Two-Pronged Intervention Increases Uptake
Of Circumcision Among Men in Zambia

A sexual risk reduction intervention increased demand for male adult circumcision, according to a cluster randomized controlled trial conducted in 2012–2014 in Zambia.[1] Men who participated in a program designed to increase the supply of and demand for male medical circumcision were more likely to opt for the procedure by 12 months postintervention than were men in the control group (odds ratio, 2.5). In addition, after circumcision, condom use increased among men in the intervention group, but not among those in the control group, indicating that newly circumcised men did not start engaging in risky behavior that might have nullified the HIV-prevention benefits of the circumcision.

The study was designed to assess the effects of combining increased availability of circumcision with a comprehensive sexual risk reduction and circumcision promotion intervention among men who had little interest in circumcision but were at high risk for HIV. The intervention, called Spear and Shield, is a culturally tailored program that addresses attitudes, beliefs and preferences related to male circumcision.

The researchers recruited 13 urban community health centers in Lusaka District to take part in the trial. Centers were eligible if they had at least 50 HIV voluntary counseling and testing clients each month and had at least five health care providers and counselors available to receive circumcision training and sexual risk reduction training, but did not have trained personnel providing circumcisions on a regular basis. Five centers were randomly assigned to the experimental group, five to the control group and three to an observation-only group. Before randomization, providers at all centers received male circumcision training; after randomization, counselors at the intervention sites were trained to provide the Spear and Shield intervention to eligible clients, while those at the control sites were trained to provide a video-based endemic disease prevention program that focused on cholera, malaria, tuberculosis and waterborne diseases. No changes in services

were instituted at clinics in the observation-only group, and outcomes for those centers are not reported here. Men who underwent voluntary HIV counseling and testing at the intervention or control sites were eligible to participate in the trial if they were 18 or older, uncircumcised and HIV negative; were not requesting circumcision at their current visit; and did not have diseases of the foreskin or penile abnormalities in need of repair.

The Spear and Shield intervention consisted of four weekly 90-minute group sessions that discussed strategies to prevent HIV and other STIs, with an emphasis on circumcision; participants were given opportunities to interact with peers who had undergone the procedure as well as with circumcision providers. The disease prevention program for the control group also included four weekly sessions; in both the intervention and control groups, participants' female partners were invited to attend sessions held specifically for them. In addition, participants in both groups received a week's supply of male condoms, female condoms or both after the first three sessions; after the fourth session, all participants received a month's supply of condoms. At study entry, after completing their assigned program, and at follow-up evaluations six and 12 months later and (when applicable) three months after circumcision, participants completed assessments that included questions on sexual behavior. Circumcisions were verified by clinic record review, provider interviews and voluntary physical examinations. The 800 men who enrolled in the trial were recruited in 2012–2013 and completed follow-up in 2014.

The outcomes of interest were the likelihood of circumcision by 12 months postintervention and trends in condom use after circumcision. In addition to conducting descriptive analyses, the researchers generated Kaplan-Meier curves to show the cumulative incidence of circumcision over time by study group. Multilevel logistic regression was used to compare the odds of circumcision between the experimental and control groups, and a

linear mixed model was used to examine condom use over time among circumcised men.

The mean age of the participants at baseline was 27 (range, 18 to 57). About half were unemployed (51%), and a similar proportion reported an annual income equivalent to less than US$100 (53%). Sixty-six percent had 12 or more years of education, 43% were married or cohabiting, and 39% had at least one child. Most participants (88%) either had never considered circumcision, were not considering undergoing the procedure in the next six months or were considering the possibility of circumcision sometime in the next six months but had not made any decisions; the remainder were planning to undergo the procedure in the next 30 days (12%). A higher proportion of men were unemployed in the control group than in the experimental group, but no other differences in demographic characteristics were apparent by study group.

Overall, 40% of men in the intervention group underwent circumcision during the study, as did 24% of those in the control group. At six months postintervention, the proportions were 27% in the intervention group and 15% in the control group; they were 42% and 24%, respectively, among men who completed 12 months of follow-up. Multivariable regression analysis revealed that men in the intervention group were more likely to have undergone circumcision by 12 months postintervention than were men in the control group (odds ratio, 2.5). The results were similar in sensitivity analyses that included self-reported circumcisions that could not be verified, or that excluded men who had already planned to be circumcised.

Condom use was assessed among circumcised participants who reported sexual activity within 2–3 months of circumcision. At baseline, condom use was lower in the experimental group than in the control group (2.5 vs. 3.5 on a scale ranging from 1 to 5). However, during the 12 months of follow-up, condom use increased among participants in the experimental group at an estimated

rate of 0.06 points per month; condom use among participants in the control group did not change.

The researchers note that their study was limited by the small number of participating clinics (which may affect external validity) and by the fact that only surgical circumcision, rather than new nonsurgical or minimally invasive options, was offered (which may have affected acceptability). Despite these limitations, the researchers suggest that their study lends support to the idea that combined approaches (i.e., behavioral interventions and environmental changes) work synergistically "to achieve outcomes that neither could accomplish by themselves." They conclude that scaling up interventions that simultaneously increase the demand for and availability of circumcision "might be one of the best and most cost-effective ways to significantly affect HIV rates in high-incidence countries."–*L. Melhado*

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Removal of User Fees Associated with Increases In Delivery at Facilities

The removal of user fees in Kenya, Ghana and Senegal resulted in 3.1 additional facility-based deliveries per 100 live births, representing a 5% increase, according to an analysis of Demographic and Health Survey (DHS) data from an array of Sub-Saharan African countries.[1] The estimated increase was smaller than that reported in prior analyses of individual countries, in part because those studies, unlike the current one, did not account for the increases that likely would have occurred even if user fees had still been required. Rates of caesarean delivery did not change following elimination of user fees; neonatal mortality declined by 9%, although the decrease was not statistically significant.

The new analysis used DHS data collected between 1997 and 2012 to examine whether levels of the three outcomes—delivery at a facility, caesarean delivery and neonatal mortality—changed when countries eliminated user fees for facility-based delivery services. Three

countries in Sub-Saharan Africa eliminated some or all such fees during the study period and served as the intervention group: Ghana, which eliminated fees for deliveries at all public, private and faith-based facilities in 2003 (selected regions) and 2005 (elsewhere); Kenya, which removed fees for deliveries at public dispensaries and health centers, but not at hospitals, in 2007; and Senegal, which eliminated fees at public facilities in most of the country in 2005–2006.

The comparison group consisted of a pool of seven countries (Cameroon, Congo, Ethiopia, Gabon, Mozambique, Nigeria and Tanzania) that did not change their delivery fee policies. Although three of these countries had existing policies that exempted women from paying fees for maternity care, these exemptions were not widely known and were rarely enforced. In addition, because changes in fee policies in Ghana and Senegal were implemented in stages, women who gave birth during the transition period before fees were eliminated in their region of residence were included in the comparison group.

To assess the relationship between removal of user fees and the three outcomes, the researchers used difference-in-differences regressions, which examined whether outcomes changed to a greater extent in countries with policy changes than in those without. All analyses adjusted for women's characteristics (age, area of residence, education, wealth and whether the woman had given birth previously), area fixed effects (which take into account regional characteristics) and year fixed effects (to account for time trends). In addition, to ensure appropriate comparisons, the investigators adjusted the make-up of the comparison groups for each outcome so that trends in the outcome were similar in the intervention and comparison groups prior to the removal of policy fees. For example, the comparison group for caesarean delivery excluded Nigeria, where the rate of such deliveries declined at an unusually high rate in 1995–2003; after that exclusion, the six remaining comparison countries and the three intervention countries had statistically similar rates of change in caesarean delivery levels prior to the fee removals. They also examined change levels by year to see if patterns (e.g., lags in improvements) were consistent with implementation of a new policy.

The difference-in-differences analysis of facility deliveries yielded an average marginal effect of 3.1, which can be interpreted

as indicating that removal of fees was associated with an additional 3.1 deliveries per 100 births, after adjustment for covariates. This represented a 5% relative increase in the proportion of deliveries that occurred in facilities.

Fee exemptions were also associated with an estimated reduction in neonatal mortality of 2.9 deaths per 1,000 births (a 9% relative decrease), although the change fell short of statistical significance. No change was apparent in the level of caesarean deliveries. The associations between covariates and the three outcomes were consistent with findings from prior studies: First births, education level, urban residence and wealth were positively associated with facility deliveries and caesarian deliveries; first births were positively associated, and education and wealth were negatively associated, with neonatal mortality.

Because prepolicy trends in the three outcomes were more extreme in Senegal than in the other two countries that removed user fees, the researchers also conducted sensitivity analyses to examine whether data from Senegal were driving the results. One analysis revealed that removal of user fees in Ghana and Kenya resulted in 3.8 additional facility deliveries per 100 live births; another indicated that the policy change in Senegal reduced the rate of neonatal mortality by 4.3 deaths per 1,000 live births. In both analyses, the set of comparison countries was adjusted so that the parameters of the main analyses were met (i.e., prepolicy trends had to be similar in intervention and comparison countries); in each case, the result was statistically significant.

Finally, the analysis of potential lag effects found that the increase in facility deliveries was greater in the year after implementation than in the year of implementation, suggesting, according to the researchers, that "the policy change took some time to be fully implemented, which is a plausible scenario for a large national-scale program."

The investigators noted that the estimated increase in facility-based deliveries was smaller in their study than in prior studies (3.1 vs. 5–12 per 100). However, those studies, which focused on single countries, simply compared pre- and postpolicy levels and did not account for existing trends (and hence for increases in facility deliveries that likely would have occurred even without the elimination of user fees). If the current study had used that approach, it would have found statistically significant changes in all three outcomes—8.6 additional facility deliveries per 100 births, 1.3

additional caesarean deliveries per 100 births and 9.5 fewer neonatal deaths per 1,000 live births.

Limitations of the study, according to the authors, include its reliance on self-reported data and the lack of consistency in fee removal policies among countries. Nonetheless, the findings suggest that eliminating user fees "led to substantial increases in facility-based deliveries" and were consistent "with a meaningful reduction in neonatal mortality." Even after fees were eliminated, however, the proportion of births that took place in facilities was still less than 60%, indicating that other barriers—such as geographical access, transportation costs and cultural barriers—"need to be simultaneously addressed in efforts to reduce maternal and neonatal mortality."
—*P. Doskoch*

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Parental HIV Status Linked to Sexual Debut In Sub-Saharan Africa

Adolescents in Sub-Saharan Africa who live in HIV-affected households are more likely than their peers to initiate sexual activity.[1] According to an analysis of Demographic and Health Survey (DHS) data collected in 2003–2008 from 19 countries, adolescents aged 15–17 who lived with at least one HIV-positive adult had 27% higher odds of having ever had sex than did adolescents who were not living with an HIV-positive adult (odds ratio, 1.3). However, unlike some prior research, the study did not find that orphans have an elevated risk of sexual activity, once poverty level and other household circumstances are taken into account.

Although considerable research has examined the vulnerabilities of children orphaned by AIDS, much less attention has been paid to those of children living with an HIV-positive household member. To address this gap in the literature, the researchers analyzed DHS data from 19 of the 21 Sub-Saharan countries with HIV-test data from 2003 to 2008 (the other two countries were excluded for technical reasons). Like all DHS surveys, these collected information from nationally representative samples of men and women of reproductive age; the current analysis was restricted to 22,620 adolescents aged 15–17.

In addition to questions on social and demographic characteristics, respondents were asked about their maternal and paternal orphanhood status; whether they were enrolled in school; their level of media exposure; the household's possessions and amenities (from which information the DHS estimates household wealth); the sex of, the age of and their relationship to the household head; and whether they had ever had sex. Results of HIV tests administered to household members were used to classify adolescents according to whether they lived with an HIV-positive adult. The researchers constructed multilevel logistic regression models to assess the associations, stratified by sex, of living with an HIV-positive adult and of maternal or paternal orphanhood with the initiation of sexual activity.

Overall, 11% of respondents lived with an HIV-positive adult, though the proportion varied widely, ranging from 2% in Ethiopia to 44% in Swaziland. In the 10 countries for which data on orphanhood were available, 7% of respondents were maternal orphans; the proportion was lowest in Liberia (4%) and highest in Zimbabwe (17%). The proportion of adolescents who were paternal orphans was 13% in the pooled sample, and ranged from 11% in Liberia to 34% in Lesotho.

Thirty-two percent of adolescent females and 25% of adolescent males had ever had sex. Again, these proportions varied considerably across countries. For example, in Rwanda, 9% of females aged 15–17 had ever had sex, while this was true for 60% of their counterparts in Liberia. For males, the proportion was lowest in Ethiopia (3%) and highest in Côte d'Ivoire (52%).

In multilevel logistic regression analyses that adjusted for household circumstances (household wealth, adolescent's relationship to head of household, and age and sex of household head) and other covariates, young women who lived with an HIV-positive adult had elevated odds of having had sex (odds ratio, 1.3). In addition, age was positively associated with having had sex (2.0 per year), while young women had reduced odds of having had sex if they were attending school (0.4), were Protestant rather than Catholic or orthodox (0.8), were not the head of their household (0.02–0.04), were in the richest wealth quintile rather than the poorest (0.7) or lived in a household in which the head was younger than 25 rather than aged 25–59 (0.8).

For males, the results of the regressions typically mirrored those for females. Age and living with an HIV-positive adult were associated with elevated odds of having ever had sex (odds ratios, 1.8 and 1.2, respectively), while being in school, not being a head of household and being in the richest wealth quintile were associated with reduced odds of having had sex (0.4–0.6). In addition, as levels of education and media exposure increased, so did the odds of males' being sexually experienced (1.4–1.9); living in a household with a head who was aged 60 or older was also associated with elevated odds of having had sex (1.2). Although in intermediate regression models, paternal orphanhood was positively associated with males' having had sex, the association was not significant when the authors adjusted for household circumstances.

Finally, regressions run on the full sample yielded results similar to those for males, albeit with some slight differences in odds ratios. The odds of having had sex were 27% greater among adolescents in households with an HIV-positive adult than among youth in other households (odds ratio, 1.3). In addition, being female was associated with elevated odds of having ever had sex (1.2), while being a maternal orphan was associated with reduced odds (0.8).

The researchers acknowledge several limitations. First, the data were cross-sectional; therefore, it was not possible to determine the temporal ordering of household HIV status and adolescent sexual debut. Second, orphanhood data were available for only about half of the included countries; however, supplemental analyses indicated that inclusion or exclusion of the orphanhood variable did not affect the other estimates. Finally, data limitations precluded exploration of regional- or country-level associations. Despite these limitations, the researchers conclude that their findings support the argument that adolescents in HIV-affected households are vulnerable to sexual initiation and underscore "the importance of extending current efforts in the region to address the plight of other children in HIV/AIDS–affected households, beyond orphans."–*L. Melhado*

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Decline in Unmet Need Is Not Main Reason for Rise In Contraceptive Prevalence

Although contraceptive prevalence has increased substantially in Sub-Saharan Africa during the past two decades, for the most part the gains have not been driven by a decline in unmet need, according to an analysis of Demographic and Health Survey (DHS) data.[1] Examining trends in 22 countries that had multiple DHS surveys between 1990 and 2011, the investigators found that, on average, contraceptive prevalence rose by 13 percentage points—from 17% to 30%—between a country's first and most recent surveys. However, the proportion of women with unmet need fell by a mean of only four percentage points, a decline smaller than the simultaneous decrease in the proportion of women with no need (e.g., those wanting more children soon).

Few studies have examined longitudinal changes in unmet need and lack of need among cohorts of women. However, Madsen and colleagues note that DHS data offer a useful substitute. Because the surveys in a particular country are typically administered about five years apart, one can use consecutive surveys to track changes in contraceptive use and nonuse among five-year cohorts of women; for example, a random sample of 25–29-year-old woman in a given survey will draw from the same pool of women as a sample of 20–24-year-old women in the previous survey, simulating a longitudinal cohort study.

The current study used this approach to analyze DHS data collected between 1990 and 2011 from 22 countries in Sub-Saharan Africa. All countries had at least two surveys during that period, and most had four; in nearly all cases, the earliest survey for a particular country was conducted before 1998 and the most recent after 2005. For each survey, women aged 15–49 who were married or in a union were categorized, according to standard DHS definitions, as either being contraceptive users, having unmet need, having no need or being infecund.

The investigators examined trends in these four categories in two ways. First, they performed period analyses to assess changes in the prevalence of the categories among women in each five-year age-group (e.g., whether the prevalence of contraceptive use, unmet need, no need and infecundity among 20–24-year-olds in a country's first survey differed from the prevalence among 20–24-year-olds in subsequent surveys). These analyses included both descriptive and regression analyses.

Second, as noted earlier, the investigators performed cohort analyses in which women in each five-year age-group were assumed to represent the same population as the next oldest five-year age-group in the following survey. Although the mean interval between surveys was, in fact, about five years, 21% of surveys were either less than four years apart or more than 6.5 years apart. Nonetheless, the authors retained these outliers in order to maintain comprehensive coverage and adequate sample size; supplementary analyses indicated that retention of the full sample did not meaningfully affect the results.

Period analyses revealed that, on average, contraceptive prevalence in a given country rose by 13 percentage points (from 17% to 30%) between a country's first and last surveys (mean interval, 14 years). At the same time, countries had mean declines of four percentage points in the proportion of women with unmet need, five points in the proportion with no need and four points in the proportion who were infecund. Consistent with these findings, a multiple linear regression model more closely linked the increase in contraceptive prevalence to a decline in lack of need (coefficient, –1.25) than to a decline in unmet need (–1.08).

Period analyses by age-group revealed that increases in contraceptive prevalence were largest (12–14 percentage points) among women aged 20–44 and smallest (nine percentage points) among women aged 15–19 or 45–49. The pattern was similar for the decline in unmet need, which was largest among women in the middle age-groups (4–6 percentage points among women aged 25–39) and smallest among the youngest and oldest women. In contrast, declines in the proportion of women with no need were greatest among younger women (5–8 percentage points among women aged 15–29), and declines in infecundity were greatest among women 35 or older (6–9 points).

The cohort analysis was restricted to the four youngest age-groups (women aged 15–34 at the earliest surveys), because women in older cohorts aged out of DHS surveys too quickly to allow analysis of long-term trends.

Between the first and last surveys, women aged 15–19 and 20–24 at baseline had substantial increases in contraceptive use (23 and 18 percentages points, respectively); these increases were made possible by substantial reductions in the proportions of women with no need (22 and 21 points), rather than by the small declines in the proportion with unmet need (3 and 2 points). Increases in contraceptive use were smaller among women aged 25–29 and 30–34 (14 and six points), but again these gains were likely attributable to decreases in the proportions of women with no need (23 and 26 points); the declines in unmet need were much smaller (four and eight points). Not surprisingly, the prevalence of infecundity rose slightly in the two youngest cohorts (by 2–5 points) and to a much larger extent in the two older ones (by 13–28 points).

Cohort analyses for individual countries generally matched those for the full sample. In all 22 countries, declines in the proportion of women with no need exceeded declines in the proportion with unmet need among women aged 20–24 at baseline; in 19 countries, the same was true among women aged 30–34 at baseline.

Additional DHS data indicated that intention to use contraceptives—one of the strongest predictors of future use—rose substantially (by 16 percentage points) between the first and last surveys among women with no need, but barely increased (by three points) among women with unmet need.

The researchers note that the large declines that have occurred in the proportion of young married women with no need suggests that "efforts to expand the acceptability of, access to and use of family planning are succeeding among young women"—individuals who in the past typically would have had no need for contraceptives because they wanted children soon after marrying. However, the relatively minor progress that has occurred in reducing levels of unmet need—or in increasing intention to use contraceptives among those with unmet need—suggests that programs need to do more to "address the complex and multifaceted reasons" for nonuse, including "health-related concerns" such as side effects.—P. Doskoch

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Nurses in Mexico Provide Safe, Successful Medication Abortions

Nurses can provide early medication abortion as well as physicians, according to a randomized controlled noninferiority trial conducted at three Ministry of Health facilities in Mexico City.[1] Virtually all of the medication abortions provided by nurses and physicians were successful (98% and 99%, respectively), and only 10% of women needed surgery or additional medication to complete the procedure. Regardless of the type of provider they used, the vast majority of women received a prescription for contraceptives (99%), and 97% of them left the facility with a method; 99% of women were comfortable with their nurse or physician.

Although abortion was legalized in Mexico City in 2007, demand for the procedure has exceeded the capacity of physicians to provide it. Allowing midlevel providers to perform abortions may help increase availability. To examine whether nurses' medication abortion care was comparable with that of physicians, the researchers conducted a randomized trial from November 2012 to January 2013 at two clinics and a hospital that collectively provided half of legal abortions in Mexico City. Women with a gestational duration of up to 70 days who were seeking an abortion were eligible if they were at least 18 years old; had never had a legal medication abortion and were willing to undergo one; had no medical history of contraindications for the procedure; and provided their social and demographic characteristics and follow-up contact information. Some 1,017 women were randomized; the 884 who returned for follow-up were included in the primary (intention-to-treat) analysis and received abortion care from either a physician (450) or a nurse (434).

The two provider groups comprised seven nurses and eight physicians who had never provided a medication abortion or had done so only under supervision. Each group was trained in medication abortion provision and related skills, such as abdominal and transvaginal ultrasound, for about two weeks.

Women had similar characteristics across provider groups. Two-thirds were aged 20–29, about half were single and four in 10 had attended at least some high school or technical school. Roughly equal proportions were students (25%), homemakers (29%) or workers (33%). The average duration of gestation was 50 days. At women's first visit, per Ministry of Health guidelines, providers performed an ultrasound to assess gestational age, had women take a 200-mg dose of oral mifepristone and gave them 800 mg of misoprostol to take at home after 24 hours. To help women avoid having an unwanted pregnancy in the future, providers also presented several postabortion contraceptive options for women to consider.

Follow-up visits took place one to two weeks later. In addition to verifying that the abortion was complete (via ultrasound, a symptom checklist and questions about women's bleeding history), providers offered women their chosen contraceptive method, if any, or told them where it was available. Women then completed a survey assessing their satisfaction with their care. In some cases, women required manual vacuum aspiration or more medication (800 mg misoprostol) to complete the abortion; nurses chose to administer additional misoprostol more often than physicians (10% of cases vs. 5% of cases).

Nurses and physicians alike achieved high success rates: Among women treated by physicians, 99% had a medication abortion with no follow-up surgery, as did 98% of women treated by nurses. The difference in rates was well within the preset noninferiority margin of 5%. When the analysis was limited to women who completed treatment according to study protocols, the results confirmed that nurses were as competent as physicians in their management of medication abortion care (98% vs. 99% success rates).

Similar proportions of women received a prescription for contraceptives from physicians and nurses (99% in each group); most women chose the pill, the IUD or the injectable. At the follow-up visit, almost all women in both groups received one or more methods (97% of each group), but a higher percentage of women in the physicians' group than of their counterparts in the nurses' group obtained an IUD (31% vs. 24%), while women in the nurses' group were more likely than those treated by physicians to receive condoms (19% vs. 11%) or emergency contraceptive pills (2% vs. 0%). Three-quarters of women in each group were very satisfied with their care; nearly all felt comfortable with their nurse or physician (99%) and had confidence in their technical skills (99%).

While nurses performed as well as physicians in all aspects of medication abortion management, contraceptive counseling and method provision, the researchers explain that nurses may have preferred to take a conservative approach toward treating possibly incomplete abortions, and therefore prescribed an extra dose of misoprostol more frequently than did physicians. Because nurses tended to give their patients the methods they routinely offered during their regular duties (i.e., condoms and emergency contraception), the researchers recommend that nurses be trained in IUD insertion to increase their confidence in prescribing and providing this method. Potential study limitations include the possibility that nurses consulted physicians at their facility, thus "contaminating" the results. However, the authors note that discussions between participating nurses and physicians were unlikely, since the two types of providers were working in separate rooms, and add that any impact on the study would have been mitigated by the benefits of having had all providers work under the same conditions. Overall, they conclude, the findings are consistent with those of previous studies that assessed midlevel providers' performance of tasks traditionally limited to physicians, and indicate that nurses can successfully augment physician provision of medication abortion care in Mexico and "help address the high demand for safe abortion" in the country. —S. Ramashwar

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In Pakistan, Poor and Rural Women Must Travel Farther To Give Birth in a Facility

Poor and rural women in Pakistan are disadvantaged in terms of their access to institutional delivery services, according to a geographic analysis of data from nine districts.[1] On average, married women who reported giving birth within the past three years lived seven kilometers by road from the nearest health facility offering delivery care; the average distance ranged from five kilometers among the wealthiest women to 10 kilometers among the poorest. Women's odds of delivering in a facility decreased by 3% per additional kilometer

of distance from the nearest facility, although this association held only in rural areas. Living within 10 kilometers of a facility offering basic or comprehensive emergency obstetric care was positively associated with institutional delivery (odds ratios, 1.8 and 1.7, respectively).

To examine relationships between geographic and economic access to a health facility and institutional delivery, researchers linked survey data for individual women and health facilities in study districts with data on distance between the primary sampling unit of women's residence and health facilities in those districts. The individual data were drawn from a 2005 survey that asked married women in selected households in primary sampling units about their health care before, during and after delivery, as well as about their social and demographic characteristics. Household wealth was measured in quartiles (lowest, lower middle, upper middle and highest) on the basis of such criteria as ownership of certain household amenities and types of construction materials used for the household's dwelling. The sample of women was restricted to the 4,435 women who reported giving birth in the past three years.

Facility data were drawn from a 2008 survey of all health facilities, ranging from large public teaching and district hospitals to private registered clinics and community pharmacies. A structured questionnaire was used to ask individuals in charge of facilities about the type and level of available reproductive health care; it included questions about staff, equipment and client amenities. The sample included all 763 facilities that offered obstetric care services before 2005. Of those, 547 were considered able to provide only "normal delivery" care (i.e., assisted vaginal delivery in a health facility that lacked an operating room), 91 could also provide "basic emergency obstetric care" (assisted deliveries, manual extraction of the placenta and removal of retained products) and 125 could further provide "comprehensive emergency obstetric care" (cesarean sections and blood transfusions).

In addition, as part of the individual and health facility surveys, the exact locations of primary sampling units and facilities were determined using global positioning system (GPS) devices. The researchers used the GPS data to create georeferenced digital maps that included health facilities, district and subdistrict boundaries, rivers and roads, and then used global information system software to calculate exact road distances between prima-

ry sampling units and health facilities within each district. Two measures of geographic access to services were created: the distance from each primary sampling unit to the nearest health facility, and the highest level of delivery care within 10 kilometers of each primary sampling unit. Multilevel mixed-effects logistic regression analyses were conducted to examine associations between geographic access, wealth status and institutional delivery.

Most women (84%) lived in a rural area; 20% lived in households in the lowest wealth quartile, 24% in the lower middle, 27% in the upper middle and 29% in the highest. On average, the primary sampling unit in which women lived was seven kilometers from the nearest health facility offering delivery care. Twenty-eight percent of women lived within 10 kilometers of a facility offering only normal delivery care, 14% within 10 kilometers of a facility offering basic emergency obstetric care, and 37% within 10 kilometers of a facility offering comprehensive emergency obstetric care; the remaining 21% of women lived more than 10 kilometers from a facility.

Overall, the distance between a woman's place of residence and the nearest district health facility was smaller among wealthier women than among poor women. The average distance to a facility ranged from five kilometers among the wealthiest women to 10 among the poorest; 88% percent of the wealthiest women lived within 10 kilometers of a health facility, compared with 62% of the poorest. Geographic access to a health facility also varied by urban or rural residence. The average distance to a facility was eight kilometers in rural areas and only one kilometer in urban areas. In addition, although 75% of rural women lived within 10 kilometers of a facility, only 27% lived that close to comprehensive emergency obstetric care; in comparison, all urban women lived within 10 kilometers of a facility, and 85% lived that close to the highest level of care. The difference in geographic access to health facilities by wealth held in rural areas, but not urban ones: For rural women, the average distance to the nearest facility ranged from six kilometers in the highest wealth quartile to 12 in the lowest, whereas for urban women, the average distance to the nearest facility was similar across wealth quartiles (1.1–1.6 kilometers).

Thirty-two percent of women reported that their most recent delivery had occurred in a health facility, while 68% had delivered at home. In multilevel regression analyses,

the odds of institutional delivery decreased by 3% per kilometer from the nearest health facility (odds ratio, 0.97); in separate analyses by rural and urban residence, this association was significant only among rural women (0.98). Women who lived within 10 kilometers of a facility offering basic or comprehensive emergency obstetric care had greater odds than women who lived further than 10 kilometers from any health facility of delivering in an institution (1.8 and 1.7, respectively); no association was found between living within 10 kilometers of a facility offering only normal delivery services and institutional delivery. Increased wealth and education were independently and positively associated with institutional delivery in all multilevel regression models (odds ratios, 1.3–4.5).

The authors acknowledge several limitations of their study, including that their measures of geographic access were based on distances to health facilities within a district, and that they lacked information on travel cost, travel time and quality of care. Even so, the findings suggest that geographic distance, poverty and low education are all barriers to Pakistani women's use of institutional delivery services, especially in rural areas. The authors conclude that the "disadvantages can be minimized by upgrading existing facilities at district and subdistrict levels to provide comprehensive emergency care and by expediting the transport of poor rural women to these facilities when life-threatening childbirth complications occur."–*J. Rosenberg*

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Poor User Adherence May Explain Lack of Efficacy In HIV Prophylaxis Trial

Daily prophylactic treatment with one of three tenofovir-based regimens did not reduce the risk of HIV acquisition among women at high risk for the infection, according to a randomized, placebo-controlled trial conducted in South Africa, Uganda and Zimbabwe.[1] Failure to follow the treatment protocol may have contributed to the lack of efficacy: Although the mean rate of adherence was 86−90% (depending on the method of assessment), teno-

fovir was detected in only 25–30% of plasma samples from a random sample of participants assigned to one of the intervention regimens.

Several randomized trials have found pre-exposure prophylaxis with oral or topical tenofovir to be effective in reducing the risk of HIV acquisition, though none of them focused on women of reproductive age. While those studies were in progress, researchers initiated a randomized, placebo-controlled trial to compare the effectiveness of oral tenofovir with that of topical tenofovir in preventing HIV infection and to assess the safety of the treatments.

Women aged 18–45 at 15 sites in the three study countries were eligible for the trial if they had had vaginal intercourse in the prior three months; were using an effective contraceptive (hormonal method, IUD or sterilization); had normal kidney, hematologic and liver function; and were neither pregnant (or planning to become pregnant in the next two years) nor breast-feeding. Participants were randomly assigned to one of five regimens: 300 mg oral tenofovir and a placebo; oral tenofovir-emtricitabine (300 mg tenofovir and 200 mg emtricitabine) and a placebo; two placebos; vaginal 1% tenofovir gel; or vaginal placebo gel. Participants were instructed to use the products every day, and were provided with HIV risk-reduction counseling, adherence counseling, hepatitis B immunization and condoms. HIV testing was performed monthly, and testing for other STIs was done at enrollment and annually thereafter (or if necessary). Other monitoring included monthly interviews and pregnancy testing, quarterly tenofovir plasma testing and biannual pelvic examinations. Adherence was assessed monthly through interviews and in-clinic counts of empty pill bottles, unused pills or unused vaginal applicators, and every three months via audio computer-assisted self-interview (ACASI); the latter was also used to assess participants' condom use and sexual practices. Study products were withheld (temporarily or permanently) if women became pregnant, started breast-feeding, or had adverse effects or a positive HIV test.

Women were followed for 12–36 months.

However, mean follow-up was only slightly more than a year, as the trial was terminated ahead of schedule (in 2012) because of lack of intervention efficacy. Analyses included Cox proportional-hazard models (to assess time to HIV seroconversion), Kaplan-Meier plots (to estimate the cumulative probability of infection), generalized-estimating-equation models (to identify characteristics associated with tenofovir detection) and Cox regression analyses (to identify characteristics associated with HIV acquisition and assess the association between tenofovir detection and HIV acquisition).

In all, 5,029 women enrolled in the trial. Participants were similar across the five study groups: Their mean age was 25, 21% were married, 92% had at least some secondary education, 85% reported condom use at last sex and 71% used an injectable for contraception. On average, women had had 1.5 live births, and they had had 2.5 episodes of vaginal sex in the week before enrollment. Ninety-one percent of participants remained in the study until their final scheduled visit; overall, the study yielded 5,509 person-years of follow-up. Across groups, the mean rate of adherence was 86% when assessed by remaining product count, 90% when assessed in face-to-face interviews and 88% when assessed by ACASI.

The incidence of HIV infection was 5.7 per 100 person-years, and was particularly high among women who were younger than 25 (8.0 per 100 person-years) or unmarried (7.2 per 100). The effectiveness of oral tenofovir was −49.0%, meaning that the risk of infection was 49% greater among women receiving this regimen than among women receiving placebo (hazard ratio, 1.5), though the association was only marginally significant. Infection rates in the oral tenofovir-emtricitabine and the vaginal tenofovir gel groups did not differ from those in the respective placebo groups.

In a randomly selected subcohort, tenofovir was detected in only 30% of quarterly plasma samples from the oral tenofovir group, 29% of samples from the oral tenofovir-emtricitabine group and 25% of samples from the vaginal tenofovir gel group. Moreover, 58% of

participants in the oral tenofovir group, 50% of those in the oral tenofovir-emtricitabine group and 57% of those in the vaginal tenofovir gel group had no tenofovir detected in any quarterly plasma sample.

After adjustment for study site, the baseline characteristics associated with tenofovir detection were being older than 25 (odds ratio, 1.6), being married (2.2), having an independent income (1.4) and having more than one child (1.8). Some supplementary analyses suggested that HIV risk was reduced among participants with better adherence; for example, vaginal tenofovir gel users who had detectable levels of tenofovir at their first quarterly visit were less likely to acquire HIV than were those without detectable levels (hazard ratio, 0.3). Finally, the risk of adverse effects was similar across study groups, with the exception that mildly elevated serum creatinine levels were more common among women in the oral tenofovir-emtricitabine group than among those in the oral placebo group (1.3% vs. 0.2%).

The researchers note that although the lack of efficacy seen in the study contrasts with the findings of most previous trials, it is consistent with results of another trial in which user adherence was low. They add that a limitation of the study is that they were unable to measure or control for women's likelihood of HIV exposure, and that this likelihood may have differed between women who used the study products and those who did not. They suggest that the lack of both efficacy and adherence has "implications for biomedical prevention research" and "for the implementation of interventions with proven efficacy"; in particular, the results "reaffirm the need for effective and acceptable prevention interventions for women at high risk for sexual acquisition of HIV-1 and suggest that more accurate measures are critical for the estimation of product use during biomedical HIV-1–prevention trials."–*L. Melhado*

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