HTPN 078: an enhanced case management study to achieve viral suppression among viremic HIV-positive men who have sex with men in the United States

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Objective(s): After identifying and recruiting men who have sex with men living with HIV and virally unsuppressed, this study attempted to enhance treatment and care via case management to increase the proportion who achieved viral suppression.

Design: Participants were randomized into one of two study arms: standard of care (SOC) or enhanced case management (CM) intervention. Participants were followed for 12 months with quarterly study assessments, with blood collected for $CD4^+$ cell count testing, HIV viral load testing (primary prespecified outcome), and plasma storage.

Methods: Participants identified via respondent-driven sampling and direct recruitment and were invited to participate in the randomized controlled trial. The CM intervention provided a wide range of support services including, health education, clinical care coordination, medication adherence support, and social service assistance. The month-12 assessment included questions about healthcare utilization, stigma, substance use, and mental health.

Results: Among the 144 participants virally unsuppressed at baseline, most had had a previous positive HIV test result; were Black, non-Hispanic, gay and bisexual men, aged 22–50. Among the 128 participants at the last study visit, 68 were virally suppressed,

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with no statistically significant difference between the CM and SOC arms (viral suppression 42% and 53%, respectively; adjusted odds ratio = 0.62 [$P = 0.15$; 95% confidence interval: 0.32, 1.2]).

Conclusions: Reaching targets of at least 90% sustained viral suppression among all people with HIV will likely require more than an individual-level CM approach that addresses barriers to optimal care and treatment at multiple levels.

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Introduction

Since the beginning of the HIV epidemic, gay, bisexual, and other men who have sex with men (MSM) have been the most affected population in the United States [1]. According to a recent Centers for Disease Control and Prevention (CDC) report, 67% of all new infections in the United States were diagnosed in MSM [2] even though this group represents, at most, 4–5% of US adult men [1]. Racial and ethnic disparities characterize this epidemic with greatest burdens among Black, Latinx, and multiracial MSM [3]. The HIV Prevention Trials Network (HPTN) 061 study found a 3% incidence rate in Black MSM with a 5.9% incidence rate in those 18–29 years old [4]. Additionally, the highest incident rates of HIV infection are among MSM in the Southern United States [5]. Racial and geographic disparities among MSM are not limited to HIV prevalence and incidence burdens. Nonwhite and Southern MSM have lower rates of regular HIV testing, less awareness of HIV status, later presentation for HIV care, poorer adherence to antiretroviral therapy (ART), and lower rates of viral suppression than among other MSM [6,7].

The continuum of care has been used to characterize HIV burden and understand gaps in response to the HIV epidemic [8]. According to CDC estimates, of the 1.2 million estimated people with HIV (PWH) in the United States, 14% do not know they are living with HIV [9], only 50% are in continuous care, and only 56% have sustained viral suppression [9]. Modeling studies point to the need to increase viral suppression among PWH to reduce HIV transmission among MSM in the United States [10,11].

Although there is some observational evidence that improved care coordination and patient navigation can have a positive impact on HIV care engagement and viral suppression [12] and also evidence for case management reducing sexual risk behaviors and syphilis among MSM with HIV [13], there is a paucity of evidence for enhanced case management having a direct effect on HIV viral suppression in rigorous controlled trials. One study showed that patient navigation, with or without financial incentives, did not have a beneficial effect on HIV viral suppression among hospitalized patients with HIV and substance use [14], with the literature suggesting that multiple factors are associated with lower odds of sustained HIV viral suppression, including demographic factors, drug and alcohol use, mental health symptoms, homelessness, transportation to appointment needs, as well as provider characteristics [15].

To address health disparities and to improve outcomes for all MSM, it is critical to reach higher proportions of MSM with HIV who are not virally suppressed, enhance their linkage to care, and increase their ability to achieve and maintain HIV suppression. These goals are central to the current "Ending the HIV Epidemic: A Plan for The United States" (EHE) [16]. Intervention strategies and packages that can achieve these goals must be acceptable, feasible, and scalable. The HPTN 078 study attempted to address two critical steps in the continuum of care for MSM: enhance outreach and recruitment of MSM with HIV infection, but not virally suppressed, through respondent driven sampling (RDS) and direct recruitment [17], and enhance treatment and care via case management to increase the proportion of MSM who achieved sustained viral suppression. This report is focused on the outcome of the second aim of the HPTN 078 study.

Methods

Study design

The primary goal of HPTN 078 was to find MSM with HIV who were not virally suppressed and to randomize them into one of two arms receiving either the standard of care (SOC, see below) or an enhanced case management (CM) intervention designed to improve viral suppression rates. RDS and direct recruitment methods were used to identify and recruit participants at clinical research sites in the following cities: Atlanta, GA, Boston, MA, Baltimore, MD, Birmingham, AL (see Beyrer *et al.* [17] for a full description of participant outreach, identification,

and screening). The primary endpoint of the study was viral suppression at 12 months. An endpoint of 24 months was originally planned for HPTN 078, but concerns about slow recruitment of viremic men led to the decision to halt recruitment and follow participants for only 12 months.

Study eligibility

Study enrollment criteria included: age at least 16 years in Birmingham and Boston; and at least 18 years in Atlanta and Baltimore; assigned male sex at birth; have a self-reported history of anal intercourse with another man; be living with HIV and not virally suppressed (defined as having a viral load $\geq$1000 copies/ml); be able to receive HIV treatment at one of the participating clinics chosen by each site; and have no current plan to relocate in the 24 months following enrollment. Individuals were excluded from the study if they were unable or unwilling to provide consent, were participating in another linkage or ART adherence study, or had any condition that, in the opinion of the site's Investigator of Record, would make participation in the study unsafe, complicate interpretation of study outcome data, or otherwise interfere with achieving the study objectives. Individuals who self-identified anywhere along the transfeminine spectrum (e.g. transgender women, female, genderqueer, etc.) were included as long as they met study eligibility criteria.

Study enrollment

At the enrollment visit, participants were consented and randomized (1:1 in blocks of size 2 or 4, randomly chosen, and stratified by study site) to the intervention (CM) or control (SOC) arm of the study (Fig. 1). Neither participants nor study personnel were blinded to the intervention assignment. To prevent cross-contamination between the arms, after randomization, all enrollment and follow-up procedures were conducted by the study case manager for those enrolled into the intervention arm and by another staff member for those enrolled into the control arm. Participants in both study arms signed a release of their medical information, provided contact information, were offered the option to have their sexual partners tested for HIV (as a courtesy and potential benefit to study participation), had blood taken for plasma storage, and were provided with referrals for syphilis or hepatitis C (HCV) treatment if they were diagnosed with these conditions during screening. Participants in both study arms also completed a computer-assisted self-interview (CASI) that included questions about substance use and mental health (note: all participants completed a CASI at initial screening in which they were asked questions about demographic information, gender and sexual orientation identity, healthcare coverage, housing stability, and stigma (HIV and sexual orientation) [17]). For SOC, sites followed their normal procedures to link participants to HIV care. For CM, the intervention began at this visit with the case manager working with the participant to ensure linkage to and engagement in care with their preferred clinic.

Participants attended in-person follow-up study visits at months 3, 6, 9, and 12. At each follow-up visit, contact information was confirmed, social impacts (an undesired change in a person's relationships, experiences, interactions, rights, and/or community status that occurs as a direct result of participating in a research study) were collected, and blood was collected for $CD4^+$ cell count testing, HIV viral load testing, and plasma storage.

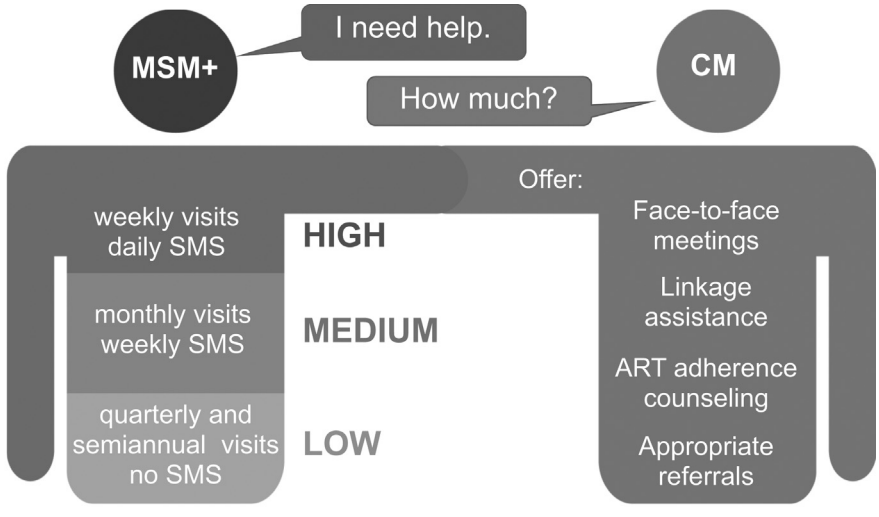

Fig. 1. Enhanced case management (CM) intervention improves linkage to care, ART initiation, treatment adherence, and retention in care. ART, antiretroviral therapy.

Participants enrolled in the CM arm met with their case manager and underwent the components of the intervention (see below). The final follow-up visit at month 12 (M12) included the following additional procedures: syphilis testing; completion of a CASI; and optional participation in a semi-structured qualitative interview. All sites provided participants with their syphilis test results and referral for care (if needed) per their normal site procedures. The substance use and mental health data collected (i.e. substance abuse and mental illness symptoms screener [SAMISS]) [18] were recorded separately from other assessments. The protocol developed for the original 24-month data collection cycle had an automatic check procedure in place to ensure complete data collection for the final study visit. When the follow-up duration was changed to 12 months, this automatic check procedure was discontinued. Inadvertently, SAMISS data at M12 were not collected from the Alabama site, which resulted in missing SAMISS data.

Case management intervention

The CM intervention was designed to improve linkage to care, ART initiation, treatment adherence, and retention in care. Each site hired a full-time case manager for the duration of the intervention. To qualify, candidates were required to have at least a bachelor's degree in a health-related discipline; some counseling experience; at least 2 years of experience in HIV/AIDS education, clinical care, or case management; and experience working with diverse populations, ideally with the MSM community. As part of the intervention, each case manager was trained to use motivational interviewing (MI), a strength-based, patient-centered counseling approach found to be effective as part of other HIV prevention behavioral interventions [19–23]. Case managers received three face-to-face MI training sessions and were provided with ongoing telephone support from an MI training expert. By using the MI approach, the case managers aimed to strengthen the participants' motivation for and commitment to change by focusing on participant choice and autonomy for engaging in care and ART adherence. The case managers also provided a wide range of support services including education, clinical care coordination, medication adherence support, and social assistance. When needed, case managers were capable of making appropriate referrals (Fig. 2).

Additionally, to support participant adherence to HIV treatment and care, the study included a communication platform shown to be effective in other HIV behavioral interventions [24–27], through which participants could choose to receive automated medication adherence and refill reminders, motivational messages, and appointment reminders for both study and non-study visits. The platform was also designed so that participants could ask their case managers for help in response to the automated messages. All messages delivered through this platform could be sent via text, voicemail, or e-mail, and were completely customizable.

A key element of the enhanced CM intervention was that the frequency and type of interactions with the case manager, as well as the tailored messaging, were driven by participants. Their choice ranged from a minimum of contact (only monthly texts and required study visits) to having daily support (Fig. 2). Receiving this CM intervention did not preclude receipt of case management provided in the clinical care setting. Thus, participants may have been also receiving SOC case management services, comparable to participants in the SOC arm, in addition to the study interventions ().

Standard of care

Individuals in the control arm were provided with SOC linkage to care, ART initiation, ART adherence support, and retention in care at their HIV clinic. It is worth noting that these were highly resourced and good quality care settings affiliated with academic medical centers in each of the four cities, without substantive differences across the sites. They had no interactions with a study case manager, and they did not receive any messages via the communication platform, but all participants in SOC had access to case management in these care sites. Other services were provided in some cases by SOC case managers.

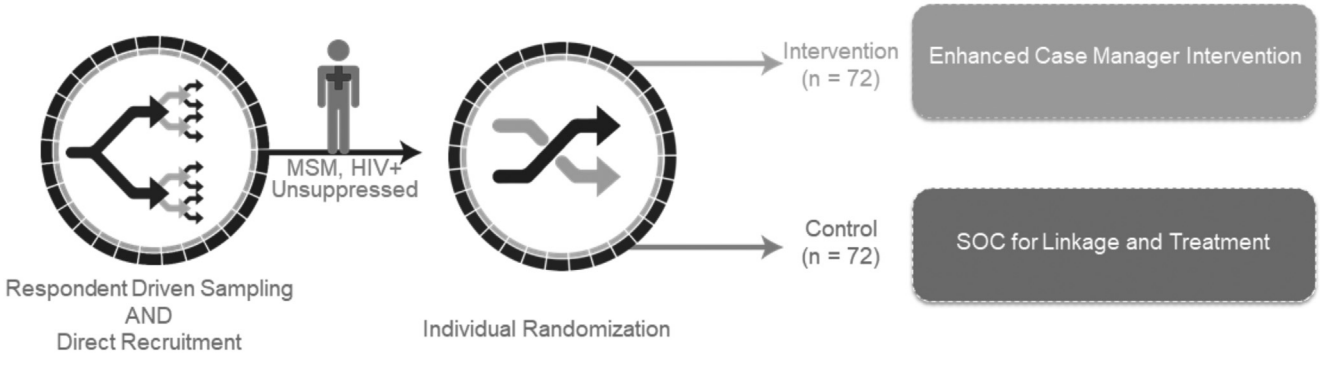

Fig. 2. Intervention assignment diagram.

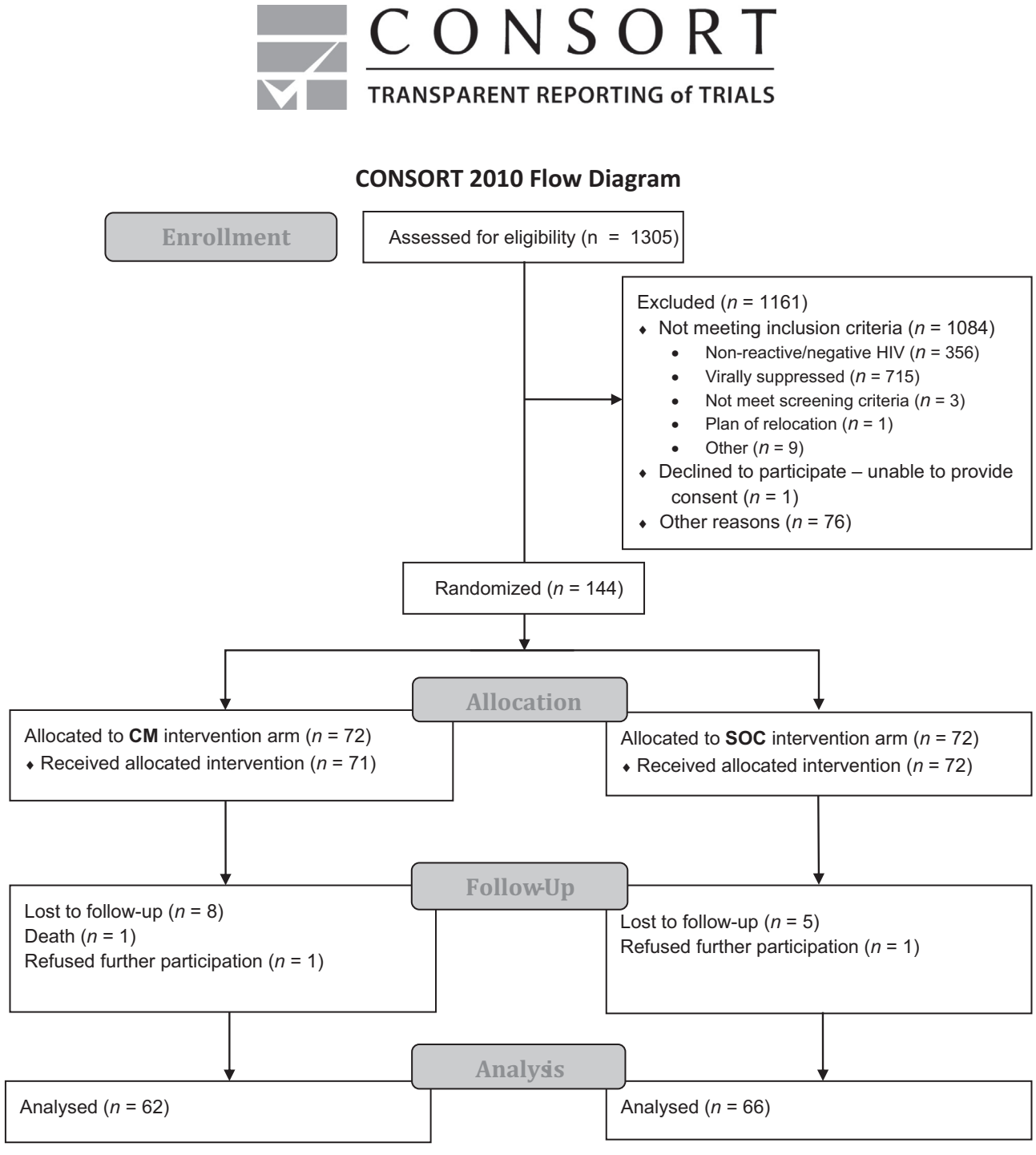

Fig. 3. Consort flow diagram.

Study follow-up

For those randomized to the intervention arm, the case manager had contact with each participant at least monthly to confirm their contact information, check-in regarding HIV and ART management, and collect any social impacts due to study participation. Participants could choose if this monthly contact was in person, by text message, e-mail, or phone call. No monthly contact was made by members of the study team with participants randomized to the control arm.

Statistical analysis

The primary outcome was viral suppression. Individuals who failed to return for follow-up were treated as unsuppressed. Data were summarized as counts and percentages. The analysis of viral suppression by CM

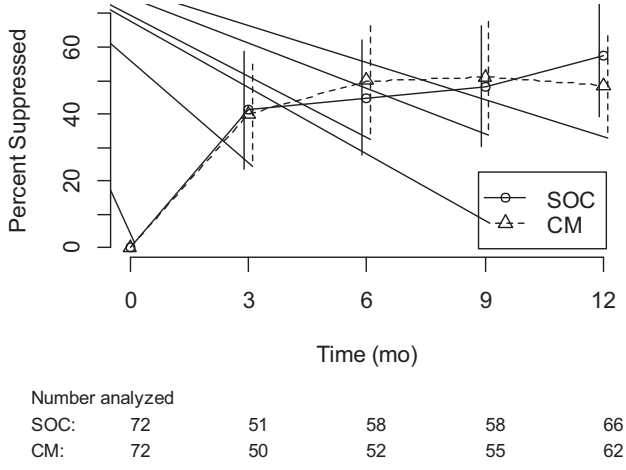

Fig. 4. Viral suppression plot.

intervention arm was intention to treat and based on a logistic regression adjusted for site. Fisher's exact test was used to evaluate the relationship between viral suppression and other characteristics, and a chi-square test for trend was also conducted for ordinal characteristics. Prespecified secondary predictors of viral suppression are shown in Table 3, and exploratory predictors are shown in Table 4. *t*-tests were used to compare the CM intervention intensity (number of encounters, number of activities) between those who were virally suppressed and unsuppressed in the CM intervention arm at 12 months. The study was originally designed to enroll 356 PWH which would have provided 90% power to detect an 18 percentage-point increase in viral suppression at M24 (e.g. 24–42%) after accounting for loss to follow-up. Due to slower than anticipated recruitment, enrollment was stopped after 144 individuals were enrolled, follow-up was shortened to 12 months, and the primary outcome was changed to viral suppression at M12.

Ethical review

The local institutional review board for each study site approved the protocol prior to study implementation. Participants provided written informed consent prior to any study procedures. HPTN 078 is registered on ClinicalTrials.gov (NCT02663219).

Results

Sample

We recruited and screened a total of 1305 persons between March 2016 and December 2017; 154 were determined eligible for the study. The primary reasons why people were ineligible were because they were not living with HIV, or were living with HIV, but were virally suppressed (see CONSORT diagram). The study enrolled 144 participants who were living with HIV

Table 1. Baseline demographics and health characteristics by study arm.

Participants	Overall 144 *N* (%)	CM arm 72 *n* (%)	SOC arm 72 *n* (%)
Age			
18–21	7 (5)	3 (4)	4 (6)
22–30	36 (25)	21 (29)	15 (21)
31–40	34 (24)	15 (21)	19 (26)
41–50	39 (27)	19 (26)	20 (28)
51–60	26 (18)	13 (18)	13 (18)
> 60	2 (1)	1 (1)	1 (1)
Mean	39	39	39
Race[a]			
Native American	1 (0.7)	1 (1.4)	0 (0)
Black	121 (84)	62 (86.1)	59 (81.9)
White	19 (13.2)	9 (12.5)	10 (13.9)
Other	8 (5.6)	3 (4.2)	5 (6.9)
Latino/Hispanic			
Yes	10 (7)	3 (4)	7 (10)
No	134 (93)	69 (96)	65 (90)
Sex			
Male	139 (97)	71 (99)	68 (94)
Female	1 (1)	0 (0)	1 (1)
Transgender female	3 (2)	1 (1)	2 (3)
Gender non-conforming	1 (1)	0 (0)	1 (1)
Sexual orientation			
Gay	114 (79)	58 (81)	56 (78)
Bisexual	23 (16)	12 (17)	11 (15)
Heterosexual	5 (3)	2 (3)	3 (4)
Other	2 (1)	0 (0)	2 (3)
Education			
High school diploma or less	56 (38)	28 (39)	28 (39)
Education beyond high school	88 (61)	44 (62)	44 (62)
Employment			
Full-time	27 (19)	13 (18)	14 (19)
Part-time	20 (14)	11 (15)	9 (13)
Not employed	97 (67)	48 (67)	49 (68)
Marital status			
Married or living with partner	20 (14)	7 (10)	13 (18)
Have primary or main partner, not living together	2 (1)	1 (1)	1 (1)
Single/divorced/widowed	122 (85)	64 (89)	58 (81)
Healthcare coverage			
Yes	116 (81)	59 (82)	57 (79)
No	28 (19)	13 (18)	15 (21)
Stable housing			
Yes	128 (89)	65 (90)	63 (88)
No	16 (11)	7 (10)	9 (13)
Syphilis status			
Active	51 (35)	27 (38)	24 (33)
Nonactive	13 (9)	7 (10)	6 (8)
Negative	80 (56)	38 (53)	42 (58)
HCV antibody			
Negative	122 (85)	57 (79)	65 (90)
Positive	22 (15)	15 (21)	7 (10)
$CD4^+$ cell count			
<200	42 (29)	24 (33)	18 (25)
200–350	34 (24)	16 (22)	18 (25)
351–500	28 (19)	16 (22)	12 (17)
>500	40 (28)	16 (22)	24 (33)
Mean	357	337	377
Substance use			
Yes	20 (14)	8 (11)	12 (17)
No	117 (81)	60 (83)	57 (79)
Prefer not to answer	7 (5)	4 (6)	3 (4)
Ever on ART[b]			
Yes	124 (87)	64 (89)	60 (83)
No	18 (13)	7 (10)	11 (15)
Missing	2	1	1

The table shows baseline demographic and health characteristics for study participants in each study arm. ART, antiretroviral therapy; CM, case manager study arm; HCV, hepatitis C virus; *N*, number; SOC, standard of care study arm.
[a]Participants could choose multiple races, if applicable, instead of choosing only one race.
[b]Percent of the nonmissing number of observations (overall, $n = 142$; CM, $n = 71$; SOC, $n = 71$).

and virally unsuppressed (defined as having a viral load $\geq$ 1000 copies/ml); most enrolled participants had a previous positive HIV test result ($n = 137$, 89%). Fifty–seven (40%) participants were recruited via RDS, and 87 (60%) were recruited via direct recruitment. Table 1 shows the baseline demographic and health characteristics of the enrolled participants, by study arm. The average age of participants was 39 years; most were aged 22–50. The study cohort was predominately comprised of Black, non-Hispanic, gay and bisexual men. Most participants were educated, unemployed, single, stably housed, and did not have a history of substance use treatment. There were high rates of HCV and syphilis among the sample [28,29]. The majority had access to healthcare. At baseline, the mean $CD4^+$ cell count was 357 cells/μl, and median HIV-1 viral load was 19 459 copies/ml; 124 (86%) reported previous ART use. Of the 144 enrolled, 143 were alive at M12, and 129 of those (90%) completed the M12 visit. One of the 129 participants did not have viral load data at the final visit (Supplemental Figure 3, http://links.lww.com/QAD/C680) and one participant never received any aspect of the CM intervention.

Table 2. Viral suppression by visit and study arm.

Participants	Overall 144 *N* (%)	CM arm 72 *n* (%)	SOC arm 72 *n* (%)
Baseline	**144**	**72**	**72**
Suppressed	0 (0)	0 (0)	0 (0)
Unsuppressed (VL $\geq$ 200)	144 (100)	72 (100)	72 (100)
Not done/not collected	0	0	0
Viral load (*N* = no. unsuppressed)			
Mean VL	77 979	60 239	95 718
Median VL	19 459	17 922	22 100
25th	6368	6158	7125
75th	57 573	55 353	63 884
1st Visit, month 3[a]	**144**	**72**	**72**
Suppressed	41 (28)	20 (28)	21 (29)
Unsuppressed (VL $\geq$ 200)	60 (42)	30 (42)	30 (42)
Not done/not collected	43	22	21
Viral load (*N* = no. unsuppressed)			
Mean VL	53 967	54 787	53 148
Median VL	13 047	14 115	11 921
25th	2526	1675	2850
75th	64 250	51 644	73 395
2nd Visit, month 6[a]	**144**	**72**	**72**
Suppressed	52 (36)	26 (36)	26 (36)
Unsuppressed (VL $\geq$ 200)	58 (40)	26 (36)	32 (44)
Not done/not collected	34	20	14
Viral load (*N* = No. unsuppressed)			
Mean VL	51 608	57 884	46 509
Median VL	20 250	30 700	19 509
25th	5654	860	3584
75th	79 721	85 247	72 612
3rd Visit, month 9[a]	**144**	**72**	**72**
Suppressed	56 (39)	28 (39)	28 (39)
Unsuppressed (VL $\geq$ 200)	57 (40)	27 (38)	30 (42)
Not done/not collected	31	17	14
Viral load (*N* = no. unsuppressed)			
Mean VL	90 685	39 580	136 679
Median VL	21 353	16 572	33 350
25th	4925	1461	8355
75th	86 077	55 214	93 600
4th Visit, Month 12[a,b]	**144**	**72**	**72**
Suppressed	68 (47)	30 (42)	38 (53)
Unsuppressed (VL $\geq$ 200)	60 (42)	32 (44)	28 (39)
Not done/not collected	15	10	5
Death	1	0	1
Viral load (*N* = no. unsuppressed)			
Mean VL	60 382	50 123	72 106
Median VL	15 411	21 850	8305
25th	1590	3865	795
75th	62 600	59 950	67 415

The table shows the number of participants based on study visit and study arm. Suppressed indicates that the viral load was <200 copies/ml at the study visit indicated. CM, case manager study arm; *N*, number; SOC, standard of care study arm; HIV viral load (VL, HIV RNA copies/ml). Adjusted for site:
[a]Only percentage among the nonmissing shown.
[b]aOR (95% CI; *P*): 0.62 (0.15,1.2; $P = 0.15$).

Primary outcome: viral load suppression

Table 2 and Supplemental Figure 4, http://links.lww.com/QAD/C681 show data for the primary outcome of viral suppression by study arm, at baseline and across the four quarterly study visits. Of the 144 participants enrolled, viral suppression data were available for 128 participants at the M12 visit. At M12, 47% ($n = 68$) were virally suppressed (defined here as having a viral load <200 copies/ml), with no statistically significant difference between the CM and SOC arms (42% and 53%, respectively; adjusted odds ratio [OR] = 0.62 [$P = 0.15$, 95% confidence intervals [CI] = 0.32, 1.2]). There were no significant differences in viral suppression between the CM and SOC arms at any of the other quarterly visits. Nearly one-third of the participants achieved viral suppression by the M3 visit. Viral suppression rates increased over time among participants in both arms. In addition, we saw no significant difference in frequency of encounters in those who were unsuppressed compared to those who were suppressed in the CM arm ($P = 0.43$) (Supplementary Table 5, http://links.lww.com/QAD/C684). However, there was a significant increase in the number of CM activities in those who were unsuppressed compared to those who were suppressed in the CM arm ($P = 0.02$) (Supplemental Tables 6, http://links.lww.com/QAD/C685–7, http://links.lww.com/QAD/C686).

Predictors of viral load suppression

Given the lack of difference in viral suppression rates between study arms, we next evaluated demographic, health, and psychosocial characteristics that may have been associated with viral suppression. We first evaluated the association of viral suppression with baseline demographic and health characteristics (Supplemental Table 3a, http://links.lww.com/QAD/C682) along with self-reported alcohol and substance use, psychiatric symptoms, and stigma (i.e. HIV and sexual orientation) at baseline (Supplemental Table 3b, http://links.lww.com/QAD/C683). With the exception of marital status ($P = 0.02$), none of these baseline characteristics were significantly different between men who were vs. were not virally suppressed at M12. We next explored

Table 3. Baseline demographics and health characteristics by HIV viral load at month 12.

Participants	Overall 144 *N* (%)	Suppressed (<200) 68 *N* (%)	Unsuppressed 60 *n* (%)	Not collected 16 *n* (%)	*P* value[a]
Age					
18–21	7 (5)	3 (4)	3 (5)	1 (6)	0.66
22–30	36 (25)	16 (24)	15 (250)	5 (31)	
31–40	34 (24)	16 (24)	15 (25)	3 (19)	
41–50	39 (27)	18 (26)	17 (28)	4 (25)	
51–60	26 (18)	15 (22)	8 (13)	3 (19)	
> 60	2 (1)	0 (0)	2 (3)	0 (0)	
Mean	39	40	39	37	
Race					
Native American	1 (1)	0 (0)	0 (0)	1 (16)	0.61
Asian	0 (0)	0 (0)	0 (0)	0 (0)	
Black	121 (84)	57 (84)	53 (88)	11 (69)	
HI/Pacific	0 (0)	0 (0)	0 (0)	0 (0)	
White	19 (13)	9 (13)	3 (5)	7 (44)	
Other	8 (6)	4 (6)	4 (7)	0 (0)	
Latino or Hispanic					
Yes	10 (7)	4 (6)	6 (10)	0 (0)	0.51
No	134 (93)	64 (94)	54 (90)	16 (100)	
Self-identified gender					
Male	139 (97)	66 (97)	57 (95)	16 (100)	0.59
Female	1 (1)	0 (0)	1 (2)	0 (0)	
Transgender female	3 (2)	2 (3)	1 (2)	0 (0)	
Gender non-conforming	1 (1)	0 (0)	1 (2)	0 (0)	
Sexual orientation					
Gay/Lesbian/Homosexual	114 (79)	54 (79)	47 (78)	13 (81)	0.64
Two-spirit	23 (16)	9 (13)	11 (18)	3 (19)	
Straight/heterosexual	5 (3)	4 (6)	1 (2)	0 (0)	
Other	2 (1)	1 (1)	1 (2)	0 (0)	
Education					
High school diploma or less	56 (39)	28 (41)	20 (33)	8 (50)	0.46
Education beyond high school	88 (61)	40 (59)	40 (67)	8 (50)	
Employment					
Full-time employment	27 (19)	13 (19)	11 (18)	3 (19)	1.00
Part-time employment	20 (14)	10 (15)	9 (15)	1 (6)	
Not employed	97 (67)	45 (66)	40 (67)	12 (75)	
Marital status					
Married/civil union/legal partnership	4 (3)	0 (0)	3 (5)	1 (6)	0.02
Living with primary or main partner	16 (11)	12 (18)	3 (5)	1 (6)	
Have primary or main partner, not living together	2 (1)	1 (1)	1 (2)	0 (0)	
Single/divorced/widowed	122 (85)	55 (81)	53 (88)	14 (88)	
Healthcare coverage					
Yes	116 (81)	54 (79)	48 (80)	14 (88)	1.00
No	28 (19)	14 (21)	12 (20)	2 (13)	
Stable housing					
Yes	128 (89)	63 (93)	53 (88)	12 (75)	0.55
No	16 (11)	5 (7)	7 (12)	4 (25)	
Substance use treatment					
Yes	20 (14)	9 (13)	9 (15)	2 (13)	0.37
No	117 (81)	57 (84)	46 (77)	14 (88)	
Prefer not to answer	7 (5)	2 (3)	5 (8)	0 (0)	
Every taken ART[b]					
Yes	124 (86)	59 (87)	52 (87)	13 (81)	0.78
No	18 (13)	9 (13)	7 (12)	2 (13)	
Missing	2	0	1	1	

The table shows the baseline demographics and health characteristics of participants based on viral suppression status. Suppressed indicates that the viral load was <200 copies/ml at the month 12 study visit. Numbers in parentheses indicate percentages, ranges (min/max), or quartiles (Q1, Q3). CM, case manager study arm; *N*, number; SOC, standard of care study arm; HIV viral load (VL, HIV RNA copies/ml). ART, antiretroviral therapy; Min, minimum, Max, maximum, 1–5; Q, quartile; SAMISS, Substance Abuse and Mental Illness Symptoms Screener.
[a]*P*-values are from Fisher exact test. For race, not being mutually exclusive among racial categories, we conducted alternative comparison between Black ''Yes/No'' and VL suppression status.
[b]Percent of the nonmissing number of observations.

whether self-reported alcohol and substance use, psychiatric symptoms, and stigma were associated with viral suppression at M12 (Table 5). We found that participants who achieved viral suppression reported having four or more drinks on one occasion more frequently than those who were not virally suppressed ($P = 0.01$). Other associations were not statistically significant.

Table 4. Comparison of month 12 virally suppressed and nonsuppressed on SAMISS questionnaire – baseline SAMISS[a] and Stigma.

Question	Value[b]	Suppressed at month 12 (VL< 200)	Unsuppressed at month 12 (VL ≥ 200)	*P* value[c]	Chi square test for trend *P* value
Q1. How often do you have a drink containing alcohol?					
	SAMISS not taken	4/68 (6%)	1/60 (1%)	0.49	0.53
	Never	11/68 (16%)	12/60 (18%)		
	Monthly or less	23/68 (34%)	18/60 (26%)		
	2–4 times/month	12/68 (18%)	18/60 (26%)		
	2–3 times/week	12/68 (18%)	7/60 (10%)		
	4 or more times/week	5/68 (7%)	3/60 (4%)		
	Response not valid	1/68 (1%)	1/60 (1%)		
Q2. How many drinks do you have on a typical day when you are drinking?					
	SAMISS not taken	4/68 (6%)	1/60 (1%)	0.84	0.61
	None	17/68 (25%)	17/60 (25%)		
	1 or 2	27/68 (40%)	27/60 (40%)		
	3 or 4	15/68 (22%)	10/60 (15%)		
	5 or 6	3/68 (4%)	4/60 (6%)		
	7–9	1/68 (1%)			
	Response not valid	1/68 (1%)	1/60 (1%)		
Q3. How often do you have 4 or more drinks on 1 occasion?					
	SAMISS not taken	4/68 (6%)	1/60 (1%)	0.20	0.59
	Never	25/68 (37%)	25/60 (37%)		
	Less than monthly	27/68 (40%)	17/60 (25%)		
	Monthly	9/68 (13%)	9/60 (13%)		
	Weekly	1/68 (1%)	6/60 (9%)		
	Daily or almost daily	2/68 (3%)	1/60 (1%)		
	Response not valid		1/60 (1%)		
Q4. In the past year, how often did you use nonprescription drugs to get high or to change the way you feel?					
	SAMISS not taken	4/68 (6%)	1/60 (1%)	0.81	0.53
	Never	40/68 (59%)	31/60 (46%)		
	Less than monthly	9/68 (13%)	11/60 (16%)		
	Monthly	6/68 (9%)	8/60 (12%)		
	Weekly	4/68 (6%)	5/60 (7%)		
	Daily or almost daily	5/68 (7%)	4/60 (6%)		
Q5. In the past year, how often did you use drugs prescribed to you or to someone else to get high or change the way you feel?					
	SAMISS not taken	4/68 (6%)	1/60 (1%)	0.54	0.1
	Never	56/68 (82%)	46/60 (68%)		
	Less than monthly	6/68 (9%)	8/60 (12%)		
	Monthly	2/68 (3%)	3/60 (4%)		
	Weekly		1/60 (1%)		
	Daily or almost daily		1/60 (1%)		
Q6. In the past year, how often did you drink or use drugs more than you meant to?					
	SAMISS not taken	4/68 (6%)	1/60 (1%)	0.66	0.87
	Never	33/68 (49%)	32/60 (47%)		
	Less than monthly	19/68 (28%)	12/60 (18%)		
	Monthly	6/68 (9%)	9/60 (13%)		
	Weekly	3/68 (4%)	4/60 (6%)		
	Daily or almost daily	3/68 (4%)	2/60 (3%)		
Q7. How often did you feel you wanted or needed to cut down on your drinking or drug use in the past year, and were not able to?					
	SAMISS not taken	4/68 (6%)	1/60 (1%)	0.91	0.89
	Never	38/68 (56%)	35/60 (51%)		
	Less than monthly	14/68 (21%)	11/60 (16%)		
	Monthly	2/68 (3%)	4/60 (6%)		
	Weekly	5/68 (7%)	4/60 (6%)		
	Daily or almost daily	5/68 (7%)	5/60 (7%)		
Q8. In the past year, when not high or intoxicated, did you ever feel extremely energetic or irritable and more talkative than usual?					
	SAMISS not taken	4/68 (6%)	1/60 (1%)	0.59	
	Yes	27/68 (40%)	22/60 (32%)		
	No	37/68 (54%)	37/60 (54%)		
Q9. In the past year, were you ever on medication or antidepressants for depression or nerve problems?					
	SAMISS not taken	4/68 (6%)	1/60 (1%)	0.18	
	Yes	17/68 (25%)	23/60 (34%)		
	No	47/68 (69%)	36/60 (53%)		
Q10. In the past year, was there ever a time when you felt sad, blue, or depressed for more than 2 weeks in a row?					
	SAMISS not taken	4/68 (6%)	1/60 (1%)	0.47	
	Yes	27/68 (40%)	29/60 (43%)		
	No	37/68 (54%)	30/60 (44%)		
Q11. In the past year, was there ever a time lasting more than 2 weeks when you lost interest in most things or activities that usually give you pleasure?					
	SAMISS not taken	4/68 (6%)	1/60 (1%)	0.86	
	Yes	27/68 (40%)	26/60 (38%)		
	No	37/68 (54%)	33/60 (49%)		

Table 4 (*continued*)

Question	Value[b]	Suppressed at month 12 (VL< 200)	Unsuppressed at month 12 (VL ≥ 200)	*P* value[c]	Chi square test for trend *P* value
Q12. In the past year, did you ever have a period lasting more than 1 month when most of the time you felt worried and anxious?					
	SAMISS not taken	4/68 (6%)	1/60 (1%)	0.28	
	Yes	23/68 (34%)	27/60 (40%)		
	No	41/68 (60%)	32/60 (47%)		
Q13. In the past year, did you have a spell or an attack when all of a sudden you felt frightened, anxious, or very uneasy when most people would not be afraid or anxious?					
	SAMISS not taken	4/68 (6%)	1/60 (1%)	0.72	
	Yes	26/68 (38%)	22/60 (32%)		
	No	38/68 (56%)	37/60 (54%)		
Q14. In the past year, did you ever have a spell or an attack when for no reason your heart suddenly started to race, you felt faint, or you could not catch your breath?					
	SAMISS not taken	4/68 (6%)	1/60 (1%)	0.33	
	Yes	17/68 (25%)	21/60 (31%)		
	No	47/68 (69%)	38/60 (56%)		
Q15. During your lifetime, as a child or adult, have you experienced or witnessed traumatic events that involved harm to yourself or to others?					
	SAMISS not taken	4/68 (6%)	1/60 (1%)	0.71	
	Yes	41/68 (60%)	35/60 (51%)		
	No	23/68 (34%)	24/60 (35%)		
Q16. In the past year, have you been troubled by flashbacks, nightmares, or thoughts of the trauma?					
	SAMISS not taken	4/68 (6%)	1/60 (1%)	0.35	
	Yes	22/68 (32%)	23/60 (34%)		
	No	19/68 (28%)	12/60 (18%)		
	Question was skipped	23/68 (34%)	24/60 (35%)		
Q17. In the past 3 months, have you experienced any events or received information that was so upsetting it affected how you cope with everyday life?					
	SAMISS not taken	4/68 (6%)	1/60 (1%)	0.34	
	Yes	18/68 (26%)	22/60 (32%)		
	No	46/68 (68%)	37/60 (54%)		
Q18. Have had nightmares about it or thought about it when you did not want to?					
	SAMISS not taken	4/68 (6%)	1/60 (1%)	0.72	
	Yes	25/68 (37%)	25/60 (37%)		
	No	39/68 (57%)	34/60 (50%)		
Q19. Tried hard not to think about it or went out of your way to avoid situations that reminded you of it?					
	SAMISS not taken	4/68 (6%)	1/60 (1%)	0.23	
	Yes	30/68 (44%)	34/60 (50%)		
	No	34/68 (50%)	25/60 (37%)		
Q20. Were constantly on guard, watchful, or easily startled?					
	SAMISS not taken	4/68 (6%)	1/60 (1%)	0.72	
	Yes	25/68 (37%)	25/60 (37%)		
	No	39/68 (57%)	34/60 (50%)		
Q21. Felt numb or detached from others, activities, or your surroundings?					
	SAMISS not taken	4/68 (6%)	1/60 (1%)	0.72	
	Yes	28/68 (41%)	28/60 (41%)		
	No	36/68 (53%)	31/60 (46%)		
1. Internalized Stigma[d]					
	Mean (Min, Max)	2.1 (1, 5)	2.0 (1, 5)	0.40	
	Median (Q1, Q3)	2 (1, 3)	2 (1, 3)		
2. HIV Stigma[e]					
	Mean (Min, Max)	2.9 (1, 5)	2.9 (1, 5)	0.65	
	Median (Q1, Q3)	3 (3, 4)	3 (2, 4)		
3. Community Stigma[f]					
	Mean (Min, Max)	0.3 (0, 1)	0.3 (0, 1)	0.33	
	Median (Q1, Q3)	0 (0, 1)	0 (0, 1)		

The table shows the baseline demographics and health characteristics of participants based on viral suppression status. Suppressed indicates that the viral load was <200 copies/ml at the month 12 study visit. Numbers in parentheses incidate percentatges, ranges (min/max), or quartiles (Q1, Q3). CM, case manager study arm; *N*, number; SOC, standard of care study arm; HIV viral load (VL, HIV RNA copies/ml). ART, antiretroviral therapy; Max, maximum, 1–5; Min, minimum; Q, quartile; SAMISS, Substance Abuse and Mental Illness Symptoms Screener.

[a]SAMISS questions Q22–24 are only available at month 12; CASI questions Q73–79 (engagement in LGBT community) and Q15 (prior ART use) are only available at baseline.

[b]The ''missing'' category was not included in the statistical test.

[c]If variable/question is categorical then the p value is from Fisher's exact test for independence; if variable is numeric then the p value is from Wilcoxon rank sum test.

[d]Average exclude variables with value = 99 (prefer not to answer) from the average.

[e]Average exclude variables with value = 99 (prefer not to answer) from the average.

[f]Calculate the percentage ''Yes'' responses among the variables with responses 1 or 2; exclude 77 (don't know) and 99 (prefer not to answer).

Table 5. Comparison of month 12 virally suppressed and nonsuppressed on month 12 SAMISS[a] and Stigma.

Question	Value[b]	Suppressed at month12 (VL < 200)	Unsuppressed at month12 (VL ≥ 200)	*P* value[c]	Chi square test for trend *P* value[d]
Q1. How often do you have a drink containing alcohol?		*n* = 68	*n* = 60		
	SAMISS not taken	19 (28%)	14 (21%)	0.70	0.79
	Never	10 (15%)	12 (18%)		
	Monthly or less	21 (31%)	18 (26%)		
	2–4 times/month	6 (9%)	5 (7%)		
	2–3 times/week	10 (15%)	6 (9%)		
	4 or more times/week	1 (1%)	3 (4%)		
	Response not valid/Missing	1 (1%)	2 (2%)		
Q2. How many drinks do you have on a typical day when you are drinking?					
	SAMISS not taken	19 (28%)	14 (21%)	0.22	0.74
	None	12 (18%)	17 (25%)		
	1 or 2	22 (32%)	15 (22%)		
	3 or 4	11 (16%)	6 (9%)		
	5 or 6	3 (4%)	6 (9%)		
	Response not valid/Missing	1 (1%)	2 (2%)		
Q3. How often do you have 4 or more drinks on 1 occasion?					
	SAMISS not taken	19 (28%)	14 (21%)	0.01	0.83
	Never	20 (29%)	26 (38%)		
	Less than monthly	22 (32%)	6 (9%)		
	Monthly	3 (4%)	7 (10%)		
	Weekly	3 (4%)	4 (6%)		
	Daily or almost daily	0 (0%)	1 (1%)		
	Response not valid/Missing	1 (1%)	2 (2%)		
Q4. In the past year, how often did you use nonprescription drugs to get high or to change the way you feel?					
	SAMISS not taken	19 (28%)	14 (21%)	0.92	0.74
	Never	34 (50%)	31 (46%)		
	Less than monthly	6 (9%)	4 (6%)		
	Monthly	3 (4%)	5 (7%)		
	Weekly	1 (1%)	1 (1%)		
	Daily or almost daily	4 (6%)	4 (6%)		
	Response missing	1 (1%)	1 (1%)		
Q5. In the past year, how often did you use drugs prescribed to you or to someone else to get high or change the way you feel?					
	SAMISS not taken	19 (28%)	14 (21%)	0.19	0.09
	Never	41 (60%)	36 (53%)		
	Less than monthly	6 (9%)	3 (4%)		
	Monthly	1 (1%)	2 (3%)		
	Weekly	0 (0%)	1 (1%)		
	Daily or almost daily	0 (0%)	3 (4%)		
	Response missing	1 (1%)	1 (1%)		
Q6. In the past year, how often did you drink or use drugs more than you meant to?					
	SAMISS not taken	19 (28%)	14 (21%)	0.09	0.29
	Never	26 (38%)	27 (40%)		
	Less than monthly	15 (22%)	6 (9%)		
	Monthly	5 (7%)	4 (6%)		
	Weekly	2 (3%)	6 (9%)		
	Daily or almost daily	0 (0%)	2 (3%)		
	Response missing	1 (1%)	1 (1%)		
Q7. How often did you feel you wanted or needed to cut down on your drinking or drug use in the past year, and were not able to?					
	SAMISS not taken	19 (28%)	14 (21%)	0.75	0.93
	Never	35 (51%)	31 (46%)		
	Less than monthly	6 (9%)	6 (9%)		
	Monthly	3 (4%)	4 (6%)		
	Weekly	1 (1%)	3 (4%)		
	Daily or almost daily	3 (4%)	1 (1%)		
	Response missing	1 (1%)	1 (1%)		
Q8. In the past year, when not high or intoxicated, did you ever feel extremely energetic or irritable and more talkative than usual?					
	SAMISS not taken	19 (28%)	14 (21%)	0.83	
	Yes	17 (25%)	17 (25%)		
	No	31 (46%)	28 (41%)		
	Response missing	1 (1%)	1 (1%)		
Q9. In the past year, were you ever on medication or antidepressants for depression or nerve problems?					
	SAMISS not taken	19 (28%)	14 (21%)	0.07	
	Yes	18 (26%)	9 (13%)		
	No	30 (44%)	36 (53%)		
	Response missing	1 (1%)	1 (1%)		
Q10. In the past year, was there ever a time when you felt sad, blue, or depressed for more than 2 weeks in a row?					
	SAMISS not taken	19 (28%)	14 (21%)	0.84	

Table 5 (*continued*)

Question	Value[b]	Suppressed at month12 (VL < 200)	Unsuppressed at month12 (VL ≥ 200)	*P* value[c]	Chi square test for trend *P* value[d]
	Yes	20 (29%)	20 (29%)		
	No	28 (41%)	25 (37%)		
	Response missing	1 (1%)	1 (1%)		
Q11. In the past year, was there ever a time lasting more than 2 weeks when you lost interest in most things or activities that usually give you pleasure?					
	SAMISS not taken	19 (28%)	14 (21%)	0.68	
	Yes	18 (26%)	19 (28%)		
	No	30 (44%)	26 (38%)		
	Response missing	1 (1%)	1 (1%)		
Q12. In the past year, did you ever have a period lasting more than 1 month when most of the time you felt worried and anxious?					
	SAMISS not taken	19 (28%)	14 (21%)	0.83	
	Yes	21 (31%)	18 (26%)		
	No	27 (40%)	27 (40%)		
	Response missing	1 (1%)	1 (1%)		
Q13. In the past year, did you have a spell or an attack when all of a sudden you felt frightened, anxious, or very uneasy when most people would not be afraid or anxious?					
	SAMISS not taken	19 (28%)	14 (21%)	0.83	
	Yes	18 (26%)	18 (26%)		
	No	30 (44%)	27 (40%)		
	Response missing	1 (1%)	1 (1%)		
Q14. In the past year, did you ever have a spell or an attack when for no reason your heart suddenly started to race, you felt faint, or you could not catch your breath?					
	SAMISS not taken	19 (28%)	14 (21%)	0.64	.
	Yes	11 (16%)	13 (19%)		
	No	37 (54%)	32 (47%)		
	Response missing	1 (1%)	1 (1%)		
Q15. During your lifetime, as a child or adult, have you experienced or witnessed traumatic events that involved harm to yourself or to others?					
	SAMISS not taken	19 (28%)	14 (21%)	0.54	
	Yes	27 (40%)	22 (32%)		
	No	21 (31%)	23 (34%)		
	Response missing	1 (1%)	1 (1%)		
Q16. In the past year, have you been troubled by flashbacks, nightmares, or thoughts of the trauma?					
	SAMISS not taken	19 (28%)	14 (21%)	0.78	
	Yes	13 (19%)	12 (18%)		
	No	14 (21%)	10 (15%)		
	Question was skipped	22 (32%)	24 (35%)		
Q17. In the past 3 months, have you experienced any events or received information that was so upsetting it affected how you cope with everyday life?					
	SAMISS not taken	19 (28%)	14 (21%)	0.20	
	Yes	14 (21%)	19 (28%)		
	No	34 (50%)	26 (38%)		
	Response missing	1 (1%)	1 (1%)		
Q18. Have had nightmares about it or thought about it when you did not want to?					
	SAMISS not taken	19 (28%)	14 (21%)	0.11	
	Yes	10 (15%)	17 (25%)		
	No	38 (56%)	28 (41%)		
	Response missing	1 (1%)	1 (1%)		
Q19. Tried hard not to think about it or went out of your way to avoid situations that reminded you of it?					
	SAMISS not taken	19 (28%)	14 (21%)	0.41	
	Yes	22 (32%)	25 (37%)		
	No	26 (38%)	20 (29%)		
	Response missing	1 (1%)	1 (1%)		
Q20. Were constantly on guard, watchful, or easily startled?					
	SAMISS not taken	19 (28%)	14 (21%)	1.00	
	Yes	20 (29%)	18 (26%)		
	No	28 (41%)	27 (40%)		
	Response missing	1 (1%)	1 (1%)		
Q21. Felt numb or detached from others, activities, or your surroundings?					
	SAMISS not taken	19 (28%)	14 (21%)	0.68	
	Yes	20 (29%)	21 (31%)		
	No	28 (41%)	24 (35%)		
	Response missing	1 (1%)	1 (1%)		
1. Internalized Stigma[e]					
	Mean (Min, Max)	2.1 (1, 5)	2.0 (1, 5)	0.70	
	Median (Q1, Q3)	2 (1, 3)	2 (1, 3)		
2. HIV Stigma[f]					
	Mean (Min, Max)	2.9 (1, 5)	2.9 (1, 5)	0.21	

Table 5 (*continued*)

Question	Value[b]	Suppressed at month12 (VL < 200)	Unsuppressed at month12 (VL ≥ 200)	*P* value[c]	Chi square test for trend *P* value[d]
	Median (Q1, Q3)	3 (3, 4)	3 (2, 4)		
3. Community Stigma[g]					
	Mean (Min, Max)	0.3 (0, 1)	0.3 (0, 1)	0.43	
	Median (Q1, Q3)	0 (0, 1)	0 (0, 1)		

The table shows the baseline demographics and health characteristics of participants based on viral suppression status. Suppressed indicates that the viral load was <200 copies/ml at the month 12 study visit. Numbers in parentheses incidate percentatges, ranges (min/max), or quartiles (Q1, Q3). *N*, number; HIV viral load (VL, HIV RNA copies/ml). Max, maximum, 1–5; Min, minimum; Q, quartile; SAMISS, Substance Abuse and Mental Illness Symptoms Screener.
[a]SAMISS questions Q22–24 are only available at month 12; CASI questions Q73–79 (engagement in LGBT community) and Q15 (prior ART use) are only available at baseline.
[b]The ''missing'' category was not included in the statistical test.
[c]If variable/question is categorical then the p value is from Fisher's exact test for independence; if variable is numeric then the p value is from Wilcoxon rank sum test.
[d]A Chi square test for trend is also conducted to take account of the trend of variable values if the categorical variable is ordinal.
[e]Average exclude variables with value = 99 (prefer not to answer) from the average.
[f]Average exclude variables with value = 99 (prefer not to answer) from the average.
[g]Calculate the percentage ''Yes'' responses among the variables with responses 1 or 2; exclude 77 (don't know) and 99 (prefer not to answer).

Discussion

HPTN 078 engaged MSM who were PWH and were not virally suppressed and evaluated the impact of a CM intervention on linkage to care and viral suppression. By the final study visit, nearly half of the men (42% in the CM arm and 54% in the SOC arm) achieved viral suppression, which is a notable achievement for this cohort but falls short of national EHE goals. There was no significant difference in viral suppression between the study arms. Although the trial was underpowered for our original objectives, the 95% CI for the intervention effect does exclude a beneficial effect of CM greater than an odds ratio of 1.20. Furthermore, most participant characteristics (i.e. sociodemographic, health, and psychosocial factors) were not associated with viral suppression after 12 months of follow-up although the power to detect such associations was low.

Most study participants reported a prior HIV diagnosis and were, therefore, aware of their status prior to study participation. Likely reasons for viremia among PWH include not being on ART, poor ART adherence, or treatment failure due to inadequate ART regimen and/or drug resistance. HIV drug resistance was detected in 44 (31%) of 143 individuals at study baseline [30]. Given the recruitment challenges of this often neglected population [17], it is noteworthy that the study team was able to engage these men and retain the majority (90%) of participants in the study for 12 months and that nearly half achieved viral suppression over the course of one year. Also worth noting is that this study was conducted in cities in which EHE efforts were being implemented, perhaps contributing to viral suppression improvements regardless of study arm. It is also possible that study engagement, in and of itself, given the numerous incentivized study visits scheduled, facilitated re-engagement in care and treatment across both study arms, thus, potentially diluting intervention impact and leading to viral suppression for nearly half of these men who were not receiving or adhering to optimal ART when recruited into the study. A study of MSM and transgender women in a sub-Saharan Africa observational cohort (HPTN 075), without an intervention to improve ART use or achieve viral suppression, found that, over 12 months, the proportion of participants using ARV drugs increased from 28.1% to 59.4% and the proportion with VLs <400 copies/ml increased from 21.9% to 57.8%; this demonstrates the feasibility of recruiting a predominantly MSM cohort and achieving increased ART uptake and HIV viral suppression without implementing an intervention [31]. In HPTN 078, we observed that viral suppression incrementally increased over the course of the 12-month observation period. Given the potency of current ART regimens, many people starting ART are able to achieve viral suppression relatively quickly (i.e. within 1-2 months) [32]. However, many of the HPTN 078 study participants took longer to achieve viral suppression with an incremental number achieving viral suppression at 3, 6, and 12 months of observation. Social determinants of health and other factors may have limited access to optimal HIV care and treatment impeding more rapid and sustained viral suppression.

It was surprising that so few of the variables measured in this study were associated with viral suppression. It may be that the variables measured were limited, and/or we did not adequately measure the most relevant and important social determinants of health. A paper was recently published which evaluated qualitative data collected during exit interviews with study participants and study case managers in this study which provides greater insight into our main study findings, an in-depth description of the multiple barriers to adherence faced by this largely ''out of care'' population, as well as a more

nuanced understanding of the benefits and challenges of implementing MI into case management [33–35].

Unfortunately, the CM intervention did not enhance viral suppression in comparison to the SOC arm of the study. We believe that the most likely explanation for the lack of an intervention effect in our study is the fact that the clinical care sites where SOC participants were referred by the study team and received their HIV care were able to provide adequate case management services to most patients, including our study participants. This would mean that the enhancements we provided in the CM intervention (i.e. counselors trained to use MI, use of the communication platform) were not significantly distinct from SOC, nor powerful enough as added components, to make a difference in HIV clinical outcomes among our study participants above and beyond the impact of study participation itself, within a one-year timeframe. It is also possible that individuals with multiple intersecting barriers to viral suppression need more than MI to support their complex care needs. Also, since the frequency and type of interactions with CM, as well as use of the communication platform, was determined by the participants, there was a wide range of intervention exposure. Many participants did not perceive a need for, or want, the enhanced case management that was offered to them. Even when we looked at dose intensity, the number of encounters did not enhance intervention impact on viral suppression. However, participants with a greater number of activities with their case managers were actually less likely to be virally suppressed at the end of the study. One possible explanation for this may be that those who needed a lot of help asked for it and received it from the case managers, but the increased supportive activities remained insufficient for greater achievement of viral suppression. Further, and unfortunately, there was a gap between the availability of participants' viral load data and the timing of the CM sessions. Thus, the case managers were not able to provide counseling that could have been more closely directed to lack of viral suppression in real time.

The study cohort was comprised predominantly of men who reported that they were aware of their HIV status before being tested in the HPTN 078 study; many of the enrolled participants also reported having had HIV care engagement prior to study participation. The number of younger participants (i.e. aged 21 years and under) was also small; the average age of the participants was 39 years, with most between the ages of 41–50. We do not know whether the CM intervention, with its communication platform, may have improved viral suppression among younger men and among men who were newly diagnosed with HIV. Finally, the intervention was not designed to address broader social determinants of health, including social and structural barriers such as intersectional stigma, racism, and lack of culturally sensitive care from providers in healthcare settings. More comprehensive interventions (e.g. at the community, healthcare facility, interpersonal, and individual levels) may be needed to address the multiple societal and behavioral challenges among disenfranchised MSM in the United States.

Conclusion

HPTN 078 was a randomized controlled trial comparing an enhanced CM intervention to SOC in four US cities. The study enrolled participants who were mostly older, non-White, and economically disadvantaged with high unemployment; most reported prior knowledge of their HIV-positive status. All had viral loads >1000 copies/ml at study entry, and nearly half achieved viral suppression (<200 copies/ml) within 12 months with no statistically significant difference between the two study arms. It is possible that engagement in care facilitated through study recruitment and participation alone contributed to viral suppression among many of the participants within the course of one year. Reaching targets of at least 90% sustained viral suppression among PWH will likely require an integrated strategies approach that addresses barriers to optimal care and treatment at multiple levels. Further research is needed to achieve this goal, to help end the HIV epidemic among disenfranchised populations in the US and across the globe.

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Ethical approval: All procedures performed in studies involving human participants were performed in accordance with the ethical standards of the local institutional review board for each study site that approved the protocol prior to study implementation.

Informed consent: Informed consent was obtained from all individual participants in the study.

Conflicts of interest

There are no conflicts of interest.

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