



Effectiveness of a Viral Load Suppression Intervention for Highly Vulnerable People Living with HIV

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Published online: 16 May 2019
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Abstract

We examine the effect of the Undetectables Intervention (UI) on viral loads among socially vulnerable HIV-positive clients. The UI utilized a toolkit that included financial incentives, graphic novels, and community-based case management services. A pre-post repeated measures analysis ($n = 502$) through 4 years examined longitudinal effects of the intervention. Logistic models regressed social determinants on viral loads. Finally, in-depth qualitative interviews ($n = 30$) examined how UI shaped adherence. The proportion of virally suppressed time-points increased 15% (from 67 to 82% pre to post-enrollment, $p < 0.0001$). The proportion of the sample virally suppressed at all time-points increased by 23% (from 39 to 62% pre to post-enrollment, $p < 0.0001$). African Americans and the homeless were the most likely to be unsuppressed at baseline, but, along with substance users, benefitted the most from UI. The intervention shaped adherence through two pathways, by: (1) establishing worth around adherence, and (2) increasing motivation to become suppressed, and maintain adherence.

Keywords HIV · Antiretroviral adherence · Financial incentives · Social determinants of health · Viral load suppression · HIV transmission · Medication adherence · Vulnerable populations

Resumen

Examinamos el efecto de la Intervención los Indetectables (II) sobre cargas virales entre clientes de VIH que son socialmente vulnerables. La II utilizó un conjunto de servicios y recursos que incluía incentivos financieros, novelas gráficas, y servicios de manejo de casos basados en la comunidad. Un análisis repetitivo pre y post- ($n = 502$) sobre cuatro años examino longitudinalmente los efectos de la intervención. Modelos logísticos incluyeron determinantes sociales sobre cargas virales. Finalmente, entrevistas cualitativas a profundidad examinaron como la II afectó adherencia a la medicación. La proporción de puntos en tiempo de cargas virales suprimidas aumento 15% (de 67% preinscripción a 82% postinscripción, $p < 0.0001$). La proporción de la muestra de cargas virales suprimidas a todos puntos en tiempo aumento por 23% (de 39% preinscripción a 62% postinscripción, $p < 0.0001$). Afroamericanos y gente sin hogar fueron más probable de no tener cargas virales suprimidas en la línea de base, pero, junto con individuos que usan sustancias, fueron los que beneficiaron más de la II. La intervención dio forma a la adherencia a través de dos rutas, por: (1) estableciendo valor a la adherencia, y (2) aumentando motivación para suprimir la carga viral y mantenerse adherente.

Introduction

Effective antiretroviral therapy (ART) that durably suppresses the amount of human immunodeficiency virus (HIV) in the blood will sustain optimal health for a person with HIV infection and effectively eliminate the risk of ongoing sexual transmission [1, 2]. However, underlying social and behavioral determinants prevent some individuals and communities from benefiting equally from HIV treatment advances. Barriers to ART adherence for people with HIV (PWH) include lack of stable housing [3–5], food insecurity

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[6, 7], engaging in commercial sex [8], incarceration [8, 9], substance use [10, 11], and mental illness [12, 13]. These barriers undermine sustained viral suppression, with substance use [14], homelessness [15], food insecurity [15], and mental illness [16] contributing significantly to virologic failure. As a result, scholars have highlighted the role of social drivers in poor HIV health outcomes, calling for interventions designed to address social and structural barriers as an essential component of effective strategies to reduce HIV health inequities and end the HIV epidemic [17, 18].

Effective interventions to boost medication adherence include cognitive behavioral therapy (CBT) [19–21], motivational interviewing (MI) [22, 23], case management [24, 25], HIV care coordination [26], community-based directly observed therapy (DOT) [27], the utilization of adherence devices such as pill boxes, electronic reminders, and electronic medication packages [28, 29], and engaging clients in peer specialist support [30].

Financial incentives may also be an effective and relatively inexpensive intervention to boost medication adherence among marginalized clients [31–35]. A meta-analysis examining the effect of incentives on medication adherence in general found a significant effect across studies [32], although reviews of the literature on ART adherence have shown mixed results [35, 36]. While one recent study found significant but modest effects of incentives on ART adherence [37], others found no difference between groups [38, 39]. Few studies have examined the effectiveness of financial incentives in community-based settings where they are linked to a suite of other evidence-based adherence services. Moreover, the scholarship on financial incentives summarized above assumes that they operate through a rational cost–benefit analysis on the part of recipients, without empirically establishing this vector of decision-making.

This study addresses these research gaps by examining the effect of the Undetectables Intervention (UI) on viral load suppression among socially vulnerable HIV-positive clients at a large health and social services organization in the city of New York. The UI was implemented over a 24-month period beginning March 1, 2014 and ending February 29, 2016, in six agency settings located in the neighborhoods of downtown Brooklyn, East New York, and the lower eastside of Manhattan. The details of the UI have been discussed elsewhere [40, 41] and are described here in brief.

Drawing on the Integrated Model of Behavior [42], the intervention consisted of several modules that sought to engage with the processes that shape health behaviors by establishing health-seeking norms, improving attitudes, increasing self-efficacy around adherence, and addressing influential precursor factors in the external environment. The first element of the UI consisted of a superhero-themed social marketing and patient education campaign that employed graphic novels to valorize medication adherence

as a heroic act to protect individual and community health [43]. The second key UI element comprised participants being assigned to interdisciplinary adherence support teams that consisted of medical doctors, case managers, and clinical social workers. Trained by a team from the University of Pennsylvania in CBT and MI modalities of engagement (over multiple booster sessions throughout the course of the intervention), adherence teams engaged in periodic sessions with participants, monitored their viral loads, and linked them to housing, psychiatric care, substance use support, and medical treatment. Monthly meetings bringing together all teams (across the various agency locations) focused on emerging barriers to adherence, and ways to address them. Finally, the financial incentive element rewarded participants with viral loads at or below 50 c/ml at their quarterly assay, with a \$100 gift card.

Methods

Procedures

To examine the impact of the UI on viral load suppression among PWH confronted by significant psychosocial challenges such as substance use and homelessness, we conducted a pre-post repeated measures analysis utilizing multiple time-points, followed by qualitative exit interviews with some participants of the intervention. The pre-post analysis examined the effectiveness of the intervention over time, while the exit interviews explored barriers, facilitators, and potential mechanisms for the observed effect.

In the pre-post analysis, RNA viral load reports post-intervention (i.e. after participant enrollment in UI) were compared to at least two viral load reports prior to the intervention. The multiple pre-intervention time-points allowed us to obtain a stable baseline to assess pre-intervention effects of treatment-as-usual. Client-level data for the final sample ($n = 502$) were obtained from client medical records.

Next, we conducted 30 semi-structured qualitative exit interviews with UI participants to examine the way the intervention shaped health behaviors regarding ART adherence.

Recruitment of Participants

For the pre-post analysis, participants in the intervention who had viral loads from at least two pre- and two post-intervention time-points were included in the study to ensure sufficient timepoints for analysis. The intervention enrolled 804 participants over the course of two years. Of these, 302 did not have at least two timepoints each in the pre and post-initiation period for various reasons, such as being new enrollees in the agency or in the intervention, and attrition. This left 502 participants who were included in the study.

For the qualitative exit interviews, snowball sampling methods were utilized to recruit UI participants, with the initial cohort of recruits ($n=4$) being referred to the study by case managers implementing the intervention. Subsequently, participants were referred by those who had previously completed the interviews themselves. Recruitment ended when conceptual saturation was reached, whereby no new themes emerged from the analysis of the interviews [44].

Measures

Outcome Variables

Drawing on the concept of cumulative exposure to HIV viremia [45], we examined the proportion of time spent virally suppressed as our outcome of interest. Viral suppression was tracked using two standards: < 200 copies/ml, a commonly used public health indicator of viral suppression, and < 50 copies/ml, an indicator of undetectable viral load that was incentivized by the intervention. Since participants in the intervention enrolled on a rolling basis throughout the two-year study period, this measure of time spent virally suppressed standardizes across cases with differing numbers of time-points. Quarterly viral load assays were conducted by the agency's primary care clinics.

Correlates

Substance use, mental illness, homelessness, and demographic data were obtained from client records documenting clinical assessments and diagnoses.

Analysis

Analysis of variance models were utilized to compare the proportion of time spent virally suppressed, and the proportion of participants with suppressed viral loads at all time points, before and after enrollment. Logistic regression models were utilized to examine the effect of participant characteristics on viral load suppression over time. We utilized an intent-to-treat approach for participants included in the analyses (those with at least two viral loads reported in agency records prior to UI enrollment), retaining attriters in the analyses, and controlling for attrition in the models.

For the qualitative arm, we used NVIVO (N6) [46] to analyze the data. Drawing on a grounded theory approach using sensitizing concepts [47, 48], thematic analyses were employed to identify concepts and themes. Initial sensitizing themes such as norms, attitudes, efficacy, and external precursors with respect to adherence were drawn from the Integrated Model of Behavior [42], then re-analyzed to fit the data more closely and to account for emerging themes from the interviews. Two research team members coded

ten interviews in an initial round, developing the first set of codes. Codes were retained when the research team, comprising organizational members familiar with the setting and the community, reached consensus about their salience, meaning, accuracy, and reproducibility [49, 50]. The two coders applied these codes to subsequent interviews, adding to them when new themes emerged. In order to ensure intercoder agreement, discrepancies in codes, as well as new, emergent codes were discussed by the research team.

Results

The sample constituted an extremely socially vulnerable population of PWH: 50% had a mental illness diagnosis (95% confidence interval [CI] 0.46–0.52), 63% used illicit drugs (95% CI 0.59–0.67) and 60% experienced homelessness during the study period (sleeping in a shelter or other emergency housing or on the street) (95% CI 0.56–0.64). The mean age of the sample was 45 (95% CI 44–46), with 71% being African American (95% CI 0.67–0.75), 20% Latino (95% CI 0.17–0.24), 27% women (95% CI 0.23–0.31), and 2% transgender (95% CI 0.1–0.3).

Of the 30 participants who completed the qualitative exit interviews, 57% were women, 10% transgender, 53% identified as heterosexual, 77% identified as Black or African American, 13% as Latino/a or Hispanic, and 3% as Mixed. The average age of this sample was 46.

We present results of the quantitative analysis examining the impact of the UI, followed by the qualitative analysis examining the mechanism of its effect.

Quantitative Results

A significant proportion of participants transitioned from a detectable viral load at the last assay before enrolling in the UI, to an undetectable viral load at their first assay after joining the program (we describe this as an enrollment effect). In all, 13% ($v_l < 50$ c/ml) of the sample experienced an enrollment effect. We identify transitioning from detectable immediately prior to enrollment, to undetectable at the last viral load collected during the study period, as an intervention effect. We found that 18% ($v_l < 50$ c/ml) of the sample experienced an intervention effect (Table 1). Using the alternative measure of < 200 c/ml for viral load suppression, 11% of the sample experienced an enrollment effect and 13% an intervention effect (Table 1).

There was a significant increase in the proportion of undetectable time-points, as well as the proportion of the sample that was undetectable at all time-points, pre to post-enrollment (Table 1). On average, the mean proportion of undetectable time-points ($v_l < 50$ c/ml) for each participant increased significantly from 58 to

Table 1 Intervention effects (n = 502)

	VL ^a < 50 copies/ml (95% Confidence Interval)		VL < 200 copies/ml (95% Confidence Interval)	
Proportion with an enrollment effect	12.6 (10.1, 15.0)		10.6 (8.3, 12.8)	
Proportion with an intervention effect	17.9 (15.1, 20.8)		13.4 (10.8, 15.9)	
	Pre-enrollment	Post-enrollment	Pre-enrollment	Post-enrollment
Proportion of time-points suppressed	57.9 (54.8, 61.1)	74.6* (71.8, 77.5)	67.0 (64.0, 70.0)	82.4* (79.9, 84.8)
Proportion of sample suppressed at all time-points	26.3 (22.4, 30.2)	46.2* (41.8, 50.6)	39.0 (34.8, 43.3)	61.8* (57.5, 66.0)

^aViral load*Paired *t* test $p < 0.0001$

75% pre to post-enrollment, an increase of 17% (95% CI 13.84–19.56%, $p < 0.0001$). The proportion of participants who were undetectable at all assessed time-points pre to post-enrollment increased from 26 to 46%, a difference of 20% (95% CI 15.32–24.52%, $p < 0.0001$). Using the alternative measure of < 200 c/ml for viral load suppression, the mean proportion of suppressed time-points for each participant increased 15% post-enrollment (from 67 to 82% pre to post-enrollment, 95% CI 12.66–18.13%, $p < 0.0001$) and the proportion of participants virally suppressed at all time-points increased by 23% (from 39 to 62% pre to post-enrollment, 95% CI 18.11–27.31%, $p < 0.0001$).

For vl < 50 c/ml, African Americans (AOR = 0.42, 95% CI 0.26, 0.68) and homeless clients (AOR = 0.52, 95% CI 0.34, 0.79) were half as likely as their counterparts to be virally undetectable (vl < 50 c/ml) at baseline, the last assay prior to enrollment (Table 2). However, African Americans were twice as likely as their counterparts to experience an enrollment effect (AOR = 2.26, 95% CI 1.13, 4.51). Moreover, African Americans (AOR = 1.86, 95% CI 1.06, 3.31) and substance users (AOR = 1.87, 95% CI 1.07, 3.25) were almost twice as likely as their counterparts to experience an intervention effect. Finally, after controlling for viral load at baseline, no risk factor was negatively associated with durable viral suppression (undetectable at all time-points) post-intervention (not shown).

Of the study sample, 14% were disenrolled from the intervention (i.e. had at least two follow-up time-points post-enrollment, but dropped out before the study ended), for reasons that included voluntary disenrollment, relocation, death, incarceration, or loss to follow-up. In analyses utilizing available time-points, attrition was not associated with any of the outcomes after controlling for other correlates.

Table 2 Regressing viral loads on correlates (n = 502)

	Suppressed at baseline ^b AOR ^c (95% CI ^f)	Enrollment effect ^c AOR (95% CI)	Intervention effect ^d AOR (95% CI)
VL ^a < 200 c/ml			
African American	0.52 (0.30, 0.91)	NS	NS
VL < 50 c/ml			
African American	0.42 (0.26, 0.68)	2.26 (1.13, 4.51)	1.87 (1.06, 3.31)
Homeless (literal)	0.52 (0.34, 0.79)	NS	NS
Substance use	NS ^g	NS	1.87 (1.07, 3.25)

^aViral load^bOdds of being suppressed immediately pre-enrollment^cOdds of transitioning to being suppressed immediately pre to post-enrollment^dOdds of transitioning to suppressed from pre-enrollment to last follow-up^eAdjusted odds ratio^fConfidence interval^gNot significant

Qualitative Results

Our results indicate that the UI increased ART adherence by: (1) attaching worth to viral suppression; and (2) increasing motivation to achieve and maintain suppression. Moreover, motivation was boosted by: (a) demonstrating at enrollment the collective and personal benefits of viral suppression, and (b) sustaining adherence through: (i) establishing a healthy orientation, (ii) improving material well-being, and (iii) engaging participants in supportive services and health-seeking relationships with providers (Fig. 1).

Establishing Meaning to Staying Adherent

The financial incentives element included in the UI, far from simply commodifying the act of medication adherence, actually expanded the meaning attached to becoming virally suppressed by signaling to suppressed participants that they were appreciated. One participant notes, “It is a lot of work to remember to be on time and then come for the appointments, so I think it is a reward not a bribe” (mixed-race man, 47 years old). Describing the manner in which the incentives improved his self-esteem, an African American male participant noted, “the money feels good. I am doing something right, I am taking care of myself” (African American man, 55 years old). Discussing the role of the incentives in helping him recognize that he was part of a larger effort to end AIDS, another participant states, “When they pay me for being suppressed...they are telling me that I am doing my part...in ending this in New York. And maybe for the whole world. That’s what the card means, you know? No

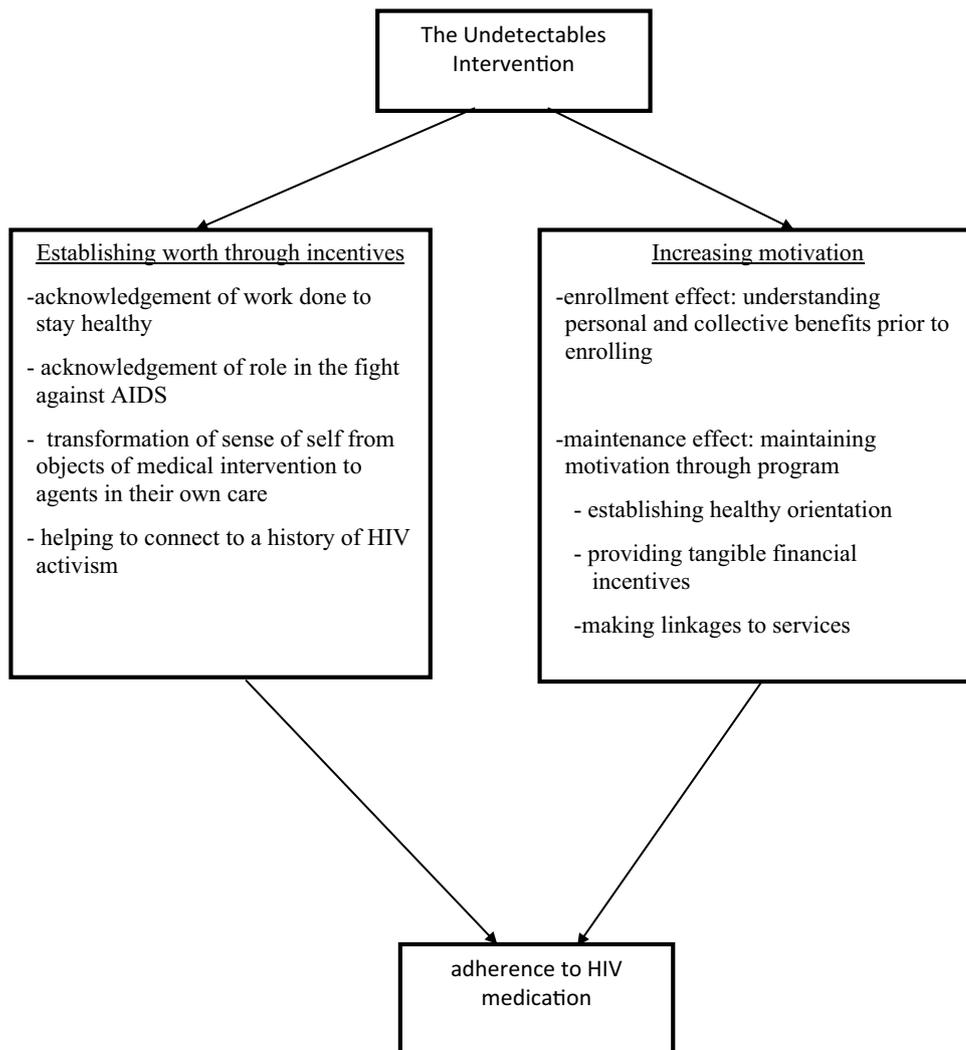
one has told me that before. Getting that [card] reminds me that I’m in this with everyone else” (African American man, 65 years).

The feeling of being collaborative agents, rather than mere objects of medical intervention invoked a sense of history for some participants. Three participants note:

You get tired of being talked down to by doctors because you have this disease. Being part of this program where I’m earning money to stop the epidemic—that makes me feel like I’m part of the old days, you know? Those days when this was a movement and a struggle and we were doing things for the community (Latina woman, 53 years).

I’m old enough to remember the ACT-UP era. This program—that’s what it reminds me of. The money is like saying screw you, we deserve this. We are telling you how to treat us. You don’t tell us how to have sex, or who to

Fig. 1 The pathway to viral load suppression



have sex with. We earned this (African American man, 56 years old).

The vouchers, the money—it all makes me feel like I'm coming to work, you know? Not just a clinic. I'm not being looked at as a diseased person. I'm earning money for coming in. It's a job—and the job is fighting AIDS (Latino man, 28 years old).

The act of being paid for staying adherent was transformative for participants because it reversed the stigma of being a PWH, encouraging participants instead to view themselves as active collaborators in the fight against AIDS, as part of a larger movement, and perhaps even as torch-bearers of a new era in HIV activism. These subjective elements triggered by the financial incentives of the UI were key in building worth around the concept of staying adherent and virally undetectable.

Increasing Motivation

Providing further evidence of the enrollment and maintenance effects that emerged in the quantitative analysis, our qualitative results indicate that the UI increased motivation to join the program and adhere initially, and maintained adherence through benefits.

Enrollment Effect The incentives provided a new goal to “over-programmed” PWH, signaling to them that they were part of a unique intervention to suppress their viral loads. One participant says, “It was beyond what you were used to hearing every day about taking your meds, you know? It was a new program. I wanted that card, to be part of it” (African American woman, 42 years old).

The graphic novels featuring superheroes in the fight against HIV also played a crucial role in motivating clients to join and reach suppression. A transgender woman (African American, 37 years old) analyses the way the novels connected with the way she aspired to present herself visually, a crucial aspect of her transgender identity, “I take care of my skin and diet and my meds. It is like superwoman, we have the superwomen in comic books at Housing Works. I think Trans women want to be that, superwomen. We are big (laughs) and powerful, we want to beat this thing and use our powers to get what we want.” Another participant states, “I love them (the comics)...I joined Undetectables after she [his wife] got me the books... It is like I have super powers now, I am strong” (African American man, 46 years old).

Maintenance Effect The UI incentives helped to maintain adherence for enrolled participants by: (1) inculcating a health-seeking orientation, (2) providing tangible material benefits and helping clients resist inappropriate transactions

that involved their medication, and (3) successfully linking to services through the adherence toolbox.

Inculcating a health seeking orientation: By showcasing the ability to maintain health through viral suppression, the UI helped to shape a health-seeking orientation among participants. One participant notes for instance, “I started to do it for the card, but as I progress, I see the possibility of surviving. I want to survive more than getting the card now” (African American woman, 46 years old). An older African American woman (60 years old) vehemently asserted her will to live by stating, “No, no, I do not want to die any more. I have to live, card or no card now.” Similarly, another older African American woman (55 years old) states, “A hundred dollars to save your life? That is a no brainer. It gives you great incentive to take your medication.” The transgender woman (37 years old) who discussed the importance of looking good earlier, emphasized the non-monetary salience of the gift cards by noting, “Gotta be on top of your health. The gift card is like the icing on the cake. The cake itself is you doing what you are supposed to do.”

Eventually, the intervention helped to shape health-seeking norms around adherence. One participant notes, “I was horrible with taking my medication, always horrible. Then I thought that, that's why they have this program because I am not the only one...I started doing what others in the program were doing—taking the meds, attending appointments...you know, even supporting others to do it” (African American woman, 24 years old). Another woman (African American, 50 years old) describes the transformative effect of being around people motivated by the incentives to stay healthy, “Seeing people get better and then the others [not in the program] who got worse, people dying. Here today, gone tomorrow. I did not want to become a statistic. I wanted to live.”

Providing tangible material benefits: The incentives constituted tangible rewards that allowed participants to improve their quality of life. Participants reported that gift cards helped to defray costs for food, shoes, essential clothes, and medicine. An older African American woman (62 years old) echoed several others' thoughts when she said, “I try to make it last, you know. It is like having money in the bank. You can buy things.” When the cards were used to defray costs of self-care and entertainment, they helped to improve participants' mental status and self-esteem. One participant who applied the cards to the cost of watching movies noted, “It makes me feel better to be able to pay for ordinary things that others can do, like watching movies” (African American man, 75 years old).

Participants were aware of the opportunity of selling their ART medication on the street. One noted, “You get fifty, may be twenty on the streets. Yes, they still approach me on the streets for the meds. Pharmacies will buy them, people on streets buy them and sell them to other countries”

(African American woman, 27 years old). However, the amount of the available incentive was considered sufficient to outweigh the financial benefits of selling medication. One participant pointed out, “Selling pills is another thing that the program has put a stop to. The gift card helps (with that)” (Transgender Latina woman, 30 years old). Another participant noted, “They just give you 25 dollars on the street. They do not even give you that much money, I am better off in the program getting my hundred dollars every four months” (White man, 57 years old).

The incentives thus constituted a substantive and tangible material benefit to participants that allowed them to experience an improvement in their circumstances, and resist the financial transactions that undermine adherence.

Linkages to Services and Support The incentives significantly increased motivation to engage in treatment services at the agency. An African American man (36 years old) note, “The card was a first step. And then I got connected to other stuff. The messages I get reminding me really help.” Describing the way engagement in treatment became salient over the long run, another said, “I gotta go to my groups, man. That’s how I keep being undetectable and getting that card” (Mixed race man, 50 years old).

The incentives encouraged participants to develop their own networks of support. Two participants noted:

We help each other get the incentive cards now. I have a friend ring me up, you know, like a buddy. I ring her up too. We check on each other: ‘Have you taken the pills? Please take them’ (African American woman, 56 years old).

My daughters ring me up every day now and ask, ‘Have you taken the medicines?’ They love their father, I do not know why. My buddy also calls and checks in with me (African American man, 65 years old).

Finally, the intervention fostered improved communication with physicians in the integrated care teams. Describing these conversations, two participants reported:

The program has helped me and (my primary care physician) talk more. I like her better than my Philly doctor. I used to see him only a few times a year, here she keeps me on my toes (African American man, 38 years old).

We have that kind of relationship. My doctor tells me, ‘you have to up it, the tests are not good.’ I like that we can talk like this (White man, 38 years old).

The UI thus supported linkages to care and improved the quality of services in significant ways that ultimately helped clients stay adherent in the program.

Discussion

The Effectiveness of the UI

By increasing and maintaining adherence to ART, the UI significantly increased time spent virally suppressed in a population of socially vulnerable PWH. The large increases, pre to post-enrollment in proportion of time-points virally suppressed and proportion of persons virally suppressed at all time-points indicate large effect sizes of the intervention. Both the quantitative and the qualitative analyses indicate that these increases in rates of viral suppression were achieved through an enrollment effect (i.e. transition from unsuppressed to suppressed status from pre- to post-enrollment), and an enduring intervention effect (i.e. transition to suppressed status from immediately pre-enrollment, to last time-point).

Significant disparities in viral load suppression rates at baseline associated with markers of social vulnerability disappeared post-enrollment. Some groups who were more at-risk immediately prior to enrollment in the UI, including African Americans and persons experiencing homelessness, were less likely to be at-risk after participating in the program, and substance users were almost one and a half times more likely than non-substance users to experience an enduring intervention effect. These results indicate that the some of the most socially marginalized clients benefitted from the intervention even more than their counterparts.

The Mechanism of Effectiveness

The qualitative results highlight the two pathways through which the UI increases adherence: (1) by establishing meaning and worth connected to staying adherent, and (2) by increasing motivation.

Participants emphasized the manner in which the financial incentives, the social marketing campaign, and the engagements with their UI integrated care teams connected them to their contribution to the fight against AIDS, creating positive meaning around their role in staying adherent. Moreover, providing further evidence for themes that emerged in the quantitative analyses, the qualitative results indicate that motivation was increased significantly during enrollment, and was maintained over time in the program. The enrollment effect was triggered by the incentives and the graphic novels, while motivation to adhere was maintained through establishing a healthy orientation, rewarding healthy behavior, and making linkages to services.

Taken together, these results amplify and build upon recent findings on the effectiveness, mechanism and cost

effectiveness of financial incentives for ART adherence. When used in conjunction with integrated health and social services and a suite of other evidence-based supports, financial incentives can be a crucial tool for addressing the barriers to ART treatment effectiveness that confront economically and socially marginalized PWH.

Implications for Practice and Research

The HIV epidemic is concentrated in socially marginalized communities, with scholarship continuing to highlight the salience of the social drivers of the disease [16, 17]. The UI represents a multimodal and multilevel response, in a community-based agency setting, to the complex challenges facing PWH living in poverty who negotiate significant social barriers. Future research needs to scale-up the intervention across agencies working in similarly marginalized communities to examine the feasibility and effectiveness of implementing the UI in a larger context. Moreover, the salience of enrollment and maintenance effects in this study (in both, the quantitative and the qualitative analyses) underlines the importance of recruiting and retaining socially marginalized clients in adherence interventions through a toolkit of interventions and incentives. Future research and practice in the ART adherence field need to focus on these dimensions of interventions.

Limitations

Since this was not a randomized control trial (RCT), relationships are associational and not causal. The study utilized the conditions of a natural experiment with variable numbers of time-points and differing enrollment dates, in a community-based care setting in which randomization was logistically and ethically impracticable. While our analyses accounted for these factors through the use of appropriate outcome variables and triangulating results through multiple models, future research that utilizes a comparison group would further test the outcomes of the UI as an integrated approach to adherence support. Cost-effectiveness analyses are also needed to examine the case for including financial incentives as a relatively inexpensive component of ART adherence support systems for PWH who face social and structural barriers to durable viral load suppression. The qualitative sample does not mirror the demographic profile of the sample for the quantitative analyses: men constitute 40% of the qualitative sample compared to 70% of the latter sample. The results of the qualitative analyses should therefore be generalized to the quantitative sample with caution. Finally, this sample constitutes a socially marginalized population living in poverty, with over half experiencing some form of homelessness during the study. Financial incentives

are more salient for this sample than others that are not as financially challenged, making the intervention possibly less effective for the latter.

Acknowledgements We thank the Robin Hood Foundation for funding this study. We thank Housing Works for supporting the intervention and this study. We also thank Farnaz Malik, Michelle Davidson, and Paige Andrews for providing support for the study.

Funding This study was funded by a Robin Hood Foundation Grant.

Compliance with Ethical Standards

Conflict of interest Toorjo Ghose declares that he has no conflict of interest. Virginia Shubert declares that she has no conflict of interest. Vaty Poitevien declares that she has no conflict of interest. Sambuddha Choudhuri declares that he has no conflict of interest. Robert Gross declares that he has no conflict of interest.

Ethical Approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

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

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