



Published in final edited form as:

Sex Transm Infect. 2010 February ; 86(1): 71–73. doi:10.1136/sti.2009.038158.

Enrollment of young adolescents in a microbicide acceptability study

Mary B. Short, PhD^{1,2}, Gregory D. Zimet³, William Black¹, and Susan L. Rosenthal, PhD^{1,4}

¹Department of Pediatrics, University of Texas Medical Branch, Galveston, Texas, USA

²Department of Psychology, University of Houston-Clear Lake, Houston, Texas, USA

³Department of Pediatrics, Indiana University School of Medicine, Indianapolis, Indiana, USA

⁴Department of Pediatrics, Columbia University School of Medicine, New York, USA

Abstract

Background—Clinical trials of microbicides should include adolescent participants. There may be unique challenges including obtaining informed consent, meeting eligibility criteria and adherence to study demands. We report on our experience enrolling young adolescents in a microbicide surrogate acceptability study and the implication of our experience for other types of clinical trials.

Methods—Adolescent females were enrolled in a microbicide surrogate acceptability study for 6 months which required parental consent. They were asked to use the product every time they had coitus. They had face-to-face interviews at intake, 3 and 6 months, and completed weekly phone diaries.

Results—Of the 208 enrolled, 95 participants were between 14 and 17 years. Ten were pregnant at intake, and 15 did not have sex during the study. Of the remaining 70 adolescents, 46 (66%) used the product at least once during the 6-month period, and all but seven attended a face-to-face interview after intake.

Conclusions—It will be possible to include young adolescents in clinical studies, even if parental consent is required. However, there will be challenges, and researchers need to anticipate those challenges and reduce barriers to enrolling young adolescents.

Corresponding Author: Dr. Susan Rosenthal, Morgan Stanley Children's Hospital, 3959 Broadway, 1st Floor, Room 101 Central, New York, NY 10032, USA; slr2154@columbia.edu.

Contributors MBS had a role in all aspects of the study and manuscript preparation, including questionnaire development, data collection, data analysis, manuscript preparations and manuscript revisions. GDZ was involved in the manuscript preparation and revisions for this submission. WB was involved in data analysis, manuscript preparation and manuscript revisions for this submission. SLR had a role in both the development and running of this study, as well as the supervision of all research staff and professionals involved in this study. She was also involved in data analysis, manuscript preparation and manuscript revisions for this submission.

Competing interests None.

Ethics approval Ethics approval was provided by the University of Texas Medical Branch. Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

INTRODUCTION

There is great hope that microbicides, substances that are inserted into a woman's vagina, could provide a method for sexually transmitted infection (STI) prevention that is under women's control. Given adolescents' heightened risk for STI, microbicides could be particularly helpful for this age group, and adolescent females have expressed willingness to try such products.¹ No microbicides are currently available, though several are in different phases of clinical trials, predominantly with adult women. It is essential for a number of reasons that prospective microbicides be evaluated for safety and efficacy in clinical trials, which include adolescents. For example, adolescent girls do not yet have a mature gynaecological tract² and may have less vaginal lubrication during intercourse.^{3, 4}

There are, however, several challenges to enrolling adolescents in microbicide trials. First, parental consent might be required, which could be a barrier. In addition, there may be difficulties with enrolling a sufficient number of eligible adolescents. Finally, once enrolled, there are questions regarding the ability of adolescent girls to adhere to the study demands associated with a clinical trial (e.g., repeated study visits, and use of product as directed). We have been able to gather preliminary information on these key issues through a longitudinal study of microbicide surrogate use and acceptability among adolescent girls 14–17 years of age. Therefore, the purpose of this manuscript is to report on our experiences with enrolling young adolescents with the hope that it can aid planning for other types of clinical trials of microbicides in adolescents.

METHODS

The data from the present study came from a larger 6-month study of the issues and variables associated with the acceptability and use of a microbicide surrogate in adolescent ages 14 through 21 years. The primary results from this larger study have been presented elsewhere, including recruitment information, information on reasons for use, and partner characteristics and acceptability.^{5–8} For the purposes of the current manuscript; we present the data and our experiences of those under 18 years of age, in order to highlight the issues associated with inclusion of young adolescents.

The adolescents were recruited through school-based health clinics and local colleges, and through snowball sampling (participants referring other girls). Once a girl was identified as being interested in participating in the study, she was contacted by phone and was given a thorough explanation of the study. At this time, girls who were under 18 were told that they needed parental consent. This included explaining to the adolescent that although her sexual experience status would not be disclosed to her parents, her parents might assume she was sexually experienced, since the study consent form required her 'to use a vaginal product in the context of romantic relationships' and that participants would 'strongly be encouraged to use condoms if engaging in sexual activity.' Although a history of heterosexual vaginal intercourse was an inclusion criterion, the participants did not have to be planning to have intercourse during the course of the 6 months.

Once the girl expressed continued interest, parental consent was sought. The parents were contacted over the phone and given a description of the study.

Once the parents agreed to let their adolescent participate, girls were allowed to bring in a witnessed signed consent form, if a parent did not accompany them to the first research visit. However, if the research coordinator had any concerns about whether the parent understood the study process when it was described on the phone, she then had an option of requiring parental attendance. Even though no records were kept regarding required parental attendance, this was estimated to have occurred only once or twice across subject recruitment.

In a 2-year time period, the larger study recruited 208 adolescents aged 14 through 21 years. Of these girls, 95 were 14–17 years old (the focus of this paper), and all of them needed parental consent to participate. As stated above, the adolescents were told that their sexual experience status would not be shared with their parents, although their parents might make an assumption that they were sexually experienced based on the nature of the study. Given the convenience sampling, it is not known for how many adolescents the parental consent requirement presented a barrier to participation. However, getting parental consent may present a barrier for getting enough participation in clinical trials from this age group.

After the girls and parents signed the consent form, participants were interviewed at intake, and at 3- and 6-month follow-up visits, and completed weekly phone interviews about their sexual activity. More specifically, during the weekly interviews, girls were asked if they had engaged in sexual intercourse over the previous week. If they answered ‘yes’, they were asked how many times they had sexual intercourse and the number of times they used the vaginal product. All participants received \$3 for each phone interview and \$30 for each face-to-face interview.

During the intake, the participants were told that scientists were developing products that would be used to protect against STIs. They were shown two vaginal moisturizers, a gel, Replens Vaginal Moisturizer (Warner Welcome, Morris Plains, New Jersey) and a suppository, Lublin Inserts (Bradley Pharmaceuticals, Fairfield, New Jersey) and given directions on how to use the products. Participants could choose between one or both formulations and were asked to use these products before having sexual intercourse over the 6 months of the study. Although the participants were told to use this product when they had intercourse, agreeing to do so was not an inclusion criterion of the study. The study was approved by the IRB at University of Texas Medical Branch.

RESULTS

Demographics

The 95 participants had a mean age of 15.94; eight participants were 14 years, 24 were 15 years, 29 were 16 years, and 34 were 17 years. Participants were 50% African-American, 34% Hispanic and 16% Caucasian. Of the 95 girls, the mean numbers of weeklies completed was 15.75, with a range of 1–23.

Eligibility criteria

Given that it was not a clinical trial, this study had minimal exclusion criteria, and the participants were not being asked to use an experimental product. Thus, participants who might have been excluded from other types of trials (pregnant, STI on intake) were allowed to participate. Also, due to the sensitivity regarding adolescent sexuality, we did not want to be at any risk for being perceived as encouraging sexual behaviour. Thus, adolescents did not have to anticipate any rates of sexual behaviour during the course of the 6-month study. We, in fact, planned our sample size assuming that some adolescents would remain abstinent for the entire time. Of the 95 adolescent girls enrolled, 10 were pregnant at intake. Furthermore, 15 did not have intercourse during the study time frame. Given that these girls would have been either excluded or dropped from analyses in a clinical trial, the remainder of this manuscript reports on the 70 participants who were not pregnant at intake and had intercourse during the study period.

Product use and attendance

Of the 70 younger adolescents described above, 46 (66%) of the participants used the product at least once during the study.

More detailed data on product use are presented in table 1. For this table, percentage of use was calculated by taking the number of sexual acts reported by the participant and dividing that number by the number of times the participant reported that they used the product. However, use of the product was not a clear study demand for this study, but it most likely would be a demand of a microbicide clinic trial.

With regards to follow-through with the face-to-face interviews, all but seven girls were seen for an additional visit after intake. Fifty-eight (83%) attended both the 3- and 6-month interview. Of those who attended at least one follow-up interview (n=463), 42 (67%) used the product.

DISCUSSION

The nature of this study differed in many important ways from a clinical trial, and the purpose of the study was not to examine clinical trial participation. Despite this significant limitation, we believe that our experience can be informative regarding issues that need to be addressed to successfully enroll adolescents under 18 years of age in a clinical trial.

We were able to recruit a reasonable number of adolescent girls into a microbicide surrogate study, even with the requirement of parental consent. Moreover, we were able to retain the majority of girls for two follow-up appointments. Attendance at our follow-up visits might have been better if participants were using an experimental product and were more concerned about ensuring safety. In addition, it is possible that a greater percentage of the adolescents would have used the product if absolute willingness to use the moisturiser had been an inclusion criterion. However, potential difficulties with adherence to use of microbicides are not unique to adolescents, as the interpretation of a recent microbicide study was hampered due to poor adherence by adult participants.⁹

As noted, we had a high rate of pregnancy at enrolment. At the minimum, study staff will have to be prepared to manage pregnancies in young adolescents and the confidentiality issues they can present between adolescent, study staff and parents. It also does suggest that screen failure rates may differ and possibly be higher in adolescent populations than in adult populations. While screen failure rates likely are population-specific and study-requirement-specific, adult clinical trials have shown screen rates to be between 30 and 49%.^{9–13} Most of those screen failure rates were for medical reasons, and we do not have that information for our sample. However, when comparing the rates of pregnancy at intake in our sample, rates were equal for those who were 18–21 years and those under 18 years. Careful consideration of the management of pregnancy diagnosis at intake will need to be considered.

The need in a microbicide clinical trial for participants to have sexual intercourse in a consistent manner also may pose a challenge for young adolescents. In the present study, several of the girls did not have intercourse during the research period. If an inclusion criterion involves a stated plan to have regular intercourse over a specified period of time, it is possible that enrolment of adolescents will be limited to those with a steady regular sexual partner or those who are commercial sex workers. In addition, societal opposition may be encountered if, as part of a clinical trial, adolescents as young as 15–16 years of age are asked to commit to having regular intercourse. However, clinical trial researchers will need to address these issues because even though this is a ‘vulnerable’ population, clinic trials are still needed in this population to get approval.

Our experience, therefore, suggests that it should be possible to include adolescents in microbicide clinical studies. Nonetheless, there will be challenges. Planning and resource allocation should anticipate a relatively high rate of screen failures and assume that some analyses will be limited to participants for whom there are follow-up data and who used the microbicide. In addition, our study team was formed to examine adolescents’ sexual health; thus they had special interest and training in the unique development needs of adolescents and their parents and in ways to engage both in the research process. It is possible that the degree of success that we achieved in enrolment and follow-up may have been related to the extensive adolescent-specific experience of the research staff.

Despite the differences between this study and a microbicide clinical trial, it is hoped that the description of our experiences will encourage discussion of how to include adolescents in all stages (Phase I to Phase III) of microbicide research in a variety of cultural contexts. Furthermore, it is important to remember that inclusion of adolescents is consistent with the Belmont Report’s¹⁴ requirement of justice (i.e., inclusion of at-risk participants).

Acknowledgments

We would like to thank The Teen Health Center. We also would like to acknowledge our research team (E Brown, S Ramos, J Oakes, EA Zubowicz) for their outstanding work in collecting and managing the data. Thank you also to T Moench, for his critical review of this manuscript. Finally, we wish to thank all the girls for their participation in this research study.

Funding Support was received from the National Institute of Child Health and Human Development (R01 HD4015101) and the National Institutes of Allergy and Infectious Diseases (U19 A161972, and N01 A150042) of the National Institutes of Health. The GCRC is funded by a grant (M01 RR 00073) from the National Center for Research Resources, NIH, and USPHS.

REFERENCES

1. Short MB, Succop PA, Ugueto AM, et al. Predictors of using a microbicide-like product among adolescent girls. *J Adolesc Health*. 2007; 41:357e62. [PubMed: 17875461]
2. The question of enrolling adolescents. Global Campaign for Microbicides. 2005 <http://www.global-campaign.org/clientfiles/chapter6.pdf>.
3. Tanner AE, Zimet GD, Fortenberry JD, et al. Young women's use of a microbicide surrogate: The role of internal and contextual factors in acceptability and sexual pleasure. *J Sex Res*. 2009; 46:1e9. [PubMed: 19205999]
4. Tanner AE, Short MB, Zimet GD, et al. Research on adolescents and microbicides: a review. *Adolesc Pediatr Gynecol*. 2009; 22:285e91.
5. Auslander BA, Rupp R, Short MB, et al. Male partners of young women: assessing their attitudes towards topical microbicides. *J Adolesc Health*. 2008; 42:626e8. [PubMed: 18486872]
6. Short MB, Auslander BA, Succop PA, et al. Relationship context associated with microbicide-like product use. *J Pediatr Adolesc Gynecol*. 2009; 22:285e91. [PubMed: 19616456]
7. Short MB, Succop PA, Rupp R, et al. Adolescents' reason for using a microbicide-like product over time. *Int J STD AIDS*. 2008; 19:115e17. [PubMed: 18334065]
8. Short MB, Succop PA, Ugueto AM, et al. Predictors of using a microbicide-like product among adolescent girls. *J Adolesc Health*. 2007; 41:357e62. [PubMed: 17875461]
9. Skoler-Karppoff S, Ramjee G, Ahmed K, et al. Efficacy of Carraguard for prevention of HIV infection in women in South Africa: a randomized, double-blind, placebo-controlled trial. *Lancet*. 2008; 372:1977e87. [PubMed: 19059048]
10. Joshi SN, Dutta S, Kumar BK, et al. Expanded safety study of Praneem polyherbal vaginal tablet among HIV-uninfected women in Pune, India: a phase II clinical trial report. *Sex Transm Infect*. 2008; 84:343e47. [PubMed: 18426844]
11. Kilmarx PH, van de Wijgert JH, Chaikummao S, et al. Safety and acceptability of the candidate microbicide Carraguard in Thai Women: findings from a Phase II Clinical Trial. *J Acquir Immune Defic Syndr*. 2006; 43:327e34. [PubMed: 16980907]
12. Morrow K, Rosen R, Richter L, et al. The acceptability of an investigative vaginal microbicide, Pro 2000 Gel, among women in a Phase I clinical trial. *J Womens Health*. 2003; 12:655e66.
13. Williams DL, Newman DR, Ballagh SA, et al. Phase I safety trial of two vaginal microbicide gels (Acidform or BufferGel) used with a diaphragm compared to KY jelly used with a diaphragm. *Sex Transm Dis*. 2007; 34:977e84. [PubMed: 18080349]
14. Office of Human Subjects Research. [accessed 20 Jan 2009] The Belmont report: ethical principles and guidelines for the protection of human subjects research. [Online]. <http://ohsr.od.nih.gov/guidelines/belmont.html>

Key Points

Microbicides clinical trials in adolescents will be challenging.

Issues of parental consent, eligibility criteria and study demands may be difficult to deal with in the adolescent population.

Given our results, it appears that microbicide clinical trials will be feasible, but special attention will need to be paid to these challenging issues.

Table 1

Description of product use (n=70)

No use	34% (n=24)
No used at least once	66% (n=46)
Mean no of uses per sexual act (n=44)*	3.73 (range 1 to 17)
Percentage used 10% or less per sexual act	10% (n=4)
Percentage used 10-25% of the time per sexual act	28% (n=11)
Percentage used 26-50% of the time per sexual act	20% (n=8)
Percentage used 51-99% of the time per sexual act	12% (n=5)
Percentage used 100% of the time per sexual act	30% (n=12)

* Since frequency of use was only reported on weekly interviews and not face-to-face interviews, data are not available for six of the subjects regarding the number of times they used the product, since those subjects only reported it on a face-to-face interview.