INCLUSION OF MINORS IN CLINICAL TRIALS FOR PREVENTION OF SEXUALLY TRANSMITTED INFECTIONS: A REVIEW OF EXISTING REGISTERED STUDIES

Lily F. Hoffman, MA, Marina Catallozzi, MD, Nefertinenene K. Francis, MA, Lawrence R. Stanberry, MD, PhD, Susan L. Rosenthal, PhD

Columbia University- College of Physicians & Surgeons

**Purpose:** Adolescents, particularly 15 to 17 year olds, continue to be disproportionately burdened by sexually transmitted infections (STIs). In order to develop new bio-medical options (e.g., microbicides) for STI prevention and treatment that are safe and effective in young adolescents, they will need to be included in clinical trials. Yet, investigators often limit trials to those over 18 to avoid the issues around consent and parental involvement associated with enrolling minors. This study aimed to describe the status of the inclusion of minors in studies for the prevention of STIs and HIV by conducting a systematic search of clinical trials listed on registries in the US and abroad.

**Methods:** We searched clinicaltrials.gov (the registry of the NIH) and International Standard Registered clinical/social study Number (ISRCTN), the primary clinical trial registry recognized by WHO and ICMJE. We used the following search terms (microbicide OR PrEP) AND (STD OR HIV OR STI OR HSV) WITH (Gel OR ring OR film) and prevention/sexually transmitted diseases WITH (gel). In clinicaltrials.gov 133 studies were identified, 29 failed to meet inclusion criteria. An additional eight unique studies were identified in ISRCTN for a final sample size of 112. Studies were coded regarding inclusion of minors based on their answers to the specific questions on the databases.

**Results:** Of the 112 studies, only 9.8% (n = 11) included minors, of which only one exclusively targeted minors. Six of the eleven studies included both male and female participants. Eight of the eleven studies were at least partially sponsored by a governmental agency. Roughly half of the studies including minors were conducted in the U.S/Puerto Rico only. Characteristics of the studies (gender, government sponsored, location) did not differ between those that included minors and adult-only studies. However, minors were under-represented in Phase 0-II studies (1/11 versus 57/101) (p = 0.004) and over-represented in studies of HIV infected individuals (5/11 vs 17/101, p=0.023).

**Conclusions:** It is concerning that minors are not included in more STI or HIV prevention studies given that minors are disproportionately likely to acquire new infections. While it may be justifiable to exclude minors in early phase studies to avoid any untoward effects, given that they are part of the target population, eventually minors need to be included to know if products are safe in their developing bodies. Since factors influencing the exclusion of minors remain unclear, future research needs to understand the barriers to inclusion of minors and help investigators and IRBs overcome those barriers.

**Sources of Support:** None
14.

**ADDINe TO THE HIV PREVENTION PORTFOLIO: THE ACHIEVEMENT OF STRUCTURAL CHANGES BY COALITIONS TARGETING TO REDUCE HIV RISK IN ADOLESCENTS AND YOUNG ADULTS THROUGH COMMUNITY MOBILIZATION IN URBAN AREAS ACROSS THE US AND PUERTO RICO**

Kate S. Chutuape, MPH; Adaline Z. Muyeed, PhD; Nancy Willard, MS; Lauren B. Greenberg, MPH; Jonathan Ellen, MD

1. Johns Hopkins University, School of Medicine; 2. Westat; 3. Johns Hopkins School of Medicine

**Purpose:** Opportunities to control risk factors that contribute to HIV transmission and acquisition extend far beyond individuals and include addressing social and structural determinants of HIV risk, such as inadequate housing, poor access to healthcare and economic insecurity. The infrastructure within communities, including the policies and practices that guide institutions and organizations, should be considered crucial targets for change. This paper examines the extent to which 13 community coalitions across the U.S. and Puerto Rico were able to achieve “structural change” objectives (SCO) (i.e., new or modified practices or policies) as an intermediate step toward the long-term goal of reducing HIV risk among adolescents and young adults (12-24 years old). Additional areas of inquiry includes which community sectors offered opportunity for buy-in for coalitions; and the level of community mobilization required to achieve structural changes.

**Methods:** The study sample is the total number of objectives (N=245) completed by the C2P coalitions over five years. Objectives were considered “complete” when a series of actions led to the adoption of the intended change (i.e., acceptance of a new policy) or integration of a new or modified practice by the entity, organization or system that was targeted. A systematic review and cross-coding process involving study team members and program coordinators, to classify the completed objectives as "structural" or "individual", as conceptualized. Univariate and bivariate descriptive analyses were run on all variables of interest to examine the overall profile of completed objectives and the comparison of the characteristics for individual versus structural changes. Statistical tests of association were performed to investigate potential differences between individual and structural change objectives. Fisher’s exact tests were used for categorical variables and non-parametric Wilcoxon tests for continuous variables.

**Results:** The study resulted in the completion of 245 objectives with 70% categorized as structural in nature. Common types of SCOs focused on creating new linkages between two or more organizations to increase youths’ access to HIV or health-related services, modifying organizational policies to increase provider competency around youth and LGBT culture, modifying policies within schools etc. Coalitions targeted social services (23%), education (22%) and government (20%) as primary community sectors to adopt structural changes. A median of 12 key actors and six new key actors contributed to accomplishing structural changes. Structural change objectives required a median of seven months to complete. The structural changes achieved offer new ideas for community health educators and practitioners seeking to bolster their HIV prevention agenda.

**Conclusions:** Opportunities to control factors that contribute to HIV acquisition and transmission extend far beyond individuals. The infrastructure within communities, including the policies and practices that guide institutions and organizations, should be considered crucial targets for intervening as public health professionals seek to expand their repertoire of HIV prevention strategies. Through this research, a
range of achievable structural changes emerged and provide a platform for communities to pursue a holistic HIV prevention agenda. 

Sources of Support: The Adolescent Trials Network for HIV/AIDS Interventions (ATN) from NIH [U01 HD 040533 and U01 HD 040474] through NICHD, with supplemental funding from NIDA and NIMH.

---

15. RE-FOCUSING HIV PREVENTION MESSAGES: A QUALITATIVE STUDY IN RURAL UGANDA

Sanyukta Mathur, DrPH¹, Dina L. Romo, MD², Mariko Rasmussen, MPH³, Neema Nakyanjo, MA⁴, Fred Nalugoda, PhD⁴, John S. Santelli, MD, MPH, FSAHM¹

¹Columbia University Mailman School of Public Health; ²Columbia University Medical Center; ³Columbia University School of Public Health; ⁴Rakai Health Sciences Program

Purpose: The human immunodeficiency virus (HIV) remains an epidemic of global concern. To support the increasing emphasis on biomedical interventions for prevention requires a renewed and re-framed focus on prevention messages to motivate engagement in risk-reduction activities. This study examines youth and adult perceptions of HIV prevention messages and HIV risk assessment in a generalized HIV epidemic context in Uganda

Methods: We conducted 24 focus groups (FGs) and 24 in-depth individual interviews (IDIs) with four age groups (adolescents 15-19, young adults 20-24, adults 25-34 and older adults 35-44) from three communities (two rural, one periurban) in Rakai, Uganda. Semi-structured field guides focused on general attitudes about 1.HIV/AIDS in the community, 2.HIV prevention messages and the sources of these messages and 3.larger social policies that could influence sexual risk behaviors. IDIs focused on HIV prevention messages received during key life events (eg. puberty, marriage, migration, pregnancy) and respondents were probed on the most prominent HIV prevention message received and how this message affected their HIV risk perception, behavior or services accessed. All discussions were recorded in Luganda and translated and transcribed into English. A systematic within-case and across-case analysis was applied. Codes of emergent themes were created for FG and IDI transcripts. Once coded, data matrices summarized and compared responses by age and sex

Results: There were a total of 218 respondents, ages 15-44 years in the 24 FGs, each discussion included approximately nine participants. IDIs included 8 participants in each of the 3 communities representing the same age groups as in FGs. Emerging themes included: 1.generational differences in perspectives of HIV risk and prevention messages; 2.persistent gender differences in the frequency, content, mode, and salience of HIV prevention messages received; 3.misinformation and misconceptions about HIV treatments and HIV transmission. Generational differences included older respondents identifying personal experience with the effects of HIV as opposed to adolescents and young adults identifying awareness of HIV only due to prevention messages. Persistent gender differences manifested as women in all age groups receiving comparatively more messages related to individual sexual practices (eg. abstinence, being faithful to their partner) throughout their lifetime; adolescent and younger men reported an emphasis on service-based messages about condom use and, more recently, male circumcision. Whereas women received more HIV/AIDS direct education through interpersonal
interactions (health providers, teachers, parents), males received messages through public sources such as the radio or during class time. Misinformation and misconceptions were universally reported as respondents felt that decreased fear of AIDS as a deadly/debilitating illness led to the abandonment of protective behaviors among HIV-positive individuals. Younger respondents felt that ART treatment made it difficult to tell who is HIV-positive thus fueling the epidemic.

**Conclusions:** Despite concerted health-education efforts over the last three decades in Rakai, there are gaps in health-education, ways the messages are delivered, and their salience. If ignored, these gaps could hamper future HIV behavioral and biomedical prevention efforts. Shifts in HIV education are needed to address these gaps to foster engagement in risk reduction strategies and adoption of newer biomedical approaches to HIV prevention

**Sources of Support:** NIH-5R01HD061092-05

16.

**EPIDEMIOLOGIC IMPACT OF HPV VACCINATION AND EVIDENCE FOR HERD IMMUNITY OVER THE FIRST 8 YEARS AFTER VACCINE INTRODUCTION IN A COMMUNITY**

Lea E. Widdice, MD1, Lili Ding, PhD1, David I. Bernstein, MD1, Darron R. Brown, MD, MPH2, Eduardo L. Franco, DrPH3, Bin Huang, PhD1, Jessica A. Kahn, MD, MPH1

1Cincinnati Children’s Hospital Medical Center; 2Indiana University School of Medicine; 3McGill University

**Purpose:** The aims of this study were to determine trends in vaccine-type HPV prevalence in young women over the eight years after HPV vaccine introduction in a community, in order to assess the epidemiologic impact of vaccine introduction and characterize herd immunity.

**Methods:** We recruited three independent samples of sexually experienced young women 13-26 years of age from an urban teen health center, sexually transmitted disease clinic, and public health clinic. Women were recruited before widespread HPV vaccine introduction (wave 1: all participants were unvaccinated) and at three years (wave 2) and seven years (wave 3) after vaccine introduction. Participants completed surveys assessing demographic characteristics and behaviors and underwent testing for cervicovaginal HPV; samples were analyzed for 36 HPV types using the Roche Linear Array assay. Vaccination status was determined by medical record review; vaccination was defined as receipt of one or more HPV vaccine doses. We determined the prevalence of type-specific HPV among unvaccinated women at waves 1, 2, and 3, and among all women at waves 2 and 3, and examined whether vaccination and study wave were associated with vaccine-type HPV (HPV6, 11, 16, and/or 18) using logistic regression.

**Results:** We recruited 1180 women in the three waves: their average age was 19 years in each wave. All vaccinated participants received the quadrivalent vaccine. Across the three waves, vaccination rates increased from 0 to 59.2% to 71.3%. Vaccine-type HPV prevalence in all women decreased across the three waves from 32.2% to 14% to 8.1% (overall relative decline 74.8%). Among unvaccinated women, vaccine-type prevalence decreased from 32.2% to 18.6% to 18.3% (overall decline 43.2%). HPV16 prevalence in all women decreased from 17.4% to 9.1% to 5.1% (overall decline 70.7%). Among
unvaccinated women, HPV16 prevalence decreased from 17.4% to 13.2% to 10.4% (overall decline 40.2%). In contrast, the prevalence of any HPV type changed from 66.0% to 76.5% to 63.8% (overall decrease 3.3%), and in unvaccinated women changed from 66.0% to 73.1% to 67.8% (overall increase 2.7%). Logistic regression analyses demonstrated that among unvaccinated participants, decreases in vaccine-type HPV prevalence were significant from waves 1 to 2 (OR 0.48, 95% CI 0.31-0.08) and 1 to 3 (OR 0.48, 95% CI 0.28-0.80), but not 2 to 3 (OR 0.99, 95% CI 0.54-1.8). Among vaccinated participants, decreases in vaccine-type HPV prevalence were significant from wave 2 to 3 (OR 0.34, 95% CI 0.16-0.70). The interaction between vaccination and study wave was significant: vaccine-type HPV prevalence was lower among vaccinated than unvaccinated participants in both waves 2 and 3, and the effect of vaccination on decreasing the odds of vaccine-type HPV prevalence in wave 3 was significantly greater than in wave 2.

Conclusions: Over the first 8 years after HPV vaccine introduction, vaccine-type HPV decreased by about 75% among all women, demonstrating high effectiveness in a community setting even in sexually experienced young women who may have already been exposed to HPV. We also found substantial evidence for herd immunity.

Sources of Support: R01 AI073713 and R01 AI104709 from NIAID (Jessica Kahn, PI)

17.

SELF-DISCLOSURE OF HIV-STATUS AMONGST HIV INFECTED ADOLESCENTS IN WESTERN KENYA

Hilary T. Wolf, MD1, Patricia Ong’wen, MD, MPH2, Matthew E. Levy, BS3, Maureen E. Lyon, PhD, FSAHM4, Lawrence J. D’Angelo, MD, FSAHM4, Zachary Kwen, PhD2, Craig R. Cohen, MD, MPH5

1Georgetown University Medical Center; 2Kenya Medical Research Institute; 3George Washington University Milken Institute School of Public Health; 4Children’s National Medical Center; 5University California San Francisco

Purpose: HIV is one of the leading causes of mortality amongst adolescents in sub-Saharan Africa (SSA). HIV self-disclosure is an important part of acceptance of an adolescent’s health status and potentially improves adherence to care and reduction of HIV transmission. Few studies have assessed the process of disclosure. The purpose of this study was to: (1) describe patterns of HIV status self-disclosure and (2) assess factors associated with HIV self-disclosure among HIV-infected adolescents aged 15-19 in Western Kenya.

Methods: 115 HIV infected adolescents ages 15-19 were surveyed regarding information on demographics and factors related to the process of HIV self-disclosure, using a survey developed by Centers for Disease Control investigators.

Results: The mean age of the 115 HIV-infected adolescents who were included in the study was 16.8 (SD=1.4), 70% were female, 7% were married, 72% attended school, 49% had access to a cell phone and 45% reported ever having vaginal, oral or anal sex. The mean age at which participants first learned about their HIV status was 12.7 years (SD=3.3). All but one of the 115 participants reported that somebody besides their healthcare provider was aware of their HIV status. However, 52% of participants
reported that they had not self-disclosed their HIV status to anyone. Among participants who self-disclosed, 62% of participants reported that they had self-disclosed to at least one person who had a supportive reaction, 25% reported an indifferent reaction, 29% reported a surprised reaction and 7% reported a negative reaction defined as angry or blaming. None of the participants reported a sad reaction after self-disclosing their status. Of the sexually active subjects, 57% had not disclosed their HIV status to their sexual partners and 43% had not disclosed their sexual activity to their healthcare providers. Sixty-three percent of participants reported that none of their friends knew about their HIV status. In multivariable analysis, females were 2.8 (95% CI 1.2, 6.5, p=.020) times more likely than males to have self-disclosed their HIV status to someone. Those who had access to a mobile phone were 2.2 (95% CI 1.0, 4.7, p=.048) times more likely to have self-disclosed his/her HIV status. In bivariate analysis participants who reported having been sexually active were 2.6 (95% CI 1.1, 5.1, p=.023) times more likely than non-sexually active participants to have self-disclosed his/her HIV status. In multivariate analysis this was no longer significant in part due to co-linearity, as female gender and history of sexual activity were strongly correlated with each other (ch2=10.2, p<.001).

**Conclusions:** While most participants had somebody who knew about their HIV status, less than half had self-disclosed their status to anyone and of those teens who were sexually active, only 43% had informed their sexual partners. Future studies should investigate the effect that this has on adherence to care and develop interventions, which may improve self-disclosure. Further research is also needed to investigate why having a cell-phone improved the likelihood of self-disclosure in this population.

**Sources of Support:** Georgetown University Medical Center, Department of Pediatrics; District of Columbia Center for AIDS Research (P30AI117970)

---

**EFFECTIVENESS, IMMUNOGENICITY, AND SAFETY OF GARDASIL™ IN PRE-ADOLESCENTS AND ADOLESCENTS – 10 YEARS OF FOLLOW-UP**

Rituparna Das, M.D., PhD  
*Merck Research Laboratories*

**Purpose:** Quadrivalent HPV vaccine has previously been shown to be generally effective, immunogenic, and safe in pre-adolescents and adolescents aged 9-15, through 96 months after vaccination. We describe final (month 126 post dose 1) effectiveness, immunogenicity, and safety data for the long-term follow-up study of GARDASIL™ in this population (V501-Protocol 018).

**Methods:** In the base study of V501-Protocol 018, 1781 sexually naïve boys and girls were assigned to GARDASIL or saline placebo at day 1, months 2 and 6. At the end of the base study (month 30), the placebo group received GARDASIL™. Those vaccinated with GARDASIL in the base study are the early vaccination group (EVG). Those vaccinated with GARDASIL during months 30-36 are the catch-up vaccination group (CVG). As this extension study does not have a placebo arm, effectiveness was estimated by calculating the incidence of the primary endpoints (HPV6/11/16/18 persistent infection or
related disease) and comparing these rates with those from previous phase 3 studies in men and women aged 16-26.

**Results:** A total of 1575 subjects (1116 in the EVG and 459 in the CVG) had follow-up in this long-term extension study. The median follow-up time was 7.9 years in EVG and 7.2 years in the CVG. Ten subjects were detected to have persistent infection of ≥ 6-month duration with vaccine-type HPV (0.3/100 person-years at risk among females in the EVG and CVG, 0.6/100 person-years at risk among males in the EVG, and 0.4/100 person-years at risk for males in the CVG). The infection persisted to 12 months in only 2 of these subjects. For comparison, incidence of HPV 6/11/16/18 persistent infection in female and male placebo recipients from previous phase 3 studies were 6/100 person-years at risk and 4/100 person years at risk respectively. No cases of HPV 6/11/16/18-related disease were observed in this population over the follow-up period. For each of HPV types 6, 11, and 16, the vaccination-induced anti-HPV response persisted long-term. Depending on HPV type, 89%-96% remained seropositive through Month126. Lower vaccination-induced anti-HPV 18 responses were seen over time and were consistent with the persistence profile observed in other studies of GARDASIL™. None of the cases of persistent infection were attributed to HPV type 18. No serious adverse events were reported between months 96 and 126.

**Conclusions:** No breakthrough cases of cervical/genital disease related to HPV types 6, 11, 16, and 18 were observed among preadolescents and adolescents vaccinated with GARDASIL™ during the long-term follow-up period. Although 10 cases of persistent infection were detected, a majority (8/10) were of <12 months duration. Anti-HPV 6, 11, 16, and 18 antibody responses generated post-vaccination with GARDASIL™ persisted over time. Additionally, the safety profile of GARDASIL™ during the follow-up period remained favorable.

**Sources of Support:** This study was sponsored by Merck & Co., Inc.