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Linkage Case Management and Posthospitalization Outcomes in People With HIV

The Daraja Randomized Clinical Trial

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IMPORTANCE Despite the widespread availability of antiretroviral therapy (ART), people with HIV still experience high mortality after hospital admission.

OBJECTIVE To determine whether a linkage case management intervention (named "Daraja" ["bridge" in Kiswahili]) that was designed to address barriers to HIV care engagement could improve posthospital outcomes.

DESIGN, SETTING, AND PARTICIPANTS Single-blind, individually randomized clinical trial to evaluate the effectiveness of the Daraja intervention. The study was conducted in 20 hospitals in Northwestern Tanzania. Five hundred people with HIV who were either not treated (ART-naive) or had discontinued ART and were hospitalized for any reason were enrolled between March 2019 and February 2022. Participants were randomly assigned 1:1 to receive either the Daraja intervention or enhanced standard care and were followed up for 12 months through March 2023.

INTERVENTION The Daraja intervention group (n = 250) received up to 5 sessions conducted by a social worker at the hospital, in the home, and in the HIV clinic over a 3-month period. The enhanced standard care group (n = 250) received predischarge HIV counseling and assistance in scheduling an HIV clinic appointment.

MAIN OUTCOMES AND MEASURES The primary outcome was all-cause mortality at 12 months after enrollment. Secondary outcomes related to HIV clinic attendance, ART use, and viral load suppression were extracted from HIV medical records. Antiretroviral therapy adherence was self-reported and pharmacy records confirmed perfect adherence.

RESULTS The mean age was 37 (SD, 12) years, 76.8% were female, 35.0% had CD4 cell counts of less than 100/μL, and 80.4% were ART-naive. Intervention fidelity and uptake were high. A total of 85 participants (17.0%) died (43 in the intervention group; 42 in the enhanced standard care group); mortality did not differ by trial group (17.2% with intervention vs 16.8% with standard care; hazard ratio [HR], 1.01; 95% CI, 0.66-1.55; $P = .96$). The intervention, compared with enhanced standard care, reduced time to HIV clinic linkage (HR, 1.50; 95% CI, 1.24-1.82; $P < .001$) and ART initiation (HR, 1.56; 95% CI, 1.28-1.89; $P < .001$). Intervention participants also achieved higher rates of HIV clinic retention (87.4% vs 76.3%; $P = .005$), ART adherence (81.1% vs 67.6%; $P = .002$), and HIV viral load suppression (78.6% vs 67.1%; $P = .01$) at 12 months. The mean cost of the Daraja intervention was about US $22 per participant including startup costs.

CONCLUSIONS AND RELEVANCE Among hospitalized people with HIV, a linkage case management intervention did not reduce 12-month mortality outcomes. These findings may help inform decisions about the potential role of linkage case management among hospitalized people with HIV.

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Visual Abstract

Editorial

Supplemental content

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In 2022, about 630 000 people died from AIDS-related causes worldwide, with two-thirds of these deaths occurring in sub-Saharan Africa.[1,2] Despite successes in expanding the availability of HIV testing and treatment worldwide, people living with HIV still experience high rates of hospitalization,[3] and hospitalized people with HIV continue to have poor outcomes.[4,5] Improving care for hospitalized people with HIV will be critical for ending AIDS deaths.[6,7]

A 2022 systematic review pooled data from 29 cohorts and 92 781 all-cause hospitalizations for people with HIV worldwide. In total, 21% of all hospitalized people with HIV died in the first year after hospital discharge,[4] with even higher mortality rates reported from sub-Saharan Africa (30%).[4,8] Factors associated with posthospital mortality included more severe immunosuppression, less than primary-level education, longer hospitalization, and delayed linkage to HIV clinic care.

Linkage case management strategies targeted to the specific needs of hospitalized people with HIV accelerate post-discharge HIV clinic linkage and improve posthospital outcomes including time to initiation of antiretroviral therapy (ART).[9,10] One clinical trial of a peer mentor intervention for hospitalized people with HIV reported no benefit for post-hospital HIV clinic attendance or viral load suppression.[11] Another clinical trial of a case management intervention in hospitalized people with HIV and substance use disorders in the US yielded mixed results.[12] Working with the principal investigator of that trial (L.R.M.), an evidence-based, linkage case management strategy was adapted to the specific needs of hospitalized people with HIV in Tanzania.[13] This study hypothesized that a low-cost, case management intervention could reduce posthospital mortality in people with HIV by facilitating early HIV clinic linkage and ART initiation.

Key Points

Question Can a linkage case management intervention decrease mortality among people with HIV in Tanzania during the first year after hospital discharge?

Finding In this randomized clinical trial that involved 500 hospitalized people with HIV, a linkage case management intervention did not reduce 12-month mortality (17.2% with intervention vs 16.8% with standard care; hazard ratio, 1.01; 95% CI, 0.66-1.55; *P* = .96).

Meaning Among hospitalized people with HIV, linkage case management did not reduce 12-month mortality.

Methods

Study Design

This was a multisite randomized clinical trial conducted in Northwestern Tanzania. The protocol has been previously published.[13] Participants were enrolled from 20 inpatient health facilities in the Mwanza region (**Figure 1**). Data from the region revealed similar trends in posthospital mortality for people with HIV as in other areas of sub-Saharan Africa,[4] with 31% mortality in the first 3 months after hospital discharge, low rates of HIV clinic linkage in the first month after hospital discharge, and a strong association between HIV clinic nonlinkage and mortality.[8] According to Tanzanian national guidelines,[14] as with other countries in sub-Saharan Africa, HIV testing is recommended for all hospitalized patients. The hospital HIV team is consulted for every hospitalized person with HIV who is newly diagnosed or has discontinued ART. According to national guidelines, ART can be initiated in hospitalized people with HIV but only after completion of evaluation for opportunistic infections.[14] Hospitalized people with HIV are then scheduled to return to the hospital's HIV clinic within 2 weeks after discharge. All of these procedures are consistent with current World Health Organization (WHO) recommendations.[6] Outpatient HIV treatment services are provided free of charge.[14]

Ethical Approvals and Protocol

The study was approved by the ethical review committees of the National Institute for Medical Research in Tanzania (NIMR/HQ/R.8a/Vol. IX/2811), Weill Cornell Medicine (1804019134), and the London School of Hygiene and Tropical Medicine (16173). Written informed consent was obtained.[13] Intervention participants were not compensated for completing intervention sessions or phone calls. All participants were compensated with approximately US $4 per visit for participating in the baseline and 12-month follow-up surveys.

Three months after trial commencement, the protocol was revised to expand enrollment from a single hospital to all hospitals in Mwanza region and to reduce the period required to be not taking ART for discontinuation from more than 3 months to more than 7 days. These changes, made to increase enrollment and the generalizability of trial results, were approved by all ethical committees and reflected on ClinicalTrials.gov. There were no changes made to outcome measures. The final version of the protocol is available in Supplement 1). No interim analyses were conducted.

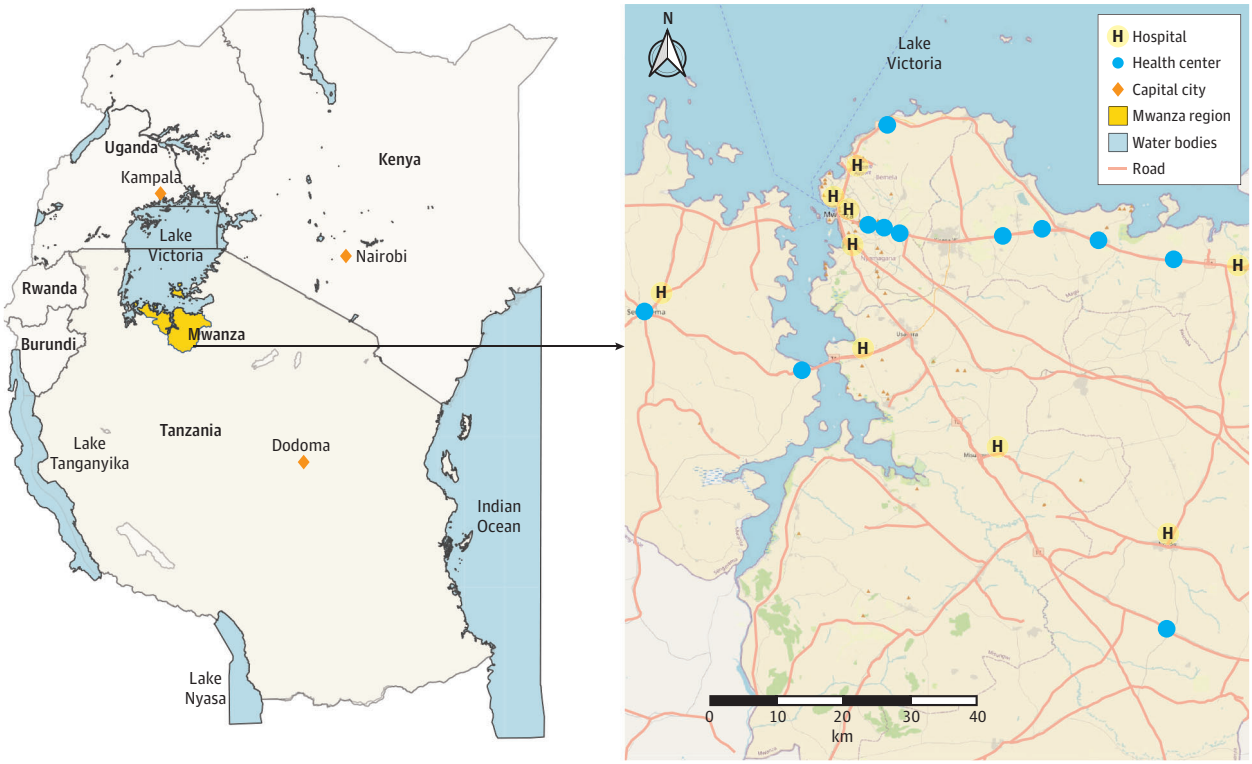
Study Population

People with HIV hospitalized for any reason at the participating health facilities were eligible for the study if they met the following criteria: (1) aged 18 years or older; (2) ART-naive or discontinued ART for more than 7 days before screening; (3) living in Mwanza region and planning to remain in the region for the next 24 months; (4) mental capacity to consent; and (5) access to a mobile phone. Informed consent was initiated at the time of discharge planning, approximately 2 to 3 days before discharge. A research nurse provided detailed information about the study.[13]

Randomization

Participants were randomized to the intervention or control group in a 1:1 ratio using a block randomization (4 per block) on the day before discharge. The allocation sequence was prepared before trial initiation and then sealed inside 500 numbered, opaque envelopes, which were opened by the

Figure 1. Map of the 20 Enrollment Sites for the Daraja Trial in Tanzania



Sites for enrollment included hospitals and health centers. All referral, regional, and district hospitals located in Mwanza region of Tanzania were included in this trial. All health centers within the study area also had inpatient facilities and were included.

research coordinator when participants were ready for randomization.

Intervention

Conceptual Model

The conceptual model guiding the intervention (eFigure 1 in Supplement 2), adapted from the Andersen Behavioral Model of Healthcare Utilization for Vulnerable Populations, builds on a pathway that requires access to health care in the form of HIV clinic linkage and ART initiation.[15] The Anti-Retroviral Treatment and Access to Services (ARTAS)[9,10] linkage case management intervention, guided by a similar conceptual model,[16] was adapted to specific challenges faced by people with HIV in Tanzania, including unemployment, traditional health beliefs, lack of transportation, lack of social support, stigma, and low perceived need for HIV care.[13] The adaptation process followed the steps of the ADAPT-ITT model (eAppendix 1 in Supplement 2).[17] The intervention was named "Daraja" ("bridge" in Kiswahili), envisioning that Daraja could bridge the gap between the hospital, the HIV clinic, and better health.

Linkage Case Management

Participants assigned to the intervention group received 5 sessions delivered by a social worker over a 3-month period. Each session lasted about 45 minutes. The first and second sessions were conducted in the hospital and in the participant's home, respectively. Three more sessions occurred either at the HIV clinic or at the participant's location of choice. The first session consisted of building rapport and identifying the participant's strengths. Sessions 2 to 4 focused on developing plans to achieve the participant's goals. The 2 most common goals were "return to work" and "live a healthy life with HIV." The fifth session focused on transitioning case management responsibilities to the participant's HIV primary care team. Social workers were also available by phone to speak with participants. During sessions 3 to 5, if the participant was too weak to walk, the social worker provided a voucher worth US $2 to facilitate travel.

The Daraja intervention was delivered by social workers with a degree in sociology or social work who underwent a minimum of 2 weeks of training on the 4 core components of the intervention: building an effective working relationship, utilizing the participant's strengths, facilitating the participant's ability to achieve their goals, and engaging formal and informal community resources. Training of social workers and implementation of the Daraja intervention were guided by the principles of Strength-Based Case Management, as in the original ARTAS intervention.[9,10] Five social workers conducted the intervention across all study sites (eTable 3 in Supplement 2). The number of participants treated by each social worker ranged from 21 to 77.

Enhanced Standard Care

All control group participants received a 30-minute counseling session by a trained nurse about the benefits of ART and HIV clinic attendance. To maximize clinic linkage in the control group, hospital nurses escorted participants to the hospital's HIV clinic, where an appointment was scheduled within 2 weeks.

Intervention Fidelity

An independent social scientist observed approximately 5% of sessions conducted by each social worker, rating the fidelity of the intervention session using a semistructured form assessing the 4 core elements of Daraja (eAppendix 2 and eTable 1 in Supplement 2).

Measures of Effectiveness

Baseline surveys were administered by research nurses after informed consent had been obtained but before randomization. These surveys were conducted in Kiswahili, using questions that have previously been translated and used in East Africa on demographics, alcohol use,[18,19] depression,[20] employment, HIV-related stigma,[21] social support,[22] and health-related quality of life.[23] Discharge diagnoses were provided by attending clinicians and were categorized according to WHO's *International Statistical Classification of Diseases and Related Health Problems, Tenth Revision* codes.

Safety

According to the safety monitoring plan (Supplement 1) and with support from the data and safety monitoring board, participants were monitored for loss of confidentiality, stigma, and other social harms secondary to the intervention.

Prespecified Outcomes

The primary outcome was all-cause mortality at 12 months. Death was confirmed by death certificates, hospital records, and/or verbal autopsy performed with 1 of the participant's designated alternate contacts.[24,25] Cause of death was assigned using a validated algorithm in accordance with WHO's verbal autopsy standards.[24,25] Secondary outcomes included (1) time to HIV clinic linkage after discharge; (2) time to ART initiation after discharge; (3) retention in care at 12 months, defined by an active ART prescription at 12 months provided at an HIV clinic visit; (4) ART adherence at 12 months, defined by a perfect score on the 3-day recall questionnaire[26] confirmed by pharmacy refill records; (5) achieving viral load suppression within 12 months, defined by an HIV RNA level of less than 1000 copies/μL; and (6) the incremental cost to implement and sustain the intervention. Secondary outcomes were extracted from medical records except ART adherence and the intervention cost. Time to HIV clinic linkage and ART initiation were determined by the date of the first HIV clinic visit and ART prescription abstracted from the medical record. ART adherence required both perfect adherence by self-report and an active prescription for ART. For patients who transferred care to another HIV clinic, medical record extraction was conducted at that site. Twelve-month outcomes were determined among all participants who were alive and remained in the study at 12 months. All outcomes were assessed by the research nurses, who underwent more than 1 month of trial-specific training. The research nurses were masked to intervention assignment. Additional prespecified secondary outcomes that were not included in this analysis were self-efficacy, stigma, social support, perceived need for HIV services, physical weakness, and intervention acceptability.

Statistical Analysis

The statistical analysis plan is contained in eAppendix 3 in Supplement 2. Outcomes were determined as described a priori.[13] The primary analysis compared all-cause mortality between the intervention and control groups using the log-rank test following the intention-to-treat principle. Time to linkage and ART initiation were also compared between groups using a log-rank test following the intention-to-treat principle. All time-to-event outcomes were analyzed by Kaplan-Meier curves and summarized in terms of Cox regression hazard ratios. Participants who withdrew from the study were censored at the time of withdrawal. Twelve-month HIV clinic retention, ART adherence, and HIV viral load suppression were treated as binary outcomes and compared between groups using the Fisher exact test. Participants who died or withdrew were excluded from these 12-month outcomes. Due to the individually randomized group treatment design of the study, additional sensitivity analyses were conducted to account for potential clustering at the level of intervention social workers. A robust standard error was calculated to adjust within-cluster correlation for outcomes. All statistical tests were 2-tailed with a significance level of .05. Data analyses were performed using R version 4.2 (R Core Team). A detailed micro-costing analysis was also conducted to estimate the resources needed to implement and sustain the Daraja intervention.[27]

Sample Size and Statistical Power

We performed sample size and power calculations for the primary outcome (12-month mortality) in the 2 independent study groups. With 500 participants and 10% lost to follow-up, the study had at least 80% power with $\alpha = .05$ to detect a 10% or greater absolute difference in all-cause mortality between the intervention group and the control group across the range of expected mortality rates.

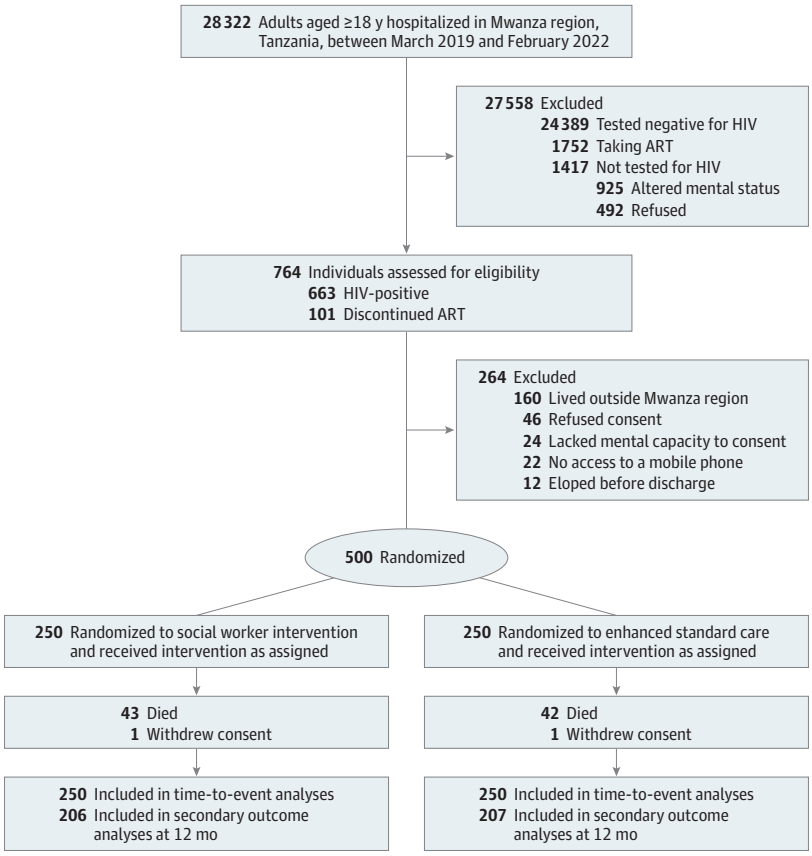
Results

Screening, Enrollment, and Follow-Up

Screening and enrollment were conducted between March 2019 and February 2022, with a pause from April 3, 2020, until August 18, 2020, due to COVID-19 directives from the Tanzanian government. Final follow-up was completed in March 2023.

During the study period, 28 322 newly admitted patients were screened (**Figure 2**). Of these, 663 newly diagnosed and 101 people with HIV who discontinued ART were eligible for enrollment, yielding 764 potential participants, among whom 500 were enrolled and randomized. From each trial group, 1 participant withdrew during follow-up. Two participants from

Figure 2. Flow of Patients Through the Daraja Trial



ART indicates antiretroviral therapy.

the control group were lost to follow-up by phone but could still be tracked by HIV clinic medical record extraction.

Baseline Characteristics

Baseline characteristics are presented in **Table 1**. The mean age was 37 years (SD, 12 years), 76.8% were female, and 35% had CD4 cell counts of less than 100/μL. Of the 500 participants, 402 (80.4%) were newly diagnosed with HIV and 98 (19.6%) discontinued ART. Exactly half earned less than US $2.15 per day, in comparison with 49% of the general population.[28] Only 8.0% of the study population had health insurance, in comparison with 15% of the general population.[29] Specific hospital discharge diagnoses are provided in eTable 4 in Supplement 2.

Primary Outcome

The primary outcome of all-cause mortality at 12-month follow-up did not differ by group (**Figure 3**; $P = .96$). Death occurred in 17.0% (85/500) of participants and did not differ by trial group (17.2% with the intervention vs 16.8% with standard care). The unadjusted hazard ratio for death in the intervention group was 1.01 (95% CI, 0.66-1.55).

Secondary Outcomes

The Daraja intervention reduced time to HIV clinic attendance and ART initiation (Figure 3; $P < .001$ for both). Hazard ratios for clinic linkage and ART initiation by Cox regression were 1.50 (95% CI, 1.24-1.82) and 1.56 (95% CI, 1.28-1.89), respectively. Intervention participants also achieved higher rates of HIV clinic retention (87.4% vs 76.3%; $P = .005$), ART adherence (81.1% vs 67.6%; $P = .002$), and HIV viral load suppression (78.6% vs 67.1%; $P = .01$) at 12 months (**Table 2**; eFigure 2 in Supplement 2). For HIV virologic suppression, the results were similar when using a definition of less than 200 copies/μL in a sensitivity analysis (77.2% [159/206] vs 66.7% [138/207]; difference, 11% [95% CI, 2%-19%]; rate ratio, 1.16 [95% CI, 1.03-1.31]; $P = .02$ by Fisher exact test).

The median time spent per client on all intervention activities was 4.3 hours (IQR, 3.5-5.1 hours). The resources/costs associated with the intervention are described in eAppendix 4 and eTable 2 in Supplement 2. Assuming that the fixed costs for Daraja are spread over the first 12 months of the intervention, the average cost to conduct the intervention for a single patient at any point in year 1 would be approximately US $22. The average cost to treat a patient in subsequent years would fall to US $17.

Exploratory Outcomes

Intervention Fidelity

Of the 250 intervention participants, 76.8% (192/250) completed all 5 sessions of the intervention. In total, 85.8% (1072/1250) of the expected sessions were successfully completed.

Table 1. Baseline Characteristics of Participants

Characteristics	Linkage intervention (n = 250)	Standard care (n = 250)
Sex, No. (%)		
Women	190 (76)	194 (78)
Men	60 (24)	56 (22)
Age, mean (SD), y	38 (12)	36 (11)
Married or cohabitating, No. (%)	131 (52)	117 (47)
Head of household, No. (%)	133 (53)	126 (50)
Education level, No. (%)[a]		
Less than primary	85 (34)	81 (32)
Completed primary	158 (63)	163 (65)
Complete secondary	7 (3)	6 (2)
Source of income, No. (%)		
Small trade or unskilled labor	156 (62)	148 (59)
Skilled labor worker or professional	35 (14)	46 (18)
Farmer	34 (14)	30 (12)
Unemployed	25 (10)	26 (10)
Income <5000 Tanzanian shillings (US $2.15) per d, No. (%)[b]	143 (57)	156 (62)
Health insurance, No. (%)	22 (9)	18 (7)
Alcohol use category by AUDIT score, No. (%)[c]		
Abstainee (score 0)	201 (80)	190 (76)
Low risk (score 1-7)	27 (11)	33 (13)
Hazardous use/dependence (score >7)	22 (9)	27 (11)
Depression category by PHQ-9 score, No. (%)[d]		
None (score 0-4)	95 (38)	100 (40)
Mild (score 5-9)	103 (41)	84 (34)
Moderate or severe (score >9)	52 (21)	66 (26)
HIV-related stigma score (self-reported), mean (SD)[e]	2.3 (0.9)	2.3 (0.9)
Social support by Social Provisions Scale score, mean (SD)[f]	34.8 (4.7)	34.7 (4.3)
Health-related quality of life by SF-12 score, mean (SD)[g]		
Physical component score	38 (9)	37 (9)
Mental component score	45 (12)	45 (12)
HIV/ART status, No. (%)		
Newly diagnosed HIV	211 (84)	191 (76)
Discontinued ART (≥7 d)	39 (16)	59 (24)
CD4 cell count, /μL, No. (%)	n = 249	n = 248
0-100	86 (34)	89 (36)
101-200	35 (14)	31 (12)
>200	128 (51)	128 (51)
Enrollment hospital, No. (%)		
Sekou Toure Regional Hospital	90 (36)	85 (34)
Nyamagana District Hospital	32 (13)	39 (16)
Igoma Health Center	36 (14)	30 (12)
Bugando Referral Hospital	16 (6)	23 (9)
Buzuruga Health Center	16 (6)	21 (8)
Other hospital or health center	60 (24)	52 (21)
Hospital stay, median (IQR), d	4 (2-6)	4 (2-7)
Enrollment before onset of COVID-19 in Tanzania, No. (%)[h]	105 (42)	104 (42)
Reason for hospital admission, No. (%)[i]		
Medical, infectious	153 (61)	156 (62)
Medical, noncommunicable	33 (13)	41 (16)
Obstetric or gynecological	48 (19)	39 (16)
Surgical	16 (6)	14 (6)

Abbreviations: ART, antiretroviral therapy; AUDIT, Alcohol Use Disorders Identification Test; PHQ-9, Patient Health Questionnaire 9; SF-12, 12-Item Short Form Health Survey.

[a] Primary school consists of the first 7 years of standard education. Primary school is followed by 4 years of secondary school.

[b] Income below the poverty line for Tanzania according to the World Bank threshold.[28]

[c] Alcohol abuse categories as defined by the AUDIT score on a scale of 0 to 40.[19]

[d] Depression categories as defined by the PHQ-9 score on a scale of 0 to 27.[20]

[e] HIV/AIDS-related stigma score quantifying perceived negative attitudes and acts of discrimination against people with HIV on a scale of 0 to 4 with higher scores indicating more stigma.[21,23]

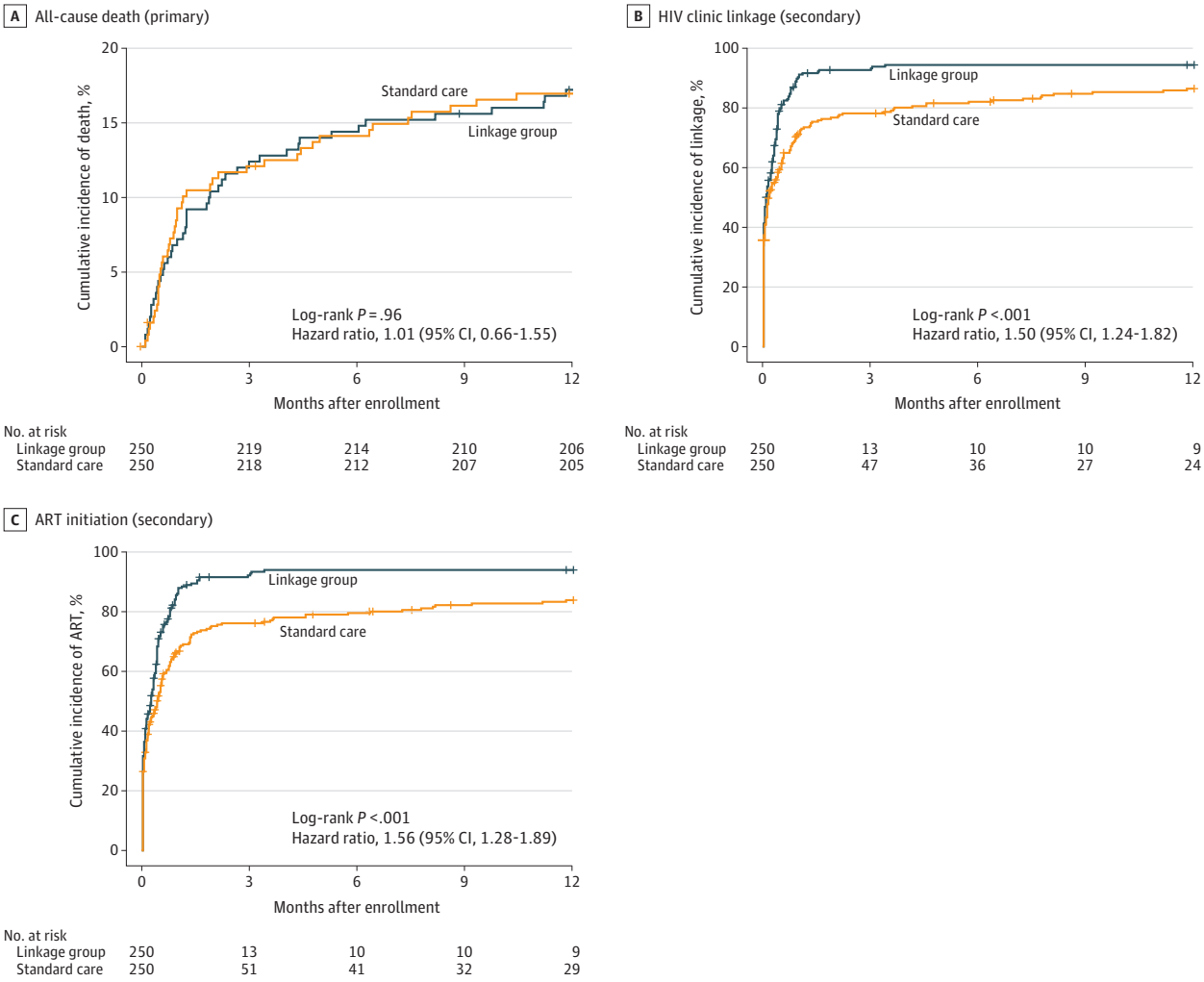
[f] Perceived social support as quantified by the 10-question Social Provisions Scale on a scale of 0 to 40 with higher scores indicating more social support.[22]

[g] Health-related quality of life as quantified by the SF-12 on a scale from 0 to 100 for both physical and mental components, with higher scores indicating better quality of life.[23]

[h] Before and after April 6, 2020, the date that the first case of COVID-19 was reported in the Mwanza Region of Tanzania.

[i] Reason for hospital admission was classified based on *International Statistical Classification of Diseases and Related Health Problems, Tenth Revision* categories.

Figure 3. All-Cause Mortality and Secondary Outcomes



ART indicates antiretroviral therapy. All participants were followed up for 12 months after enrollment. Hazard ratios at 12 months are shown. Linkage is defined by the first clinic visit after enrollment (discharge).

Table 2. Secondary Outcomes

12-mo Outcomes[a]	Linkage intervention (n = 206)[b]	Standard care (n = 207)[b]	Difference (95% CI)	Rate ratio (95% CI)[c]	*P* value[d]
Retention in HIV care	180 (87.4)	158 (76.3)	11.1 (3.7-18.4)	1.14 (1.04-1.25)	.005
ART adherence	167 (81.1)	140 (67.6)	13.4 (5.1-21.8)	1.20 (1.07-1.34)	.002
Viral load suppression (<1000 copies/μL)	162 (78.6)	139 (67.1)	11.5 (3.0-20.0)	1.18 (1.04-1.32)	.01

[a] Retention in care was defined by an active ART prescription at 12 months provided by an HIV clinic visit. ART adherence was defined by a perfect score on the 3-day recall questionnaire confirmed by HIV pharmacy refills.

[b] Binary outcomes at month 12 were assessed for participants alive at month 12 who did not withdraw from the study.

[c] Rate ratio by Poisson regressions with robust standard errors.

[d] Based on Fisher exact test.

Of the 178 sessions that were missed, 49.4% (88/178) were missed because a participant died before completion of the 3-month intervention period. A total of 4.9% (52/1072) of the intervention sessions were rated for fidelity, and the mean fidelity score was 2.96 of 3.

Post Hoc Analyses

A sensitivity analysis was conducted to account for potential correlation across outcomes. Clusters were defined according to social worker designation, health facility type, and reason for admission, separately. There was no difference in the

effect size of the intervention when accounting for clustering by social worker, health facility type, or reason for admission (eAppendix 5 and eTable 5 in Supplement 2).

Causes of death were HIV related for all except 1 participant who died in a mining accident. Analysis of the causes of death among patients who were pregnant or undergoing surgery did not provide any evidence of differential mortality in these groups (eAppendix 5 and eTable 6 in Supplement 2).

By 1 month after enrollment, 87.6% (219/250) of intervention participants had attended the HIV clinic vs 69.6% (174/250) of control participants (difference, 18% [95% CI, 11%-25%]; rate ratio, 1.26 [95% CI, 1.15-1.38]; $P < .001$ by Fisher exact test). By 3 months, 87.6% (219/250) had started ART vs 72.8% (182/250) of controls (difference, 15% [95% CI, 8%-22%]; rate ratio, 1.20 [95% CI, 1.10-1.32]; $P < .001$).

Adverse Events

No adverse events associated with the Daraja intervention occurred.

Discussion

This was a randomized, multicenter clinical trial of a linkage case management intervention adapted for hospitalized people with HIV living in northwestern Tanzania. This low-cost linkage case management intervention failed to reduce 12-month posthospital mortality (primary outcome) but led to meaningful effects in accelerating the HIV continuum of care after hospital discharge among newly diagnosed people with HIV and those who discontinued ART. Intervention recipients who survived to 12 months had higher rates of HIV clinic retention, ART adherence, and viral load suppression. These findings are important for researchers and clinicians in the field of HIV, as well as those working with other potentially stigmatizing conditions diagnosed during hospitalization that require engagement in postdischarge clinical care, such as tuberculosis and sexually transmitted infections.

This linkage case management intervention reduced time to HIV clinic linkage and ART initiation after hospital discharge. These findings are encouraging considering the cost of the intervention in relationship to other sociomedical interventions in sub-Saharan Africa.[30-33] These findings are similar to the first trial of the ARTAS linkage case management intervention, which demonstrated a 15% increase in HIV clinic linkage within 6 months.[9] Two subsequent trials of social interventions for hospitalized people with HIV—both from the US and both published in 2016—yielded mixed results. The first of these trials tested a peer mentor intervention and concluded that "more intense and system-focused interventions warrant further study."[11] A subsequent study of a linkage case management intervention adapted from ARTAS applied to hospitalized people with HIV with substance use disorders, coupled with financial incentives, failed to demonstrate any benefit of case management on viral suppression but did show some short-term benefits on HIV care engagement.[12]

In the current trial, the benefits of case management persisted to 12 months. The intervention was associated with a greater than 10% absolute increase in continued engagement in HIV care and viral load suppression. Long-term viral load suppression may have additional public health benefits such as reduced HIV transmission, although this was beyond the scope of the current trial. These findings support the hypothesis that for people with HIV, hospitalization is "a critical event in the continuum of care"[34] and "an opportunity to engage patients when they are particularly apt to consider behavior change, given their acute illness."[11] Hospitalization may offer a new angle to achieve the elusive 95-95-95 targets through testing and reengagement in HIV care.

There are several possible explanations for the failure of the intervention to reduce posthospital mortality. First, hospitalized people with HIV often present, as many patients did before the availability of ART, with multiple opportunistic infections and advanced illness. Reducing posthospital mortality will likely require earlier diagnosis and improved management of opportunistic infections.[6] Rapid urine-based screening for tuberculosis with the TB-LAM antigen test may be part of the solution.[35] Second, rapid viral load assessment with drug resistance testing may be necessary for hospitalized people with HIV to identify HIV viral replication due to inadequate ART as well as to adjust ART in cases of HIV drug resistance. Of 786 hospitalized people with HIV taking stable ART who were enrolled in 1 recent trial in Malawi and South Africa, 32% had virologic failure.[36] Resistance to at least 2 ART drugs was common and was associated with increased mortality. Third, in some hospitalized people with HIV with terminal disease, the only way to prevent death might be through interventions addressing stigma and targeting early diagnosis.[37]

One major strength of this trial was the high rate of HIV testing, with more than 28 000 hospitalized adults undergoing testing during the study period. The routine application of clinician-initiated testing and counseling for HIV according to the WHO guidelines at study sites ensured that all hospitalized people with HIV could be screened for enrollment, whether they previously knew of their diagnosis or were newly diagnosed.[6] Another strength was the low rate of study withdrawal, suggesting that the study procedures, including the intervention, were feasible for participants. In addition, the intervention team also achieved a high rate of treatment exposure. This suggests that the intervention was acceptable to the target population, but further investigation is needed to formally establish this acceptability.

Limitations

First, the generalizability of these findings beyond Tanzania is unknown; however, the overall posthospital mortality rate observed in the trial is consistent with rates reported in prior observational studies[4] and clinical trials[12] in both Africa and the US, suggesting these findings are applicable to other populations. Second, application of enhanced standard care in the control group may have reduced mortality in the control group, leading to an underestimation of the intervention effect. For patients who are highly amenable to starting or restarting ART, enhanced nurse counseling and accompaniment to the clinic may be sufficient to promote posthospital HIV clinic linkage and use of ART. Third, although 12-month all-cause mortality

was the primary outcome, perhaps HIV clinic linkage and ART initiation may be more reasonable targets for case management interventions after hospitalization. Additional clinical trials are needed to test this hypothesis. Fourth, intervention social workers were employed by the research study rather than by health care facilities. Implementation research is needed to determine if a similar intervention could be carried out by health facility social workers or other staff.

Conclusions

Among hospitalized people with HIV, a linkage case management intervention did not reduce 12-month mortality outcomes. These findings may help inform decisions about the potential role of linkage case management among hospitalized people with HIV.

ARTICLE INFORMATION

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