AIDS and Behavior
https://doi.org/10.1007/s10461-018-2200-8

ORIGINAL PAPER

# Ugandan Study Participants Experience Electronic Monitoring of Antiretroviral Therapy Adherence as Welcomed Pressure to Adhere

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**Abstract**
Many new technologies monitor patients' and study participants' medical adherence. Some have cautioned that these devices transgress personal autonomy and ethics. But do they? This qualitative study explored how Ugandan study participants perceive the effect of electronic monitoring of their adherence to antiretroviral therapy (ART) on their freedoms to be non-adherent and pursue other activities that monitoring may inadvertently expose. Between August 2014 and June 2015, we interviewed 60 Ugandans living with HIV and enrolled in the Uganda AIDS Rural Treatment Outcomes (UARTO) study, a longitudinal, observational study involving electronic adherence monitors (EAMs) to assess ART adherence. We also interviewed 6 UARTO research assistants. Both direct and indirect content analysis were used to interpret interview transcripts. We found that monitoring created a sense of pressure to adhere to ART, which some participants described as "forcing" them to adhere. However, even participants who felt that monitoring forced them to take medications perceived using the EAM as conducive to their fundamental goal of high ART adherence. Overall, even if monitoring may have limited participants' effective freedom to be non-adherent, participants welcomed any such effect. No participant rejected the EAM on the grounds that it would limit that effective freedom. Reports that monitoring altered behaviors unrelated to pill-taking were rare. Researchers should continue to be vigilant about the ways in which behavioral health monitoring affects autonomy, but should also recognize that even autonomy-limiting monitoring strategies may enable participants to achieve their own goals.

## Introduction

Does monitoring medical adherence place individuals under pressure to take medications or adhere to prescribed behaviors? Does it otherwise limit their personal autonomy? If so, is such pressure ethically unacceptable when it improves medical adherence and health? Electronic adherence monitors (EAMs) take many forms, including pill bottles that transmit the timing of bottle openings [1], pills that indicate ingestion [2], and drug metabolite detectors [3]. As a host of new EAMs have become available, questions about potential autonomy effects of these devices impact the ethics of their use and may guide further device development, as well as the studies that use them. EAMs have been used in numerous research studies to characterize adherence, particularly for treatment of HIV [1, 4–6], as well as other chronic conditions like hypertension [7] and asthma [8]. As EAMs enter clinical use [9–11], both academic papers and the popular press have warned that they could constitute "Big Brother" in healthcare, and some have warned of damage to "autonomy" [12–15]. However, precisely what these authors mean by "autonomy" and the specific ways in which these devices could and do affect it have not been fleshed out. Nor has the ethical importance of these effects been studied.

We have previously posited two ways in which EAM may limit individuals' autonomy [16]. First, the knowledge that researchers or clinicians closely monitor one's adherence could pressure an individual into taking medications or adhering to prescribed behaviors even when she does not want to. To some, that pressure would infringe upon what they take to be a right to be non-adherent [17–21], which is

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Published online: 20 June 2018

said to hold even when an individual's non-adherence may increase risk of disease transmission to others [22]. Second, observation of routine health behaviors may be thought to limit individuals' freedom to carry out activities unrelated to these behaviors, so as to avoid embarrassment or observation (e.g. avoiding travel to specific locations out of fear that the device would reveal locations). Likewise, scholars worry that surveillance from telemonitoring devices—close cousins of EAMs—may result in "inhibition and self-censorship" [23].

However, we know little about what individuals think about their autonomy when their medication-taking is monitored, or how they value the different forms of autonomy that monitoring may affect. In this study, we investigated research participants' attitudes towards the potential effect of adherence monitoring on autonomy to be non-adherent and to otherwise behave as they please. We focused on use of two specific EAMs: Medication Event Monitoring System (MEMS) and Wisepill. MEMS has been used for over 25 years and Wisepill for 10 years; together, several hundred studies that used these technologies have been published [24, 25]. We studied research participants in a cohort study of individuals taking HIV antiretroviral therapy (ART) in southwestern Uganda.

## Methods

### Parent Study

Our interviewees were participants in and research assistants (RAs) for the Uganda AIDS Rural Treatment Outcomes (UARTO) study [4]. UARTO was a longitudinal, observational study of 750 individuals initiating HIV antiretroviral therapy (ART) that took place between 2005 and 2015 in Mbarara, Uganda. Mbarara is a medium-sized city (population ~80,000) in southwest Uganda located approximately 260 km from Kampala, surrounded by numerous rural farming communities. All participants received HIV-related care and free ART through the Mbarara Regional Referral Hospital Immune Suppression Syndrome (ISS) Clinic. UARTO was ongoing at time of our interviews. In UARTO, data on non-adherence were used to understand behavioral determinants and biological consequences of incomplete adherence.

From 2005 to 2011, MEMS caps were used to monitor adherence by tracking each time a participant's pill bottle was opened. Adherence data were downloaded at each study visit. From 2011 to 2015, UARTO used the Wisepill device. MEMS (WestRock, Switzerland) is a pill bottle that is electronically outfitted to record date and time stamps of opening that can be downloaded at clinic visits (Fig. 1a). The Wisepill device (Wisepill Technologies, South Africa) is a pill bottle that electronically records when it is opened, and sends this adherence information to researchers via cellular networks in real time (Fig. 1b). RAs investigated interruptions in wireless EAM signal transmission lasting more than 48 h through a brief interview to determine the cause of the lapse, as well as a blood draw to assess HIV RNA levels. Because technical problems could not always be confirmed immediately, or occurred concurrently with non-adherence, blood draws were performed initially for all lapses. However, as the study progressed and technical failures became rarer and more easily identifiable, blood draws were done only during signal lapses with documented device functionality. Participants were informed that a blood draw did not necessarily indicate presumed non-adherence and they could decline it at any time. The technology and functionality involved with the EAMs was explained to participants at enrollment. While RAs were involved in collecting adherence data, and had frequent interactions (once or more per month) with participants during routine study visits and when following up adherence lapses, they did not view the data themselves or provide adherence counseling per study protocol. Notably, neither EAM collected location information or other identifiable data.

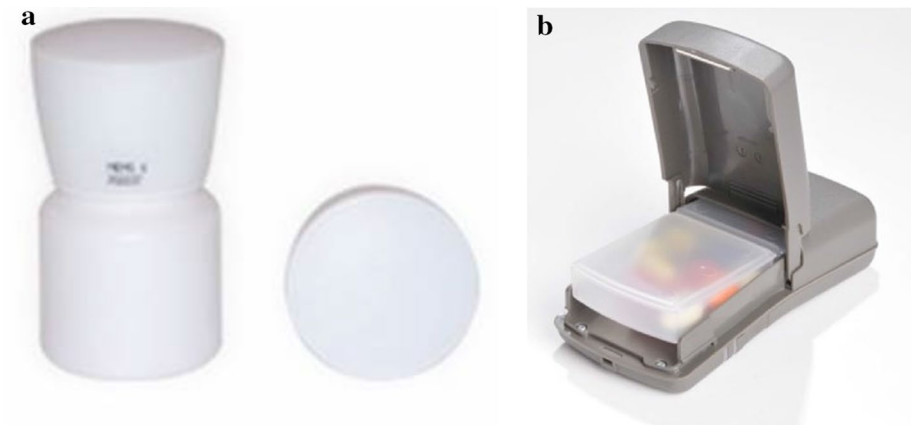


**Fig. 1** The MEMS (**a**) and Wisepill (**b**) devices

All UARTO participants used an EAM upon enrolment, although participants who subsequently declined to use the device or who moved out of the study catchment area (approximately 60 km from the research offices) could continue participating in non-monitoring aspects of the study. Per standard practice for research studies in this setting, UARTO participants received small incentives (e.g., a bar of soap), and a transport refund for study visits.

## Qualitative Data Collection

Semi-structured interviews were conducted from August 2014 to June 2015. First, we conducted exploratory interviews with UARTO participants who used the wireless EAM (n = 20). Our aim was to understand general impressions of wireless EAM use. Interview domains covered likes and dislikes of using the device, as well as the experience of participating in UARTO. Results of exploratory interviews informed subsequent data collection.

Second, we conducted in-depth interviews with three groups: 1) UARTO participants who used the wireless EAM (n = 20, distinct from exploratory interviewees), 2) UARTO participants who did not use the wireless EAM (n=20), and 3) UARTO RAs (n = 6). We ventured that enrolling both EAM users and individuals who had declined use of the device would reveal a broad range of attitudes surrounding EAM use, and that interviewing RAs would contextualize participants' experiences. Due to timing of the qualitative interviews, all UARTO participants had been enrolled in UARTO (and had been taking antiretroviral therapy) for at least six months prior to being interviewed, and all were ages 18 or older.

During interviews, participants were asked about a range of potential ethical considerations that we had proposed in prior theoretical work [16]. Specifically, questions focused on autonomy, trust, dependence, privacy and confidentiality, researchers' ancillary care obligations, and the role of social support in adherence monitoring studies. Here we report results relating to autonomy. Our autonomy-specific questions sought to understand whether monitoring:

1. affected pill-taking behavior,
2. created a sense of pressure to be adherent, and whether this pressure caused participants to feel upset or otherwise negative about their research experience
3. affected adherence-unrelated behaviors, such as travel plans, daily activities, or interactions with others.

Interviews were conducted in Runyankole (the local language in Mbarara) or English, according to participants' preferences.

## Qualitative Data Analysis

Using direct content analysis, we assessed the relevance, in participants' eyes, of theoretically-identified autonomy considerations surrounding EAM use [16]. We also employed an inductive content analysis approach [26] to identify additional exploratory themes. Initial analysis began with review and discussion of 20% of interviews by two researchers (JIC and BB), with substantial input from two additional researchers (JEH and AM), to identify relevant content. Content was then organized as codes in a codebook. Codebook development was iterative and involved defining codes and identifying illustrative quotes from interview transcripts. The final codebook was then imported into NVivo version 11, and two researchers (JIC and BB) used this software to code all interviews, with approximately 25% of interviews coded by both researchers to determine inter-rater reliability. Discrepancies in coding were discussed to reach consensus.

## Quantitative Assessments

All UARTO participants who joined our study completed a baseline demographic survey, as well as the general items of the decision-making preferences subscale—which assesses individuals' preferences for making their own medical decisions versus ceding decisions to doctors or other care providers—and the information-seeking preferences subscale—which assesses preferences surrounding how much information individuals want regarding their health—of the Autonomy Preferences Index (API) [27]. Survey questions were translated into Runyankole for non-English speakers. The API has been used widely to measure patient preferences for autonomy in medical research [28], although by design the index measures autonomy preference in clinical, not research, scenarios. The autonomy subscales were computed by coding responses from 0 to 4, with 4 indicating greatest preference for autonomy. Scores from each question were summed, and the total was scaled from 0 to 100, with 0 indicating no preference for autonomy, 50 indicating ambivalence, and 100 indicating greatest preference for autonomy. While both the API and a modified HIV-specific API [29] use case vignettes as part of the decision-making preferences scale, these vignettes were designed for use in Western settings and were dropped due to lack of face validity in our study setting. Because we adapted the API for use in our setting, our aim was to use data gathered via its subscales to help contextualize qualitative findings. While not validated for this population, the adapted API may add some understanding of decision-making as it relates to healthcare autonomy in this setting. All quantitative data were entered into a secured electronic database using Research Electronic Data Capture (REDCap) version 6 [30].

We used descriptive statistics to summarize demographic and API data. Differences between EAM users and non-users were analyzed with Fisher Exact and Wilcoxon rank-sum tests.

## Results

### Participant Characteristics

Participant characteristics are summarized in Table 1. We recruited a total of 66 participants in this study. Forty were EAM users enrolled in the UARTO study, 20 were UARTO participants who did not use the EAM, and six were UARTO RAs. EAM users were younger than EAM non-users [median age: 41 (IQR 35–46) vs. 45 (IQR 42–50) respectively, p = 0.03], had shorter duration of participation in UARTO [mean 5.5 years (standard deviation 2.7 years) vs. 8.0 years (standard deviation 1.1 years), p < 0.001], and had lower monthly non-salaried income [median non-salary income: USD 12 (IQR 4–36) vs. USD 63 (IQR 24–81), p=0.04].

### Quantitative Findings on Autonomy Preferences

Among both EAM users and EAM non-users, we found low preference for shared decision-making, but high preference for information seeking (Table 2). We found no significant difference in preferences for shared medical decision-making

**Table 1** Participant characteristics

| UARTO Participants | EAM users (n = 40) | EAM Non-users (n = 20) | p value (difference between EAM users and non-users) |
|---|---|---|---|
| Age (median, [IQR]) | 41 [35–46] | 45 [42–50] | 0.03 |
| Female (%) | 70 | 65 | 0.77 |
| Literate (%) | 90 | 85 | 0.68 |
| Education level (n [%]) | | | 0.77 |
| Never attended school | 4 [10] | 2 [10] | |
| Primary | 23 [57.5] | 11 [55] | |
| O-Level[a] | 9 [22.5] | 3 [15] | |
| A-Level[a] | 1 [2.5] | 3 [15] | |
| University/vocational | 5 [12.5] | 1 [5] | |
| Post-graduate | 0 [0] | 0 [0] | |
| Socioeconomic status | | | |
| Earns a salary? (n [%]) | 8 [20%] | 5 [25%] | 0.74 |
| Monthly salary (median [IQR]) (USD)[b] | $65 [$44 - $130] | $116 [$87 - $116] | 0.42 |
| Monthly non-salaried income (median [IQR]) (USD)[b] | $12 [$4 - $36] | $63 [$24 - $81] | 0.04 |
| Monthly household expenditures (median [IQR]) (USD)[b] | $75 [$39 - $148] | $87 [$22 - $171] | 0.67 |
| Time from UARTO enrollment to interview (years, mean [SD]) | 5.5 [2.7] | 8.0 [1.1] | <0.0001 |
| UARTO RAs | n = 6 | | |
| Age (median, [IQR]) | 36 [34–38] | | |
| Female (n [%]) | 4 [66] | | |

*UARTO* Uganda AIDS Rural Treatment Outcomes study, *EAM* electronic adherence monitor, *IQR* interquartile range, *USD* United States Dollar, *SD* standard deviation, *CAB* Community Advisory Board, *REC* Research Ethics Committee

[a]In the Ugandan education system, O-Level indicates completion of secondary school. A-Level is two-year, post-secondary, pre-university schooling

[b]Monetary conversion calculated at 1 US Dollar = 3445 Ugandan Shillings (as of January 12, 2015)

**Table 2** Autonomy Preferences Index subscale scores

| Autonomy Preferences Index (mean [SD]) | Overall (n = 60) | EAM users (n = 40) | EAM non-users (n = 20) | p value (EAM users vs. non-users) |
|---|---|---|---|---|
| Shared Decision-Making Subscale | 42 [9.0] | 43 [9.4] | 41 [8.4] | 0.58 |
| Information-Seeking Subscale | 70 [6.9] | 70 [7.4] | 70 [5.9] | 0.27 |

($p = 0.58$) or information seeking ($p = 0.27$) between EAM users and non-users.

## Overview of Qualitative Findings

Overall, we found that for many participants monitoring did create a sense of pressure to adhere. Some participants described monitoring as a potential infringement of their autonomous choice to take medications, feeling that it "forced" them, as they put it, to ingest ARVs. Others described how monitoring, in their words, "motivated" them to take their medications, which they perceived as a positive effect of monitoring. Nearly all participants, however, felt that adherence was in their best interest, and that, whether through force or motivation, monitoring helped them achieve their personal goal of taking ART as prescribed. No participant described modifying adherence-unrelated behaviors because of being monitored. Notably, no participant referenced incentives or travel reimbursements when discussing motivation to adhere.

## Adherence Monitoring Creates a Sense of Pressure to Take Medications

Participants said that monitoring sometimes created pressure to be adherent to ART even when they otherwise had not wanted to take their medications. This pressure was perceived either as motivating or as forcing ART adherence. In Runyankole, both the term for "motivate" (*akacipa nikampaririza*) and "force" (*akacupa nikangyema*) can have positive connotations more closely associated with "motivate" in English. However, in our interviews, participants consistently used these terms in distinct ways, with "motivate" carrying positive connotations and "force" bearing negative connotations.

### Monitoring "Forces" Adherence

Several participants emphasized fear of damaged relationships or of perceived punishment (e.g. via a blood draw) if they did not take their medications. In these cases, participants felt that monitoring forced them to take their medications. These feelings implied a negative outcome for detected non-adherence. One participant described:

> Respondent (R): *Those who started drugs before us set a bad example. They were not taking their drugs well. But for us when we began with [the EAM], it used to force us to take our drugs because we never wanted it to report us.*
> Male EAM user, Age 40

Another participant contextualized this sentiment, connecting the concepts of pressure to take medications with fear of losing a valued relationship with RAs:

> R: *The truth is that when you know that you have the device to report you and you do not want to spoil your relationship with your doctor and researchers, you make sure that you take your medication so as to maintain a good relationship with them.*
> Female EAM user, Age 42

Blood draws in the UARTO study were disliked, and when monitored, participants at times felt forced to take medications in order to avoid blood draws stipulated by the study's protocol:

> R:*…you do not want your RA to come and do a blood draw. So you find that you are forced to take your medication well. Generally, if we never had it, we would not be taking our medication the way we are taking it.*
> Female EAM user, Age 42

Other participants described their perception of monitoring and fear of revealing socially undesirable non-adherence as a potential source of pressure to take medications:

> R: *Because it forces you to take your drugs, because you know that it can report you. So you end up taking [ARVs] anyway even if you never wanted to take them.*
> Female EAM user, age 45

> Interviewer (I): *You also said that you fear that the device will report you, please tell me more about this fear you talked about.*
> R: *I said it's like a child who fears to be reported for doing wrong because he knows he will be punished…I fear that they will know that am careless about my life and I do not want that to happen.*
> Female EAM user, age 45

However, for most participants, the relationship between monitoring and feeling forced to take medications was more nuanced. Most participants held that good adherence was in their best interests and maintained that it was their personal overarching goal. So even when feeling forced to take medications because the monitor would reveal non-adherence, participants frequently welcomed this pressure, and saw it as a tool to their own ends:

> R: *It has helped me like I told you. Sometimes you can be busy but something forces you to stop what you are doing and you first take your medicine because you do not want your doctor to know that you delayed. But otherwise if it was not there you would probably keep busy and you take at any time later.*
> Female EAM user, age 32

I: *Does this device cause feelings of obligation or resentment? Do you sometimes feel like you do not want to take your medication but you end up taking it because you have the device that will report you?*
R: *We should be happy that we have a device that reminds us.*
I: *But does this happen, that you get feelings of obligation or resentment sometimes*?
R: *Yes I sometimes have these feelings. It's like when you are in school and you have to go for night and early morning prep. You do not like it but you are forced to do it by force from the teachers but in the end it's always for the student's good.*
Female EAM user, Age 42

#### Monitoring "Motivates" Adherence

In contrast to feeling forced, many participants said that monitoring motivated them to take medications, typically using the word "motivation" to explain how EAMs helped them to achieve an immediate goal of taking medications. They linked monitoring to motivation to take medications in three primary ways. First, and most commonly, they felt that good adherence was important to RAs, who "cared about" them; participants achieved satisfaction when monitoring enabled them to demonstrate good adherence:

R: *I told you when you have it [the EAM], there is something that you feel telling you to open [the EAM] because you know that someone will see a message that you have taken your medicine and this motivates you.*
I: *So is it the device that motivates you or is it someone whom you want to see the message that you have taken your drugs?*
R: *For sure it is both because they all go hand in hand, I have to have the device and open it for someone to be able to see the message.*
I: *So how does this make you feel?*
R: *I feel good because I know that someone who cares about me has seen that am doing as she instructed me to do.*
Male EAM user, Age 39

Second, monitoring motivated participants to take medications in order to avoid imposing additional work on RAs, a feeling that RAs confirmed:

I: *What do you like about using [the EAM]?*
R: *I like it a lot because on my side I was lazy to take drugs but now it encourages me and motivates me to take my drugs.*
I: *How?*
R: *Because I know that if I do not take my drugs it will report me to the RA and I do not want this to happen since it will disturb her to come here and find out why.*
Female EAM user, Age 62

I: *What do you think [the EAM] helps them with?*
R: *It reminds them to take their drugs…Because they knew that we were monitoring them so it was in their head that if they don't take their drugs we would know…you know when you have someone watching and he cares about you, you take your drugs. Maybe they would think they would let us down if they don't take their drugs…We always had to make sure we go to their home even when it was shining or raining so they would feel they are bothering us even when it was our job.*
RA 1

Third, many participants understood the study's aim to be demonstration of good adherence among the study population. Motivation to take medications arose from the desire to further what they perceived to be this objective. Monitoring provided the crucial link between adherence behavior and researchers' perceived ability to fulfill study aims:

I: *How does [the EAM] motivate you?*
R: *I feel happy to know that they are doing their research on me well as they planned as I take my drugs well too. They benefit and I benefit as well.*
Male EAM user, Age 60

All three of these mechanisms of motivation arose from the sense that adherence was in participants' own best interests, combined with the perceived positive effects of participants' adherence on study team members'—and particularly RAs'—satisfaction, as well as study success.

### Adherence Monitoring Rarely Altered Behaviors Unrelated to Adherence

Participants reported only few instances in which monitoring made them alter their adherence-unrelated behavior. Monitoring infrequently changed their behavior by prompting actions to enable EAM use or signal transmission, such as climbing to the top of a hill to enable the cellular signal to be sent:

R: *They first gave me one that was faulty it used to lose network so my RA used to come a lot to my place due to this network issue. This device had failed to grab network in my house I had to first go to a hilly place because my house was like on a valley and I used to first go to a hilly place for the device to be able to send a message.*
Male EAM user, Age 64

Participants, however, did not raise concerns about the device restricting behaviors unrelated to adherence, such as travel plans or daily activities.

### Limitations on Freedom to be Non-adherent did not Prompt Rejection of the EAM

No participant who rejected the wireless EAM described limitations to her freedom to be non-adherent or to her ability to pursue other activities as reasons for why she rejected the wireless EAM. Rather, reasons for refusing the EAM included concerns about device fragility, inconvenience of using the device, and concerns about disclosure of HIV status (e.g., if seen with the EAM).

## Discussion

When electronic adherence monitoring is said to constrain personal autonomy, two potential allegations are implied. First, that monitoring pressures adherence against individuals' true wishes, and second, that monitoring constrains individuals' freedom to carry out activities unrelated to adherence, primarily through self-censorship given knowledge that one's behaviors are being observed.

Did participants of this study perceive monitoring as autonomy-limiting? Most participants felt that monitoring helped them to achieve their goal of taking medications as prescribed. However, one could argue that because monitoring constituted an external pressure on many participants' decision-making surrounding adherence, it created autonomy-limiting effect. Individuals are typically thought to have the right to be non-adherent to medication, and can and often do make informed, autonomous decisions to not take prescribed medications.

Our data suggest that participants specifically *welcomed* monitoring as a strategy to improve their adherence. Even participants who at times felt that monitoring "forced" them to adhere held that adherence was aligned with their self-stated overarching goals and personal good. One participant described feeling like a student under the supervision of "teachers" (namely, her RAs) who oversaw her adherence. Although this made her feel that she was being forced to take her medications, ultimately she acknowledged that this was "for [her] own good". Other studies have shown that participants sometimes "cede decisional authority" to care providers in order to pursue courses of action that they fundamentally desire but "find themselves resisting" [31]. In our population and setting, participants valued achieving adherence more than they valued fulfilling the right to be non-adherent, and did not mind pressure against personal drivers of non-adherence when it enabled them to achieve another, more desired goal: ART adherence.

These findings illustrate how what philosophers would call participants' "first-order" desires (e.g. wanting to skip taking medications) can be in tension with their "higher-order" desires, namely, preferences about these first-order desires (e.g. wanting to cease wanting to skip taking medications) (Table 3). When a higher-order desire serves a third, deeper desire (e.g. to remain healthy), then the higher-order desire is accepted as successfully "repudiating" the first-order desire. Some philosophers identify autonomy with a state in which a person's higher-order desires govern her choices [32, 33].

However, in practice, when a participant is a capacitated adult, most bioethicists understand autonomy to include respect for her first-order desires, even without higher-order desires or with some that repudiate her first-order desires [17]. In our case, all interviewees were deemed capacitated, both in general and on the specific matter of ART adherence. Therefore, most bioethicists would catalogue deliberate pressure against many participants' first-order desire to not take medications as limiting their personal autonomy in certain respects—whether or not these bioethicists would see that pressure as permissible and/or as autonomy-boosting overall.

Our own view is that even if EAMs to some extent constrained our participants' first-order desires to be non-adherent, from an ethical standpoint, this mattered little. While the ethics of paternalistic conduct in general are being debated, many bioethicists maintain that some limitation of autonomy to fulfill first-order desires, which helps individuals fulfill higher-order desires and their ultimate desires, is justifiable, or in fact increases personal autonomy [31, 34, 35]. Additionally, some ethicists do not consider all first-order desires worthy of preservation [36], and preferences not to adhere to ART may be considered a case in point, for instance, because it is usually irrational to skip lifesaving

**Table 3** Key terms

| Term | Definition | Example |
|---|---|---|
| Autonomy | Authority and agency to govern one's own actions | Ability to decide for oneself when to take a medication or not |
| First-order desire | A basic desire to do something or not to do something | Momentary desire to not take a pill |
| Higher-order desire | A desire to have one first-order desire (e.g. over another) | Desire to lack the momentary desire to not take a pill (e.g. in the service of an ultimate desire to stay healthy) |

treatment. Admittedly, according to some conceptions of autonomy, pressure that serves a person's own ultimate goals can remain impermissible and contrary to that person's personal autonomy. However, our participants described monitoring as a relatively mild form of pressure to take ART, which preserved some ability to be non-adherent, hence limiting any ethical transgression. Indeed, despite monitoring, in the UARTO study, adherence remained suboptimal (median 86%) [37], potentially in part due to personal choice. Finally, because non-adherence to ART may pose risks not only to the individual patient but also to others (e.g. through increased risk of transmission and spread of resistant strains), some have argued that people living with HIV have a degree of duty to take antiretrovirals for the benefit of public health [38].

Personal autonomy is a cornerstone of "Western" bioethics [17, 39]. However, much prior theoretical and empirical work has criticized the primacy of personal autonomy in global health research and clinical care. Such work, which has largely focused on the informed consent process, argues that the importance of autonomy is often projected onto individuals whose cultures may rather emphasize communitarian or family approaches to decision making [40–46]. Empirical work has also supported the notion that personal autonomy is not a paramount concern among research participants or field workers in at least some parts of sub-Saharan Africa. For instance, research from Kenya suggests that RAs prioritize improving participants' health over preserving the participants' autonomy [47]. Our results extend these findings beyond informed consent, to attitudes towards personal autonomy in choices about medication adherence. Specifically, even when feeling forced to adhere, the autonomy to fulfill first-order desires in decision making surrounding ART adherence was deemed less important than other, more pressing considerations like preserving health, potentially in light of the higher-order preference to have different, more pro-health first-order desires.

Our quantitative findings suggest that these qualitative results may be based on underlying attitudes towards medical decision-making in this community: participants expressed desire for health information, but placed less emphasis on making medical decisions for themselves. Instead, according to the decision-making preferences scale of the API that we employed, participants leaned towards ceding authority over medical decisions to care providers. It is therefore not entirely surprising that participants were minimally perturbed when feeling forced to adhere. This finding underscores other research using the API from the developed world [31,48].

Ware and colleagues conducted a qualitative study of similar participants from this setting who were enrolled in a nine-month randomized controlled trial involving EAM and a text message adherence promotion service [49]. They described how EAM monitoring led to a sense of "being seen adhering", which in turn led them to "have no choice but to take the medication every day". Participants in Ware et al., like in our study, generally interpreted pressure to adhere positively. In contrast to the participants described in Ware et al., our population was drawn from a study in which participants were observed for a longer period of time, resulting in more longitudinal contact with study staff, the EAM, and ART. The emphasis that participants in our study placed on close relationships with RAs, and the fear of losing these relationships or the benefits gained from them, may reflect this long-term contact. RAs similarly suspected that the intricacies of close relationships with participants contributed to adherence motivation. Ware et al. did not observe these relationship-based effects, potentially due to the comparatively shorter duration of the trial they investigated. Our results suggest that such longitudinal relationships may affect decision-making surrounding adherence when participants are monitored.

Importantly, monitoring was not reported to affect participants' ability to pursue activities unrelated to adherence, and participants generally did not express fears that researchers might learn more about them through use of the EAM than merely about their adherence. The wireless EAM used in the UARTO study had limited capacity to detect or report activities beyond simple medication timing, and participants had qualitatively accurate understandings of these limited capabilities. It remains possible, however, that future EAMs that enable more invasive monitoring (e.g., ingestion monitors [50]) would impede personal autonomy in this way, and further study of novel devices is needed.

Our study has several limitations. First, we only interviewed participants in the UARTO study. The viewpoints they expressed may not fully reflect the range of perspectives on EAMs in this community, and some characteristics of the study (e.g. blood draws) may have colored participants' perspectives in ways that will be less relevant for dissimilar studies. We were unable to interview individuals who declined participation in UARTO altogether, and we do not know if autonomy concerns factored into their decision not to participate. Furthermore, there were differences in age, duration of UARTO participation, and income between EAM users and non-users, suggesting that social factors may have affected the decision to use or reject the EAM. In particular, the younger age of EAM users than non-users may indicate generational differences in receptiveness to new technologies. Second, participants were all drawn from a single site in Uganda and used (or had declined) variations of a single type of device that was being used to study a single disease (HIV). Third, because the API was designed to measure autonomy preferences in clinical settings and was modified to be relevant for our study participants, it may not provide generalizable information on autonomy preferences

in this population. Rather, we used it to provide information to contextualize our qualitative results. Finally, we interviewed participants only once, and were therefore unable to capture changes in attitudes over time. Future research could investigate how experience with monitoring changes over the course of a longitudinal monitoring study.

Our results have several implications. First, they argue that it is necessary for researchers to be vigilant about the ways in which monitoring systems affect participants' ability to make and act upon their own choices surrounding medication adherence. Second, they suggest that the unrestricted ability to be non-adherent, free from any pressure to take medications that monitoring might create, was less desirable to participants than taking medications as prescribed. In fact, monitoring promoted their ultimate goals in this instance. Third, we corroborate previous findings from this resource-limited remote setting that associated HIV adherence monitoring with perceptions of caring treatment [49]. Fourth, although research subjects using EAM theoretically accept potential limitations to their autonomy to fulfill first-order desires when they autonomously provide informed consent, the nature of these potential limitations has not previously been described. Specifically, our analysis outlines the effects of specific monitoring strategies on participants' ability to take medications and otherwise behave as they choose. These considerations should inform future EAM-based study design and consent processes. Finally, as we asked in the introduction, is pressure to adhere ethically unacceptable when it improves adherence and health? Our empirical evidence tends to supports the theory that such pressure to adhere may be ethically acceptable, particularly when the pressure confers significant benefit, is generally welcomed by those experiencing the pressure, and aligns individuals' behaviors with their goals.

## Conclusion

Among participants of a longitudinal cohort study in Uganda, EAM of ART appears to have influenced decision-making surrounding adherence, and at times was reported to have forced adherence. However, even when seen as forcing adherence, monitoring was generally perceived as a positive feature of the device and of the research support system. Participants had few concerns that EAM would impinge upon their freedom to make choices unrelated to adherence.

Altogether, these findings suggest that participants favored, at least in retrospect, fulfilling their ultimate goals (preservation of their health through adherence) over both fulfilling more momentary desires (e.g. non-adherence due to inconvenience of taking pills) and the unrestricted autonomy to fulfill the latter desire. As electronic monitoring devices become more prevalent in medical research, researchers should remain cognizant of potential autonomy transgressions arising from monitoring, but also of how monitoring may enable participants to achieve their own fundamental health goals.

**Acknowledgements** We would like to thank the individuals who participated in this study. This study was supported by an NIH/NIAID grant R21 AI108329.

## Compliance with Ethical Standards

**Ethical Approval** This study was reviewed and approved by the IRB at Partners Healthcare/Massachusetts General Hospital, the Research Ethics Committee at MUST, and the Uganda National Council of Science and Technology. Notably, one member of our study team (JEH) was also involved with UARTO; however, she was not directly involved in data collection and the interviewers for our study were not members of the UARTO study staff.

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