SUPPLEMENTAL DIGITAL CONTENT

A. Weight Estimation

1. Treatment weights corresponding to the probability of HC use at t-1

The denominator of the HC use weight is a product of three pooled logistic regression models for the probabilities of using each type of HC (COC, POP, injectable) at a given visit. The common predictors of HC use in these models are the time-fixed covariates measured at baseline and age category, number of days since baseline, STI status before the current visit, last reported HC type, diaphragm use frequency, condom use frequency, new sexual partner and coital frequency before the current visit. For each of the last five covariates, we also added an interaction of the covariate value with the number of days since it was last measured.

There were 20 participants missing some of the time-fixed covariates; their missing covariates are imputed and a binary indicator for each imputed covariate is used in the model to account for possible uncertainty in the covariate values. Missing education was imputed using multinomial model with study site as predictor; missing housing and number of life-time partners are each imputed using site, education and age as predictors; missing risk and partner risk are imputed using all other baseline characteristics except housing (for some of which are missing); baseline sex frequency, condom use and diaphragm use are each imputed using baseline HC use and all baseline characteristics except housing, risk and partner risk (for some of which are missing).

For the binary POP model, the current COC use status is also included; for the injectable model, the current POP and COC uses are also included. For the overall effect of HC use, the numerator is the marginal distribution of the HC type. For the effect modification analysis, the effect modifier of interest is included as a predictor in both the numerator and denominator of the weights. When the effect modifier is baseline HSV-2, we only consider patient-visits with t>1 to ensure that the effect modifier proceeds the treatment of interest.

2. HC availability weights corresponding to the probability of not missing HC data at t-1

Some patients have missing HC data due to missed visits or interview error. There are a total of 36084 patient-visits in the analysis including 2997 (8.3%) patient visits with missing HC data. Of these, 2934 (98%) are due to a missing visit.To adjust for potential bias we included a second set of weights for availability of HC data. We used a pooled logistic regression model for the probability of not missing HC data at a given visit, with independent variables the time-fixed covariates, the number of days since follow up, age category, number of missing HC reports thus far and number of missing visits thus far. These weights are stabilized by the marginal distribution of HC availability in the overall effect analysis. For the effect modification analysis, the effect modifier of interest is included as a predictor in both the numerator and denominator of the weights.

2. Censoring weights corresponding to the probability of not having been censored by time t.

To adjust for potential bias due to right censoring, a third set of weights are included. The probability of not having been censored by visit t is a product of the three probabilities: not using implant t-1, not becoming pregnant by t-1, and remaining in the study by t. Each of these probabilities is estimated by first fitting a model for instantaneous risk and then multiplying those risks through visits up to either t-1 or t, correspondingly. The model for probability of reporting implant use at a given visit, conditional on observed

history, is the same as that for the three main HC types. The model for not becoming pregnant at a given missed visit is the same; but at a given realized visit, HC use, new sexual partner, coital frequency, condom use frequency and diaphragm use frequency reported at that visit is also included in the model (some patients fail to report some of these covariates, in which case they are imputed and imputation indicators are included to adjust for uncertainty in their values). The model for remaining in the study at any given visit uses predictors variables the time-fixed covariates, the number of days since follow up, age category, number of missing visits thus far, and the STI status at previous visit. The numerators for these censoring weights are the marginal distributions (or conditional on effect modifier, in the case of effect modification) of the corresponding dependent variables.

B.Nonparametric Bootstrap Percentile Method

A bootstrap sample is generated by sampling with replacement n=4913 patients (and all their visits) from the study population. For each bootstrap sample, we reran the imputation procedures for some missing predictor values in the models, and refit the weight models and the MSM to obtain a bootstrap HR estimate. We repeat this procedure 10000 times to obtain a boostrap distribution for the original HR estimates. The 95% CI of an estimate is given by the 2.5 and 97.5 percentiles of the bootstrap distribution.