Understanding and informing interventions to improve antiretroviral adherence: three papers on antiretroviral adherence in sub-Saharan Africa

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Abstract

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The widespread availability of antiretroviral therapy (ART) for HIV infection in Sub-Saharan Africa (SSA) has resulted in decreased morbidity, mortality, and transmission of HIV. This region, however, still represents the majority of the global burden of HIV. Furthermore, levels of retention in care and medication adherence, critical determinants of ART effectiveness, are currently suboptimal, and, thus, continue to be the target of many interventions. This dissertation is comprised of three chapters related to understanding ART adherence and interventions to improve it.

Chapter 1 quantitatively describes and examines the distribution of poor adherence to antiretroviral therapy in a study of HIV-positive patients in Zambia. In a novel application of the Lorenz curve, a tool used commonly in economics, this analysis characterized the concentration of medication non-possession in a network of clinics in order to identify "hotspots" and predictors of poor adherence. Results extend previous studies by revealing that even though average adherence is high, lapses in adherence are common and concentrated among a minority of patients, and also in certain clinics. This concentration and variability varies with time on ART. Furthermore, a small fraction of patients accounts for the majority of days of medication non-possession, with the size of this group increasing with time on ART. This suggests that targeted interventions may represent a preferable overall strategy as compared to those targeting all patients to improve adherence. Furthermore, there was high variability across clinics suggesting that interventions targeting clinic "hotspots" may also represent an efficient use of resources to improve ART adherence.

Chapter 2 presents the results of the first qualitative study to examine conditional incentives for ART adherence and their potential pathways of action among people living with HIV. This study was conducted within a study of conditional food and cash transfers to increase retention in care and adherence to ART among HIV-positive food insecure recent adults in Shinyanga, Tanzania. Although financial and in-kind incentives have been shown to improve outcomes along the HIV care cascade, results are mixed, and there is little evidence about the pathways through which incentives work. Results of this qualitative study and analysis revealed that incentives acted through three primary

pathways to potentially increase retention in care and adherence to ART: 1) addressing competing needs and offsetting opportunity costs associated with clinic attendance, 2) increasing motivation and 3) alleviating stress associated with attending clinic, worry about providing for oneself and one's family, and providing hope for a better future. The first pathway was the strongest, which was consistent with field observations and discussions with local clinic staff, research staff, and Ministry of Health officials. Participants did not report any harmful events associated with the incentives, and reported a variety of beneficial spillover effects on household welfare. Understanding these pathways can help improve design and targeting of future food or cash incentive interventions.

Chapter 3 focused on intrinsic motivation within the aforementioned study of food and cash transfers for ART adherence in Tanzania. Some critical of incentives argue that incentives can 'crowd out' intrinsic motivation, making the individual less likely to engage in the desired behavior after the incentive is removed, potentially leading to limited durability of effect and causing harm in the long term. This hypothesis was examined among recent antiretroviral treatment initiates in Tanzania by comparing participants' level of intrinsic motivation before receiving transfers to the level once the transfer period ended. The analysis revealed that, not only did intrinsic motivation not decrease after the transfer period ended, but that the level of intrinsic motivation increased overall and within study arms. Furthermore, the change in motivation did not differ by study arms. As the first study to empirically examine the crowding out hypothesis regarding incentives in a real-world, resource-limited setting, these results suggest that incentive interventions in such settings should not be impeded by concerns of crowding out intrinsic motivation.

Together these chapters contribute to improving our understanding of antiretroviral adherence and intervention response. The Lorenz curve and medication possession analysis provides a more comprehensive and detailed measurement and illustration of adherence and its variability across individuals and clinics in Zambia. Such information is critical to targeting and designing future interventions. Next, by examining an ongoing intervention to improve adherence in Tanzania, we were able to elucidate and examine the potential pathways of action of food and cash transfers. Furthermore, we found no evidence that these incentives decreased intrinsic motivation. Knowledge gleaned from this deep exploration of the incentives' mechanism of action in a real-world setting not only informs refinement of the intervention, but also helps to fill the gap in understanding how and when these interventions may work.

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INTRODUCTION

Burden and impact of HIV

As of 2012, HIV/AIDS had infected 75 million people and resulted in 36 million deaths.[1] Globally, an estimated 35.3 million people are currently living with HIV of which 25 million live in Sub Saharan Africa. Although there has been a 33% decrease in HIV incidence since 2001, there were 2.3 million new infections in 2012 of which 1.6 million occurred in Sub Saharan Africa.[2] This translates into 6,300 new HIV infections per day in 2012 with 95% of these in low and middle-income countries. No other disease to date has decreased life expectancy as dramatically as HIV/AIDS, however public sector provision of antiretroviral therapy (ART) has greatly contributed to its rebound.[3] Furthermore, since it primarily affects young adults, HIV/AIDS has strong economic and social impacts on society, resulting in an increased loss of productivity and increase in orphans and child-led households.[4]

Antiretroviral therapy

Through a combination of increased funding, development of new antiretroviral (ARV) medications, capacity building and development work, antiretroviral therapy (ART) is now a widely available and highly effective method of combating the AIDS epidemic.[5,6] The advent of ART has shifted HIV from a deadly disease towards a treatable chronic condition. ART has been repeatedly shown to reduce the morbidity and mortality of the individual,[7-9] as well as significantly reduce the risk of transmission.[10-13] In the past five years the WHO guidelines for ART eligibility have expanded, with the CD4 cutoff doubling from 250 to 500 cells/mm^3.[14] Results of recent randomized trials showed a beneficial effect of ART for all HIV-infected individuals regardless of CD4 count.[15,16] This prompted updated WHO guidelines (full guidelines to be released in 2016) that recommend starting all HIV-individuals on ART at any CD4 count.[17]

The HIV care continuum

The mantra of "seek, test, treat, retain"[18,19] outlines the main steps in the HIV care and treatment cascade, which begins by testing individuals for HIV and continues by linking them to care, initiating ART, retaining them in care, and ultimately ensuring that they are virally suppressed. When examined closely, these steps can signal key intervention points to address weaknesses in cascade completion. The care continuum can be divided into three distinct phases: HIV testing, pre-ART care, and ART care.[20] Individuals must first be sought out or seek care themselves, often at a health facility or in the community, and then be tested for HIV. Those who are HIV-positive enter the pre-ART care phase where they are assessed for ART eligibility by clinical staging or CD4 count. This often requires at least one return visit to the health facility. If they are not eligible for ART, they are advised to remain engaged in care and be periodically evaluated for ART eligibility. If they are eligible, they typically receive some amount of education and counseling and subsequently initiate ART. In Tanzania and Zambia, the focus of this dissertation, this process requires at least three visits, which typically occur over the course of several weeks. Although eligibility guidelines have been expanded, these are not yet in practice in all settings. Once on ART, individuals must return to the clinic at regular intervals (often monthly to quarterly) to receive medical care and refill prescriptions.

Though it initially appears to be a linear process, there are many points in the HIV care continuum where individuals can disengage. For example, many people are lost to the health system between testing and treatment before beginning ART.[20,21] A meta-analysis of Sub-Saharan Africa found that roughly 30% of people were lost between testing and receiving CD4 count results with roughly 50% of those remaining being eligible for ART. Of those eligible, only an estimated 62% started ART.[22] Among those who are eligible and initiate ART, the importance of retention in care is compounded by its inextricable link to ART adherence and viral suppression,[23,24] and thus better health outcomes. Each gap or entry/exit point in the HIV care continuum indicates a potential opportunity for an intervention to maximize the effectiveness of HIV care and treatment and minimize loss from the continuum. While acknowledging the importance of interventions at all stages of the care continuum, this dissertation will focus on retention and adherence.

Retention in care and adherence are required attributes of successful HIV treatment and prevention programs. Focusing on the treatment of people living with HIV (PLWH), high levels of adherence are required to receive the benefits of ART, including increased survival, viral suppression, reduced morbidity, higher quality of life, and reduced risk of progression to AIDS.[25-27] Furthermore, non-adherence increases the risk of developing drug resistance.[28] Meta-analysis of ART-adherence in Sub-Saharan Africa estimate 77% adherence, although there is much variability (range 30-100%).[29] In the current landscape, these estimates of retention in care give pause to viewing universal test and treat as a primary strategy to end the HIV epidemic without accompanying interventions to increase retention. Estimates suggest that of the minority of PLWH that initiate ART, only 65% are retained in care at 3 years,[20] with death estimated to account for 40-60% of those lost to follow-up.[30,31] In addition to its individual clinical benefits, many HIV prevention programs are based on ART including prevention of mother to child transmission (PMTCT), pre-exposure prophylaxis (PrEP), treatment as prevention (TasP), and post-exposure prophylaxis (PEP).[32,33] The efficacy of such programs is directly related to adherence.[13,32] Thus, the success of ART for both treatment and prevention hinges on adherence or interventions to increase adherence, as much as on the biological efficacy of the agent,[33] making adherence and retention in care essential factors to long-term success of ART scale up.[34]

Efforts to quantify and collect data on patterns of patient loss to follow-up have led to a deeper understanding of this continuum and help to inform future interventions. However, thus far, these efforts[29,32,35] mostly focus on point estimates and fail to adequately quantify and investigate the distribution of retention or adherence in the target population. In chapter 1, I present an innovative application of an economic method to improve the way we measure and think about adherence, with the goal of informing more effective and efficiently targeted interventions. I then examine an intervention designed to improve adherence in chapters 2 and 3.

Barriers to retention and adherence

From a public health and policy perspective, it is important to closely examine the many barriers to retention and adherence to determine which are appropriate targets for intervention. Previous studies have identified non-disclosure,[25] stigma, alcohol abuse,[25] food insecurity,[36-39] costs and difficulty following drug regimens,[29] and availability of drugs as key barriers to ART adherence. Food insecurity is of particular interest and is defined as existing "whenever the availability of nutritionally adequate and safe foods or the ability to acquire acceptable foods in socially acceptable ways is limited or uncertain".[40] It is a unique barrier to both adherence and retention as it acts across individual and structural levels, and is often considered "syndemic" with HIV/AIDS. [37,41-49] In many locations, including Tanzania and Zambia, ART is provided free of charge, but ART-users report other related costs, such as transportation, user fees, and waiting times as major obstacles to adherence and retention.[31,50,51]Other costs often cited as barriers include those for missing work, childcare, and other competing costs such as food.[34,38] Importantly, all of these factors also affect retention in care.[31]

In-kind and financial incentives as interventions

As recognition of food insecurity as a barrier to retention in care and ART adherence increases, food assistance has gained momentum as a way to overcome these barriers among food insecure PLWH.[52-54] Of the five studies that have examined the impact of food assistance on ART adherence in sub-Saharan Africa, three found higher levels of ART adherence among those receiving food.[52,55-58] In addition to ART adherence, food assistance has also been positively associated with retention in care.[53,59] Based on these limited results, food assistance appears to be a promising intervention to increase ART adherence and retention to care among PLWH, though it has yet to be rigorously evaluated in a randomized trial.

Financial incentives have been shown to improve outcomes along the HIV care continuum.[60-67] To date, however, there have only been a handful of trials examining the effects of financial incentives on adherence among PLWH. All four studies took place in the US in populations with a history of treatment failure or drug use/abuse, which are at higher risk of non-adherence than the general population. Given this, it is encouraging that all studies noted either an increase in adherence or decrease in viral load during follow-up.[64] However, in all three randomized studies of cash transfers and ART adherence that examined durability, adherence returned to baseline levels once the incentives were removed.[64] Some critical of incentives argue that incentives can 'crowd out' intrinsic motivation, making the individual less likely to engage in the desired behavior after the incentive is removed, potentially leading to limited durability of effect and causing harm in the long term. [64,68] This hypothesis will be explicitly examined in chapter 3. Although the evidence on the value of using incentives to increase adherence is growing, how or why these incentives work is unknown. In chapters 2 and 3 I will explore what people use them for and whether they may have unintended consequences.

Food versus cash assistance

Despite the promising outlook of food assistance as an intervention to address the deleterious effects of food insecurity, [52,55-57,69]there is an ongoing debate over the relative value of food versus cash transfers. Chapters 2 and 3 of this dissertation focus

specifically on a randomized trial examining the impact of food and cash incentives on ART adherence.[70] While the trial will evaluate whether food and cash incentives are equivalent in the Tanzanian setting, these chapters aim to provide explanations for how and why the transfers may or may not work and whether this differs by transfer type. There are many reasons why either food or cash may be the superior transfer type, and these vary by context. First of all, distribution of food is costly and often labor-intensive, prompting many to suggest cash as an alternative. For example, a cost-effectiveness analysis found that the cost of distribution was equal to the cost of food, effectively doubling the cost of the intervention.[69] Meanwhile, the cost of distributing cash is much lower and sometimes nearly zero.[71] Proponents of cash argue that cash offers greater freedom of choice to the recipient, is easier and cheaper to distribute, and is more efficient according to microeconomic theory.[72] However, directly providing food results in higher food consumption (compared to cash) [72] and is acceptable when markets are performing poorly, i.e. there is little food available for purchase or food prices are very high.[71] One hypothesis to explain this difference is that food assistance often impacts both those otherwise unable to afford food and those who would not purchase an adequate amount of food even if they had the required cash.[71] Thus, in addition to the monetary value, food may nudge behavior in the desired direction, whereas cash alone has no such implicit suggestion for use attached to it.

Adherence and retention in care are critical components of the HIV care cascade and must be improved in order to help end the HIV epidemic. This dissertation aims to describe and illustrate of the concentration of adherence across individuals and clinic to inform intervention development and also to explore mechanisms of action of an ongoing intervention to improve adherence.

Chapter 1: Non-adherence to antiretroviral therapy among HIV-infected patients in Zambia is concentrated among a minority of patients and highly variable across clinics

ABSTRACT:

Background: The distribution of poor adherence to antiretroviral therapy (ART) in an HIV-positive patient population indicates whether barriers to medication use are concentrated within particular sub-populations or are otherwise crosscutting. We quantified the medication possession ratio (MPR) and characterized the distribution of medication non-possession in a network of clinics in Zambia to identify "hotspots" and predictors of poor adherence.

Methods: We analyzed a population of adults on ART for more than 3 months who made at least one clinic visit between March 1, 2013 and February 28, 2015. Pharmacy refill and clinical information were obtained through the electronic medical record system used in routine care. MPR was calculated as the number of days of ART dispensed over the total number of days the patient should have been on ART using pharmacy records. We constructed a Lorenz curve, plotting the cumulative proportion of days of medication non-possession against the cumulative proportion of patients to visualize the distribution of poor adherence. We used a multi-level logistic regression model to examine clinic and individual-level factors associated with MPR.

Results: Among 131,767 patients in 56 clinics (64% female, median age 34 years [IQR 29-41], median CD4 count at ART initiation 351 cells/μl [IQR 220-517]), the median MPR was 85.8 [IQR 70.8-96.8] indicating that patients were not in possession of ART 14.2% of the time. After 1 year on ART, 45.6% of patients had 100% medication possession, the next 43.9% accounted for the bottom 50% of medication non-possession and the final 10.5% contributed the top 50%. Over time, a greater proportion of patients contributed to days of non-possession. In multi-level logistic regression, disclosure of HIV status, and more recent ART initiation were associated with higher MPR, while WHO Stage 3 or 4 at enrollment in care and being male sex were linked to lower MPR. Across clinics, median MPR ranged from 49.1 to 98.5 and clinic accounted for 12% of the total variability in MPR after adjusting for individual and other clinic-level characteristics.

Conclusions: A small fraction of patients account for the majority of days of medication non-possession, especially early after ART initiation. Further characterization of patient sub-populations where non-adherence is concentrated is needed to target interventions. The greatest amount of variability in MPR was explained by the clinic. Health systems interventions targeting clinic "hot spots" may represent an efficient use of resources to improve ART adherence.

INTRODUCTION

Although adherence to antiretroviral therapy (ART) among people living with HIV in resource limited settings is high on average,[29] understanding the variability in adherence across patients—in addition to the average level—offers additional insights. Consider, for example, a population of patients where average medication adherence is 80%. If all patients in this population exhibited 80% adherence, we would suspect that barriers to adherence in this setting might be broad and systematic. Stock outs or local economic shocks would be barriers that could affect all patients equally. On the other hand, an average of 80% adherence might also represent a setting in which most patients had 100% adherence while a minority had very poor adherence. Such a skewed distribution would imply that the magnitude of barriers to adherence differs substantially between individuals. Distance from home to clinic and socioeconomic status, for example, might be highly variable in a population of patients.[73] Interventions should be systematic and broad if little variability in adherence exists, but would be more efficient if targeted in settings where adherence differs markedly between individuals.

Presently, most studies on adherence focus on population averages and offer limited information on quantifying variability. Although spread is often touched upon in quantities such as the interquartile range, which often accompanies reports of medians,[29,74] these figures do not show the extent to which adherence lapses are concentrated. An analysis that pooled results of previous US studies using electronic monitoring to measure adherence showed that adherence varied non-linearly over time and that trend varied across study sites,[75] but it did not provide estimates of the distribution of adherence across patients or within sites. Another reported notable differences in means across sites in Tanzania, Uganda, and Zambia, but the variability in differences within sites was not reported.[35] Likewise systematic reviews and meta-analyses pool averages across studies, but variability within patients in a particular study are often not included in such summaries.

To characterize variability in adherence to HIV treatment, we examined individual medication refill data from a large network of health clinics in Zambia. We borrow a technique originally used to describe income inequality, the Lorenz Curve, to highlight the extent to which variability in adherence is concentrated in a population.[76] We also explored individual and clinic-level predictors of high adherence. The goal is to use this understanding of the distribution of adherence to inform the type and targeting of interventions to more effectively and efficiently improve adherence.

METHODS

Patients

This is a secondary data analysis of electronic medical records of patients attending a Zambian clinic supported by the Center for Infectious Disease Research in Zambia (CIDRZ). To best characterize the contemporary patient experience, we limited our analysis to the current adult (18 years or older) clinic population, defined as individuals who were on treatment had any HIV care visit between January 1, 2013 and February 28, 2015. We further limited the analysis to those on ART for at least 3 months. CIDRZ is a Zambian non-governmental organization that supports HIV care and treatment services at a network of 78 government and private clinics across 4 of 10

provinces in Zambia. For this analysis, we excluded CIDRZ-supported private clinics and clinics where a large randomized trial was ongoing because these clinics had access to additional financial and human resources that limit their representativeness of the typical Zambian HIV treatment experience. We constructed a retrospective cohort, with observation time beginning on the first visit date after January 1, 2013 and continuing until the earliest of: 90 days past their last appointment date, death, official transfer, or database closure on February 28, 2015 (sensitivity analysis on cut-off choice results is presented in Appendix Table 1.1). Observation time was limited to 90 days after the last documented pharmacy appointment because Zambian consolidated guidelines[77] consider patients lost to follow up (LTFU) at greater than 60 days and clinics reported they often remove patient files from the records room after 90 days – therefore they cease to contribute metrics of adherence but rather are no longer considered part of the cohort of interest.

Measurements

Basic information about the clinics such as province and clinic type (e.g., urban clinic, rural clinic, hospital) was obtained from administrative data. Clinic size and the year the clinic started operating were determined empirically as the number of patients currently attending that clinic and the year of first recorded visit. Sociodemographic and clinical characteristics of patients, including all visit and appointment dates, were obtained from the patient's electronic medical record in the Zambian national data system, SmartCare (visit date completion outlined in Appendix Table 1.2). Sex, education level, disclosure of HIV status, marital status, and WHO stage were documented through routine clinical care at time of enrollment in care, while baseline CD4 count was defined as the last CD4 count recorded between 6 months prior to and 7 days after ART initiation.

Analyses

We measured adherence with the medication possession ratio (MPR), or the proportion of time on treatment that a patient actually has ART in their possession. MPR is recognized as a reliable measure of adherence,[35,52,70,78-81] with previous studies showing a strong association between MPR and viral load or treatment failure[78,79] and poor clinical outcomes.[82-91] Using visit and appointment dates from pharmacy records, we calculated MPR as the number of days of ART dispensed over the total number of days during the observation period. For example, pharmacy visits were usually given at 4 or 8 week intervals and 30 or 60 days of ART were given out for that interval. Because 2-3 extra pills are given at each pharmacy pick-up, in our analysis patients began to accrue days of medication non-possession 3 days after a missed pharmacy visit. These pills were later accounted for by adding 2 days to total medication possession for every on-time visit. After the last recorded pharmacy appointment and exhaustion of pill supply given on that date, patients accrued days of medication non-possession until the earliest date among: death, transfer, database close, or 90 days past appointment date. A dichotomized outcome of "good" MPR was defined as MPR>80%, since adherence above this level has been associated with lower levels of drug resistance, reduced mortality, and improved CD4 response in previous studies.[82,86]

We examined the distribution of MPR in each clinic using boxplots. We then constructed a Lorenz curve[76] by plotting the cumulative proportion of days of medication non-possession in the population against the cumulative proportion of patients in the population to visualize the

distribution of lapses in adherence. Because time on ART is associated with adherence, we stratified the curve by time on ART observed (0-6 months, 6 months-1 year, 1-2 years, 2-3 years, 3-5 years) to increase interpretability. To contribute to a stratum, the patient had to be observed for the entire period of time on ART defined by that stratum. For example, to contribute to the 0-6 months stratum, the patient's entire 0-6 months on ART had to occur during the observation period. Each patient could thus contribute to multiple strata they were observed for that length of time on ART.

We used a multi-level, mixed effects logistic regression model and mixed effects Poisson model (results shown in appendix) to identify individual and clinic-level characteristics associated with individual MPR>80% and calculate resulting odds ratios. Covariate selection was based on directed acyclic graphs that encode hypothesized causal relationships to include confounders and exclude colliders.[92,93] We used a random intercept term for clinic. Sex, education level, disclosure of HIV status, marital status, and WHO stage were measured at enrollment into care; year of ART initiation and baseline CD4 count were measured at time of ART initiation; age, days on ART, clinic type, province, and clinic size were determine at the end of the observation period. We used the mi suite in Stata[94] to implement multiple imputation to address missing predictor values for five variables (baseline CD4 category, education, marital status, disclosure, and WHO stage), as they were assumed to be missing at random conditional on other measured covariates (summary in Appendix Table 1.3).[95] Intracluster correlation was calculated to determine the percent of variability in MPR attributable to clinic. All analyses were conducted with Stata version 13.0 (StataCorp LP, College Station, Texas). This study was approved by the institutional review boards at the University of California, Berkeley; University of California, San Francisco; and the University of Zambia.

RESULTS

Patient and Clinic Characteristics

A total of 131,767 patients from 56 clinics were included in this analysis, collectively accounting for 1,175,666 pharmacy visits (Table 1). The median age was 34 [interquartile range (IQR) 29-41] and 64% were women. The median time on ART was 3.47 years [IQR 1.52-5.98 years], with 42% of patients initiating ART between 2013-2015. Median CD4 count at ART initiation was 351 [IQR 220-517], and 35% were WHO stage 3 or 4 at initiation. The majority (52%) of patients attended clinics in Lusaka province and the majority (86.4%) had disclosed their HIV status to someone at the time of enrollment. Forty-three percent of the clinics were in Lusaka province (Table 2) and 43% were urban clinics. The median current clinic population size was 1,770 [IQR 889-3,966].

Variability in MPR

Median MPR among all patients 85.8% [IQR 70.8-96.8] indicating patients were not in possession of ART 14.2% of the time. The Lorenz curve revealed differences in distribution of medication non-possession by period of time on ART (Figure 1). During the first six months on ART, 49% of patients accrued zero days of medication non-possession, and thus had a 100% MPR. This proportion decreased for longer time on ART, and only 12.7% of patients had 100% MPR during years 3-5 on ART. Furthermore, the proportion of patients contributing to the top 50% of medication non-possession also increases with time. During the first 6 months on ART,

11% of patients account for the top 50% of days of medication non-possession. Though still a minority, this group increases to 19% for the period of 3-5 years on ART. For example, we find that between 1 and 2 years on ART, 27% of patients had 100% medication possession, with the next 61% of patients accounting for the bottom 50% of medication non-possession and the final 12% of patients contributing the top 50% of days of medication non-possession.

In addition to individual heterogeneity by time on ART, MPR also varied by clinic with median clinic MPR ranging from 49.1% to 98.5% (Figure 2A). Similarly, by clinic, the percent of patients contributing zero days of medication non-possession ranged from 3.8% to 46.1% (Figure 2B), while the percent of patients with MPR>80% ranged from 7.2-89.2% by clinic (Figure 2C).

Multi-level predictors of MPR > 80%

In multi-level multivariable analyses (Table 3) disclosure of HIV status (OR = 1.14, 95% CI: 1.0-1.3), more recent ART initiation, CD4 >200 cells/μL at ART initiation, attending a hospital for care as compared to lower level clinic (OR = 1.7, 95% CI: 1.17-2.47), being married or widowed, and receiving care in Lusaka or Southern Province were significantly and positively associated with MPR>80% (Table 3). In contrast, college education (OR = 0.81, 95% CI: 0.73,-0.90), WHO stage 3 (OR = 0.86, 95% CI: 0.82,-0.91) or 4 (OR = 0.77, 95% CI: 0.70-0.84) at enrollment, and attending an urban clinic (OR = 0.67, 95% CI: 0.52-0.86) or a clinic in Western Province (OR = 0.60, 95% CI: 0.45-0.78) were associated lower MPR. (Risk ratio results from an equivalent Poisson regression are shows in Appendix Table 1.4) .The intraclass correlation (ICC=0.12) indicates clinic accounted for 12% of the total variability in MPR even after adjusting for individual sociodemographic and clinical characteristics as well as and clinic characteristics (A graphical illustration of the differences between predicted MPR by clinic using a model with and without fixed effects for clinic is included as Appendix Figure 1.1).

DISCUSSION

In a large cohort of 131,767 patients from four provinces and 56 clinics in Zambia, we found MPR to be high (83%) on average but highly variable across both individuals and clinics. In the first year on ART, nearly 50% of patients had perfect adherence, while approximately 10% of patients accounted for 50% of the days of non-adherence. Both individual characteristics such as recent ART initiation lower WHO stage, female sex, and clinic characteristics were associated with MPR>80%. These results suggest that even though average adherence is high, lapses in adherence are common and concentrated among certain individuals in certain clinics at certain times after starting ART. However, even after adjustment for individual and measured clinic characteristics, clinic accounted for 12% of the variability in MPR. The concentrated nature of the problem reveals the presence of “hotspots” of poor-adherence that can guide further investigations. Additionally, these hotspots suggest that targeted interventions may represent a preferable overall strategy as compared to those targeting all patients to improve adherence.

Visualizing MPR using the Lorenz curve provided novel insights into the distribution of adherence within a patient population. The Lorenz curve specifically summarizes the concentration of the outcome, in our case medication non-possession, in a way that traditional summary statistics such as mean and standard deviation or median and interquartile range do not. In other words, the information available in a Lorenz curve can also be conveyed in a series of

numbers, perhaps for example, that 50% of persons do not contribute to medication non possession, 60% contribute 7%, 70% contribute 15%, etc. A single Lorenz curve, however, shows all of these data points and offers a synthesis of the extent of distributional inequality. Furthermore, by comparing curves over time or across subpopulations, a comparative summary of the distributional inequality changes is also made immediately clear.

We identified factors associated with less than 80% adherence. There was no major difference by age, but males were less likely to have MPR>80%, which is consistent with literature suggesting lower adherence among males.[96-98] Adherence did not differ by much between those who had no education and those who had basic primary or secondary education, however adherence was lower among those with a college or university education. This is possibly because highly educated patients tend to switch to private clinics or health providers over time. Although adherence differed by marital status, the effect size was generally small. We found that those who had disclosed their HIV status at baseline were more likely to have MPR>80, which is consistent with the literature, even though the effect size is not dramatic.[99,100] The factor most associated with adherence was year of ART initiation with those initiating more recently much more likely to have MPR>80%. This is consistent with our Lorenz curve findings that early after ART initiation, many patients have perfect adherence, and this number decreases over time. Clinically, the sicker patients, those with lower CD4 counts and WHO stage 2 or 4 were less likely to have MPR>80%. This is likely due to access issues related to severity of illness, and perhaps also a higher rate or unreported mortality.[101]

Identifying clinic "hotspots" offers immediate information for systems improvement activities.[102] Both measured and unmeasured clinic level factors associated with lower adherence indicate that at least some of the drivers of adherence are likely rooted in the organizational and structural characteristics of the clinic or community. The odds of having MPR>80% differed significantly by province, being higher in Lusaka and Southern provinces, which are home to the capital and other larger urban centers, and lower in Western province compared to Eastern province. Western province was associated with lower overall adherence which may be explained by the fact that seasonal flooding makes clinics difficult to reach at certain times of the year. We found no association between clinic size and MPR. Hospitals were associated with higher MPR than rural health centers – a finding inconsistent with previous literature suggesting greater adherence and retention in lower level health clinics.[103,104] On the other hand, urban centers were less likely to have MPR>80%. Beyond these measured factors, an additional 12% of the variance in adherence was due to unmeasured clinic characteristics. Many of these remaining factors, such as management, human capital, integrity and quality of care, and data quality are difficult to measure quantitatively but should be the focus of future research. Some of this variability may also be due to differential migration patterns at each clinic; anecdotally, however, migration was only reported as a factor potentially impacting MPR by <5 clinics. Strategies such as positive deviance also suggest that understanding processes at the highest performing clinics may offer a generalizable solution to improvement of delivery.

This study has limitations. MPR was calculated based only on pharmacy visit and appointment dates, rather than conducting pill counts of doses distributed and number remaining when the patient returns. To increase accuracy of this method, we based assumptions of number of pills distributed and the number returned on information from local clinicians and pharmacists

regarding actual practices at the clinics. Another inherent limitation is that lost to follow up, transfers, and deaths, are not comprehensively captured in the data system, and some visits may not be accurately documented. Patients who appear lost to follow-up may have disengaged from care, but they may also be in care at another clinic or have died. To address this unknown patient status, we capped the time of observation at 90 days after the last appointment. In case of an undocumented patient death or transfer to care at another clinic before this date, we would likely underestimate MPR. However, for those who truly disengaged, this method would result in an overestimate of MPR. Previous research suggests that approximately 50% of those LTFU are in care elsewhere, so overall, this is likely a conservative estimate of MPR.[105]

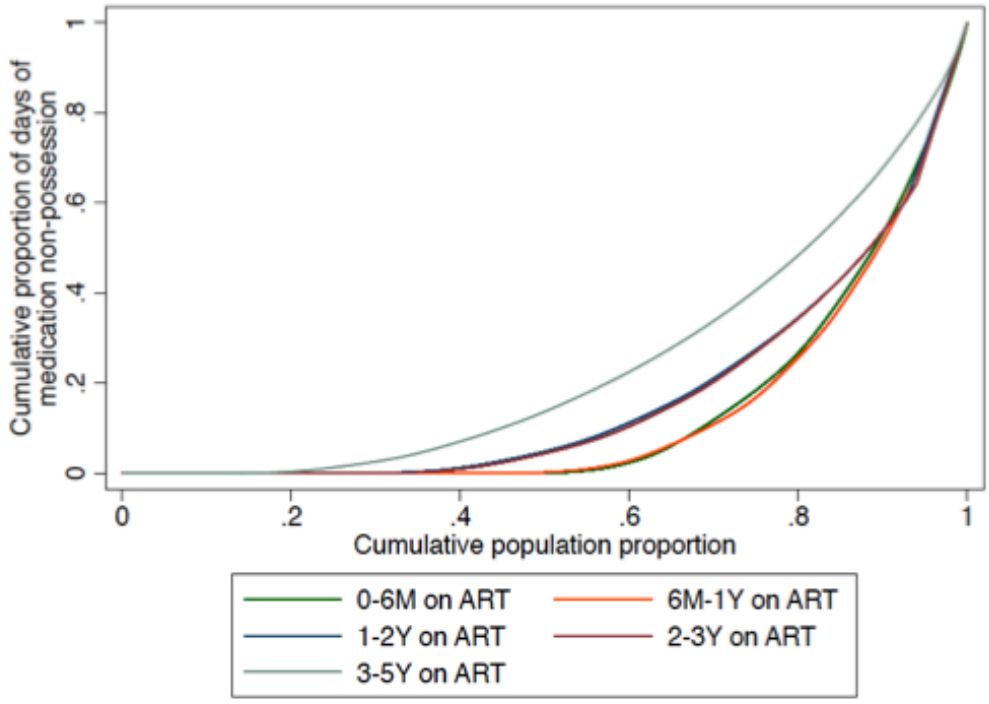
CONCLUSION

In summary, we found a high degree of variability in MPR that differed most strongly by time on ART and clinic. The Lorenz Curve illustrates that a small fraction of patients account for the majority of days of medication non-possession, especially early after ART initiation. Further characterization of these patients is needed to better target individual-level interventions. The difference across time on ART, also noted in other studies,[75] suggests that interventions to increase retention and adherence should adapt to how long a patient has been on ART. In addition to individual considerations, we need to increasingly shift our focus to clinic-level interventions as clinic explained much of the variability in MPR. Further work to illuminate the specific factors at work on the clinic-level can aid in the development of clinic-level interventions that likely target structural and organizational factor. Health systems interventions targeting lower performing clinics may represent an efficient use of resources to improve ART adherence.

Table 1. Sociodemographic and clinical characteristics of patients on ART>3 months attending CIDRZ-supported clinics in Zambia (N = 131,767)	
	N (%)
Female	84763 (64.3)
Year of ART initiation	
2004-2006	14244 (10.8)
2007-2009	32378 (24.6)
2010-2012	29694 (22.5)
2013-2015	55451 (42.1)
Marital Status	
Single	11233 (8.5)
Married	69063 (52.4)
Divorced	13530 (10.3)
Widowed	13627 (10.3)
Unknown	1839 (1.4)
Education	
None	7414 (5.6)
Lower-Mid Basic	37608 (28.5)
Upper Basic/Secondary	48513 (36.8)
College or University	5092 (3.9)
Disclosed HIV Status at baseline	113800 (86.4)
Baseline WHO Stage	
1	47231 (35.8)
2	27739 (12.1)
3	41380 (31.4)
4	4799 (3.6)
Province	
Eastern	24890 (18.99)
Lusaka	68653 (52.38)
Southern	16310 (12.44)
Western	21205 (16.18)
Facility Type	
Rural	12531 (9.56)
Urban	73746 (56.27)
Hospital	44781 (34.17)
Clinic opening year	
2003	69729 (53.2)
2004	42704 (32.58)
2005+	18625 (14.21)
	Median [IQR]
Age	34 [29, 41]
Time on ART (days)	1267 [556, 2,178]
CD4 at ART initiation	351 [220, 517]
Clinic Size (in hundreds)	1589 [681, 3,521]

Table 2. Characteristics of clinics attended by patients	
	N (%)
Total	56 (100)
Province	
Eastern	11 (20)
Lusaka	24 (43)
Southern	10 (18)
Western	11 (20)
Facility Type	
Rural	18 (32)
Urban	24 (43)
Hospital	14 (25)
Clinic opening year	
2003 or before	16 (29)
2004	25 (45)
2005+	11 (20)
	Median [IQR]
Clinic size	1,770 [889, 3,966]
Clinic MPR (%)	82.4 [75.1, 86.75]

Figure 1. Lorenz curve of days of medication non-possession stratified by time on ART and percent of patients contributing to non-possession



Percent of Patients contributing to Medication non-possession

Time on ART	Perfect Adherence	Bottom 50% of non-possession	Top 50% of non-possession
0-6M	49.39	39.56	11.05
6M-1Y	45.63	43.88	10.49
1-2Y	27.25	61.14	11.61
2-3Y	29.32	59.06	11.62
3-5Y	12.7	68.17	19.13

Note: Bottom 50% of non-possession refers to the percent of the population that accounted for the lower 50% of medication non-possession. Top 50% of non-possession refers to the percent of the population that accounted for the higher 50% of medication non-possession

Figure 2. A. Box plot of medication possession ratio by clinic (median range: 49.1-98.5); B Bar graph of the percent of patients with perfect adherence by clinic (range: 3.75-46.05%); C Bar graph of the percent of patients with good adherence (MPR > 80%) by clinic (range: 7.2-89.2%)

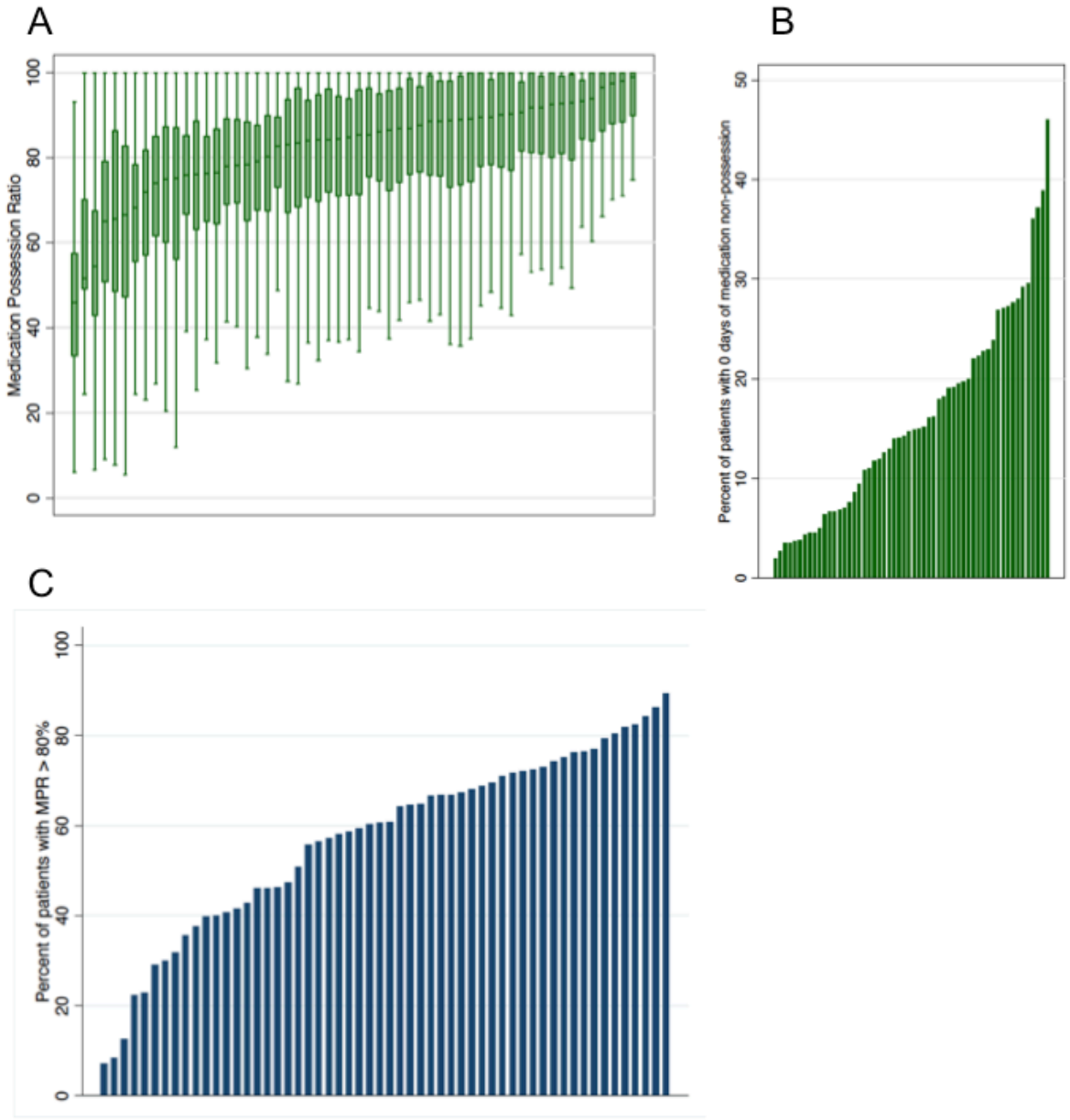


Table 3. Results of multi-level logistic model of MPR>80[a]

	Odds Ratio	95% Confidence Interval	P-value
Age	1.01	(1.01, 1.02)	>0.001
Male	0.88	(0.85, 0.91)	>0.001
Education			>0.001*
None	Ref		
Lower-Mid Basic	1.1	(1.02, 1.19)	0.011
Upper Basic/Secondary	1.02	(0.93, 1.11)	0.661
College or University	0.81	(0.73, 0.9)	>0.001
Disclose	1.14	(1, 1.3)	0.047
Marital Status			0.004*
Single	Ref		
Married	1.1	(1.04, 1.16)	0.002
Divorced	1.02	(0.95, 1.09)	0.548
Widowed	1.08	(1, 1.16)	0.039
Unknown	1.17	(0.9, 1.51)	0.233
Year of ART initiation			>0.001*
2004-6	Ref		
2007-09	2.64	(2.2, 3.18)	>0.001
2010-12	7.76	(5.45, 11.05)	>0.001
2013-15	21.19	(13.37, 33.6)	>0.001
CD4 count at ART initiation			>0.001*
<200	Ref		
200-349	1.11	(1.06, 1.16)	>0.001
350-499	1.14	(1.08, 1.21)	>0.001
>500	1.16	(1.09, 1.23)	>0.001
WHO Stage at enrollment			>0.001*
1	Ref		
2	0.98	(0.92, 1.05)	0.584
3	0.86	(0.82, 0.91)	>0.001
4	0.77	(0.7, 0.84)	>0.001
Facility Type			>0.001*
Rural	Ref		
Urban	0.67	(0.52, 0.86)	0.002
Hospital	1.7	(1.17, 2.47)	0.007
Province			>0.001*
Eastern	Ref		
Lusaka	1.53	(1.22, 1.92)	>0.001
Southern	1.67	(1.38, 2.02)	>0.001
Western	0.6	(0.45, 0.78)	>0.001
Clinic Size (per 100)	1.00	(1.00, 1.01)	0.480
ICC	0.12		

[a] Model was adjusted for year clinic opened and time on ART (results not shown)
*P-value from Wald test of equivalence across all levels of variable

Chapter 2: *It helps me live, sends my children to school, and feeds me*: A qualitative study of pathways through which food and cash incentives may improve retention in care and antiretroviral adherence among adults living with HIV in Tanzania

ABSTRACT

Background:
Financial and in-kind incentives have been shown to improve outcomes along the HIV care cascade. However, investigation into the potential pathways through which they work remains limited. Understanding the mechanisms through which these incentives impact health outcomes and for which populations they work best is critical to increase the effectiveness of future incentive-based programs. To identify the pathways through which incentives may improve retention in care or adherence to antiretroviral therapy (ART), we conducted a qualitative study within an ongoing trial of conditional food and cash incentives for HIV-positive food insecure adults in Shinyanga, Tanzania.

Methods:
Participants met trial eligibility criteria of 1) at least 18 years of age, 2) started ART within the past 90 days (at enrollment), 3) food insecure according to the Household Hunger Scale, and 4) body mass index >16 kg/m^2. Eligibility for this study further required that participants had been randomized to the food or cash incentive group and received at least 3 of 6 possible incentives as of the interview date. We purposively sampled eligible participants and conducted in-depth interviews to examine how they used the incentive and the process behind these decisions to elucidate potential pathways through which incentives may work to improve retention in care and adherence to ART.

Results:
Among the 29 study participants, there were 16 women and 13 men, of whom 17 had received food incentives while 12 received cash. We found that the incentives acted through three primary pathways to potentially increase retention in care and adherence to ART: 1) addressing competing needs and offsetting opportunity costs associated with clinic attendance, 2) increasing motivation and 3) through a mental health pathway whereby the incentives reportedly alleviated stress associated with attending clinic and providing for oneself and one's family. Participants did not report any harmful events associated with the incentives, but reported a variety of beneficial spillover effects on household welfare.

Conclusion:
This is the first qualitative study to examine conditional incentives and their potential pathways of action among people living with HIV. Understanding how incentives are used and how they impact outcomes can improve the design of future interventions. Based on the pathways identified here, economic and opportunity cost barriers and the mental health status of the target population should be a focus when implementing a food or cash incentive intervention.

INTRODUCTION

The widespread availability and use of antiretroviral therapy (ART) has shifted HIV from a deadly disease towards a treatable chronic condition. The cascade of HIV care begins with HIV testing and continues by linking and retaining individuals in care and successfully treating PLWH (i.e., virally suppressed) for the rest of their lives.[20] However, there are many points in the cascade such as linking to care after testing, initiating ART, and being retained in care, where an individual may disengage and experience suboptimal health outcomes. Thus, interventions to reduce such leaks in the cascade are in high demand. In resource-limited settings, such as Sub-Saharan Africa, only 62% of eligible patients are estimated to start ART,[22] and only 65% of ART initiates are retained in care at 3 years,[20] with death estimated to account for 40-60% of those lost to follow-up.[30,31]

Financial incentives have been shown to improve HIV prevention and treatment outcomes in some, but not all, studies, and reasons for this heterogeneity often remain unexplored. Several studies have demonstrated that financial incentives can lead to behavior that reduces HIV incidence[60-62], increases HIV testing[63,66,67], increases linkage to care after diagnosis[65], and increases ART adherence,[52,55-57,60-67] while others have shown null effects.[106-108] As an illustration of this unexplained heterogeneity, it is unclear, why cash incentives reduced sexually transmitted infections among young girls in Malawi[62] and young adults in Tanzania,[61] but a cash incentive conditional on school attendance did not prevent HIV infection among young women in South Africa.[106]

In addition to heterogeneous effects on the intervention's primary behavioral outcome (e.g., school attendance) across studies, both positive and negative spillover effects have been reported. These spillover effects, defined here as effects not directly related to the targeted behavior or outcome, also vary in type and magnitude by study. Potentially harmful spillover effects previously reported include an increase in risky sexual behavior among men in the Malawi Incentives Project[109] and an increase in obesity among participants in Mexico's *Oportunidades* program.[110] Meanwhile, positive spillover effects were observed in Mexico and South Africa when reproductive health and HIV-related risk behavior improved as a result of anti-poverty programs that distributed cash incentives targeted to households with children.[111-117] Without knowing how or why incentives work, and for whom they work best, we are unable to explain conflicting results, prevent undesirable effects, and maximize positive spillover effects.

Literature examining the pathways through which incentives operate is sparse, and quantitative data from impact evaluations, although valuable, cannot explain these complex, often context-dependent mechanisms of action that could help explain observed heteorogeneity. In contrast, qualitative research can provide a more in-depth understanding of how incentives may work– information that could be widely applicable to the spectrum of cash and in-kind assistance programs currently being implemented.[64,118]

Since there are virtually no empirical data describing how cash or in-kind incentives are used by PLWH and there is an equal paucity of data about why those decisions are made, we looked to qualitative studies of cash incentives in other contexts, specifically anti-poverty programs and programs to increase engagement with health systems. Qualitative research about incentive use

in the context of anti-poverty programs focuses mostly on the benefits and uses of the incentives, highlighting potential reasons for differential use and decision making which may be informative.[119] A review on qualitative research on incentives aiming to support engagement with the health system explores how conditional cash incentives increased the use of health services in different programs across four countries. It concludes that the incentives worked both to lift financial constraints and to incentivize engagement with the health facilities, but that the effects were limited by social factors impeding the desired behavior such as traditional beliefs, gender and social norms, and poverty.[120] In addition, a qualitative study in India exploring why conditional cash incentives for hospital births did not improve health outcomes, including neonatal and maternal mortality, despite increasing the number of hospital-based births, found that poor quality of care coupled with emotional and psychological costs (not overcome by the incentive) hampered improved health outcomes.[121] Together, these findings demonstrate the complexity of the potential pathways that incentives may act through in various contexts, and highlight the importance of understanding the mechanisms through which incentives change behavior and the populations for which they work best in order to maximize benefits, minimize adverse outcomes, and better target incentive-based programs in the future.[30,35-38]

We examined the potential pathways through which incentives may work in the context of ART adherence among PLWH .We conducted a qualitative study within an ongoing trial of conditional food and cash incentives to increase retention in care among HIV-positive food insecure adults in Shinyanga, Tanzania. The goal of this research was to identify the pathways through which incentives may act to improve retention in care, and to evaluate whether economic and psychological theories support these pathways.

METHODS

Study Setting and Population

This study was ancillary to a randomized control trial evaluating the effectiveness of conditional food and cash incentives to improve adherence to ART among food-insecure HIV patients who recently initiated ART in Shinyanga, Tanzania (NCT01957917).[70] Patients were eligible for the trial if they were at least 18 years of age, had started ART within the past 90 days, were food insecure, according to the Household Hunger Scale,[122] and were not severely malnourished. In total, 805 patients were recruited from two government hospitals and one government health clinic and randomized into one of 3 arms: nutritional assessment and counseling (NAC; control), NAC plus monthly food incentive, or NAC plus cash incentive. All patients in the food or cash arms were eligible for up to 6 monthly incentives conditional on attending routine physician-given appointments (within a +/-4 day window). Food incentives consisted of 12 kg maize meal, 5 kg beans, and 5 kg groundnuts (peanuts). Cash incentives included requisite fees and were delivered via m-pesa, a mobile-money platform accessible throughout the region. The food and cash incentives were of equivalent value at 22,500 TSH ($10-12 with varying conversion rate), which is approximately 30% of regional GDP per capita per month (10.5% of GDP per household with median of 3 members).[123] Participants were given the following instructions regarding the use of their incentive(s): “This food/cash is to help you stay healthy as you continue your HIV treatment. You can use the food/cash as you wish to help you with your health.” In the parent study, surveys were administered and blood samples for viral load were

collected at baseline, 6, and 12 months. Preliminary data indicate that both medication and visit adherence were higher in the cash group compared to either food or NAC only.[124]

To participate in the qualitative study, participants had to be enrolled in the parent study, randomized to either the food or cash incentive group, and have received at least 3 of 6 possible incentives at the time of interview to ensure adequate exposure to the program and facilitate discussions about the incentive. Since previous studies indicated differential incentive usage by gender, head of household, and incentive type (food/cash),[71,72] participants were purposively selected from these joint strata in an effort to represent the perspective of each sub-group. The interviews were distributed across study sites roughly in proportion to total study enrollment to increase diversity of participant viewpoints.

Ethical Statement

This study was approved by the Committee for Protection of Human Subjects at University of California Berkeley and by the National Institute for Medical Research in Tanzania.

Theoretical Framework and interview guide development

Three theories directed the development of the in-depth interview guide. The first is neoclassical microeconomic theory, which suggests that incentives help overcome economic constraints to positive health behaviors. Since the food and cash incentives were designed to mitigate food insecurity, which has been associated with decreased ART adherence,[125] we incorporated questions to explore whether the incentives addressed opportunity costs or other basic needs that would otherwise preclude clinic attendance.[118,125,126] The incentives can potentially have a price effect, income effect, or both.[71,127] Based on consumer demand theory, individuals will demand or consume more of a good if the price is lowered; in this case a price effect implies that the incentive lowers the cost of coming to clinic. An income effect, on the other hand, implies that the incentives are large enough to relieve broader economic constraints, not limited to clinic-related costs that could impact adherence.[64] The resulting interview guide included questions examining competing needs, incentive use, how recipients make decisions about incentive use, and the structural factors influencing these decisions.

The second is behavioral economic theory, which theorizes that individuals fail to engage in healthy behaviors due to systematic biases or shortcuts. For example, standard economic theory predicts that individuals may choose behaviors with immediate rewards over those with long-term rewards and immediate costs (like adherence to ART or attending clinic) because they place a low value on, or "discount", the long-term benefits of the behavior.[64,128,129] Behavioral economic theory extends this assertion by predicting that the incentives may not act solely through discounting, but instead by counteracting non-standard barriers such as inertia (i.e., it is very hard for people to change routines that didn't previously include taking medications or attending the clinic regularly) and self-control (i.e., it is very difficult for people to restrain behaviors perceived as more gratifying than being healthy). Incentives, such as food and cash incentives, may theoretically work either by increasing the short-term benefits of the costly behavior, counteracting inertia, or reducing barriers to beneficial self-control. In this study, incentives were intended to increase the short-term benefit of coming to the clinic, and thus we aimed to explore individual's perceptions and preferences for present versus future goals and how that impacts decisions about incentive use.

We also drew constructs from Self Determination Theory, which distinguishes between intrinsic motivation, engaging in an activity because it evokes positive feelings, and extrinsic motivation, engaging in an activity for a separate consequence or reward.[130] To further explore this phenomenon, we incorporated questions into the interview guide about pre-existing motivation to come to clinic and take ART and motivation during the incentive period. Questions explicitly examining mental health were not included in the interview guide; the mental health pathway arose unprompted from the interviews.

After an internal review and revision of the interview guide based on feedback from local research assistants, a pilot study of four interviews was conducted September-November 2014 to further refine the guide. The interviews followed a semi-structured approach in that questions and probes were pre-specified to ensure consistent data collection, but the interviewer was free to change the wording or sequence of the questions and probes during the course of the interview.[131] After each pilot interview, the guide was further revised to increase participant understanding of questions and depth of response (the interview guide is included as Appendix Item 2.1). This iterative process of interview guide design is characteristic of qualitative research.[131]

Data Collection

Recruitment

We created eligible patient lists for each strata (joint strata of gender, incentive group, and head of household status) based on the baseline survey from the randomized trial and verified the number of incentives received by each before their next clinic visit. On their next HIV primary care visit, potentially eligible patients were approached by a researcher (A.M.) who explained the study. Interested patients provided written informed consent and completed the in-depth interview on the same day. Participants were reimbursed with a small token of appreciation for their time (kanga cloth or cellphone talk time) valued at approximately $5.

In-depth interviews

Interviews were conducted between February and May 2015. Each in-depth interview lasted 30-60 minutes, took place at a private space at the health facility, and was conducted in Kiswahili by a Tanzanian interviewer trained in qualitative research methods and research ethics. The interviews were audio recorded with the permission of each participant and later transcribed verbatim and then translated into English by local staff. In addition, the interviewer created written memos in English at the completion of each interview to record any non-verbal attributes, emerging ideas, and suggestions to improve subsequent interviews. The interviewer and investigator debriefed in weekly meetings to discuss emerging themes, defined here as recurring patterns or categories of ideas that emerge across interviews.[131] The target sample size was 32, and the final sample size was determined by examining theme saturation, both overall and within strata.

Analysis

We developed an initial list of deductive codes, such as ‘motivation’, that represented key aspects of the theoretical framework and hypothesized mechanisms of action. English transcripts of the interviews were independently read and coded by two researchers (NC and MB) using the

same codebook in either Atlas.ti or Dedoose qualitative data analysis software (software choice was based on access and preference), and coded transcripts were compared. Intercoder agreement for a set of 13 codes representing the main themes and theoretical framework was evaluated (pooled Cohen's kappa = 0.81). The two coders met weekly to resolve coding and interpretation differences and to identify and discuss emerging themes and new inductive codes to be incorporated into the codebook. For example, though not included in our initial codebook, many narratives mentioned mental health and how the incentive helped to relieve stressors or negative thoughts, so a code was developed for this inductive theme and we returned to previously coded transcripts to incorporate it.

To examine differences and similarities in narratives within and across themes, code sorts were evaluated and compared to the theoretical framework.[131] For example, through examining quotes coded as *incentive use,* we found that many patients were using the incentive for entrepreneurial activities, and that became a potential pathway through which incentives may overcome economic barriers to ART adherence. Once pathways through which incentives were acting and themes emerged from the coding analysis, we considered the consistency of cases supporting and refuting those pathways and themes through systematic review, reduction and interpretation of the data.[132] The transcripts were revisited once consensus was made on both the inductive and deductive codes to fully develop the observed incentive pathways and compare these findings back to the three theoretical frameworks. Narratives corresponding to each pathway were further analyzed to examine patterns or inconsistencies across sub-groups.

RESULTS

Participant Characteristics

Among the 29 study participants, there were 16 women and 13 men, and 17 had received food incentives while 12 had received cash (Table 1). Only one person refused to participate in the study.

How incentives were used

Food

All participants receiving food incentives reported using it for personal and household consumption. No one reported selling the food themselves, but one participant claimed to know someone who sold some of the food, and another reported sharing some with a friend. A strong sense of obligation to consume the food was common in the participant narratives. Some expressed that they didn't feel enough ownership of the incentive to use it for anything but consumption [Table 2, Quote 1] whereas others felt that using the food for anything but consumption was incomprehensible [Quote 2]. Meanwhile, others, linking the food to the study and clinic, felt they should use the food to better themselves [Quote 3]. Lastly, some patients, likely those who were severely food insecure, didn't consider using the food for anything but eating [Quote 4]. Benefits of food other than consumption were sparsely noted and included using the money normally spent on food to start a business [Quote 5] or to pay for school fees [Quote 6].

Cash

Participants reported that the extra cash provided by the incentives allowed them to spend money in a variety of ways, including food and basic needs, entrepreneurial activities, savings, and children's school fees. Some participants were struggling to meet their basic needs more than others, and for them especially, all of the cash went towards food, rent and basic needs. One woman, who was not head of household, felt she could not consider using the cash for anything but food [Quote 7]. Others were able to use the funds for rent, and other needs, in addition to food [Quotes 8 and 9]. The perceived benefits were mostly related to improved physical and mental condition as many cited an increase in number of meals consumed, ability to feed other members of the household, and increased energy allowing them to be more productive. For example, one woman reported that she was able to start a business after restoring her own health and even use the profits from that business to pay for school fees for her children [Quote 10]. In this case, the benefits of the cash incentive included personal health, livelihood activities, and investments in children's health or education.

Entrepreneurial activities were more commonly reported among cash recipients compared to food recipients, despite being asked the same interview questions and similar probes. In addition to the woman described above who started her own business, one 32-year-old married man used the cash incentive to improve his pre-existing business by purchasing a cart to save money in daily rental fees [Quote 11]. Here again, the benefits multiply; this man's ability to save and purchase his own cart temporarily freed up enough capital so that his wife could also start a business. These benefits appeared more concentrated in those who already had a small amount of money with which to meet basic survival needs and for whom the incentive provided some additional income, as they did not mention a pressing need to buy food and, could instead imagine and act on longer-term goals.

While some participants reported investing in and saving for entrepreneurial activities to provide a better future and sustainable income, other participants simply saved the money to have some degree of financial cushion for the unexpected [Quote 12]. There was frequent commentary on the uncertainty of the future and certainty of death, and many felt driven to either start a business or simply save cash to help support their families in the case of, what they felt was inevitable, their own death. With this in mind, participants viewed their children as their legacy, their best hope for the future, and wanted to invest everything in them, with a strong focus on education. They frequently reported using at least some of the cash to purchase school supplies or pay school fees, like one father who felt empowered to support his child's education and additional classes with the incentive [Quote 13].

Potential action pathways of the incentives

We found that the incentives acted through three primary pathways to potentially increase retention in care and adherence to ART: 1) addressing competing needs and offsetting opportunity costs associated with clinic attendance, 2) increasing motivation, and 3) through a mental health pathway whereby the incentives reportedly alleviated stress associated with attending clinic, reduced worry about providing for oneself and one's family, and provided hope for a better future (Figure 1).

How food and cash incentives address competing needs and offset opportunity costs

One pathway through which incentives were found to increase retention and adherence was by alleviating economic barriers to attend clinic. This pathway had the strongest support in participant narratives. In many instances, this manifested as a price effect reducing opportunity cost, meaning that individuals could come to clinic instead of spending the day looking for food or money, which was a commonly reported reason for missing visits at the clinic [Quote 14]. For such patients who may have previously weighed their decision to go to clinic against other daily needs, the incentive offset the lost opportunity costs normally associated with going to clinic. For example, one woman who received food assistance emphasized that the incentive was enough to offset the time, inconvenience, and actual cost of coming to clinic even for those who hated coming [Quote 15]. Analogously, others gave specific examples of how receiving the incentive enabled them to pay expenses associated with clinic attendance, such as transportation, and explicitly cited the incentives' ability to help provide for their families [Quote 16]. Another woman reported using the cash to purchase cotrimoxazole and another prescription that the clinic was unable to provide. Thus, the incentives likely act through a price effect pathway by reducing structural barriers and addressing opportunity cost imbalances to effectively reduce the price of attending clinic.

Given that most participants reported using the incentives for food and other basic needs, the incentive also appeared to act through an income effect by relieving broader economic constraints not directly related to clinic costs. Many participants reported using the transfers to meet immediate basic needs such as buying food or paying rent [Quotes 8, 9, and 13], and/or to start or support entrepreneurial activities that would provide sustained income to meet these basic needs long term [Quotes 10,11]. Several participant narratives pointed to income effects as playing a role. For example, such participants reported that receiving the incentive allows them to fulfill those basic needs and expenses unrelated to clinic costs, and keeps them coming to clinic [Quote 17]. Thus, the incentives seemed to reduce economic constraints and meet basic non-clinic needs at home to facilitate clinic attendance and ART adherence, behaviors in which they were already motivated to engage.

How incentives affected motivation to attend clinic

Many patients expressed a high level of motivation to take ART, which stemmed from an ingrained belief in the effectiveness of ART stemming from both clinic messaging [Quotes 18 and 19] and personal experiences witnessing or experiencing dramatic improvements in health after initiating ART [Quote 20]. However, very few explicitly reported that the incentive changed their desire or motivation to come to clinic. One man, with a nuanced and sophisticated understanding of his own motivation, explicitly said that the incentives did not motivate him to come to clinic and that he had to come regardless of the offer of the incentive or his ability to afford transportation [Quote 16]. On the other hand, it was apparent that participants correctly linked the incentives to clinic attendance [Quote 21: *"I come here for my medications and my [food] certificate."*] and thus it is difficult to infer that the incentive did not impact motivation to come to clinic, even if such an effect was not explicitly and verbally expressed by participants. Most participants said that the incentive did not motivate them, but the interviewer reported non-verbal cues such as eyes brightening and tone getting more excited when they discussed the incentives. Although this doesn't directly translate into motivation, it does suggest that participants were excited about the incentives and very conscious of them. It is important to note that despite linking the incentive to coming to the clinic and checking in with a research

assistant, most participants had a limited understanding of the conditionality of the incentive, specifically that patients had to attend their scheduled appointment within a 4 day window to receive the incentive. For example, one man reported knowing that he had to check in with the research assistant in the office after picking up his ART from the pharmacy, but did not know he had to come to his visit on time to receive the incentive [Quote 22]. Though these individuals did not clearly understand or remember the specific requirements, the incentive seemed to act as a motivator by giving people an additional reason to go to clinic when they might otherwise have chosen not to.

How incentives may reduce mental health barriers to adherence

Many participants reported that receiving the incentives reduced stress, worry, and depression (often expressed in Kiswahili as 'many thoughts' or 'bad thoughts'), and fostered a sense of peace because they were now able to meet their basic needs. These results suggest that mental health may have improved temporarily among transfer recipients. Although no participants were able to explicitly link this mental health improvement with increased adherence or clinic attendance, we infer this as a likely pathway given the strong association between mental health and adherence present in the existing literature.[133-137] Participants reported that a sense of happiness and mental freedom arose from the ability to attend clinic (which often required a full day) and the absence of worry about where the next meal would come because they would be receiving the incentive, or had a previous incentive remaining at home or saved. One woman expressed the soothing feeling of knowing that she would be able to eat and get transport home, a sentiment echoed by others [Quote 23]. In addition, some, like this man and his wife, simply expressed relief, as the burden worries about meeting basic needs was lifted through receipt of the incentives [Quote 24]. In addition to stress relief, improved physical condition also inspired more positive thoughts and a sense of hope and direction among some, like this man who received food incentives [Quote 25] and ultimately wanted to do HIV outreach in the village to educate others. This evidence in the context of what is known about the relationship between mental health and adherence suggests that improvement of mental health is another pathway through which these incentives may act.

DISCUSSION

This qualitative study explored how participants chose to use food and cash incentives received as part of an ongoing randomized trial, and identified three pathways through which the incentives may impact retention in care and adherence to ART if they are shown to be effective. Participant narratives suggested that patients used the incentives in a wide variety of ways, and that ultimately, if the incentives are shown to be effective, they are likely acting through one or a combination of the pathways: 1) offsetting opportunity costs and competing needs; 2) providing motivation to attend clinic; and 3) reducing mental health barriers associated with adherence. Overall, participants did not report harmful events associated with the incentives and instead reported a variety of beneficial spillover effects on household welfare, including: investments in productive assets or businesses, covering school-related expenses for children, saving, and covering expenditures for other basic needs such as rent and paying off debt.

While most reported consuming the food provided in the food baskets, those receiving cash incentives understandably reported more varied uses including purchasing food, entrepreneurial

activities, paying school fees, and saving. Many receiving cash reported using at least part of the incentive to purchase food and using the remainder to address other needs, including saving it up over the course of several months, which was typically not possible with food in this climate without proper storage facilities. Given the fungible nature of cash, it is difficult to clearly determine how cash affected household consumption from qualitative data. However, the objective of this analysis was to identify the uses of the cash incentives as perceived by the patients. While some in the food group reported using the cash that would normally be spent on food to start a business or cover other expenses, such uses may be underreported from food recipients who did not clearly link food with offsetting other costs. Giving them food may also have served as an informal signal from the program that they were to consume the food, whereas cash does not naturally come with such a signal. Furthermore, the non-fungible nature of food helps to explain why people prefer to consume than sell, as selling these smaller allotments of food is not common, would likely be perceived as suspicious, and would sell below market value (personal conversations with local study team). A quantitative analysis of data in the ongoing trial will provide more insight into how food and cash incentives were used. However, results from this qualitative study may be consistent with literature showing that people receiving food incentives have higher food consumption while those receiving cash have greater freedom of choice for use.[71,72] If true, it may be that food incentives have more of a short-term effect, while the transfer is ongoing, and cash incentives have long-term effects due to these additional more sustainable uses.

Of the three pathways through which the incentives may impact retention and adherence identified in this study, offsetting opportunity costs and meeting basic economic needs had the most support. These pathways suggest that the incentive had both a price and income effect, with the majority experiencing a reduced price to attend clinic by offsetting opportunity costs, and some also meeting basic needs not directly related to clinic attendance. The noted reduction in opportunity cost is consistent with the context of a food-insecure population and feedback from local and regional health officials who reported that needing to work or find food is one of the most common reasons that patients become lost to follow-up (personal communication with Regional Medical Officer). Coming to clinic is typically a full day consisting of travel time, early morning arrival, check-in, educational session, waiting for and seeing a clinician, and lastly picking up the next prescription of ART before traveling home. Furthermore, many used the transfer to relieve broader economic constraints and meet basic needs (i.e. rent, children's education fees, food), which likely also facilitated clinic attendance (income effects). By offsetting the opportunity costs lost by attending clinic (i.e. not being able to work or search for work or food that day), and meeting basic needs, the incentives may increase retention and adherence to ART.

Another pathway through which the incentives may act is by motivating patients to come to clinic, through the incentive's effect as external motivation. Although patients did not directly express that the incentives motivated them, potentially because of social desirability bias, most clearly linked receiving the incentives with checking in with research staff at the clinic, or more generally, coming to clinic. However, most did not fully understand the conditionality nor how it was enforced. Thus, this pathway, though plausible and likely for a few participants, appears to be the weakest pathway among the three, and any activity through it is likely to occur in combination with either or both of the stronger pathways outlined here.

The final pathway outlined here has the second highest level of support, emerged naturally from the data, and is consistent with prior work linking mental health to ART adherence,[134] food insecurity,[39] poverty,[138] and cash incentives.[139,140] In this study, many participants reported feeling "free" because they knew they had food or money to buy food and pay other expenses. Increased levels of anxiety, depression, and other mental health disorders is a noted effect of extreme poverty,[138] and these afflictions have also been identified as barriers to ART adherence.[134] Furthermore, food insecurity impacts HIV morbidity and mortality through a mental health pathway,[39] which is especially relevant in this context of providing conditional incentives to food-insecure PLWH. Previous research within cash incentive programs found that receipt of cash incentives was associated with a significant reduction in depression symptoms both among households receiving incentives in Kenya's cash incentive program for orphans and vulnerable children,[139] and among mothers receiving incentives through the *Oportunidades* program in Mexico.[140] In our study, participants not only reported that a mental burden had been removed as a result of receiving the incentives, but also reported a renewed sense of hopefulness, gratitude, and happiness that the clinic cared about them and their struggles with HIV and poverty. In addition to the mental health effects associated with poverty and food insecurity, participants in this study are also coping with a relatively new HIV diagnosis, which may be overwhelming. It is thus not surprising that many reported characteristics of improved mental health as a result of receiving the incentives. More attention should be paid to the interaction between the mental health effects of poverty and HIV and how interventions may improve overall health by addressing these circumstances.

There were important limitations to this study. First, as this study took place before the trial concluded, we do not yet have definitive evidence that the incentives improve retention in care and ART adherence or whether that effect differs by incentive type. However, preliminary data suggests that they do, and our findings support those data. Secondly, while many participants reported improvements in health and productivity as a result of receiving the incentive, they were also all recent ART initiates. While this strengthens the study by increasing homogeneity of the study population, it is at the same time difficult to disentangle the effects of the incentives from the positive impact of ART on physical and emotional quality of life at the beginning of treatment.[141] Lastly, social desirability bias is an important consideration, especially in participants' responses about motivation to come to clinic and how the incentive may have impacted that. Since they are told how important it is to come to clinic, they may not have explicitly and/or verbally reported that the incentive motivated them because of perceived social pressure to not conflict clinic orders, lack of self-awareness of true motivations, or unease admitting they were motivated by the incentive and sometimes didn't want to come to clinic, despite confirmation of confidentiality and probes directed at this specific issue. Furthermore, motivation often has a strong sub-conscious characteristic, and being able to vocalize reasons for a given behavior is limited by not only by what can be comfortably admitted, but also by self-awareness of the source of motivation.

This study also had myriad strengths. Trial results were unknown at the time of data collection and analysis which limits our ability to interpret results, but it also limits any interviewer or investigator bias that may have been introduced by knowing the results before conducting the interviews or analysis. Furthermore, conducting this study within a trial context allows us to

directly examine both incentive types in otherwise identical circumstances. This is the first qualitative study we are aware of that examined incentive uses and potential pathways of action among PLWH.

The pathways outlined here are non-obvious in both scope and strength, and this can be leveraged in future intervention designs. For example, if the motivation pathway is assumed at the outset, conditionality may be crucial to the intervention. However, if the dominant pathway is through offsetting opportunity costs, conditionality may be less important or unnecessary. Furthermore, if offsetting opportunity costs is the dominant pathway, other non-incentive based interventions (e.g., shortening clinic wait time) may also be highly effective if targeted towards that barrier. However, while effective in reducing opportunity costs, such interventions likely won't also help patients to meet basic needs. The mental health pathway elucidated here, and consistent with many other findings, also warrants greater attention in design and implementation. We acknowledge that different pathways may be more or less active for a given patient, therefore interventions, such as incentives, that give patients some freedom to choose how to address their multiple barriers are more desirable on a population level.

CONCLUSION

Food and cash incentives may impact retention in care and adherence to ART through one, or a combination, of several pathways. This study identified and described three likely pathways, and will further inform the interpretation of the trial results and future intervention design. By understanding how the incentives are used and how they may impact the desired outcome, we can improve the design of future interventions by varying amount, conditionality, and target population to increase effectiveness. Further consideration of the specific economic and opportunity cost barriers to a desired health behavior and also mental health status of the target population should be a focus when implementing a food or cash incentive intervention.

Table 1. In-depth interview participants stratified by gender, incentive group, and head of household (HoH) status in Shinyanga Region, Tanzania (N = 29)							
Men (N = 13)				Women (N = 16)			
Food (N = 8)		Cash (N = 5)		Food (N = 9)		Cash (N = 7)	
HoH	non-HoH	HoH	non-HoH	HoH	non-HoH	HoH	non-HoH
4	4	4	1	4	5	4	3

Table 2. Selected quotes from in-depth interviews illustrating categories of incentive uses and pathways of action

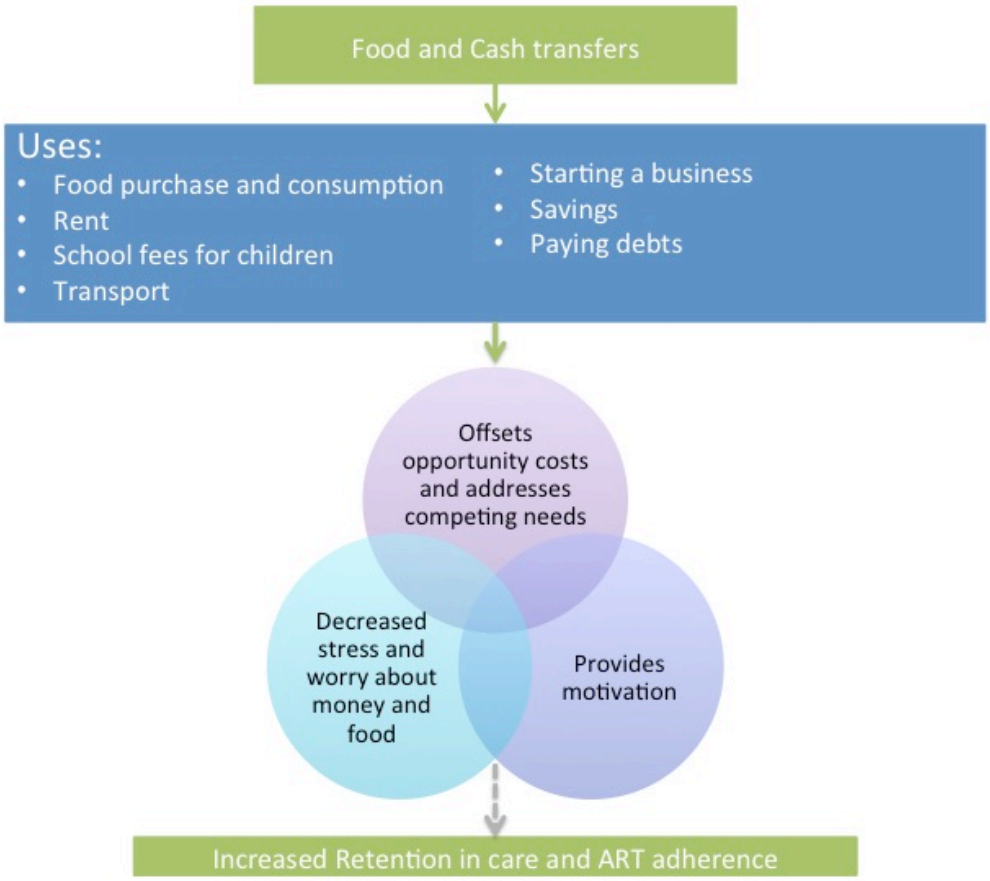
Category	Gender	Head of Household Status	Incentive type	Quote Number	Quote
Incentive Usage					
Food consumption	F	HoH	Food	1	*"I ate it by myself. I just can't disburse it to others because I have not planted it. I ate and finished it by myself."*
Food consumption	M	Not HoH	Food	2	*"You must be insane to sell the food that was given to you."*
Food consumption	M	HoH	Food	3	*"I came to a conclusion by myself that the food was given to me because of my health, body and my inability to get food. I thought that the food was to help me with the condition that I had. I thought it was to build up my health quickly. This food didn't come to me for business purposes and that's why I ate it together with my family and the children."*
Food consumption	F	Not HoH	Food	4	*"I used it well because we were given food that we can use daily...we are supposed to eat daily so I did my best in eating it daily"*
Entrepreneurial Activities	M	HoH	Food	5	*"I have bought six goats since I have started to take the medications….I was not able to buy goats before because every amount of money I was getting was finished in buying food. There were moments where I was able to make up to one hundred thousands shillings but all of that was ending in buying food and paying rent but things have changed since I started to receive food because the money that was supposed to buy food is now used of other family uses."*
Food offsetting other costs	F	HoH	Food	6	*"I can speak of that in general terms, I was taking flour, beans and groundnuts to my house whenever I received them…This means that they have reduced the amount of money that I would have used to buy flour so I can use it for paying my child's school fees."*
Buy food with money	F	Not HoH	Cash	7	*"The amount we were receiving was so little so I thought that I couldn't use it for other things apart from caring for my health. Sometimes I was not able to work to get any money so I had to use the little that I had to strengthen my health. I had to buy little food*

Buy food with money	F	HoH	Cash	8	*"[The money] has helped me because, when I was receiving that money. I bought food, I could live peacefully, I was able to pay the house rental fee. I was sleeping in peace knowing that I am going to pay it. I was also sleeping peacefully because I knew that I was going to receive money in the next month and will be able to pay the fee."*
Buy food with money, includes children	F	HoH	Cash	9	*"The money was sent when I was in need, I would struggle for two months but was relieved with the money that was sent, it helped me in buying food for myself and my two little children. The food I was buying was helpful and the money was also helpful because I could get my other needs too and that would have been different if I were to receive food only."*
Entrepreneurial Activities	F	Not HoH	Cash	10	*"I started to buy fruits after receiving the money, I bought a lot of oranges and stored them at home, and I was eating one orange per day. I started that business after feeling better; I was able to buy at least three fruits for use at home. [Money from the project and my new business] helped me in paying my child's school fee. I was able to make thirty eight thousand shillings to pay for my child who is in standard five. I took him from my parent's home and we stayed together. I was also able to send my last born child to standard one. I also paid thirty eight thousand for his primary education."*
Entrepreneurial Activities	M	HoH	Cash	11	*"I received that amount of money for six months; it has helped me to buy my own cart…I just saved it in my MPESA account until I bought a cart…I own a cart now. I no longer rent other people's carts. I was paying five thousand shillings weekly to the cart owner. I have my own cart now. That money has helped me…. My wife is running a food kiosk. I gave her a capital. That money comes from the amount that I was offering to the cart owner weekly. I now give five thousand to my wife every weekend. She has used that for the food kiosk so that we develop."*
Savings	F	Not HoH	Cash	12	*"You have to save some money as you keep receiving it…I took twenty thousand and put it aside. You can fall sick someday, can't you? You will use money in such a situation."*
Children	M	HoH	Cash	13	*"I think it's good if this project continues because it empowers me, my family and helps in my child's schooling. My child's school requirement is for each child to attend extra classes so I need to have money for that, for examinations and other school contributions. There are a lot of needs that are relieved by that money so I will keep on thanking God if this project continues."*

Pathway					
1. Addressing competing needs and offsetting opportunity costs to attend clinic					
Reduction in opportunity cost	M	HoH	Food	14	"*The food has helped me this way, in the beginning I had to first go look for food and then go to the clinic, but I can now go to the clinic knowing that I have left something at home and I am going to receive another thing at the clinic."*
Reduction in opportunity cost	F	Not HoH	Food	15	"*They would have come even if they hate it. Some hate...you know you may spend the whole day here at the clinic so you know that the whole day routine has been destroyed if you come here and it's much more difficult when you don't have something to eat. We always come here early in the morning and leave at 3 pm, so going home at that time not knowing what to eat and where to get it is so sad. There are a lot of troubles when you come here even if you are very early you won't leave that early, that's how the clinic is. He will not be bothered by spending the whole day at the clinic because he knows that he will find food at home [because of the incentive] and that's different if one was to stay here for the whole day not knowing what to eat and where to get it*."
Motivated by how incentive addresses needs	M	HoH	Cash	16	*"I was away for sometime so I had to borrow some money from someone for transport fare so that I can attend the clinic on time and then would return the loan after receiving money from the project so it has somehow motivated me...Receiving money doesn't motivate me to use my medications, I am using medications for my health, the money I receive motivates me through the services that it provides for my family and not in my medications…I am supposed to come to the clinic when my medications are finished, I have to come to the clinic whether it's there or not."*
Meeting basic needs motivates clinic attendance	F	Not HoH	Cash	17	"*This project is really helping me, I can't stop coming here. It helps me live, sends my children to school and feeds me*"
2. Motivating patients to attend clinic					
Strong motivation to take ART	F	HoH	Food	18	"*I can't stop taking my medications, I can't forget to take them. I will be devaluing my children if I don't take the medications intentionally or forget to take them. That will not be fair to them. I will leave them with their grandmother while they are still young, why shouldn't I continue with my medications so that I can pull them until they are grown up? They are saying that we can live long if we continue to use the medications"*

Strong motivation to take ART	F	HoH	Cash	19	"*We were told that we should take these medications for life and at the same time daily once we have started to take them. I was also scared [when I forgot to take ART] because we were taught that the virus will awaken with an abnormal speed if we stop taking the medications*."
Strong motivation to take ART	M	HoH	Cash	20	"*I was in a very bad state, I didn't believe that I could get healed, I was in despair. I am feeling well right now that I have used the medications and followed the nurse's instructions and advice. I can even do a casual labor if there is any…I couldn't even carry a five-liter jerry can during those days. All I could do was eat and sleep only*."
Linked incentive with clinic	M	Not HoH	Food	21	*"I come here for my medications and my [food] certificate."*
Understanding of study	M	HoH	Money	22	*R: He told me that I will be receiving it through MPESA; I really received money through it. (MPESA is the money incentive system by the Vodacom mobile network)* *I: Did he tell you that you will be receiving money without doing anything? Were you supposed to do something to receive that money?* *R: I was supposed to pass there after taking my medications.*
3. Reduce mental health barriers to adherence					
Reduced stress worrying about resources	F	Not HoH	Cash	23	*"My heart was soothed, I felt like some of my problems were taken away. I was able to get help in transport and food. There were moments in which I was coming here with an empty stomach but I was able to eat and get transport to home."*
Sense of Relief	M	HoH	Cash	24	*We were so relieved both I and my wife after receiving that money because we knew it will cater for our little needs. It helped us in a lot of ways.*
Renewed direction and hope	M	HoH	Food	25	*"I was so happy and went home with comfort [after receiving the first installment]. I still have that comfort to this day and I am happy. It was different from other days in which I had no direction...I started to see changes in my body after I have used that food. I started to see changes in my body, the changes brought hope."*

Figure 1. Proposed pathways through which food and cash incentives may impact clinic attendance and ART adherence



Chapter 3: Do incentives undermine intrinsic motivation? Increases in intrinsic motivation within an incentive-based intervention for people living with HIV

ABSTRACT

Background:
Cash and in-kind incentives have been shown to improve several health behaviors and outcomes across settings. However, some critical of incentives argue that incentives can 'crowd out' intrinsic motivation, making the individual less likely to engage in the desired behavior after the incentive is removed, potentially leading to limited durability of effect and causing harm in the long term. We examined this hypothesis in a trial of food and cash incentives among people living with HIV (PLWH) who were recent antiretroviral treatment (ART) initiates in Tanzania.

Methods:
Participants included in this analysis met trial enrollment criteria: 1) at least 18 years of age, 2) started ART within the past 90 days, 3) food insecure according to the Household Hunger Scale, and 4) had a body mass index >16 kg/m^2 and for the current study also 1) started ART prior to the day the baseline survey was administered and 2) completed the 6-month and/or 12-month survey. In-person surveys were administered at baseline, 6, and 12 months. Intrinsic motivation was measured using the autonomous motivation section of the Treatment Self-Regulation Questionnaire (TSRQ, range: 0-3). To determine if intrinsic motivation changed differentially across arms, we compared the change in TSRQ score from baseline to 6 and 12 months within and across arms using T-tests and linear regression.

Results:
Among the 446 participants who met the inclusion criteria (mean age 37, 67% female), the intrinsic motivation score was 2.79 at baseline and 2.91 at 6-months. Intrinsic motivation increased from baseline to 6 months both for the overall study population (0.13 point increase, $p < 0.001$, Cohen's $d = 0.29$) and within arms: food arm (0.15, $p<0.001$, Cohen's $d = 0.37$), cash arm (0.11, $p<0.001$, Cohen's $d = 0.25$), and comparison arm (0.08, $p = 0.160$, Cohen's $d = 0.21$). The change in motivation did not differ significantly by study arm (food v. comparison 0.07, 95% CI: -0.07, 0.21; cash v. comparison 0.03, 95% CI: -0.11, 0.17). Motivation continued to increase and these relationships were similar at 12 months.

Conclusion:
This is the first study to empirically examine the crowding out hypothesis regarding incentives in a real-world, resource-limited setting among PLHIV. We found no evidence to support that hypothesis in this context. Although further research is needed to examine this relationship in different settings and with incentives of different amount and duration, given these results, incentive interventions in resource limited settings should not be impeded by concerns of crowding out intrinsic motivation.

INTRODUCTION

Financial incentives, such as cash transfers, have been shown to increase a variety of health behaviors and positive health outcomes including health care utilization,[142] immunization rates, [143] child health status, [143] mental health, [139] exercise,[144] and medication adherence.[64] Cash transfer programs for poverty alleviation are now standard practice in Latin America and rapidly increasing in Asia and Africa. In the realm of HIV, financial incentives can improve outcomes related to HIV prevention and care including reducing HIV incidence[60,61,145], increasing HIV testing[63,66,67] and linkage to care after diagnosis[65], and increasing antiretroviral (ART) adherence.[64]

Although cash transfers have shown great promise as a public health intervention, it is critical to ensure that they are do no long-term harm, for example, increase behaviors with negative health effects or reduce motivation to do desired behaviors during or after the intervention period. Self Determination Theory (SDT), the principal psychological theory of human motivation, is often cited as an explanation of how incentives facilitate behavior change. It distinguishes between intrinsic motivation, engaging in an activity because of joy or other positive feelings generated from doing the activity, and extrinsic motivation, engaging in an activity because of some separate positive or negative consequence.[146] In the context of incentives, the incentive serves as an extrinsic motivator to do the desired behavior. SDT also suggests that under certain conditions where autonomy, competence, and relatedness to others are fostered, extrinsic motivation can be internalized and transformed to intrinsic motivation. [147,148] Ideally, under this theory, incentives would be provided as a source of external motivation under conditions that facilitate it becoming internalized.

Some critical of incentives argue that they may 'crowd out' intrinsic motivation, making the individual *less* likely to engage in the desired behavior after the incentive period compared to baseline.[149] If true, a consequence is that incentives may have limited durability of effect and cause harm in the long term. [64,68] Experimental evidence supporting the 'crowding out' hypothesis is largely rooted in the field of psychology, with the most recent studies occurring in education. These studies often occur in a laboratory-like, controlled setting where individuals are given a task, such as completing a puzzle or editing papers, and are then given free-choice time.[150] Whether or not they continue with the task and for how long during free-choice time is compared between a group receiving a reward, monetary or otherwise, and the group not receiving the reward. A meta-analysis of 128 of these studies found that those receiving the reward spend less time on the task in their free choice time compared to those without the reward, though the measure of effect was small (overall Cohen's d = -0.21).[150-152] However, others contend that incentives do not hamper intrinsic motivation under most conditions, citing the limited generalizability and narrow focus of most experiments.[153,154]

The crowding out theory has not been examined in real world settings where the incentivized behavior may be beneficial and improve the individual's health, as is the case with adherence to HIV treatment or keeping scheduled appointments. For example, many studies on human motivation conducted in education focus on short-term performance-based incentives (e.g., getting a high test score)[149] that are not necessarily directly linked the desired outcome of increasing learning. Furthermore, although a recent study of conditional cash transfers to

increase gym attendance showed a reduction in attendance post-incentive, the level did not drop *below* baseline gym attendance levels nor below that of the control group suggesting that the program did not cause long-term harm (e.g., reduction in intrinsic motivation) or a reduction in the beneficial behavior.[144] This study did not occur in a laboratory setting and is likely a more accurate representation of incentive response and motivation in a real-world setting.

The few studies examining the effect of incentives on adherence to ART have targeted populations with poor adherence in the US. While all noted an increase in adherence or decrease in viral load during follow-up, in the few studies that measured post-incentive outcomes, adherence levels returned to baseline, suggesting lack of durability of the incentives' effect.[64] However, no study has empirically examined whether incentives 'crowd out' intrinsic motivation in the context of HIV and treatment adherence, thus it remains a question of important consequence. For example, if these incentives are crowding out intrinsic motivation, then these interventions are having a negative effect that should be taken seriously and weighed carefully by implementers. However, if there is no evidence for crowding out, then successful incentive interventions should not be hampered by this concern. We had the unique opportunity to examine whether crowding out occurred in a study of conditional food and cash transfers in Tanzania using an empirical measure of intrinsic motivation.[155] We aimed to explore whether levels of internal motivation change between baseline and after participants have received up to six food or cash transfers, and whether this difference varies by study arm. Our goal is to understand how receiving a transfer may impact intrinsic motivation in a real world resource-limited setting.

METHODS

Population and Setting

This is a secondary analysis of data from a randomized controlled trial evaluating the impact of food and cash transfers on adherence among HIV-positive adults in Shinyanga, Tanzania (clinicaltrials.gov: NCT01957917).[70] Participants were recruited from two government hospitals and one government health clinic in Shinyanga region, Tanzania, which is a largely dry and agrarian region. The facilities were located in peri-urban areas and served patients who both live in town and in distant rural areas.

In the parent study, eligible patients met the following inclusion criteria at the time of enrollment: 1) at least 18 years of age; 2) living with HIV infection; 3) initiated ART for HIV infection ≤90 days before enrollment; and 4) food insecure, as measured by the Household Hunger Scale.[156,122] PLWH who were severely underweight (BMI<16.0) were excluded from the study, as these individuals require therapeutic food support (ready-to-use food products) for nutritional recovery. In total, 805 patients were recruited and randomized in a 1:3:3 ratio into one of 3 arms: nutritional assessment and counseling (NAC; comparison group), NAC plus monthly food transfer, or NAC plus cash transfer. The food and cash transfers were of equal value, and patients in the food or cash arms were eligible for up to 6 monthly transfers conditional on attending routine physician-given appointments (within a +/-4 day window). At baseline, 6, and 12 months, in-person surveys were administered and data was extracted from patients' medical files.

This analysis was limited to patients who completed the baseline and 6-month survey and/or 12-month survey, and excluded those who started ART on the day of enrollment, as they were not asked questions regarding motivation to take ART at that time.

Measurements

Primary outcome

Intrinsic motivation was measured at baseline (before incentives), 6 months (after completion of incentive period), and 12 months (6 months post-incentive) using the autonomous motivation section of the Treatment Self Regulation Questionnaire (TSRQ), originally designed to assess motivations and reasons for staying in a weight loss program.[155] The TSRQ was modeled after self-regulation questionnaires by Ryan and Connell,[157] and is based on Self-Determination Theory.[146] The autonomous section of this scale measures the extent to which individuals choose to engage with a specific health behavior because of its importance to them (intrinsic motivation), rather than its importance to others or in response to external stimuli (extrinsic motivation). Since its original conception, TSRQ has been used to examine the relationship between autonomous motivation and weight loss maintenance and exercise,[155] smoking cessation, glucose control among patients with diabetes,[158] adherence to medication for chronic health conditions,[159] and adherence to ART.[160] It has also been further validated in the contexts of tobacco use, diet and exercise.[161]

Participants who were on ART at baseline rated their agreement to statements describing reasons they may take their HIV medication as prescribed using a 3 point Likert Scale (1 = *not at all true*, 2 = *somewhat true*, 3 = *very true*). For example, participants were asked, "The reason you take your HIV medication as it was prescribed to you is because taking your HIV medication is consistent with your life goals". Consistent with previous studies,[155,160-162] the measure of intrinsic motivation was defined as the average score across the 5 statements. Change in motivation from baseline to 6 months, was defined as the difference in score between the 6-month survey and baseline. Likewise, change in motivation at 12 months was defined as the difference in score between the 12-month survey and baseline.

Exposure

We aimed to determine if intrinsic motivation changed between baseline and post-transfer period and whether that difference varies between transfer groups. Thus, the primary exposure was the randomly assigned study arm: food transfers, cash transfers, or comparison group.

Covariates

We examined heterogeneity in the change in motivation by additional factors representing determinants of intrinsic motivation as theorized by SDT. Deci and Ryan suggest that factors that enhance competence, autonomy, or relatedness will enhance intrinsic motivation and, conversely, factors that undermine these will decrease intrinsic motivation.[148] Additionally, Williams linked autonomous motivation, that coming from within, with self-rated current health, severity of illness, and perceived barriers in an investigation of the relationship between motivation and medication adherence.[159] Factors that control behavior, like rigid social roles or inability to make decisions about your own behavior, may also undermine autonomous self-regulation. With this in mind, we proposed to examine heterogeneity of change in motivation across age, gender, head of household status, marital status, education, religion, working status,

number of people in the household, food insecurity (according to the Household Hunger Survey),[122], whether or not the individual has children, inability to go to school or work due to illness, role in decision making regarding own health care, self-rated health (1-10 scale), and barriers to care (Appendix Table 3.1). All factors were self-reported in the survey at baseline. We created an index of barriers to care that was the sum of responses (0 = *not a problem*, 1 = *somewhat of a problem*, 2 = *big problem*) to questions about 11 barriers to getting medical advice or treatment when sick (e.g. getting permission to go or getting money needed for treatment).

Analysis

To determine whether intrinsic motivation changed between baseline and post-transfer periods and whether that change was different across arms, we conducted paired t-tests among the total study population (pooled across randomization arms) and also within arms. Effect size was expressed as Cohen's d statistic for each test. Cohen's d is a standardized measurement of the difference between two means and is calculated as difference in means divided by the standard deviation. In general, an effect of 0.2 is considered small, 0.5 medium, and above 0.8, large.[163] We compared the change in intrinsic motivation between arms using linear regression. These same methods were repeated to compare the change in motivation between baseline and 12 months. To examine heterogeneity across potential determinants of intrinsic motivation, we added the variable of interest and the two-way interaction term between the determinant and arm to the model. The Liu method was used to control false discovery rate in order to account for multiple testing in this subgroup analysis (*multproc* package in Stata).[164] To examine the impact of loss to follow-up (197 participants did not complete the 6 month survey), we repeated the analysis with inverse probability of censoring weights to account for differential attrition. Probability of censoring was predicted using pooled logistic regression and included arm, age, food insecurity status at baseline, education, clinic, baseline working status, sex, marital status, and barrier score as main-term predictors. All analysis was conducted in Stata version 13 (College Station, TX).

RESULTS

Overall, 469 participants were included in the analysis, of whom 446 completed both the baseline and 6-month surveys (N = 195 food arm; N = 207 cash arm, N = 45 comparison arm) and 270 completed the baseline and 12 month surveys (Figure 1). The average age was 37, 67% were female, 27% had no education, 89% had children, 76% were Christian, and 38% were married (Table 1). At baseline, the majority of participants were currently working (61%) and 60% were head of household. Average self-rated health at baseline was 8.25 out of 10, although 56% of participants had been unable to work or attend school due to illness in the past 12 months.

The mean intrinsic motivation score was 2.79 at baseline (range: 1-3), 2.91 (range: 1-3) at 6-months, which was after the opportunity to receive food or cash transfers, and 2.95 at 12 months (range: 2-3), which was 6 months after incentives had ended. (Distributions for each item in the subscale are included in Appendix Table 3.2). The level of intrinsic motivation significantly increased overall over both time periods and within each study group (Table 2). Among all patients, the intrinsic motivation score increased by 0.13 points at 6 months (95% CI (0.09,

0.17), Cohen's d = 0.29), and 0.19 points at 12 months (95% CI (0.14, 0.24), Cohen's d = 0.49). We also observed increases in intrinsic motivation in each incentive arm. The increase in intrinsic motivation at 6 months was 0.15 points in the food arm (95% CI (0.09, 0.21), Cohen's d = 0.37), 0.11 points in the cash arm (95% CI (0.05, 0.18), Cohen's d = 0.25), and 0.08 points in the comparison arm (95% CI (-0.03, 0.19), Cohen's d = 0.21) (Figure 2 A). At 12 months, the increase in motivation from baseline was 0.22 points in the food arm (95% CI (0.14, 0.31), Cohen's d = 0.52), 0.16 points in the cash arm (95% CI (0.10, 0.22), Cohen's d = 0.47), and 0.19 points in the comparison arm (95% CI (0.05, 0.34), Cohen's d = 0.49) (Figure 2 B). There was not a significant difference in change in motivation by arm at either time point, although the increase in motivation was slightly greater in the food group. For example, at 6 months the change in motivation in the food arm was 0.07 points greater than that of the comparison (95%CI: -0.07, 0.21), and the change in the cash arm was 0.03 points greater than that of the comparison (95% CI: -0.11, 0.17) (Table 3). Weighting the models by the inverse probability of censoring did not significantly change the results (Table 3).

Analysis of heterogeneity revealed no differences in change in motivation within subgroups outlined in Appendix Table 3.1. Initially, only age appeared to significantly modify the effect of study arm (p = 0.05), but after adjusting for multiple comparisons, this was no longer significant (critical p-value = 0.002).

DISCUSSION

We examined change in intrinsic motivation between baseline and the end of the transfer period and 6-months post-transfer in a trial of food and cash transfers for HIV-positive adults in Shinyanga, Tanzania. We found that intrinsic motivation to take ART significantly increased both overall and within the food and cash incentive arms. However, there was no difference in the size of the increase by study arm and there was no evidence of heterogeneity by proposed determinants. To our knowledge, this is the first study to empirically examine the crowding out hypothesis regarding incentives in a real-world, resource-limited setting. We found no evidence to support the crowding out hypothesis in the context of incentives used to improve adherence to HIV treatment.

The idea that incentives undermine intrinsic motivation has historically been an argument against their use. [68,150] Empirical data from this sample in Tanzania shows, contrary to the crowding out hypothesis, that intrinsic motivation is higher post-incentive compared to baseline. This relationship was robust to both adjustment for patient characteristics and inverse probability of censoring weighting to account for loss to follow-up. It also held for both 6 and 12 months of follow-up. In addition to the quantitative data presented here, qualitative data from in-depth interviews suggests that participants are using the incentives to both overcome economic constraints and offset opportunity costs to attending clinic (see Chapter 2). This suggests that the transfer is not merely an extrinsic motivator, and in fact, that it may have little impact on motivation to attend clinic.

When considering incentives, there is an important difference between giving an incentive to someone who is economically constrained, for whom the incentive makes the behavior possible, and giving an incentive to someone with sufficient resources where the incentive may provide

additional motivation, not originally present, to engage in the behavior.[165] Context likely plays an important role in how incentives may impact motivation. This particular intervention targeted a vulnerable population, recent ART initiates, and was designed to address food insecurity and overcome economic constraints, such as reductions in employment and productivity often experienced prior to and immediately after starting ART.[166,167] It was valued to be consistent with cash transfers provided through the Tanzania Social Action Fund to avoid coercive effects and was designed to be short term. It may be that the crowding out hypothesis applies differentially to situations where the incentive is primarily acting as an extrinsic motivator compared to those where the incentive operates through a different mechanism. Perhaps an incentive can crowd out motivation for an activity that people have little motivation or desire to do in the first place and for which the incentive is the primary motivator, but less so for behaviors in which individuals are highly motivated to engage. Even though the baseline scores were very close to the maximum score possible on the scale, we still observed significant increases after the conclusion of the intervention period. While we cannot definitively refute the crowding out hypothesis in all arenas, our results suggest that this incentive intervention in this context did not reduce the level of intrinsic motivation for treatment adherence among HIV-infected adults.

There are several limitations to this analysis. First, the level of motivation was measured by the TSRQ scale, and there is little evidence of this scale being used in low-income countries. Although it has been validated for many health outcomes in myriad settings, and questions were reviewed and vetted with local staff and translated appropriately, it was not directly validated in this setting. This scale was chosen to build on and represent previous work done in this arena, but this may not be the best way to measure intrinsic motivation in this setting. On one hand, observed behavioral data, such as clinic attendance after the transfer period is over, may be a better indicator. However, such a measurement captures multiple behavioral drivers beyond intrinsic motivation, such as ability to access care, experience with providers, illness, migration, and other socioeconomic and psychosocial factors and it would be difficult to equate this behavior with intrinsic motivation directly. Given its limitations, the TSRQ scale was the best-suited measurement tool for this application at this time. Secondly, since the baseline scores were already rather high on the scale, there may be ceiling effects, where the participants are unable to score any higher on the scale. This may limit our ability to test whether external incentives were internalized in the form of increased intrinsic motivation since those in the transfer arms could not possibly score higher. Furthermore, this was a secondary analysis of trial data, and thus was not powered to detect a change in motivation, nor heterogeneity by subgroup. Although the increase in motivation was statistically significant overall and within both the food and cash arms, we cannot rule out lack of power as the reason for the non-significant increase in the comparison arm and non-significant differences between groups. Similarly, lack of power may explain why we did not find significant heterogeneity among subgroups.

This analysis also had several strengths, the most significant of which was that it was done within the context of a randomized trial, which limited confounding by unmeasured factors. Secondly, the intervention and measurements were standardized and implemented in the same manner across arms. The trial design also allowed us to measure intrinsic motivation at baseline, immediately at the conclusion of the incentive period, and also 6-months after the incentives had ceased providing a clear comparison of motivation levels and outcomes, something often missing

from other incentive studies. Furthermore, the TSRQ was developed in line with self-determination theory, the underlying theory of the crowding out hypothesis. Using the sub-scale of this widely used tool increases comparability of our results to other studies. This scale has been used with many health outcomes and has been validated across settings in the developed world. Of note, the distribution of responses in our study (baseline intrinsic motivation 2.79 out of 3; 6-month: 2.91) is similar to other studies that have used this instrument. In the first use of the TSRQ autonomous scale used in a weight loss study, the mean was 13.8 out of 15 [155]; in a review of studies on smoking and/or diet and exercise 3 of 4 sites had a mean of roughly 6 out of 7;[161] in a study of patients with heart failure, nearly half of participants had the maximum score of 7;[162] and in a study specifically looking at ART use, the mean TSRQ score for autonomous motivation was 6.5 out of 7.[160] Lastly, the results of the sensitivity analysis using IPCW to account for loss to follow-up were consistent with the unadjusted and adjusted results of complete cases, which demonstrates the robustness of our results.

CONCLUSION

This is the first study to empirically examine the crowding out hypothesis in the context of an incentive intervention in a resource-limited setting. Further research is needed to explore this relationship in different settings and with incentives of different amount and duration. However, given these results, incentive interventions for treatment adherence should not be held back due to concerns of crowding out intrinsic motivation.

Figure 1. Participants included and excluded from analysis

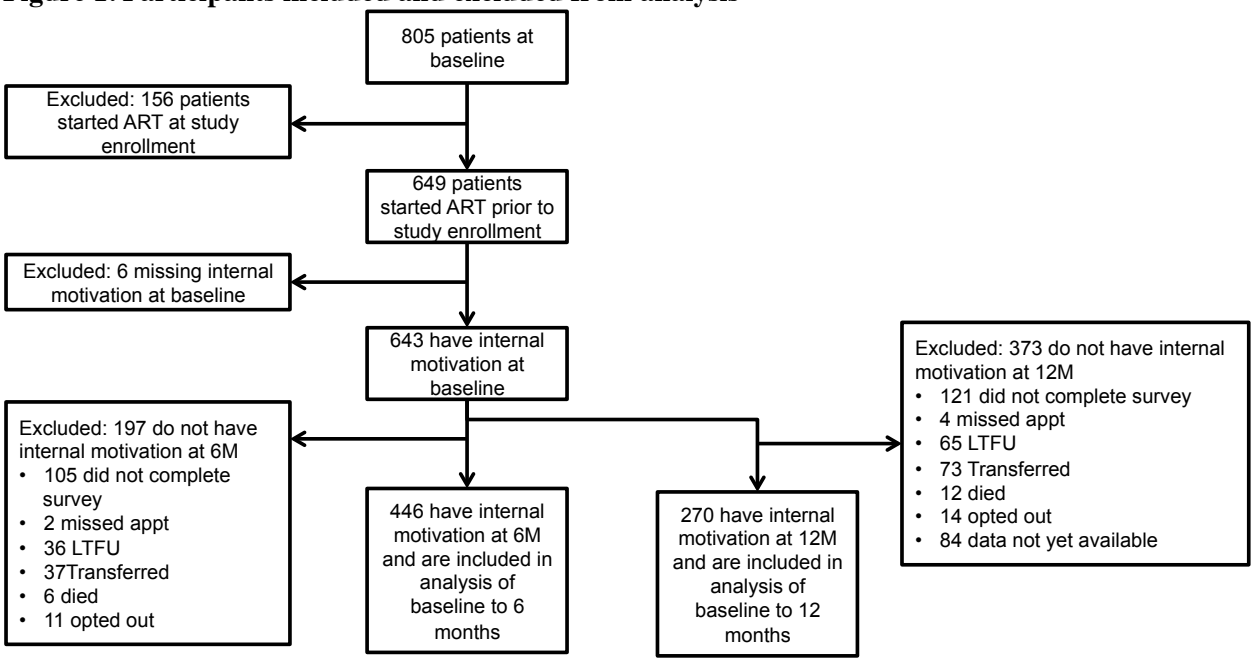


Table 1. Characteristics of participants completing both baseline and 6-month surveys, Tanzania, 2014-2015

Characteristic	N	(%)
Total	446	(100)
Study Arm		
Food transfers	194	(44)
Cash transfers	207	(46)
Comparison	45	(10)
Female	299	(67)
Education		
None	122	(27)
Any	324	(73)
Religion		
Christian	340	(76)
Islam	77	(17)
None	29	(7)
Marital Status		
Single	64	(14)
Married	172	(38)
Unmarried with partner	18	(4)
Divorced/Widowed/Separated	192	(44)
Currently Working	272	(61)
Head of Household	268	(60)
Who has the final say on decisions about how or when you obtain your own healthcare		
You alone	320	(72)
Your partner/spouse	29	(7)
Someone else alone	11	(3)
You jointly	85	(19)
Baseline Household Hunger Scale (HHS)		
Moderate hunger	266	(60)
Severe hunger	180	(40)
6-month HHS		
Little to no hunger	160	(39)
Moderate hunger	210	(50)
Severe hunger	46	(11)
Has children	394	(89)
Unable to work or attend school due to illness	248	(56)
	Mean	**(SD)**
Age (years)	37.07	(10.43)
Number in household	3.74	(2.08)
Self-rated health (1-10 scale)	8.25	(1.46)
Barriers to care (max 22)	2.53	(2.04)
Internal motivation at baseline	2.79	(0.36)
Internal motivation at 6M	2.91	(0.23)

Table 2. Paired T-tests comparing intrinsic motivation scores at 6 and 12 months to baseline[a]

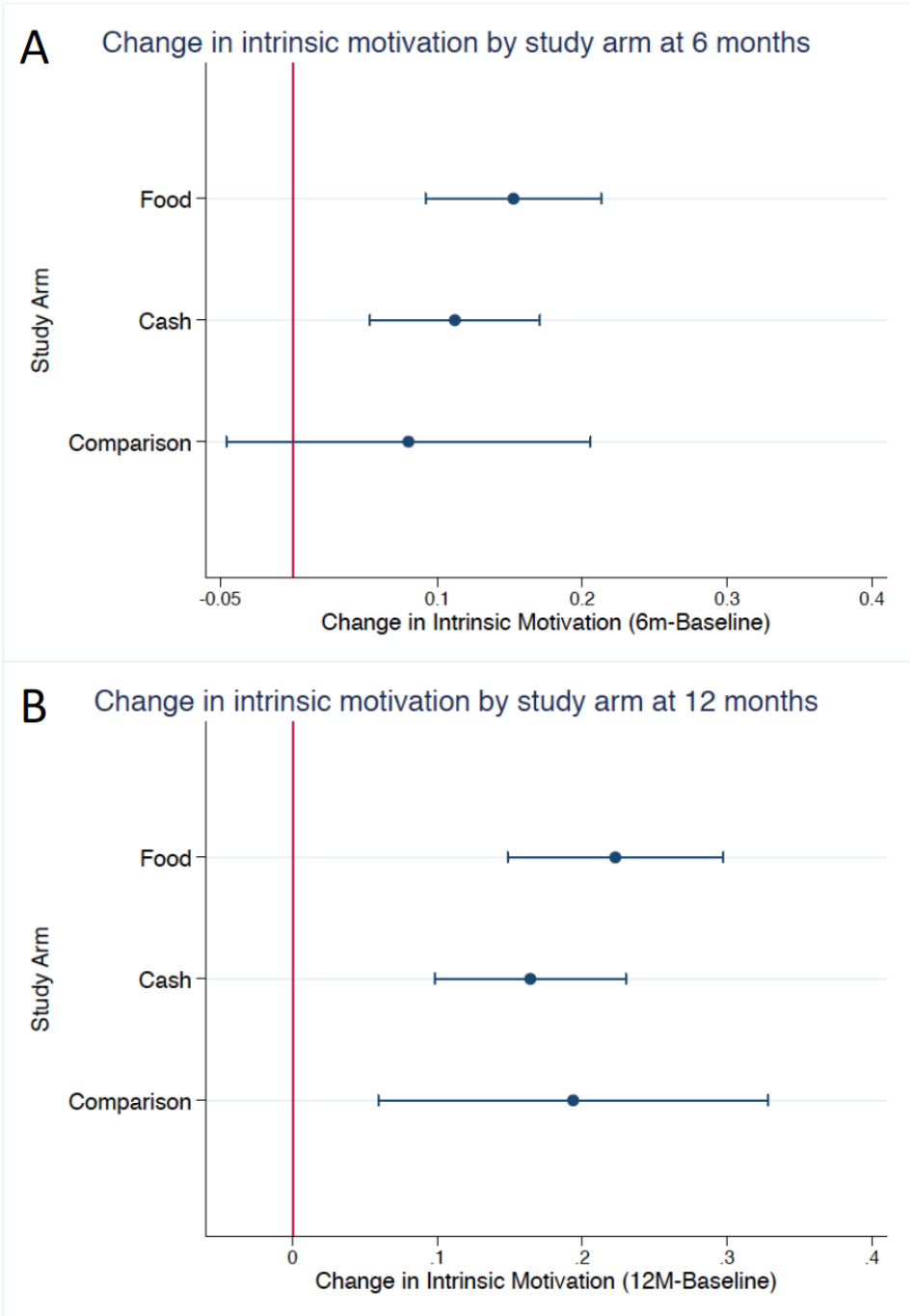
Comparison of 6-month values to baseline (N = 446)							
	N	**Baseline**	**6-Month**	**Difference (6M-baseline)**	**SD**	**95% CI**	**Cohen's d**
Overall	446	2.79	2.91	0.13	0.43	(0.09, 0.17) **	0.29
Food Transfer Arm	194	2.77	2.92	0.15	0.42	(0.09, 0.21) **	0.37
Cash Transfer Arm	207	2.80	2.91	0.11	0.45	(0.05, 0.18) **	0.25
Comparison Arm	45	2.79	2.87	0.08	0.38	(-0.03, 0.19)	0.21
Comparison of 12-month values to baseline (N = 270)							
	N	**Baseline**	**12-Month**	**Difference (12M-baseline)**	**SD**	**95% CI**	**Cohen's d**
Overall	270	2.76	2.95	0.19	0.39	(0.14, 0.24) **	0.49
Food Transfer Arm	104	2.72	2.94	0.22	0.43	(0.14, 0.31) **	0.52
Cash Transfer Arm	134	2.79	2.95	0.16	0.35	(0.10, 0.22) **	0.47
Comparison Arm	32	2.76	2.95	0.19	0.39	(0.05, 0.34) *	0.49

*p<0.05 **p<0.001

[a] Intrinsic motivation was the average score of a 3 point Likert scale on 5 questions from the autonomous motivation scale of the TSRQ

Note: Baseline values for the 6 and 12 month comparisons are different due to different sample size and different individuals included in each analysis

Figure 2. Mean change in intrinsic motivation by study arm with 95% confidence intervals at 6 months (N = 446) and 12 months (N = 270)[ab]



[a] The red line at 0 indicates no change in intrinsic motivation
[b] The mean change in intrinsic motivation is presented along with the estimated 95% confidence interval

Table 3. Linear regression model of change in intrinsic motivation across study arm

Change in intrinsic motivation (6M-baseline) (N = 446)						
	Unadjusted[a]			Adjusted[b]		
Group	Coefficient	95% CI	p-value	Coefficient	95% CI	p-value
Comparison	Ref		0.479	Ref		0.375*
Food Transfers	0.070	(-0.07, 0.21)	0.308	0.050	(-0.02, 0.13)	0.162
Cash Transfers	0.030	(-0.11, 0.17)	0.650	0.040	(-0.03, 0.11)	0.277
Identical models with inverse probability of censoring weights						
	Unadjusted[a]			Adjusted[b]		
Group	Coefficient	95% CI	p-value	Coefficient	95% CI	p-value
Comparison	Ref		0.430	Ref		0.573*
Food Transfers	0.07	(-0.05, 0.19)	0.271	0.04	(-0.03, 0.11)	0.300
Cash Transfers	0.02	(-0.10, 0.14)	0.752	0.03	(-0.05, 0.10)	0.465
Change in intrinsic motivation (12M-baseline) (N = 270)						
	Unadjusted[a]			Adjusted[b]		
Group	Coefficient	95% CI	p-value	Coefficient	95% CI	p-value
Comparison	Ref		0.508	Ref		0.842*
Food Transfers	0.03	(-0.12, 0.18)	0.710	-0.01	(-0.07, 0.05)	0.767
Cash Transfers	-0.03	(-0.18, 0.12)	0.698	0.002	(-0.06, 0.07)	0.932
Identical models with inverse probability of censoring weights						
	Unadjusted[a]			Adjusted[b]		
Group	Coefficient	95% CI	p-value	Coefficient	95% CI	p-value
Comparison	Ref		0.364			0.829*
Food Transfers	0.03	(-0.12, 0.18)	0.682	-0.01	(-0.08, 0.06)	0.811
Cash Transfers	-0.04	(-0.18, 0.10)	0.594	0.003	(-0.06, 0.07)	0.923

[a]Model only contains study arm
[b]Adjusted for clinic, sex, age, education, baseline intrinsic motivation, and baseline food insecurity (HHS category)

*Wald test for equivalence of all arms

CONCLUSION

Together these chapters provide novel perspectives on adherence to ART in sub-Saharan Africa. The initial examination of adherence and how it is concentrated across individuals and clinics highlighted the need to replace universal solutions with more data-driven strategic interventions. Then, within the context of an intervention to improve adherence, the results from a qualitative study outlined pathways through which the intervention acts. Understanding this mechanism can inform future intervention design and help to explain observed results. Lastly, an exploration of whether the intervention caused harm by crowding out intrinsic motivation found that intrinsic motivation actually increased over time post-intervention. This suggests that incentives in this context do not negatively impact intrinsic motivation and should continue to be implemented.

Chapter 1 illustrated the high degree of variability in medication possession ratio within and between clinics. The novel application of the Lorenz curve further highlighted the inequality of this distribution and concentration of poor adherence among patients attending 56 HIV clinics. While further characterization of these patients is needed to better target individual-level interventions, these results can immediately inform interventions at the clinic-level. Utilizing this data to target and provide additional support to clinics with low levels of adherence will be critical to improve the efficiency and effectiveness of HIV programming. Such targeting at the clinical level is quite feasible and can be advanced through development and use of a dashboard that highlights important indicators, such as median MPR, that can be reviewed in real-time to inform and support programming. Further work to explore clinic-level drivers of this variability including management quality is planned. Meaningful data use, as demonstrated in this approach, can improve the data-to-care linkage and help improve resource allocation and patient care within and across programs.

Chapter 2 explored the pathways of action of food and cash incentives for food-insecure PLWH in Shinyanga Region, Tanzania. This study found that the strongest pathway through which the incentives acted was by offsetting opportunity costs and meeting basic economic needs. This was consistent with our field observations and discussions with local clinic staff, research staff, and Ministry of Health officials. Recipients also reported improved mental health as a result of the incentive. This was an unexpected finding, but is consistent with previous literature. In the future we hope to explore this relationship further and also collect quantitative measurements on participants' mental health status to confirm this relationship. The weakest pathway found was that the incentive motivated patients to attend the clinic. Although this was difficult for patients to be aware of and articulate, it did not seem to be a strong behavioral driver. Together these findings and previous knowledge about barriers to retention and adherence suggest that food and cash incentives can be an effective way to overcome barriers to positive health outcomes. Cash transfers are less costly to implement, maximize patient choice, offer the greatest propensity for positive spillover effects, and may have longer-term effects compared to food transfers. Furthermore, initial analysis of the randomized trial results show that the impact of cash transfers on adherence is greater than that of food transfers. Future work should thus aim to optimize the cash transfer delivery system and develop ways to bring such programs to scale to improve the health of patients living with HIV in developing countries and resource-limited settings.

Chapter 3 explored the concern that providing incentives may crowd out intrinsic motivation, leaving recipients worse off after the incentive is removed. To directly explore this issue, we measured intrinsic motivation at baseline, 6-months (post-incentive), and 12-months (6-months post-incentive). This was the first study of incentives in low-resource settings to explicitly examine intrinsic motivation. Levels of intrinsic motivation were high at baseline and increased over time. We found no evidence to support the crowding out hypothesis. These results are consistent with the pathways of action identified in chapter 2, as the incentives do not appear to be acting solely through motivation pathways, if at all. In similar settings where incentives likely act by offsetting opportunity costs and meeting basic economic needs, concerns of crowding out intrinsic motivation should not impede further rollout of potentially beneficial incentive programs.

In summary, this body of work presents novel approaches to understanding and addressing ART adherence in sub-Saharan Africa. Application of a tool traditionally used in economics provided new insight into understanding the scope and magnitude of poor-adherence across clinics in Zambia. These results are being used to better understand clinic variability and to offer programs and support to under-performing clinics. Meanwhile, an in-depth exploration of the mechanism of incentives, not often undertaken in such studies, revealed pathways that help explain why the incentives were effective. In addition, an unexpected pathway through improved metal health was discovered, and this warrants additional attention in the future. Further examination of the incentives' impact on intrinsic motivation found no evidence of the crowding out hypothesis. The findings highlight the need to empirically test theories in real-world settings where context may have a strong effect. Given these findings, crowding out is no longer a reasonable objection to incentive interventions in this setting. This multi-disciplinary approach to adherence has provided new insights and tool to further our understanding and inform future interventions.

REFERENCES

1. Organization WH. Global Health Observatory. 2013; http://www.who.int/gho/hiv/en/.
2. UNAIDS. *Global Report: UNAIDS report on the global AIDS epidemic 2013*2013.
3. Bor J, Herbst AJ, Newell M-L, Bärnighausen T. Increases in Adult Life Expectancy in Rural South Africa: Valuing the Scale-Up of HIV Treatment. *Science.* February 22, 2013 2013;339(6122):961-965.
4. Piot P. Global AIDS Epidemic: Time to Turn the Tide. *Science.* June 23, 2000 2000;288(5474):2176-2178.
5. Organization WH. *Global Update on HIV Treatment 2013: Results, Impact, and Opportunities*.
6. Mayer KH. Thinking about an AIDS end game. *The Lancet.* 2013;382(9903):1462-1464.
7. Siegfried N, Uthman OA, Rutherford GW. Optimal time for initiation of antiretroviral therapy in asymptomatic, HIV-infected, treatment-naive adults. *The Cochrane database of systematic reviews.* 2010(3):CD008272.
8. Ray M, Logan R, Sterne JA, et al. The effect of combined antiretroviral therapy on the overall mortality of HIV-infected individuals. *AIDS (London, England).* Jan 2 2010;24(1):123-137.
9. Cain LE, Logan R, Robins JM, et al. When to initiate combined antiretroviral therapy to reduce mortality and AIDS-defining illness in HIV-infected persons in developed countries: an observational study. *Annals of internal medicine.* Apr 19 2011;154(8):509-515.
10. Nosyk B, Audoin B, Beyrer C, et al. Examining the evidence on the causal effect of HAART on transmission of HIV using the Bradford Hill criteria. *AIDS (London, England).* Apr 24 2013;27(7):1159-1165.
11. McNairy ML, Cohen M, El-Sadr WM. Antiretroviral therapy for prevention is a combination strategy. *Current HIV/AIDS reports.* Jun 2013;10(2):152-158.
12. Cohen MS, Chen YQ, McCauley M, et al. Prevention of HIV-1 infection with early antiretroviral therapy. *The New England journal of medicine.* Aug 11 2011;365(6):493-505.
13. Cohen MS, Smith MK, Muessig KE, Hallett TB, Powers KA, Kashuba AD. Antiretroviral treatment of HIV-1 prevents transmission of HIV-1: where do we go from here? *Lancet.* Nov 2 2013;382(9903):1515-1524.
14. Organization WH. *Consolidated Guidelines on the use of Antiretroviral Drugs for Treating and Preventing HIV Infection: Recommendations for a Public Health Approach* June 2013 June 2013.
15. Group TISS. Initiation of Antiretroviral Therapy in Early Asymptomatic HIV Infection. *New England Journal of Medicine.* 2015;373(9):795-807.
16. Group TTAS. A Trial of Early Antiretrovirals and Isoniazid Preventive Therapy in Africa. *New England Journal of Medicine.* 2015;373(9):808-822.
17. WHO. *Guideline on when to start antiretroviral therapy and on pre-exposure prophylaxis for HIV* September 2015 2015.
18. Berkelman R. The United States government's response to HIV/AIDS today: 'test and treat' as prevention. *Journal of public health policy.* Aug 2012;33(3):337-343.

19. Hull MW, Wu Z, Montaner JS. Optimizing the engagement of care cascade: a critical step to maximize the impact of HIV treatment as prevention. *Current opinion in HIV and AIDS.* Nov 2012;7(6):579-586.
20. Kranzer K, Govindasamy D, Ford N, Johnston V, Lawn SD. Quantifying and addressing losses along the continuum of care for people living with HIV infection in sub-Saharan Africa: a systematic review. *Journal of the International AIDS Society.* 2012;15(2):17383.
21. Rosen S, Fox MP. Retention in HIV care between testing and treatment in sub-Saharan Africa: a systematic review. 20110803 DCOM- 20111213 (1549-1676 (Electronic)).
22. Mugglin C, Estill J, Wandeler G, et al. Loss to programme between HIV diagnosis and initiation of antiretroviral therapy in sub-Saharan Africa: systematic review and meta-analysis. *Tropical medicine & international health : TM & IH.* Dec 2012;17(12):1509-1520.
23. Mugavero MJ, Amico KR, Westfall AO, et al. Early retention in HIV care and viral load suppression: implications for a test and treat approach to HIV prevention. *Journal of acquired immune deficiency syndromes (1999).* Jan 1 2012;59(1):86-93.
24. Mugavero MJ, Westfall AO, Zinski A, et al. Measuring retention in HIV care: the elusive gold standard. *Journal of acquired immune deficiency syndromes (1999).* Dec 15 2012;61(5):574-580.
25. Lyimo RA, de Bruin M, van den Boogaard J, Hospers HJ, van der Ven A, Mushi D. Determinants of antiretroviral therapy adherence in northern Tanzania: a comprehensive picture from the patient perspective. *BMC public health.* 2012;12:716.
26. Mannheimer S, Friedland G, Matts J, Child C, Chesney M. The consistency of adherence to antiretroviral therapy predicts biologic outcomes for human immunodeficiency virus-infected persons in clinical trials. *Clinical infectious diseases : an official publication of the Infectious Diseases Society of America.* Apr 15 2002;34(8):1115-1121.
27. Bangsberg DR, Perry S, Charlebois ED, et al. Non-adherence to highly active antiretroviral therapy predicts progression to AIDS. *AIDS (London, England).* Jun 15 2001;15(9):1181-1183.
28. Sethi AK, Celentano DD, Gange SJ, Moore RD, Gallant JE. Association between Adherence to Antiretroviral Therapy and Human Immunodeficiency Virus Drug Resistance. *Clinical Infectious Diseases.* October 15, 2003 2003;37(8):1112-1118.
29. Mills EJ, Nachega JB, Buchan I, et al. Adherence to antiretroviral therapy in sub-Saharan Africa and North America: a meta-analysis. *JAMA : the journal of the American Medical Association.* Aug 9 2006;296(6):679-690.
30. Rosen S, Fox MP, Gill CJ. Patient Retention in Antiretroviral Therapy Programs in Sub-Saharan Africa: A Systematic Review. *PLoS Med.* 2007;4(10):e298.
31. Geng EH, Bangsberg DR, Musinguzi N, et al. Understanding reasons for and outcomes of patients lost to follow-up in antiretroviral therapy programs in Africa through a sampling-based approach. *Journal of acquired immune deficiency syndromes (1999).* Mar 2010;53(3):405-411.
32. Nachega JB, Uthman OA, Mills EJ, Quinn TC. Adherence to Antiretroviral Therapy for the Success of Emerging Interventions to Prevent HIV Transmission: A Wake up Call. *Journal of AIDS & clinical research.* Oct 22 2013;2012(Suppl 4).
33. Padian NS, McCoy SI, Karim SS, et al. HIV prevention transformed: the new prevention research agenda. *Lancet.* Jul 16 2011;378(9787):269-278.

34. Govindasamy D, Kranzer K, Ford N. Strengthening the HIV cascade to ensure an effective future ART response in sub-Saharan Africa. *Transactions of the Royal Society of Tropical Medicine and Hygiene.* Jan 2014;108(1):1-3.
35. Denison JA, Koole O, Tsui S, et al. Incomplete adherence among treatment-experienced adults on antiretroviral therapy in Tanzania, Uganda and Zambia. *AIDS (London, England).* Jan 28 2015;29(3):361-371.
36. Musumari PM, Wouters E, Kayembe PK, et al. Food insecurity is associated with increased risk of non-adherence to antiretroviral therapy among HIV-infected adults in the Democratic Republic of Congo: a cross-sectional study. *PloS one.* 2014;9(1):e85327.
37. Weiser SD, Tuller DM, Frongillo EA, Senkungu J, Mukiibi N, Bangsberg DR. Food insecurity as a barrier to sustained antiretroviral therapy adherence in Uganda. *PloS one.* 2010;5(4):e10340.
38. Ivers LC, Cullen KA, Freedberg KA, Block S, Coates J, Webb P. HIV/AIDS, undernutrition, and food insecurity. *Clinical infectious diseases : an official publication of the Infectious Diseases Society of America.* Oct 1 2009;49(7):1096-1102.
39. Weiser SD, Young SL, Cohen CR, et al. Conceptual framework for understanding the bidirectional links between food insecurity and HIV/AIDS. *Am J Clin Nutr.* Dec 2011;94(6):1729S-1739S.
40. Anderson SA. Core indicators of nutritional state for difficult-to-sample populations. *The Journal of nutrition.* Nov 1990;120 Suppl 11:1559-1600.
41. Goudge J, Ngoma B. Exploring antiretroviral treatment adherence in an urban setting in South Africa. *Journal of public health policy.* 2011;32 Suppl 1:S52-64.
42. Nagata JM, Magerenge RO, Young SL, Oguta JO, Weiser SD, Cohen CR. Social determinants, lived experiences, and consequences of household food insecurity among persons living with HIV/AIDS on the shore of Lake Victoria, Kenya. *AIDS Care.* Dec 07 2011:1-9.
43. Weiser SD, Frongillo EA, Ragland K, Hogg RS, Riley ED, Bangsberg DR. Food insecurity is associated with incomplete HIV RNA suppression among homeless and marginally housed HIV-infected individuals in San Francisco. *Journal of general internal medicine.* Jan 2009;24(1):14-20.
44. Wang EA, McGinnis KA, Fiellin DA, et al. Food insecurity is associated with poor virologic response among HIV-infected patients receiving antiretroviral medications. *Journal of general internal medicine.* Sep 2011;26(9):1012-1018.
45. McMahon JH, Wanke CA, Elliott JH, Skinner S, Tang AM. Repeated assessments of food security predict CD4 change in the setting of antiretroviral therapy. *Journal of acquired immune deficiency syndromes (1999).* Sep 1 2011;58(1):60-63.
46. Weiser SD, Fernandes KA, Brandson EK, et al. The association between food insecurity and mortality among HIV-infected individuals on HAART. *Journal of acquired immune deficiency syndromes.* Nov 1 2009;52(3):342-349.
47. Weiser SD, Tsai AC, Gupta R, et al. Food insecurity is associated with morbidity and patterns of healthcare utilization among HIV-infected individuals in a resource-poor setting. *AIDS (London, England).* Jan 2 2012;26(1):67-75.
48. Singer M. *Introduction to syndemics: a critical systems approach to public and community health*. San Francisco: Jossey-Bass.

49. Reddi A, Powers MA, Thyssen A. HIV/AIDS and food insecurity: deadly syndemic or an opportunity for healthcare synergism in resource-limited settings of sub-Saharan Africa? *AIDS (London, England).* 2012;26:115-117.
50. Hardon AP, Akurut D, Comoro C, et al. Hunger, waiting time and transport costs: time to confront challenges to ART adherence in Africa. *AIDS Care.* May 2007;19(5):658-665.
51. Zachariah R, Harries AD, Manzi M, et al. Acceptance of anti-retroviral therapy among patients infected with HIV and tuberculosis in rural Malawi is low and associated with cost of transport. *PloS one.* 2006;1:e121.
52. Cantrell RA, Sinkala M, Megazinni K, et al. A pilot study of food supplementation to improve adherence to antiretroviral therapy among food-insecure adults in Lusaka, Zambia. *Journal of acquired immune deficiency syndromes (1999).* Oct 1 2008;49(2):190-195.
53. Ivers LC, Chang Y, Gregory Jerome J, Freedberg KA. Food assistance is associated with improved body mass index, food security and attendance at clinic in an HIV program in central Haiti: a prospective observational cohort study. *AIDS research and therapy.* 2010;7:33.
54. Sztam KA, Fawzi WW, Duggan C. Macronutrient supplementation and food prices in HIV treatment. *The Journal of nutrition.* Jan 2010;140(1):213S-223S.
55. Tirivayi N, Koethe JR, Groot W. Clinic-Based Food Assistance is Associated with Increased Medication Adherence among HIV-Infected Adults on Long-Term Antiretroviral Therapy in Zambia. *Journal of AIDS & clinical research.* 2012;3(7):171.
56. Posse M, Tirivayi N, Saha U, R B. The effect of food assistance on adherence to antiretroviral therapy among HIV/AIDS patients in Sofala Province, Mozambique: A retrospective study. *Journal of AIDS & clinical research.* 2013;4(3).
57. Serrano C, Laporte R, Ide M, et al. Family nutritional support improves survival, immune restoration and adherence in HIV patients receiving ART in developing country. *Asia Pacific journal of clinical nutrition.* 2010;19(1):68-75.
58. Kawana BM, Mofu MJ, Siamusantu WS, et al. Cash or Food? Which Works Better to Improve Nutrition Status and Treatment Adherence for HIV Patients Starting Antiretroviral Therapy2014. Located at: IDS Special Collection.
59. Lamb MR, El-Sadr WM, Geng E, Nash D. Association of adherence support and outreach services with total attrition, loss to follow-up, and death among ART patients in sub-Saharan Africa. *PloS one.* 2012;7(6):e38443.
60. Björkman-Nyqvist M, Corno L, de Walque D, Svensson J. Evaluating the impact of short term financial incentives on HIV and STI incidence among youth in Lesotho: a randomized trial. Paper presented at: 7th IAS Conference on HIV Pathogenesis, Treatment, and Prevention2013; Kuala Lumpur.
61. de Walque D, Dow WH, Nathan R, et al. Incentivising safe sex: a randomised trial of conditional cash transfers for HIV and sexually transmitted infection prevention in rural Tanzania. *BMJ open.* 2012;2:e000747.
62. Baird SJ, Garfein RS, McIntosh CT, Ozler B. Impact of a cash transfer program for schooling on prevalence of HIV and HSV-2 in Malawi: a cluster randomized trial. *Lancet.* 2012.
63. McCoy SI, Shiu K, Martz TE, et al. Improving the Efficiency of HIV Testing With Peer Recruitment, Financial Incentives, and the Involvement of Persons Living with HIV Infection. *Journal of acquired immune deficiency syndromes.* Feb 11 2013.

64. Galarraga O, Genberg BL, Martin RA, Barton Laws M, Wilson IB. Conditional Economic Incentives to Improve HIV Treatment Adherence: Literature Review and Theoretical Considerations. *AIDS and behavior.* Jan 31 2013.
65. Solomon S, Srikrishnan A, Vasudevan C, et al. The Impact of Voucher Incentives on Linkage to Care and ART Initiation among Drug Users: Chennai, India. Paper presented at: 19th Conference on Retroviruses and Opportunistic Infections2012; Seattle.
66. Haukoos JS, Witt MD, Coil CJ, Lewis RJ. The effect of financial incentives on adherence with outpatient human immunodeficiency virus testing referrals from the emergency department. *Acad Emerg Med.* Jul 2005;12(7):617-621.
67. Thornton R. The Demand for and Impact of Learning HIV Status: Evidence from a Field Experiment. *American Economic Review.* 2008;98(5):1829–1863.
68. Gneezy U, Meier S, Rey-Biel P. When and why incentives (don't) work to modify behavior. *J Economic Perspectives.* 2011;25(4):191-209.
69. Posse M, Baltussen R. Costs of providing food assistance to HIV/AIDS patients in Sofala province, Mozambique: a retrospective analysis. *Cost effectiveness and resource allocation : C/E.* 2013;11(1):20.
70. McCoy SI, Njau PF, Czaicki NL, et al. Rationale and design of a randomized study of short-term food and cash assistance to improve adherence to antiretroviral therapy among food insecure HIV-infected adults in Tanzania. *BMC infectious diseases.* 2015;15(1):490.
71. Ahmed A, Quisumbing A, Nasreen M, Hoddinott J, Bryan E. *Comparing Food and Cash Transfers to the Ultra Poor in Bangladesh.* Washington D.C.: International Food Policy Research Institute;2009.
72. Gentilini U. *Cash and Food Transfers: A Primer.* Rome: World Food Programme;2007.
73. Tuller DM, Bangsberg DR, Senkungu J, Ware NC, Emenyonu N, Weiser SD. Transportation Costs Impede Sustained Adherence and Access to HAART in a Clinic Population in Southwestern Uganda: A Qualitative Study. *AIDS Behav.* Mar 13 2009.
74. Ortego C, Huedo-Medina TB, Llorca J, et al. Adherence to highly active antiretroviral therapy (HAART): a meta-analysis. *AIDS Behav.* Oct 2011;15(7):1381-1396.
75. Wilson IB, Bangsberg DR, Shen J, et al. Heterogeneity among studies in rates of decline of antiretroviral therapy adherence over time: results from the multisite adherence collaboration on HIV 14 study. *Journal of acquired immune deficiency syndromes (1999).* Dec 15 2013;64(5):448-454.
76. Lorenz MO. Methods of Measuring the Concentration of Wealth. *Publications of the American Statistical Association.* 1905/06/01 1905;9(70):209-219.
77. Zambia MoH. Zambia Consolidated Guidelines for Treatment and Prevention of HIV Infection2013.
78. Kabore L, Muntner P, Chamot E, Zinski A, Burkholder G, Mugavero MJ. Self-Report Measures in the Assessment of Antiretroviral Medication Adherence: Comparison with Medication Possession Ratio and HIV Viral Load. *Journal of the International Association of Providers of AIDS Care.* Mar-Apr 2015;14(2):156-162.
79. Wu P, Johnson BA, Nachega JB, et al. The combination of pill count and self-reported adherence is a strong predictor of first-line ART failure for adults in South Africa. *Current HIV research.* 2014;12(5):366-375.
80. Hong SY, Fanelli TJ, Jonas A, et al. Household food insecurity associated with antiretroviral therapy adherence among HIV-infected patients in Windhoek, Namibia. *Journal of acquired immune deficiency syndromes (1999).* Dec 1 2014;67(4):e115-122.

81. Weidle PJ, Wamai N, Solberg P, et al. Adherence to antiretroviral therapy in a home-based AIDS care programme in rural Uganda. *Lancet.* Nov 4 2006;368(9547):1587-1594.
82. Chi BH, Cantrell RA, Zulu I, et al. Adherence to first-line antiretroviral therapy affects non-virologic outcomes among patients on treatment for more than 12 months in Lusaka, Zambia. *International journal of epidemiology.* Jun 2009;38(3):746-756.
83. Goldman JD, Cantrell RA, Mulenga LB, et al. Simple adherence assessments to predict virologic failure among HIV-infected adults with discordant immunologic and clinical responses to antiretroviral therapy. *AIDS research and human retroviruses.* Aug 2008;24(8):1031-1035.
84. Hong SY, Jerger L, Jonas A, et al. Medication possession ratio associated with short-term virologic response in individuals initiating antiretroviral therapy in Namibia. *PloS one.* 2013;8(2):e56307.
85. Hong SY, Jonas A, DeKlerk M, et al. Population-based surveillance of HIV drug resistance emerging on treatment and associated factors at sentinel antiretroviral therapy sites in Namibia. *Journal of acquired immune deficiency syndromes (1999).* Apr 1 2015;68(4):463-471.
86. McMahon JH, Jordan MR, Kelley K, et al. Pharmacy adherence measures to assess adherence to antiretroviral therapy: review of the literature and implications for treatment monitoring. *Clinical infectious diseases : an official publication of the Infectious Diseases Society of America.* Feb 15 2011;52(4):493-506.
87. Messou E, Chaix ML, Gabillard D, et al. Association between medication possession ratio, virologic failure and drug resistance in HIV-1-infected adults on antiretroviral therapy in Cote d'Ivoire. *Journal of acquired immune deficiency syndromes (1999).* Apr 2011;56(4):356-364.
88. Messou E, Kouakou M, Gabillard D, et al. Medication possession ratio: predicting and decreasing loss to follow-up in antiretroviral treatment programs in Cote d'Ivoire. *Journal of acquired immune deficiency syndromes (1999).* Jul 1 2011;57 Suppl 1:S34-39.
89. Salinas JL, Alave JL, Westfall AO, et al. Medication possession ratio predicts antiretroviral regimens persistence in Peru. *PloS one.* 2013;8(10):e76323.
90. Vinikoor MJ, Joseph J, Mwale J, et al. Age at antiretroviral therapy initiation predicts immune recovery, death, and loss to follow-up among HIV-infected adults in urban Zambia. *AIDS research and human retroviruses.* Oct 2014;30(10):949-955.
91. Vinikoor MJ, Schuttner L, Moyo C, et al. Short communication: Late refills during the first year of antiretroviral therapy predict mortality and program failure among HIV-infected adults in urban Zambia. *AIDS research and human retroviruses.* Jan 2014;30(1):74-77.
92. Hernan MA, Hernandez-Diaz S, Robins JM. A structural approach to selection bias. *Epidemiology (Cambridge, Mass.* Sep 2004;15(5):615-625.
93. Hernan MA, Hernandez-Diaz S, Werler MM, Mitchell AA. Causal knowledge as a prerequisite for confounding evaluation: an application to birth defects epidemiology. *American journal of epidemiology.* Jan 15 2002;155(2):176-184.
94. LP SC. Stata Multiple-Imputation Reference Manual: Release 13. 2013.
95. White IR, Royston P, Wood AM. Multiple imputation using chained equations: Issues and guidance for practice. *Statistics in medicine.* Feb 20 2011;30(4):377-399.

96. Koole O, Tsui S, Wabwire-Mangen F, et al. Retention and risk factors for attrition among adults in antiretroviral treatment programmes in Tanzania, Uganda and Zambia. *Tropical medicine & international health : TM & IH.* Dec 2014;19(12):1397-1410.
97. Dewing S, Mathews C, Lurie M, Kagee A, Padayachee T, Lombard C. Predictors of poor adherence among people on antiretroviral treatment in Cape Town, South Africa: a case-control study. *AIDS Care.* 2015;27(3):342-349.
98. Safren SA, Biello KB, Smeaton L, et al. Psychosocial predictors of non-adherence and treatment failure in a large scale multi-national trial of antiretroviral therapy for HIV: data from the ACTG A5175/PEARLS trial. *PloS one.* 2014;9(8):e104178.
99. Labhardt ND, Bader J, Ramoeletsi M, et al. Clinical and socio-demographic predictors for virologic failure in rural Southern Africa: preliminary findings from CART-1. *Journal of the International AIDS Society.* 2014;17(4 Suppl 3):19666.
100. Unge C, Sodergard B, Marrone G, et al. Long-term adherence to antiretroviral treatment and program drop-out in a high-risk urban setting in sub-Saharan Africa: a prospective cohort study. *PloS one.* 2010;5(10):e13613.
101. Geng EH, Odeny TA, Lyamuya RE, et al. Estimation of mortality among HIV-infected people on antiretroviral treatment in east Africa: a sampling based approach in an observational, multisite, cohort study. *The Lancet HIV.* 2015.
102. Wand H, Ramjee G. Targeting the hotspots: investigating spatial and demographic variations in HIV infection in small communities in South Africa. 20101112 DCOM-20110309 (1758-2652 (Electronic)).
103. Bedelu M, Ford N, Hilderbrand K, Reuter H. Implementing antiretroviral therapy in rural communities: the Lusikisiki model of decentralized HIV/AIDS care. *The Journal of infectious diseases.* Dec 1 2007;196 Suppl 3:S464-468.
104. Loubiere S, Boyer S, Protopopescu C, et al. Decentralization of HIV care in Cameroon: increased access to antiretroviral treatment and associated persistent barriers. *Health policy (Amsterdam, Netherlands).* Oct 2009;92(2-3):165-173.
105. Geng EH, Nash D, Kambugu A, et al. Retention in care among HIV-infected patients in resource-limited settings: emerging insights and new directions. *Current HIV/AIDS reports.* Nov 2010;7(4):234-244.
106. A. Pettifor CM, A. Selin, X. Gomez-Olivé, J. Hughes, R., Wagner WM, I. Mokoena, S. Eshleman, E. PiwowarManning,, R. Twine AJ, C. Marcus, P. Andrew, J. Wang, Y., Xing LM, E. Hamilton, Y. Agyei, S. Allison, P. Sato, E., Townley ST, K. Kahn, HPTN 068 Study Team. HPTN 068 conditional cash transfer to prevent HIV infection among young women in South Africa: results of a randomized controlled trial. *International AIDS Society Conference*. Vancouver, British Columbia, Canada2015.
107. Kohler HP, Thornton R. Financial Incentives and HIV PreventionDecember 22, 2009.
108. Q. Abdool Karim KL, A. Kharsany, H. Humphries, F., Ntombela NS, C. Baxter, J. Frohlich, L. van der Elst, S., Karim A. Impact of conditional cash incentives on HSV-2 and HIV prevention in rural South African high school students: results of the CAPRISA 007 cluster randomized controlled trial. Paper presented at: International AIDS Society Conference2015; Vancouver, British Columbia, Canada.
109. Kohler H, Thornton RL. Conditional Cash Transfers and HIV/AIDS Prevention: Unconditionally Promising? *World Bank Economic Review.* 2012/06/01 2012;26(2):165-190.

110. Fernald LC, Gertler PJ, Hou X. Cash component of conditional cash transfer program is associated with higher body mass index and blood pressure in adults. *The Journal of nutrition.* Nov 2008;138(11):2250-2257.
111. Ladmadrid-Figueroa H, Angeles G, Mroz T, et al. Heterogeneous impacts of the social programme Oportunidades on use of contraceptive methods by young adult women living in rural areas. *Journal of Development Effectiveness.* 2010;2(1):74-86.
112. Feldman BS, Zaslavsky AM, Ezzati M, Peterson KE, Mitchell M. Contraceptive use, birth spacing, and autonomy: an analysis of the Oportunidades program in rural Mexico. *Stud Fam Planning.* 2009;40(1):51-62.
113. Hernandez-Prado B, Salomon JEU, Villalobos MDR, Figueroa JL. *Impact of Oportunidades on the Reproductive Health of Its Beneficiary Population.* Cuernavaca: Instituto Nacional de Salud Publica;2005.
114. Steklov G, Winters P, Todd J, Regalia F. Demographic Externalities from Poverty Programs in Developing Countries: Experimental Evidence from Latin America. *Department of Economics Working Paper Series*. Washington, D.C.: American University 2006.
115. Huerta M, C., , Hernandez D. *Algunos aspectos de salud reproductiva de la población beneficiaria de Progresa*2000.
116. Sosa-Rubi SG, Walker D, Servan E, Bautista-Arredondo S. Learning effect of a conditional cash transfer programme on poor rural women's selection of delivery care in Mexico. *Health policy and planning.* Nov 2011;26(6):496-507.
117. Cluver L, Boyes M, Orkin M, Pantelic M, Molwena T, Sherr L. Child-focused state cash transfers and adolescent risk of HIV infection in South Africa: a propensity-score-matched case-control study. *The Lancet Global Health.* 2013;1(6):e362 - e370.
118. Pettifor A, MacPhail C, Nguyen N, Rosenberg M. Can money prevent the spread of HIV? A review of cash payments for HIV prevention. *AIDS Behav.* Oct 2012;16(7):1729-1738.
119. Valentina Barca SB, Jeremy Holland, Mosope Otulana, Pamela Posarny *Qualitative research and analyses of the economic impacts of cash transfer programmes in Sub-Saharan Africa* Rome: Food and Agriculture Organization of the United Nations and Oxford Policy Management.
120. Adato M, Roopnaraine T, Becker E. Understanding use of health services in conditional cash transfer programs: insights from qualitative research in Latin America and Turkey. *Social science & medicine (1982).* Jun 2011;72(12):1921-1929.
121. Coffey D. Costs and consequences of a cash transfer for hospital births in a rural district of Uttar Pradesh, India. *Social science & medicine (1982).* Aug 2014;114:89-96.
122. Ballard T, Coates J, Swindale A, Deitchler M. *Household Hunger Scale: Indicator Definition and Measurement Guide.* Washington, D.C.: Food and Nutrition Technical Assistance II Project, AED;2011.
123. Programme UND. Tanzania Human Development Report 2014: Economic Transformation for Human Development. 2015.
124. McCoy SI, Njau PF, Fahey C, et al. A randomized study of short-term conditional cash and food assistance to improve adherence to antiretroviral therapy among food insecure adults with HIV infection in Tanzania. *21st International AIDS Conference*. Durban, South Africa2016.

125. Young S, Wheeler AC, McCoy SI, Weiser SD. A Review of the Role of Food Insecurity in Adherence to Care and Treatment Among Adult and Pediatric Populations Living with HIV and AIDS. *AIDS and behavior.* Jul 11 2013.
126. Heise L, Lutz B, Ranganathan M, Watts C. Cash transfers for HIV prevention: considering their potential. *Journal of the International AIDS Society.* 2013;16(1):18615.
127. de Walque D, Dow WH, Medlin C, Nathan R. Stimulating Demand for AIDS Prevention: Lessons from the RESPECT Trial. 2012.
128. Frederick S, Loewenstein G, O'Donoghue T. Time Discounting and Time Preference: A Critical Review. *Journal of Economic Literature.* 2002;40(2):351-401.
129. Loewenstein G, Brennan T, Volpp KG. Asymmetric paternalism to improve health behaviors. *JAMA : the journal of the American Medical Association.* Nov 28 2007;298(20):2415-2417.
130. Deci EL, Ryan RM. Self-Determination Theory: A Macrotheory of Human Motivation, Development, and Health. *Canadian Psychology.* 2008;49(3):182-185.
131. Ulin P, Robinson E, Tolley E. *Qualitative Methods in Public Health: A Field Guide for Applied Research.* San Francisco, CA: Jossey-Bass; 2005.
132. Miles MB, Huberman AM. *Qualitative Data Analysis: An Expanded Sourcebook*: SAGE Publications; 1994.
133. Safren SA, Mayer KH, Ou SS, et al. Adherence to Early Antiretroviral Therapy: Results From HPTN 052, a Phase III, Multinational Randomized Trial of ART to Prevent HIV-1 Sexual Transmission in Serodiscordant Couples. *Journal of acquired immune deficiency syndromes (1999).* Jun 1 2015;69(2):234-240.
134. Nel A, Kagee A. Common mental health problems and antiretroviral therapy adherence. *AIDS Care.* Nov 2011;23(11):1360-1365.
135. Anuradha S, Joshi A, Negi M, Nischal N, Rajeshwari K, Dewan R. Factors influencing adherence to ART: new insights from a center providing free ART under the national program in Delhi, India. *Journal of the International Association of Providers of AIDS Care.* May-Jun 2013;12(3):195-201.
136. Starace F, Ammassari A, Trotta MP, et al. Depression is a risk factor for suboptimal adherence to highly active antiretroviral therapy. *Journal of acquired immune deficiency syndromes (1999).* Dec 15 2002;31 Suppl 3:S136-139.
137. Huynh AK, Kinsler JJ, Cunningham WE, Sayles JN. The role of mental health in mediating the relationship between social support and optimal ART adherence. *AIDS Care.* 2013;25(9):1179-1184.
138. Lund C, De Silva M, Plagerson S, et al. Poverty and mental disorders: breaking the cycle in low-income and middle-income countries. *The Lancet.*378(9801):1502-1514.
139. Kilburn K, Thirumurthy H, Halpern CT, Pettifor A, Handa S. Effects of a Large-Scale Unconditional Cash Transfer Program on Mental Health Outcomes of Young People in Kenya. *The Journal of adolescent health : official publication of the Society for Adolescent Medicine.* Feb 2016;58(2):223-229.
140. Ozer EJ, Fernald LC, Weber A, Flynn EP, VanderWeele TJ. Does alleviating poverty affect mothers' depressive symptoms? A quasi-experimental investigation of Mexico's Oportunidades programme. *International journal of epidemiology.* July 7, 2011 2011.
141. Wouters E, Meulemans H, Van Rensburg HC, Heunis JC, Mortelmans D. Short-term physical and emotional health outcomes of public sector ART in the Free State province

of South Africa. *Quality of life research : an international journal of quality of life aspects of treatment, care and rehabilitation.* Nov 2007;16(9):1461-1471.
142. Gaarder MM, Glassman A, Todd JE. Conditional cash transfers and health: unpacking the causal chain. *Journal of Development Effectiveness.* 2010/04/13 2010;2(1):6-50.
143. Lagarde M, Haines A, Palmer N. The impact of conditional cash transfers on health outcomes and use of health services in low and middle income countries. *The Cochrane database of systematic reviews.* 2009(4):Cd008137.
144. Acland D, Levy MR. Naiveté, Projection Bias, and Habit Formation in Gym Attendance. *Management Science.* 2015;61(1):146-160.
145. Baird SJ, Garfein RS, McIntosh CT, Ozler B. Impact of a cash transfer program for schooling on prevalence of HIV and HSV-2 in Malawi: a cluster randomized trial. *Lancet.* 2012.
146. Deci E, Ryan RM. *Intrinsic Motivation and Self-Determination in Human Behavior*: Springer US; 1985.
147. Deci E, Ryan RM. Facilitating optimal motivation and psychological well-being across life's domains. *Canadian Psychology.* 2008;49(1):14-23.
148. Ryan RM, Deci EL. Self-determination theory and the facilitation of intrinsic motivation, social development, and well-being. *The American psychologist.* Jan 2000;55(1):68-78.
149. Deci EL, Koestner R, Ryan RM. The undermining effect is a reality after all—Extrinsic rewards, task interest, and self-determination: Reply to Eisenberger, Pierce, and Cameron (1999) and Lepper, Henderlong, and Gingras (1999). *Psychological Bulletin.* 1999;125(6):692-700.
150. Deci EL. The effects of contingent and noncontingent rewards and controls on intrinsic motivation. *Organizational Behavior and Human Performance.* 1972/10/01 1972;8(2):217-229.
151. Deci EL, Koestner R, Ryan RM. A meta-analytic review of experiments examining the effects of extrinsic rewards on intrinsic motivation. *Psychol Bull.* Nov 1999;125(6):627-668; discussion 692-700.
152. Sullivan GM, Feinn R. Using Effect Size—or Why the P Value Is Not Enough. *Journal of Graduate Medical Education.* 2012;4(3):279-282.
153. Cameron J. Negative Effects of Reward on Intrinsic Motivation—A Limited Phenomenon: Comment on Deci, Koestner, and Ryan (2001). *Review of Educational Research.* March 1, 2001 2001;71(1):29-42.
154. Carton JS. The differential effects of tangible rewards and praise on intrinsic motivation: A comparison of cognitive evaluation theory and operant theory. *The Behavior Analyst.* Fall 1996;19(2):237-255.
155. Williams GC, Grow VM, Freedman ZR, Ryan RM, Deci EL. Motivational predictors of weight loss and weight-loss maintenance. *Journal of personality and social psychology.* Jan 1996;70(1):115-126.
156. Deitchler M, Ballard T, Swindale A, Coates J. *Introducing a Simple Measure of Household Hunger for Cross-Cultural Use.* Washington, D.C.: Food and Nutrition Technical Assistance II Project, AED;2011.
157. Ryan RM, Connell JP. Perceived locus of causality and internalization: examining reasons for acting in two domains. *Journal of personality and social psychology.* Nov 1989;57(5):749-761.

158. Williams GC, Freedman ZR, Deci EL. Supporting autonomy to motivate patients with diabetes for glucose control. *Diabetes care.* Oct 1998;21(10):1644-1651.
159. Williams GC, Rodin GC, Ryan RM, Grolnick WS, Deci EL. Autonomous regulation and long-term medication adherence in adult outpatients. *Health psychology : official journal of the Division of Health Psychology, American Psychological Association.* May 1998;17(3):269-276.
160. Kennedy S, Goggin K, Nollen N. Adherence to HIV Medications: Utility of the Theory of Self-Determination. *Cognitive Therapy and Research.* 2004/10/01 2004;28(5):611-628.
161. Levesque CS, Williams GC, Elliot D, Pickering MA, Bodenhamer B, Finley PJ. Validating the theoretical structure of the Treatment Self-Regulation Questionnaire (TSRQ) across three different health behaviors. *Health education research.* Oct 2007;22(5):691-702.
162. Stamp KD, Dunbar SB, Clark PC, et al. Family partner intervention influences self-care confidence and treatment self-regulation in patients with heart failure. *European journal of cardiovascular nursing : journal of the Working Group on Cardiovascular Nursing of the European Society of Cardiology.* Feb 11 2015.
163. Cohen J. *Statistical Power Analysis for the Behavioral Sciences*: L. Erlbaum Associates; 1988.
164. Newson R, The AST. Multiple-test procedures and smile plots. *Stata Journal.* 2003;3(2):109-132.
165. Linnemayr S, Rice T. Insights from Behavioral Economics to Design More Effective Incentives for Improving Chronic Health Behaviors, with an Application to Adherence to Antiretrovirals. *Journal of acquired immune deficiency syndromes (1999).* Feb 25 2016.
166. Bor J, Tanser F, Newell M-L, Bärnighausen T. Nearly Full Employment Recovery Among South African HIV Patients On Antiretroviral Therapy: Evidence From A Large Population Cohort. *Health affairs (Project Hope).* 2012;31(7):10.1377/hlthaff.2012.0407.
167. Thirumurthy H, Zivin JG, Goldstein M. The Economic Impact of AIDS Treatment: Labor Supply in Western Kenya. *The Journal of human resources.* Summer 2008;43(3):511-552.

APPENDIX

Table 1.1 Summary of Individual and Clinic Median MPR with 60, 90, and 120 day cut-off periods past last given appointment

	Individual Level MPR		Clinic Level MPR	
	Median	[IQR]	Median	[IQR]
60 day cutoff	86.3	[72.6, 96.8]	84.2	[79.0, 88.2]
90 day cutoff	85.8	[70.8, 96.8]	83.6	[78.4, 87.6]
120 day cutoff	85.7	[69.5, 96.8]	83.1	[77.8, 87.0]

Table 1.2 Summary of chart review from 2 clinics: All pharmacy visits recorded in medical files of 50 patients randomly selected from each clinic and the percent of those visits captured in the electronic medical record system, SmartCare, by year after accounting for typographic errors

Year	Pharmacy visits in medical file	Pharmacy visits not in SmartCare	
	N	N	(%)
2013	330	18	(5)
2014	358	36	(10)
2015	66	5	(8)

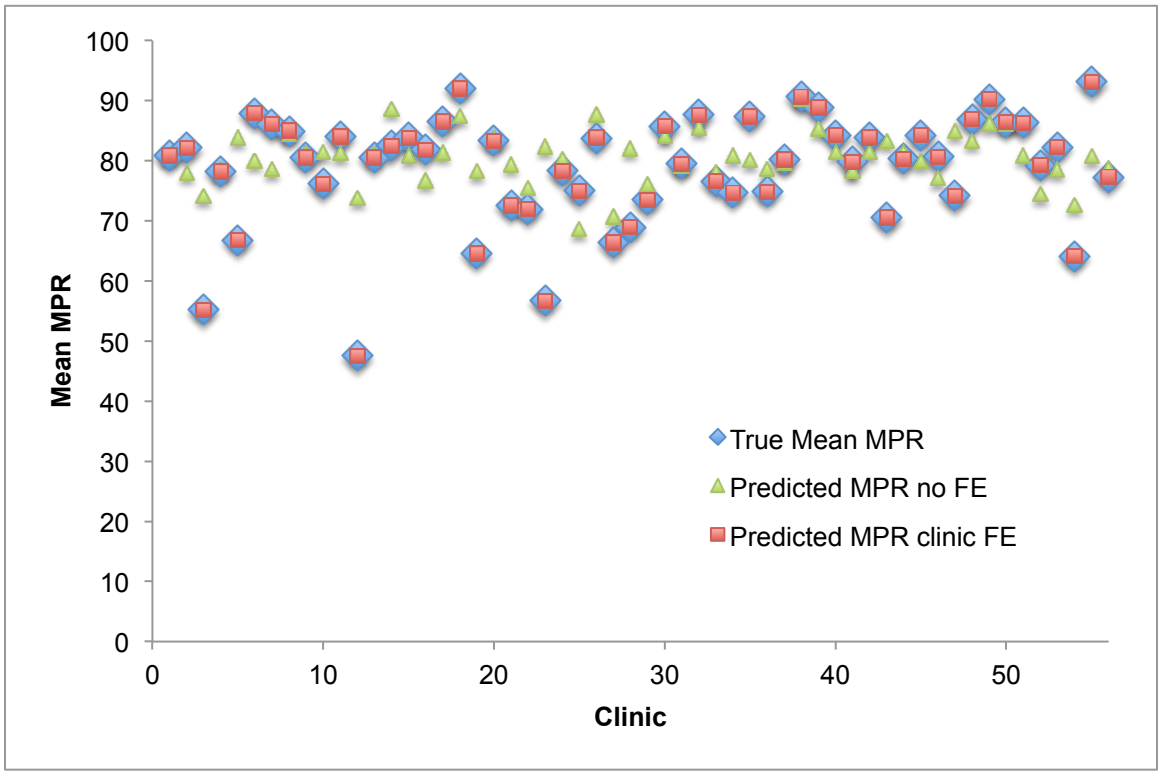
Table 1.3 Summary of missing data	
Covariate	**N (%)**
Female	0 (0)
MPR	675 (0.5)
Year of ART initiation	0 (0)
Marital Status	22,475 (17)
Education	32,624 (25)
Disclosed HIV Status at baseline	16,264 (12)
Baseline WHO Stage	10,618 (8)
Province	0 (0)
Facility Type	0 (0)
Clinic opening year	675 (0.5)
Age	0 (0)
Time on ART (days)	675 (0.5)
Baseline CD4	62,014 (47)
Clinic Size (in hundreds)	0 (0)

Table 1.4. Adjusted Risk Ratios from Multi-level Poisson Model of Medication Possession Ratio>80%

	Risk Ratio	Standard Error	95% Confidence Interval	
Age	1.00	0.00	(0.003, 0.005)	***
Male	0.96	0.01	(-0.055, -0.033)	***
Education				***
None	Ref			
Lower-Mid Basic	1.03	0.01	(0.005, 0.059)	*
Upper Basic/Secondary	1.00	0.02	(-0.026, 0.036)	
College or University	0.93	0.02	(-0.114, -0.031)	**
Disclose	1.05	0.03	(-0.003, 0.108)	
Days on ART	1.00	0.00	(0, 0)	***
Marital Status				**
Single	Ref			
Married	1.04	0.01	(0.016, 0.059)	**
Divorced	1.01	0.01	(-0.012, 0.039)	
Widowed	1.03	0.01	(0.003, 0.055)	*
Unknown	1.06	0.05	(-0.04, 0.155)	
Year of ART initiation				***
2004-6	Ref			
2007-09	1.41	0.03	(0.289, 0.397)	***
2010-12	2.04	0.05	(0.618, 0.806)	***
2013-15	2.91	0.07	(0.933, 1.205)	***
Baseline CD4 count				***
<200	Ref			
200-349	1.04	0.01	(0.021, 0.055)	***
350-499	1.05	0.01	(0.031, 0.07)	***
>500	1.05	0.01	(0.03, 0.074)	***
WHO Stage at enrollment				***
1	Ref			
2	0.99	0.01	(-0.031, 0.015)	
3	0.95	0.01	(-0.073, -0.034)	***
4	0.91	0.02	(-0.127, -0.061)	***
Facility Type				**
Rural	Ref			
Urban	0.83	0.14	(-0.478, 0.111)	
Hospital	1.25	0.15	(-0.082, 0.53)	
Province				**
Eastern	Ref			
Lusaka	1.20	0.08	(0.019, 0.344)	*
Southern	1.09	0.10	(-0.122, 0.292)	
Western	0.83	0.08	(-0.358, -0.022)	*
Clinic size (per 100)	1.01	0.00	(0, 0.011)	
Clinic start year				
2003	Ref			
2004	1.15	0.07	(-0.014, 0.292)	
2005+	1.30	0.14	(-0.036, 0.558)	

* p<0.05, ** p<0.01, *** p<0.001

Figure 1.1. Mean MPR by clinic: empirical mean (blue), predicted mean without fixed effects for clinic (green), and predicted mean with fixed effects for clinic (red).



Item 2.1 In-depth interview guide

Experience with ART and the clinic

- Tell me about first knowing about HIV infection and your first time coming to this clinic. What happened? [probe about feelings and staff interactions]
- You've now been taking ART for about 6 months. How do you think about taking your ART now compared to when you first started? How has it become easier or harder?
    - You're now an expert, what would you tell someone else who is just starting? [probe for motivation]
- Can you tell me about the last time you were unable to return to clinic to get more pills before you ran out? What happened then? What barriers do you face?
    - Is this what everyone else thinks too? Give me an example.
    - Optional: [Are you the same or different from your friends/family/people in your community with what you think about this? Give me an example.]
- Tell me about a time when you forgot to take your ART or maybe took them late. What happened? Why?
    - Do these things (running out of pills or forgetting to take them) also happen to friends or other people in the community? How do they manage it?

Experience in Study

- Walk me through the day you enrolled in the study.
    - How was your experience with the research assistant?
    - How did you feel to be approached and then enter into the study?
- Who did you tell about the study?
    - What did you tell them?
    - What did they say?
        - *[probe for: gender/power…..]*

Experience with Transfers

- Remind me how many transfers have you received so far?
- What were the expectations about how you were to use the transfer?
- What happened the day you received/picked the first transfer?
    - How did you feel?
    - Where were you? (For cash transfer)
- How did you use the transfer? (probe about other uses apart from study intentions)
- Did you tell anyone about the transfer? What was that discussion like? How did you decide you were going to use the transfer at that time? Who was a part of that decision? Why?
- Did this differ for each transfer? How did this change as you received more transfers? Did you anticipate the next transfer?
- Have you heard from other people in the program who had similar or different experiences? What did they say?

- In this study, some people get transfers every month and some people don't. When do you get the transfers? Why do you get transfers? What is the reason that people get transfers in this project? Why do you get transfers? Have you ever not received a transfer as planned? Why was that?
- Did getting a transfer help you to get to clinic? Did the thought of getting the transfer motivate you to come to clinic?

Parting thoughts

- What do you think about this program?
- What do you think about it only going on for 6 months? Should it be longer/shorter?
- What else would you like to tell me about your experience with the study and with the transfers?

Things to probe on:

- Make sure question is answered
- Probe more when:
    - **Gender and power** issues are touched upon
    - Thinking (or not) **thinking about the future** and **how decisions made** now may impact the future
        - Life goals and aspirations
        - Hopes for the future
        - Expectations for the future
    - **Motivations** to stay in care and take ART
        - Why you come to clinic
        - Why you take ART

Table 3.1. Rational for determinant inclusion in heterogeneity analysis

Determinant	Rational for inclusion
Female	Due to cultural norms females may feel lower levels of self-efficacy and higher degrees of external control (thus lower autonomy).
Education	Level of education may be associated with competence and autonomy.
Religion	Religion may be associated with competence and autonomy. Religion may also increase relatedness.
Marital Status	Competence, autonomy, and relatedness likely differ by marital status.
Currently Working	Whether a person is currently working may be associated with competence and autonomy
Head of Household	Being head of household may be associated with competence and autonomy.
Decision making about own healthcare	An individual's involvement in making decisions about their own health care may be linked to autonomy and competence.
Baseline HHS	Food insecurity level may be associated with competence and autonomy.
6M HHS	Food insecurity level may be associated with competence and autonomy.
Has children	Having children may be associated with competence, autonomy, and relatedness.
Unable to work or attend school due to illness	This is a reflection of severity of illness which has been previously associated with intrinsic motivation and is also likely associated with autonomy.
Age (years)	Age may be associated with competence and autonomy.
Number in household	The number of people living in a household may be associated with autonomy and relatedness.
Self-rated health (1-10 scale)	This is a reflection of severity of illness and self-rated current health which has been previously associated with intrinsic motivation and is also likely associated with autonomy.
Barriers to care (max 22)	Perceived barriers have previously been associated with intrinsic motivation and may also be associated with competence and autonomy.

Appendix Table 3.2 Distribution of answers to each question in the TSRQ sub-scale at each time point

	Baseline (N =643)		6-months (N =446)		12 months (N =270)	
Item	Mean	(SD)	Mean	(SD)	Mean	(SD)
The reason you take your HIV medication as it was prescribed to you is…						
Because you feel that you want to take responsibility for your own health	2.76	(0.46)	2.93	(0.29)	2.97	(0.18)
Because you have carefully thought about it and believe it is very important for many aspects of your life	2.81	(0.47)	2.91	(0.31)	2.94	(0.24)
Because taking your HIV medication is consistent with your life goals	2.78	(0.50)	2.89	(0.36)	2.93	(0.30)
Because you personally believe it is the best thing for your health	2.83	(0.46)	2.91	(0.34)	2.95	(0.21)
Because it is an important choice you really want to make	2.79	(0.50)	2.93	(0.30)	2.96	(0.22)