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HHS Public Access

Author manuscript

AIDS Behav. Author manuscript; available in PMC 2016 November 01.

Published in final edited form as:

AIDS Behav. 2016 November ; 20(11): 2662–2673. doi:10.1007/s10461-016-1322-0.

What Time is it? Adherence to Antiretroviral Therapy in Ethiopia

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Abstract

This study assessed adherence to antiretroviral therapy (ART) among people living with HIV/AIDS in Ethiopia and explored the sociocultural context in which they relate to their regimen requirements. Data were collected through semi-structured in-depth interviews with 105 patients on ART and observations held at the study clinic. We analyzed data using both qualitative and quantitative methods. Our findings indicate that study participants are highly adherent to dose but less adherent to dose schedule. Strict dose time instructions were reported as stressful and unrealistic. The discrepancy between adherence to dose and dose schedule could be explained by time perception, difficulty with the strictness of medication regimens, or beliefs about dose timing adherence. Care providers should acknowledge the complexities of medication practices and engage in shared decision-making to incorporate patients' perspectives and identify effective interventions.

Keywords

Antiretroviral therapy; Adherence to dose; Adherence to schedule; Dose timing; HIV; Ethiopia

Introduction

Despite early success in adherence to antiretroviral therapy (ART) in African countries [1–3], researchers increasingly have pointed out that adherence will likely decline over time [4] as people continue to experience the challenges of sustaining long-term adherence to multi-drug antiviral medications [5, 6]. Suboptimal adherence to ART is associated with treatment failure, development of drug resistance, increased risk of HIV transmission, disease progression, and higher numbers of HIV-related deaths [7–12]. In such resource-poor settings, with poor monitoring systems and limited access to second-line treatment [2, 13], adherence behaviors must be understood and addressed to mitigate treatment failure [4] and implement effective adherence interventions.

Over the last few decades, a number of studies have quantified patient adherence practices among people living with HIV/AIDS (PLWHA) in sub-Saharan Africa [1, 14–16]. Reviews of studies conducted in the region indicate that, on average, 77 % of adults on ART have

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achieved high levels (>80 %) of ART adherence, which is comparable to or better than adherence in other settings [17, 18]. Yet, 35 % of people who begin ART are no longer engaged in care after 36 months [19]. A similar percentage of people develop immunological failure for various reasons, including poor adherence and sub-therapeutic drug concentration [20] as well as drug resistance mutation [21–23], emphasizing the need to better understand how people integrate long-term medication practices into their daily lives.

PLWHA navigate a multitude of factors to adhere to their regimens, which require strict compliance with dosage, medication schedules (dose timing), and dietary restrictions [24–26]. For example, patients must follow instructions regarding appropriate time intervals between doses [27], as dose mistiming may be associated with poor clinical outcomes [28, 29]. Yet, the extent to which dose scheduling must be maintained remains unclear. Patients and clinicians conceptualize missed or delayed doses variably [24] and very few studies have accounted for dose timing when measuring adherence [28, 30]. The relationship of viral rebound with dose timing has not been investigated as thoroughly as its relationship with missing doses. Although a recent study reported a higher risk of viral rebound and resistance after missing consecutive doses than after simply mistiming a dose [31], we must understand the effects of dose timing on adherence if we are to identify and fully understand all risky adherence patterns [28]. That is, even if dose timing is less critical than it once was for clinical success, it is possible that poor dose timing correlates with risky adherence patterns, especially in settings where people are more likely to keep track of time using social cues rather than by using a clock.

A wide range of behavioral, structural, and sociocultural factors are associated with poor adherence. Of these, sociocultural factors such as stigma, fear of disclosure, lack of social support, use of traditional healers, social norms, and gender inequalities can have profound negative effects on adherence across various African settings [6, 14, 16, 32–36]. In response, qualitative inquiries are increasingly exploring how people perceive and integrate the requirements of ART [37] and identifying the strategies they use to manage their therapy in light of their beliefs, experiences, and social realities [34, 37]. This is encouraging considering the need to understand medicine-taking behavior from the patient's perspective [38]. However, social processes and contextual factors influencing adherence are extremely diverse and have not been explored sufficiently [16]. The evidence base for the effects of various intervention strategies is also limited [39, 40]. It is, therefore, important to study medication practices in a wide range of settings and diverse sociocultural contexts if we are to understand their complexities [34, 41], and this gap in the literature in part motivated our inquiry.

The current study assessed adherence to ART using a self-report method [42] among PLWHA receiving ART in Ethiopia, with the following two goals. First, we wanted to assess whether or not patients take their medicine (adherence to dose) and the extent to which they follow the prescribed regimen (including adherence to dosing schedule). Second, we wanted to understand the sociocultural context within which PLWHA understand and relate to their ART adherence requirements, especially regarding regular dose timing. Since notions of time and schedule are differentially constructed and practiced, people relate in multiple ways

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to a regimen expectation premised on clock time. We argue that, to address causes of incomplete adherence, we need to understand how people navigate their regimen recommendations from their perspectives and within the sociocultural contexts in which they live.

Methods

Participants

This study was part of a larger mixed-methods study conducted among seropositive people receiving care at the HIV clinic of a teaching hospital in Addis Ababa, Ethiopia. Study participants were randomly selected clinic attendees seeking follow-up visits or prescription refills as a routine part of care. Clinic nurses randomly chose every other or every third patient from the day's list (depending on the total number of patients on a given day) to inform them about the research. Interested potential participants were referred to the research team for further explanation and clarification of the study's nature, purpose, and potential risks.

Patients were eligible for participation if they were 18 years of age or older and had been receiving ART for at least 6 months prior to the study. People with a serious or acute illness that impairs their ability to reflect on illness experiences were excluded from the study. A total of 112 eligible patients were invited to participate; 105 participated, while five refused to participate due to fear of inadvertent disclosure, aversion to being audiotaped, or unwillingness to commit the estimated time that the interview would require. Two people agreed to participate but did not appear for the interview. Most participants preferred to be interviewed on the day of or the day after their most recent clinic visits, although some returned to be interviewed two or more days following their interviews (but no more than a week later). To avoid any potential threat to internal validity, participants were given a very general explanation about the research in reference to their overall experience with their care. No specific reference was made to adherence so that their responses would not be affected by their knowledge of the research. Individuals who agreed to participate were asked to provide written consent and were paid 20 birr (equal to a little over 2 dollars) to cover transportation, as was customary at the clinic. The Institutional Review Boards of Northwestern University, the National Science and Technology Commission of Ethiopia, and Addis Ababa University approved the study.

Data Collection

Data were collected through semi-structured in-depth interviews with 105 people on ART and observations at the study clinic between May and October 2008. Adherence data were collected using an interview schedule, consisting of standardized questions adapted from Chesney et al.'s instrument for adherence to antiretroviral medication [43].

Observations—The first author observed clinic practices over the course of fieldwork to understand how participants' clinic experiences may relate to their medication practices. Observation sessions were conducted at varying hours of the day and lasted 2–4 h. The first month was devoted to understanding clinic procedures and routines while developing

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rapport with clinic staff. Subsequently, observations concentrated on the physical and social environments of the clinic, the length of clinic visits, patient volume, privacy, waiting times, and the nature of patient–provider interactions—especially on the subject of adherence to medication. A checklist was used to focus observations. Brief field notes were taken during observation periods, and comprehensive summaries of important observations were written at the end of each day. Field notes were revisited periodically and observations were clarified by personal communications with clinic staff as needed, in keeping with the iterative and interactional process of data collection [44].

Interviews—All in-depth interviews were conducted by the first author in Amharic (the official language of Ethiopia). Interviews lasted 75 min on average, with some approaching 2 h in length. The interview guide was pretested on four people at the same clinic for clarity, cultural appropriateness, and validity of translation and it was updated to incorporate the preliminary findings. Interviews were conducted at the clinic in a room that offered privacy and all sessions were digitally recorded with permission. The interviews were designed to explore participants' daily experiences with ART and the challenges they encountered as they managed their illness and medications. Observational notes were written about all participants following each interview.

Adherence Data—Participants were asked about the types of medications they were prescribed, the times they were prescribed to be taken, and the number of pills taken at each dose; morning and evening doses were counted separately for people on twice-a-day regimens. Regimens and dosing instructions were confirmed by examining each patient's chart. We used 3- and 7-day recall reports to assess the number of prescribed doses of medication taken (number of pills taken/number of pills prescribed) over the three most recent and seven most recent days, respectively [30, 45]. Although 3- and 7-day self-reported adherence measures often result in overestimates of adherence [30], we decided to use them to provide context for our qualitative discussion by quantifying adherence based on a reasonable reliance on memory, especially for the time component. All subjects were asked: "Did you take your medication yesterday?" "Did you take your medication the day before yesterday?" And, "Did you take your medication 3 days ago?" The questions were extended to a 7-day period for the 1-week adherence measure. People who were on twice-a-day regimens were asked about each of the day's doses separately. We used the term 'missed dose' to denote any dose that was not taken on the calendar day for which it was prescribed [24].

Adherence to dose-time instructions was measured by the question, "Have you altered the way you are supposed to take your HIV medications over the last 3 days/7 days?" [27] Participants who responded "yes" were asked to reflect on adherence within dose-time windows based on their recollection of the number of instances and alterations of the schedule by standard clock time. When it was impossible to ascertain the time lapse, subjects were then asked to estimate adherence lapses by reference to social time indicators such as the length of a Sunday church service or the lengths of familiar local radio/TV shows. Subjects on twice-a-day regimens—the most common regimen in the research setting—were asked about morning doses and evening doses separately for all 3 days/7 days.

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To address the challenges inherent to the self-report method [26], this study employed additional techniques and precautions to encourage people to report their pill-taking practices accurately. The first author assured participants that the research team had no institutional relationship with the clinic and promised confidentiality, assuring them that the study would not compromise their relationships with the clinic. Adherence questions were introduced by acknowledging that the inconvenience of regular pill-taking normalizes non-adherence [26]. Participant trust was evident in the majority of cases; participants reported how they experienced departures from their prescribed medication regimens or dose schedules, most of which they had not shared with healthcare providers. Furthermore, time-of-day social markers that were common to subjects' daily routines and social positions were used to help reduce recall bias. Questions were phrased simply, using appropriate phrasing and, when necessary, were phrased in two or three ways to avoid misinterpretation.

Data Analysis

Data from semi-structured in-depth interviews and observations were analyzed thematically using an inductive and iterative process of qualitative analysis, while adherence data were analyzed quantitatively.

All field notes from observations, including personal communications, were reviewed, summarized, and iteratively examined to identify patterns and themes through reading, categorization, and contrasting. Congruency with and differences from interview findings were closely examined. Methodological and theoretical memos were written throughout the data-collection and analysis period to inform analytic ideas and identify potential core categories [44, 46, 47].

Recorded interviews were translated into English soon after the interviews to maximize the degree of fidelity to the data. Emerging analytical insights from preliminary analyses were validated and elaborated during subsequent interviews with other participants. The first author translated half of the interviews. Two qualified research assistants translated the remaining interviews and the first author reviewed all transcripts for completeness against the digital record. Interview transcripts were entered into HyperRESEARCH (version 2.8.3; Researchware Inc.,www.researchware.com) for data handling. The first author performed all the coding. After initial coding, the coder listened to audio records again to double-check coding accuracy and revisited full transcripts and notes to ground developing analyses.

Although theoretical sampling was not employed to recruit participants, data were analyzed using an inductive approach informed by grounded theory [44, 48]. We employed three-step coding processes. The first stage involved line-by-line analysis of transcribed interviews to identify provisional explanatory concepts that were relevant to each specific question from our large qualitative dataset. Next, we thoroughly condensed codes into categories and subcategories based on similarities of content. Finally, we examined patterns within and between categories and interpretively identified underlying relationships using the constant comparative method [44] to generate more fully integrated thematic explanations of participant' diverse experiences with their regimen recommendations [48].

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Data on adherence to medication, along with basic socio-demographic information, were entered into Statistical Package for Social Sciences (SPSS, Version 19.0) for analysis [49]. Each of the adherence measures (3- and 7-day) was calculated using two metrics. First, adherence to dose was calculated as the proportion of doses taken in the last 3 days/7 days divided by the total prescribed dose, calculated as a continuous variable ranging from 0 to 100 %. Second, adherence to schedule instructions was calculated as the proportion of doses taken within a 30-min window of a pre-specified dose time divided by the total number of possible doses. Both the adherence-to-dose and adherence-to-dose-schedule measures were dichotomized as adherent or non-adherent at a 95 % threshold [7].

While there is no consensus in the literature about what constitutes 'on-time dosing,' prior studies have chosen a ±1-h compliance window to indicate taking medication on time [28]. However, the construct for the dose-time window in this study was limited to 30 min because we wanted to be as sensitive as possible to participants' sense of time. Many Ethiopians use social time to mark events or parts of the day and being "on time," i.e., using "clock time," is less relevant as a temporal orientation. According to Westerners, most Ethiopians "run late." For instance, the majority of interviewees arrived at the clinic between one and one-and-a-half hours later than their specified interview times. When asked how late they thought they were, many said simply "a little," even if they were more than an hour late. Similarly, when told that interviews might last 1 h, many participants regarded that as "a very long time." However, when the researcher asked participants if they thought that their interviews had been lengthy, most said "not at all," even after 90–115 min of interview time. In addition, translating gross time into measured time has not yet been fully developed; therefore, a window of ±30 min is assumed to be the closest estimate to the widely observed ±1-h time window. For this reason, any medication dose taken outside of this ±30-min window around established dose times was considered non-adherent for that dose.

We present the findings of this study in two sections. The first section describes respondent characteristics followed by a presentation of adherence rates to dose alone and to dose schedule using both recall periods. We then present the qualitative data to contextualize and better understand the quantitative adherence results. Data pertaining to how PLWHA navigate their medications, in particular the work involved in observing dose schedule, and how participants differentially relate to ART schedule requirements, are presented in the second section. Qualitative data obtained from interviews and observations are presented simultaneously and marked as such.

Results

Participant Characteristics

The average age of participants was 38 years (range: 21–58 years) and 59 % were women (see Table 1). The majority were followers of Orthodox Christianity (63 %) and 37 % were never married. About 42 % had experienced elementary-level or no education; 31 % were unemployed. Over two-thirds had no regular income or earned less than 50 dollars a month.

The length of time over which participants had been taking ART ranged from 6 to 76 months (mean = 37.6 months). Most were antiretroviral-naïve and had started treatment at the study

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clinic only when medications had become freely available through the national ART program in January 2005. The majority (76.2 %) of the study participants were being treated with first-line, fixed-dose combination ART, mostly on a twice-a-day regimen consisting of one non-nucleoside reverse transcriptase Inhibitor, generally nevirapine or efavirenz, and two nucleoside reverse transcriptase inhibitors, generally lamivudine and stavudine or zidovudine. A considerable portion of the participants (23.8 %) were being treated with second-line drugs after the failure of a first-line regimen, which was monitored by periodic CD4 counts (the proxy determinant of treatment success) or inferred clinically.

Self-Reported Adherence to ART

The estimated mean adherence-to-dose rate using both 3- and 7-day recall data was 95.8 %, (95 % CI, 93–99 %), with nearly all participants reporting 100 % adherence ($N = 102$ for the 7-day recall rate). A significant majority, 97 subjects (92.4 %), reported optimal adherence to dose (taking 95 % of their prescribed medication) in the last 3 days prior to interviews. In the same recall period, the number of participants reporting optimal adherence to dose schedule dropped to 70 (66.7 %). Using 7-day recall data, optimal adherence to dose was achieved by 90 (85.7 %) of the participants compared with 60 (57.1 %) who were adherent to dose schedule. Failure to report dose time lapses by reference to clock time was more prevalent when using the longer (7-day) recall interval. Nine (8.6 %) of the study participants could not report taking their medications “on time” using the 7-day recall period, compared with three (2.9 %) using the 3-day recall period, because they either were unable to quantify the delay in clock time or simply did not know when they had taken their medication.

Managing Dose Timing

Almost all participants stated that they were informed about their medications and given specified instructions. The need for strict on-time dosing was often mentioned at the top on the list and people were expected to observe a self-determined or provider-assigned clock time for taking medication. Observations at the clinic also confirmed that instructions given to patients who were going to start ART as well as those who came for follow-up visits consistently emphasized the importance of regular dose timing. This stress on clock time is perceived as a peculiar requirement for the typical medication practice that is imposed on seropositive individuals, as expressed by a respondent: “ART has to be taken for a lifetime just like other medications for chronic conditions…. The only unique requirement with ART is the fact that we have to take it ‘on-time’ all the time. No compromise!” (Male, age 31). Meeting these expectations often involves prioritizing activities. Some seropositive people work hard at conforming to clock time and observe this norm of punctuality as though it were a full-time job that takes precedence over any other activity. Such people are engaged in coordinating pill-taking with standard dose time around the clock. The following interviewee stressed this:

> Just like your main job, you have to take it seriously. My goal of the day is taking the medicine. It’s the first thing on my to-do list…. Watching time is my main job. The rest of my daily activity is secondary. (Male, age 38)

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Several participants who reported being adherent to their dose schedules benefited from the use of devices or social support mechanisms to conform to dose schedules, as described by the following participants:

> My pills time is 10 in the morning and 10 in the evening. Initially, I found it so hard to keep track of my dose time. Fortunately, I was given an alarm clock… which made my life a lot easier…. Also, if I am home, my children always tell me the time. They say, "It is your medication time, Mom," even though they do not know what the medication is for. (Female, age 38)

> I have an alarm clock next to my bed, which is helping me to get used to taking the medicine on time. These days I even have some gut feelings when time for the medication is approaching. (Male, age 57)

Others, however, fail to consistently observe on-time dosing instructions, as the medication regimen does not fit easily into their daily routines. Even those who accepted the expectations often modified them. We looked for patterns of particular kinds of events that made people take their medication early or late but no clear pattern emerged. Three themes were identified based on the reasons participants offered for deviating from/disregarding medication schedules: poor orientation to clock time, regimen strictness, and beliefs about dose-timing adherence. We discuss these reasons in turn below.

Poor Orientation to Clock Time—Irrespective of socioeconomic status, age, or gender, many respondents reported instances of missing dose times. In particular, for people who lack contact with or access to clock time (usually because they are illiterate), it was difficult to incorporate dose timing into their routines even if they wanted to. The following interviewee depicts this type of divergence from standard time:

> I am told to take my pills at 8 in the morning and 8 in the evening. But I take my pills just by guessing…. I'm illiterate. I'm ashamed to ask [what the time is]… as I worry that people might know why. I do not have any control on time. (Female, age 40)

Lived experience of time is expressed in terms such as "now and then" and "a while" by those who have not associated their experience of social time with clock time. Observations at the clinic also noted that timepieces are not easily accessible; a majority of interviewees did not wear a wristwatch or carry other accessories that indicate clock time (such as cellular phones) [field note]. For such individuals, expecting strict adherence to a time schedule is unrealistic.

Many participants noted it was difficult to characterize their pill-taking experience by dose timing. This was widely observed during the interviews when subjects had to strain to report their experiences of time lapses. Even some participants who were well-versed in clock time (those who wore wristwatches, were engaged in day-to-day activities that demanded awareness of clock time, or were better educated than the rest of the sample), were unable to characterize their dose-timing experiences, suggesting a potential disconnect between the subjective sense of time passing and standardized clock time.

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> I often forget to take my medication on time…. If I am on the road, I do not keep track of the time and I do not even know how long the lapse was. (Male, age 30)
>
> I do not remember exactly how late I take my meds, but I usually miss my schedule during the daytime. (Female, age 28)

Even when people try to harmonize dose time with clock time, the subjective experience of duration may not align with standardized clock time. Consider how one participant described such an occurrence: "I was late by 10 min because I started watching live soccer right before my pill time, and I did not want to get up and take my pills until they [the players] went for a break" (Male, age 40). Based on the length of time it takes to complete one half of a soccer game (45 min), it is very likely that—even accounting for other "breaks" in a soccer broadcast—the lapse was considerably longer than the reported 10 min. Ultimately, medication practices are strongly influenced by such sociocultural factors as time perceptions and the norms governing punctuality.

Regimen Strictness and Social Life—Some respondents found instructions for "on-time" doses highly demanding, intimidating, and at times stressful enough that they stopped meeting regimen recommendations. One participant expressed this situation as follows: "It [the regimen recommendation] is so suffocating. It is very stressful to know that you have to be punctual all the time. Even minutes… the instructions they gave us when we start the medication are so strict that we have to be conscious about minutes and seconds. I think being punctual all the time is not humanly possible, and I came to a conclusion that my anxiety about time is not going to make any difference" (Female, age 29). Some people felt that the expected norm of punctuality was unattainable or impeded their participation in routine social activities:

> I am very much forgetful, and my work situation does not allow me to take my pills on time. It is really impossible. (Female, age 28)
>
> Adhering to the dose schedule is never easy for me. If I am at home I try to keep the time. But if I am traveling, it is just impossible to be punctual. I am planning to visit my sister this evening, and I am not sure if I will be able to take my pills on time. (Male, age 40)

The difficulty of meeting the expectations accompanying this highly structured regimen often stems from the fact that most people do not know how to safely integrate their regimens into their lives. In a number of counseling sessions and follow-up clinic visits we observed, conversations between patients and healthcare workers regarding medication adherence were short and too prescriptive to reasonably address any concern from the patients' perspectives. The provider speaks and the patient listens; the latter do not seem to sense their entitlement to ask questions, much less to delve into practicalities [field note]. Thus, they incorporate regimen recommendations as they see fit and create practical ways to be as adherent as possible. Many participants reported that they intentionally modify dose time in relation to what is going on in their lives, especially when they are attending social events, observing religious practices such as long-term fasting, or trying to control HIV disclosure and stigma, as illustrated in the following quotes:

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> I take them [pills] when it is convenient. But I skip my dose to not let people know about my pills and be suspicious [of my HIV status]. I skip my dose time quite often. (Male, age 39)

> But during fasting, the way the medication is taken is not convenient…. I eat at 6:00 and I take my pills at 9:00. Then I take the morning dose at 4 o'clock in the morning [last time when one can eat or drink]. (Female, age 27)

Younger participants were more comfortable maneuvering their pill spacing, and strict adherence to dose schedule often eroded with time as people who initially observed regular dose timing slowly modified their practice, as illustrated by the following respondent:

> I know that I have to take my meds on time… twice a day, at 8 a.m. and 8 p.m. I was pretty much strict on time when I started the medication. I used to be too conscientious. But as time goes by, I mean… when you take the medication for a while you tend to normalize the activity…. Nowadays, I just know that I have to take it twice a day. (Female, age 30)

Beliefs About Dose-Timing Adherence—Adherence to dose-time instructions is also influenced by one's belief about its relevance, which is often primed by information offered by healthcare providers. Although participants were told that they need to take their medications regularly, information about deciding what is best when a dose or dose schedule has been missed, or how to respond to a delayed dose, was poorly communicated. During individual interviews, many participants mentioned their concerns about determining the proper degree of flexibility for adhering to a dose schedule and asked whether the interviewer has reliable information. The questions we heard being asked included: "How much of a delay is too detrimental to treatment success?" "What would happen to me if my doses were taken too closely to each other?" "How many hours of delay would be so long that I am better off skipping?" "Given my situation (family, work, medical…), how can I best take the medication without risking treatment failure?" and, "Does the timing of taking my pills really matter?" [field note].

There are, however, no clear instructions clarifying a safe dose time range in the context of an ART regimen or a shared agreement about acceptable dose timing. Care providers themselves had varying perceptions of adherence, as shown in the following contrasting statements by two physicians. A second-year medical resident at the clinic said, "It is a matter of disciplining patients so that they won't dare to mess with their medication schedule. Otherwise, time lapse may not have any real impact for some drugs. Some of the drugs have a half-life as long as 4 days." Another doctor (a third-year resident) said, "I would say ±2 h is the best bet to ensure treatment success" [field note].

Lingering uncertainties surrounding adherence to dose time led some PLWHA to question its relevance and convinced them that it is not required. Thus they departed from their medication schedules, believing that taking the medication at a regular time was unnecessary or insignificant. Such people allow themselves a degree of flexibility based on what they believe is good enough, which is mostly not skipping doses altogether. One interviewee said:

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> I follow my medication regimen appropriately. There are times when I take my pills later or earlier than 8 o'clock. I don't think this is a problem at all. I take my dose even if it is late. (Male, age 42)

In contrast, however, when missing a schedule was believed to cause immediate illness or death, people tended to observe adherence strictly. Such people were also keen to report even trivial lapses in dose time. Respondents who had personally experienced negative effects of non-adherence were often actively engaged in reorienting themselves to clock time and attempted to socialize themselves to adopt the norm of punctuality. One participant stated:

> Adhering to dose schedule is an obligation that I have to fulfill in order to stay alive. I learned that the hard way. I became sick and bedridden for messing up with my dose time. If I die who would support the three children that I am raising?… I would not mess up my dose time now. (Female, age 49)

Discussion

This study produced two main findings. First, we found that PLWHA in our study sample achieved high levels of self-reported adherence to dose but lower levels of adherence to dose schedule. Second, we found that time perception, difficulty with the strictness of medication regimens, and beliefs about dose timing adherence were the most common impediments to regular pill-taking. This may explain the discrepancy between the dose and dose schedule adherence rates.

Over 90 % of participants in the current study had achieved optimum adherence (>95 %) in the previous 3 days, similar to the results of other studies in Ethiopia [50–53]. Adherence to dose schedule in the same time period declined to 67 %. This discrepancy between the two adherence rates (dose and dose schedule) illustrates two interesting points. First, even in light of the known tendency of self-report data to overestimate adherence, the data clearly revealed the difference between the adherence-to-dose and adherence-to-schedule measures. Second, as evidence develops supporting the concept that dose adherence is more important than dose timing [31], our data indicate that adherence to ART in this setting is excellent. Even those who were only loosely oriented to Western time were highly dose-adherent.

Our qualitative data also revealed how challenging and burdensome patients found incorporating "time" into medication taking to be. There were considerable delays in some cases, while others could not measure delays accurately because of their lack of experience with clock time. Following clock time was challenging for many people, particularly those who were not involved in social activities traditionally bound by clock time. For such participants, clock time has minimal salience in their lives and aligning dose time with clock time needs extra work because it does not come naturally [54]. Such practices indicate potentially risky adherence patterns and could cause problems when they result in adherence levels that are below what is required for clinical success. Thus, adherence conversations are crucial to understanding how individual patients regularly perceive and operationalize time and address risky adherence patterns earlier.

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Yet time perception only partially explains the difficulties encountered with dose timing. PLWHA have to simultaneously deal with many other difficulties, such as concealing HIV status, managing stigma, maintaining/striving for financial security, and keeping up with their spiritual lives. Many participants purposefully disregard dose timing as they work to develop self-efficacy related to taking medication. While some patients integrate medication taking into their social environments [55], others—often younger patients and those on ART for longer time periods—adjusted their dose schedules. These adjustments would relieve them of the psychological tension and potential negative consequences (e.g., stigma, unintended disclosure) of pill-taking during social events.

What patients believe about ART is also an important factor informing their relationship with dose time [27, 56]. In our study, lack of belief in the relevance of regular dose timing among PLWHA was rooted in uncertainties about optimal compliance time windows. Evidence suggests that advances in HIV medications with less restrictive dose regimens means that exact dose timing may not be required for current HIV medications [12, 57] and missing doses seem more critical than adhering precisely to a dose schedule [31]. Nevertheless, there is no clear consensus among either researchers or practitioners as to what constitutes a safe dose lapse range or how it should be measured [24]. This conceptual discrepancy may produce confusion, supporting previous arguments that inadequate medical information may be a foundation on which alternative strategies and practices are built [55] or may allow people to become less adherent [58].

Regardless of the scientific ambiguity, however, the strict dose-timing instructions that care providers gave participants in this study were very stressful and likely influenced adherence negatively. Such perceived overemphasis on dose timing adds to the difficulty involved in adhering to an already complex regimen. Ethiopian HIV guidelines raised the CD4 cell count threshold for initiation of ART to 350 cells/ml in 2012 [59], and this threshold was increased again to 500 cells/ml in 2013 [60]. With more people being eligible for ART while they are healthier, the unrealistic demand for on-time dosing might frighten and discourage people who could benefit from early initiation of ART. Adherence to a dose schedule requires that patients distinguish acceptable from unacceptable flexibility [54] without experiencing debilitating stress over strict time directives. Providers and patients therefore need a shared understanding of optimal adherence that takes the context of individual patients' lives into account.

We argue that patients exercise considerable personal agency when they deviate from their regimen recommendations. To understand how patients integrate their treatment into their unique lives and play an active role in this important process, a patient-centered approach is essential [38, 61]. Our study revealed that, despite their concerns, patients were reluctant to ask questions about their treatment during clinic visits. We acknowledge that in some cases a participant's reluctance might have been associated with the briefness of the visits. However, it was clear in other cases that participants did not feel fully entitled to interfere with a clinical procedure and were uncertain about the appropriateness of doing so while providers were focused on giving instructions, as they had not seen that happen at the clinic. Care providers should appreciate individual differences and learn to listen and negotiate with their patients rather than giving strict directives. This could establish a practice of shared

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decision-making [61, 62] that would allow patients to discuss their concerns and induce providers to offer one-on-one support to patients through applicable adherence interventions. It also confirms the critical role of communication factors in achieving agreement between patients and care providers [63, 64] and establishing a high quality patient–provider relationship [38]. However, the paternalistic approach that characterizes the doctor–patient relationship at work in the study area would incorporate neither patients' perspectives nor their health beliefs, both of which are essential factors in adherence [38, 58, 65]. Although empowering patients to actively engage in their care is necessary to discussion-based adherence support, in a social context where the power balance strongly leans towards the provider, we believe that care providers should take the initiative to implement shared decision-making.

No matter why patients deviate from recommended dose times, our study highlighted the difficulty of assessing such deviations by presenting the prevalent notion of time in the study area. Several factors, including the socially based time-management norm in Ethiopian society, might explain these difficulties in translating gross time into standard clock time and estimating the observed sense of duration. Thus, time estimations in societies favoring social time are likely to be misleading simply because few people reconcile social time with standard clock time. Since self-report is by far the easiest and the most feasible method of assessing adherence [26], paying attention to socio-cultural contexts and demanding a reasonable level of commensuration skills—the ability to compare social time with clock time—might increase its sensitivity. Therefore, researchers conducting adherence studies in non-Western cultures should account for aspects of research design that are premised on careful dose timing. Assessing adherence to HIV treatment would be more accurate and less burdensome if patients were asked to rate their regimens in more general terms rather than asking about individual dose experience [30, 66, 67], especially in reference to dose timing.

Regarding the study's limitations, we note first that reliance on the self-report method did not provide an objective adherence measure. The caregiving site where we conducted our study did not routinely collect plasma viral loads, so we cannot examine the relationship of these self-reports to immunological measures of treatment success. Second, this study was conducted in a clinical setting with patients who had been on ART for at least 6 months, and who therefore had chosen to engage in care. Therefore, it might not capture the experiences of people who have dropped out of care. Third, although the researchers took time perception in the study area into consideration when assessing adherence to dose timing and tried to validate the dose-timing data against standard social activities such as Sunday church services, TV programs, news time on the radio, public school dismissal time, or government work hours, such efforts could perhaps reduce the discrepancy between actual time and reported time but could not guarantee precision in estimates of dose timing. The challenge of measuring time accurately therefore may limit the validity of the study's findings to some extent. Finally, although our sample reflected a socio-demographically diverse group of people in Ethiopia, it presented the experiences of PLWHA in a very particular social setting and in one clinical context, which might restrict generalizability. We believe, however, that the insights we gathered from learning about medication practices are valuable and can be applied elsewhere.

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One of the major strengths of this study is its use of multiple sources of data [68]. The rich explorative account of social realities uncovered in the interviews and field observations [41] explained why adherence rates revealed by the quantitative findings would differ when factoring in dose timing. The interviewer inquired into adherence data in a way that made it possible to present question items in multiple ways, thus minimizing misinterpretation, and to cross-check responses. It also made it possible to explore time perception, commensuration skills, and cultural contexts that could affect medication practices as well as adherence measurement. Having all the interviews conducted by the first author, who speaks the local language, avoided the use of interpreters or the involvement of clinic staff in data collection. This is likely to minimize social desirability bias by eliminating incentives for participants to misrepresent their experiences.

In conclusion, this study contributes to an emerging body of knowledge about medication practices in non-Western settings by focusing on adherence practices among PLWHA in Ethiopia through observation and interview data. We studied a population with a high rate of adherence to dose but wide variation in dose timing. Care providers in such settings would benefit from engaging in adherence conversations that help patients safely map regimen instructions onto the social environments that give life its rich complexity.

Acknowledgments

This study was supported by the department of Sociology and The Graduate School of Northwestern University, and by Grant Number T32HS000011 from the Agency for Healthcare Research and Quality.

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Table 1

Socio-demographic and treatment characteristics of participants (*N* = 105)

Characteristic	*N* (%)
Female	62 (59)
Age (Mean = 37.7)	
18–29	21 (20)
30–49	53 (50.5)
50 and above	31 (29.5)
Religion	
Orthodox Christian	66 (62.9)
Other Christians	24 (22.9)
Muslim	13 (12.4)
No religion	2 (1.9)
Marital status	
Never married	39 (37.2)
Married	31 (29.5)
Separated/divorced/widowed	35 (33.3)
Education	
Elementary or no education	44 (41.9)
High school/vocational training	46 (43.8)
College	15 (14.3)
Employment	
Employed in formal sectors	30 (28.6)
Self-employed	43 (41)
Unemployed	32 (30.5)
Income	
Under 50 dollars a month	74 (70.5)
Months on ART	
6–24	40 (38.1)
25–48	58 (55.2)
49 and above	7 (6.7)
ART regimen	
First line regimen	80 (76.2)
Second-line regimen	25 (23.8)