Strategies to Accelerate HIV Care and Antiretroviral Therapy Initiation Following HIV Diagnosis: a Randomized Trial

Running: Accelerated linkage to care for HIV

Christopher J Hoffmann(1, 2); Tonderai Mabuto(2; 4); Sibuse Ginindza (2); Katherine L Fielding(3; 4); Griffths Kubeka(2); David W Dowdy(1); Gavin J Churchyard(2, 3, 4); Salome Charalambous (2, 4);

1. Johns Hopkins University School of Medicine and Bloomberg School of Public Health, Baltimore, USA

2. The Aurum Institute, Johannesburg, South Africa

3. London School of Hygiene & Tropical Medicine, London, UK

4. The University of the Witwatersrand School of Public Health, Johannesburg, South Africa

Corresponding Author:

Christopher J Hoffmann; 725 N Wolfe St; Suite 211; Baltimore, MD 21205

choffmann@jhmi.edu

Funding: United States Agency for International Development (USAID) Cooperative Agreement AID-OAA-A-12-00028.

Presented in part at the Conference on Retroviruses and Opportunistic Infections 2016, Boston, Massachusetts, USA February 22-25, 2016. Abstract 113LB.

Disclosures: all authors report no financial disclosures or other conflicts of interest

Word Count: 3478

Abstract

Objective

Determine the effectiveness of strategies to increase linkage to care following testing HIV positive at mobile HIV testing in South Africa.

Design

Unmasked randomized controlled trial.

Methods

Recruitment of adults testing HIV-positive and not currently in HIV care occurred at seven mobile HCT units in urban, peri-urban, and rural South Africa with those consenting randomized 1:1:1:1 into one of four arms. Three strategies were compared to standard of care (SOC): point-of-care CD4 count testing (POC CD4), POC CD4 plus longitudinal strengths-based counselling (care facilitation; CF), and POC CD4 plus transport reimbursement (transport). Participants were followed-up telephonically and through clinic records and analyzed with an intention to treat analysis.

Results

From March 2013 to October 2014, 2,558 participants were enrolled, of whom 160 were excluded post-randomization. Compared to the SOC arm where 298 (50%) reported having entered care , linkage to care was 319 (52%) for POC CD4, hazard ratio (HR) 1.0 [95% confidence interval (CI): 0.89, 1.2, p=0.6]; 331 (55%) for CF, HR 1.1 (95% CI: 0.84, 1.3, p=0.2); and 291 (49%) for transport, HR 0.97 (95% CI: 0.83, 1.1, p=0.7). linkage to care verified with clinical records occurred for 172 (29%) in the SOC arm; 187 (31%) in the POC CD4 arm, HR 1.0 (95% CI: 0.86, 1.3, p=0.6); 225 (38%) in the CF arm, HR 1.4 (95% CI: 1.1, 1.7, p=0.001); and 180 (31%) in the transport arm, HR 1.1 (95% CI: 0.88, 1.3, p=0.5).

Conclusions

Care facilitation improved verified linkage to care from 29 to 38%.

43 Key words: HIV; linkage to care; counseling; transportation; randomized trial; Africa

44

Introduction

HIV treatment reduces HIV related illness, HIV-associated deaths, and has the potential to end the AIDS epidemic through reducing HIV transmission.[1] Success with reducing HIV morbidity, mortality, and transmission depends on the combination of HIV diagnosis early after infection and rapid initiation of antiretroviral therapy (ART) .[2-5] Considering these factors, the World Health Organization, UNAIDS, and other global and national bodies, including the government of South Africa, have endorsed policies to provide ART to all people living with HIV.[6,7]

In many regions of the world, many or most of those living with HIV have failed to engage in care. In South Africa, 86% of people living with HIV are estimated to be aware of their status [8], but only a third of those diagnosed are receiving ART, even among those who were ART eligible.[9,10] This attrition between testing and ART initiation occurs due to the substantial attrition between testing HIV positive and engaging in HIV care[11]. Denial of HIV diagnosis, fear of morbidity from HIV disease, lack of health self-efficacy, inadvertent disclosure of status associated with seeking care, seeking alternative forms of healing, cost of travel to and from clinic, and burdens of wait time and clinic enacted stigmatization all contribute to the failure of people diagnosed with HIV to link to care. [12,13] Despite the catalogue of factors associated with this failure, there are few demonstrated effective approaches to improve the transition from testing HIV positive to clinic engagement and ART initiation.[12,14]

We sought to address the failure to engage in care by aligning known individual-level barriers with pragmatic strategies for individuals testing HIV positive at mobile HIV counseling and testing (HCT) units. Mobile HCT, as well as other non-facility approaches to HIV testing, is increasing in importance with greater efforts to reach the untested and undiagnosed groups who may not be ill enough to seek acute care at a clinic or hospital.[15,16] To engage individuals testing HIV positive in care, we adapted approaches of point-of-care CD4 (POC-CD4) count testing, strengths-based case management, and transport assistance.[17-20] We hypothesized that combinations of engagement strategies may be necessary to

overcome barriers; thus, we paired counselling and transport assistance with POC-CD4 count testing in addition to a POC-CD4 only arm and a standard of care arm. In this randomized trial we assessed whether these strategies decreased (i) time to linkage to care within 90 days and 180 days and (ii) mortality within 180 and 365 days of enrollment and (iii) increased ART initiation within 180 days of enrollment.

Methods

Study design

This was an individually randomized pragmatic trial.[21] Seven mobile HCT units were deployed in two districts in South Africa, a rural district and an urban / peri-urban district. The mobile units were deployed in communities, workplaces, commercial shopping areas, and public events as part of routine HCT service delivery. HCT procedures were standardized across units, provided free-of-charge, performed by trained counsellors, and followed South African National HCT Policy Guidelines. Small incentives were provided for HIV testing (value $0.25-$1.00). Following testing HIV positive, participants were encouraged to receive care at the most convenient government or private clinic (over 200 in the areas where the mobile HCT units were deployed). During the period of recruitment the national ART initiation threshold was a CD4 count of <350 cells/mm^3. This study adhered to the Declaration of Helsinki and was approved by the University of the Witwatersrand Human Research Ethics Committee, the Johns Hopkins University School of Medicine Institutional Review Board, the London School of Hygiene & Tropical Medicine Research Ethics Committee, and research committees of Ekurhuleni District and Limpopo Province, South Africa. **The full protocol is available as S1 Appendix.**

Participants

Clients were eligible to participate if they tested HIV-positive (regardless of prior HIV testing), were ≥18 years old, capable of providing informed consent, reporting not currently receiving HIV-related care, and anticipating remaining in South Africa for at least six months for follow-up. All participants completed written informed consent prior to enrollment.

Randomization and masking

Participants were randomized in the ratio of 1:1:1:1 into four study arms using random block sizes and stratified by the seven mobile HCT units. Study assignments were generated by the trial statistician and were placed in sealed opaque envelopes with participant identification numbers on the outside. Research assistants sequentially assigned participant identification numbers and opened the envelope in

the presence of the participant. Due to the behavioral nature of the strategies and need for the research assistant to explain strategy specific procedures, the assignment arm was unmasked from the participant and the field worker enrolling the participant. The randomization arm was masked to research staff collecting outcome data and the investigators prior to the final analyses.

Procedures

Standard of care: In the standard of care (SOC) arm, participants were counseled on the importance of HIV care and provided a referral letter to the clinic closest to their place of residence or the clinic of their choice.

POC-CD4 count testing: This included the standard of care as well as a portable battery-powered POC-CD4 test platform (PIMA, Alere Inc. Waltham, Massachusetts, USA) which used capillary blood to provide CD4 count enumeration within 20 minutes. Following testing, the participant received printed results and counselling on the health implications. We hypothesized that knowledge of CD4 count and the health implications of that value would convince skeptical participants of the HIV diagnosis and motivate participants to link to care.

Care facilitation: This included the standard of care, POC CD4 count testing, and up to five care facilitation sessions. The counselling sessions were discontinued after five sessions had occurred, 90 days had passed since enrolment, or the participant requested stopping. The counselling was structured around modified strengths-based counselling based on the United States Centers for Disease Control and Prevention (CDC) antiretroviral treatment and access to services (ARTAS) counselling approach.[18] Care facilitators had formal training as either a social worker or auxiliary social worker and received two days of didactic and practical training in strengths-based case management and ongoing assessments and coaching. After a participant was randomized to this arm, the research assistant contacted a care facilitator via cell phone to introduce the participant to the care facilitator. Subsequently the care facilitator and participant arranged times and places for counselling sessions, either telephonic or in-

person. We hypothesized that individualized strengths-based counseling could assist participants in overcoming concerns and uncertainties around HIV status disclosure, internalized stigma, and linkage to care.

Transport reimbursement: This included the standard of care, POC CD4 count testing, and reimbursement for travel to a clinic at a standard rate of US$6 for urban or peri-urban and US$10 for rural residents for up to three clinic visits within 90 days of randomization. Following a participant notifying that they had visited a clinic (using a toll-free number or text message), reimbursement was made through cell phone transfer, automated teller machine, or a designated grocery store chain. We hypothesized that limited financial resources for transport may be a barrier to linkage to care.

Baseline characteristics, locator information, and national identification number were obtained following randomization. For study follow-up, participants were contacted telephonically at 30 and 60 days to verify contact information and after 90 days and 180 days to ascertain care status. Telephonic contact was attempted at least three times, at different times of the day and on different days. When the participant was not reached and next-of-kin telephone numbers were available, contact via the next-of-kin was attempted at least three times, at different times of the day and on different days. Home visits were attempted for all participants with unsuccessful telephonic contact. At least three attempts were made to visit the reported, or updated, place of residence.

Clinical records were reviewed for all participants who reported linkage to care. Clinical records included clinic paper records, electronic records, or national laboratory system electronic laboratory results. If no records were located, the participant was re-contacted to ask whether care entry occurred, asked again at which clinic, and asked about different names that may have been used to register for care. Electronic district health and laboratory records (not clinic specific) were also searched for participants unable to be contacted via telephone or home visits. Linkage to care was considered

verified if any clinical records indicated an HIV related clinic visit. Finally, national identification numbers were periodically matched with the South African national population registry to identify participants who had died.

Outcomes

Linkage to care was defined as receiving HIV-specific care at any allopathic medical facility in South Africa. Participants without care status data (self-report of verified) were classified as having linked to care. The primary outcome was time to linkage to care, by self-report, within 90 days of enrollment. Secondary outcomes were time to linkage to care as verified by clinical records within 90 days, and time to death 90, 180, and 365 days from enrollment. We also assessed self-reported and verified ART initiation within 180 days (regardless of eligibility criteria), all as *a priori* exploratory outcomes. Given a hypothesis that the interventions may benefit some demographic groups more than others, we planned, *a priori*, to assess for interactions between study arm and the following subgroups for the primary outcome: sex, age group (≤30/>30 years), urban or rural residence, employment status, distance from the place of residence to the nearest or preferred clinic (<5km/≥5km), self-reported cost of travel to the clinic (>/≤US$2), and presence of symptoms at enrollment.

Distance from a participant's residence and the nearest clinic was calculated using the Haversine Formula by inputting GPS coordinates of the place of residence (based on an estimate using Google Earth) and the GPS coordinates of the nearest clinic or favored clinic as stated by the participant.[22]

Statistical analysis

The sample size was calculated to identify a 15% or greater increase in linkage to care; an increase that may be meaningful from a policy perspective. Assumptions for calculating the sample size were that 40% of participants in the standard of care arm would enter care by 90 days, a conservative type I error as low as 1.67% (equivalent to 5% Bonferroni correction for multiple comparisons), and loss from study follow-up of 10% of participants.[11,23,24] Under these scenarios, a sample size of 625 participants per arm

would achieve greater than a 90% power to detect a 15% or greater difference between the standard of care arm and any one of the three strategy arms.

Analysis was based on intention-to-treat, including all randomized participants, except for those excluded post-randomization due to confirmation that they were already in HIV care prior to study enrollment. We used Kaplan-Meier curves to graph the cumulative risk for linkage to care and ART initiation outcomes. For the primary outcome we used Cox proportional hazards regression with three pairwise comparisons of each of the three intervention arms versus standard of care, adjusting for randomization strata (mobile unit). Proportional hazards assumptions were tested using log-log plots and Schoenfeld residuals. A secondary analysis was planned adjusting for any major imbalances by study arm, with the exception of mode of transport to clinic because of likely reporting bias as the question was asked after randomization. Time at risk was measured from date of randomization to earliest of (i) date of linkage to care; (ii) date of death; or (iii) 90 days after enrollment. Participants without follow-up were considered not to be in care or on ART at the 90 or 180 day time point. Secondary and exploratory outcomes were similarly assessed.

Stata 13 was used for all analyses (STATA Corp. College Park, Texas, USA). This trial is registered with ClinicalTrials.gov, NCT02271074 and the South African National Research Ethics Council DOH-27-0713-4480.

Role of funding source

The sponsor of the study had no role in the design of the original study protocol, data collection, data analysis, data interpretation, writing of the report, or decision to submit the manuscript for publication. CJH, TM, SG, and KLF had full access to all the data in the study. CJH had final responsibility for the decision to submit for publication, and all authors approved the decision to submit.

Results

From 13 March 2013 to 30 October 2014, 3,739 adults tested HIV-positive at the mobile HCT units, 2,930 were screened for eligibility, and 2,711 (92%) met eligibility criteria. Primary reasons for ineligibility were not being part of the strategy target population because they were already receiving HIV care (129; 4.4%) or that they expected to be unavailable for follow-up (expecting to leave South Africa within 6 months; 75; 2.5%). Of the 2,711 who were eligible, 2,558 gave consent (94%) and were randomized (**Figure 1**). After randomization, 152 participants were identified as being in care at the time of enrolment and eight to have a second enrolment in the study; they were excluded from all analyses. We were able to contact or find clinical records for 2,133 participants (89%) to determine linkage to care status at 90 days post-enrollment (range 88 to 90% by study arm; chi square test for difference by study arm, p=0.7).

Overall 1,472 (61%) participants were female, the median age was 33 years (interquartile range, [IQR]: 27, 41), the median distance from place of residence to a clinic was 4.0 km (IQR: 1.5, 12), and 959 (40%) participants reported reaching the clinic from their residence by walking (**Table 1**). Among participants in the three study arms that received POC-CD4 count testing, the median CD4 count was 427 cells/mm^3 (IQR: 287, 595); 629 (35%) had a CD4 count <350 cells/mm^3 meeting South African ART initiation criteria in place during enrollment. The baseline characteristics were balanced overall by study arm with the exception of reported mode of transport to a clinic.

Overall, 1,239 (cumulative risk 52%) participants self-reported linkage to care by 90 days at 272 different clinics; 298 (50%) for SOC, 319 (52%) for POC-CD4 count, 331 (55%) for care facilitation, and 291 (49%) for transport reimbursement. Compared to standard of care, there were no differences between strategy arms (**Table 2 & Figure 2**). We found no subgroup differences by study arm (p for interactions all > 0.1; **S2 Appendix**).

For the outcome of verified linkage to care by 90 days, 172 (29%) participants had verified care entry in the standard of care arm, 187 (31%) in the POC CD4 arm, 225 (38%) in the care facilitation arm, and 180 (31%) in the transport reimbursement arm (**Figure 3**). Hazard ratios were as follows: POC CD4 count, 1.0 (95% CI: 0.86, 1.3; p=0.6); care facilitation, 1.4 (95% CI: 1.1, 1.7; p=0.001), and transport reimbursement 1.1 (95% CI: 0.88, 1.3; p=0.5), all versus the SOC arm (**Table 2**). The effect of each intervention on 180 day self-reported and verified linkage to care was similar to the effect measured over 90 days (**Table 2**). Variation in percentage or participants reporting unverified entry ranged from 17-21% by study arm (chi-square for difference: p=0.2).

Forty patients died within a year of enrollment (six within the first 90 days). We found no difference between study arm and mortality (**S2 Appendix**).

By 180 days after enrollment, 373 participants (15%) had verified ART initiation. For verified ART initiation, the hazard ratios were 1.2 (95% CI: 0.91, 1.6; p=0.2) for POC CD4 count, 1.4 (95% CI: 1.1, 1.9; p=0.02) for care facilitation; and 1.2 (95% CI: 0.89, 1.6; p=0.2) for transport reimbursement, versus the SOC arm (**Table 2**). Among the 629 participants in the POC CD4 count arms meeting the ART initiation threshold (CD4<350 cells/mm^2), 207 (33%) had verified ART initiation by 180 days from enrollment.

Considering uptake of the strategies, POC-CD4 count test results were delivered on the same day to 1,764 of the 1,807 (98%) participants in POC-CD4 count testing arms. Of the participants in the care facilitation arm, 377 (62%) requested and received at least one session, 218 (36%) had two or more sessions, and 101 (17%) had three or more sessions. Of the 758 total sessions, 69% were face-to-face and 31% were telephonic. Among participants in the transport reimbursement arm 285 (48%) submitted at least one transport claim; 67% of those with self-reported and 74% of those with verified 90 day linkage to care. Reasons for not requesting reimbursement included residing close enough to walk to the clinic and not understanding the procedures for reimbursement.

Discussion

Increasing ART initiation following HIV diagnosis, especially following diagnosis in non-clinic sites such as mobile HCT units, is essential to reach asymptomatic individuals, men, and youth to achieve targets for HIV treatment and prevention [16,25-28]. This has become especially important with universal test and treat policies, including the policy introduced in 2016 in South Africa.[29] Engagement in care following diagnosis is necessary to deliver the potential of test and treat to reduce illness, death, and HIV transmission. In this study of 2,398 people testing positive for HIV in mobile units across rural, peri-urban, and urban South Africa, only 52% self-reported initiating HIV care, and only 29% had clinic verified linkage to care within 90 days. None of the tested strategies improved the primary outcome of self-reported time to linkage to care. Using the outcome of clinically verified linkage to care, POC CD4 plus care facilitation lead to a 40% increase in linkage to care by 90 days (HR 1.4, p=0.001, versus standard of care).

These results provide a generalizable description of large attrition in the care continuum following testing HIV positive at non-clinic sites. Linkage to care was lower than previously reported following clinic-based HIV testing [11,30] though consistent with studies of linkage to care following mobile and household HCT.[23,30,31] There are several reasons why mobile compared to clinic-based HCT may achieve lower rates of linkage to care. In clinic-based HCT, individuals seeking care are usually symptomatic, creating a motivation to initiate treatment to relieve symptoms [26,27]. Equally important, the individual has overcome initial barriers to clinic entry when seeking acute care or HIV testing at the clinic. Despite the lower linkage to care following mobile testing, mobile and other non-clinic based testing, when compared to clinic-based testing, generally reach a larger proportion of asymptomatic individuals, those with higher CD4 counts, men, and young adults.[13]

In this study, self-reported linkage to care was notably higher than verified linkage to care. This difference may be attributable to participants misrepresenting their care status as was acknowledged by

some participants at follow-up interviews and has previously been reported.[31,32] Over-reporting of linkage to care may have been driven by the social desirability bias.[33] It is also possible that clinical records were not located for all participants who had successfully linked to care. The use of three distinct sources of verification minimized, but likely did not eliminate, this problem.

This study has several limitations. One is that participant self-report appeared to over-ascertain linkage to care. Given the suggestion of misreporting by participants, verified linkage to care may be more accurate. A key strength is that we did verify linkage to care by contacting participants and conducting paper record and electronic record searches at over 200 clinics. An additional potential limitation is that we made contact with participants at 30 and 60 days following enrollment, contact that may have increased linkage to care, particularly in those arms without ongoing scheduled contact. In addition, not all participants in the care facilitation and transport reimbursement arms utilized care facilitation or made reimbursement claims. This was partly due to difficulties in receiving reimbursement and challenges in having care facilitation sessions, either due to lack of transport or access to a phone. Important strengths of the study are its large sample size relative to other studies of linkage to care in the global South, 95% enrollment among eligible individuals, the number of clinics involved, and the geographic diversity of the population covered.

The findings of this study are particularly relevant in South Africa where HIV programs are adopting universal treatment for all people living with HIV. Identifying effective approaches to engaging individuals in care is essential to achieve ART initiation and retention on ART. Through the longitudinal counselling provided in the care facilitation arm that started before, or at the time of a care visit or ART initiation, we have demonstrated an approach to increasing care engagement and ART initiation. The implications for program implementers and policy makers include the potential role of longitudinal tailored interpersonal communication to achieve improved care engagement. We studied communication delivered independently from clinics; however, approaches of integrating counselling

with traditional clinical care or community-based care and ART delivery may be a more efficient and fits with current approaches to expedite ART initiation. While there are likely ancillary benefits of POC CD4 count testing and transport reimbursement, our results suggest that neither were an effective strategy to improve linkage to care or ART initiation in this setting. Finally, achieving the ambitious target of 90% of diagnosed patients entering into care and initiating ART will likely require multiple approaches that address a spectrum of barriers, including lack of patient self-efficacy, community level stigma, and clinic and health service delivery challenges. Future research needs to assess strategies for linkage to care that address multiple levels, including individual counselling and improved clinical service delivery.[34] Research questions emerging directly from this work include whether care facilitation can be further optimized to increase linkage to care, how it is best delivered in a universal test and treat setting, and whether group care facilitation or other forms of health communication could also be successful.

In summary, this trial suggests that strengths-based longitudinal care facilitation may improve care engagement and ART initiation, but also illustrates the challenges of linking and retaining newly-diagnosed patients into care. As South Africa and other low and middle income countries diagnose more people living with HIV through mobile, house hold, and self-testing and adopt ART treatment for all people living with HIV, there is an even more pressing need to find ways to engage asymptomatic individuals in care.

1. UNAIDS. *AIDS by the numbers.* Geneva, Switzerland2015.
2. Cohen MS, Chen YQ, McCauley M, et al. Prevention of HIV-1 infection with early antiretroviral therapy. *NEnglJ Med.* 2011;365(6):493-505.
3. Tanser F, Barnighausen T, Grapsa E, Zaidi J, Newell ML. High coverage of ART associated with decline in risk of HIV acquisition in rural KwaZulu-Natal, South Africa. *Science.* 2013;339(6122):966-971.
4. Johnson LF, Mossong J, Dorrington RE, et al. Life expectancies of South African adults starting antiretroviral treatment: collaborative analysis of cohort studies. *PLoS medicine.* 2013;10(4):e1001418.
5. Hoffmann CJ, Lewis JJ, Dowdy DW, et al. Mortality associated with delays between clinic entry and ART initiation in resource-limited settings: results of a transition-state model. *Journal of acquired immune deficiency syndromes.* 2013;63(1):105-111.
6. Lundgren JG, JM; Rockstroh, JK; Furrer, H. *EACS Guidelines Version 8.0.* London2015.
7. WHO. *Guideline on when to start antriretroviral therapy and on pre-exposure prophylaxis for HIV.* Geneva, Switzerland2015.
8. Johnson LF, Rehle TM, Jooste S, Bekker LG. Rates of HIV testing and diagnosis in South Africa: successes and challenges. *AIDS.* 2015;29(11):1401-1409.
9. Shisana OR, T; Simbayi, LC; Zuma, K; Jooste, S; Zunga, N; Labadarios, D; Onoya, D. *South African national HIV prevalence, incidence, and behaviour survey, 2012.* Cape Town, South Africa: HSRC;2014.
10. UNAIDS. *Global Report: UNAIDS report on the global AIDS epidemic 2013.* Geneva, Switzerland2013.
11. Rosen S, Fox MP. Retention in HIV care between testing and treatment in sub-Saharan Africa: a systematic review. *PLoSMed.* 2011;8(7):e1001056.
12. Brennan A, Browne JP, Horgan M. A systematic review of health service interventions to improve linkage with or retention in HIV care. *AIDS Care.* 2014;26(7):804-812.
13. Govindasamy D, Ford N, Kranzer K. Risk factors, barriers and facilitators for linkage to antiretroviral therapy care: a systematic review. *AIDS.* 2012;26(16):2059-2067.
14. Govindasamy D, Meghij J, Kebede Negussi E, Clare Baggaley R, Ford N, Kranzer K. Interventions to improve or facilitate linkage to or retention in pre-ART (HIV) care and initiation of ART in low- and middle-income settings--a systematic review. *J Int AIDS Soc.* 2014;17:19032.
15. . *Consolidated Guidelines on the Use of Antiretroviral Drugs for Treating and Preventing HIV Infection: Recommendations for a Public Health Approach*. 2nd ed. Geneva2016.
16. Suthar AB, Ford N, Bachanas PJ, et al. Towards universal voluntary HIV testing and counselling: a systematic review and meta-analysis of community-based approaches. *PLoS medicine.* 2013;10(8):e1001496.
17. Vojnov L, Markby J, Boeke C, Harris L, Ford N, Peter T. POC CD4 Testing Improves Linkage to HIV Care and Timeliness of ART Initiation in a Public Health Approach: A Systematic Review and Meta-Analysis. *PloS one.* 2016;11(5):e0155256.
18. Gardner LI, Metsch LR, Anderson-Mahoney P, et al. Efficacy of a brief case management intervention to link recently diagnosed HIV-infected persons to care. *AIDS.* 2005;19(4):423-431.
19. Nsigaye R, Wringe A, Roura M, et al. From HIV diagnosis to treatment: evaluation of a referral system to promote and monitor access to antiretroviral therapy in rural Tanzania. *J IntAIDS Soc.* 2009;12(1):31.

20. Wynberg E, Cooke G, Shroufi A, Reid SD, Ford N. Impact of point-of-care CD4 testing on linkage to HIV care: a systematic review. *J Int AIDS Soc.* 2014;17:18809.
21. Loudon K, Treweek S, Sullivan F, Donnan P, Thorpe KE, Zwarenstein M. The PRECIS-2 tool: designing trials that are fit for purpose. *BMJ.* 2015;350:h2147.
22. Siedner MJ, Lankowski A, Tsai AC, et al. GPS-measured distance to clinic, but not self-reported transportation factors, are associated with missed HIV clinic visits in rural Uganda. *AIDS.* 2013;27(9):1503-1508.
23. Govindasamy D, van Schaik N, Kranzer K, Wood R, Mathews C, Bekker LG. Linkage to HIV care from a mobile testing unit in South Africa by different CD4 count strata. *Journal of acquired immune deficiency syndromes.* 2011;58(3):344-352.
24. Larson BA, Brennan A, McNamara L, et al. Early loss to follow up after enrolment in pre-ART care at a large public clinic in Johannesburg, South Africa. *TropMedIntHealth.* 2010;15 Suppl 1:43-47.
25. Chang W, Chamie G, Mwai D, et al. Implementation and Operational Research: Cost and Efficiency of a Hybrid Mobile Multidisease Testing Approach With High HIV Testing Coverage in East Africa. *Journal of acquired immune deficiency syndromes.* 2016;73(3):e39-e45.
26. Mabuto T, Latka MH, Kuwane B, Churchyard GJ, Charalambous S, Hoffmann CJ. Four models of HIV counseling and testing: utilization and test results in South Africa. *PloS one.* 2014;9(7):e102267.
27. Meehan SA, Naidoo P, Claassens MM, Lombard C, Beyers N. Characteristics of clients who access mobile compared to clinic HIV counselling and testing services: a matched study from Cape Town, South Africa. *BMC Health Serv Res.* 2014;14:658.
28. Kadede K, Ruel T, Kabami J, et al. Increased adolescent HIV testing with a hybrid mobile strategy in Uganda and Kenya. *AIDS.* 2016;30(14):2121-2126.
29. Department of Health RoSA. Implementation of the universal test and treat strategy for HIV positive patients and differnetiated care for stable patients. In: Health Do, ed. Pretoria2016.
30. Bassett IV, Regan S, Luthuli P, et al. Linkage to care following community-based mobile HIV testing compared with clinic-based testing in Umlazi Township, Durban, South Africa. *HIV Med.* 2014;15(6):367-372.
31. Genberg BL, Naanyu V, Wachira J, et al. Linkage to and engagement in HIV care in western Kenya: an observational study using population-based estimates from home-based counselling and testing. *Lancet HIV.* 2015;2(1):e20-26.
32. MacKellar DA, Williams D, Storer N, et al. Enrollment in HIV Care Two Years after HIV Diagnosis in the Kingdom of Swaziland: An Evaluation of a National Program of New Linkage Procedures. *PloS one.* 2016;11(2):e0150086.
33. Fisher RJK, J.E. Social-desirability bias and the validity of self-reported values. *Psychology & Marketing.* 2000;17(2):105-120.
34. Hoffmann CJ, Mabuto T, McCarthy K, Maulsby C, Holtgrave DR. A Framework to Inform Strategies to Improve the HIV Care Continuum in Low- and Middle-Income Countries. *AIDS Educ Prev.* 2016;28(4):351-364.

Other Information

Contributors

CJH: conceptualized the study, acquired funding, supervised study implementation, completed formal analysis, and wrote the original draft of this manuscript; TM: contributed to conceptualization, managed data curation, administered study activities, and reviewed and edited manuscript drafts; SG: contributed to the formal analysis; KLF: was the study statistician, conceptualized the statistical approach, reviewed all statistical output, interpreted results, and reviewed and edited manuscript drafts DD: conceptualized components of the analysis plan and reviewed and edited manuscript drafts; GJC: managed stakeholder engagement and reviewed and edited manuscript drafts; SC contributed project administration, managed stakeholder engagement, and reviewed and edited manuscript drafts.

Conflicts of interest

We declare no conflicts of interest.

Acknowledgements

We gratefully acknowledge the funder of this study, the United States Agency for International Development (USAID) Cooperative Agreement AID-OAA-A-12-00028. In addition, we acknowledge the effort of the study team and the involvement of all the participants.

Registration

This trial is registered with ClinicalTrials.gov, NCT02271074 and the South African National Research Ethics Council DOH-27-0713-4480.

Funding

United States Agency for International Development (USAID) Cooperative Agreement AID-OAA-A-12-00028. The funders had no role in data analysis, writing of the manuscript, or decision to submit for publication.

Tables and Figures

Supplemental Digital Content

S1 Appendix: Study Protocol.pdf

S2 Appendix: Subgroup and Mortality Results.pdf