Title

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Impact of short message service and peer navigation on linkage to care and antiretroviral therapy initiation in South Africa

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Objective: We examine the efficacy of short message service (SMS) and SMS with peer navigation (SMS + PN) in improving linkage to HIV care and initiation of antiretroviral therapy (ART).

Design: I-Care was a cluster randomized trial conducted in primary care facilities in North West Province, South Africa. The primary study outcome was retention in HIV care; this analysis includes secondary outcomes: linkage to care and ART initiation.

Methods: Eighteen primary care clinics were randomized to automated SMS ($n = 7$), automated and tailored SMS + PN ($n = 7$), or standard of care (SOC; $n = 4$). Recently HIV diagnosed adults ($n = 752$) were recruited from October 2014 to April 2015. Those not previously linked to care ($n = 352$) contributed data to this analysis. Data extracted from clinical records were used to assess the days that elapsed between diagnosis and linkage to care and ART initiation. Cox proportional hazards models and generalized estimating equations were employed to compare outcomes between trial arms, overall and stratified by sex and pregnancy status.

Results: Overall, SMS ($n = 132$) and SMS + PN ($n = 133$) participants linked at 1.28 [95% confidence interval (CI): 1.01–1.61] and 1.60 (95% CI: 1.29–1.99) times the rate of SOC participants ($n = 87$), respectively. SMS + PN significantly improved time to ART initiation among non-pregnant women (hazards ratio: 1.68; 95% CI: 1.25–2.25) and men (hazards ratio: 1.83; 95% CI: 1.03–3.26) as compared with SOC.

Conclusion: Results suggest SMS and peer navigation services significantly reduce time to linkage to HIV care in sub-Saharan Africa and that SMS + PN reduced time to ART initiation among men and non-pregnant women. Both should be considered candidates for integration into national programs.

Trial registration: NCT02417233, registered 12 December 2014; closed to accrual 17 April 2015.

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Keywords: antiretroviral therapy initiation, cluster randomized trial, HIV, linkage to care, peer navigation, short message service, South Africa

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Introduction

In South Africa where there are 7.8 million people with HIV (PWH) [1], improving early HIV diagnosis, linkage to care, treatment initiation, retention in care, and adherence to antiretroviral therapy (ART) could bring substantial gains in HIV prevention [2,3]. In 2014, before universal treatment was available in South Africa, an estimated 37.8% of HIV-positive men and 55.0% of women were aware of their status [4]. In addition, numerous studies have noted a lack of linkage post-HIV testing and further extensive losses from care, hampering effective epidemic control [5–7]. Even following the introduction of universal treatment, data from the 2017 South African national survey estimated that only 67% of men and 72% of women living with HIV who knew their status were on ART [8], a significant gap in ART coverage among PWH, especially among men [9]. The gaps in HIV status knowledge and treatment uptake have resulted in only 43% of men and 58% of women living with HIV overall achieving viral suppression [10].

As universal access to ART was being introduced, few interventions had proven efficacious in linking patients to HIV care and promoting early ART initiation in resource-limited settings [11–15]. Among feasible strategies with the potential to improve care engagement outcomes, short message service (SMS or text messaging) and personal support interventions have demonstrated promise both prior to and following universal ART access [11,12,16–18] and could be cost-effective [19–21]. SMS interventions, including appointment reminders and/or check-in messages eliciting a response from the participant, were shown to improve clinic attendance [22–27]. Similarly, personal support interventions that focus on peer-facilitated navigation of health systems and/or support and encouragement to remain in care have led to improvements in linkage to and retention in care, albeit not consistently [16,28–34].

We examine the efficacy of SMS alone and the efficacy of adding peer navigation to a basic SMS package (SMS + PN) to improve linkage to care and retention through the implementation of the I-Care cluster randomized trial in primary health clinics and community health centers in North West Province, South Africa [35]. The program followed participants for 1 year to assess care engagement. Retention outcomes have been published: briefly, individuals in the SMS + PN arm had 1.77 greater odds of being retained in care over 1 year than those in standard-of-care (SOC) clinics. The SMS-only intervention did not improve retention [36]. Herein, we report the intervention effects on the secondary trial outcomes of linkage to HIV care and ART treatment initiation during the first 6 months of participant follow-up among intervention participants who had no history of linkage to care prior to the study.

Methods

Study setting

The trial was conducted in the Bojanala Platinum District of North West Province, where HIV prevalence in the adult population is estimated at 22.7% [8] and ART uptake is lower than the national average, with approximately 61% of PWH aware of their status on ART [10]. Two sub-districts were selected to participate in the study to represent a range of rural and urban experiences: Moses Kotane, which is largely rural, and Rustenburg, which is a mix of peri-urban and urban areas, including Rustenburg, the most populous city in North West province. Health facilities included community health centers and primary health clinics, both of which are public clinics offering HIV testing and treatment; hospitals were not included in the study.

Randomization

Randomization procedures have been described in detail elsewhere [35,36]. Among 61 ART-initiating health facilities within the two study sub-districts, 18 were selected for participation, following the exclusion of facilities that participated in a pilot test of the interventions [37], those not meeting a minimum number of ART patients, and facilities that were either scheduled to close, too distant to access consistently or that served mobile populations unlikely to be retained in research. The sample size of 18 clinics was based on a goal of recruiting a minimum of 600 clients, assuming 80% power to observe a 15% difference (50 vs. 65%) or more in patient retention between any two study arms [36]. The remaining 18 facilities were randomized to one of the three study arms: seven to SMS, seven to SMS + PN, and four to SOC (Fig. 1). We randomized sites using methods described by Hayes and Moulton [38]; briefly, we stratified by sub-district and employed balanced (restricted) randomization based on patient load and clinic functionality indicators [35]. Clinic allocation was not blinded.

Recruitment

Clinic staff assisted with recruiting patients between October 2014 and April 2015, using two strategies. First, all patients who presented for HIV testing or those returning to collect their initial $CD4^+$ test results were approached by clinic staff about their interest in participating in the study. If interested, the clinic staff escorted the prospective patient to study personnel or requested a phone number for contact at a more convenient time. Second, staff enumerated all patients in the clinic HIV care registers who entered care in the past year and systematically selected a sub-sample (every 5th or 10th entry), depending on the clinic patient load. Clinic staff then contacted each selected participant, assessed interest, and elicited permission for contact by study staff [35]. Research staff assessed eligibility criteria. Those who were 18 years or older, had access to a mobile

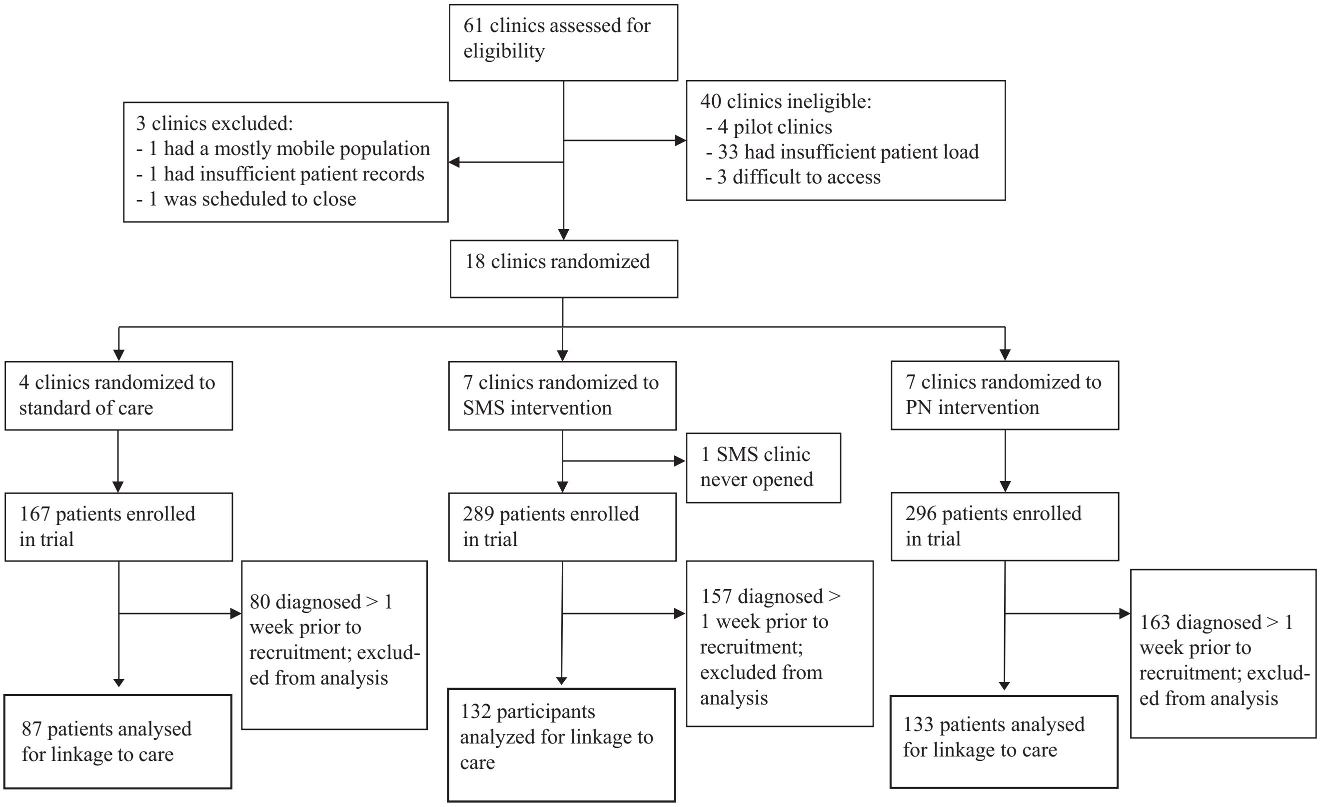

Fig. 1. Trial profile, clinic allocation, participant enrollment, and analytic sample.

phone, were willing to receive automated text messages with HIV-related content, and had been diagnosed with HIV within the past year were eligible and scheduled for an enrollment visit.

I-Care intervention design

Short message service

The SMS strategy included three types of messages delivered from an automated system that determined messaging based on sex, clinical/ART status, and clinic visit dates, data which were kept current through clinical record extraction. Reminder messages were sent prior to scheduled clinic visits and following missed visits. Behavioral messages were sent every 2 weeks and addressed engagement in care (e.g. blood tests every 6 months will help you keep track of your health. Ask your nurse when your next blood test should be); medication adherence or awareness (e.g. Be smart! Take your meds with you to work or travel. Have a plan for how you will take them when away from home); and healthy living (e.g. reduced alcohol consumption). Finally, every other week participants received two-way check-in messages to assess whether participants were encountering any difficulties or needed assistance. Participants were able to respond free of charge with a numeric response indicating if they were okay (input 1) or if they needed to talk to someone (input 2). Though the messaging system (CommConnect; Dimagi, Inc, Boston, Massachusetts, USA) was free to participants, they received approximately five US dollars' worth of airtime at enrollment and again at the 6- and 12-month follow-up visits. A full description of messaging content was published previously [35].

Short message service + peer navigation

Participants in the SMS + PN condition also received appointment reminders and automated bi-weekly behavioral messages identical to those in the SMS-only condition, however, check-in messages were personalized and sent by peer navigators. These check-in messages were not scripted. Navigators completed training prior to commencing direct one-on-one patient contact. The training consisted of 1 week of intensive didactic and skills-building materials related to rapport building, listening skills, identifying barriers to care and prevention, setting and monitoring behavior change goals, and ethics [37]. Following the training, they began delivering services under supervision. Throughout the study, the navigators were required to meet weekly with a supervisor to review their work with each client. Supervisors met biweekly with study investigators. Navigators were HIV-positive adults in care who worked with participants to develop strategies for overcoming barriers to care through monthly in-person meetings and text/phone check-ins, with additional contacts as needed. The project employed both male and female navigators so that sex matching would be possible if requested by a client. However, most clients did not request a sex-matched navigator. Navigators provided assistance to an average of 13 patients over the course of the trial and were closely supervised by a trained research assistant, who helped troubleshoot challenges and ensured client contacts and meetings were recorded.

Standard of care

SOC participants did not receive messages or services. SOC clinic personnel received the same training regarding proper completion of patient forms as intervention clinic personnel, to ensure consistency of data quality. Participants in the SOC arm completed surveys at the same intervals as intervention participants.

Procedures

Research personnel were stationed at all clinics, including SOC clinics, to assist with recruitment, conduct interviews, extract data, and provide support to the clinics. At enrollment, participants responded to a demographic and behavioral survey, including socio-demographic characteristics and current HIV treatment status, following informed consent. Surveys were repeated at 6- and 12-month follow-up appointments. Data on clinical care visits were extracted from patient files biweekly, as described in detail in the published protocol [35]. All procedures were approved by the Institutional Review Board at the University of California, San Francisco, the Human Subjects Division at the University of Washington, and the Human Sciences Research Council Research Ethics Committee in South Africa. The Policy, Planning, Research, Monitoring and Evaluation Committee for the North West Provincial Department of Health also reviewed and approved the protocol.

Measures

The clinic randomization arm of SMS, SMS + PN, or SOC is the primary exposure. Linkage to care was determined by capturing days elapsed from the diagnostic visit to the first follow-up care visit among recently diagnosed participants (diagnosed the day of enrollment or enrolled within 7 days of diagnosis). Days to linkage to care was analyzed as a continuous variable for hazards analysis and then dichotomized for further analysis at two cut-points: within 90 days, reflecting South African clinical standards at the time, and within 30 days, reflecting more stringent international recommendations for immediate referral following diagnosis [39] and aligning with concurrent research in South Africa [40]. We also assessed the time to ART initiation, defined as the time between the diagnostic visit and receipt of medication, for those who were ART eligible on the date of diagnosis. Of note – at the time of the study start, national ART eligibility criteria included $CD4^{+}$ cell count 350 cells/μl or less, pregnancy, or tuberculosis (TB) co-infection; criteria were expanded 2 months into accrual to $CD4^{+}$ cell count 500 cells/μl or less in January 2015; 49 people (13.9%) in this analysis were recruited prior to January 2015.

Statistical analysis

A total of 752 participants (289 in SMS, 296 in peer navigation, and 167 in SOC) were enrolled in the trial across 17 clinics; however, the analysis of linkage outcomes is limited to participants recruited at the HIV testing visit only to ensure that there was no previous care (and thus previous linkage) history. Participants recruited from care registers were, by definition, already linked into the system, even if not currently retained. For that reason, analyses of linkage to care outcomes were restricted a priori to 352 participants enrolled on or within 7 days of their HIV diagnosis (representing approximately half of the total study participants), to ensure that exposure to the intervention preceded linkage to care outcomes.

All analyses are intent-to-treat and conducted using Stata version 13 (StataCorp, College Station, Texas, USA). Kaplan–Meier survival function plots were generated and survival analysis was performed with Cox models to compare rates of linkage to care and ART initiation between arms. Binary markers of linkage to care and ART initiation were assessed for differences by intervention arm using generalized estimating equations (GEE) accounting for clustering at the clinic level; results from GEE analyses are included as supplemental tables. All analyses were stratified by sex. Because linkage and ART initiation practices differ during pregnancy, including triage into immediate ART initiation, we also conducted analyses excluding women who were pregnant at diagnosis. We utilized robust standard errors as these are unbiased in a setting where the coefficient of variation is less than 0.20 [41]. Sensitivity analyses to adjust for potential confounding [42] employed targeted maximum likelihood estimation [43] and are described in supplemental content, http://links.lww.com/QAD/C742.

Results

Eighteen primary healthcare facilities were randomized; however, one clinic allocated to the SMS condition was under construction and did not open in time for the study. A total of 752 participants (289 in SMS, 296 in peer navigation, and 167 in SOC) were enrolled in the trial across 17 clinics. For analyses of linkage to care outcomes ($n = 352$), the average cluster size of participants was 20.7, with a range of 4–37 participants per clinic. The intraclass correlation coefficient (ICC) for linkage to care at 30 days was 0.025 (0.000–0.077), which aligns with the ICC utilized for trial sample size calculations.

The analytic cohort was comprised of 62% women and 38% men, with 22% having only primary education or less, 83% being South African citizens, and 29% residing in households living below the national poverty line (Table 1). Just over three-quarters of participants qualified

Table 1. Distribution of characteristics across trial arms, among 352 participants enrolled within 1 week of HIV diagnosis, I-Care cohort, North West Province, 2014–2015.

	SOC			SMS			SMS + PN			
	N = 87			N = 132			N = 133			
Participant characteristics[a]	n	%	95% CI	n	%	95% CI	n	%	95% CI	Chi-squared (arm) P value
Sex										0.697
Male	30	34.48	25.11–45.24	53	40.15	32.04–48.84	51	38.35	30.39–46.98	
Female	57	65.52	54.76–74.89	79	59.85	51.16–67.96	82	61.65	53.02–69.61	
Age										0.461
18–24	15	17.24	10.56–26.87	22	16.67	11.17–24.13	12	9.02	5.16–15.32	
25–34	43	49.43	38.89–60.01	52	39.39	31.33–48.07	52	39.10	31.09–47.74	
35–44	18	20.69	13.32–30.69	36	27.27	20.28–35.60	45	33.83	26.22–42.39	
45+	11	12.64	7.06–21.62	22	16.67	11.17–24.13	24	18.05	12.34–25.62	
Marital status										0.322
Married/living together	25	28.74	20.07–39.30	52	39.39	31.33–48.07	53	39.85	31.79–48.50	
Unmarried	59	67.82	57.11–76.93	73	55.30	46.64–63.66	68	51.13	42.57–59.62	
Separated/widowed	3	3.45	1.09–10.36	6	4.55	2.03–9.84	12	9.02	5.16–15.32	
Educational attainment										0.826
Complete primary or less	17	19.54	12.39–29.43	34	25.76	18.94–34.00	27	20.30	14.24–28.10	
Partial secondary	36	41.38	31.36–52.17	44	33.33	25.73–41.91	72	54.14	45.52–62.51	
Complete secondary or more	34	39.08	29.25–49.89	53	40.15	32.04–48.84	33	24.81	18.13–32.96	
Pregnancy at diagnosis[b]										0.109
No	22	38.60	26.62–52.14	50	63.29	51.93–73.35	54	65.85	54.75–75.45	
Yes	35	61.40	47.86–73.38	28	35.44	25.52–46.80	26	31.71	2.24–42.75	
South African citizen/resident										0.776
No	12	13.79	7.91–22.95	20	15.15	9.93–22.43	27	20.30	14.24–28.10	
Yes	75	86.21	77.05–92.09	111	84.09	76.72–89.45	106	79.70	71.90–85.76	
Below the poverty line (R400)										0.862
No	62	71.26	60.70–79.93	88	66.67	58–09–74.27	85	63.91	5.53–71.71	
Yes	21	24.14	16.16–34.43	36	27.27	20.28–35.60	41	30.83	23.49–39.28	
Harmful drinking										0.304
No	78	89.66	81.09–94.60	120	90.91	84.57–94.80	111	83.46	76.04–88.91	
Yes	9	10.34	5.40–18.91	8	6.06	3.03–11.75	19	14.29	9.25–21.42	
Eligible for ART[c]										0.492
No	24	27.59	19.08–38.10	34	25.76	18.94–34.00	28	21.05	14.88–28.92	
Yes	63	72.41	61.90–80.92	98	74.24	66.00–81.06	105	78.95	71.08–85.12	
WHO staging at diagnosis										0.202
Asymptomatic (stage 1)	50	57.47	46.69–67.58	81	61.36	52.69–69.37	56	42.11	33.91–50.76	
Symptomatic (stages 2–4)	7	8.05	3.83–16.14	18	13.64	8.71–20.72	32	24.06	17.48–32.16	
Missing staging data	30	34.48	25.11–45.24	33	25.00	18.28–33.19	45	33.83	26.22–42.39	
Travel time to the nearest facility										0.364
0–30 min	42	48.28	37.80–58.90	60	45.45	37.06–54.11	78	58.65	49.99–66.80	
30–60 min	43	49.43	38.89–60.01	66	50.00	41.44–58.56	45	33.83	26.22–42.39	
60–90 min	2	2.30	0.56–8.96	5	3.79	1.57–8.87	10	7.52	4.06–13.51	

ART, antiretroviral therapy; CI, confidence interval; PN, peer navigation; SMS, short message service; SOC, standard of care.
[a]Numbers differ slightly due to missing data.
[b]Among 215 women (missing data on 3 women).
[c]$CD4^+$ cell count 500 cells/μl or less, pregnancy, or TB coinfection.

for ART at the time of study entry; with 41% of female participants being pregnant at enrollment and automatically qualified for immediate ART initiation. There were no significant differences in participant characteristics between trial arms (Table 1).

Linkage to care findings

Overall, 23.86% did not link to care within 90 days (28.74% in the SOC arm, 26.52% in the SMS arm, and 18.05% in the SMS + PN arm). Among those who linked to care within 120 days (95% of all linkages), the median time to linkage to care was 7 days [interquartile range (IQR) = 4–28] for SMS participants, 7 days (IQR: 7–22) for SMS + PN participants and 20 days (IQR: 7–36) for the SOC group. Kaplan–Meier survival curves (Fig. 2) demonstrate that participants linked to care at greater rates in both intervention arms, most prominently during the first 10–30 days of care, following a short period of very rapid linkage in all three arms (likely representing those fast-tracked into care due to poor health or pregnancy). Results from hazards models demonstrate that both SMS and SMS + PN interventions improve time to linkage to care (Figs. 2a and c): on average, those in the SMS and SMS + PN arms linked at a rate of 1.28 [95% confidence interval (CI): 1.01–1.61] and 1.60 (95% CI: 1.29–1.99) times higher, respectively, than those in the SOC arm. When pregnant women were excluded, the effect estimates for SMS and SMS + PN arms were higher: 1.58 (95% CI: 1.14–2.21) and 1.85 (95% CI: 1.39–2.44), respectively, compared with participants in

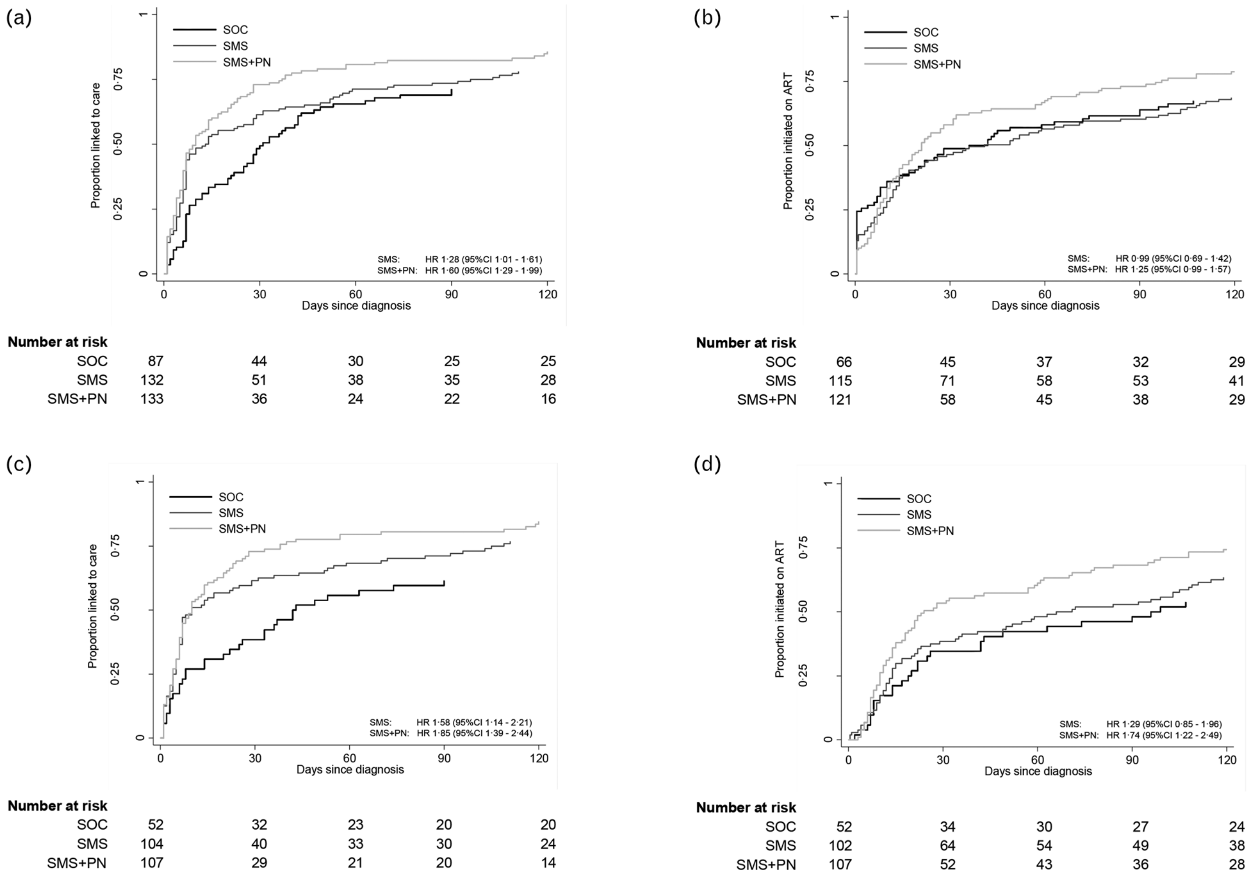

Fig. 2. Kaplan–Meier plots. By randomization arm, time to (a) linkage to care for all newly diagnosed participants; (b) antiretroviral therapy initiation for all newly diagnosed participants; (c) linkage to care excluding women who were pregnant at diagnosis; and (d) antiretroviral therapy initiation excluding women who were pregnant at diagnosis. Standard of care (SOC) is in black, short message service (SMS) is in dark grey, and SMS with peer navigation (SMS+PN) is in light grey.

the SOC arm. When stratified by sex, hazards analyses indicated that SMS was significantly associated with increased linkage to care for non-pregnant women and that SMS + PN demonstrated significant effects for men, all women, and non-pregnant women compared with SOC participants (Table 2). We observed similar findings examining linkage to care as a binary outcome at 30 days and 90 days (Supplemental Table 1, http://links.lww.com/QAD/C743). Furthermore, sensitivity analyses confirmed the above findings and suggest potentially greater effects of the SMS + PN intervention (Supplemental Table 3, http://links.lww.com/QAD/C745).

Antiretroviral therapy initiation findings

Overall, about a third of participants (34.94%) did not initiate ART (36.78% in the SOC arm, 40.15% in the SMS arm, and 28.57% in the SMS + PN arm). Among those who linked to care, almost all of those who were indicated to start ART did initiate treatment (100% started ART in the SOC and SMS arms and all but two in the SMS + PN arm initiated treatment). Overall, Findings from hazards models indicate that SMS + PN participants initiated ART 1.74 (95% CI: 1.22–2.49) times faster than those in the SOC arm when excluding pregnant women (Figs. 2b and d). In stratified hazards analyses, men and non-pregnant women in SMS + PN clinics initiated ART at greater rates: 1.83 (95% CI: 1.03–3.26) and 1.68 (95% CI: 1.25–2.25) times that of men and non-pregnant women in the SOC arm, respectively (Table 3). No differences in time to ART initiation were noted for SMS participants. Findings were similar in binary, GEE analyses, such that when excluding pregnant women, odds of ART initiation within 30 and 90 days were significantly increased in the SMS + PN clinics as compared with the SOC clinics (Supplemental Table 2, http://links.lww.com/QAD/C744).

Discussion

Our data demonstrate that overall both the SMS and SMS + PN interventions improved the time to linkage to care and that the SMS + PN intervention hastened the time to ART initiation. When stratified by sex, men experienced a doubling in linkage rates in the SMS + PN arm compared with men in SOC, and close to a doubling of ART initiation rates as well. Among women, effects

Table 2. Proportion and rate of linkage to care by the trial arm and stratified by sex and pregnancy in the I-Care cohort, North West Province, 2014–2015.

	Proportion linked within 90 days		Rate of linkage to care (marginal Cox model)[a]		
	N	%	Hazards ratio	95% CI	*P* value
Overall[b]					
SOC	62/87	71.26	1.00	–	–
SMS	97/132	73.48	**1.28**	**1.01–1.61**	**0.04**
SMS + PN	109/133	81.95	**1.60**	**1.29–1.99**	**<0.01**
Overall[c]					
SOC	32/52	60.38	1.00	–	–
SMS	74/104	70.48	**1.58**	**1.14–2.21**	**0.01**
SMS + PN	86/107	79.63	**1.85**	**1.39–2.44**	**<0.01**
Men					
SOC	20/30	66.67	1.00	–	–
SMS	39/53	73.58	1.36	0.73–2.52	0.33
SMS + PN	44/51	86.27	**2.06**	**1.24–3.42**	**<0.01**
All women					
SOC	42/57	73.68	1.00	–	–
SMS	58/79	73.42	1.24	0.93–1.65	0.15
SMS + PN	67/82	81.71	**1.36**	**1.06–1.73**	**<0.01**
Non-pregnant women					
SOC	12/22	52.17	1.00	–	–
SMS	35/51	67.31	**1.93**	**1.45–4.57**	**<0.01**
SMS + PN	42/56	73.68	**1.76**	**1.35–2.29**	**<0.01**

CI, confidence interval; PN, peer navigation; SMS, short message service; SOC, standard of care. Values in bold represent significant findings.
[a]Proportional hazards models adjusted for clustered data.
[b]Includes all women.
[c]Excludes pregnant women.

were most apparent in the non-pregnant population, where both interventions demonstrated significant improvements in time to linkage to care and SMS + PN participants experienced more rapid ART initiation. Effects were attenuated when including pregnant women in the analyses, likely given their rapid triage into care for

Table 3. Proportion and rate of treatment initiation by the trial arm and stratified by sex and pregnancy in the I-Care cohort, North West Province, 2014–2015.

	Proportion initiating care within 90 days		Rate of ART initiation (marginal Cox model)[a]		
	N	%	Hazards ratio	95% CI	*P* value
Overall[b]					
SOC	55/87	63.A22	1.00	–	–
SMS	79/132	59.85	0.99	0.69–1.42	0.94
SMS + PN	95/133	71.43	**1.25**	**0.99–1.57**	**0.06**
Overall[c]					
SOC	25/52	48.08	1.00	–	–
SMS	55/104	52.88	1.29	0.85–1.96	0.23
SMS + PN	71/107	66.36	**1.74**	**1.22–2.49**	**<0.01**
Men					
SOC	15/30	50.00	1.00	–	–
SMS	29/53	54.72	1.28	0.64–2.54	0.48
SMS + PN	35/51	68.63	**1.83**	**1.03–3.26**	**0.04**
All women					
SOC	40/57	70.18	1.00	–	–
SMS	50/79	63.29	0.88	0.61–1.27	0.49
SMS + PN	60/82	73.17	1.03	0.85–1.25	0.77
Non-pregnant women					
SOC	10/22	45.45	1.00	–	–
SMS	26/51	50.98	1.31	0.94–1.82	0.11
SMS + PN	36/56	64.29	**1.68**	**1.25–2.25**	**<0.01**

ART, antiretroviral therapy; CI, confidence interval; PN, peer navigation; SMS, short message service; SOC, standard of care. Values in bold represent significant findings.
[a]Proportional hazards models adjusted for clustered data.
[b]Includes all women.
[c]Excludes pregnant women.

prevention of mother to child transmission across study arms. The data indicate that both interventions merit consideration for scale-up, though sex-specific programming may be warranted.

The PN + SMS intervention demonstrated consistently significant effects in our study population. Evidence of the effect of peer-based programming on linkage to care has been growing in recent years [31–33]. In a study in Soweto, peer navigation resulted in significantly more PWH linked to care in a shorter amount of time than a passive referral, but did not lead to more referred PWH initiating treatment [31]. Another South African study found that providing a peer-based behavioral intervention for PWH who were not on ART that assisted via clinical navigation and psychosocial support was feasible and acceptable and showed preliminary efficacy [32]. Additional studies have demonstrated a positive effect of peer support or lay worker programming on linkage to care and retention in care in sub-Saharan Africa [34,44–48]. Our findings are among the first to demonstrate that using peer navigation with SMS reminders is a useful tool to accelerate both linkage (among women and men) and treatment initiation (among men and non-pregnant women): findings which are welcome with few interventions to date proving successful in this critical moment of engagement in care.

The SMS-only approach also demonstrated improvements in linkage to care, though in stratified analyses these improvements were only significant among non-pregnant women, with a non-significant effect trending in the hypothesized direction among men. SMS did not significantly impact time to ART initiation, although effects trended in the hypothesized direction for men and non-pregnant women. Although there is evidence that SMS approaches can improve ART adherence and viral suppression [18,49], there are few studies documenting whether SMS can impact the timing of linkage to care or ART initiation. One observational study demonstrated reductions in both times to clinic return and treatment initiation in participants who received seven days of daily SMS messages and transport reimbursement as compared with pre-intervention clients, though effects of the SMS and reimbursements cannot be estimated separately [23]. Consistent with our findings, a trial in Botswana found no evidence of an effect on timely $CD4^+$ draw or treatment initiation using an SMS-based intervention among pregnant women [50]. The attenuation of intervention impact when pregnant women are included may be attributed to two issues. First, pregnant women were already triaged into immediate initiation, so the intervention was less likely to impact their linkage to care. Second, a substantive number of pregnant women travel during pregnancy, returning to a native village to be with female relatives during the birth and post-partum period [51–53]. For pregnant women with potential discontinuity in care, a key intervention strategy would be to improve referral services to ensure continuity across clinics within a healthcare system that is not set up to accommodate for mobile populations [54,55]; it is possible that navigators (likely virtual navigators) could assist with this strategy in the future.

For both men and women, SMS may be a good first-step option for those who only require appointment reminders or have fewer barriers to care whereas the peer navigation approach is likely more adept at addressing the needs of people who face significant barriers and require emotional support and encouragement. In addition, programmatic evaluations have shown that peer support programming leads to an improved sense of social support and reductions in stigma [56]. This may explain the benefit for men in the SMS + PN arm vs. SMS-only; men may require more support to enter care [57]. Generally, men test less frequently, enter care at later stages of disease progression, take longer to link to care after testing, are less frequently retained and virally suppressed, and experience higher levels of attrition from HIV care and AIDS-related mortality [58–61]. Men's concern about HIV-related stigma and inadequate social support have been found to be key barriers affecting treatment initiation [62,63]. Data also indicate that men worry more about attending clinics, as working-age men, unlike reproductive-age women and certainly pregnant women, have few plausible reasons for seeking care outside of HIV and other stigmatized conditions [64]. Having peer support through the early to mid-stages of HIV care engagement may be important for those who perceive stigma associated with clinic attendance and require additional social support for linkage to care [65]. Ongoing peer mentorship that normalizes treatment uptake and adherence may also be a strategy to engage men [66].

The current study, while rigorous, has limitations. Intervention allocation was not blinded. Trial sites included government clinics in two peri-urban and rural sub-districts, as a result, findings may not be generalizable to clients attending private clinics, residents of other provinces, or large metropolitan centers. The findings may also not be generalizable to all patients or facilities within the district given that facility selection excluded those which were too distant to access consistently or that served primarily mobile populations unlikely to be retained in research. Nearly half of the potential participants identified in the clinic registers could not be reached as either contact information was not available or phone numbers were not current. Further, participants were only eligible if they had access to a mobile phone. Though 94% of residents in north west province have access to mobile phones and 92% use cell phones exclusively [67,68], the most impoverished PWH (potentially up to 5–10% of the target population for the study) may have been excluded from this sample for not having access to a mobile phone upon screening. One clinic originally assigned to the SMS arm never opened (it was under construction), though sensitivity analysis should have addressed any potential resulting imbalance. Finally, it is possible that some participants were misclassified as not linked to care or initiating treatment when in fact they had linked elsewhere. We did attempt to track participants to non-study clinics and confirm whether they were receiving services elsewhere, however, transfers are poorly documented. We have no reason to believe this misclassification would be differential between arms. This intervention was conducted prior to universal ART access and while the findings are still highly relevant, not all patients were ART-eligible during the study. This may have impacted peer navigators' abilities to encourage follow-up or may have discouraged some from engaging with the SMS system. Finally, viral load outcomes were not included in this study; we cannot infer whether the observed improved linkage to care (SMS and SMS + PN) or ART initiation (SMS + PN) would result in improved viral suppression in the intervention groups as compared with SOC.

The current policy climate in South Africa might enable adapting SMS and/or peer navigation. Indeed, techniques that target multiple steps in the care cascade and show efficacy in strengthening both linkage to care following HIV testing and treatment initiation are needed [14]. South Africa has already introduced 'MomConnect,' an SMS appointment reminder system with well-baby information for pregnant women [69]. South Africa is also rolling out a re-engineering of primary healthcare, which includes the deployment of a cadre of community health workers to conduct home-based prevention and care visits. These ward-based outreach teams (WBOTs) are integrated into primary healthcare facilities and provide community-level outreach for early detection of health conditions, follow-up support, and ultimately, linkage to the facility for services, including HIV testing and HIV/TB care. Aspects of peer navigation would fit well within the WBOT model, and, as the WBOT package of services is reviewed, integration of peer navigators for HIV-care engagement should be considered.

Our findings indicate that peer navigation coupled with SMS reminders can improve linkage to HIV care and ART initiation as well as retention in HIV care in South Africa [36], where scalable interventions are sorely needed to meet the 95–95–95 goals. It will be important to explore whether the more intensive SMS + PN intervention could be targeted to the clients that require comprehensive support and whether the less intensive SMS-only intervention could be sufficient for those who need reminders but do not have major barriers to accessing care. It is also important that the cost-effectiveness of these interventions at different levels of intensity be estimated and utilized to determine the potential benefits of stepping up interventions to link and retain clients in care in the sub-Saharan African setting. Studies on the cost-effectiveness of such interventions are scant and have been identified as a gap in the literature [12,17]. To address this, cost estimates of the interventions in the I-Care study are forthcoming.

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Conflicts of interest

There are no conflicts of interest.

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