

# “We are Getting Those Old People Things.” Polypharmacy Management and Medication Adherence Among Adult HIV Patients with Multiple Comorbidities: A Qualitative Study

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**Introduction:** Improvements in treatment have led to a growing population of older adults living with HIV. As this population ages, polypharmacy, or the use of more than five medications, may become more common among people living with HIV (PLWH).

**Methods:** Two qualitative focus groups (N=7, N=8) were conducted among a sample of patients who participated in a larger study regarding differential medication adherence. Open-ended questions and probes focused on barriers and facilitators to multiple medication management as well as differential adherence.

**Results:** Overall, patients were able to manage their polypharmacy. Social support facilitated adherence while long-term antiretroviral (ARV) use, medication-specific requirements and emotional fatigue were barriers to management. A small number of participants reported differential adherence that prioritized non-HIV medications over ARVs due to more immediate effects of non-adherence.

**Discussion:** Findings suggest that PLWH have learned to manage their polypharmacy, but still face significant challenges adhering to multiple medications in the long-term. Future research may focus on the emotional toll of long-term ARV use and how patients' own management strategies may be leveraged to promote adherence.

**Keywords:** HIV/AIDS, polypharmacy, medication management, medication adherence

## Introduction

Over the past three decades, the adoption of potent combination antiretroviral therapy (ART) has dramatically reduced viral transmission, disease progression, and death among individuals infected with human immunodeficiency virus (HIV).<sup>1–3</sup> As a result, HIV infection is evolving in some contexts, from a lethal disease to a chronic one, resulting in greater disease prevalence as life expectancy among people living with HIV (PLWH) improves.<sup>4</sup> As patients live longer, polypharmacy, defined as the use of five or more prescription medications for chronic conditions, is growing among this population.<sup>5</sup> A recent audit to quantify polypharmacy in a large cohort in the United Kingdom showed that among patients prescribed ART, 71% were taking medications other than ART with a median number of two ART formulations and a median number of four total medications including non-ART medications.<sup>6</sup>

The drivers of polypharmacy are multifaceted and impact PLWH of all ages. From diagnosis, PLWH may manage multiple-medication regimens for their HIV alone. High incidence of HIV among young adults<sup>7</sup> may contribute to earlier and longer-term polypharmacy among PLWH. HIV infection itself and long-term use of certain antiretrovirals (ARVs) are associated with increased risk of cardiovascular disease,<sup>8,9</sup> osteoporosis,<sup>10</sup> diabetes mellitus (DM) and other metabolic disorders (ie dyslipidemia, hyperlipidemia and insulin resistance)<sup>11</sup> and in turn, increased medication burden.

Finally, it is predicted that by 2035, 75% of PLWH will be over age 50, thereby increasing the likelihood of polypharmacy that comes with age among this population.<sup>12</sup> A recent study estimated that by 2030, 84% of PLWH will have at least one age-related comorbid condition and that 30% will have more than two.<sup>13</sup>

Polypharmacy has been linked to decreased medication adherence in the general population and also among PLWH.<sup>5,6,14</sup> Differential adherence to ART and other medications for comorbidities is not well understood. One study of pharmacy claims data found a positive relationship between number of comorbidities and ART discontinuation.<sup>15</sup> Conversely, results from a study of PLWH with DM indicated that participants were more adherent to ART than to their DM medications and that ART was perceived as more necessary than DM medications.<sup>16</sup> Moreover, the factors associated with ART non-adherence (ie, concerns about ARVs) were different from those associated with DM non-adherence (ie, DM symptom burden).<sup>16</sup> Even within ARVs, studies have demonstrated variability in which medication is taken most consistently, often resulting in variable resistance patterns and virologic failure overall.<sup>17,18</sup>

Poor ART adherence due to polypharmacy presents a serious health concern for PLWH and is associated with increased risk of hospitalization and death.<sup>19,20</sup> As the population of older adults living with HIV grows, a greater understanding of the impact of polypharmacy on medication management and adherence is needed.<sup>5</sup> We utilize qualitative focus group data from a sample of adult HIV patients receiving care at a large HIV/AIDS clinic to examine patient perspectives on polypharmacy management and medication adherence.

## Materials and Methods

### Study Setting and Population

Focus group discussion (FGD) participants were recruited from a New York metropolitan area HIV clinic. All clinic patients have a comprehensive care team comprised of medical providers, nursing staff, pharmacists, health educators, social workers, a dietician, and research team, if applicable. Providers emphasize the importance of ARV adherence as part of patient visits. As needed, patients who are at risk for non-adherence may receive daily reminder calls and/or video-observed therapy by health educators. Nursing staff and the pharmacy team also educate patients on ARVs and adherence, assist in ensuring all patients have adequate refills on their medications, and supply patients with pill trays and carriers to facilitate ARV adherence.

Participants (FGD=2; N=7, N=8) were recruited from a sample of patients who were participating in a larger trial of a medication adherence mobile application. Participants were eligible for the larger trial if they were taking at least one additional non-HIV-related chronic medication.

### Data Collection

After enrolling in the trial, patients were invited by study staff to participate in a FGD. Participants were consented prior to the start of each FGD. Informed consent included publication of anonymized responses. FGDs lasted approximately one hour and participants received dinner during the FGD and a \$50 gift card following participation. FGDs were conducted by trained qualitative investigators (*RS & KGB*) in a private conference room at the clinic where participants receive HIV-related care. *RS* (PhD) is a clinical research psychologist who identifies as a white cisgender female. At the time of data collection, *KGB* (MPH) was a research coordinator who identifies as a white cisgender female. Both *RS* and *KGB* worked closely with clinical staff on several research projects, including the present study for which *RS* was the Principal Investigator. *KGB* also conducted enrollment and data collection for the larger trial in which this qualitative research was embedded. Investigators followed a semi-structured interview guide (available upon request) that focused on medication management and adherence.

### Analysis

FGDs were audio-recorded and transcribed verbatim. The data were analyzed inductively using an iterative approach adapted from the Framework Method.<sup>21</sup> Transcripts were reviewed by one study team member and emergent themes were organized into an analytic matrix; a second study team member reviewed the matrix and disagreements were

reviewed and reconciled by both investigators. Finally, illustrative quotes were selected relating to salient themes and subthemes.

## Ethical Approvals

All study procedures were approved by the Northwell Health Institutional Review Board (IRB# 17–0063) and were in line with guidelines set for by the Declaration of Helsinki. All participants completed informed consent during enrollment for the larger study and again before their FGD participation, which included information pertaining to the publication of anonymized responses.

## Results

Quantitative data for the 15 FGD participants were extracted from the larger trial. Mean age of participants was 57 years (SD=11.2; range= 33–73) (Table 1). The majority of participants (60%) identified as female. 47% percent of participants identified as Black/African American, 20% as white, and 33% other/unknown; 13% identified as Hispanic. On average, participants were clinic patients for 13 years (range: 5–30). Thirteen participants (87%) had an undetectable HIV viral load at the baseline study visit. Mean absolute CD4 cell count at the baseline study visit was 618 cells/7.7 cells/  $\mu$ L (SD=375.0; range=79–1405), with 7 participants who had absolute CD4 cell counts less than 500 cells/ $\mu$ L and 1 participant with a count less than 200 cells/ $\mu$ L. Participants had a mean of 4.4 (SD=2.0; range=1-8) comorbidities

**Table 1** Demographic and Clinical Characteristics of Focus Group Discussion Participants (N=15)

Characteristics	FGD (n=15)
<b>Age, mean (SD, range)</b>	57.0 (11.2, 33–73)
<b>Sex, n (%)</b>	
Female	9 (60.0)
Male	6 (40.0)
<b>Race, n (%)</b>	
Black/African American	7 (46.6)
White	3 (20.0)
Other/unknown	5 (33.3)
<b>Ethnicity, n (%)</b>	
Hispanic	2 (13.3)
Non-Hispanic	12 (80.0)
Missing	1 (6.7)
<b>Years at clinic, mean (range)</b>	13.0 (5–30)
<b>Viral load, n (%)</b>	
Undetectable	13 (86.7)
Detectable	2 (13.3)
<b>Absolute CD4 cell count, mean (SD, range)</b>	618 cells/7.7 cells/ $\mu$ L (375.0, 79–1405)
<b>Number of comorbidities requiring chronic medication, mean (SD)</b>	4.4 (2.0)
<b>Number of chronic medications, mean (range)</b>	5.67 (3–11)

requiring chronic medication. The most common comorbidities included were hypertension, diabetes, hyperlipidemia, and osteoporosis. FGD participants were taking 5.67 (range: 3–11) chronic medications, on average, with only four participants taking fewer than 5 medications.

Two overarching themes emerged from the data: “Polypharmacy complicates medication management” and “Polypharmacy as a barrier to medication adherence” with subthemes identified within each theme.

## Polypharmacy Complicates Medication Management

Participants described polypharmacy regimens that included ART, medications for comorbidities and over-the-counter supplements.

I take one in the morning and three at night. All pills. Atripla, Tegretol for my seizures and vitamin D.

I take 5 and I am on the same regimen...doctor said simplify and I said I have been oversimplifying with doctor, this is the simplest I can get under the circumstances, not like other people that can take one pill a day that are very fortunate and lucky and blessed by that.

## Complications from Long-Term ART Use

Participants felt that in addition to aging, polypharmacy was also a result of long-term ART use. Patients describe two ways by which ART use resulted in polypharmacy. For some participants, ART use necessitated additional medications to manage side effects from long-term use.

I think age is a big factor to this too, because you then will have osteoporosis, you will have arthritis, you have all these different types of things and then they have to give you vitamin D...add a pill...add a pill, but I truly believe that it is also the medication. Because the side effects of the medication, they will tell you. You have to get tested for lactic acid, have to get tested all the time for the damage to your liver, damage to your kidneys and it says you might get diabetes, have to medication for a certain period of time. These are things we have to deal with on an everyday basis.

## Polypharmacy Resulting from Aging/Comorbidities

Other participants tied ART use directly to the development of additional comorbidities.

We are getting older and we are getting different things because of age. I get that, definitely we're getting older and we're getting older illnesses. I also believe that is like a double edge sword for me. We're getting older. We're getting those old people things and then the HIV medicine, I do feel exacerbates the other illnesses [...] I look at my daughter who is 32 and she gets old people illnesses that she shouldn't have at this age. It exacerbates things.

## Methods to Assist in Polypharmacy Management

Participants described a variety of methods they employed to manage their polypharmacy. One participant reported being able to remember to take their medication without reminders while several others described using cues that were part of their daily routine to remember to take their medications. Such tools were adapted over time as medication regimens changed and participants developed new comorbidities.

In the beginning, I was such a hot mess with taking the medication [...] then [clinic staff] told me [I] should make an appointment with a health educator [...] She showed me about the pill trays and told me it should be taken every day at the same time so relate it to something that you do every day. I used to watch Manuela at nighttime [...] so I used to leave the pill box on the TV with a little bottle of water and when Manuela came on, it's right there when I turned the TV on, I took my medication. That's how I got started trying to and I got a lot better.

Requirements related to when medications must be taken led patients to develop carefully timed regimens. Medication and food interactions also influenced participants' management of their polypharmacy.

It is like my vitamins with my Biktarvy, either I have to take my vitamins 2 hours after or take the vitamins then take the HIV medication 6 hours. I take the HIV. I just forget to or sometimes I will just take a handful and fill my mouth at night of the vitamins.

[...] I figured out how each one worked individually with or without food, why, the reasoning and especially with the thyroid to get things started because if you take the Synthroid with the medications, it knocks out most of the Synthroid and then it doesn't really work for your thyroid. I figured out a routine for myself and it worked out for almost 20 years for myself.

For several participants polypharmacy was itself a tool for medication management.

So the diabetes is what triggers me to take my HIV medications not the other way around. I don't really need the reminders because I check my sugar 4x a day and the insulin pump depending on what the numbers are then I have to pump, let me take my insulin, oh yeah I have to take my Victoza which is once a day as well, oh yeah I have to take my cholesterol pill because people with diabetes they want to monitor your heart so you have to take cholesterol pill.

For many participants, granting themselves permission to be flexible was integral to successful management of their polypharmacy.

The regimen was rigid. I did not deviate from it. However, after having the kid, I see it like this...I know there is that window period, but I am not going to succumb my life to a clock. I am already succumbing my life. As long as I know I take my medications every day, I don't care if I come in from a party. This thing doesn't know my life is very dynamic. It doesn't have a set clock.

## Polypharmacy as a Barrier to Medication Adherence

Participants reported high medication adherence overall. However, the majority of participants discussed fluctuations in medication adherence over time due to a variety of factors including long-term pill burden and mental health challenges.

### Long-Term Polypharmacy and Adherence Fatigue

Nearly all the participants described what one woman termed "pill burn" or fatigue from years of medication that may impact adherence.

[...] so several times I have had pill burn [...] I've gone a month without taking my pills, a month [...] It is not a physical. It is more mental, emotional. I get that mentally, but I get it physical as well.

For me, it is a commitment [...] and [medication] is the saddest reminder of my mortality. So, you kind of get that pill burn. You take [the] same pills. It is like the folks who take the pills at the same time every day. After a while, sometimes they just get burnt out and say you know what, I am skipping a day, I am tired of this mess. I just want one day to be free and not think of it and just do.

Long-term polypharmacy also contributed to general forgetfulness related to medication.

When you take medications for so many years, I feel like I almost get very forgetful. It is like one day blends into the next kind of and all the pills look the same. Yes, brain fog...like did I take this already or did I not?

### Mental Health Challenges and Adherence

Though not necessarily related to polypharmacy, mental health challenges were a significant barrier to medication adherence.

I was always adherent to my medicine, but when I slip into a depression. Like now, I have been missing a lot, the last two months and that never happened to me. It is what it is...you know, whatever, that's how I feel now at this point. If I take it, I take it, if I don't, I don't. It is how I feel and I have earned how I feel...depression stops me from taking it.

I signed up for [reminders], but then I realize, this doesn't help [...] My mood determines whether or not I need it. There are days I am just like look, if I am determined, I am not going to take it. You can bing, bing, ring all you want. I don't want to do it.

## Differential Medication Adherence

In terms of differential medication adherence, there was no consensus among participations about prioritizing one medication over another. Some participants suggested they prioritize non-HIV medications over HIV medications because failure to take medications for comorbidities have a more immediate effect on their health and well-being. Others reported greater difficulty remembering to take medications for comorbidities compared to their ARVs.

The HIV pill is one thing because I don't see the damage or I don't see the virus. So if I skip a day after I had been adherent for two months, in my opinion, there are not going to be major consequences. But diabetes, if I go 2 hours. I just ate and if I don't take my insulin if I don't start putting the numbers in my pump, my glucose is going to shoot up to 250–300. Okay, the HIV is easy. It is the comorbidity. It is keeping up with that one, that's the problem for me.

I am really good with my antivirals, but the other medication that doesn't seem to work in the same fashion. I forget. Because I know if I don't take them together, even though sometimes life happens and then you're tired, you're out all day long, you come home, you're exhausted and the only thing you are thinking about is shower and bed and you forget and then you wake up the next morning, oh my gosh.

## Adherence Facilitators

Despite these challenges, instrumental and emotional support from friends and family and in the clinical setting promoted medication adherence among participants.

I used to have issues early on taking medications couple years back, grandson born so then I have been taking them on a regular basis. I also have the buddy system. My wife, she will remind me when I used to miss. My daughter. So we kind of work on each other also.

With my medical providers, they are all primarily from [health system]. I do that on purpose so they can all share information. I get a redundancy with the endocrinologist about my HIV stuff. I get redundancy with Infectious Disease about my diabetes. It is like okay, sort of reinforcement.

## Discussion

Two focus group discussions were conducted with patients from a New York metropolitan area HIV clinic to explore patient perceptions of their polypharmacy and its impact on medication management and adherence among PLWH. Findings suggest that patients believed their polypharmacy to be a direct result of their ART regimen, either due to the use of additional medications to manage ART-induced side effects or because they believe that long-term ART use contributed to the development of comorbidities that necessitate additional chronic medications. In turn, polypharmacy was a serious barrier to medication management and adherence. Patients describe developing tools and coping strategies to effectively manage their polypharmacy and the role that instrumental support from family and clinical staff plays in promoting medication adherence.

Participants believed their comorbidities to be premature in relation to their age and the consequence of long-term HIV infection and ARV treatment. Despite a growing body of literature,<sup>8–11</sup> several patients reported that their provider often downplayed the connection between ART and comorbidities and attributed them to lifestyle factors like obesity. Participants described various tools for managing polypharmacy including reminders, pill boxes and using one medication as a cue for another. Future interventions to support adherence in the context of polypharmacy might leverage patients' existing routines to improve management.

Though participants described successfully managing their polypharmacy, nearly every participant cited a time when they were less adherent to their medications. Notably, poor adherence was more often related to mental health challenges than to polypharmacy, a phenomenon that has been observed elsewhere.<sup>22</sup> Despite the health concerns associated with nonadherence,<sup>18</sup> participants suggested that allowing themselves periods of nonadherence actually improved their overall adherence by preserving their psychosocial well-being, a phenomenon that has not been explored in-depth in existing adherence literature.

Consistent with existing literature,<sup>16,17</sup> there was no consensus regarding differential adherence across medications. Several participants suggested they prioritize non-HIV medications over HIV medications because failure to take medications for comorbidities has a more immediate effect on their health and well-being, while others reported greater difficulty remembering to take medications for comorbidities compared to their ARVs, perhaps due to the perceived severity of their HIV. Of note, there is a comprehensive team, including pharmacists, that regularly checks in on patients regarding their ARV medication adherence thereby maximizing the chance for high levels of ARV adherence. It is unclear, however, the extent to which HIV primary care providers reinforce adherence to non-ARV chronic medications, which is an area for further research.

Findings should be understood in the context of the study's limitations. Though our relatively small sample size may have limited our findings, research suggests that two focus group discussions can be sufficient for reaching thematic saturation<sup>23</sup> and our analysis suggests that saturation was reached with respect to our research questions. Because the larger trial included individuals taking one or more additional medications, some FGD participants may not fulfill the technical definition of polypharmacy (ie, 5 or more medications). However, the average number of medications among participants was 5.67, suggesting most participants were experiencing polypharmacy. The generalizability of this study is limited by the clinic-based study population, as individuals who are less connected to care may face greater challenges to managing their medications, and the focus group participants were particularly healthy in that all except two had undetectable HIV viral loads. Future research should focus on polypharmacy in lower-resourced or non-clinic connected populations, including those in low- and middle-income countries, where more accessible ART may contribute to a similar increase in life expectancy and polypharmacy among PLWH.

## Conclusion

Despite these limitations, our findings have important implications for potential interventions to facilitate medication adherence among PLWH as this population ages. Such interventions may focus on the emotional toll of managing long-term polypharmacy. Management tools may also need to be tailored to individual perceptions of severity of their HIV and other comorbidities and should provide clear information related to potential medication interactions. Finally, interventions to promote successful polypharmacy management should leverage patients' own strategies to promote adherence, not just to ARVs but also to other chronic medications.

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## Disclosure

The authors report no conflicts of interest in this work.

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