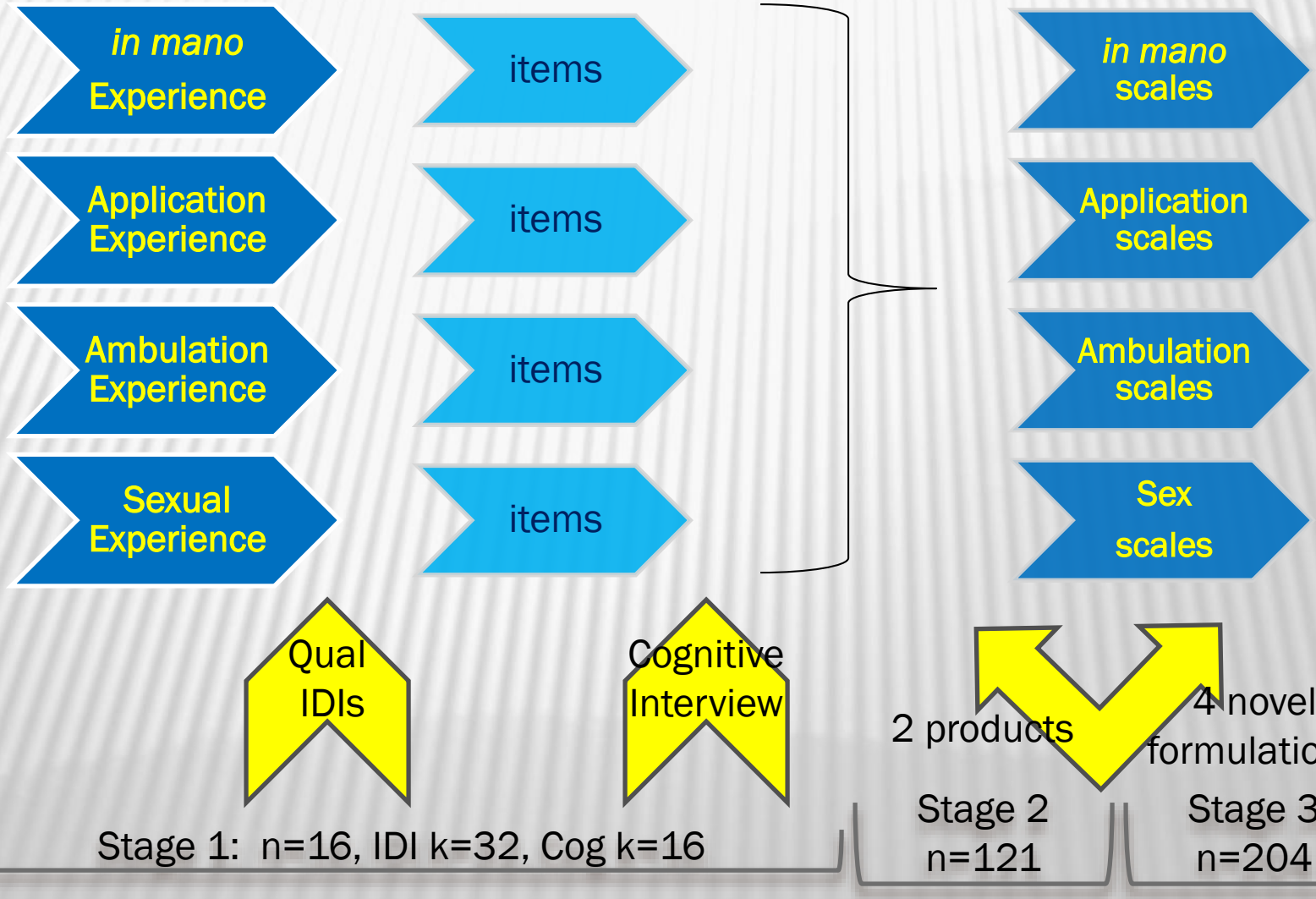
DOI: 10.1089/aid.2013.0099

PRECLINICAL STUDIES/DRUG DEVELOPMENT

Designing Preclinical Perceptibility Measures to Evaluate Topical Vaginal Gel Formulations: Relating User Sensory Perceptions and Experiences to Formulation Properties

Kathleen M. Morrow,[1,2] Joseph L. Fava,[1] Rochelle K. Rosen,[1,3] Sara Vargas,[1,2] Julia G. Shaw,[1] E. Milu Kojic,[4,5] Patrick F. Kiser,[6] David R. Friend,[7] David F. Katz,[8] and The Project LINK Study Team

PROJECT LINK: THE MAKING OF USPE SCALES



LINK FORMULATIONS

Gel Primary Composition	3% HEC		1.25% Carbopol		3% HEC; 2.5% Carbopol		2% HEC; 1.73% Carbopol	
	Undiluted	Diluted	Undiluted	Diluted	Undiluted	Diluted	Undiluted	Diluted
Viscosity at 1s (pa-s)	96	40	250	184	1474	1079	492	287
Residual Stress (Pa)	13	0	129	87	182	172	120	72
Volume (mL)	3.5	3.5	3.5	3.5	2	2	3.5	3.5
Area Coated at 2.5 min (cm^2)	53	67	35	35	20	20	35	36
Area Coated at 6 min (cm^2)	57	76	35	36	20	20	35	37
*Diluted with 20% Vaginal Fluid Simulant								

FIG. 3. Perceptibility Scales for Sexual Activity.

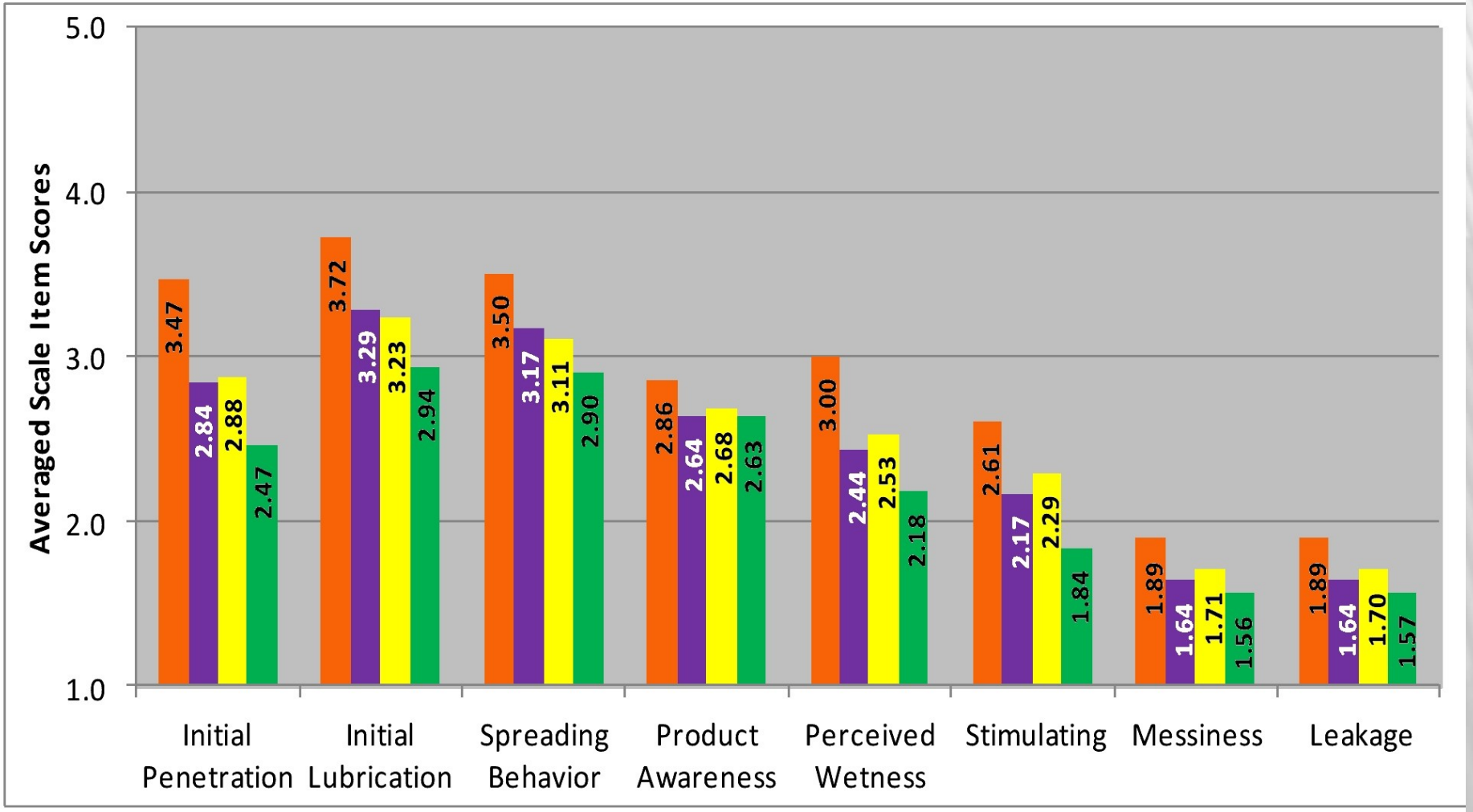
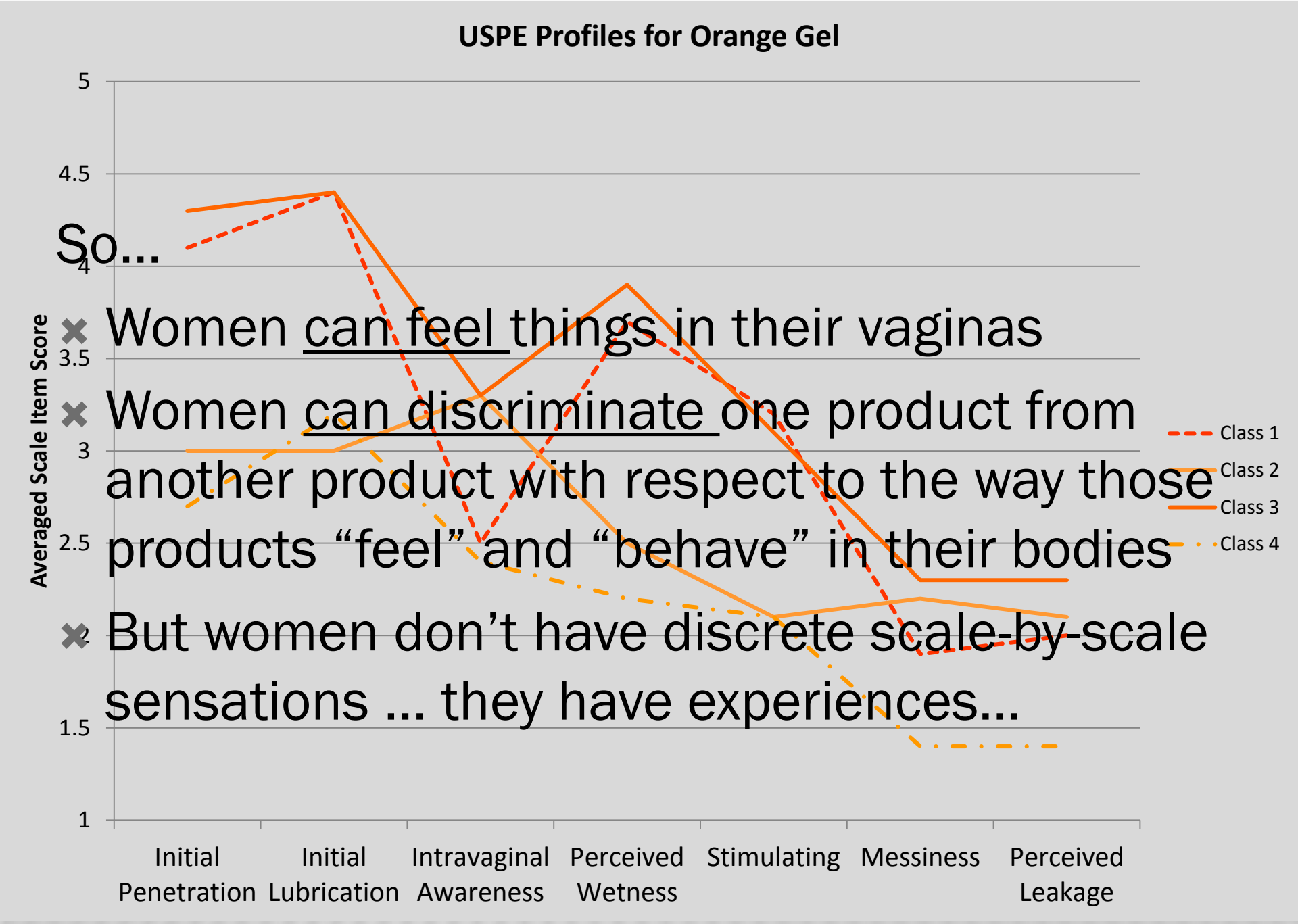


Figure 3. Averaged scale item scores for each Perceptibility Scale for Sexual Activity. 1=do not agree at all; 2=agree a little; 3=agree somewhat; 4= agree a lot; and 5= agree completely. Primary constituents for each gel were: 3% hydroxyethylcellulose (HEC) (orange); 1.25% carbopol (yellow); 2% HEC and 1.73% carbopol (purple); and 3% HEC and 2.5% carbopol (green). Pair-wise comparisons are presented in Table 6.



So…

- Women can feel things in their vaginas
- Women can discriminate one product from another product with respect to the way those products "feel" and "behave" in their bodies
- But women don't have discrete scale-by-scale sensations … they have experiences…

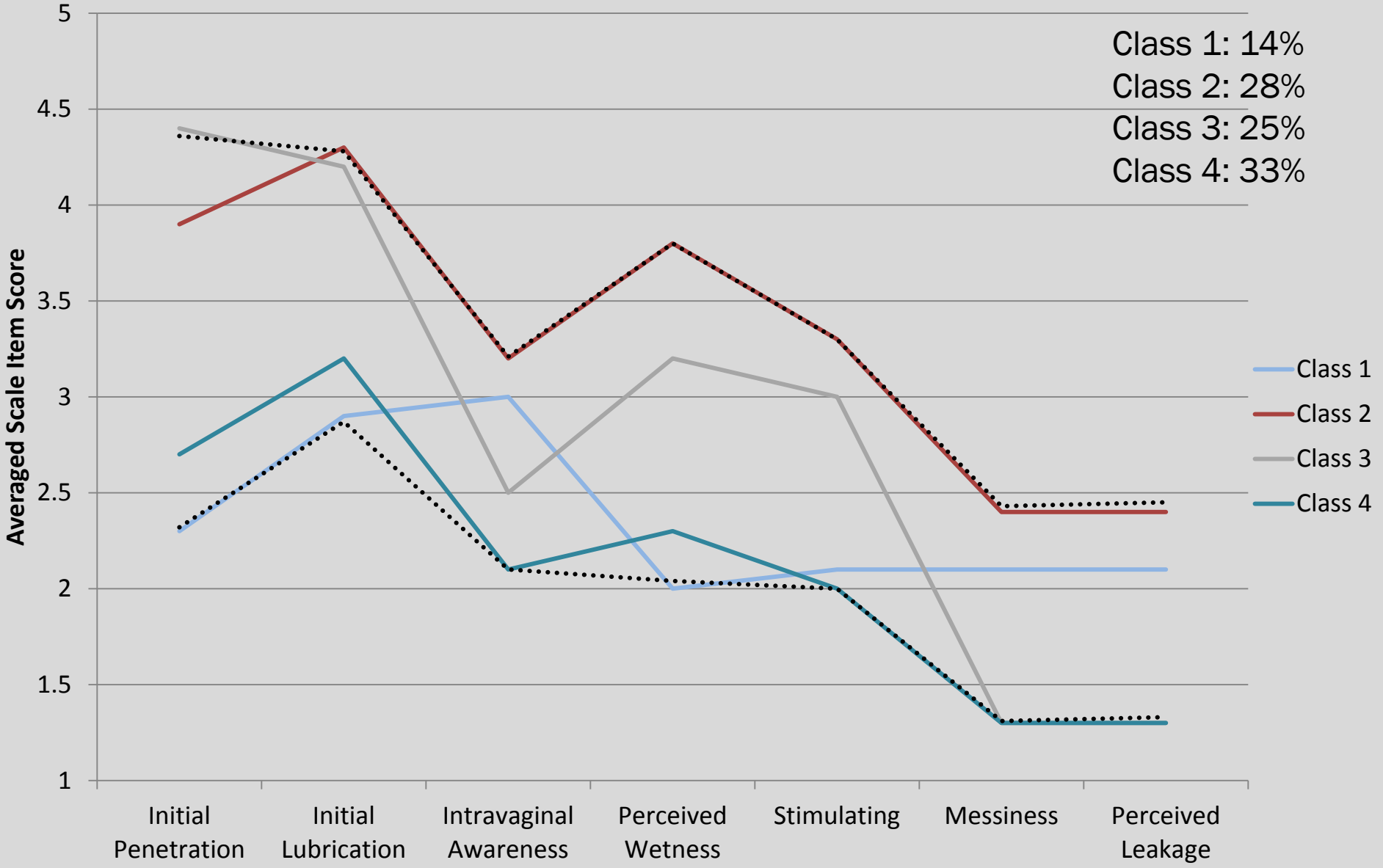
CHOICE OF GEL…?

No single gel was preferred:

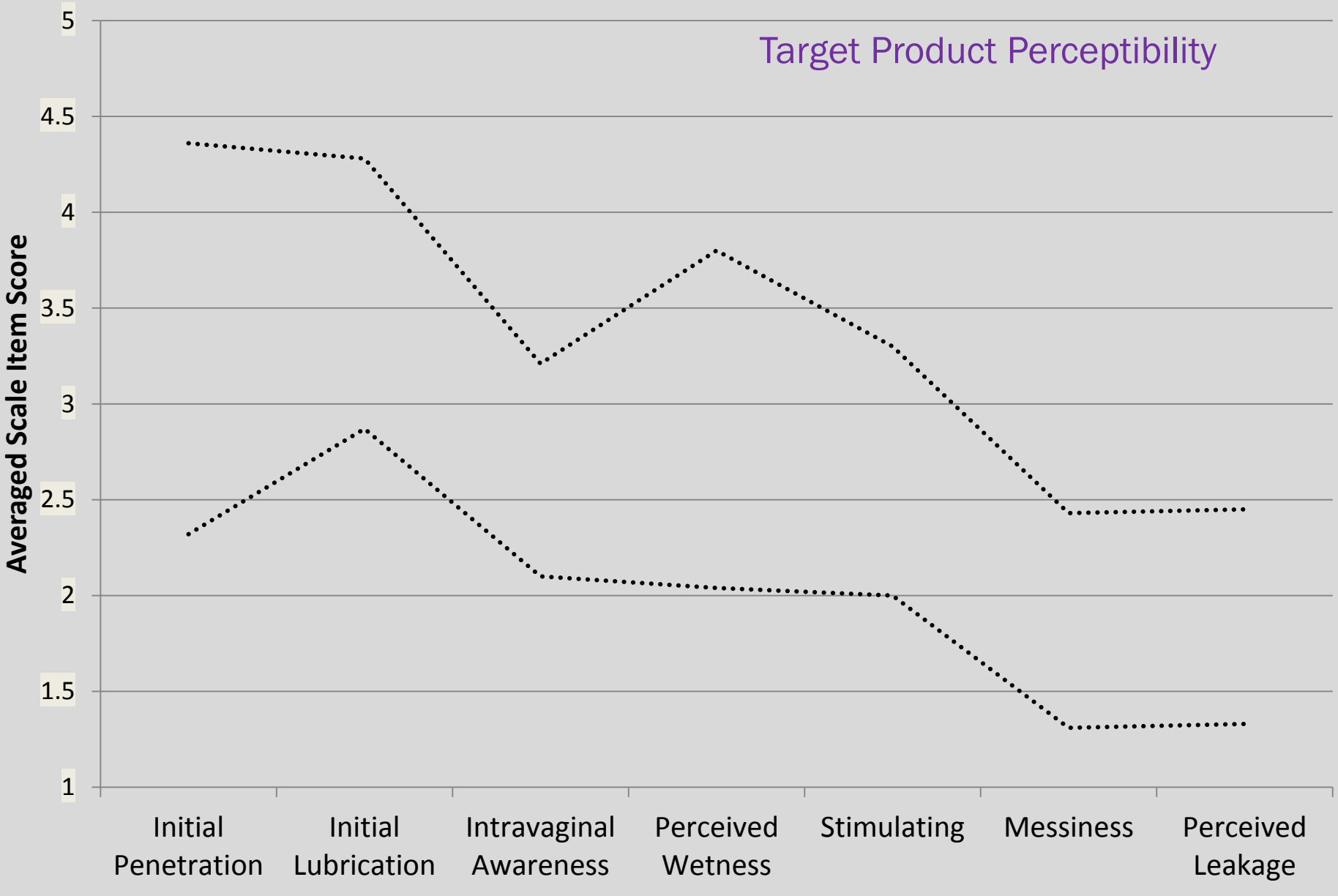
- 34% chose Orange [low viscosity, low residual stress];
- 15% chose Green [high viscosity, high residual stress];
- 51% chose 1 of 2 gels w/more complicated profiles:
  - Purple (26%)
  - Yellow (25%)

So… if a specific gel isn't *chosen* then what *is*…?

CHOICE-EXPERIENCE PATTERNS



“THE SWEET SPOT”



BETWEEN CLASS DIFFERENCES

	Class 1	Class 2	Class 3	Class 4
Age (years)	28.8 (7.5)	29.7 (8.6)	27.7 (7.9)	29.0 (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%

*$p<0.05$ for between-*class* difference

… neither sociodemographics nor behavioral history differentiated classes of choice-experience patterns

WHAT DO USERS WANT?

- There is no one answer
- The scale most correlated with class is Initial Penetration.
  - If all the scales are put into the model to predict class, the most associated is **Initial Penetration**: thus Initial Penetration, in this parameter space, is most predictive of choice experience.
  - The next two most correlated with class (which is determined by choice product) are Intravaginal Awareness and Perceived Wetness
- What does this mean? (educated guess)
  - It's important that a product provide the "best" initial penetration experience (whichever way they like it); that their awareness of it conveys the "right" message; and that they feel as much like "normal" as possible

CONSIDERATIONS…

- The LINK data only applies to a gel parameter space - and a limited one at that
  - We are currently conducting analyses for vaginal films and suppositories
  - We have not yet psychometrically validated similar USPE constructs for intravaginal ring use

CONCLUSION-1

- Microbicide effectiveness is predicated on optimal drug delivery AND optimal use adherence.
- Both drug delivery (and resulting efficacy) - and use are impacted by rheological and other biophysical properties of gel formulations.
- Clinical trials have been challenged by low adherence, obviating proof of concept.

CONCLUSION-2

- If we can understand the correspondence between product properties and the **user experience** elicited by those properties, we can:
  - Develop products that meet a defined set of parameters most likely to “hit the sweet spot”
  - Develop educational materials or behavioral interventions that help users “cope” with use sensations and experiences that cannot be changed due to their impact on efficacy
  - Make products people will use, increasing the likelihood of improved **adherence** and **impact on HIV incidence.**

THANK YOU!!

KMORROW@LIFESPAN.ORG