

1 **Title Page**

2 **Title: Factors associated with poor linkage to HIV care in South**
3 **Africa: secondary analysis of data from the Thol'impilo trial**

4 **Authors:** Jienchi Dorward, MBChB, BSc, MSc. London School of Hygiene & Tropical Medicine,
5 London, United Kingdom and Centre for the AIDS Programme of Research in South Africa
6 (CAPRISA), Durban, South Africa

7 Tonderai Mabuto, MPH. The Aurum Institute, Johannesburg, South Africa and School of Public
8 Health, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, South
9 Africa

10 Salome Charalambous, MBBS, MSc, PhD. The Aurum Institute, Johannesburg, South Africa
11 and School of Public Health, Faculty of Health Sciences, University of the Witwatersrand,
12 Johannesburg, South Africa

13 Katherine L Fielding, BSc, MSc, PhD. London School of Hygiene & Tropical Medicine, London,
14 United Kingdom and School of Public Health, Faculty of Health Sciences, University of the
15 Witwatersrand, Johannesburg, South Africa

16 Christopher J Hoffmann, MD, MPH. Johns Hopkins University, Baltimore, USA

17 **Correspondence:** Jienchi Dorward, CAPRISA, Doris Duke Medical Research Institute, Nelson
18 R Mandela School of Medicine, University of KwaZulu-Natal, Private Bag X7, Congella 4013,
19 South Africa. Tel: +27 31 2604511 Fax: +27 31 2604549 Email: jienchi.dorward@gmail.com

Meetings where parts of data presented: Primary analysis of Thol'impilo trial presented at Conference on Retroviruses and Opportunistic Infections (CROI); Boston 2016.

Conflicts of Interest and Source of Funding: All authors report no financial disclosures or other conflicts of interest. The Thol'impilo trial was funded by a United States Agency for International Development (USAID) Cooperative Agreement AID-OAA-A-12-00028.

Running title: Risk factors for poor linkage-to-care

Word count: 3494

Abstract

Background: Poor linkage to HIV care is impeding achievement of UNAIDS 90-90-90 targets. This study aims to identify risk factors for poor linkage-to-care after HIV counselling and testing (HCT), thereby informing strategies to achieve 90-90-90.

Setting: The Thol'impilo trial was a large randomised controlled trial performed between 2012-2015 in South Africa, comparing different strategies to improve linkage-to-care amongst adults aged >18 years who tested HIV-positive at mobile clinic HCT.

Methods: In this secondary analysis, sociodemographic factors associated with time to linkage-to-care were identified using Cox regression.

Results: Of 2398 participants, 61% were female, with median age 33 years (interquartile range, [IQR]: 27-41) and median CD4 count 427 cells/mm³ (IQR: 287-595). 1101 (46%) had clinic verified linkage-to-care within 365 days of testing HIV-positive. In adjusted analysis, younger

age (<30 vs >40 years: adjusted hazard ratio [aHR] 0.58, 95% CI 0.50-0.68; 31-40 vs >40 years aHR 0.81, 95% CI 0.70-0.94, test for trend $p<0.001$), being male (aHR 0.86, 95% CI 0.76-0.98, $p=0.028$), not being South African (aHR 0.79, 95% CI 0.66-0.96, $p=0.014$), urban district (aHR 0.82, 95% CI 0.73-0.93, $p=0.002$), being employed (aHR 0.81, 95% CI 0.72-0.92, $p=0.001$), non-disclosure of HIV (aHR 0.63, 95% CI 0.56-0.72, $p<0.001$) and having higher CD4 counts (test for trend $p<0.001$), were all associated with decreased hazard of linkage-to-care.

Conclusion: Linkage-to-care was low in this relatively large cohort. Increasing linkage-to-care requires innovative, evidence based interventions particularly targeting individuals who are younger, male, immigrant, urban, employed and reluctant to disclose their HIV status.

Key words: Linkage-to-care, HIV care cascade, 90-90-90, HIV counselling and testing, South Africa

Introduction

Increased access to antiretroviral therapy (ART) has changed the face of the global HIV epidemic, with an estimated 17.0 million people on ART in 2015, and annual AIDS-related deaths down by 43% compared to 2003.¹ In order to achieve universal ART coverage, and with the aim of ending the AIDS epidemic by 2030, UNAIDS have set the 90-90-90 targets, which focus on increased HIV testing (90% of PLHIV to know their status), increased linkage to HIV care (90% of PLHIV who know their status to be on ART), and optimal adherence and retention in care (90% of PLHIV on ART to be virally suppressed).² Achieving these targets would result in viral suppression amongst 73% of all PLHIV.

60 Attaining high levels of population viral suppression has promise as an HIV prevention strategy,
61 and is being tested in several large clinical trials in Southern Africa using a universal test and
62 treat approach.³ Two such studies, ANRS Treatment as Prevention (TasP) and PopART
63 HPTN071, have reported high levels of home based HIV testing coverage (92% and 87-90%
64 respectively), but poor linkage to HIV care (36% and 50% respectively at 6 months after
65 diagnosis).^{4,5} Despite 93% of those on ART being virally suppressed in TasP, poor linkage-to-
66 care resulted in population viral suppression of only 42%, and no decrease in HIV incidence.⁴

67 Recent evidence suggests that community based HIV counselling and testing (HCT), combining
68 mobile clinic and home based approaches, can rapidly achieve population wide testing targets
69 (the 'first 90').⁶ Mobile clinic HCT reaches different populations compared to home and
70 healthcare facility HCT,⁷ and has been shown to test higher proportions of 'hard to reach'
71 groups.⁸ However, low linkage-to-care from mobile HCT remains problematic, with a systematic
72 review finding only 37% in care 2-10 months after testing HIV-positive.⁸ Increasing linkage-to-
73 care from mobile HCT will be crucial to achieving the 90-90-90 targets.

74 The evidence regarding interventions that improve linkage-to-care from community based HCT
75 is mixed. Point of care (POC) CD4 count testing at diagnosis,^{9,10} care facilitation counselling¹¹
76 and peer support^{12,13} have led to increased linkage-to-care in some studies, but these results
77 have not been consistently replicated.^{11,14,15} Further evidence regarding effective interventions,
78 and which individuals these interventions should target, is needed for each HCT modality,
79 especially given the differences in the populations that each modality reaches.^{7,8} Studies of
80 mobile HCT suggest that individuals who have not disclosed their HIV status,¹⁶⁻¹⁸ or have CD4

counts >350 cells/ mm³^{16,19} have decreased linkage-to-care, while the evidence regarding other individual factors (e.g. age, sex, income and education level) is varied.^{16–21}

Here, we aim to identify sociodemographic factors associated with time to linkage-to-care, using data from an individually randomised controlled trial (RCT) which assessed mobile clinic HCT interventions in South Africa.

Methods

Study design and setting: The Thol'impilo trial

The Thol'impilo trial was a large, pragmatic, RCT conducted between 2013-2015 in Gauteng and Limpopo provinces.¹¹ Mobile HCT units were used in workplaces, community spaces, commercial shopping areas and public events. Adults aged >18 years who tested HIV-positive, were not currently receiving HIV care, were able to provide informed consent and planned to remain in South Africa for at least six months were eligible for enrolment. At enrolment, participants were randomised to receive either routine referral to HIV clinic of their choice (standard of care [SOC]), or SOC and POC CD4 testing, or SOC and POC CD4 testing and care facilitation counselling,²² or SOC and POC CD4 and transportation assistance vouchers. Participants were followed up by telephone and/or home visits at 90, 180 and 365 days to assess disclosure of HIV status and self-reported linkage to HIV care. Self-reported linkage-to-care at any public or private health facility in South Africa was verified by the study team, who visited the facility to perform case note abstraction using clinical charts, registers and/or electronic records. If no records were found, the participant was re-contacted to clarify which facility they had attended and possible names they may have used. Additional searches were

then performed using this information. National Health Laboratory Service (NHLS) data, (matched on name, date of birth, clinic and date range), were searched for further evidence of linkage-to-care for all participants, irrespective of self-report. Individuals were defined as having verified linkage-to-care if any evidence of registering for or receiving HIV care was found, including but not limited to ART initiation. The primary outcome was self-reported linkage-to-care within 90 days of testing HIV-positive and has been reported elsewhere.¹¹ In brief, using Cox regression, there was no difference in self-reported linkage-to-care at 90 days between the four arms. However, there was increased verified linkage-to-care at 90 days in the POC CD4 and care facilitation counselling arm compared to SOC (hazard ratio [HR] 1.4, 95% confidence interval [CI] 1.1-1.7, $p=0.001$). Overall, 31.9% of participants had verified linkage-to-care within 90 days of testing HIV-positive.¹¹

Study enrolment occurred between March 2013 and October 2014, during which time the South African Department of Health CD4 threshold for ART initiation was <350 cells/mm³. This was expanded to <500 cells/mm³ in January 2015.²³

Population included in this secondary analysis

All individuals enrolled into the Thol'impilo trial, excluding individuals found, post-enrolment, to be already in HIV care, were included in this secondary analysis.

Definition of outcomes and explanatory variables

Sociodemographic data were collected at study enrolment. Participants were asked to choose (or if unable to choose, were recommended) a suitable HIV clinic to which they could be referred for ongoing HIV care. Distance from home to HIV referral clinic was calculated using

global positioning system (GPS) data. Participants were asked at follow up whether they had disclosed their HIV status, and if so, the date of disclosure. These data were used to generate a time updated explanatory variable for disclosure prior to linkage-to-care.

In follow up interviews some participants acknowledged inaccurately reporting linkage-to-care to the study team, presumably due to social desirability.^{16,17} Therefore, for the present analysis, verified linkage-to-care by 365 days after testing HIV-positive was used as the primary outcome. Individuals who had no verified linkage-to-care were censored at death or at 365 days after testing HIV-positive (whichever was earliest). A second analysis was performed amongst a subset of participants with verified linkage-to-care, to assess factors associated with changing referral clinic; defined as verified linkage-to-care at a different clinic from the clinic they chose/were referred to at enrolment. This was conducted to provide further insight into supporting and documenting linkage-to-care following HCT.

Statistical methods

A descriptive analysis of the data was performed to explore the baseline characteristics of the study population. Associations between baseline variables and time to linkage-to-care were analysed using Cox regression and Kaplan Meier proportions. Ordered categorical variables were tested for a linear trend and departures from linear trend using the likelihood ratio test (LRT). Sociodemographic variables which were associated with linkage-to-care in univariable analysis (LRT $p < 0.1$), and for which there were no missing data (complete case analysis), were included in a multivariable Cox regression model and retained if $p < 0.1$. Proportional hazards were assessed by testing for interactions between each variable and time period (0-90 days versus 90-365 days in accordance with recommended timelines for analysing linkage-to-care).²⁴

Sensitivity analyses were conducted, in which variables with incomplete data (income, distance to clinic, disclosure and CD4 count) were included in separate multivariable models. Evidence from a previous study¹⁷ suggested that sex may modify the effect of disclosure on linkage-to-care and was explored *a priori* in multivariable analysis.

The subset of participants who had verified linkage-to-care were included in a second analysis to assess the association between sociodemographic variables and the outcome of changing referral clinic. As this outcome was common, log-binomial models were used.²⁵ Variables that were associated with changing referral clinic in univariable analysis were included in a multivariable log-binomial model using a similar modelling approach as for the primary outcome.

Stata 14.0 was used for all analyses (STATA Corp. College Park, Texas, USA). Ethical approval for this secondary analysis was obtained from the London School of Hygiene & Tropical Medicine Ethics Committee (ref:11180 /RR/4515). Overall approval was obtained from the University of the Witwatersrand and Johns Hopkins University. The Thol'impilo trial was registered with ClinicalTrials.gov, NCT02271074. All participants completed written informed consent.

Results

Baseline characteristics

A total of 2558 participants were enrolled in the Thol'impilo trial between March 2013 and October 2014, of whom 2398 were eligible for this analysis. Participants were predominantly female (61%), employed (57%) and of South African origin (86%) (see Table, Supplemental

Digital Content 1), with median age of 33 years (interquartile range, [IQR]: 27, 41). The majority (62%) were tested in the urban/peri-urban district of Ekurhuleni (Gauteng province), as opposed to rural Sekhukhune (Limpopo province). Routine HIV testing (as opposed to testing due to symptoms or concern of having been exposed to HIV) was reported by 81% of participants, and first time testing by 35%. Baseline characteristics were similar between study arms.¹¹ Of the 1769 who had a POC CD4 result, median CD4 count was 427 cells/mm³ (IQR: 287-595) and 64% had a CD4 count >350 cells/mm³. Baseline data on income were missing for 21% of participants. Lack of formal addresses complicated the identification of home GPS co-ordinates, meaning that distance from home to referral clinic was missing for 5% of participants. Data on disclosure of HIV status to another adult was collected at some point during follow up for 1982 (83%) participants. 1214 (51%) participants reported disclosure of HIV status to another adult prior to linking to any care, while 768 (32%) had not yet disclosed their HIV status, or if they had, had done so after linkage-to-care.

Linkage-to-care

Participants were followed up to endpoint or censoring date over 1539 person-years at risk. At 365 days, 1101 (46%) participants had verified linkage-to-care, with median time to verified linkage-to-care of 30 days (IQR: 5, 126). 624 (26%) participants had no verified linkage-to-care but remained in follow up, and 640 (27%) were lost to follow up, despite multiple attempts at telephone contact/home visits and searching of National Health Laboratory Service and national civil registry death records. A further 33 (1.4%) died before linking to care.

In univariable analysis there was evidence that younger age (test for trend $p < 0.001$), male sex, being employed, testing in the more urban district, not being from South Africa, attaining

secondary education or higher, higher household incomes (test for trend $p=0.002$), routine HIV testing, non-disclosure of HIV status, and higher CD4 count (test for trend $p<0.001$) were associated with decreased hazard of linkage-to-care (Table 1 and Figure 1). In a complete case, adjusted analysis younger age (<30 vs >40 years: adjusted hazard ratio [aHR] 0.58, 95% CI 0.50-0.68; 31-40 vs >40 years aHR 0.81, 95% CI 0.70-0.94), being male (aHR 0.86, 95% CI 0.76-0.98), testing in the more urban district (aHR 0.82, 95% CI 0.73-0.93), being employed (aHR 0.81, 95% CI 0.72-0.92) and not being South African (aHR 0.79, 95% CI 0.66-0.96) were all associated with decreased hazard of linkage-to-care (Table 1). In separate sensitivity analyses (each adjusting for age, sex, country of origin, employment status and district), having a higher CD4 count (test for trend $p<0.001$), non-disclosure of HIV status (aHR 0.63, 95% CI 0.56-0.72) and higher household income (test for trend $p=0.03$) were also associated with decreased hazard of linkage-to-care (Table 1), while distance from home to referral clinic was not associated with time to linkage-to-care (test for trend $p=0.13$). Adjusting for study arm did not confound any of the above associations.

In adjusted analyses, there was evidence of non-proportional hazards for sex and CD4 count (Table 2). The hazard for linkage-to-care was similar for men and women in the first 90 days after enrolment (aHR 0.95, 95% CI 0.81-1.11), but decreased for men compared to women after 90 days (aHR 0.69, 95% CI 0.54-0.87, p -value for interaction $p=0.021$). Further, the effect of CD4 count on linkage-to-care was strongest in the first 90 days since enrolment (p -value for interaction $p=0.001$). There was some evidence that the effect of non-disclosure on time to linkage-to-care was stronger in men (aHR 0.53, 95% CI 0.42-0.66) compared to women (aHR 0.70, 95% CI 0.60-0.82, p -value for interaction $p=0.04$), when adjusting for age, country of origin, district and employment.

Changing referral clinic

Of the 1101 participants who linked to care, 485 (44%) had linked to a different clinic from the clinic they chose/were referred to following testing HIV-positive at enrolment. In adjusted analysis, younger age (<30 versus >40 years: adjusted risk ratio [aRR] 1.21, 95% CI 1.02-1.43), testing in the more urban district (aRR 1.37, 95% CI 1.17-1.60), living further from the referral clinic (>10 versus <5km: aRR 1.43, 95%CI 1.20-1.70), and not intending to walk to clinic (aRR 1.44, 95% CI 1.22-1.70) were associated with increased risk for changing referral clinic (Table 3).

Discussion

In this relatively large cohort, verified linkage-to-care at 365 days was low (46%), which is consistent with other studies from mobile HCT in Southern Africa.^{16,18,19,21,26} Identifying and supporting those individuals at risk of not linking to care will be crucial to increasing ART coverage and achieving the 90-90-90 targets. Here, we present evidence that younger age, male sex, being employed, testing in a more urban district, not being from South Africa, higher CD4 counts and non-disclosure of HIV status (especially for men) were associated with decreased hazard of linkage-to-care.

Previous findings from Southern Africa on the association between age and linkage-to-care from mobile HCT have been mixed. Two studies found evidence of an association between younger age and decreased linkage-to-care in adjusted analyses.^{17,21} Four studies found no evidence of any association, but were variously limited by using self-reported linkage-to-care,^{16,18-20} not conducting an adjusted analysis^{16,18,20} and not using time to event analysis.^{16,20} This may explain

the difference with results presented here, which showed a dose response relationship between younger age and decreased hazard of linkage-to-care. Furthermore, a large, recent study of time from HIV *infection* to linkage-to-care in rural South Africa, found a strong association between younger age and longer time to linkage-to-care.²⁷ Given high HIV incidence rates amongst young people (particularly women) in South Africa^{28,29} it is crucial that interventions to increase HCT and subsequent linkage-to-care are targeted at this group.

Linkage-to-care was similar for men and women up to 90 days, but was lower in men during the 90-365 days after testing. This is consistent with the literature, in which studies from both home and mobile HCT with shorter follow up times (less than 180 days) have failed to demonstrate an association between sex and linkage-to-care,^{16,18,21,30-32} in contrast to studies with longer follow up.^{17,27,33} This may be due to sex differentiated behavioural factors over time, or women becoming pregnant during follow up and therefore continuing to link to integrated HIV and antenatal care.

HIV care in the South African public system is free of charge, regardless of citizenship status. Nevertheless, our finding that non-South Africans were less likely to link to care is consistent with literature identifying barriers to accessing healthcare for immigrants,³⁴ which include xenophobia,³⁵ language problems and misconceptions by service providers regarding healthcare legislation.³⁶ Given the high proportion of foreign nationals living in some parts of South Africa,³⁷ further research into interventions that promote equitable linkage-to-care is needed.

Work places were often used as mobile HCT sites by the study team, and this is reflected in the high proportion (57%) of employed participants compared to national averages.³⁸ Being

employed was a risk factor for decreased hazard of linkage-to-care. This association has only been shown in one previous study from mobile HCT,¹⁶ although difficulty finding time to attend clinic due to work commitments has been reported as a barrier to entering care in previous qualitative studies.³⁹ Opening clinics outside of working hours, or liaising with employers to increase clinic access may increase linkage-to-care for employed PLHIV.

Distance from home to referral clinic was not associated with time to linkage-to-care in univariate or multivariate sensitivity analysis. Nevertheless, participants in the more urban district were less likely to link to care compared to the rural district. This may be due to differences in rural/urban lifestyle, more mobile populations in urban centres,⁴⁰ or variations in the quality of health services between districts. Anecdotal reports and clinic use data (unpublished) suggested that patient numbers and waiting times were lower in the rural clinics covered by the Thol'impilo trial. Previous qualitative studies from Southern Africa have reported long clinic waiting times and poor quality services to be important barriers to care.^{39,41} Research into cost-effective interventions that remove clinic-level barriers to facilitate linkage-to-care is needed.⁴²

The association between higher household income and decreased hazard of linkage-to-care, albeit weak, is difficult to explain, and has not been demonstrated in previous studies.

Individuals with higher incomes may be more likely to attend private clinics, where verification of linkage-to-care was more difficult (although still sought). However, this should not have been a major problem as only 2% of study participants chose to be referred to a private/non-governmental clinic at enrolment.

274 Disclosure of HIV status was not ascertained at baseline (as participants had only just tested
275 HIV-positive) but was captured at some point during follow up for 83% of participants. Amongst
276 these participants there was a strong association between disclosure of HIV and subsequent
277 linkage-to-care, which is consistent with other studies from Southern Africa.^{16–18,31} However, the
278 mechanism of the association, and potential interaction with male sex, requires further
279 investigation. Disclosure may directly lead to assistance with accessing care, or be a marker of
280 more supportive social networks and/or decreased stigma, that facilitates engagement with HIV
281 services.⁴³ If it is the former, then carefully supporting individuals to disclose their HIV status
282 through, for example, more regular and targeted counselling, may increase linkage-to-care.

283 The effect of CD4 count was strongest in the first 90 days from enrolment, possibly due to the
284 motivating effect of knowing one's CD4 count decreasing with time. Individuals with CD4 counts
285 >350 cells/mm³ were not eligible for ART during the study enrolment period, and are also less
286 likely to suffer from HIV related illness, so they may not have felt the need to enter into HIV
287 care. Some participants with CD4 >350 cells/mm³ also reported being turned away by clinic staff
288 due to not being eligible for ART (despite the need for non-ART HIV care like TB screening).
289 Now that international and South African national guidelines advocate the removal of CD4
290 thresholds for ART initiation,⁴⁴ it will be crucial to establish whether individuals with higher CD4
291 counts remain less likely to link to care.

292 Lastly, there is increased interest in initiation of ART on the day of diagnosis as a strategy to
293 increase linkage to and retention in care.^{45,46} Our finding that a large proportion (44%) of
294 individuals who entered into care did so at a different clinic from that which they were referred to
295 has implications for the design of same day ART initiation interventions. If individuals test HIV-

296 positive in community HCT, and are started on ART that day, arrangements must be flexible
297 enough for participants to receive follow up at a range of clinics other than the one to which they
298 are originally referred. This is particularly relevant for younger individuals and those who test in
299 urban districts, where there are likely to be a wider range of nearby clinics to choose from. It is
300 possible that concerns regarding disclosure of HIV status lead some participants to change
301 clinic selection. If this was an important factor in clinic switches, a similar phenomenon may be
302 observed after facility based HCT. Clients may seek care at a different clinic after testing HIV-
303 positive to minimize disclosure of their status within the community.

304 This is the largest Southern African study assessing socio-demographic factors associated with
305 linkage-to-care following mobile HCT that we are aware of. Weaknesses of the study include
306 missing data for some variables, lack of data on internal migration and mobility of participants,
307 difficulties establishing home GPS co-ordinates, and the potential for selection bias due to
308 difficulties contacting participants and subsequent loss to follow up. Furthermore, despite
309 extensive efforts by the study team, inadequate record keeping in clinics may have led to
310 underestimation of verified linkage-to-care. Overall, the large sample size, including urban and
311 rural districts, long follow up time, adjustment for multiple potential confounders which were
312 measured at baseline, verification of linkage-to-care using clinic and national laboratory records,
313 inclusion of linkage-to-care at any health facility, and use of time to event analysis, strengthen
314 the evidence presented here when compared to previous studies of linkage-to-care from mobile
315 HCT.

Conclusions

Low rates of linkage-to-care, as seen in this large cohort, remain a significant challenge to the achievement of the 90-90-90 targets and universal test and treat as a successful HIV prevention strategy.⁴ While recent evidence suggests that a combination of mobile and home based HCT can rapidly attain the 'first 90',⁶ effective, evidence based interventions that increase linkage-to-care are urgently needed to reach the 'second 90'. Our analysis demonstrates that, particularly when using mobile HCT, these interventions should focus on individuals who are younger, male, immigrant, urban, employed, and reluctant to disclose their HIV status.

Acknowledgments

We would like to thank the United States Agency for International Development (USAID) Cooperative Agreement AID-OAA-A-12-00028 for funding the study, as well as the study team and participants for their work and involvement.

References

1. Joint United Nations Programme on HIV/AIDS. *Global AIDS Update 2016*. Geneva, Switzerland; 2016.
2. Joint United Nations Programme on HIV/AIDS. *90-90-90 An Ambitious Treatment Target to Help End the AIDS Epidemic*. Geneva, Switzerland; 2014.

- 335 3. Hayes R, Fidler S, Cori A, et al. HIV Treatment-As-Prevention Research: Taking the Right
336 Road at the Crossroads. *PLoS Med.* 2015;12:1-6.
- 337 4. Iwuji CC, Orne-Gliemann J, Balestre E, et al. The impact of universal test and treat on HIV
338 incidence in a rural South African population: ANRS 12249 TasP trial, 2012–2016 [FRAC0105LB].
339 In: *Proceedings of the 21st International AIDS Conference*. Durban; 2016.
- 340 5. Hayes R, Floyd S, Schaap A, et al. A universal testing and treatment intervention to
341 improve HIV control: One-year results from intervention communities in Zambia in the HPTN
342 071 (PopART) cluster-randomised trial. *PLoS Med.* 2017;14:1-22.
- 343 6. Chamie G, Clark TD, Kabami J, et al. A hybrid mobile approach for population-wide HIV
344 testing in rural east Africa: An observational study. *Lancet HIV.* 2016;3:e111-e119.
- 345 7. Labhardt ND, Motlomelo M, Cerutti B, et al. Home-Based Versus Mobile Clinic HIV
346 Testing and Counseling in Rural Lesotho: A Cluster-Randomized Trial. *PLoS Med.*
347 2014;11:e1001768.
- 348 8. Sharma M, Ying R, Tarr G, et al. A systematic review and meta-analysis of community
349 and facility-based approaches to address gaps in HIV testing and linkage in sub-Saharan Africa.
350 *Nature.* 2015;528:S77-S85.
- 351 9. Wynberg E, Cooke G, Shroufi A, et al. Impact of point-of-care CD4 testing on linkage to
352 HIV care: a systematic review. *J Int AIDS Soc.* 2014;17:18809.

- 353 10. Vojnov L, Markby J, Boeke C, et al. POC CD4 Testing Improves Linkage to HIV Care and
354 Timeliness of ART Initiation in a Public Health Approach: A Systematic Review and Meta-
355 Analysis. *PLoS One*. 2016;11:e0155256.
- 356 11. Hoffmann CJ, Mabuto T, Ginindza S, et al. Strategies to Accelerate HIV Care and
357 Antiretroviral Therapy Initiation After HIV Diagnosis. *J Acquir Immune Defic Syndr*. 2017;75:540-
358 547.
- 359 12. Barnabas R V, Rooyen H Van, Tumwesigye E, et al. Initiation of antiretroviral therapy and
360 viral suppression after home HIV testing and counselling in KwaZulu-Natal, South Africa, and
361 Mbarara district, Uganda: a prospective, observational intervention study. *Lancet HIV*.
362 2014;1:e68-e76.
- 363 13. Aliyu MH, Blevins M, Audet CM, et al. Integrated prevention of mother-to-child HIV
364 transmission services, antiretroviral therapy initiation, and maternal and infant retention in
365 care in rural north-central Nigeria: a cluster-randomised controlled trial. *Lancet HIV*.
366 2016;3:e202-11.
- 367 14. Bassett I V, Coleman SM, Giddy J, et al. Sizanani: A Randomized Trial of Health System
368 Navigators to Improve Linkage to HIV and TB Care in South Africa. *J Acquir Immune Defic Syndr*.
369 2016;73:154-160.
- 370 15. Govindasamy D, Meghij J, Negussi EK, et al. Interventions to improve or facilitate linkage
371 to or retention in pre-ART (HIV) care and initiation of ART in low- and middle- income settings -
372 a systematic review. *J Int AIDS Soc*. 2014;17:19032.

- 373 16. Govindasamy D, van Schaik N, Kranzer K, et al. Linkage to HIV care from a mobile testing
374 unit in South Africa by different CD4 count strata. *J Acquir Immune Defic Syndr*. 2011;58:344-
375 352.
- 376 17. Hatcher AM, Turan JM, Leslie HH, et al. Predictors of Linkage to Care Following
377 Community-Based HIV Counseling and Testing in Rural Kenya. 2012:1295-1307.
- 378 18. Govindasamy D, Kranzer K, Van Schaik N, et al. Linkage to HIV, TB and non-
379 communicable disease care from a mobile testing unit in Cape Town, South Africa. *PLoS One*.
380 2013;8:1-11.
- 381 19. Larson BA, Schnippel K, Ndibongo B, et al. Rapid point-of-care CD4 testing at mobile HIV
382 testing sites to increase linkage to care: an evaluation of a pilot program in South Africa. *J*
383 *Acquir Immune Defic Syndr*. 2012;61:e13-7.
- 384 20. van Zyl MA, Brown LL, Pahl K. Using a call center to encourage linkage to care following
385 mobile HIV counseling and testing. *AIDS Care*. 2015;27:921-925.
- 386 21. Parker LA, Jobanputra K, Rusike L, et al. Feasibility and effectiveness of two community-
387 based HIV testing models in rural Swaziland. *Trop Med Int Heal*. 2015;20:893-902.
- 388 22. Mabuto T, Charalambous S, Hoffmann CJ. Effective Interpersonal Health Communication
389 for Linkage to Care After HIV Diagnosis in South Africa. *J Acquir Immune Defic Syndr*.
390 2017;74:23-28.

- 391 23. South African National Department of Health. *National Consolidated Guidelines for the*
392 *Prevention of Mother to Child Transmission of HIV (PMTCT) and the Management of HIV in*
393 *Children, Adolescents and Adults*. Pretoria, South Africa; 2015.
- 394 24. Fox MP, Rosen S. Retention of Adult Patients on Antiretroviral Therapy in Low- and
395 Middle-Income Countries. *J Acquir Immune Defic Syndr*. 2015;69:98-108.
- 396 25. Localio AR, Margolis DJ, Berlin JA. Relative risks and confidence intervals were easily
397 computed indirectly from multivariable logistic regression. *J Clin Epidemiol*. 2007;60:874-882.
- 398 26. Bassett I, Regan S, Luthuli P, et al. Linkage to care following community-based mobile
399 HIV testing compared with clinic-based testing in Umlazi Township, Durban, South Africa. *HIV*
400 *Med*. 2014;15:367-372.
- 401 27. Maheu-Giroux M, Tanser F, Boily M-C, et al. Determinants of time from HIV infection to
402 linkage-to-care in rural KwaZulu-Natal, South Africa. *AIDS*. 2017;31:1017-1024.
- 403 28. Shisana, O, Rehle, T, Simbayi LC, Zuma, K, Jooste, S, Zungu N, Labadarios, D, Onoya DEA.
404 South African National HIV Prevalence, Incidence and Behaviour Survey, 2012. *HSRC Press*.
405 2014:194.
- 406 29. Dellar RC, Dlamini S, Karim QA. Adolescent girls and young women: key populations for
407 HIV epidemic control. *J Int AIDS Soc*. 2015;18:19408.
- 408 30. Larson BA, Brennan A, McNamara L, et al. Early loss to follow up after enrolment in pre-
409 ART care at a large public clinic in Johannesburg, South Africa. *Trop Med Int Heal*. 2010;15:43-
410 47.

- 411 31. Medley A, Ackers M, Amolloh M, et al. Early Uptake of HIV Clinical Care After Testing
412 HIV-Positive During Home-Based Testing and Counseling in Western Kenya. *AIDS Behav.*
413 2013;224-234.
- 414 32. PLazy M, Farouki K El, Iwuji C, et al. Access to HIV care in the context of universal test
415 and treat²: challenges within the ANRS 12249 TasP cluster-randomized trial in rural South
416 Africa. *J Int AIDS Soc.* 2016;19:20913.
- 417 33. Genberg BL, Naanyu V, Wachira J, et al. Linkage to and engagement in HIV care in
418 western Kenya: an observational study using population-based estimates from home-based
419 counselling and testing. *Lancet HIV.* 2015;2:e20-e26.
- 420 34. Vearey J. Learning from HIV: Exploring migration and health in South Africa. *Glob Public*
421 *Health.* 2012;7:58-70.
- 422 35. Crush J, Tawodzera G. Medical Xenophobia and Zimbabwean Migrant Access to Public
423 Health Services in South Africa. *J Ethn Migr Stud.* 2014;40:655-670.
- 424 36. Vearey J. Migration, access to ART, and survivalist livelihood strategies in Johannesburg.
425 *African J AIDS Res.* 2008;7:361-374.
- 426 37. Statistics South Africa. *Mid-Year Population Estimates 2015.* Pretoria, South Africa;
427 2015.
- 428 38. Statistics South Africa. *Quarterly Labour Force Survey Quarter 4:2016.* Pretoria, South
429 Africa; 2016.

- 430 39. Govindasamy D, Ford N, Kranzer K. Risk factors, barriers and facilitators for linkage to
431 antiretroviral therapy care. *AIDS*. 2012;26:2059-2067.
- 432 40. Tanser F, Bärnighausen T, Vandormael A, et al. HIV treatment cascade in migrants and
433 mobile populations. *Curr Opin HIV AIDS*. 2015;10:430-438.
- 434 41. Layer EH, Kennedy CE, Beckham SW, et al. Multi-level factors affecting entry into and
435 engagement in the HIV continuum of care in Iringa, Tanzania. *PLoS One*. 2014;9:e104961.
- 436 42. Amanyire G, Semitala FC, Namusobya J, et al. Effects of a multicomponent intervention
437 to streamline initiation of antiretroviral therapy in Africa: a stepped-wedge cluster-randomised
438 trial. *Lancet HIV*. 2016;3:e539-e548.
- 439 43. Maeri I, El Ayadi A, Getahun M, et al. "How can I tell?" Consequences of HIV status
440 disclosure among couples in eastern African communities in the context of an ongoing HIV
441 "test-and-treat" trial. *AIDS Care*. 2016;28:59-66.
- 442 44. World Health Organisation. *Consolidated Guidelines on the Use of Antiretroviral Drugs*
443 *for Treating and Preventing HIV Infection: Recommendations for a Public Health Approach – 2nd*
444 *Ed*. Geneva, Switzerland; 2016.
- 445 45. Rosen S, Maskew M, Fox MP, et al. Initiating Antiretroviral Therapy for HIV at a Patient's
446 First Clinic Visit: The RapIT Randomized Controlled Trial. *PLOS Med*. 2016;13:e1002015.
- 447 46. Labhardt ND, Ringera I, Lejone TI, et al. Same day ART initiation versus clinic-based pre-
448 ART assessment and counselling for individuals newly tested HIV-positive during community-

449 based HIV testing in rural Lesotho – a randomized controlled trial (CASCADE trial). *BMC Public*
450 *Health*. 2016;1-8.

451

452 **Figure captions**

453 Figure 1: Kaplan Meier estimates for linkage to care by 365 days, by risk factor

454

Tables

Table 1: Analysis of factors associated with verified linkage-to-care at 365 days (n=2398)

Variable		Linked to care at 365 days (n/N)	KM risk of linkage-to-care by 90 days	Unadjusted HR	p-value	Adjusted HR * (95% CI)	p-value
Age, years	>40	333/602	0.39	1	<0.001	1	<0.001 [†]
	31-40	395/833	0.34	0.80		0.81 (0.70-0.94)	
	18-30	373/963	0.26	0.60		0.58 (0.50-0.68)	
Sex	Female	713/1472	0.33	1	0.006	1	0.028
	Male	388/926	0.31	0.84		0.86 (0.76-0.98)	
Country of origin	South Africa	977/2062	0.33	1	<0.001	1	0.014
	Other	124/336	0.25	0.71		0.79 (0.66-0.96)	
District	Rural	464/916	0.37	1	<0.001	1	0.002
	Urban/peri-urban	637/1482	0.29	0.78		0.82 (0.73-0.93)	
Employment	Unemployed	505/1026	0.34	1	0.006	1	0.001
	Employed/Other	596/1372	0.30	0.85		0.81 (0.72-0.92)	
Highest level of education	None/primary	272/548	0.36	1	0.034	-	-
	Secondary/higher	829/1850	0.31	0.86		-	
Dwelling	Formal	718/1542	0.33	1	0.374	-	-
	Informal	383/856	0.31	0.95		-	
Household income, South African Rand/month (n=1899)	<1000	291/585	0.34	1	0.022	1 ^{††}	0.032 [†]
	1001-2000	249/519	0.35	0.97		1.00 (0.84-1.19)	
	2001-4000	222/501	0.31	0.86		0.95 (0.79-1.15)	
	>4000	114/294	0.25	0.72		0.75 (0.60-0.95)	

Distance to referral clinic, km (n=2279)	<5	605/1303	0.32	1	0.991	-	-
	5-10	170/360	0.31	1.01		-	
	>10	284/616	0.34	1.01		-	
CD4, cells/mm ³ (n=1769)	<200	138/223	0.51	1	<0.001	1 ^{††}	<0.001
	201-350	228/408	0.44	0.83		0.87 (0.70-1.07)	†
	351-500	209/471	0.28	0.57		0.59 (0.47-0.73)	
	>500	255/667	0.24	0.47		0.46 (0.37-0.57)	
Relationship status	No relationship	181/361	0.36	1	0.166	-	-
	Co-habitation	681/1496	0.32	0.87		-	
	No co-habitation	239/541	0.30	0.84		-	
Walk to clinic?	No	688/1439	0.33	1	0.041	-	-
	Yes	413/959	0.30	0.88		-	
Routine HIV test?	No	234/466	0.37	1	0.024	-	-
	Yes	867/1932	0.31	0.84		-	
Previous HIV test and result	No test	373/845	0.31	1	0.530	-	-
	Positive	92/190	0.34	1.07		-	
	Negative	612/1306	0.32	1.12		-	
	Unknown result	24/57	0.30	0.91		-	
Disclosed HIV status? (n=1982)	Yes	644/1214	0.38	1	<0.001	1 ^{††}	<0.001
	No	356/768	0.32	0.85		0.63 (0.56-0.72)	1

*Age, sex, country of origin, employment and district adjusted for each other in complete case analysis.

†Test for linear trend

††Separate models, each adjusting for age, sex, country of origin, employment and district, were used for household income, CD4 and disclosure of HIV status, due to incomplete data.

KM Kaplan-Meier; HR Hazard Ratio; CI confidence interval

Table 2: Interaction between time since enrolment and sex (n=2398), and time since enrolment and CD4 count (n=1769)

Variable	Strata	Time since enrolment, days	
		<90	90-365
		Adjusted HR ^{††} (95% CI)	Adjusted HR ^{††} (95% CI)
Sex [*]	Female	1	1
	Male	0.95 (0.81-1.11)	0.69 (0.54-0.87)
CD4 [†] , cells/mm ³	<200	1	1
	201-350	0.86 (0.68-1.08)	0.94 (0.58-1.52)
	351-500	0.49 (0.38-0.63)	0.99 (0.63-1.56)
	>500	0.38 (0.30-0.49)	0.76 (0.49-1.19)

* p-value for interaction 0.021; [†] p-value for interaction 0.001; ^{††} adjusted for age, sex, country of origin, employment and district

HR hazard ratio; CI confidence interval

Table 3: Factors associated with changing referral clinic (n=1101)

Variable		Changed clinic (%)	Unadjusted RR (95% CI)	p-value	Adjusted RR * (95% CI)	p-value
Age, years	>40	135/333 (40.5)	1	0.023	1	0.048
	31-40	164/395 (41.5)	1.02 (0.86-1.22)		1.05 (0.88-1.25)	
	<30	186/373 (49.9)	1.23 (1.04-1.45)		1.21 (1.02-1.43)	
Sex	Female	312/713 (43.8)	1	0.791	1	0.604
	Male	173/388 (44.6)	1.02 (0.89-1.17)		1.04 (0.90-1.19)	
District	Rural	199/464 (42.9)	1	0.508	1	<0.001
	Urban/peri-urban	286/637 (44.9)	1.05 (0.91-1.20)		1.37 (1.17-1.60)	
Walk to clinic?	Yes	142/413 (34.4)	1	<0.001	1	<0.001
	No	343/688 (50.0)	1.44 (1.24-1.69)		1.44 (1.22-1.70)	
Distance to referral clinic, km (n=1059)	<5	228/605 (37.7)	1	<0.001	1	<0.001
	5-10	80/170 (52.9)	1.40 (1.18-1.67)		1.37 (1.15-1.64)	
	>10	142/284 (50.0)	1.32 (1.14-1.55)		1.43 (1.20-1.70)	

* Adjusted for all other variables in the table, n=1059 due to 42 participants with missing data for distance to clinic.

RR hazard ratio; CI confidence interval

Figure 1: Kaplan Meier estimates for linkage to care by 365 days, by risk factor

