Higher Levels of Education Associated With Greater Access to Safe Abortion in Brazil

In Brazil, women with higher levels of education are more likely to terminate a pregnancy, and less likely to experience complications after the termination, than those with less education, according to a cross-sectional study conducted among female and male civil servants in Campinas, Sao Pãulo.[1] Despite the country's strict abortion laws, more than half of respondents who had had (or whose partner had had) an unwanted pregnancy reported that the pregnancy ended in abortion. The only measured characteristic associated with opting to terminate an unwanted pregnancy was education level: Respondents with at least some college education were more likely than others to say that an unwanted pregnancy had resulted in abortion (prevalence ratio, 1.6). After an abortion, women with some college education were less likely than those with lower levels of education to need medical care (13% vs. 38%) and hospitalization (8% vs. 28%).

Although abortion is restricted to women who were raped or whose life is endangered by their pregnancy (and, since 2012, in cases of fetal anencephaly), an estimated one million induced abortions occur in Brazil each year; only a small proportion can be classified as legal. And, despite scant data, it is generally believed that women's risk of complications from unsafe abortion increases as socioeconomic level decreases. Using education level as a proxy for socioeconomic status, the researchers sought to assess the association between education level and induced abortion, and to examine women's access to physician-performed abortions and their risk of complications.

In January 2010, the researchers sent self-administered questionnaires to 15,800 male and female civil servants; the survey was resent after a month to increase the response rate. In all, 1,660 questionnaires were returned (response rate, 11%). Women were asked if they had ever had "an absolutely unwanted pregnancy," whether they had felt the need to terminate the pregnancy and, if so, what they had done; men were asked the same questions about their female partners. The survey also collected social and demographic information that referred to the time of the unwanted pregnancy, including age, number of children, marital status, education level and contraceptive use. The researchers used chi-square tests to assess differences in reports of unwanted pregnancy and induced abortion by social and demographic characteristics; multivariate Poisson regression models were constructed to assess associations between demographic variables and induced abortion, the need for medical care and the need for hospitalization.

Nearly three-quarters of participants (73%) were women. Overall, 18% of respondents reported that they or a partner had had an unwanted pregnancy; the proportion was even higher (24%) among respondents who had not attended college. At the time of their unwanted pregnancy, almost half of participants were aged 18–24, nearly three-fourths had no children and a similar proportion were not in a stable union; 45% had at least some college education. Thirty-three percent of respondents had not been using contraceptives, while 23% had been using a hormonal or surgical method or an IUD, and 45% had been using a barrier method, a behavioral method (rhythm or withdrawal) or both.

Among respondents reporting an unwanted pregnancy, 56% had had (or their partner had had) an induced abortion. At the time of the pregnancy, 20% of those reporting an abortion had been in a stable union, and 54% had been using a barrier method, a behavioral method or some combination thereof. Fifty-six percent had some college education. The most common reason for having had an abortion—given by 37% of both men and women—was that the respondent had not wanted to be a single parent. In bivariate analyses, living in a stable union, having attended college, and using barrier or behavioral contraceptive methods were associated with an elevated likelihood of having had an abortion; college attendance was the only characteristic that remained statistically significant in the multivariate regression analysis (prevalence ratio, 1.6).

Sixty-two percent of induced abortions had been performed by physicians, 10% by midwives and 2% by providers with no formal training; 26% were self-induced. Misoprostol was used in 18% of abortions, and unspecified medicines in 12%; medication was provided by physicians or midwives in 5% of abortions, and 26% of respondents reported self-administering drugs. Three percent of respondents said catheters and herbs had been used, and some women had used more than one method. Seventy-six percent of abortions reported by respondents with some college education had been performed by a physician, compared with only 41% of those among respondents with less education.

Twenty-three percent of women who had had an abortion had needed medical care afterward; 17% had required hospitalization. Women whose abortion had been performed by a physician were less likely than those who had used another provider or self-induced to need medical care (12% vs. 40%) or require hospitalization (8% vs. 30%). Moreover, respondents with some college education were less likely than those with less education to report a need for medical care (13% vs. 38%) or hospitalization (8% vs. 28%) after the abortion. Finally, regression models revealed that having an abortion performed by a physician was associated with a lower likelihood of requiring medical care or hospitalization after an abortion (prevalence ratio, 0.3 for each).

The researchers note several limitations. The sample was not representative of the Brazilian population or even (because of the low response rate) civil servants. Furthermore, those who participated may have done so because they had relatively liberal views on abortion, and because most of the abortions had occurred years or even decades earlier, the hospital admission rates might not reflect current risk. Despite these limitations, the researchers suggest that their study provides objective evidence that less educated women face an elevated risk of having complications from unsafe abortion, underscoring "the so-

cial inequalities associated with abortion in Brazil."–*L. Melhado*

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Pakistani Study Finds High Abortion Rate and Low Level Of Contraceptive Use

Despite legal restrictions that limit women's access to abortion, the incidence of the procedure in Pakistan is high, and the abortion rate has increased during the past decade.[1] According to a recent national study, women in Pakistan had an estimated 2.25 million abortions in 2012, equivalent to an abortion rate of 50 abortions per 1,000 women of reproductive age–nearly double the rate estimated for 2002 (27 per 1,000). Low levels of contraceptive use have resulted in high levels of unintended pregnancy, and more than half of the estimated 4.2 million unintended pregnancies in 2012 ended in abortion.

The data come from two nationally representative surveys fielded in 2012 as part of the study–the Health Facilities Survey and the Health Professionals Survey–and from existing national data sets, including the 2012–2013 Pakistan Demographic and Health Survey. The Health Facilities Survey assessed Pakistan's capacity to provide quality postabortion care and ascertained the number of women treated for postabortion complications. It included 266 facilities: all large public and private teaching hospitals and a sampling of smaller facilities. Researchers used a questionnaire adapted from a previous national abortion study, conducted in 2002, to maintain comparability between the studies; it was administered in face-to-face interviews with senior medical officials and providers working in obstetrics and gynecology departments. The Health Professionals Study focused on providers', researchers' and administrators' perceptions of abortion provision (e.g., the types of providers women use and the likelihood of complications). Researchers interviewed 102 respondents, who were chosen on the basis of their knowledge of and experience with abortion. Both surveys were conducted in the country's four major provinces (Baluchistan, Khyber Pakhtunkhwa, Punjab and Sindh), where more than 90% of the population of Pakistan resides.

The researchers applied the data to an established method for indirectly estimating abortion incidence in settings where the procedure is not reliably tracked and where induced abortions may be passed off as or mistaken for miscarriages. They first used weighted data from the Health Facilities Survey to estimate the number of women treated in a facility for complications of either miscarriage or induced abortion; in 2012, these women totaled 712,000. Reducing this number by the estimated number of women treated for miscarriage (calculated from data on the biological likelihood of miscarriage and the province-specific likelihood that women who have a miscarriage will obtain care in a facility), the researchers estimated that 623,000 women were treated in facilities for complications from induced abortion alone

This number, however, excludes women who did not obtain facility-based treatment for abortion complications (e.g., because they feared legal ramifications and social stigma) or who did not have complications at all. Using data from the Health Professionals Survey, the researchers estimated the proportion of women having induced abortions who obtain postabortion care from a facility (taking into account women's wealth and place of residence, the type of abortion provider, the probability of complications and the probability that women with complications would seek medical care). For Pakistan overall, that proportion was estimated to be about 28%. By applying it to the estimated number of women obtaining medical care for induced abortion complications, the researchers calculated that 2.25 million women had induced abortions in 2012. They further estimated that 4.2 million of the nine million total pregnancies in Pakistan that year were unintended.

The national abortion rate for 2012 was 50 per 1,000 women aged 15–49; it ranged from 35 in Khyber Pakhtunkhwa to 60 in Baluchistan. A previous study reported an abortion rate of 27 per 1,000 in 2002, although that study did not include private facilities and thus likely underestimated abortion incidence. Private facilities accounted for 62% of postabortion care cases in 2012. Although no data on private-sector care are available from the earlier study, national surveys indicate that a large increase occurred between 2002 and 2012 in the proportion of births that take place in private-sector facilities, suggesting that a similar trend may have occurred for abortion. That, combined with the relatively small change in the complication treatment rate for public facilities (from 7.3 to 6.0 cases per 1,000 women aged 15–49), leads the researchers to conclude that the abortion rate likely "increased substantially" between 2002 and 2012.

Fifty-four percent of Pakistan's 4.2 million unintended pregnancies ended in induced abortion in 2012, and another 34% (1.4 million) ended in unplanned births. While the unintended pregnancy rate varied little by province, the proportion ending in abortion was much higher in Sindh and Baluchistan (62%) than in Khyber Pakhtunkhwa (40%).

The researchers conclude that the apparent increase in the abortion rate, accompanied by the high level of unintended pregnancy, is consistent with the major changes in fertility and fertility preferences observed over the past decade. These figures, they add, indicate "the very high level of unmet need for contraception and the high level of unwanted childbearing" in Pakistan–and thus the "urgent" need "for policymakers and service providers is to improve access to quality contraceptive services." They point out that despite the private sector's large and expanding role in providing abortions, postabortion care and health care overall, it has yet to become a major provider of contraceptive services.–*H. Ball*

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Bivalent HPV Vaccine Is Efficacious Among Women Older Than 25

The bivalent human papillomavirus (HPV) vaccine, which generates immunity to the cancer-causing types 16 and 18 of the virus, appears to be effective in protecting women older than 25 against infection and precancerous cervical lesions, according to a randomized trial conducted in 12 countries, including several developing nations.[1] An interim analysis from the trial found that women with no history of HPV infection or disease who received all three doses of the vaccine had an 81% reduction in the risk of six-month persistent infection or precancerous cervical

changes associated with HPV 16 or 18, compared with similar women in a control group who received a placebo.[1] Furthermore, the vaccine protected against persistent infection with two other cancer-causing HPV types to which it was not designed to generate immunity. About one in 10 women in both the overall vaccine group and the control group reported a serious adverse event, but very few were related to the vaccine.

Although licensed in some countries for use among older individuals, HPV vaccines are generally aimed at teenagers and young adults. To examine vaccine efficacy among older women, the trial, known as the VIVIANE study, enrolled healthy nonpregnant, non–breast-feeding women older than 25 from Australia, Canada, Mexico, the Netherlands, Peru, Philippines, Portugal, Russia, Singapore, Thailand, the United Kingdom and the United States between 2006 and 2010. Enrollment in the seven-year trial was age-stratified such that approximately 45% of women were aged 26–35, 45% were aged 36–45 and 10% were 46 or older. To explore the vaccine's effects among women previously exposed to the virus and to mirror real-world conditions, the study design specified that up to 15% of women in each age-group could have a history of HPV infection or disease, defined as having had two or more abnormal Pap smears in a row, an abnormal colposcopy, or cervical biopsy or treatment after an abnormal smear or colposcopy.

Participants were randomly assigned to receive the bivalent HPV vaccine (marketed as Cervarix) or a control vaccine on a double-blind basis. Cervical samples were collected for HPV DNA testing every six months and Pap testing every 12 months, and blood samples were collected every 6–12 months to assess levels of HPV antibodies. The interim analysis was performed after all women had completed the 48-month visit. For each group, the investigators computed the rate of HPV 16 or 18 infection lasting at least six months or of precancerous cervical changes (cervical intraepithelial neoplasia of grade 1 or higher, CIN1+); they calculated vaccine efficacy as 1 minus the rate ratio (the rate of events in the HPV vaccine group divided by the rate in the control group).

During the trial, 5,752 women received at least one dose of HPV vaccine or placebo and were included in the total vaccinated cohort; on average, women were 37 years old. At baseline, about one-third in each group tested positive for HPV 16 and a similar proportion for HPV 18; one-fourth had had six or more lifetime sexual partners.

Main efficacy analyses were based on the 4,505 women who received all three planned doses of vaccine or placebo, had normal or low-grade cervical cytology at baseline and had no history of HPV infection or disease; the mean duration of follow-up in this cohort was 40 months. The rate of persistent infection or CIN1+ associated with HPV 16 or 18 was 0.1 cases per 100 woman-years among women in the vaccine group and 0.6 cases per 100 woman-years among those in the control group; the difference translated to an overall vaccine efficacy of 81%. By age-group, efficacy was 84% among 26–35-year-olds and 77% among 36–45-year-olds; there were no cases of persistent infection or CIN1+ among women 46 or older. The vaccine had 94% efficacy against HPV 16 or 18 when assessed by an alternate cytology classification (atypical squamous cells of undetermined significance or greater, ASCUS+). And, in an apparent cross-protective effect, it was 79% and 77% effective against persistent HPV 31 and HPV 45 infections, respectively.

The vaccine also showed efficacy, although to a lesser extent, in supplementary analyses using other cohorts. For example, in analyses that excluded women who had had high-grade cytology or a history of HPV infection at baseline, but included women even if they had missed one or two doses, the vaccine had 74% efficacy against persistent infection or CIN1+ associated with HPV 16 or 18; among all women, regardless of cytology and HPV history, who received at least one dose, the vaccine's efficacy was 44%. In post hoc exploratory analyses restricted to women who had a history of HPV infection at baseline, but included women even if they had missed one or two doses, the rate of persistent infection or CIN1+ associated with HPV 16 or 18 was 1.5 cases per 100 woman-years in the vaccine group and 2.9 cases per 100 woman-years in the control group. Vaccine efficacy for all vaccinated women excluding this subset was 42%—similar to that for all vaccinated women as a whole.

Safety results, assessed among the total vaccinated cohort, showed that a larger proportion of women in the HPV vaccine group than of peers in the control group reported an injection-site reaction when specifically asked about this side effect (85% vs. 67%). Overall, 10% of women in the vaccine group and 9% of those in the control group experienced serious adverse events; however, fewer than 1% of these events in each group were considered to be related to vaccination. Among women who conceived during the study, rates of spontaneous abortions and congenital anomalies were similar in the two groups.

"Adolescent girls before sexual debut will probably continue to be the main priority for population-level, publicly funded [HPV] vaccination programmes," the investigators maintain. However, women continue to acquire new HPV infections during their adult life and may also become reinfected or have reactivation of latent infection, they note. "Our findings lend support [to] the contention that women older than 25 years can benefit from HPV vaccination, including those who have been previously exposed to HPV," they conclude.–*S. London*

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Gains in Education May Explain Decline in HIV Among Ugandan Girls

Trends in HIV incidence among youth in Rakai, Uganda, during a recent 12-year period varied substantially by sex and age, according to a prospective population-based cohort study.[1] Among women aged 15–19, the rate of new infections declined by more than four-fifths during the study period; however, no change was found among women aged 20–24 or among men in either age-group. In addition, school enrollment increased, particularly among 15–19-year-olds, and rates of sexual initiation and marriage generally decreased; medical circumcision increased among males. The majority of the decline in HIV incidence among teenage women, according to the researchers, can be explained by the reduction in sexual initiation, which in turn was related to higher school enrollment.

In the study, Santelli and colleagues analyzed data from 15–24-year-olds who took part in one or more of the nine rounds of the Rakai Community Cohort Study that were conducted between 1999 and 2011. This period—the third decade of the HIV epidemic in

the district—saw implementation of multiple HIV prevention and treatment programs, and came soon after introduction of a new national policy of universal primary education that abolished tuition fees. During community surveys conducted roughly annually, participants completed questionnaires about their demographic, behavioral, reproductive and health characteristics, and provided specimens for HIV and STI testing. The investigators evaluated trends in HIV acquisition and in risk factors; used univariate and multivariate analyses to assess correlations between these trends; and performed decomposition analysis to determine the extent to which various risk factors may have contributed to changes in HIV incidence.

Analyses were based on 22,164 participants aged 15–24 residing in 43 communities. The researchers found that the rate of new HIV infections acquired between survey rounds was consistently higher among female youth (10–16 per 1,000 person-years) than among their male counterparts (6–10 per 1,000 person-years). Over the study period, women aged 15–19 had an 86% reduction in HIV incidence (from 17 to 2 new infections per 1,000 person-years); in contrast, women aged 20–24 and men of either age-group had no change in HIV incidence. Overall, the prevalence of HIV infection fell among females (from 9% in 1999 to 6% in 2011), whereas it remained unchanged among males (2–3%).

Trends in risk factors showed that the proportion of youth enrolled in school increased among all subgroups, but especially among teenage women (from 26% to 59%) and men (from 43% to 66%); similarly, the proportion who had ever had sex decreased among all youth, but the decline was greatest among 15–19-year-old women (from 76% to 50%) and men (from 63% to 41%). The proportion who had ever been married fell among teenage women (from 46% to 24%), teenage men (from 5% to 1%) and men aged 20–24 (from 52% to 37%). Roughly one in six young men had been circumcised early in the study, but more than one in three had been by the end. Among sexually experienced youth, the proportion reporting two or more partners in the past year fell among all subgroups, but especially among 15–19-year-old women (from 11% to 6%) and men (from 39% to 20%). There was minimal change in consistent condom use over the past year with primary and other partners, other than slight increases with primary partners among 15–19-year-old women and 20–24-year-old men; of note, only 7% of women aged 20–24 reported always using condoms with their primary partner at the end of the study period. The prevalence of alcohol use in the past month declined in all groups.

In multivariate analyses, sexually experienced women who were enrolled in school had a lower risk of acquiring HIV than did their nonenrolled counterparts (incidence rate ratio, 0.3); sexually experienced women reporting more than two partners in the past year had a sharply higher risk of HIV than their peers reporting none (6.0). Among sexually experienced males, HIV infection was positively associated with having had more than two partners in the past year (rather than none), having ever been married and having used alcohol in the past month (2.2–5.8).

Decomposition analysis found that 71% of the reduction in HIV incidence among women 15–19 could be attributed to the decline in sexual initiation in this group, while the other 29% could be attributed to decreased acquisition of HIV among those who were sexually experienced. Further analyses indicated that the entire decline in sexual initiation was likely because of increased school enrollment.

The authors acknowledge several limitations of their study. For example, behaviors were self-reported, and the findings may not apply to all of Uganda or to other Sub-Saharan African countries. In addition, the survey did not capture data on school performance and developmental transitions, such as puberty, that may have influenced school enrollment. Nonetheless, the authors comment that their study's results reinforce earlier findings that, for teenage Ugandan women, schooling may have a protective effect against HIV infection. They suggest that increasing access to education may be a key prevention strategy in this setting; however, they add that "the absence of a reduction in HIV acquisition among young adult men and women suggests that multiple HIV prevention efforts with youth are needed to reach the goal of an AIDS-free generation."—*S. London*

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Low Levels of Sexual and Reproductive Health Knowledge Found Among Students in Sri Lanka

A survey conducted in Sri Lanka reveals low levels of sexual and reproductive health knowledge among students aged 16–19.[1] For example, only one in 10 could correctly identify a method of contraception, and fewer than 1% correctly answered all four of the survey's primary sexual knowledge questions. The survey also examined sexual attitudes and behaviors, and found that males were more likely than females to consider sexual relationships acceptable among youth their own age (21% vs. 8%). Just 2% of the adolescents had had sexual intercourse; 57% of these youth had used contraceptives at first sex, and 63% had ever used contraceptives.

The lack of information on the reproductive and sexual health needs of adolescents in Sri Lanka has been highlighted as an area of national concern. To help identify these needs and to inform reproductive health policy, in 2010 researchers conducted the first survey in 10 years to assess the sexual and reproductive health knowledge, attitudes and behaviors of in-school teenagers. Students from randomly selected government schools in Badulla District (an area socioeconomically similar to the rest of the country) were eligible for inclusion if they were aged 16–19, were attending grades 11–13 and had been registered in a state school between July 2007 and June 2009. The self-administered survey, which was completed by 2,020 students (response rate, 90%), included questions on social and demographic characteristics, socioeconomic status, sexual and reproductive knowledge, attitudes toward premarital sex, and sexual behaviors. The researchers computed descriptive statistics and used chi-square testing to identify statistical differences between males and females in sexual knowledge, attitudes and behaviors.

Overall, 26% of the respondents were male and 74% were female, reflecting the sex ratio in state schools. The majority of students were aged 16–17; almost all of the students were Sinhalese (97%) and Buddhist (96%). Nine percent characterized their home environment as poor, most often because of financial difficulties or paternal alcoholism. Levels of parental closeness were high: Nine-tenths of

participants reported being very close to their mother, and two-thirds reported being very close to their father. Although 57% of females and 34% of males identified their parents as their most important source of general support, only 45% of females and 3% of males identified them as their most likely source of support and information concerning sex. About one-third of males and one-fifth of females said they had no one with whom to discuss sexual matters; their most preferred sources of information on sexual issues were health personnel (midwives and public health inspectors; 20%) and doctors (18%).

The four questions that served as indicators of reproductive health knowledge revealed substantial deficits. Fewer than 25% of respondents were aware that it is possible to acquire an STI at first sex, and a similarly small proportion knew that it is possible to become pregnant at first sex. Just one in 10 correctly identified a contraceptive method, and even fewer (6%) could identify a way to prevent STI transmission. Only 0.4% of respondents answered all four questions correctly.

The respondents also fared poorly when asked to identify the phase of the menstrual cycle during which conception is most likely to occur; most said they did not know, and none of those who answered did so correctly. Moreover, although 83% of students had heard of AIDS and 77% of gonorrhea, much smaller proportions had heard of syphilis (22%) and trichomoniasis (7%).

Attitudes toward sex were assessed with questions about the acceptability of various types of relationships. Males were more likely than females to believe that it is acceptable for youth their own age to have relationships that are more than friendship (39% vs. 24%) or to have sexual relationships (21% vs. 8%). Eighty-three percent of young women agreed or strongly agreed that females should be virgins at marriage, and 53% believed that males should be. Among young men, 66% believed that females should be virgins at marriage, while 44% believed that males should be.

Three percent of respondents said they themselves had engaged in some sort of sexual activity; 23% of these youth said the experience had been nonconsensual. Two percent of students indicated that they had had intercourse. Among these respondents, more than half of males reported that they had wanted their first intercourse to occur and were glad it had happened; none of the females expressed similar sentiments, because all felt they had been too young. Contraceptive use at first sex was reported by 57% of sexually experienced respondents, and ever use by 63%.

The authors note several limitations. The results cannot be generalized to adolescents who do not attend state schools or to Sri Lanka's ethnic minorities, who were underrepresented in the survey. Students may have underreported sexual activity. Furthermore, to assuage the anxiety of stakeholders, the most sensitive survey questions were phrased in ways that might have resulted in ambiguity for the respondents (and hence in reporting errors); for example, the phrase "intimate sexual relationship" was used to indicate intercourse. Despite these limitations, the researchers note that their findings indicate an "alarmingly low" level of sexual knowledge among surveyed youth. Given the high degree of school attendance in Sri Lanka, they suggest that the country is well-equipped to provide adequate sex education to the majority of adolescents; the characteristics of effective sex education programs in other developing countries could be used to develop "a more comprehensive and effective programme." The researchers note that greater efforts are needed to provide sexually active students with information, support and access to contraceptives (which in Sri Lanka are typically available only to married individuals), and conclude that to address the needs of adolescents, "it is essential that the [study] findings are translated into concrete action at policy and practice levels."—*L. Melhado*

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Longer Use of Combination Antiretroviral Therapy Associated with Reduced Risk of Cervical HPV

Women infected with HIV may have a lower risk of testing positive for cervical human papillomavirus (HPV) if they have been taking combination antiretroviral therapy (cART) for a longer period of time, according to a prospective cohort study conducted in South Africa.[1] Relative to peers who were not receiving this therapy, study participants who were receiving cART had a reduction of two-thirds in the unadjusted odds of HPV types associated with a high risk of cervical cancer and a reduction of one-half in the unadjusted odds of HPV 16, one of the main cancer-causing types. Although these associations were no longer statistically significant after adjustment for covariates, duration of therapy remained an important indicator of risk: With each additional month that a woman used cART, the adjusted likelihood of testing positive fell by 5% and 6%, respectively, for high-risk types and for HPV 16.

Between November 2009 and October 2011, investigators enrolled in the study nonpregnant, cancer-free South African women who were infected with HIV and had never taken cART. During twice-yearly follow-up visits, the women provided clinical, obstetric and sexual behavior data; underwent a Pap test; and gave blood samples for assessment of CD4 cell count and HIV viral load, and cervical samples for HIV and HPV DNA testing. The investigators used bivariate analyses to compare baseline characteristics between women who did and did not initiate cART, and modeled the probability of detection of HPV using multivariate logistic regression analysis as a function of whether women were on cART at a given visit and of the length of time they had been on this therapy.

The 300 women studied were 35 years old, on average. Overall, 68% initiated cART after meeting the criteria in government guidelines; all were started on a regimen containing a non-nucleoside analogue reverse transcriptase inhibitor, standard practice at the time. About 46% of women who initiated cART and 65% of those who did not were black, and the majority (69% and 80%, respectively) had a partner. Mean duration of follow-up was 19 months among those who initiated cART and 12 months among those who did not. On average, the women who started cART stayed on this therapy for 16 months.

Results showed that 94% of women tested positive for at least one high-risk type of HPV (type 16, 18, 31, 33, 35, 39, 45, 52 or 58) at some time during follow-up, and 42% specifically tested positive for HPV 16. In unadjusted analyses, relative to peers who were not using cART, women who were had a roughly 80% reduction in the odds of testing positive for any type of HPV (odds ratio, 0.2), a 70% re-

duction in the odds of testing positive for any high-risk HPV (0.3) and a 50% reduction in the odds of testing positive for HPV 16 (0.5). Risk fell by 7–9% with each additional month on this therapy.

After adjustment for other factors potentially associated with or affecting HPV acquisition or detection, the associations of cART use with HPV positivity were no longer statistically significant. But risk was still inversely associated with the duration of cART: With each additional month on this therapy, the adjusted odds fell by 4% for any HPV, 5% for high-risk HPV and 6% for HPV 16 (odds ratios, 0.94–0.96 per month).

In other adjusted findings, sexually active women were more likely than other women to test positive for any type of HPV (odds ratio, 1.8) and for HPV 16 specifically (1.8), and the odds of testing positive for any HPV was positively associated with the level of HIV DNA found in cervical cells (1.3). The risk of HPV 16 fell with each month elapsed since excisional treatment of cervical neoplasia (0.96).

Further analysis showed that the reduction in odds seen among women taking cART was smaller for all low-risk types of HPV combined than for HPV 16 (ratio of odds ratios, 1.4). In contrast, the reduction in odds for all high-risk types of HPV combined was statistically indistinguishable from that for HPV 16.

Study strengths included the use of a clearly defined outcome, adjustment for a wide range of variables and assessment of associations with different types and groups of HPV, according to the investigators; limitations included the possible influence of unmeasured confounders and inability to conclude that cervical HIV and HPV are causally related. They speculate that the conflicting results of previous studies of the association of cART with HPV detection may have been due in part to a differential risk reduction seen with this therapy across viral types. Taken together, the study's findings suggest that cART protects against HPV infection "in a time-dependent and immunology-driven manner," according to the investigators. "Reducing cervical HPV co-infection in women living with HIV infection should be seen as one of the many benefits of initiating the combination anti-HIV medication," they conclude.–*S. London*

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Male Circumcision Linked to Reduction In Risk of Syphilis

Circumcision may protect both men and their partners from syphilis, according to an analysis of data from an HIV prevention trial conducted in Uganda and Kenya.[1] During the study's three-year follow-up period, the risk of a new syphilis infection was lower among circumcised men than among their uncircumcised peers (hazard ratio, 0.6), and lower among their partners than among the partners of uncircumcised men (0.4). In analyses that stratified participants by HIV status, circumcision was associated with reductions in syphilis risk among HIV-infected men (0.4), HIV-infected women (0.5) and women without HIV (0.3), though not among men without HIV.

Data from at least three clinical trials have shown that circumcision reduces the risk of HIV acquisition among heterosexual men, and observational studies have suggested that it may also reduce transmission of HPV, herpes and other STIs. At least some of these benefits may extend to women as well. Evidence concerning syphilis transmission is less conclusive, however; although observational studies suggest that circumcision reduces the risk of syphilis, two clinical trials have failed to show protective effects, and no data are available on women.

In the current study, Pintye and colleagues analyzed syphilis data from a prospective clinical trial (the Partners PrEP Study) designed to examine whether pre-exposure therapy reduced the risk of HIV transmission between HIV-serodiscordant partners. All participants received HIV prevention services, including referrals for circumcision, and those randomized to the treatment group received antiretroviral drugs. Participants were recruited from 2008 to 2010 and followed for up to three years; the placebo group was discontinued in 2011 when an interim analysis revealed convincing evidence that outcomes were superior in the treatment group. Throughout follow-up, uninfected partners had monthly counseling visits and infected partners had quarterly visits; testing for syphilis was done annually or at interim visits if clinically indicated.

At enrollment, participants provided information on their demographic characteristics, medical history and sexual behavior in the past 30 days; circumcision status was determined via physical exam at baseline and annually thereafter. The relationship between circumcision and syphilis incidence was assessed using Andersen-Gill survival models that treated circumcision as a time-dependent event (i.e., researchers were able to account for circumcisions that occurred during follow-up). Analyses were conducted separately for men and women by HIV status to examine whether the relationship between circumcision status and syphilis incidence differed by HIV status. All statistical models adjusted for age at enrollment, whether the participant had had unprotected sex in the past 30 days and serum level of HIV RNA in the infected partner; other demographic and behavioral variables were not included in models because they did not have a meaningful impact on odds ratios.

The analytic sample consisted of 4,716 couples; the HIV-infected partner was male in 38% of couples and female in 62%. Median age at enrollment was 36 for men and 30 for women; nearly all couples were married. On average, couples had had sex four times in the past month; one-fourth had had unprotected sex during that time. Men were more likely than women to report having had an outside partner in the past month (14% vs. 1%), though women were more likely to have a curable STI (10% vs. 5%).

Nearly half (46%) of men were circumcised when they entered the study. Compared with their uncircumcised peers, circumcised men had slightly higher levels of education and had more children, and in the past month they were less likely to have had unprotected sex with their partner or to have had sex with an outside partner. They were also less likely to have laboratory-confirmed syphilis (2% vs. 6%) at study enrollment; their partners had a reduced prevalence of infection as well (2% vs. 5%). In multivariate analyses, the odds of syphilis infection at enrollment were reduced among both men and their partners, regardless of HIV status, if the man was circumcised (odds ratios, 0.3–0.5).

During follow-up, 221 new cases of syphilis emerged—122 among men and 99 among women. In multivariate analyses, circumcision was associated with a 42% reduction in the risk of syphilis infection among men (hazard ratio, 0.6). The risk of infection was reduced to an even greater extent among men with HIV (0.4); among men without HIV, the risk reduction fell short of statistical signifi-

cance. Among women, having a circumcised partner was associated with reductions in the risk of syphilis incidence for the full sample (0.4), those with HIV (0.5) and women without HIV (0.3).

Findings were generally similar (though not necessarily statistically significant) in sensitivity analyses that excluded possible cases of treatment failure (i.e., individuals who tested positive after a previous syphilis infection was detected and treated); that excluded cases in which only one partner had a positive syphilis test; or that were restricted to men who were circumcised during follow-up.

Limitations of the study, according to the authors, include that syphilis testing was done annually (unless men had symptoms that warranted interim testing); hence, cases that were treated by outside providers (including cases that were indirectly treated when men received antibiotics for unrelated conditions) may have gone undetected. Moreover, the circumcision status of any outside partners who transmitted the infection to study participants was not known, potentially leading to misclassification. Nonetheless, the authors note that the study is the first to find that circumcision reduces the risk of syphilis infection in men with HIV or among women of any HIV status. "If confirmed," the authors note, the results "suggest that male circumcision could significantly reduce syphilis incidence and related sequelae in both men and their female partners," which would be a particular public health benefit in settings where HIV is highly prevalent.–*P. Doskoch*

REFERENCE

1. Pintye et al., Association between male circumcision and incidence of syphilis in men and women, *Lancet Global Health,* 2014, 2(11):e664–e671, doi: 10.1016/S2214-109X(14)70315-8, accessed Jan. 15, 2015.