

Incentivising safe sex: a randomised trial of conditional cash transfers for HIV and sexually transmitted infection prevention in rural Tanzania

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ABSTRACT

Objective: The authors evaluated the use of conditional cash transfers as an HIV and sexually transmitted infection prevention strategy to incentivise safe sex.

Design: An unblinded, individually randomised and controlled trial.

Setting: 10 villages within the Kilombero/Ulanga districts of the Ifakara Health and Demographic Surveillance System in rural south-west Tanzania.

Participants: The authors enrolled 2399 participants, aged 18–30 years, including adult spouses.

Interventions: Participants were randomly assigned to either a control arm (n=1124) or one of two intervention arms: low-value conditional cash transfer (eligible for \$10 per testing round, n=660) and high-value conditional cash transfer (eligible for \$20 per testing round, n=615). The authors tested participants every 4 months over a 12-month period for the presence of common sexually transmitted infections. In the intervention arms, conditional cash transfer payments were tied to negative sexually transmitted infection test results. Anyone testing positive for a sexually transmitted infection was offered free treatment, and all received counselling.

Main outcome measures: The primary study end point was combined prevalence of the four sexually transmitted infections, which were tested and reported to subjects every 4 months: *Chlamydia trachomatis*, *Neisseria gonorrhoeae*, *Trichomonas vaginalis* and *Mycoplasma genitalium*. The authors also tested for HIV, herpes simplex virus 2 and syphilis at baseline and month 12.

Results: At the end of the 12-month period, for the combined prevalence of any of the four sexually transmitted infections, which were tested and reported every 4 months (*C trachomatis*, *N gonorrhoeae*, *T vaginalis* and *M genitalium*), unadjusted RR for the high-value conditional cash transfer arm compared to controls was 0.80 (95% CI 0.54 to 1.06) and the adjusted RR was 0.73 (95% CI 0.47 to 0.99). Unadjusted RR for the high-value conditional cash

ARTICLE SUMMARY

Article focus

- Existing prevention strategies have had a limited impact on the trajectory of the HIV/AIDS epidemic.
- Conditional cash transfers have been used successfully in a variety of settings to promote activities that are beneficial to the participants, such as school participation or health check-ups for children.
- This trial asks whether conditional cash transfers can be used to prevent people from engaging in activities that are harmful to themselves and others, such as unsafe sex.

Key messages

- We designed and evaluated a novel intervention that tests for risky sexual behaviour repeatedly over short time intervals, reinforcing learning about safer behaviour with cash transfer incentives conditional on testing negative for a set of curable sexually transmitted infections (STIs).
- After 12 months, the results from the adjusted model showed a significant reduction in the combined point prevalence of the four curable STIs tested every 4 months by nucleic acid amplification tests in the group that was eligible for the \$20 payments, but no such reduction was found for the group receiving the \$10 payments.
- The results suggest that conditional cash transfers used to incentivise safer sexual practices are a potentially promising new tool in HIV and STIs prevention. Additional larger study would be useful to clarify the effect size, to calibrate the size of the incentive and to determine whether the intervention can be delivered cost effectively.

transfer arm compared to the low-value conditional cash transfer arm was 0.76 (95% CI 0.49 to 1.03) and the adjusted RR was 0.69 (95% CI 0.45 to 0.92). No harm was reported.

ARTICLE SUMMARY

Strengths and limitations of this study

- This paper reports the results of a novel approach for HIV and STI prevention.
- Our study methodology is rigorous, and the results are likely to advance a global conversation about economic approaches to HIV/STI prevention.
- Our main outcome measure is the combined point prevalence of four STIs repeatedly tested by nucleic acid amplification tests over the course of the year and which have been incontrovertibly linked to risky sexual activity. These biological outcomes, however, cannot be used to infer the relative importance of STI treatment seeking behaviour versus other behaviour changes, such as increased condom use or reducing riskiness of partners.
- The results reported in this study are limited to a 12-month experiment and cannot address the sustainability of improvements in STI outcomes over a longer period, particularly after the conditional cash transfers have been discontinued.

Conclusions: Conditional cash transfers used to incentivise safer sexual practices are a potentially promising new tool in HIV and sexually transmitted infections prevention. Additional larger study would be useful to clarify the effect size, to calibrate the size of the incentive and to determine whether the intervention can be delivered cost effectively.

Trial registration number: NCT00922038 ClinicalTrials.gov.

INTRODUCTION

Innovative solutions for AIDS prevention are desperately needed. The Joint United Nations Programme on HIV/AIDS reported that five people are infected for every two placed on treatment, and, in 2009, approximately 2.8 million people were newly infected.¹ Large-scale behaviour change interventions aimed at promoting safer sexual practices have proven less effective and more unreliable at stemming the tide of the epidemic than hoped.^{2–3} It has been far more difficult than was first anticipated to persuade high-risk populations to adopt safer sexual behaviours and practices that serve their longer term interests.

Conditional cash transfer programmes have become an increasingly popular approach for incentivising socially desirable behavioural change.⁴ The principle of conditionality—making payments contingent, for example, on a minimal level of schooling attendance or preventive care use—distinguishes conditional cash transfer programmes from more traditional means tested social programmes. The evaluation of conditional cash transfer programmes has shown that they can be effective at raising consumption, education and preventive health-care,⁵ as well as actual health outcomes.⁶ Similarly, ‘contingency management’ approaches have shown important substance abuse reductions by conditioning rewards on negative tests for drug or alcohol use.⁷

In the context of the staggering social, economic and human costs of the AIDS epidemic in sub-Saharan Africa, it is perhaps not as great a leap as it would first appear to apply the logic of conditional cash transfers to the private arena of human sexuality with the aim of incentivising safer sexual practices among high-risk populations. Numerous studies have documented the responsiveness of sexual behaviour to incentives, such as sex workers willing to forego condoms when clients pay extra,⁸ and increases in transactional sex in the face of household financial difficulties.⁹ Economic theory suggests several pathways through which risky sexual behaviours could be reduced by a conditional cash transfer programme that conditions payment on negative sexually transmitted infections (STIs) tests. Standard theory predicts that the incentives could operate by raising the implicit price of unsafe sex (risking losing the conditional cash transfer) or by bringing the rewards of risk avoidance much closer to the present (eg, a conditional cash transfer within weeks may be more powerful for some people than the spectre of developing AIDS many years in the future) or both. If the conditional cash transfer was sufficiently large, then this higher income could also relieve economic pressures on young women to engage in transactional sex; but even if incentives were small, recent behavioural economics research suggests that regular reminders of this new frame for viewing sexual behaviour could still ‘nudge’ individuals to overcome inertia and extricate themselves from unduly risky sexual relationships.¹⁰ In Malawi, small financial incentives have already been shown to increase the uptake of HIV testing and counselling.¹¹ In the only prior study similar to ours, a follow-on Malawi intervention promised a single cash reward in 1 year’s time for individuals who remained HIV negative, but this design had no measurable effect on HIV status.¹² By contrast, we used the above theory to design and evaluate a novel intervention that tests for risky sexual behaviour repeatedly over shorter time intervals, reinforcing learning about safer behaviour with conditional cash transfer incentives each time.

METHODS

Trial design

This study is an unblinded, individually randomised and controlled trial. It has three separate arms—a control arm with an allocation ratio of 50% and two intervention arms (low-value conditional cash transfer and high-value conditional cash transfer), with an allocation ratio of 25% each. No important changes to methods were implemented after trial commencement.

Participants

Inclusion criteria consisted of males and females, aged 18–30 years (and spouses starting at age 16 years and potentially older than 30 years), residing in one of 10 study villages within the Kilombero/Ulanga districts of the Ifakara Health and Demographic Surveillance

System¹³ in south-west Tanzania. The villages consisted of eight rural villages and two semi-urban neighbourhoods in Ifakara town, with participants evenly distributed across the villages. On average across the 10 villages, approximately 20% of the 18–30 old residents were enrolled in the study. There were three exclusion criteria: being pregnant at the time of registration, having the intention to permanently migrate out of the Ifakara Health and Demographic Surveillance System area within the next year and unwillingness to participate if assigned to the control arm. HIV-positives were eligible for enrolment.

Interventions

The intervention arm was divided into two subarms—a low-value conditional cash transfer arm eligible for up to \$30 over the course of the study (10 000 Tanzanian shillings or approximately \$10 per testing round) and a high-value conditional cash transfer arm eligible for up to \$60 (20 000 Tanzanian shillings or approximately \$20 per testing round). Those amounts were determined based on focus-group discussions in neighbouring villages conducted before the intervention started, balancing sufficient incentive levels against concerns about scalability and potential coercion. All participants were tested for STIs at baseline and then every 4 months for 1 year. Participants in the two intervention arms were eligible to receive conditional cash transfer incentive payments if they tested negative for curable STIs at the 4-, 8- and 12-month testing rounds. STIs tested at all these incentivised rounds were *Chlamydia trachomatis*, *Neisseria gonorrhoeae*, *Trichomonas vaginalis* and *Mycoplasma genitalium*, which are transmitted through unprotected sexual contact and therefore serve as a proxy for risky sexual behaviour as well as vulnerability to HIV infection.^{14–17}

Individuals in the conditional cash transfer arms were not eligible for the cash award at the 4-, 8- and 12-month testing rounds if they tested positive for any of the following: *C trachomatis*, *N gonorrhoeae* and *T vaginalis*. Those converting from negative at baseline to positive at 12 months for syphilis or herpes simplex virus 2 were also ineligible to receive the 12-month conditional cash transfer. HIV testing was conducted at baseline and month 12, but payments were not conditioned on those results because of local ethical sensitivities. *M genitalium* results did not affect conditional cash transfer eligibility because there is some uncertainty around transmission pathways; however, it was included in the combined prevalence measure used as primary outcome to increase statistical power. Individuals in the intervention arms testing positive for any of the conditioned curable STIs did not receive the conditional cash transfer but were eligible to continue as a study participant in subsequent rounds after having been treated and cured of the infection. Individuals in the control arm were not eligible for conditional cash transfer, but all other study procedures were identical between the control and intervention arms. Anyone testing positive for a STI

(regardless of arm) was offered counselling and free STI treatment (for self and partners) through health facilities of the District Ministry of Health serving the research communities. Individual pre-test and post-test counselling was provided to study enrollees at each testing interval, following Tanzania national testing guidelines. In addition, monthly group counselling sessions emphasising relationship skills training adapted from a subset of the Stepping Stones curriculum¹⁸ were also made available to all study participants in all villages but were not mandatory.

Outcomes

The biological markers used in the study were selected both due to their likely prevalence levels in the study population and due to their status within the epidemiological literature as reasonable proxies for risky sexual behaviour. The primary outcome measure, as defined in the study protocol, is the round-specific combined point prevalence of the four STIs that were regularly tested—*C trachomatis*, *N gonorrhoeae*, *T vaginalis* and *M genitalium*—at months 4, 8 and 12. This measure of combined point prevalence was constructed at study design to ensure sufficient power to detect differences in the control and treatment groups in response to the conditional cash transfer intervention. For logistical reasons, *M genitalium* testing was not conducted at baseline. We also tested for HIV, herpes simplex virus 2 and syphilis at baseline and month 12.

All STI testing was conducted by the Ifakara Health Institute microbiology laboratory in Ifakara. All test results were available within 7–10 days and were returned to participants the following week. Ten per cent of all samples, and all positives, were sent to the University of California Chlamydia Laboratory for confirmation analysis (quality control).

Specimens for chlamydia, gonorrhoea, trichomonas and *M genitalium* were collected by a self-administered vaginal swab for women. Men provided a ‘first-catch urine’ (about 20–30 ml) sample. Specimen collection among women was always observed by a nurse at the testing station. For men, the specialised receptacle used to collect a urine sample was provided only after dropping off personal belongings upon checking into the testing section of the study station. Men were asked to urinate into the study receptacle in the vicinity of the study station. Detection used GenProbe Aptima (GenProbe Inc, San Diego, California, USA) nucleic acid amplification tests.

To test for HIV, herpes simplex virus 2 and syphilis, a single venous blood sample of approximately 5–10 ml was collected from each participant at baseline and month 12. For herpes simplex virus 2, we used the Focus HerpeSelect HSV-2 ELISA IgG assay (Focus Technologies, Cypress, California, USA) to detect serum antibodies. *Treponema pallidum* was identified using rapid plasma reagin with reactive tests confirmed by *T pallidum* particle agglutination assay. Active syphilis was defined as rapid plasma reagin+/ *T pallidum* particle agglutination

assay+. For HIV, we used a series of three rapid tests for screening results (SD Bioline HIV-1/2 3.0; Standard Diagnostics, INC., Kyonggi-do, Korea), confirmation of positives (Determine® HIV-1/2; Inverness Medical Japan Co, Ltd, Tokyo, Japan), and tie-breaking (Uni-Gold HIV, Trinity Biotech plc, Bray, Ireland).

Sample size

Early study planning had initially assumed a sample size of 3000, which would have provided improved power for gender subgroup analysis in our main comparisons, but due to logistical fieldwork constraints the recruited sample size was reduced to approximately 2400. We present here the ex-post power calculations at this actual recruited sample size and actual infection rates, based on a comparison of combined STI prevalence rates of 12% between two equal-sized study arms for a single post-treatment measurement of proportions controlling for one baseline measure and assuming a two-sided alternative hypothesis. We calculated that a total sample size of 2400 individuals would be sufficient to provide at least 90% power to detect a one-third intervention-related reduction in STI point prevalence (significant at the 5% level) in both intervention arms combined. This sample size would also retain at least 80% power to detect a reduction in a single intervention arm (eg, the high-value conditional cash transfer arm) compared to the control arm, and if the prevalence was assumed to be as high as 20%, then this power rises to over 90%. Subgroup analysis by gender would not be powered at the 80% level for our main comparison of the high-value conditional cash transfer arm against controls assuming a 12% prevalence level, although it would retain approximately 90% power when comparing the combined arms against the control arm assuming 20% prevalence.

Randomisation

Individual-level randomisation took place at the study station after baseline interview and testing, with participants selecting coloured balls from an opaque bag. The randomisation took place in public view and in two stages with participants first randomly selecting one of four balls to determine their allocation to the intervention or the control arm. In order to study potential peer-effects, in randomly selected subvillages, the probability of selection in the intervention arm was 75% (three balls out of four) and in the other subvillages, it was 25% (one ball out of four); based on the distribution of participants across subvillages, we thus expected 48% of the overall sample to be randomised into the control arm. Participants randomised into the intervention arm were further invited to choose one of two balls from a second bag determining in which of the two intervention arms (low-value conditional cash transfers and high-value conditional cash transfers) they would be allocated. These highly transparent procedures were deemed necessary for acceptability of randomisation in a popu-

lation with limited formal education. Participants were not blinded to arm assignment since awareness of their eligibility for the conditional cash transfer was a critical component of the intervention.

Spousal pairs were assigned the same intervention arm and the protocol prescribed for randomisation to occur after both spouses had enrolled.

Statistical methods

Each individual was coded as per their initial randomised assignment as per an intent-to-treat design. However, individuals who were not present at any given round were treated as missing and dropped from the analysis for that round due to lack of outcome data. We report sample means at baseline to verify the balance across the three study arms. Unadjusted outcomes at the three follow-up rounds are reported using RRs, that is, the probability of being positive for any STI in the intervention arm, divided by the probability of being positive for any STI in the control arm. RRs are calculated from logistic regressions using the *margins* and *nlcom* post-estimation commands in the *Stata V.12* statistical software package. We further report adjusted outcomes using RRs to account for residual variation across arms after randomisation. Adjustments have been made for standard socioeconomic variables, such as gender, education, age, marital status, income, socioeconomic status, subvillage and baseline STI status. Age and income are continuous variables, while the other adjustment variables are categorical. We cluster SEs both at the household and at subvillage levels, accounting for the possible correlation within couples and the variation in selection probability at that subvillage level. We present a subgroup analysis by gender. We used *Stata V.12.1* (Stata Corp) for statistical analysis.

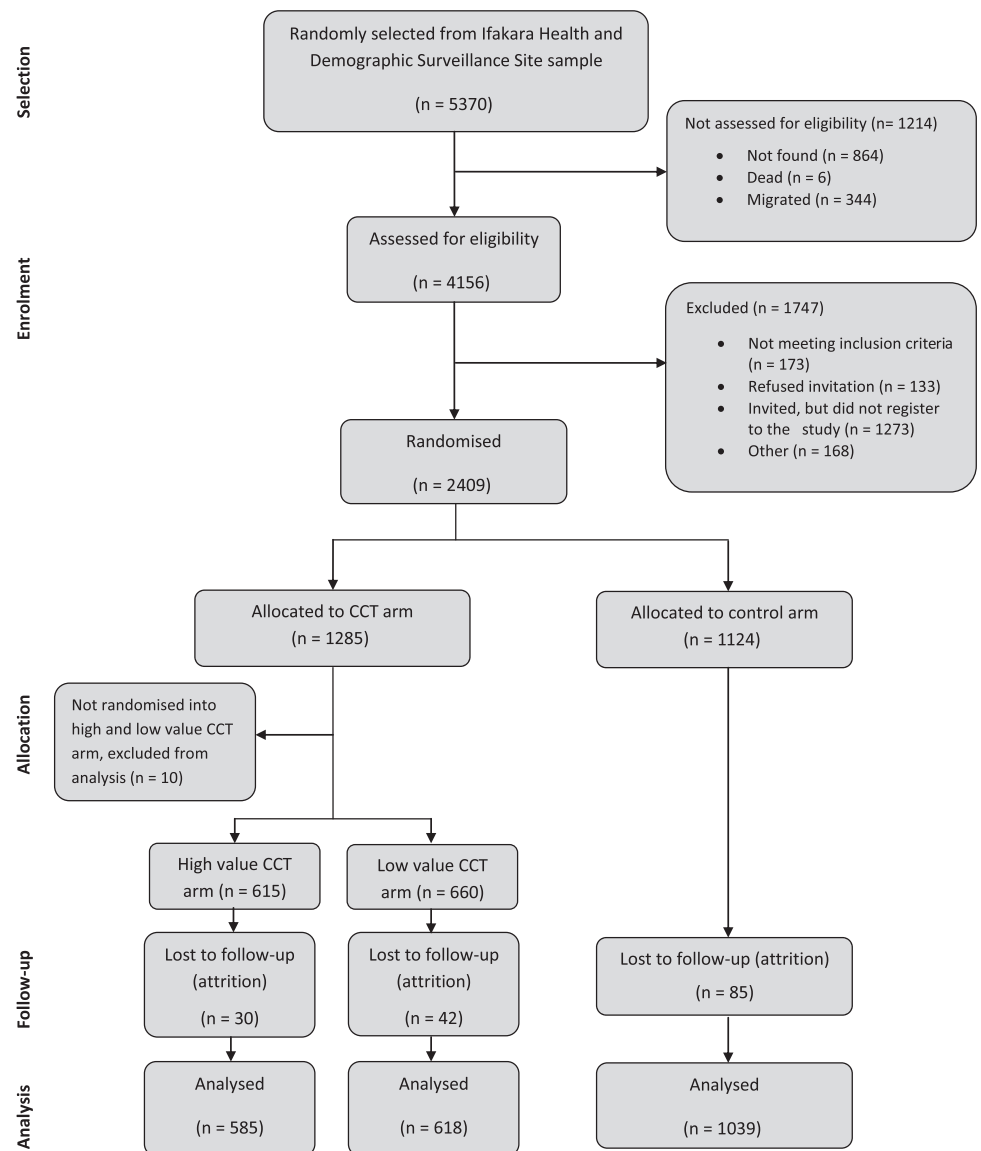
RESULTS

Participant flow

A total of 5370 individuals were randomly selected from the Ifakara Health and Demographic Surveillance System sample (figure 1). Eight hundred and sixty-four (16.1%) of those individuals were not found, six (0.1%) had died and 344 (6.4%) had migrated. Fieldworkers assessed for eligibility 4156 individuals: 173 (4.2%) did not meet the inclusion criteria, among them 35 (0.8%) were not in the study age range and 138 women (3.3%) were currently pregnant. Of those eligible, 133 (3.3%) explicitly refused to participate in the study and 168 (4.2%) declined for other reasons. All others (3682) were given an invitation to come to a study station the following week: 2409 (65.4%) registered for the study and were randomised into one of the three study arms, while 1273 did not come to the study station for registration.

Of the 2409 registered participants, 1124 (46.7%) were randomly allocated to the control arm. Among the participants, 1285 were randomly selected, in a first stage, to one of the two conditional cash transfer arms: 615 (25.5%) were randomly assigned in the high-value

Figure 1 Participant flow diagram.



conditional cash transfer arm and 660 (27.4%) in the low-value conditional cash transfer arm. Ten (0.4%) individuals assigned to the intervention arms were intentionally dropped from the analysis since they failed to be further randomised in one of the two subarms. In the control arm, 967 were tested and interviewed at round 2 (attrition 14%), 983 (attrition 12.5%) at round 3 and 1039 (attrition 7.6%) at round 4. In the high-value conditional cash transfer arm, 570 were tested and interviewed at round 2 (attrition 7.3%), 567 (attrition 7.8%) at round 3 and 585 (attrition 4.9%) at round 4. In the low-value conditional cash transfer arm, 568 were tested and interviewed at round 2 (attrition 13.9%), 567 (attrition 14.1%) at round 3 and 618 (attrition 6.4%) at round 4. Overall, attrition was lower at round 4 because the field team made extensive additional effort to contact and interview attriters. Symptomatic individuals in all study arms were particularly encouraged to come to the study station in order to receive free STI treatment. Attrition was not predicted by any of the baseline STI results, except that HIV-positive individuals at base-

line were more likely to be lost to follow-up, despite the fact the participants were clearly told that HIV status would not affect eligibility for conditional cash transfers.

Recruitment

Recruitment and baseline data collection took place from 10 February to 9 April 2009. The second, third and fourth rounds of interviews and testing took place from 9 June to 15 August 2009, 29 September to 5 December 2009 and 16 February to 1 May 2010, respectively. The conditional cash transfer intervention was stopped after 1 year, following the protocol.

Process

The intervention was well accepted and accessed by the study participants as indicated in the participant flow and the low attrition numbers. Furthermore, study participants randomised into the conditional cash transfer arms declared that the financial incentives motivated them to modify their behaviour. In the high-value conditional cash transfer arm, 317 (59.0%)

declared that the money motivated them ‘very much’ to change their behaviour and 67 (12.5%) stated that it motivated them ‘somewhat’. In the low-value conditional cash transfer arm, those numbers are 194 (37.4%) for ‘very much’ and 107 (20.6%) for ‘somewhat’.

Baseline data

Table 1 describes the baseline characteristics of the participants by study arm. The prevalence of the six STIs tested at baseline was distributed similarly across arms. Participants were also similar according to gender and education. However, individuals in the two intervention arms had slightly lower self-reported socioeconomic status, and individuals in the low-value conditional cash transfer arm also had a higher income.

We verified that there was no deviation from protocol that could have led to differential secondary spousal enrolment across arms: 604 out of the 2399 participants were spouses who joined the study after their spouse was initially invited. They were distributed as follows: 279 out of 1124 (24.8%) in the control arm, 156 (25.4%) out of 615 in the high-value cash arm and 169 (25.6%) out of 660 in the low-value cash arm. Tests for statistical differences with the control arm yielded p values of 0.673 for the high-value conditional cash transfer arm and 0.742 for the low-value conditional cash transfer arm, so differences across the three study arms in the percentage of spouses joining the study are minimal and not statistically significant.

Numbers analysed

Except for the 10 (0.4%) individuals who failed to be assigned to either the high or low-value conditional cash transfer arm, all participants tested and interviewed at

the respective rounds were included in the analysis (refer to the sample sizes in tables 1 and 2). The reductions in sample size from the unadjusted (table 2) to the adjusted analysis (table 3) were from 2105 to 2077 at round 2, from 2117 to 2092 at round 3 and from 2242 to 2211 at round 4 due to missing data on covariates in the logistic regression model (table 2 results are similar when using the smaller samples from table 3).

Outcomes and estimation

Table 2 presents the unadjusted RR ratios compared to the control group. At months 4, 8 and 12 when the outcome is the combined point prevalence of the four curable STIs tested every 4 months by nucleic acid amplification tests (columns 1–3), the RRs are not statistically different at the 5% significance level. At month 12, the number of positives was 57 (9.7%) in the high-value conditional cash transfer arm, while it was 79 (12.8%) in the low-value conditional cash transfer arm and 126 (12.1%) in the control group. At month 12, this unadjusted analysis estimated a reduction in the RR of those four curable STIs for the high-value conditional cash transfer arm of 20% (95% CI 6% increase to 46% reduction). The RRs were also not statistically different at the 5% significance level in column 4 for the combination of syphilis prevalence and new cases of HIV and herpes simplex virus 2. Those three STIs were detected by serology performed only at baseline and round 4. For the combined point prevalence of chlamydia, gonorrhoea, trichomonas, *M genitalium* at month 12, the unadjusted RRs are not statistically different than 1 at 5% significance level when men and women are considered separately (columns 5 and 6). At month 12, for the combined point prevalence of the four curable

Table 1 Summary statistics at baseline, by arm

Variables	(1) Control	(2) High-value CCT	(3) Low-value CCT
Female	561 (49.9%)	314 (51.1%)	329 (49.9%)
Age	27.2 (5.6)	27.6 (5.4)	27.6 (5.7)
Education			
None	139 (12.4%)	70 (11.4%)	79 (12.0%)
Primary	863 (76.8%)	482 (78.4%)	660 (78.3%)
Secondary	122 (10.9%)	63 (10.2%)	64 (9.7%)
Married	842 (75.0%)	474 (77.1%)	476 (72.7%)
Low SES	582 (51.8%)	344 (55.9%)	377 (57.2%)
Yearly income	239 311 (425 091)	257 017 (531 370)	283 218 (534 399)
Chlamydia	21 (1.9%)	15 (2.4%)	16 (2.4%)
Gonorrhoea	8 (0.7%)	8 (1.3%)	6 (0.9%)
Trichomonas	130 (11.6%)	88 (14.3%)	79 (12.0%)
Herpes simplex virus 2	380 (33.9%)	226 (36.8%)	225 (34.2%)
Syphilis	17 (1.5%)	8 (1.3%)	15 (2.3%)
HIV	41 (3.7%)	17 (2.8%)	27 (4.1%)
N	1124	615	660

Data are represented in means (SD) or numbers (%).

Yearly income in Tanzanian Shillings (Tsh).

At baseline, 1000 Tsh = approximately 1US\$.

Low SES corresponds to the lowest two ranks on a self-reported socioeconomic status scale from 1 to 7.

CCT, conditional cash transfer.

Table 2 Unadjusted outcomes: RR from logistic regression

	(1)	(2)	(3)	(4)	(5)	(6)
	Month 4 combined prevalence of four STIs tested by NAAT*	Month 8 combined prevalence of four STIs tested by NAAT*	Month 12 combined prevalence of four STIs tested by NAAT*	Month 12 combined measure for three STIs detected by serology at baseline and month 12†	Month 12 combined prevalence of four STIs tested by NAAT* men only	Month 12 combined prevalence of four STIs tested by NAAT* women only
High-value CCT (95% CI)	1.06 (0.74 to 1.38)	0.86 (0.60 to 1.12)	0.80 (0.54 to 1.06)	1.09 (0.76 to 1.43)	0.70 (0.34 to 1.07)	0.85 (0.55 to 1.15)
Low-value CCT (95% CI)	0.97 (0.66 to 1.28)	0.80 (0.55 to 1.04)	1.05 (0.75 to 1.35)	1.03 (0.71 to 1.35)	1.25 (0.73 to 1.77)	0.94 (0.62 to 1.25)
Number positive	246 (11.7%)	260 (12.3%)	262 (11.7%)	232 (10.4%)	99 (9.0%)	163 (14.3%)
N	2105	2117	2242	2241	1105	1137
Number positives by study arm						
Control arm	112 (11.6%)	133 (13.5%)	126 (12.1%)	104 (10.0%)	47 (9.0%)	79 (15.2%)
High-value CCT	70 (12.3%)	66 (11.6%)	57 (9.7%)	64 (11.0%)	18 (6.4%)	39 (12.9%)
Low-value CCT	64 (11.3%)	61 (10.8%)	79 (12.8%)	64 (10.4%)	34 (11.3%)	45 (14.2%)

Robust SEs in parentheses, clustered at both the household and the subvillage levels.

The reference group for the computation of the RRs is the control group.

*Chlamydia, gonorrhoea, trichomonas, *Mycoplasma genitalium*.

†HIV, herpes simplex virus 2, syphilis.

CCT, conditional cash transfer; NAAT, nucleic acid amplification test; STI, sexually transmitted infection.

STIs tested by nucleic acid amplification tests, unadjusted RR for the high-value conditional cash transfer arm compared to the low-value conditional cash transfer arm was 0.76 (95% CI 0.49 to 1.03) and was 0.56 (95% CI 0.26 to 0.87) for men only.

Table 3 presents results from adjusted regressions. Adjustments have been made for gender, education, age, marital status, income, socioeconomic status, subvillage and baseline STI status. At months 4 and 8 (columns 1 and 2), the combined prevalence of the four STIs tested by nucleic acid amplification tests is shown to have RRs lower than 1 for the two conditional cash transfer arms compared to the control arm, but not significantly so. However, at month 12 (column 3) for the combined prevalence of the STIs tested by nucleic acid amplification tests, the adjusted model estimated a 27% reduction in the RRs for the high-value conditional cash transfer arm compared to the control arm (95% CI 1% to 53% reduction), while the RR is not statistically different from 1 for the low-value conditional cash transfer arm. At month 12, for the three STIs detected by serology (without having been tested at months 4 and 8), the RR for the low-value conditional cash transfer arm is 0.82 (column 4) but is not significantly lower than the control arm (95% CI 0.60 to 1.03). In a subgroup analysis by gender (columns 5 and 6), for the four STIs tested by nucleic acid amplification tests, the RRs for the high-value conditional cash transfer arm are 0.68 for men and 0.76 for women. Those two RRs are not significantly different from each other (as confirmed by test of interaction between gender and arm, where an interaction term for woman was not significant for either conditional cash transfer arm (p values 0.648 for high-value cash transfer arm and 0.391 for low-value cash transfer arm) and is not significantly lower than 1 at the 5% level. At month 12, for the combined point prevalence of the four STIs tested by nucleic acid amplification tests, adjusted RR for the high-value conditional cash transfer arm compared to the low-value conditional cash transfer arm was 0.69 (95% CI 0.45 to 0.92) and was 0.52 (95% CI 0.23 to 0.80) for men only.

DISCUSSION

After 12 months, the adjusted results showed a significant reduction in the combined point prevalence of the four curable STIs tested every 4 months by nucleic acid amplification tests in the group that was eligible for the \$20 quarterly payments, but no such reduction was found for the group receiving the \$10 quarterly payments. Such results were not found at earlier rounds nor for unadjusted results. Furthermore, the impact of the conditional cash transfers did not differ between men and women.

Limitation

Our main outcome measure is the combined point prevalence of four STIs repeatedly tested by nucleic acid amplification tests over the course of the year and which

Table 3 Adjusted outcomes: RRR from logistic regression

(1)	(2)	(3)	(4)	(5)	(6)
Month 4 combined prevalence of four STIs tested by NAAT*	Month 8 combined prevalence of four STIs tested by NAAT*	Month 12 combined prevalence of four STIs tested by NAAT*	Month 12 combined measure for three STIs detected by serology at baseline and month 12†	Month 12 combined prevalence of four STIs tested by NAAT* men only	Month 12 combined prevalence of four STIs tested by NAAT* women only
High-value CCT (95% CI)	0.92 (0.62 to 1.20)	0.90 (0.61 to 1.18)	0.73 (0.47 to 0.99)	1.03 (0.74 to 1.32)	0.68 (0.25 to 1.10)
Low-value CCT (95% CI)	0.94 (0.63 to 1.26)	0.85 (0.58 to 1.13)	0.82 (0.60 to 1.03)	0.82 (0.60 to 1.03)	1.31 (0.73 to 1.89)
Number positive	242 (11.7%)	258 (12.3%)	257 (11.6%)	227 (10.3%)	98 (9.0%)
N	2077	2092	2211	2210	1093

Results adjusted for gender, education, age, marital status, income, socioeconomic status, subvillage and baseline STIs. Robust SEs in parentheses, clustered at both the household and the subvillage levels. The reference group for the computation of the RRs is the control group.

*Chlamydia, gonorrhoea, trichomonas, *Mycoplasma genitalium*.

†HIV, herpes simplex virus 2, syphilis.

CCT, conditional cash transfer; NAAT, nucleic acid amplification test; STI, sexually transmitted infection.

have been incontrovertibly linked to risky sexual activity. These biological outcomes, however, cannot be used to infer the relative importance of STI treatment seeking behaviour versus other behaviour changes, such as increased condom use or reducing riskiness of partners. Furthermore, the lack of a clear result on the combined measure for the three STIs that were detected by serology only at baseline and month 12 (this measure primarily reflects herpes simplex virus 2 incidence, as HIV and syphilis prevalence were somewhat lower) is puzzling and merits further study. The contrasting result with the impact of the high-value conditional cash transfers on the four curable STIs that were tested by nucleic acid amplification tests could point to the importance of treatment seeking behaviour rather than safer sexual practices. However, the interpretation of herpes simplex virus 2 results is complicated by the fact that most transmission occurs via asymptomatic shedding by partners who may be otherwise low risk,¹⁹ as well as the fact that it can be transmitted even in the context of appropriate condom use.²⁰ Furthermore, this study was not powered to directly examine HIV conversion, thus implications for HIV prevention remain speculative.

In order to study potential peer-effects, in randomly selected subvillages, the probability of selection in the intervention arm was 75% and in the other subvillages, it was 25%. This might have led to baseline imbalances. For this reason, we included subvillage indicator variables in the adjusted models. This might explain some of the differences between the results from the unadjusted and the adjusted models.

Finally, the results reported in this study are limited to a 12-month experiment and cannot address the sustainability of improvements in STI outcomes over a longer period, particularly after the conditional cash transfers have been discontinued. Nor can they address the possibility of adverse consequences to the extent that extrinsic incentives may reduce long-term intrinsic motivation to engage in safe behaviours after incentives are withdrawn. To address these questions, we will follow-up with study participants 1 year following the end of the intervention study, in the Spring of 2011, to assess whether improved outcomes have been sustained, or reversed, in the absence of a positive feedback mechanism in the form of STI testing and conditional cash transfers.

Generalisability

While these study results are important in showing that the idea of using financial incentives can be a useful tool for preventing HIV and STI transmission, it remains an initial study on a limited scale. Even though the study site is fairly representative of rural and small town environments in sub-Saharan Africa, this approach would need to be replicated elsewhere and implemented on a larger scale (in permutations requiring less administrative and laboratory capacity) before it could be concluded that such conditional cash transfer

programmes offer an efficient, scalable and sustainable HIV prevention strategy.

Interpretation

The results indicate that conditional cash transfers based on negative results of periodic screenings for incident STIs—an objectively measured marker for risky sexual behaviour—are a potentially useful tool for STI and possibly HIV prevention. The extraordinarily high social and economic cost of the current HIV and AIDS crisis suggests that prevention can be far cheaper than treatment, thus motivating the continued search for innovative and effective new prevention approaches, such as conditional cash transfers or other financial incentives.

The absence of significant impacts at rounds 2 (month 4) and 3 (month 8) suggests that the impact of the conditional cash transfer may take time to materialise, perhaps because it is not easy to extricate oneself from complicated sexual relationships, or perhaps because participants needed time to become accustomed to (and trust) the incentive mechanism. The comparison between the impacts of the conditional cash transfer intervention in the high-value conditional cash transfer arm to that in the low-value conditional cash transfer arm permits us to better understand at which threshold conditional cash transfers can be effective as an HIV and STI prevention tool. While the results showed a significant reduction in STI incidence in the arm that was eligible for the \$20 conditional cash transfers every 4 months or up to \$60 over 12 months, no such reduction was found for the arm receiving the \$10 conditional cash transfers every 4 months or up to \$30 over 12 months. This distinction must be interpreted with caution though because assignments were not masked, hence individuals in the low-value conditional cash transfer arm could have behaved differently than if they were to receive the same incentive in the absence of a higher conditional cash transfer arm. Both of these amounts represent a meaningful proportion of household income in a country where gross domestic product per capita was \$440 in 2008, and particularly among our study participants who had mean individual annual earnings of approximately \$250.

OTHER INFORMATION

Registration

This randomised control trial is registered at ClinicalTrials.gov, study identifier # NCT00922038.

Protocol

The study protocol was initially approved by the University of California; Berkeley's Institutional Review Board (Committee for Protection of Human Subjects) effective 17 December 2008; approval has been updated numerous times since to reflect protocol amendments, with the latest approval effective 11 October 2011. The Ifakara Health Institute Institutional Review Board initially approved the study on 24 July 2008. The latest

amended approval is from 11 February 2010. Tanzania's National Institute for Medical Research approved the study 5 February 2009.

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Competing interests None.

Patient consent The article does not contain personal medical information about an identifiable living individual.

Contributors DdW, WHD, RN and CAM made contributions to each part of the project, planned and designed the study, conducted the analysis, interpreted the findings and contributed to the manuscript. The Ifakara Health Institute was the main implementing agency for the project: BJ and FA managed the Ifakara laboratory testing, AM led field operations, MAM facilitated operations, KS programmed the study systems and together with RA managed the database and SM was responsible for outreach to participating communities and health clinics. EG contributed to data analysis, LP conducted in-depth interviews and ZI was project director onsite in Tanzania. From University of California, San Francisco, JM and JS set up the Ifakara Health Institute laboratory, developed laboratory protocols and were responsible for quality control. SK, JJ and EM as senior investigators have contributed throughout the project and are leading subanalyses linked to the main study in their respective fields of expertise. All authors, external and internal, had full access to all the data (including statistical reports and tables) in the study and can take responsibility for the integrity of the data and the accuracy of the data analysis. DdW and WHD are the guarantors of the study.

Provenance and peer review Not commissioned; externally peer reviewed.

Data sharing statement No additional data available.

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This document contains copies of:

- 1) First Submission Decision letter and our answers to it. Our answers in bold: p. 2**
- 2) First submission reviews and our answers (in bold) to them: p. 11**
- 3) Second submission decision: p. 20**
- 4) Second submission review and our answers (in bold) to it: p.30**

1) First round decision letter and our answers in bold.

MS ID#: BMJ/2011/883504

MS TITLE: Incentivizing safe sex: A randomized trial of conditional cash transfers (CCTs) for HIV/STI prevention in rural Tanzania

Thank you for sending us this paper, which we were pleased to have the chance to consider, and enjoyed reading. We recognise its potential importance and relevance to general medical readers, but I am afraid that we have not yet been able to reach a final decision on it. This is because several important aspects of the work still need clarifying.

We hope very much that you will be willing and able to revise your paper as explained below in the report from the manuscript meeting, so that we will be in a better position to understand your study and decide whether the BMJ is the right journal for it. We hope, too, that you will submit your revised paper (via your author area at our online editorial office <http://submit.bmj.com>) within one month.

Looking forward to hearing from you again and, we hope, to reaching a decision.

Best wishes

Domhnall

Domhnall MacAuley
BMJ Editorial

Report from the BMJ's manuscript meeting

We are able to accept only a small proportion even of the good articles submitted to us. A little over 10 % of articles reach this stage, and to do so they have to have passed preliminary screening by one or more of the editors, have received sufficiently positive external peer review, and have been discussed at the manuscript meeting.

At the manuscript meeting each article is discussed by the Editor or deputy, the rest of the BMJ's international team of research editors, and two invited

advisers: one statistician and one clinical editorial adviser. As well as the scientific merits of the paper we take into account each paper's originality and interest to a general readership in comparison with other submitted papers. We take reviewers' reports fully into account too, but the final decision on acceptance or rejection of a paper rests with the Editor.

These comments are an attempt to summarise the discussions at the manuscript meeting. They are not an exact transcript.

Members of the committee were:

Trish Groves (Chair), Jon Deeks (ext Statistician), Elizabeth Loder, Wim

Weber, Tobias Kurth, Kirsten Patrick, Domhnall MacAuley.

* Randomisation of spouses. There is likely to be correlation in couples so

should it be analysed as a cluster. The unadjusted results show little effect. There is only a benefit is when adjusted. Also no account for the number of comparisons. We suspect that with adjustment, the clustering effect

may disappear. The message of the paper might change. There are problems in the method and clustering of spouse.

We agree that correlation in couples is likely and we therefore have adapted our clustering of the standard errors to account for this. We now cluster standard errors both at the household and at sub-village levels, accounting for the possible correlation within couples and the variation in selection probability at that sub-village level. All tables have been revised accordingly. We have also updated the statistical methods sub-section to describe this. These changes do not alter the main messages of the paper.

Regarding the multiple comparisons, we had always planned to look primarily at the effect after one year, i.e. at round 4, expecting that the effect would become stronger over time during the previous rounds. We therefore do not think it is necessary to adjust for multiple comparisons across rounds.

* How did the authors choose the variables- is it based on the p values? More variables in the final model. There are many p values in table one but not for primary hypothesis. We need more explanation of how the variables were selected etc

For Table 1 and adjusted models, we chose standard socio-demographic variables such as age, gender, education, marital status, socio-economic status and income which are expected to influence behaviors. (We did not choose these variables based on p-values). We

also included baseline STI levels, but could not include the combined prevalence measure at baseline because Mycoplasma Genitalium was not tested at baseline due to logistical constraints.

*There is a potential fundamental flaw. If one tests positive in the study, one doesn't get any benefit. If looking for the money- one could get a sample from someone else which may bias the study. Participants may try to avoid a positive test.

The reviewers are correct to point out that pronounced 'gaming behavior' by participants in the CCT groups would introduce bias into the study. We adopted several strategies to reduce the likelihood that gaming could occur. Specimen collection among females was always observed by a nurse at the testing station. For males, the specialized receptacle used to collect a urine sample was provided only after dropping off personal belongings upon checking in to the testing section of the study station. Males were asked to urinate into the study receptacle in the vicinity of the study station. They would have had to risk being observed attempting to transfer the contents of 'healthy' urine into the study receptacle, and this behavior was not reported by the study staff.

We have introduced a more detailed description to clarify this point in the outcomes sub-section of the methods section.

*Power calculation difficult to follow. Need to explain exactly what the power calculation was done in terms of time measurement. Needs to be more clear- especially about reporting clearly the primary outcome in the abstract.

The sample size sub-section has now been revised to reflect the power calculations for the analysis reported. The previous power calculations were those used when the project was initially conceived, but these were updated to the currently reported power calculations during the final stages of project design and recruitment planning.

In the abstract, we now clearly states the 4 sexually transmitted infections combined for the primary outcome measure both in the methods and the results headings.

*Abstract- says is a proof of concept study.

By identifying this as a 'proof of concept' study, we hoped to acknowledge the importance of testing on a small scale whether individuals will respond to financial incentives to change their sexual behavior before evaluating whether the intervention can be delivered on a larger scale. This resonates with common understanding, but we are aware that the biomedical field employs a more precise definition (e.g. Any Phase 1b, or Phase 2 trial, regardless of sponsorship, that could generate, confirm, provide an adequate benefit-risk, or establish a dose response relationship that could be used as the basis for a decision to move forward with a registration strategy).

For clarity, we have removed the reference to “proof of concept” in the abstract and the body of the text.

* Doesn't seem to be a good idea to pay people to have a negative sample and then allow people to take their own sample. This sounds like a major problem (It may not be feasible to do it otherwise)

Please see above our answer clarifying our methods for specimen collection and the more detailed description to clarify this point in the outcomes sub-section of the methods section.

* Good clinical question, the introduction was good but the methods are very confusing.

We have made significant changes to the methods section in responding to this and other reviewers' comments. We now provide additional information on specimen collection procedures, more detail on process aspects related to administering the intervention, and greater clarity around the trial design, the primary outcome measure and its rationale and the power calculations. We have also updated the statistical methods sub-section to clarify the relative risks reported and to describe the clustering of standard errors both at the household and at sub-village levels, accounting for the possible correlation within couples and the variation in selection probability at that sub-village level.

* Need to know a lot more about the methods of sample collection. Authors need to be clear on the primary outcome.

Please see above our answer clarifying our methods for specimen collection and the more detailed description to clarify this point in the outcomes sub-section of the methods section.

Technical editor's report

- Please provide positions (job titles) for each author<P>

To do.

- The abstract must be structured with regulation headings (Objective, Design, Setting, Participants, (Interventions,) Main outcome measures, Results, Conclusions)

We have done this.

- Abbreviations should not be used and should be spelt out each time (HIV and AIDS are OK)

We have done this.

- For all confidence intervals, use format "xx to xx" (not "xx - xx") <P>

We have done this.

- Please restate the main findings in the first paragraph of the Discussion

We have done this.

End matter

- Please provide a summary points box comprising two or three points under each of the headings "What is already known on this topic" and "What this study adds"<P>

We have done this.

We have done this.

We have done this.

by both of the reviewers. You will find these at our online editorial office (at <http://submit.bmj.com>) in your author area, under this manuscript number. Please also respond to these additional comments by the committee:

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*

When you revise and return your manuscript, please take note of all the following points. The commonest reason for us to have return papers to authors after revision is that some of these points have not been attended to and we cannot, therefore, proceed to acceptance. Even if an item, such as a competing interests statement, was present and correct in the original draft of your paper, please check that it has not slipped out during revision.

a. In your covering letter please provide, point by point, your replies to the comments made by the reviewers and the editors, and please explain how you have dealt with them in the paper. It may not be possible to respond in detail to all these points in the paper itself, so please do so in the covering letter.

b. We will need the full version of your paper.

c. Please include the items below in your revised paper to comply with BMJ style

Essential items for BMJ articles

* the title of the article should include the study design eg "a retrospective analysis of hospital episode statistics"

* details of ethics committee approval, or a statement that it was not required (see <http://resources.bmj.com/bmj/authors/editorial-policies/guidelines>)

* Competing interests. A declaration about competing interests needs to be made in the manuscript. This should be composed after each author has filled in the form at www.icmje.org/coi_disclosure.pdf, and the corresponding author should keep the completed forms in case they are required later. Please then add to the manuscript a statement in the following format:

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* signed patient consent form(s), if the article gives enough personal information about any patient(s): this sometimes occurs even in research papers - for example in a table giving demographic and clinical information

about a small subgroup in a trial or observational study, or in quotes/tables in a qualitative study (see http://resources.bmj.com/bmj/authors/editorial-policies/copy_of_patient-confidentiality)

- * for a clinical trial, the trial registration number and name of register - in the last line of the structured abstract

- * a data sharing statement such as "Data sharing: technical appendix, statistical code, and dataset available from the corresponding author at <email address or url>". If there are no such further data available, please use this wording: "Data sharing: no additional data available"

- * please write the discussion section of your paper in a structured way, to minimise the risk of careful explanation giving way to polemic.

Please follow this structure:

- * statement of principal findings of the study

- * strengths and weaknesses of the study

- * strengths and weaknesses in relation to other studies, discussing important differences in results and what your study adds. Whenever possible please discuss your study in the light of relevant systematic reviews and meta-analyses (eg Cochrane reviews)

- * meaning of the study: possible explanations and implications for clinicians and policymakers and other researchers; how your study could promote better decisions

- * unanswered questions and future research

- * What this paper adds/what is already known box (as described at <http://resources.bmj.com/bmj/authors/types-of-article/research>)

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- * for studies funded or sponsored by industry (see <http://resources.bmj.com/bmj/authors/article-submission/article-requirements>):

- * a statement describing the role of the study sponsor(s), if any, in study design; in the collection, analysis, and interpretation of data; in the writing of the report; and in the decision to submit the article for publication

- * assurance, in the cover letter, that a clinical trial funded by a pharmaceutical or other commercial company follows the guidelines on good publication practice (see <http://resources.bmj.com/bmj/authors/article-submission/article-requirements>)

- * inclusion in the list of contributors the name(s) any professional medical writer(s), specifying in the formal funding statement for the article who paid the writer. Writers and authors must have access to relevant data while writing articles.

* structured abstract (see <http://resources.bmj.com/bmj/authors/types-of-article/research>)

* summary statistics to clarify your message

We do want your piece to be easy to read, but also want it to be as scientifically accurate as possible. Please include in the results section of your structured abstract (and, of course, in the article's results section) the following terms, as appropriate:

For a clinical trial:

- Absolute event rates among experimental and control groups
- RRR (relative risk reduction)
- NNT or NNH (number needed to treat or harm) and its 95%

confidence

interval (or, if the trial is of a public health intervention, number helped per 1000 or 100,000)

For a cohort study:

- Absolute event rates over time (eg 10 years) among exposed and non-exposed groups

- RRR (relative risk reduction)

For a case control study:

- OR (odds ratio) for strength of association between exposure and outcome

For a study of a diagnostic test:

- Sensitivity and specificity
- PPV and NPV (positive and negative predictive values)

2) First submission reviews and our answers (in bold) to them.

Reviewer 1 Comments...

Name: James Hargreaves

Position: Senior Lecturer, LSHTM

This is a potentially important paper - although I am not sure it is of sufficient scientific importance for publication for a general readership such as in the BMJ. It is not suitable for publication in the BMJ its current format – though this could probably be rectified.

I strongly encourage the authors to consider making the changes suggested here with regard the format of reporting - and resubmitting to the BMJ or to another public health / AIDS / STI journal. These are important, truly intersectoral studies – and I wish to encourage them. There is growing understanding of the importance of conditional cash transfers, and other social development and financial incentivisation programmes, for public health – and much interest in this within the public health sector. Much expertise in the design and delivery of these programmes lies outside the health sector as exemplified by this author group. There is much to learn in either direction between researchers in the economics and those in the public health field as this strand of research continues. One area of very clear difference is in normative approaches to reporting. I think this is an area where the public health / medical field has much to offer and I genuinely hope these authors will consider reporting their results in a format that facilitates publication in a high impact public health journal, and, even more importantly, facilitates greater understanding in the public health field and greater collaboration across disciplines.

Thank you for your comments about the interest of the study and the need for interdisciplinary exchanges. We have followed your recommendations and those of the editors to improve the reporting of our results.

Specific comments

Reporting

I refer the authors to the CONSORT statement and associated papers that outline approaches to reporting the results of clinical trials in medical / public health journals, and to literature on economic interventions reported in public health journals that adopt these standards – one example being the IMAGE study

published by Pronyk, Hargreaves et al in the Lancet 2006. As examples:

- A participant flow diagram is required, and would probably remove the need for the recruitment and numbers analysed sections of the results. Some aspects of the section “participant flow” should be in the methods (eg that potential participants were randomly selected from Ifakara DHSS), while the numbers would probably also appear in the diagram.

We have included a participant flow diagram that is included as figure 1 (separate file) and further described under the participant flow sub-section in the results section. The selection from the Ifakara Health and Demographic Surveillance System is described under the participants sub-section in the methods section.

- It is important to stipulate primary outcome measures from secondary ones and to identify when the specific analysis reported was planned (at study design; prior to a final data set being available; or during analysis of the final dataset)

In the outcomes sub-section of the methods section, we define our primary outcome measure: “The primary outcome measure, as defined in the study protocol, is the round-specific combined point prevalence of the four sexually transmitted infections that were regularly tested – *Chlamydia trachomatis*, *Neisseria gonorrhea*, *Trichomonas vaginalis*, and *Mycoplasma genitalium* – at months 4, 8, and 12. “

This primary outcome measure was planned at the study design in order to have sufficient power. We now say it explicitly in the text.

- there should be coherence between the methods of analysis implied by the sample size calculation and those conducted (the sample size calc refers to a log rank test, but this analysis does not appear to have been conducted). When the sample size was calculated had the details of the combined endpoint been pre-specified?

The sample size sub-section has now been revised to reflect the power calculations for the analysis reported. The previous power calculations were those used when the project was initially conceived, but these were updated to the currently reported power calculations during the final stages of project design and recruitment planning.

- The results in tables 2/3 should include N,s and %s as well as measures of effect. Table 1 – for binary or categorical variables – should report these as n’s / %s rather than “sample means” of binary variables.

We have made the suggested changes in all tables.

- The BMJ has previously published good guidelines for structured discussions – that start with a clear statement of the findings as the authors see them in light of their a priori hypotheses. Its not quite clear to me what this statement should say – partly because as I have said above its not very clear what the primary outcome analysis was and when this was specified. It might say that there is from this trial some evidence that a high value CCT, but not a lower value CCT, was associated with decreased prevalence of STIs, but that its unclear what behavioural changes led to this shift and secondary outcome data do not necessarily support the suggestion that this was due to a shift towards sexual behaviour that would reduce risk of HIV in this population.

As suggested, we have added a statement at the beginning of the discussion section describing the main findings of the study.

Other methodological comments

The rationale for a combined endpoint is unclear, and is perhaps difficult to justify – for reasons the authors allude to in their discussion. At the least more discussion of problems in interpretation should be discussed. The 4-bacterial STI endpoint appears to have been dominated by trichomonas – though we do not currently have any baseline or follow up data on mycoplasma genitalium so its unclear whether this was common or how many people had co-infections. The infections each have different epidemiologies, and in turn this epidemiology is different to that of HIV – which is referred to in the title of the paper and appears to be the real motivation behind the study. There are, for example differences in the age-specific prevalence of HIV and the bacterial STIs used which mean that great great caution should be taken in inferring that any effect on eg trichomonas or a bacterial STI composite could necessarily have any influence on HIV epidemiology. This is particularly important if there is any possibility that an influence of the intervention might have been to change the age of sexual partners – which is highly plausible in the case of this intervention. (I know of conference papers from Ross and White on this subject – I don't know if published). As the authors do point out – there is also the issue of treatment for bacterial STIs – which might have differed between arms here but would have had no influence on HIV epidemiology and might imply little or no change in sexual behaviour attributable to the intervention. Were sexual behaviour data not captured at all? There are well-described limitations to these data but they seem essential to at least try to get a handle on what it was that actually changed between the groups here.

I can perhaps see a rationale for the combined endpoint if this directly links

to the “condition” attached to the cash transfer – but overall I think my preference in design would have been not to use a composite marker. I would certainly encourage the authors to report in a lot more detail what happened over time to each of the specific STIs. Graphs showing the unadjusted prevalence results (and confidence intervals) over time for each of the STIs in I and C groups – and perhaps also shown stratified by sex – would be particularly useful as an adjunct to the reporting of hypothesis tests on the composite outcome.

The measure of combined point prevalence was constructed at study design to ensure sufficient power to detect differences in the control and treatment groups in response to the intervention (the conditional cash transfer). While it would have been interesting to study specific trends in prevalence rates of the various STIs tested over time, we were not powered to do so, and in any case, these specific trends would yield more insight into the specific transmission patterns of each STI and the susceptibility of the research population to infection than into sexual practices, per se. Our objective was in some ways much narrower than this, as we were seeking sufficient power to detect differences that would indicate changes in behavior as a result of the intervention, rather than transmission patterns of different STIs within this population. The impact of financial incentives on behavior relating to sexual health was in fact confirmed by our study, although the biological outcomes cannot be used to infer the relative importance of STI treatment seeking behavior versus a reduction in risky sexual activity (e.g. increased condom use, number of partners). It is true as the reviewer states that this result does not confirm a reduced risk of infection for HIV in this population, it does point to the importance of a behavioral pathway (via treatment seeking behavior or changing sexual practices).

In the text (outcome sub-section of the methods section), we have strengthened the rationale for reliance on the composite marker.

As requested, we are also providing as a supplemental table including the prevalence by study arm for each STI at each round. We provide it as additional information for the reviewers and editors, but we would think that because our study was not powered to detect reduction in individual STI prevalence and because of space limitation that table should not be included in the published paper. Of course, if the referees and editors think otherwise, we would be happy to include in this or another format.

As far as sexual behavior data are concerned, we have collected quantitative and qualitative data. We are developing separate manuscript for its analysis and it has been analyzed in the following PhD dissertation:

Packel, Laura J. Who Changes How: Strategies and Motivation for Risk Reduction Behaviors in the Context of an Economic--based HIV Prevention Intervention in Tanzania. PhD Dissertation, University of California at Berkeley, 2010.

Process data

For a complex intervention such as that reported on here it seems essential to report data on “process” as is recommended now for trials of complex interventions in public health (Anne Oakleys group have been particularly active and have published on this in the BMJ). I could imagine a number of forms such data might have taken – but the overall aim of such data would to convey to the critical reader things like: was the intervention delivered as intended; was it acceptable and accessed by participants; did intermediary markers (such as sexual behaviour) change in the direction hypothesised etc. There are obvious issues of space limitation – but some data of this type seem essential here.

We collected a significant amount of process data in conducting this study. As the reviewer indicates, space limitation makes it difficult to provide the details that would be of interest to many readers. However, we include some information about whether the intervention was acceptable and accessed by participants and how it was perceived.

We refer the reviewer to the participant flow diagram, and have added a process sub-section in the results section. We are copying here this sub-section:

“Process

The intervention was well accepted and accessed by the study participants as indicated in the participant flow and the low attrition numbers. Further, study participants randomized into the conditional cash transfer arms declared that the financial incentives motivated them to modify their behavior. In the high-value conditional cash transfer arm 317(59.0%) declared that the money motivated them “very much” to change their behavior and 67(12.5%) stated that it motivated them “somewhat”. In the low value conditional cash transfer arm, those numbers are 194(37.4%) for “very much” and 107(20.6%) for “somewhat”.”

Detailed comments

The term “group randomised trial” has a specific meaning – the randomisation of groups – and is confusing here. The trial appears to be an unblinded, individually randomised and controlled trial.

We have made the suggested modifications in the abstract and the trial design sub-section of the methods section.

The authors use the term “risk ratio” throughout – I think what they present are Odds Ratios from logistic regression models. Risk Ratios in epidemiology refer to ratios of cumulative incidence proportions – here we are talking about relative odds of prevalence. This is an important distinction – particularly so as the outcome is not particularly rare.

What we are presenting are relative risks, i.e. the probability of being STI positive in the intervention group, divided by the probability of being STI positive in the treatment group. The term relative risk ratio can be confusing, thus we now instead use the clearer term “relative risk” in the statistical methods.

I’m also not sure about the emphasis on “proof of concept” – if this phrase is to be used the concept in question should be much more clearly articulated – and the discussion of limitations should highlight how proof of this concept relates to other relevant concepts. For example, I don’t think that this study in anyway proves the concept that cash transfers can influence sexual behaviour – no data on this were collected and the overall balance from outcome results suggests that at least those behaviours relevant to shifts in HIV were not achieved. The abstract must stipulate something about what the “condition” was and how this was monitored.

We have removed the reference to “proof of concept” in the abstract and the body of the text.

The additional complexity of a sub-village level randomisation intended to allow the study of “potential peer-effects” is interesting but complex and requires a bit more detail in the limitations section. The inclusion of a fixed term for sub-village in the analysis appears to be intended to “re-correct” the results for this aspect of the design I think (we don’t see here any of these analysis on peer-effects – so in the context of this paper this design aspect feels like a limitation, though there may have been interesting reasons for this). However, there are greater difference that one would normally expect in a randomised trial between the unadjusted and adjusted results, and I wonder whether this is partly due to this group level random selection step (given that there were only 10 sub villages, and this step therefore may well have introduced imbalance). However, it might also be related to the problem of non-collapsibility of Odds

Ratios from cohorts. It may be useful to provide some more detailed baseline data on the differences between villages at baseline – and how the stratified sampling might have led to some of the baseline differences described. More on steps taken to ensure randomisation was truly blind would have been useful. As it reads it has the potential to be very easily influenced at field level. At least this should be reflected in the limitations.

First, we note that there were 10 villages and 50 sub-villages. It is true that we introduced indicator variables for each sub-village in the adjusted models to account for the different selection probability (and potentially associated peer-effects) at the sub-village level. We have added one sentence in the limitation section to account for this.

“In order to study potential peer-effects, in randomly selected sub-villages, the probability of selection in the intervention arm was 75% and in the other sub-villages, it was 25%. This might have led to baseline imbalances. For this reason, we included sub-village indicator variables in the adjusted models. This might explain some of the differences between the results from the unadjusted and the adjusted models”.

Randomization was not blind. Participants were not blinded to arm assignment since awareness of their eligibility for the conditional cash transfer was a critical component of the intervention. We believe the reviewer refers to the possibility of manipulation of the randomization at the field level. We think our very transparent procedures eliminated this risk. We added in the randomization sub-section of the methods section that the randomization step took place in public view, minimizing the potential for manipulation.

[Reviewer 2 Comments...](#)

Name: Dr Surinder Singh

Position: Senior Lecturer in General Practice

Firstly, a word of caution. There are some quite intricate statistics used in this paper and I am no expert (though, importantly I managed to acquire some help with this in that I consulted one of my senior 'stats' colleagues in the dept). If it is likely that this paper is published it ought to be looked at independently from a statistical point of view.

I liked this paper - not simply because of the subject material but because it highlights an important, perhaps all-to-simple, way of reducing high-risk behaviour in a certain population. The results are fascinating.

The introduction is fine along with the methods and the trial design, including a description of the participants and interventions. One question: I wondered why one of the key STIs being incentivised was mycoplasma genitalium (MG) when it seemed to be an unfamiliar infection to the clinicians (page 8). I understand that HIV was also not included for genuine reasons. The role of MG seemed to be ambiguous since there was no testing at baseline.

Mycoplasma Genitalium was included in the primary study endpoint calculation to increase power. However, we did not tie the CCT payments to participants to a negative test result for m Gen. While m Gen has been shown to be incontrovertibly linked to risky sexual activity, there is some uncertainty around transmission pathways. Rather than risk penalizing participants from testing positive if it was unrelated to risky behavior, we chose to use the aggregate results in the composite measure to increase power for the study. We have modified the sentence about the lack of familiarity of participants and clinicians with m Gen, and replaced it with an explanation of why m Gen can be used to increase power but is less appropriate for conditionality.

I also have a question about sample size (page 10); the description is that a log rank test is being used, however the results/tables show logistic regression (which is the entirely appropriate tool to use) - does the initial description need minor modification?

As indicated in the response to the editor's comments, the sample sub-section has now been revised to reflect the power calculations for the analysis reported. The previous power calculations were those used when the project was initially conceived, but these were updated to the currently reported power calculations during the final stages of project design and recruitment planning. As per the reviewer's intuition, we too had initially considered the log rank test to be most appropriate. However, fieldwork in preparation for project launch suggested the strong possibility of time-varying effect sizes, which led us to instead prefer an approach that would estimate separate models at each post-treatment time point.

A couple of questions/comments about the tables:

Table 1: Do we need columns 3 & 5? My understanding that as these are baseline descriptive results 'P' values are not necessary. This may be a debatable point? Also in columns 1 & 2 the figures are presented as fractions of 1 (0.499 & 0.511); would percentages be clearer (perhaps with standard deviations)?

We have modified the tables to include percentages, but we have kept the p-values in table 1 to underline the few imbalances at baseline.

Tables 2/3: Fairly clear - though why is mycoplasma genitalium included; see my comments above about MG.

We added Mycoplasma genitalium to increase statistical power. See discussion above.

Discussion - I think this is fine and is a well-written account of the what the trial has shown, including within that a robust examination of the limitations. I agree that some of the findings are perverse (positive results only seen at specific points) - but further study may shed light on this.

Generalizability: again I agree and this is well-written. For those unfamiliar with "proof of concept" - might this warrant a definition or description?

Abstract: I think this is fine and describes well what follows in the trial.

3) Second submission decision

To: Damien de Walque <ddewalque@worldbank.org>
From: dmacauley@bmj.com
Subject: BMJ BMJ/2011/883504- Manuscript Decision
Cc:

BMJ/2011/883504

Incentivizing safe sex: A randomized trial of conditional cash transfers
(CCTs) for HIV and sexually transmitted infection prevention in rural Tanzania

Dear Dr de Walque

Thank you for sending us this paper and giving us the chance to consider your work, which we enjoyed reading. We recognise the work involved in revising the manuscript to this stage and thank you for sending us this version. We asked our statistician to take a further look at the paper. He has, unfortunately, raised a number of issues relating to the paper. These do appear to be rather important and we would be unable to publish the manuscript in its current form. You will find our statisticians report on the web. I would ask you to respond to each of the points raised. Please supply your response point by point and indicate where in the manuscript you have made the changes. Some of these issues are quite fundamental and large sections of the paper will need to be rewritten. I am sorry to ask you to do this at this stage but we take our statisticians advice very seriously and we would be unable to consider your paper in its current format.

We hope that you will be able to revise and resubmit the paper and send it

back to us within one month. Please upload the revised version as a Word document via your author area at our online editorial office (<http://submit.bmj.com>) - do not resubmit the manuscript as a PDF because our system will not be able to process that.

All original research in the BMJ is published with open access. The full text online version of your article, if accepted after revision, will be the indexed citable version (full details are at <http://resources.bmj.com/bmj/about-bmj/the-bmjs-publishing-model>), while the print BMJ will carry an abridged version of your article, usually a few weeks afterwards.

We would also like you to write an abridged version of the article for the print BMJ - what is essentially an evidence abstract called BMJ pico and then email it to pico.bmj@bmjgroup.com (more details below on how to write this using a template).

If we ultimately offer you publication of your article we will be asking you to pay the BMJ a publication fee if you are able to claim that amount from your funder. Consideration of your paper is not related to whether you can or cannot pay the fee, and you need do nothing now. If we accept your paper we will write to you again to ask whether you can claim the fee from your funder.

However, because publication of research on bmj.com is definitive and is not simply interim "epublication ahead of print",

if you do not wish to abridge your article using BMJ pico you will be able to opt for online only publication. Please let us know if you would prefer this option.

Best wishes

Domhnall

Domhnall MacAuley

BMJ Editorial

Report from the BMJ's manuscript meeting

We are able to accept only a small proportion even of the good articles submitted to us. A little over 10 % of articles reach this stage, and to do so they have to have passed preliminary screening by one or more of the editors, have received sufficiently positive external peer review, and have been discussed at the manuscript meeting.

At the manuscript meeting each article is discussed by the Editor or deputy, the rest of the BMJ's international team of research editors, and two invited advisers: one statistician and one clinical editorial adviser. As well as the scientific merits of the paper we take into account each paper's originality and interest to a general readership in comparison with other submitted papers. We take reviewers' reports fully into account too, but the final decision on acceptance or rejection of a paper rests with the Editor.

These comments are an attempt to summarise the discussions at the manuscript meeting. They are not an exact transcript.

Members of the committee were: xxx (chair), yyy (statistician), zzz (editorial adviser), [and list other eds who took part]

Decision: provisional acceptance

Detailed comments from the meeting:

First and foremost, please revise your paper to respond to all of the comments by both of the reviewers. You will find these at our online editorial office (at <http://submit.bmj.com>) in your author area, under this manuscript number.

Please also respond to these additional comments by the committee:

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When you revise and return your manuscript, please take note of all the following points. The commonest reason for us to have return papers to authors after revision is that some of these points have not been attended to and we cannot, therefore, proceed to acceptance. Even if an item, such as a competing interests statement, was present and correct in the original draft of your

paper, please check that it has not slipped out during revision:

a. In your covering letter please provide, point by point, your replies to the comments made by the reviewers and the editors, and please explain how you have dealt with them in the paper. It may not be possible to respond in detail to all these points in the paper itself, so please do so in the covering letter.

b. We will need the full version of your paper. If it is accepted it will then be edited, proofed, and - after your approval - published on bmj.com with open access. This open access Online First article will not be a pre-print. It will represent the full, citable, publication of that article.

At the time of publication on bmj.com the bibliographic information is forwarded to PubMed and other indexing agencies, so the article can be searched for and cited (the citation format appears at the top of the online article). Full details are at <http://resources.bmj.com/bmj/about-bmj/the-bmjs-publishing-model>).

The citation will be year, volume, elocator (a unique identifier for that article): eg BMJ 2008;337:a145 — and this is what will appear in Medline, PubMed, and other bibliographical indexes. We will give this citation in print and online, and you will need to use it when you cite your article.

c. We would also like you to write an abridged version of the article for the print BMJ - what is essentially an evidence abstract called BMJ pico. To do this please use the appropriate template for your study's design. Please be reassured that it doesn't take long to complete this. When your BMJ pico is ready please email

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* signed patient consent form(s), if the article gives enough personal information about any patient(s): this sometimes occurs even in research papers - for example in a table giving demographic and clinical information

about a small subgroup in a trial or observational study, or in quotes/tables in a qualitative study - (see http://resources.bmj.com/bmj/authors/editorial-policies/copy_of_patient-confidentiality)

- * for a clinical trial, the trial registration number and name of register – in the last line of the structured abstract

- * a data sharing statement such as "Data sharing: technical appendix, statistical code, and dataset available from the corresponding author at <email address or url>". If there are no such further data available, please use this wording: "Data sharing: no additional data available"

- * please write the discussion section of your paper in a structured way, to minimise the risk of careful explanation giving way to polemic.

Please follow this structure:

- * statement of principal findings of the study

- * strengths and weaknesses of the study

- * strengths and weaknesses in relation to other studies, discussing important differences in results and what your study adds. Whenever possible please discuss your study in the light of relevant systematic reviews and meta-analyses (eg Cochrane reviews)

- * meaning of the study: possible explanations and implications for clinicians and policymakers and other researchers; how your study could promote better decisions

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We do want your piece to be easy to read, but also want it to be as scientifically accurate as possible. Please include in the results section of your structured abstract (and, of course, in the article's results section) the following terms, as appropriate:

For a clinical trial:

- Absolute event rates among experimental and control groups
- RRR (relative risk reduction)
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For a cohort study:

- Absolute event rates over time (eg 10 years) among exposed and non-exposed groups
- RRR (relative risk reduction)

For a case control study:

- OR (odds ratio) for strength of association between exposure and outcome

For a study of a diagnostic test:

- Sensitivity and specificity
- PPV and NPV (positive and negative predictive values)

4) Second submission review and our answer (in bold) to it.

Comments

BMJ/2011/883504

Incentivizing safe sex: A randomized trial of conditional cash transfers (CCTs) for HIV and sexually transmitted infection prevention in rural Tanzania

Damien de Walque, William H Dow, Rose Nathan, Ramadhani Abdul, Faraji Abilahi, Erick Gong, Zachary Isdahl, Julian Jamison, Boniphace Jullu, Suneeta Krishnan, Albert Majura, Edward Miguel, Jeanne Moncada, Sally Mtenga, Matthew Alexander Mwanyangala, Laura Packel, Julius Schachter, Kizito Shirima, and Carol A Medlin

Decision: Provisional Acceptance/Request Revision; **Decision Date:** 3 Oct 2011

Date Received: 17 Sep 2011

Editor: Domhnall MacAuley

Previous manuscript ID: BMJ/2011/883504

Article Types: Research

Corresponding Author: Damien de Walque

Keywords: None

Supplemental Files: 6

[Comments](#)

[Comments...](#)

Name: Jon Deeks

Position: Professor of Biostatistics

This manuscript reports results of a randomized trial of financial incentives to increase safer sexual behaviours. The study did not proceed as planned, and the results do not provide convincing evidence that the intervention works. The authors find a significant effect at one time point using an adjusted analysis, and interpret their findings as being more conclusive than probably can be justified.

We have been more explicit on the smaller sample size than originally anticipated in the “Sample size” section (this was the only key aspect in which the study did not proceed as planned). We have qualified our results in the abstract, the first paragraph of the discussion section and the summary points box.

1. There appears to be a degree of post hoc rationalization of sample size

calculations which is not made entirely clear to the reader, with a discrepancy between the sample size calculation reported in the study protocol and the calculation reported in the paper. The authors do acknowledge at the end of the sample size calculation section that they had initially intended to recruit more participants but they do not explicitly state that the calculation which is reported was undertaken post hoc and based upon the incidence observed in the study. The protocol reports a calculations based on detecting (relative) differences of a 30% magnitude or greater in the treatment arm compared to the control arm with incidence rates varying between 15%-20% across research sites and drop-out rates as high as 20% per year giving a total sample size of 3000 individuals. The paper states that the power calculation was based on an incidence rate of 12%, controlling for one baseline measure for a one-third reduction requiring 2400 individuals with no mention of any drop-out.

In the revised “Sample size” section we have now explicitly indicated that the power calculation presented is an ex-post calculation based on the observed properties of the actual recruited sample and infection rates. In the original manuscript submission we had presented the power calculations from the study protocol, but were asked to remove these. We agree with the earlier reviewers that the power calculations corresponding to our actual data analysis are most directly relevant for readers.

2. Calculation of P-values between randomized groups at baseline is illogical – the P-values indicate the probability that differences have occurred by chance – as all differences are created by randomization, they must have occurred by chance, so why calculate a probability? What is important is the magnitude of the differences, not the P-values. Please remove the P-values from Table 1 and the baseline data section of the results. The use of 2 decimal places on the percentages in this table is also not justified – it implies excessive precision.

We have removed the p-values from table 1 and from the baseline data section of the results. We have also removed the second decimal from table 2.

3. There is no mention in the statistical methods whether an intention-to-treat process was followed for the analysis and how missing data were handled (although there is a section describing how much missing data existed).

We have added the following sentences to the beginnng of the statistical methods section to clarify these two points:

“Each individual was coded as per their initial randomized assignment as per an intent-to-treat design. However, individuals who were not present at any given round were treated as missing and dropped from the analysis for that round due to lack of outcome data.”

4. I would have expected the results section to have reported on the incidence of the outcome measure – this is not mentioned at all in the text and is somewhat cryptically reported in Table 2 (wrongly labeled “sample mean”) and more appropriately in Table 3. However, the actual numbers positive are never reported by randomized group, which is highly desirable (and I believe required by the CONSORT guidelines).

We have now added the number of positives by study arms at the bottom of table 2 and we have relabeled correctly the number of positives. We also report the number of positives at month 12 in the outcomes and estimation section of the text.

5. Please note that the logistic regression model will have estimated odds ratios and not relative risks. With an incidence rate of 12% the figures will be close to relative risks but they should be described properly.

Our tables do in fact report relative risks, not odds ratios. We understand that there is some difference in use of the term relative risk, but we are using the term in the same sense as indicated in the BMJ Clinical Evidence glossary (<http://clinicalevidence.bmj.com/ceweb/resources/glossary.jsp>). Although logistic regression will yield estimated odds ratios, we have transformed the effects into relative risks using the “margins” and “nlcom” commands in *Stata 12* (using the method as recommended e.g. in: Kleinman LC, Norton EC. What’s the risk? a simple approach for estimating adjusted risk measures from nonlinear models including logistic regression. *Health Services Research* 2009; 44: 288-302). This is now explicitly stated in the “Statistical methods” section of the text.

We prefer to report the relative risks for two reasons. First, this was an interdisciplinary project, and while we believe that publication in BMJ is highly appropriate, we also want the magnitudes to be readily interpretable by other audiences as well such as economists who do not typically use odds ratios. Second is the related point referred to by the reviewer, that with an incidence rate of .12, the odds ratio will show a larger reduction than the relative risk. For example, where we report a relative risk of 0.73, the corresponding odds ratio would have been reported as 0.69. To avoid the problem of readers having to do the calculation themselves to understand how different the odds ratio is from the more interpretable relative risk, we prefer to directly report the relative risk.

6. The results section on "outcomes and estimation" focused on the statistical significance of the comparisons, with very little "estimation" of treatment effects for the main comparisons. It would be helpful to give the estimates

(with 95% CIs) in this section – for example you can state that the unadjusted analysis estimated a reduction in the odds of STI of 20% (95% CI: 6% increase to 46% reduction) at 12 months, whereas the adjusted model estimated a reduction of 27% (95% CI: 1% to 53% reduction)

We have now provided this statement of estimates of the effects for the main results (high value CCT group at month 12) for the unadjusted and adjusted model in the outcome and estimation section.

7. Tables 2 and 3 do not state what the comparator group is for computation of the relative risks (odds ratios). Inclusion of standard errors in these tables probably isn't helpful – they are figures on the log odds ratio scale. The confidence intervals are more useful, and should a reader require a standard error they could be computed from these values.

Expanded notes under tables 2 and 3 now indicate that the reference group for the computation of the relative risks is the control group. We have removed the standard errors from tables 2 and 3, retaining the confidence intervals.

8. There is no explanation of how the adjustment variables were chosen, whether they were prespecified (the protocol has no statistical methods section so I would presume that they were not prespecified) and the manner in which they were categorized or used as continuous measures. The comparison of the effect in males and females must have been undertaken using a test of interaction but this is not currently mentioned.

While the adjustment variables were not explicitly pre-specified in the protocol, they are standard socio-demographic variables. We have now indicated in the statistical methods that age and income are continuous variable and that the other adjustment variables are categorical. In the outcomes and estimation sub-section of the results section, we now make clear that we ran a test of interaction for the difference between males and females and that the interaction term for female was not significant.

9. From the results which have been obtained I am not clear that the authors can conclude with any reasonable degree of certainty that there is a benefit of this intervention. However, the headline for the discussion (and the summary points) is that there was a significant reduction for the higher \$20 payments (opening sentence of discussion). However, this reduction was only observed as being statistically significant when adjustments were made, only at one of the three time points, and only when the serum tests were not considered. It therefore

seems to be an overstatement of the findings.

We have revised the headline of the discussion to make clear that the statistically significant results were only obtained in the adjusted model and only at month 12 and not at earlier time points, for the high value cash payments and for the serum tests. We would be even more tentative if the results were only statistically significant during an early time point rather than the final time point; however the pattern of increasing effect over time is consistent with our a priori hypothesis and indeed is the reason why we structured the intervention to have multiple incentivized testing rounds. As noted in the “Interpretation” section, “the impact of the conditional cash transfer may take time to materialize, perhaps because it is not easy to extricate oneself from complicated sexual relationships, or perhaps because participants needed time to become accustomed to (and trust) the incentive mechanism.”

10. One conclusion from the trial (mentioned in the abstract) is that a further study needs to be done to clarify the magnitude of the benefit. This statement is presumptive about there being a proven benefit, and one wonders how well the case can be made for a larger trial which would be needed (probably requiring over 10,000 participants).

In the abstract and the summary box, we now say that the intervention is “potentially promising” rather than promising and we add that a larger study would be useful to clarify the effect size, to calibrate the size of the incentive, and to determine whether the intervention can be delivered cost effectively.

CONSORT 2010 checklist of information to include when reporting a randomised trial*

Section/Topic	Item No	Checklist item	Reported on page No
Title and abstract	1a	Identification as a randomised trial in the title	1
	1b	Structured summary of trial design, methods, results, and conclusions (for specific guidance see CONSORT for abstracts)	3-4
Introduction Background and objectives	2a	Scientific background and explanation of rationale	5-6
	2b	Specific objectives or hypotheses	6
Methods Trial design	3a	Description of trial design (such as parallel, factorial) including allocation ratio	7
	3b	Important changes to methods after trial commencement (such as eligibility criteria), with reasons	7
Participants	4a	Eligibility criteria for participants	7
	4b	Settings and locations where the data were collected	7
Interventions	5	The interventions for each group with sufficient details to allow replication, including how and when they were actually administered	7-8
Outcomes	6a	Completely defined pre-specified primary and secondary outcome measures, including how and when they were assessed	9-10
Sample size	6b	Any changes to trial outcomes after the trial commenced, with reasons	
	7a	How sample size was determined	10
Randomisation: Sequence generation	7b	When applicable, explanation of any interim analyses and stopping guidelines	
	8a	Method used to generate the random allocation sequence	11
Allocation concealment mechanism	8b	Type of randomisation; details of any restriction (such as blocking and block size)	11
	9	Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned	11
Implementation	10	Who generated the random allocation sequence, who enrolled participants, and who assigned	11

		participants to interventions	
Blinding	11a	If done, who was blinded after assignment to interventions (for example, participants, care providers, those assessing outcomes) and how	11
	11b	If relevant, description of the similarity of interventions	
Statistical methods	12a	Statistical methods used to compare groups for primary and secondary outcomes	12
	12b	Methods for additional analyses, such as subgroup analyses and adjusted analyses	12
Results			
Participant flow (a diagram is strongly recommended)	13a	For each group, the numbers of participants who were randomly assigned, received intended treatment, and were analysed for the primary outcome	13
Recruitment	13b	For each group, losses and exclusions after randomisation, together with reasons	13
	14a	Dates defining the periods of recruitment and follow-up	14
	14b	Why the trial ended or was stopped	14
Baseline data	15	A table showing baseline demographic and clinical characteristics for each group	p. 15+Table 1
Numbers analysed	16	For each group, number of participants (denominator) included in each analysis and whether the analysis was by original assigned groups	15-16
Outcomes and estimation	17a	For each primary and secondary outcome, results for each group, and the estimated effect size and its precision (such as 95% confidence interval)	16-17, tables 2 and 3
	17b	For binary outcomes, presentation of both absolute and relative effect sizes is recommended	
Ancillary analyses	18	Results of any other analyses performed, including subgroup analyses and adjusted analyses, distinguishing pre-specified from exploratory	16-17, tables 2 and 3
Harms	19	All important harms or unintended effects in each group (for specific guidance see CONSORT for harms)	4
Discussion			
Limitations	20	Trial limitations, addressing sources of potential bias, imprecision, and, if relevant, multiplicity of analyses	18-19
Generalisability	21	Generalisability (external validity, applicability) of the trial findings	19
Interpretation	22	Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence	19-20
Other information			
Registration	23	Registration number and name of trial registry	20-21
Protocol	24	Where the full trial protocol can be accessed, if available	21
Funding	25	Sources of funding and other support (such as supply of drugs), role of funders	12; 22-23

*We strongly recommend reading this statement in conjunction with the CONSORT 2010 Explanation and Elaboration for important clarifications on all the items. If relevant, we also recommend reading CONSORT extensions for cluster randomised trials, non-inferiority and equivalence trials, non-pharmacological treatments, herbal interventions, and pragmatic trials. Additional extensions are forthcoming: for those and for up to date references relevant to this checklist, see www.consort-statement.org.

Dear Editors,

It is a pleasure to submit, on behalf of my co-authors, our manuscript entitled “Incentivizing safe sex: A randomized trial of conditional cash transfers for HIV and sexually transmitted infection prevention in rural Tanzania” to *BMJ Open*.

We think this is an important paper reporting the results of a novel approach for HIV and STI prevention. Given the limited repertoire of proven efficacious HIV prevention interventions, this research could have an influential role in HIV prevention programming, HIV policy, and HIV research. This study provides a new avenue for HIV prevention through conditional cash transfers that can be described as a "structural" behavioral intervention that has shown to be also effective in other domains such as nutrition and education.

This paper had been submitted to *BMJ* (manuscript BMJ/2011/883504) and went through two rounds of review. We are submitting to *BMJ Open* the last version (second revision) we submitted to *BMJ*, in exactly the same format. If needed, we would be happy to make any modification requested for the *BMJ Open* format. We are also uploading a document entitled “Review History with responses at *BMJ*”. This document includes the first and second submission decision letters and reviews received at *BMJ* together with our answers to each point. Our answers are in bold. In addition, to help identify the modifications made to the manuscript during the review process, I am attaching, for both revisions, versions of the manuscript including “track changes” from the precedent version. I am confident those “track changes” versions capture all the substantial changes we made to the manuscript, but a few final corrections of typos and other formatting changes might not have been captured.

We are looking forward to receiving the feed-back from your reviewers and editors and are grateful for your consideration of our manuscript.

Best regards,

Damien de Walque

**Protocol for the
RESPECT Study (“Rewarding STI Prevention and Control in Tanzania”)
October 2010**

SECTION 1: PURPOSE AND BACKGROUND OF STUDY

At its core, the global AIDS epidemic is fueled by risky sexual behavior. Over 80% of HIV infections occur through sexual contact with an infected partner, and could have been avoided through the adoption of safer sexual behaviors. Despite isolated – and, often temporary – successes, behavior change interventions promoting safer sexual behavior have proven remarkably ineffective at stemming the tide of the epidemic. New, innovative approaches to behavior change are desperately needed, particularly for young people in their child-bearing years who are becoming sexually active. Of the 4.3 million *new* HIV infections that occur each year globally, 80 percent occur among this age group.

The primary aim of this study is to evaluate the impact of a novel behavioral intervention for preventing HIV and other sexually transmitted infections (STIs) among youth and young people in the Kilombero/Ulanga districts in southern Tanzania. This intervention uses a type of economic incentive called “conditional-cash transfers” (CCTs) to motivate safe sexual behavior among youth by linking cash rewards to negative laboratory test results from periodic STI screenings. The basic premise is that safer sexual practices can be encouraged by using CCTs to make risky decisions more costly.

The decision to have sex involves a trade-off between the short-term benefit of sexual pleasure and intimacy and the long-term (probabilistic) cost of getting pregnant or acquiring an STI (O’Donoghue and Rabin, 2000). Thus, risky decisions may be the result of realistic assessment of trade-offs and probabilities, or may result from problems associated with undervaluing the future (e.g. excessive “discounting”). Of course, this is a stylized view of the decision making process that may be conditioned and constrained by the cultural, social, and economic context. A large body of research has focused on how poverty, lack of economic opportunity, and powerlessness closes off options to the point that the individual does not experience his or her engagement in risky sexual behavior as the outcome of a deliberate “decision.”

Nevertheless, evidence from the fields of economics, behavioral economics, and clinical psychology has shown that decision-making under conditions of uncertainty is highly responsive to incentives. Applied to the area of sexual health, the evidence is suggestive of a decision-making process that is at least partially informed by an explicit assessment of costs and benefits, even among the socially and economically disadvantaged. Gertler et al. (2005) found in a study of Mexican sex workers that “risky sex” carries a 23% higher price tag than sex with condoms. In a study of informal sex workers in Western Kenya, Robinson and Yeh (2009) found that sex workers charge more for anal sex and that risky sexual activity fluctuates in response to consumption expenditures and income shocks experienced within the household. Such findings suggest that an appropriately-designed and well-targeted intervention would be able to alter the cost-benefit parameters of the decision to engage in risky sexual behavior.

We plan to conduct a two-arm randomized control trial to test the hypothesis that a system of rapid feedback and positive reinforcement – using cash as the primary incentive – can be used to promote safer sexual activity among youth and young people who are at high risk of HIV infection. CCTs have proven remarkably effective at inducing and reinforcing positive behavior change in many areas of social and health policy, but they have not yet been evaluated for their effectiveness as an AIDS prevention intervention.

In the CCT intervention to be tested in this trial, cash payments will be conditional on the avoidance of risky sexual behaviors (or, alternately, on the adoption of safe sexual behaviors). Since self-reported sexual behavior data is notoriously unreliable and subject to strong reporting biases, we will instead link cash payments to objective measures – like STI test results – that serve as proxies for risky sexual behavior. Only STIs which have been incontrovertibly linked to risky sexual activity will be linked with cash payments. Youth will be

monitored on a regular basis for STIs and will be rewarded with cash each time their STI test results are all negative.

For our study population in Tanzania, cash payments will be linked to several STI test results: Chlamydia, gonorrhea, syphilis, HSV-2, and trichomonas. With the exception of HSV-2, which can be treated but not cured, each of these STIs is curable. This is a critical point, since youth who test positive for an STI can continue to participate in the intervention after they have been treated and cured of the infection. Thus, learning is encouraged through positive reinforcement, and mistakes can be corrected and overcome. For both ethical and practical reasons, the cash transfers will not be tied to HIV status, and HIV acquisition will not result in being dropped from any arm of the study.

The proposed intervention is also likely applicable to a variety of social and cultural settings due to the nature of the intervention, which is neutral about the specific behaviors required to remain free of infection. For example, individuals may choose to abstain, use condoms, or reduce the number and concurrency of sexual partners. While information about how to prevent infection will be provided to all participants, the specific decision will rest in the hands of the individuals themselves.

Recognizing that girls and young women may lack the power to actively participate in decisions affecting their sexual/reproductive health, we have added a psychosocial intervention (gender-based counseling and life-skills training) to strengthen and reinforce the effects of the CCT intervention on behavior change. The psycho-social component of the intervention will thus serve to improve the decision-making capacity of participants by focusing on STI education, gender-power imbalances, and making deliberate choices in the domain of sexual/reproductive health. Limited empirical evidence suggests that economic interventions in combination with psycho-social support have greater impact than either type of intervention taken singly.^{i ii iii}

Because this is such a novel approach, there are many unanswered questions on how an intervention using such an approach could be – or should be – designed. What is the appropriate target population? Adolescents? Geographical hot spot areas? Set within residential communities or within social networks? What is the appropriate amount of cash to dispense? What interval of testing/payment is needed? For how long should the intervention run? What happens when the money runs out? What are the risks? How do the risks differ in different potential target population groups? What epidemiologic setting is most appropriate?

These are absolutely critical questions that have never been examined in terms of CCTs & STIs/HIV prevention, which is why we are casting a ‘wide net’ in this first study and are focusing on an epidemiological context that is ‘typical’ of the East African areas where youth are at higher-risk of HIV.

We have been careful in the design of this study to ensure that we explicitly consider each of these fundamental questions and ensure that we are using the best empirical evidence available. In some cases, that means we have been able to draw on empirical work in other areas; in other cases it means that we have built the question into the study ourselves because there is little evidence to guide intervention design decisions.

In this study, we will implement the intervention for one year in two districts in southern Tanzania and evaluate its impact by randomly assigning 18-30 year old participants and their spouses to receive either the CCT intervention or STI testing/treatment alone. A follow-up assessment will be conducted 12-months after the intervention ends. This two-year randomized trial thus has two main arms: a treatment arm which receives the CCT intervention for 1 year starting after baseline, and a control arm which does not. Both study arms will receive STI testing, basic STI/HIV counseling, and treatment five times over the 2-year period, as well as the psychosocial /group-counseling intervention for the first year. Individuals in the treatment arm will then be randomly assigned to receive either a Tsh 10,000 or Tsh 20,000 (roughly \$10 or \$20, as referred to in this protocol) cash reward group. This will further allow sub-study of the effect of varying sizes of cash transfers.

We have 3 primary research objectives:

1. Evaluate the impact of the combined CCT/counseling intervention on STI incidence overall – and by specific subgroups – during the intervention period. This will enable a characterization of the immediate and short-term effects of the intervention and to identify responsiveness in different potential target groups. Economic outcomes will be evaluated as well.
2. Examine the long-term effects of the intervention – and its withdrawal – on STI incidence and economic outcomes by conducting a final round of STI testing and surveying in the same population 12-months after the intervention has ended.
3. Compare the impact of the CCT intervention in the high-value cash transfer arm to that in the low-value cash transfer arm. This will permit us to better understand thresholds and non-linearities in the price effects, and the findings will have important implications for how the intervention could be brought to scale, if found to be effective.

In addition, the Control-R4 sample to be newly recruited at round 4 (not initially envisioned as part of the study) will be used to test the impact of enrollment in the original Control group. Specifically, the Control-R4 sample will allow testing of the effects of the extensive access to counseling, testing and treatment provided to original Control subjects in the main study. The main study was designed to test the effects of cash rewards, over and above the effects of such counseling/testing/treatment, thus the original Control group itself received extensive intervention. This original Control group intervention has so far included baseline, 4-month, and 8-month counseling/testing/treatment, as well as a year of monthly group counseling. This package of services to baseline participants is expected to result in decreased STI incidence based on prior research, but the extent of that prior research is limited, thus there is considerable scientific value in quantifying the STI benefits of this precise package of preventive efforts. The Control-R4 will serve as a comparison group to this original Control group, allowing estimation of the STI improvement due to original Control enrollment.

Study area

This study will take place in two rural districts in southern Tanzania, Kilombero and Ulanga, located in the region of Morogoro. The Ifakara Health Research and Development Center (IHRDC) manages the Ifakara Demographic Surveillance System (DSS) in this region. The Ifakara DSS site was inceptioned in September 1996 and is among the largest demographic surveillance system in all of Africa, collecting basic sociodemographic household-level information on births, pregnancies, deaths, and migration on a quarterly basis. Basic data on asset ownership, ethnicity, education levels, and economic activity is also collected, although at less frequent intervals. A baseline census was conducted between September and December 1996, and each household has been visited once every four months ever since. A total of 56 villages are covered with a population of about 95,000 people in 20,000 households.

In Tanzania and other East African countries, the majority of new HIV infections occur among young people, aged 15-30,^{iv} and the Kilombero/Ulanga district appears to be strongly affected. The infection rates in the Morogoro region as a whole are higher than many other parts of the country. At the district level, accurate data are often lacking, but the data that are available suggest a consistent pattern. Results of an antenatal survey of young mothers conducted in 2003 revealed an overall HIV prevalence of 13.0% for the Kilombero/Ulanga district as a whole. In Kilombero, overall HIV prevalence was 19.2%, compared to 9.8% in Ulanga (with apparent “hot spots” in a few areas – e.g. Lupiro).^v In addition, a 2006 study conducted by our research team found an aggregate STI prevalence rate of 19% amongst 500 youth randomly selected from five villages in the Kilombero/Ulanga DSS region.

In the last quarter of 2005, IHRDC added a youth sexual and reproductive health module to a socio-demographic survey administered within the DSS area. For this module, approximately 4000 youth between the ages of 12-24 were randomly selected from the DSS database to participate in the study. Preliminary analyses indicate that age at sexual debut is low, frequency and concurrency of partners is high, and condom use is low, all indicating the urgent need for new youth-focused prevention approaches. Among respondents who had ever had sex, 78% had their first sexual contact between the ages of 14 and 18. Among female respondents, 62% did not use a condom in their last sexual encounter, while 38% of males did not use condoms. Among out-of-school youth, 86% did not use condoms in their last sexual encounter.

Qualitative assessment of behavioral impacts of intervention

In an effort to supplement the quantitative data being collected through survey at baseline and follow up at 12 and 24 months, we will also collect qualitative data at each time point. In-depth interviews will be performed with a small sub-set (about 90-100) of the enrolled study participants just after enrollment and again after the 4-month results have been received. The qualitative data collected will help us to gain a more complete understanding of how the conditional cash transfers provided for those who remain uninfected impact the decision-making processes of participants, especially regarding sexual and reproductive health. In-depth interview transcripts will provide a more nuanced explanation as to why the cash transfers did or did not facilitate behavior change relating to risky sex and will enable us to understand why an increase in income may or may not influence perceptions of risk, gender inequities and self-efficacy in sexual reproductive health decision-making, ties with dependents, and the decision to engage in transactional sex. These qualitative data will be further supplemented by Conversational Journal data collected by local community diarists, following a methodology successfully developed by Swidler and colleagues for use studying sexual behaviors in neighboring Malawi.

Study background

Mass information, education, and communication (IEC) campaigns, typically the centerpiece of countries' AIDS prevention strategies, have been shown to have had relatively little impact on patterns of HIV transmission and the trajectory of the epidemic (Bertrand et al., 2006). Numerous studies have shown that information alone is typically insufficient to change risk behavior. However, accurate information is indisputably a basic ingredient in informed policy discourse, and IEC in conjunction with condom promotion and distribution likely results in higher condom use and significantly lower STI incidence (Bertozzi et. al., 2006). Nonetheless, in many African countries, infection rates continue to rise even as awareness about risks and consequences of HIV infection has increased within the general population (World Bank, 2006). In Tanzania, the awareness of HIV prevention methods in the youth population is high but has not fully translated into safer sexual behaviors. Almost 80% of young people know that using condoms reduces the risk of contracting HIV, but fewer than half reported using a condom the last time they had sex (MEASURE DHS, 2007).

Psycho-social interventions, such as peer-to-peer counseling, have had a significant and measurable impact on unsafe behaviors, but have not been shown to be cost-effective as a strategy for reaching young people (Hutton et al., 2003). These types of interventions may be costly when brought to scale due to the emphasis on an individualized or small group therapy approach, although there has been some experimentation with more easily scalable, community-based approaches. A multi-country trial of a community-based VCT approach is currently underway (Coates and Szekeres, 2006).

One plausible explanation for the lack of progress with behavior change interventions is that most interventions have focused exclusively on AIDS prevention messages, rather than sexual and reproductive health more broadly. These single-intervention approaches to behavior change have presumed a degree of individual control over decision making that does not speak to the reality of women's and girl's circumstances in sub-Saharan Africa, nor to the dilemma that many face in balancing economic needs, the desire to bear children, and the need to protect themselves from HIV and other STIs. Furthermore, few interventions have been developed to explicitly address critical characteristics of the risk environment, most notably poverty and gender inequalities that give rise to risky behaviors.

Many public health experts have argued that a more aggressive approach to behavior change in Africa is needed, pointing out that "instances where HIV infections appears to be falling ... [were] linked to successful programs aimed at changing behavior, notably in Kenya, Uganda, and Zimbabwe" (Jack, 2007). New, innovative prevention programs are particularly needed to reduce transmission among young people in their child-bearing years who are becoming or who have recently become sexually active. Of the 2.5 million *new* HIV infections that occur each year globally, 80 percent occur among this age group.

Adolescence and young adulthood often represents a period of risk-taking and experimentation, but it also means that young people are at their most receptive and open to change, before social and sexual norms have been firmly established. It is possible that an intervention strategy which seeks to mitigate the effects of the broader risk environment facing young people and emphasizes increased control and deliberation in decision-making will have a greater impact.

This research proposal aims to test a radically different approach to prevention, and to target the age demographic group that can derive the most benefit from it.

The proposed study is a randomized control trial to evaluate a new intervention that uses “conditional cash transfers” (CCTs) in conjunction with counseling and training to encourage safe sexual behavior among young people in East Africa. The basic premise is that safer sexual practices can be encouraged by using CCTs to make risky decisions more costly.

Conditional cash transfer (CCT) programs provide cash to poor households in exchange for their active participation in educational and health care services. CCT programs have proven remarkably popular among developing country governments, sweeping the globe from Mexico to several other Latin American countries, including Columbia, Honduras, Jamaica, and Nicaragua, and much more recently, to Africa. The principle of conditionality – which may be applied differently in practice, but generally requires families to send their children to school or to receive a range of health care services, such as nutritional counseling, childhood vaccination programs, etc. – distinguishes CCT programs from the more traditional social assistance programs which provide cash or vouchers directly to poor or otherwise distressed families with no strings attached. The CCT programs emphasize the use of market-oriented “demand-side” interventions as an instrument for longer-term human capital investments. Ideally, they are designed to complement, rather than replace, the more familiar “supply-side” investments which channel resources directly towards schools, clinics, and service providers.

International collaborative team

This research collaboration brings together investigators from the Ifakara Health and Research Development Centre (IHRDC) in Tanzania, the University of California, Berkeley, and the World Bank. This study is being reviewed by the IRBs at both the local (IHRDC) and national (National Institute for Medical Research) levels in Tanzania.

This research will be conducted in villages in the Kilombero/Ulanga districts in southern Tanzania, in close collaboration with researchers at the Ifakara Health and Research Development Centre (IHRDC). Since 1996, IHRDC has managed a Demographic Surveillance System (DSS) in these two districts covering over 95,000 people in 25 villages, one of the largest DSS in all of Africa. As part of the DSS core activities, basic socio-demographic household-level information on births, pregnancies, deaths, and migration is collected from all households in the DSS area on a quarterly basis. The Ifakara DSS has served as a platform for dozens of health studies – mostly related to malaria – since its inception. IHRDC has stringent standards for protecting confidentiality of research data and study participants which are in line with CPHS standards for U.S.-based research. All research conducted through IHRDC must be approved by a formal Institutional Review Board (IRB) at both IHRDC and the Tanzanian National Institute for Medical Research (NIMR).

Our local Tanzanian collaborators at IHRDC have extensive experience conducting research in the DSS area and are highly qualified to conduct research. They are highly knowledgeable of local community attitudes and cultural norms as well as cultural sensitivities in the DSS area. All IHRDC-based team members are native Tanzanians who speak fluent Kiswahili (the local language) and English. The local PI on our study, Dr. Rose Nathan, is a senior demographer at IHRDC and served as the director of the Ifakara DSS site for four years where she oversaw all DSS activities and associated research. The project coordinator on our study, Ms. Sally Mtenga, has worked on numerous studies in the area and currently serves as the secretary for the IHRDC Institutional Review Board. She has written and reviewed over a dozen informed consent forms for studies in the DSS area and has also led community sensitization efforts for HIV VCT programs in the area. This IHRDC research team, together with our collaborators from the World Bank and UCSF, conducted an STI prevalence

study in 2006 to assess the feasibility of this larger trial in this area. The Tanzanian collaborators at IHRDC will work closely with the US-based team throughout the design and implementation of the study to ensure that we remain respectful of cultural norms, attitudes, and sensitivities as well as of local laws.

SECTION 2: SUBJECTS

Main study

We will randomly select from the DSS database men and women aged 18-30 who live in the study villages in the Kilombero/Ulanga districts in southern Tanzania, as well as their spouses ages 16 and over.

We will select 10 villages located in or near to the Kilombero/Ulanga DSS research area where STI/HIV transmission is relatively high in the youth population (the ‘hot spots’ in the DSS). Potential sites have been identified through consideration of our own 2006 STI prevalence study that focused on 5 villages, a 2003 antenatal clinic HIV survey, as well as the location of villages in terms of their accessibility to roads, train stops, commercial centers, bars/pubs, etc. (whereby higher accessibility to each of these typically translates into higher HIV/STI transmission rates in the area).

Inclusion criteria consist of males and females, aged 18-30 (and spouses ages 16 and over) who reside in selected villages in the Kilombero/Ulanga districts in southern Tanzania and who consent/assent to participate in the study. Exclusion criteria will include: currently pregnant, intention to permanently migrate out of the DSS area within the next year, and unwillingness to participate if assigned to the control arm. These criteria will not be formally incorporated into a screening questionnaire or interview. Rather, they will simply be reiterated in all of the recruitment materials and informed consent form(s), as well as reviewed by study staff at the time of enrollment.

Prospective participants will be identified through the DSS database, oversampling lower socioeconomic status households. The local P.I. and DSS staff will randomly select potential participants from the DSS database after restricting the sampling frame to the target age group (18 to 30) and target villages of residence. Following a phase of community sensitization, fieldworkers will visit the households of the randomly-selected young men & women to invite them to participate in the study. If the individual is eligible and interested in participating in the study, that individual will be invited to the study station the following week, and may be enrolled in the study once the informed consent form is complete.

Individuals will be randomized to study arms at the individual-level, although spouses will always be placed in the same arm as each other. First sub-villages will be randomized to either “high spillover” (75% of enrollees are in treatment arm) or “low spillover” (25% of enrollees are in treatment arm) villages. Participants will then be randomly assigned to the treatment group (n=1500) or control group (n=1500), with on average a 50/50 chance of being assigned to either group. Participants assigned to the treatment group will be further randomized to either the “high-value” cash transfer group (n=750) or the “low-value” cash transfer group (n=750).

Qualitative sub-study

For the qualitative sub-study, participants will be recruited from the main study sample during the second study station visit at either baseline or month-4. A random selection of approximately 90-100 participants drawn from both the treatment and control arms will be recruited at baseline and asked if they would be willing to participate in the qualitative sub-study. At month 4, five participants from the treatment arm who tested positive for one or more STI (and therefore did not receive the cash reward) will be invited to participate. The only inclusion criteria are attendance at the study station during the time of sub-study recruitment and consenting to participate in both interviews, but we will impose quotas by gender, marital status and study arm.

Round 4 Control Group (“Control-R4”)

At the 12-month (round 4) follow-up study point we will recruit a small additional control group (to be termed “Control-R4”) to compare against our original control group enrolled at the round 1 baseline (we now term this

original control group recruited at round 1 “Control-R1”). This will allow us to test whether the intensive counseling and treatment activities given to Control-R1 over the first year of the study resulted in changed sexual behavior and decreased STI incidence, as compared to the new Control-R4 group that was not enrolled during the first year of the study. Although not originally envisioned in the study design, the decrease in STI incidence that we have observed among the Control-R1 group during the first eight months of the study suggests that there may be important scientific gains to studying the Control-R1 group as an intervention group in and of itself. In order to do so, we will draw a new random sample of community members who were eligible for the original study recruitment but who were not enrolled. To minimize the potential for contamination due to sexual mixing across control groups, we will only draw this new Control-R4 sample and make comparisons among married individuals. To enhance power, we will only enroll one person per marital couple into this new sample. Other eligibility criteria will be identical to the original baseline enrollment criteria: The individuals must have been aged 18-30 and married at the time of the initial recruitment one year ago; they must also be currently living in one of the 10 study villages, not be pregnant, and not be planning on permanently migrating out of the study area during the next year. As at baseline, potentially eligible individuals will be identified in the existing Demographic Surveillance Survey computerized database of village residents; study personnel will visit their household to explain the study and verify eligibility; and eligibles will be invited to come to the study station the following week to complete informed consent and enroll if they so choose. All Control-R4 participants will be placed in the same study group, so no randomization will occur. The Control-R4 group will receive free voluntary counseling and testing for HIV and the same set of STIs as original study participants (plus free treatment and referral as is done for original study enrollees).

Number of subjects

Main study

We plan to enroll a total of 3000 individuals in the study. Assuming a refusal/ineligibility rate of 20%, we will recruit 3600 individuals.

By convention, STI prevention trials are often powered to detect a magnitude of 30% difference in STI incidence across study arms. Thus, the proposed study has been powered to detect differences of a magnitude of 30% between aggregate STI incidence rates in the treatment versus control arm.

Power calculations are based on a comparison of aggregate STI incidence rates between two, equal-sized study arms using a log rank test and assuming a two-sided alternative hypothesis. By basing the calculations on a two-arm comparison, we ensure sufficient power to detect differences of a 30% magnitude or greater in the treatment arm compared to the control arm. Other assumptions include:

1. Annual (aggregate) incidence rates in research sites will be constant;
2. (Aggregate) incidence rates may vary between 15%-20% across research sites;
3. Total trial will be 12 months;
4. Overall annual censoring (i.e., drop-out) rates will be as high as 20% per year

Based on these assumptions, a total sample size of 3000 individuals (e.g., 1500 per main study arm) will be sufficient to provide at least 90% power to detect an intervention-related reduction in STI incidence as small as 24%, significant at the 5% level. We will retain at least 80% power to detect a reduction as small as 20% with this sample size. Collectively, these results indicate that the proposed sample size is large enough to provide ample power to detect meaningful effects for the overall effect of the intervention under a range of possible incidence rates, and making very conservative assumptions about loss to follow-up. Further, we should retain adequate power to investigate intervention effects in subgroups of participants defined by factors such as age and gender.

Qualitative sub-study

We are planning to interview 90-100 participants at each time point. We will likely need to recruit approximately 120 participants to yield 90 completed interviews. In round 2 we will include five additional interviews: three men and two women who have tested positive after 4 months will be asked to participate in an in-depth interview the week after receiving test results.

Round 4 Control Group (“Control-R4”)

In Round 4 we plan to enroll approximately 400 new individuals into the “Control-R4” study group. Based on original recruitment success, we anticipate inviting approximately 600 people in order to achieve the target enrollment. The target enrolment number of 400 was chosen based on power calculations of sample size needed to test the hypothesis that the Control-R4 STI rates at round 4 are significantly higher than the round 4 STI rates of the original control (Control-R1) group that has received counseling, testing, and free treatment over the first 12 months of the study.

SECTION 3: RECRUITMENT

Main study

We will randomly select approximately 3600 individuals, aged 18-30, from households in the study villages (3000 plus 20% extra to allow for expected refusal/ineligibility). Prospective participants will be identified through the DSS database. The DSS collects basic socio-demographic household-level information on births, pregnancies, deaths, and migration from all households in the DSS area on a quarterly basis, making it an excellent platform for drawing random samples. To minimize ‘spillover effects’ across the intervention and control groups (where 1 non-marital sexual partner is in one arm & the other partner is in the other arm), we will enroll not more than 30% of age-eligible youth from any one village, and we will designate some villages as “high treatment penetration” villages and others as “low treatment penetration” villages, by varying the percent of the eligible population who is enrolled in the treatment arm.

Following a phase of community sensitization, fieldworkers will visit the households of the randomly-selected young men & women to invite them to participate in the study. Potential participants will be given an invitation that contains information about the study, plus the informed consent form to read, and instructions to come to a nearby ‘study station’ the following week for screening & potential enrollment if they are interested in participating (see below for details on the study stations).

Qualitative sub-study

We will recruit participants for the qualitative study at two points in time using the same recruitment methods. The first recruitment will take place during the baseline visit to the study station. At the end of this visit, an interviewer for the qualitative study will verbally recruit a stratified random selection of 90-100 participants. The sample of participants selected for the qualitative sub-study will be stratified by treatment arm, gender and marital status. In addition we plan to interview approximately 10 HIV-positive participants, all in the treatment arm, and 8 participants who have spouses also enrolled in the study. We will use purposive sampling to meet these recruitment criteria if they are not met by the initial random selection of participants. All participants will be asked if they would be willing to participate in the qualitative sub-study.

The second recruitment will take place at month-4, during the second visit to the study station. All participants interviewed in at the baseline visit will be interviewed again at the 4-month visit. In addition to these interviews, immediately following their post-test counseling session, an interviewer for the qualitative study will verbally recruit a random selection of 5 participants from the treatment arm who tested positive for one or more STI (and therefore did not receive the cash reward). These participants will be asked if they would be willing to participate in the qualitative sub-study.

Round 4 Control Group (“Control-R4”)

The Control-R4 group will be selected and recruited using the same procedures described above as were used for the original baseline sample. Potentially eligible individuals will be identified in the existing Demographic Surveillance Survey computerized database of village residents; study personnel will visit their household to explain the study and verify eligibility; and eligibles will be invited to come to the study station the following week to complete informed consent and enroll if they so choose.

Recruitment Materials

Main study and Control-R4 sample

Recruitment invitations will be delivered to the households of selected individuals a few days before the study team arrives for enrollment and baseline study activities. These invitations will inform recipients that they have been randomly selected to participate in a new study. The invitations will also specify where and when the recruit should go to meet with the study team for possible enrollment and baseline data collection.

The purpose of the study will be described briefly, eligibility criteria will be detailed, and the names and institutional affiliations of the researchers will be given. The name and contact information for the in-village study representative – as well as the IHRDC study contact person – will be provided. The invitation will list the same key points about study participation that are listed in the informed consent form (and comprehension assessment). The same language will be used to ensure consistency across all communication materials.

Qualitative sub-study

Potential participants will be verbally recruited using the attached recruitment script.

SECTION 4: INFORMED CONSENT

Main study and Control-R4 sample

The main study will involve informed consent for study enrollment. The consent will also ask for agreement for long-term specimen storage and possible future research testing, as well as for linking to DSS data for future research.

All potential study participants must provide written informed consent to enroll in the main study. Participants are not required to consent to long-term specimen storage and DSS data access; participants may choose not to consent to these future research activities and still be enrolled in the study. Informed consent forms will be written and reviewed with participants in Kiswahili, the local language. Forms will be translated into Kiswahili and back-translated into English before study implementation.

Please note that we have adopted many “best practices” for obtaining informed consent and view informed consent as a process: involving the communities at outset, building participants’ understanding of the study over time before obtaining written informed consent, assessing participants’ understanding within the informed consent forms, using visual aids to enhance participants’ understanding, and monitoring participants’ understanding and perceived risks throughout the study. Specific activities relating to the informed consent process are detailed below.

Community sensitization phase

The process of obtaining informed consent will begin with a period of community sensitization several weeks before recruitment begins. In each study village, study staff will work with village leaders to build understanding of and support for the study within the villages. Study staff will give presentations at community meetings to explain the study and will encourage questions from all interested/concerned community members. A drama group will be hired to perform in each village, focusing the performance on the key points of the study

Recruitment phase

During the recruitment phase, we will continue to build and reinforce participants’ understanding of the study. Fieldworkers will visit the households of the randomly-selected young men & women to invite them to participate in the study. Potential participants will be given an invitation that contains key information about the study and instructions to come to a nearby ‘study station’ the following week for potential enrollment. The fieldworker will read the invitation aloud to potential participants as needed, depending on literacy level of the recruit, and answer any questions. Recruits will be encouraged to contact the village study representative – or any other available study staff member – with any questions that they may have about their potential involvement in the study.

Enrollment – signing of the informed consent

Potential participants are asked to visit their local ‘study station’ during the 1-week enrollment period (a few days after recruitment) to review the informed consent materials with a study interviewer and possibly enroll in the study.

When a potential participant visits the study station, he/she will meet with a study interviewer in a quiet, private area of the study station to review the informed consent materials. Before reviewing the form, the interviewer will first review the eligibility criteria for the study with the potential participant. If the individual reports that he/she is eligible and interested in participating in the study, that individual may be enrolled in the study once the informed consent form is complete.

The interviewer will then review the material in the informed consent form with the potential participant. Visual aids like calendars and samples of specimen collection materials will be available for each interviewer to use during the review to enhance participants’ understanding. The review will involve either reading the informed consent aloud to the participant or having the participant read the form (depending on the literacy level and preferences of the participant) and answering any questions the participant may have. When consent forms need to be read to non-literate potential participants by the interviewer, a witness will be present to verify that the contents of the form have been read and to sign the form.

Once the informed consent has been reviewed with the participant, the interviewer will conduct a “comprehension assessment” to ensure that the participant understands all information required to make an informed decision about whether to enroll in the study. An Informed Consent Comprehension Checklist (see attached) will assist interviewers in assessing participant comprehension and targeting follow-up educational efforts.

The checklist will not be presented to participants as a “test,” but rather as a way of double-checking that the interviewer has fulfilled their responsibility to provide all information needed for the participant to make an informed decision about enrolling in the study. The checklist is structured around eight open-ended questions that correspond with the elements of informed consent required for research in the U.S. Each question will be read to the participant, giving him or her time to respond to each one.

For each question, the checklist specifies particular points that must eventually be included in the participant’s response. If the participant does not mention one or more of the required points, the study interviewer will follow-up with another open-ended question to elicit a response about that point. All required points must be satisfactorily addressed by the participant, and checked off, before proceeding to the final informed consent decision and signing or marking of the enrollment informed consent form. Note that we have explicitly included these required points in the recruitment invitation and in the final ‘review’ section of the informed consent form to reinforce these key points.

The informed consent forms for the main study will contain a ‘review’ section where the participant and/or parents will be asked to acknowledge that they understand specified key points of the study before consenting to enroll in the main study (signing). Participants will also be asked to indicate whether they consent to the optional long-term specimen storage and/or DSS data access by initialing designated spaces. For all participants that cannot sign their name, spaces will be provided where participants may place a thumbprint.

Ongoing assessments

Study participants will be asked to resign the informed consent at each visit to the study station at which interviews are conducted and samples collected.

Qualitative sub-study

For the qualitative sub-study, participants will be recruited during their baseline visit to the study station. A random selection of 90-100 participants will be asked if they would be willing to participate in the qualitative sub-study.

Informed written consent from all persons agreeing to be part of the qualitative sub-study is required for participation. The consent form will clearly indicate that the interviews will be audio tape-recorded and that these recordings will be transcribed and translated into English by a member of the study staff. The consent form will also indicate that no other identifying information will be collected as part of study participation. The participant's name will not be associated with the recorded interview, only the study identification number will be linked to the recording. The participant will also be notified clearly that the information collected through this sub-study will be linked to other information collected from them as part of the larger cash reward study, but the linking will occur only by the use of the study identification number, not by the name or other identifying information of the participant. Finally, the consent form will include a brief description of the study and will indicate clearly what agreeing to participate means for them, address any confidentiality and potential harm concerns, explain that even after agreeing to be part of the study, the participant may chose to stop the interview at any time, and briefly explain how the data will be used.

Consent forms will be available to potential participants in Kiswahili. Forms will be translated into Kiswahili and back-translated into English before study implementation. Consent forms will be read to non-literate potential participants by the interviewer.

The consent process will take place in a private area of the study station, with only the research staff, participant, and witness (if applicable) present. All participants will be informed both verbally, and in the printed consent form that their decision to leave this study will not affect access to the usual medical care they get now or in the future, and that their decision will not affect their ability to take part in the larger cash reward study or in any other research studies.

Qualitative monitoring with Conversational Journals

We are requesting a waiver of informed consent for community members whose conversations are captured in the conversational journals. Community diarists will be anonymously reporting in nightly journals the conversations pertaining to the study that they have heard around them during their daily activities. In many cases these will be conversations in public places, thus the diarists will be observing public behavior, and no consent would ordinarily be required. However, an important subset of the conversations related to the study may be carried out in private places. For these latter conversations it would not be feasible to obtain informed consent from the conversants, thus that component of the research could not be practicably carried out without a waiver of informed consent.

To help ensure that the conversational journals will present no risk of harm any greater than that encountered from everyday life, the journalists will be instructed to record all conversations anonymously. Only those subsets of conversations directly relevant to the study will be recorded in the diary, so that a third party reading the diary should not be able to infer the identity of the conversants.

SECTION 5: STUDY PROCEDURES

Main study

OVERVIEW

The study will last about two years, beginning in late-2008 and ending in late-2010. Most of the study activities will happen in the first year. There will be four rounds of study activities in the first year (about every four months) and one round at the end of the second year.

Round 1 (early 2009)	-	Baseline
Round 2 (mid 2009)	-	4-months after baseline (Treatment group eligible for CCT)
Round 3 (late 2009)	-	8-months after baseline (Treatment group eligible for CCT)
Round 4 (early 2010)	-	12-months after baseline (Treatment group eligible for CCT)
Round 5 (early 2011)	-	24-months after baseline (post-intervention follow-up)

Each study round, all participants will be asked to come to the study station twice: once to provide a biological specimen for STI testing, and a second time (about three weeks later) to pick up test results and (if eligible) cash payments. During each study round, study counselors will provide pre- and post-counseling to all participants to ensure that the participants understand the meaning of their test results, etc. Participants will be interviewed once per study round as well. Short (10- to 15-minute) surveys will be administered during the first visit of each intervention round (Rounds 2 and 3). Longer surveys will be administered at baseline and at follow-up.

Participants will also be invited to attend the counseling “group discussions” which will be held every month in the first year.

Study activities will take place on a rolling basis over each study round. The study teams will move from village-to-village each week, visiting all 10 villages twice per round. Because of the rolling nature of study activities, we must describe the chronology in terms of calendar quarters, rounds, and study months rather than exact calendar dates.

For clarity, the intervention and study procedures are presented in detail first and then listed in chronological order.

RANDOMIZATION

This study proposes to randomize at the individual-level. Participants will first be randomly assigned to the treatment group (n=1500) or control group (n=1500), with on average a 50/50 chance of being assigned to either group. Participants assigned to the treatment group will be further randomized to either the “high-value” cash transfer group (n=750) or the “low-value” cash transfer group (n=750). Participants in all three study groups will then be randomly assigned to either receive additional counseling (n=1500) or receive no additional counseling (n=1500).

INTERVENTION PROCEDURES

All study participants will be monitored on a regular basis for several STIs that serve as proxies for risky sexual contact, will receive standard pre- and post-test counseling, and will receive free STI treatment through the local public health facilities as needed. Participants in the treatment arm will receive conditional cash transfers (CCTs) of Tsh10,000 or Tsh20,000 (approximately \$10 and \$20) each reward round that they avoid becoming infected by any of the conditioned STIs. Participants in the control arm will not be eligible to receive cash rewards for negative STI test results at any point during the study.

STI testing, STI treatment, and conditional-cash transfers

Biological markers of risky sexual behavior

The biological markers selected for the intervention have been selected from a list of STIs that are commonly used within the epidemiological literature as proxies for risky sexual behavior, and that are known to be prevalent in the Kilombero/Ulangu districts. Participants will be tested for each of the following six STIs during the five rounds of STI testing: *Chlamydia trachomatis*, *Neisseria gonorrhoeae*, *Trichomonas vaginalis*, *Mycoplasma genitalium* [Round 1 testing was not possible], *Treponema pallidum* (syphilis), and HSV-2 (herpes simplex II). Participants will not be tested for syphilis and HSV-2 in rounds 2 and 3. During the three cash payment rounds, participants in the treatment group will receive a cash payment of Tsh10,000 to Tsh20,000 each round when curable STI test results are negative (excluding *Mycoplasma genitalium*). Once participants test positive for HSV-2, they will not be tested for it again since it is a lifelong infection. Cash payments will only be conditional on HSV-2 status the first time they test positive.

We plan to test participants for HIV three times over the study period (baseline, month 12, and month 24) to measure the impact of the intervention on HIV incidence. These HIV tests are not part of the intervention *per se* because cash payments are **never** conditional on HIV status (meaning a participant may test positive for HIV and still be eligible to receive cash if all other STI test results are negative). Rather, the HIV tests are a biological measure for the overall RCT evaluation.

The battery of HIV/STI tests that we intend to use in the study have been selected to ensure that only minimally invasive procedures are needed for specimen collection, and that collection procedures can be easily performed by field staff.

HIV/STI pre-counseling

All study participants will be offered HIV/STI testing, based on the “three C’s” (informed consent, counseling and confidentiality). This expanded HIV/STI pre-test counseling builds on the recommendations of the Tanzanian Ministry of Health and Social Welfare’s National AIDS Control Programme and the World Health Organization. During pre-test counseling, the study counselor will describe the testing and post-test counseling process, discuss the confidentiality of testing and results, and individuals’ right to decline testing. The counselor will provide information on HIV/AIDS and STIs in order to clarify misinformation and/or misconceptions, ensure that any decision to take the HIV/STI tests is informed and voluntary, and prepare the participant for a positive result. The counselor will also carry out a risk assessment, help the participant develop a risk prevention/reduction plan, and explore potential obstacles and problems that participants may encounter when implementing this plan. This will include the provision of male condoms, directions for use, and information on contraceptive and disease prevention efficacy. Thus, the pre-test counseling will address the following issues at a minimum:

- Knowledge of STIs, HIV/AIDS, and difference between HIV and AIDS
- Modes of transmission
- Advantages/disadvantages of knowing one’s HIV status
- How the tests work, and what the possible results are
- Risk prevention/reduction assessment and plan, including condom demonstration

Participants will be asked to return to the study station during a specified period of time to receive their test results and post-test counseling (described in the “STI/HIV post-counseling” section below).

Specimen collection procedures

Each round of testing, participants will be asked to provide biological specimens that will be sent to the IHRDC laboratory for STI testing. All specimen collection will take place at the study station during the first visit of each study round. Specimens will be handled discreetly by study staff and will be labeled with a unique barcode to protect the confidentiality of study participants. Specimens will not be labeled with any information that directly identifies an individual participant.

Blood draw: A single venous blood sample of approximately 5-10 mL will be collected from each participant to test for syphilis, HSV-2, and HIV. We will have three certified phlebotomists as part of the field team to collect these samples. Blood-based tests will be conducted only at baseline, 12-month, and 24-month rounds. Again, the cash payments for the treatment group will **never** be conditional on the results of the HIV test(s). Once a participant tests positive for HSV-2, he/she will not be tested for HSV-2 again.

Vaginal swab sample (females only): Female participants will be asked to provide a self-administered vaginal swab sample for laboratory tests at each round. Participants will be asked to collect this sample in a private area of the study station, using a long “Q-tip” that easily inserts into the vagina. This type of specimen collection has been used successfully in numerous studies in Tanzania (ref) and in our own team’s 2006 STI prevalence study in the Kilombero/Ulunda districts. Female research study staff will explain specimen collection procedures to participants, will provide participants a diagram showing how to collect the specimen, and will be available if the participant wishes to have assistance. This sample will be used to test for four STIs: Chlamydia, gonorrhea, *M. genitalium*, and trichomonas. Vaginal swab sampling is the preferred method of sample collection for women (vs. urine or cervical samples) because it has the highest diagnostic accuracy in women and it is the easiest to collect in the field.

Urine sample (males only): Male participants will be asked to give a small sample of “first-catch urine” (about 20-30 mL) for laboratory tests each round. Male participants will be asked to not urinate for at least one hour before giving the sample. This sample will be used to test for four STIs: Chlamydia, gonorrhea, *M. genitalium*, and trichomonas.

Laboratory testing methods

All samples will be sent to the microbiology laboratory at IHRDC in Ifakara for testing. For efficiency/cost savings, we will first use pooled testing of samples, then retesting individuals' samples in those pools that indicate positive results. All test results will be available within 7-10 days and will be returned to participants the following week. Ten percent of all samples, and a subset of positives, will be sent to the University of California Chlamydia Laboratory for confirmation analysis.

Urine samples and self-collected vaginal swabs will be tested for Chlamydia, gonorrhea, *M. genitalium*, and trichomonas. Detection of these organisms will be done with the GenProbe Aptima (GenProbe Inc, San Diego, CA) assays. These nucleic acid amplified tests (NAATs) have been extensively evaluated, and are considered the most sensitive and specific NAATs available. The methodology involves target capture of specific rRNA, transcription mediated amplification, and end detection of amplicons with hybridized probes using chemiluminescence. The AC2 assay simultaneously detects CT and NG, whereas the MG and TV assays are individual analyte specific reagents (ASR). These assays have a turnaround time of 4 hrs. NAAT specimens can be pooled for testing in low-prevalence settings. We anticipate the use of a pooling protocol for some of the NAATs.

Blood specimens will be tested for herpes simplex II virus (HSV-2), *T. pallidum* (syphilis), and HIV. For HSV-2, we will use the Focus HerpeSelect HSV-2 ELISA IgG assay (Focus Technologies, Cypress, CA) to detect serum antibodies. This is a FDA approved ELISA that utilizes purified HSV recombinant glycoprotein G2 antigens immobilized on polystyrene microwells. Higher cut points needed for sera from Africa will be used. Positive results do not distinguish between active or past infection. *T. pallidum* will be identified using RPR with reactive tests confirmed by TPPA. Active syphilis is defined as RPR+/TPPA+. For HIV, we will use rapid test for initial results, confirmation of positives, and tie-breaking.

For each participant, specimens will be labeled with a dated barcode that will link their samples (and test results) to their study identification code in the laboratory computer database. All laboratory test results will be stored in a password-protected database on a computer in the laboratory, separate from all other study data. The laboratory test result reports will be automatically generated (using standard laboratory management software) for each study participant once all tests have been completed for their village in a given round. These reports will then be double-checked by laboratory staff for accuracy and then returned to study participants in a standardized format.

As part of the accuracy checking of STI result reports generated for study participants, several procedures have been implemented:

- The computer programs that translate results into reports have been extensively bug-checked.
- The data entry interface has been modified so as to reduce the possibility of results being entered into incorrect fields, and also to prevent invalid responses (such as blank spaces) from being entered.
- In addition to lab staff double-checking any data entry for accuracy, the lab director must hand-check every positive report against a raw printout of lab results, and sign a flow sheet each time he does so.
- The local Ifakara director of the Ifakara Health Institute will spot-check the result printouts for study participants against raw result printouts. This will be done prior to results being delivered to subjects each week.

HIV/STI post-counseling

Participants will be asked to return to the study station at a specified time to receive their test results and HIV/STI post-test counseling. A trained study counselor will return the results to the participant in a private, soundproof area of the study station. Post-test counseling will differ depending on whether the result is negative or positive. However, all post-test counseling will contain the following core elements:

- Confirmation of participant's readiness to receive the HIV/STI test result

- Provision of HIV/STI test results and time for reflection.
- Assessment of individual's comprehension of results and additional explanation if necessary.
- Discussion of support system.
- Discussion of partner testing and notification.
- Explanation of active measures for staying healthy (remaining negative/avoiding re-infection and transmission of STI/HIV to others)
- Referrals for additional counseling and support

Counselors will describe the window period and the importance of repeated testing as well as following the risk reduction plan for individuals who test negative for HIV/STIs. With participants who test positive, emphasis will be placed on helping the individual cope with the test result, determining sources of social support and arranging for appropriate referrals. The importance of seeking treatment – and completing treatment – will also be emphasized to ensure that those who test positive have the opportunity to test negative in the next round.

Distribution of cash payment

Following post-counseling, those participants in the treatment group who tested negative for all conditional STIs will receive their conditional-cash payment in envelope from a study staff person (who is not their counselor). The Tsh 2,500 (about \$2) inconvenience fee will be given to the participant in the same envelope. Participants who test positive for one or more STIs will not receive a conditional cash payment for that round. The participant will still receive the Tsh 2,500 inconvenience fee in an envelope from a study staff person.

CCT cash payments will only be distributed during Rounds 2, 3, and 4 (or study month 4, 8, and 12). These cash payments will serve to reward safe sexual behavior that occurred in the interval since the last test.

Lottery prizes

Control group participants who report to the study station and complete their interview at rounds 2, 3, and 4 will be eligible for a prize drawing, determined by lottery. Treatment group participants will also be eligible as long as they have tested negative for all rewarded STIs that round. All participants reporting for the interview at round 5 will be eligible for a lottery as well, regardless of their STI status. The prizes will be Tsh100,000, given to one man and one woman in each village in each round (about 1 in 150 chance of winning during each round).

Treatment of STIs

All study participants testing positive for any STI will be offered free treatment and counseling for the condition. The treatment will be administered by the health staff at the nearest health facility, and will be equivalent to the national standard of care – syndromic management of STIs. Treatment kits are provided free of charge to health facilities, but the study team will provide extras to ensure that there are sufficient kits in-stock to treat the study population.

Participants who test positive for an STI during the study will be provided with 2 vouchers (one for participant and one for them to give to a sexual partner) for free treatment at the local health clinic, to be used within one month. For confidentiality purposes, the vouchers will not include their name or name of the STI; it will contain a coded indicator of STI for use by clinic personnel. In order for treatment group participants to be eligible for rewards in the next round, they must have reported to the clinic for treatment of their STIs.

We will work with the local health centers to ensure that 1) adequate supplies of the first -line drugs are available onsite to treat the STIs included in this study; 2) the drugs will be provided free of charge to study participants; and 3) their staff members are prepared to provide STI counseling services to any study participant that requests it. The research team will prepare and provide a short refresher course on STI counseling and treatment to the local health staff.

Participants testing positive for HIV will be referred to the Chronic Disease Clinic based at St. Francis Hospital for further evaluation. This clinic provides free testing and treatment to HIV positives. Participants who are HIV positive will be permitted to remain enrolled in our study should they so choose.

Group-based counseling program

The psycho-social counseling involves a group-based program that uses participatory learning approaches such as critical reflection, role plays and drama to promote gender-equitable relationships and encourage deliberate decision-making in sexual and reproductive health (specifically, the prevention of HIV, other STIs, and unintended pregnancy). The intervention is based on Stepping Stones, a curriculum focused on gender, HIV, communication and relationship skills that addresses why people behave in the ways they do, and how to change behavior. This curriculum has been used in over 40 countries (including Tanzania) and translated into at least 13 languages.

The intervention consists of 12 monthly group sessions, each lasting approximately two hours that bring together 20-30 participants of the same sex and similar age for structured group discussions facilitated by trained study staff. It will begin with a set of activities designed to foster comfort and trust within the group and establish ground rules for the remaining sessions. Subsequent sessions will address sexual health, HIV, and STIs, gender norms and expectations; explore why people behave the way they do; and facilitate and support behavior change. Principles of confidentiality will be explained at the launch of the intervention and reinforced throughout. We will emphasize that the study will not reveal personally identifying/identified information and request participants to also maintain confidentiality. The intervention sessions will be conducted in each community in a private, confidential space. We will provide reminders about these sessions to a randomly chosen half of study participants.

DATA COLLECTION PROCEDURES

Data collection for the primary research questions will occur in conjunction with implementation of the intervention, with a few separate data collection activities involving subgroups of participants. Although we will use STI biological markers as our primary impact measure for the study, we will also gather additional information on participants, such as survey responses about sexual behavior using indicators and scales that have been validated in the epidemiologic and behavioral social science literatures. Because we will be working in partnership with our Tanzanian colleagues at IHRDC, we will have access to further socio-demographic data collected on individuals and households in the DSS research area.

Biological markers of risky sexual behavior

The same biological markers/STIs monitored as part of the intervention will be used in the study evaluation as well (described below). In addition, we will test for HIV at baseline, month 12, and month 24 so that we have a measure of the study's impact on HIV, as well as additional outcome measures. The conditional-cash payments in the intervention will never be conditional on HIV test results.

Surveys and interviews

All study participants will be interviewed five times as part of the main study. Study counselors will conduct one-on-one interviews with study participants during each study round using structured questionnaires. All questionnaires will be written and read aloud in the local language (Kiswahili) and will be administered in a private, soundproof area of the study station. Since some participants may feel uncomfortable responding to sensitive survey questions aloud, participants may respond to sensitive questions using non-verbal cues (pointing, nodding, etc.).

Baseline survey: During the first visit to the study station at baseline, study counselors will interview all participants using a structured baseline questionnaire. Participants will be asked a series of questions regarding demographics, sexual behavior, economic activity, knowledge and beliefs about HIV & STIs, etc. during a face-to-face interview with a study counselor. This baseline survey will take about one hour to complete.

Short surveys: During the 4-month and 8-month intervention rounds (Rounds 2-3), study counselors will interview all participants using a structured short questionnaire. This short survey will take 10-15 minutes to complete and will contain questions that enable us to monitor for adverse events (e.g., reported physical abuse) or study implementation problems (e.g., STI treatment availability) as well as changes in sexual behavior and economic activity.

Follow-up survey: During the 12-month and 24-month follow-up rounds, study counselors will interview all participants using a structured follow-up questionnaire. Participants will be asked a series of questions similar to those asked at baseline regarding sexual behavior, economic activity, knowledge and beliefs about HIV & STIs, etc. This follow-up survey will take about one hour to complete.

Some study participants may be asked to participate in additional surveys or interviews that are being conducted to provide additional insights into this study. The possible activities include the following:

Linking to existing DSS: Because we will be working in partnership with our Tanzanian colleagues at IHRDC, we will have access to socio-demographic data collected on individuals and households in the DSS research area. We will link existing DSS data with the data collected for this study in order to add information about the socio-demographic background and history. The main study informed consent form contains a place where participants can agree to allow us to access and utilize their DSS data. Data from the DSS will not be linked for those participants not providing consent.

Supplemental study of economic attitudes: A subset of participants may be invited to participate in a sub-study to learn more about participants' attitudes towards risk, the future and trust. At the round 3 visits participants would be invited to respond to a supplemental questionnaire, and then participate in games in which they would be eligible for small payments. If this activity is undertaken then an IRB amendment will be submitted to approve exact study details.

CHRONOLOGY OF INTERVENTION & STUDY PROCEDURES

Round 1 – Baseline

Study station visit #1 (week 1)

Total participant time: ~2.5 hours

- Informed consent for main study
- Enrollment for main study
- Baseline questionnaire
- HIV/STI pre-test counseling
- Specimen collection for STI/HIV testing (blood and urine/vaginal swab)
- Randomization
- Inconvenience fee payment

Laboratory testing (weeks 1-3)

Total participant time: 0

- Blood samples (HIV, syphilis, and HSV-2)
- Urine/vaginal swab samples (Chlamydia, gonorrhea, *M. gen*, and trichomonas)

Group counseling sessions (once per month)

Total participant time: 8 hours

Study station visit #2 (week 4)

Total participant time: ~1 hours

- Laboratory test result distribution
- HIV/STI post-test counseling
- Inconvenience fee payment

Round 2 – Month 4

Group counseling sessions (once per month)

Total participant time: 8 hours

Study station visit #1 (week 1)

Total participant time: ~1 hour

- Short questionnaire

- STI pre-test counseling
- Specimen collection for STI testing (urine/vaginal swab)
- Inconvenience fee payment

Laboratory testing (weeks 1-2)

- Urine/vaginal swab samples (Chlamydia, gonorrhea, *M. gen*, and trichomonas)

Study station visit #2 (week 3)

Total participant time: ~1 hour

- Laboratory test result distribution
- STI post-test counseling
- Cash reward payment
- Inconvenience fee payment

Round 3 – Month 8

Group counseling sessions (once per month)

Total participant time: 8 hours

Study station visit #1 (week 1)

Total participant time: ~1 hour

- Short questionnaire
- STI pre-test counseling
- Specimen collection for STI testing (urine/vaginal swab)
- Inconvenience fee payment

Laboratory testing (weeks 1-2)

- Urine/vaginal swab samples (Chlamydia, gonorrhea, *M. gen*, and trichomonas)

Study station visit #2 (week 3)

Total participant time: ~1 hour

- Laboratory test result distribution
- STI post-test counseling
- Cash reward payment
- Inconvenience fee payment

Round 4 – Month 12

Group counseling sessions (once per month)

Total participant time: 8 hours

Study station visit #1 (week 1)

Total participant time: ~1.5 hours

- Follow-up questionnaire
- HIV/STI pre-test counseling
- Specimen collection for STI/HIV testing (blood and urine/vaginal swab)
- Inconvenience fee payment

Laboratory testing (weeks 1-3)

- Urine/vaginal swab samples (Chlamydia, gonorrhea, *M. gen*, and trichomonas)
- Blood samples (HIV, syphilis, and HSV-2)

Study station visit #2 (week 3 or 4)

Total participant time: ~1 hour

- Laboratory test result distribution
- HIV/STI post-test counseling
- Cash reward payment
- Inconvenience fee payment

Round 5 – Month 24

Study station visit #1 (week 1)

Total participant time: ~1.5 hours

- Follow-up questionnaire
- HIV/STI pre-test counseling
- Specimen collection for STI/HIV testing (blood and urine/vaginal swab)
- Inconvenience fee payment

Laboratory testing (weeks 1-3)

- Urine/vaginal swab samples (Chlamydia, gonorrhea, *M. gen*, and trichomonas)
- Blood samples (HIV, syphilis, and HSV-2)

Study station visit #2 (week 3 or 4)

Total participant time: ~1 hour

- Laboratory test result distribution
- HIV/STI post-test counseling
- Inconvenience fee payment

Qualitative sub-study

We will conduct one-on-one in-depth interviews during which we will ask open-ended questions using an interview guide. Interviews will be conducted in Swahili by a Tanzanian trained in qualitative interviewing techniques.

After participants are enrolled at baseline, provide their initial lab tests, and complete the quantitative survey, a small sub-set of participants will be asked if they would be willing to participate in an in-depth interview, to take place twice during the duration of the study. The first interview will be scheduled 1-3 weeks after enrollment.

Interviews in later rounds will take place just after the STI results have been given to participants. In addition to the original participants, five interviews will be recruited at round 2 who tested positive and therefore will not receive their conditional cash transfer. These five additional people will be asked to participate in the in-depth interviews at the time they receive their test results, and will be consented at the time of the in-depth interview.

Structure and Content of Interviews

All interviews will be conducted in Swahili by trained Tanzanian interviewers hired for the purposes of this study. Interviews will be recorded with an audio tape recorder, transcribed in Swahili, and then translated into English. Participants consenting to the in-depth interviews will set up an appointment with the study interviewer. The interviews will take approximately 45 to 60 minutes. Participants will be compensated approximately \$3 (Tsh 3,000) for their time at each interview.

While the questions asked during the in-depth interview will be open-ended, an interview guide will be followed to ensure that all the relevant topic areas are covered in each interview. The qualitative data collection will focus mainly on how the cash incentive fits in with life decisions and life plans of men and women in rural Tanzania and what strategies men and women in rural Tanzania believe will be effective and plan to use in an effort to avoid infection with STIs or HIV.

Qualitative monitoring with Conversational Journals

Using a methodology developed by Watkins and Swidler termed conversational journals, we will hire ten diarists (one in each study community) who are “cultural insiders” the communities in which the CCT trial is taking place. Swidler and Watkins have very successfully used this method as part of their HIV research in Malawi (Swidler and Watkins; Tavory and Swidler). Conversational journals provide a method to get at interpretation and meaning not just at the individual level, but at more collective level, and to capture the dynamic nature of meaning and interpretation on a daily basis. Text from journals kept by the hired “cultural insiders” journaling the details of conversations that they overhear or participate in will be analyzed to try to get at interpretation and meaning.

In the context of the RCT, journalists will be instructed to capture all conversations and events that relate to the study, the researchers, the incentive, and sexual behavior and partnerships generally. Data collected from the conversational journals will not include names or identifying information of anyone that the diarists are writing about. If the diarists mistakenly include names in their notebooks, names will be redacted upon review of the journals.

Round 4 Control Group (“Control-R4”)

The Control-R4 sample group will be enrolled for only one round of the study (round 4), thus for only 3 weeks. During that round, study procedures for recruitment, enrollment, and informed consent will be identical to those at round 1 for the main sample described elsewhere (note that since all are enrolled in the same group, there will be no randomization step). After informed consent, the round 4 procedures for the Control-R4 group will be identical to those described above for the main control group (Control-R1):

- As described in the Section 7 Overview above, the Control-R4 participants will have two visits to the study station. At the initial enrolment visit they will complete a 30-minute interview, have individual pre-test counseling, and provide a blood and urine sample. At the second visit 2-3 weeks later they will receive their test results, post-test counseling, and free treatment vouchers.
- The pre and post-test counseling will be identical to that described above (the group counseling sessions in the village will have finished by round 4, so Control-R4 participants will not be involved in any group counseling).
- The blood and urine specimen collection procedures will be identical to those described above.
- The STIs tested for will be identical to those listed above at round 4 (including HIV).
- The laboratory testing procedures will be identical to those described above.
- The inconvenience fees and inclusion in the lottery will be identical to those described above for control group enrollees.
- Free STI treatment vouchers will be identical to that described above.
- The round 4 survey questionnaire for the Control-R4 enrollees will be identical to that used for the main study enrollees at round 4 (except that sections U and W will be omitted for the Control-R4 enrollees, as indicated by the questionnaire skip patterns).
- Control-R4 enrollees will not be invited to participate in any supplemental studies (such as qualitative sub-study).

Description of locations for intervention/study activities

Enrollment, STI testing, basic counseling, and surveys

‘Study stations’ will be temporary structures set up in each village that will serve as the location where intervention/study activities take place, including enrollment, specimen collection, test result and cash payment distribution, survey administration, etc. Dedicated areas will be set up within the stations that allow for privacy during specimen collection, results distribution and counseling, and survey administration. These stations will be conveniently located within each village and will be open hours that are respectful of school, employment, and other commitments. Home visits will only occur when participants fail to appear at the study station during their designated week (permission to follow-up in the home will be obtained from participants at the outset of the study). All of these strategies are in place to minimize pulling participants away from productive pursuits as well as maintain their privacy. Note the study stations will move with the field teams from village-to-village and will only be set up in each site for 2 weeks per round (one week for specimen collection and one week for results distribution).

Group counseling sessions

The intervention sessions will be conducted in each community in a private, confidential space (either a community facility or a private house, depending on what is available in a given community).

Study personnel and time

Time

Please see the time estimates for each of the study procedures listed in the chronology above. Twenty-four of these hours are spent in the group counseling sessions. Still, no more than 3.5 hours of study activities per month will ever be required.

Personnel

Please see the study procedure details above for specific listings of personnel to be involved. Here, we provide more detail about the personnel that is interacting with participants.

Phlebotomists: We will hire phlebotomists who have been certified by national authorities in Tanzania to conduct the blood draws.

Study counselors: We will hire individuals who are certified VCT counselors through Tanzania's National HIV/AIDS Programme to serve as study counselors in this study. This certification ensures that study counselors are knowledgeable about HIV/AIDS counseling and testing procedures in the Tanzanian context. Study counselors will receive additional training through this study to enable them to effectively counsel participants through the specific study-related issues. Study counselors will also facilitate group counseling sessions.

Fieldworkers / Interviewers: We will hire experienced fieldworkers/interviewers to assist with questionnaire administration and specimen processing in the field.

Laboratory staff: The microbiology laboratory staff at IHRDC, managed by Boniphace Jullu, has extensive experience in processing biological samples for large randomized trials. The lab has effective procedures in place to for maintaining participant confidentiality for all specimens.

Qualitative sub-study

Interviews will be conducted in Swahili by a Tanzanian trained in qualitative interviewing techniques.

Conversational diarists

Ten local community residents (each in a separate study village) will be hired to anonymously record conversations overheard in the village regarding the study. The interviewers will undergo training in appropriate techniques for recording data and ensuring confidentiality of the anonymous conversations recorded.

Round 4 Control Group ("Control-R4")

The Control-R4 study activities will take place at the same study station as for the main enrollees, during the same weeks, with the same study personnel. We anticipate that the initial visit will take approximately 2 hours, and the second visit to pick up results will take less than one hour.

Data Collection Instruments:

Main study

Baseline survey: During the first visit to the study station at baseline, study counselors will interview all participants using a structured baseline questionnaire. Participants will be asked a series of questions regarding demographics, sexual behavior, economic activity, knowledge and beliefs about HIV & STIs, etc. during a face-to-face interview with a study counselor.

Short surveys: During the 4-month and 8-month intervention rounds (Rounds 2-3), study counselors will interview all participants using a structured short questionnaire. This short survey will take 10-15 minutes to complete and will contain questions that enable us to monitor for adverse events (e.g., reported physical abuse) or study implementation problems (e.g., STI treatment availability) as well as changes in sexual behavior and economic activity.

Follow-up surveys: During the 12-month and 24-month follow-up rounds, study counselors will interview all participants using a structured follow-up questionnaire. Participants will be asked a series of questions similar to

those asked at baseline regarding sexual behavior, economic activity, knowledge and beliefs about HIV and STIs, etc.

Qualitative sub-study

While the questions asked during the in-depth interview will be open-ended, an interview guide will be followed to ensure that all the relevant topic areas are covered in each interview. The qualitative data collection will focus mainly on sexual reproductive health decision-making and the influence that additional income might have on the decision-making process.

Round 4 Control Group (“Control-R4”)

The round 4 survey questionnaire for the Control-R4 enrollees will be identical to that used for the main study enrollees at round 4 (except that sections U and W will be omitted for the Control-R4 enrollees, as indicated by the questionnaire skip patterns).

Identifiable Personal Information

Main study and Control-R4 sample

Identifiable personal information will be collected in this study in the form of photos and names of study participants. These photos and names will only be used to verify the identity of study participants when they come to the study station to provide a specimen, pick up results, and/or pick up cash payments. The photos and names will be stored in a password-protected computer database that will not be directly connected to any other databases containing study-related data.

Qualitative sub-study

Identifiable personal information will be collected in this study in the form of audio tape-recorded interviews. The audio tapes will not include the names of the participant; the interview will be identified on the tape recording by the participant’s study identification number.

SECTION 6: RISKS/DISCOMFORTS

Main study and Control-R4 sample

STI testing and treatment

Specimen collection

The specimen collection methods for HIV and STI testing used in this study are well-established and are in routine use across the world. Nonetheless, there are some physical, psychological, and social risks associated with these testing procedures that we must prepare for.

Physical risks

i) There is a chance that a participant may experience mild amount of pain during the blood draw or may feel dizzy following the blood draw. Light bruising at the site of the blood draw is also possible.

Trained phlebotomists will conduct the blood draws, using standard techniques to minimize pain and bruising as well as dizziness and other common responses. Since the volume of blood being collected is relatively small (only 5-10 mL), few participants are expected to experience dizziness. Juice will be available at the study station during blood draws to help any participant feeling dizzy recover. Any participant feeling dizzy will be encouraged to remain seated until they are feeling better.

ii) There is a very slight chance that needles or other specimen collection materials could be improperly handled and put participants and study staff at risk of a variety of infections.

All specimens will be collected with unused, sterile supplies. Needles will be disposed of in an appropriate 'sharps' container and swabs and urine cups will be properly disposed of immediately after processing. All study staff involved in specimen collection will be trained on the proper handling of collection materials.

iii) There are no known physical risks associated with the collection of samples from self-administered vaginal swabs or from urine. Hand sanitizer will be available for participants to wash up after collecting their own specimens.

Psychological and social risks

i) *There is a chance that a participant will feel anxious about being tested for HIV and STIs.*

It is common for people to feel anxious because of fear of the potential illness itself (HIV, in particular), fear of abandonment or divorce if found to be positive, fear of abuse within a relationship if found to be positive, or fear of being stigmatized in one's community.

During pre- and post-counseling, counselors will help participants think through responses to such possibilities to reduce anxiety (e.g., identify the support systems that exist in a participant's life that can help them respond to such possibilities, etc.). Counselors will review the meaning of each test and the range of possible test results. In the rare case that a participant is concerned about her own safety following HIV/STI testing, counselors will connect the participant with the local services for dealing with such domestic violence matters.

ii) *Some participants may experience discomfort or anxiety during the specimen collection procedures*

Female participants may be uncomfortable with collecting a vaginal swab specimen. Female study staff members will review collection instructions with participants, and will have actual sampling supplies as well as instruction sheets with simple diagrams available for facilitating communication. A private area will be set aside in the study station for female participants to collect these samples. To ensure complete privacy, only one participant will be allowed in at a time.

Some participants may be uncomfortable with needles and blood draws. The phlebotomists have also been trained on appropriate ways to work with clients who have such concerns.

Physical risks

i) *There is a very small chance that a participant who is truly positive for HIV or another STI receives a test result indicating they are negative.* Such a false negative result could delay treatment for the infected participant, prolonging the infection and any associated discomfort. A false negative result could also put future sexual partners of the participant at risk of acquiring the infection.

For each of the diagnostic methods we will be using, false negatives are unlikely.

ii) *There is also a very small chance that a participant who is truly negative for HIV or another STI receives a test result indicating they are positive.* Such a false positive result could lead to a participant unnecessarily receiving treatment for an STI they do not have.

For each of the diagnostic methods we will be using, false positives are unlikely. The testing protocols that we are using for HIV and syphilis already require that all positives undergo a confirmation test before results can be returned to study participants. Such confirmation testing significantly decreases the possibility of false positive results.

If a false positive result is not detected and a participant is treated unnecessarily, it is unlikely that the treatment itself will cause anything more than mild discomfort to the participant.

iii) *Participants who receive false positive results face the same risks as participants who receive truly positive results.*

Psychological and social risks

i) Psychological/social risks of false negatives.

ii) Participants who receive false positive results face the same risks as participants who receive truly positive results. Participants who receive false positive results, however, face additional psychological and social risks.

HIV/STI testing – results reporting

Despite the benefits to participants' learning their HIV/STI status, participants will face certain risks once their HIV/STI status is known.

Physical risks

i) There is a small chance that participants could experience physical abuse in their home – by a partner, a parent, or another household member – when their HIV/STI status becomes known.

Physical abuse of individuals within households following HIV/STI testing does occur, particularly against women, when their HIV/STI becomes known. This has been shown to occur when HIV/STI results are either positive or negative. Physical abuse occurs most often when the results indicate a couple is discordant or when the status of one partner is unknown but the other is positive (typically the woman is known and the man is unknown)

We will respond to the risk of such abuse in a number of ways. First, counselors will monitor for physical abuse of participants by 'formally' asking participants about such events in the short survey during each round of testing. In these sessions, counselors will also informally discuss how safe the participant feels at home. If there is any indication that study activities are resulting in physical abuse of a participant, the counselor will contact the study coordinator for consultation. Counselors will also help participants think through strategies for preventing or diffusing test-result-associated abuse during pre- and post-counseling.

Psychological/social risks

i) There is a small chance that participants could be abandoned – by a partner (divorce) or a parent – when their HIV/STI status becomes known.

ii) It is very likely that participants who test positive for HIV or an STI could feel anxious about notifying their partner(s) of their HIV/STI status.

iii) There is a chance that participants who test positive for HIV or an STI could feel guilty about having HIV or an STI.

HIV/STI testing – STI test results as an indicator of risky sexual behavior

i) There is a risk of treatment failure in participants who sought out treatment for any one of the treatable STIs. Treatment failure could occur because of poor patient compliance with the treatment regimen, pathogen resistance to the available treatment, unanticipated interaction with other medications, or other causes.

If a participant experiences treatment failure, he/she may test positive in a second round of testing even if he/she has not engaged in risky sex during that period. If a participant tests positive again after having already sought treatment for a given STI (and possibly not engaging in risky sex), a repeat positive test result may warp their association between STI acquisition and risky sexual practices.

ii) There is a risk that some participants may engage in risky sexual behavior but not get 'caught' because they do not 'catch' an STI during their risky encounters, and then become overconfident of their ability to avoid STIs.

iii) There is a small risk that participants may try to self-treat for STIs prior to STI testing if they have had risky sexual contact and wish to "cover it up". This could lead to unnecessary treatment.

HIV/STI testing - diagnostics

We will use among the most accurate diagnostic methods to test for HIV and STIs that are available for routine use. These laboratory-based techniques are well-established and are the standard diagnostic techniques used in the U.S., Europe, and across the world. Nonetheless, there are some physical, psychological, and social risks associated with such testing that we must prepare for.

The primary risks associated with diagnosing HIV and STIs are related to the possibility of false positive and/or false negative test results. A false positive test result means that a specimen is truly negative, but identified as positive by the diagnostic test. A false negative test result means that a specimen is truly positive, but identified as negative by the diagnostic test.

Risks unique to the treatment group

Physical risks

i) *It is possible that the intervention could exacerbate existing power imbalances in couples, leading to domestic violence*, as pressure on the couple increases to change their patterns of sexual activity. If the cash reward was expected by the parent or partner but was not received due to a positive test result, the study participant could be vulnerable to violence. Violence could also erupt if a disagreement arises over who controls the study-related money (i.e., who gets to decide how the money is spent).

We will respond to the risk of such abuse in the same ways as listed above for the abuse stemming from HIV/STI test result reporting.

ii) *It is possible that participants who receive cash payments may use the money from one round of testing (assuming they are not “caught” and test negative on the battery of tests conducted) to engage in more activities which involve physical risks (purchasing sex, alcohol or drugs, etc.).*

If such behavior does result, we believe the likelihood of recurrence is low. Frequent STI testing can help ‘catch’ any participant that has become infected during such activities and can discourage such activities in the future by withholding cash payments. Throughout the study, participants will be reminded that the intention of the cash is to reward safe sexual behaviors, and that negative test results are no guarantee that they will not become infected if they continue to engage in risky behaviors.

iii) *A few participants who do not receive a cash payment because of positive results may seek out alternate ways of obtaining/earning cash in order to deliver the cash expected by household members.* Such alternate ways may involve commercial sex work, stealing, or other risky enterprises.

We will respond to the risk of such abuse in the same ways as listed above for the abuse stemming from HIV/STI test result reporting.

iv) *Small risk that participants could be targeted (e.g., robbery, theft) because of the cash.*

Psychological/social risks

- i) Feel a loss of privacy.
- ii) Create conflict and tension in the household that does not lead to physical abuse.
- iii) Feel that the cash creates a sense of coercion to engage in certain behaviors.

Qualitative sub-study

The primary potential risk to subjects is a loss of confidentiality with regard to interview responses, HIV status, or identity and the impact of discussing sensitive subject matter about HIV status, partner’s HIV status, the decision to have or not to have children, and power dynamics in sexual relationships. We will minimize this risk

by performing initial and follow-up training of staff to ensure understanding of ethical issues in this type of research and the procedures to minimize risk. Additionally, in an effort to prevent negative impacts of discussing these sensitive issues, the interviewer will preface this set of questions as potentially sensitive and remind participants that they are under no obligation to answer and can feel free to stop the interview at any time. The participant may feel threatened by the interviewer. Every effort will be made to ensure that the participant is comfortable in the interview situation, and if the participant is uncomfortable at any point, the interview will be stopped. The interviews will be audio tape-recorded. As this is considered identifiable information, there is an associated confidentiality risk to the participant. Every effort will be made to protect the confidentiality of the participant. No names or other identifiable information will be included in the audio recording—only the study identification number will be used.

SECTION 7: BENEFITS

Main study

Individuals who choose to participate in the study will benefit in a variety of ways, independent of their group assignment.

- Participants will have five opportunities to learn whether or not they are infected with HIV or STIs. They will be tested using the best, most accurate tests that are available.
- Participants who are found to be infected with one or more of the treatable STIs (CT, GC, syphilis, M.Gen, and trich) will receive free treatment that will cure them of the infection. Participants whose test results indicate that they are infected with HIV will be referred to the VCT clinic for further evaluation. The VCT clinic only provides testing, and then refers the positives to the Chronic Care Clinic run out of the district hospital. All HIV positives are regularly monitored for CD4 count and viral load. Note that the VCT clinic provides free treatment to all HIV-positive individuals, but may not begin treatment until a patient has passed a specific clinic stage of disease.
- Free condoms will be available to all participants each time they visit the study station
- Participants will have access to trained counselors who will assist with any questions or concerns participants may have about this testing, their sexual health, etc.

Participants in the cash groups will have the opportunity to benefit from this study in other ways.

- Increase household income by up to \$60 over the one-year study (note that this is included here because the cash incentives at the heart of the CCT intervention are not compensating participants for their time in the study; rather they are incentives for rewarding positive behavior change)
- Gain more control over household spending decisions
- If this intervention is effective, some participants in the treatment group will gain skills and capacity to exert control over the conditions under which sexual activity occurs.

Participants receiving the group-counseling portion of the intervention

- Will learn more about sexual health and will gain communication and relationship skills through participating in the group discussions.

Qualitative sub-study

The individual participants will not directly benefit from enrolling in the qualitative sub-study. The potential group-level and societal-level benefits of the qualitative research will be the design and implementation of a novel HIV prevention program in Tanzania guided and informed by the discussions and responses gathered during the in-depth interview process. Such an HIV prevention program may lead to better overall health in the community and greater access to economic resources for members of the community.

The risks posed to the subjects as part of the proposed qualitative sub-study are minimal and every precaution will be taken so that these risks are avoided as much as possible. The anticipated benefits that the members of community and Tanzanian society generally will receive over the long-term include improvement of overall quality of life as regards health and economic outcomes for young women and men both regionally in the Kilombero/Ulunda Districts, and potentially nationally as well.

Importance of knowledge to be gained (main study and qualitative sub-study)

The knowledge that will be gained as a result of the proposed research includes a more complete understanding of how the conditional cash transfers provided for those who remain uninfected impact the behaviors and outcomes of participants, especially as regards sexual and reproductive health. In-depth interview transcripts will provide a more nuanced explanation as to why the cash transfers did or did not facilitate behavior change relating to risky sex as compared to those in the control group and will enable us to understand why an increase in income may or may not influence perceptions of risk, gender inequities and self-efficacy in sexual reproductive health decision-making, and the decision to engage in risky sex. This enhanced understanding will allow the eventual design of an improved HIV prevention program based on the results of both the qualitative sub-study and the larger cash reward study. Because the risks incurred by all study subjects are minimal, and the knowledge that will be gained by the responses provided in the in-depth interviews has the potential to greatly enhance the results of the quantitative data collection in the cash reward study and eventually guide and inform an HIV prevention program, the risks that the study subjects may be exposed to can be construed as reasonable. In addition, adequate warnings of the potential risks to study subjects and options for discontinuation of the interview and for skipping sensitive questions are available to all participants.

Round 4 Control Group (“Control-R4”)

The Control-R4 sample is unique in that individuals are being recruited without any chance of being randomized to the original cash incentive treatment group. Despite this, these subjects are being offered significant benefits, with very low risk:

- They will have the opportunity to learn whether or not they are infected with HIV or STIs. They will be tested using the best, most accurate tests that are available. This is a significant benefit, because STI testing is not routinely available in the study villages; STIs are generally only treated syndromically. Furthermore, existing study participants have repeatedly expressed their appreciation for the opportunity to be tested for HIV through our study. Although HIV testing is sporadically available in these communities, it is typically conducted by a local health worker who lives in the study area, and participants have expressed concern about lack of confidentiality, thus often have been unwilling to be tested in the community. By contrast, since our study employs personnel from outside the area, subjects have expressed a high degree of interest in testing through our study.
- Participants who are found to be infected with one or more of the treatable STIs (CT, GC, syphilis, M.Gen, and trich) will receive free treatment that will cure them of the infection. Participants whose test results indicate that they are infected with HIV will be referred to the VCT clinic for further evaluation. The VCT clinic only provides testing, and then refers the positives to the Chronic Care Clinic run out of the district hospital. All HIV positives are regularly monitored for CD4 count and viral load. Note that the VCT clinic provides free treatment to all HIV-positive individuals, but may not begin treatment until a patient has passed a specific clinic stage of disease.
- Free condoms will be available to all participants each time they visit the study station
- Participants will have access to trained counselors who will assist with any questions or concerns participants may have about this testing, their sexual health, etc.

Importance of knowledge to be gained (Control-R4 sample)

The Control-R4 sample will allow testing of the effects of the extensive access to counseling, testing and treatment provided to Control-R1 subjects in the main study. The main study was designed to test the effects of cash rewards, over and above the effects of such counseling/testing/treatment, thus the Control-R1 group itself received extensive intervention. This Control-R1 intervention has so far included baseline, 4-month, and 8-month counseling/testing/treatment, as well as a year of monthly group counseling. This package of services to baseline participants is expected to result in decreased STI incidence based on prior research, but the extent of that prior research is limited, thus there is considerable scientific value in quantifying the STI benefits of this precise package of preventive efforts. The Control-R4 will serve as a comparison group to this Control-R1 group, allowing estimation of the STI improvement in Control-R1.

SECTION 8: ALTERNATIVES TO PARTICIPATION

Main study and Control-R4 sample

Prospective subjects may be diagnosed and treated for STIs through local public health facilities under the national policy of syndromic treatment. Since this approach involves STI treatment based on collections of symptoms rather than laboratory diagnoses, this means that only symptomatic STIs could be identified and treated under routine care. Laboratory diagnoses of STIs are not currently available in southern Tanzania.

Voluntary counseling and treatment (VCT) services for HIV/AIDS are available to all individuals living in the Kilombero/Ulanga district. The diagnostic and counseling approach adopted by our study corresponds to that provided by VCTs in the area.

There are no alternatives to the group counseling or the cash reward that are offered by our study for STI/HIV prevention activities. Since this study is fundamentally a prevention study, an appropriate alternative for prospective subjects is to simply do nothing.

SECTION 9: CONFIDENTIALITY

Main study and Control-R4 sample

Study participants will be identified by a unique and confidential study ID. Participant names will not be used on any study-related data or specimens, and the study team will follow all confidentiality procedures that are followed by the Ifakara investigators and field team involved in DSS research. Blood samples, vaginal swabs, and urine samples will be sent to the laboratory coded only with study numbers (via barcode) and date.

Information about participation in this study will remain confidential.

- All information collected in this study will be labeled with a unique 10-digit code. Names – or any other identifying information – will never be used on surveys, biological specimens, test results, or study reports. Only anonymized study-related information will be shared with researchers who are collaborating on the conduct of this study.
- The results of STI and HIV tests will be disclosed only to the participant and their counselor. Other study staff will have access to only anonymized results. The study team will not share laboratory test results with anyone, including partner(s) or parents or friends. In line with the National VCT Guidelines, participants who test positive for HIV or any STI will be urged to notify their partner(s) so they can also seek testing and treatment.
- The study team will also not share information regarding study group assignment (e.g., control group, high-value cash group, etc.) with anyone outside of the study team.

Qualitative sub-study

In order to protect against risks to privacy of individuals or confidentiality of data, no personal identifying information will be included in the audio recording of the interview. However, the audio recording in and of itself is considered identifiable information, and therefore every effort will be made to protect the confidentiality of the recordings and of the participant. The privacy and confidentiality of the patient will be protected in the following ways:

- The interviews will take place in a private area with only the research staff interviewer and the participant present to ensure confidentiality.
- In order to protect against risks of participants feeling uncomfortable being asked questions that are sensitive in nature, participants will be assured, both verbally during the interview and on the written consent form, that they are free to skip any question that they prefer not to answer, and that they are free to discontinue the interview at any time.

- All participants will be informed both verbally during the interview and in the printed consent form that their decision to leave this study will not affect the medical care they get now or in the future, and that their decision will not affect their ability to take part in other research studies.
- The name or other identifiable information of the participant will not be audio recorded or collected in any other way. Only the study identification number will be associated with the interview.
- If the participant, in the course of the interview, states any information that would allow their identification, this information will be removed during transcription of the interview.

Dworkin and Anke Ehrhardt, “Going Beyond “ABC” to Include “GEM”: Critical Reflections on Progress in the HIV/AIDS Epidemic,” *American Journal of Public Health*, January 2007, Vol. 97, No.1.

ⁱⁱ Vun, MC. Fighting HIV/AIDS on all fronts: Cambodia’s multisectoral approach. Available at <http://www1.worldbank.org/devoutreach/july04/article.asp?id=248>.

ⁱⁱⁱ Pronyk et al “Effect of a structural intervention for the prevention of intimate-partner violence and HIV in rural South Africa: a cluster randomization trial.”

^{iv} (Tanzania Ministry of Health/NACP, 2005),

^v (Source: technical presentation given by R. Urassa,