A mixed-methods study of the technical feasibility and patient acceptability of a real-time adherence monitor in breast cancer survivors taking adjuvant endocrine therapy

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Abstract

Purpose Oral anti-cancer medications are increasingly common and endocrine therapies represent the most common oral anti-cancer medications in breast cancer. Adjuvant endocrine therapies reduce the likelihood of recurrence and mortality in the approximately 80% of women diagnosed with hormone-receptor-positive breast cancer, thus rendering adherence essential. Real-time medication adherence monitors, such as the Wisepill electronic pillbox, transmit adherence data remotely, allowing for early intervention for non-adherence. However, their feasibility and acceptability have yet to be examined among breast cancer survivors taking endocrine therapies.

Methods This study presents quantitative patient-report and technical support data and qualitative patient acceptability data on Wisepill, a common real-time adherence monitor, among 88 breast cancer survivors prescribed adjuvant endocrine therapy.

Results This mixed-methods study of a common real-time adherence monitor, among the first in breast cancer survivors taking adjuvant endocrine therapy, demonstrates its technical feasibility and patient acceptability.

Conclusion The use of wireless medication monitors that transmit real-time adherence data is uniquely promising for maximizing the benefits of adjuvant endocrine therapy by allowing for continuous tracking, ongoing communication with oncologic or research teams, and early intervention. This study demonstrates the feasibility and patient acceptability of one such real-time adherence monitor.

Keywords Breast cancer · Medication adherence · Endocrine therapy · Real-time adherence monitor

Introductions

Oral anti-cancer medications are increasingly common [1]; however, medication adherence (i.e., taking the medication in the dose, frequency, and duration as prescribed) among adults with cancer remains suboptimal [2–6]. Non-adherence is associated with poor treatment efficacy, greater health care costs, and increased hospital utilization among patients with cancer [4]. Medication adherence is a key pathway through which oncologic practice is translated into patient outcomes [5, 7]. A common class of oral anti-cancer medication is adjuvant endocrine therapy (AET), adjuvant medications that reduce recurrence and mortality among the approximately 80% of breast cancer survivors with hormone-receptor-positive tumors [8–10]. Recommendations suggest five to ten years of AET after primary treatment, making long-term adherence particularly challenging for breast cancer survivors [11]. Despite the benefits of adherence, a systematic review revealed that AET adherence after 5 years ranged from 41 to 72% [2]. The clear advantages of AET coupled with the challenges of adherence render the accurate assessment of adherence essential and early intervention for non-adherence necessary for optimizing medical outcomes among breast cancer survivors.
Current approaches for assessing medication adherence include indirect methods such as patient self-report on questionnaires and interviews, pill counts, prescription records, and more direct methods, such as serum detection and electronic medication monitors [13]. Electronic medication adherence monitors are precise and can track patterns in adherence over time without being subject to poor patient recall or social desirability. Advancements in electronic adherence monitors, such as the Wisepill real-time adherence monitor (Wisepill Technologies, Cape Town, South Africa), have eliminated the need for return visits to download device data and can remotely transmit adherence information in real time via wireless networks. Real-time adherence monitors allow for early intervention among patients who have discontinued their medications [14], as they detect lapses in adherence as they occur, providing novel opportunities to prevent treatment failure among breast cancer survivors taking AET.

In that real-time monitors represent the future of adherence assessment, it remains critical to evaluate their feasibility and acceptability in cancer populations that are commonly prescribed oral medication. Real-time monitoring of physical symptoms is well established in many cancer care settings [15, 16]; however, real-time monitoring of medication adherence is not. Despite widespread use of medication adherence monitoring among adults with HIV/AIDS [17, 18], the feasibility and acceptability of real-time medication adherence monitors such as Wisepill are not yet established among breast cancer survivors prescribed AET. The current study provides the first known published report on the use of real-time medication adherence-monitoring devices in breast cancer survivors. This study uses mixed methods to evaluate patient and technical support perspectives on Wisepill, a real-time monitor. Our patient acceptability and feasibility goals were that (1) patients would find the real-time medication adherence-monitoring devices acceptable on both quantitative and qualitative measures, (2) 95% of participants would complete the 30-day device feasibility baseline period and continue using it for the 6-month follow-up period, thus demonstrating patient feasibility of device use, and (3) participants could successfully use the monitoring device throughout baseline and 6-month follow-up with minimal contact from the research team to resolve technical issues.

Methods

Participants

Patients who were prescreened as medically eligible by electronic chart review were recruited from Rocky Mountain Cancer Centers in Colorado to participate in a values-based clinical intervention trial to promote AET adherence (clinical trial identifier: NCT03980093) [19]. The study eligibility criteria included diagnosed with Stage 0 to III hormone-receptor-positive breast cancer, completed primary cancer treatment, prescribed AET in the past 2.5 years with at least 1 year remaining, reported at least modest difficulty taking AET (see Screener), internet access to participate in the online intervention, and regular access to cell service to transmit Wisepill data. Of the 977 mailings that were sent to prescreened patients, 207 women responded, 99 were eligible, 11 women were not interested in participating after hearing more detail about the study, and 88 women enrolled. All participants provided informed consent and the University of Colorado Boulder Institutional Review Board approved the study.

Procedure

Participants were mailed a Wisepill device, a wireless electronic pillbox that sends real-time data when opened, along with instructions for its use. The device consists of a portable black rectangular box (4.33” long × 1.77” wide x 0.47” deep) that holds up to 30 large or 60 small pills (Fig. 1). The instructions included visuals, basic written instructions, and troubleshooting tips printed on a 5 × 8” laminated card. After participants received the post-mailed package with the Wisepill and the instructions, a member of the research team called to confirm that the participants were able to set up and use the device. The devices were remotely monitored online by the research team several times per week to ensure proper functioning. Wisepill works by recording events (i.e., pill box openings) on the device and sending a report of those events to the Wisepill server via a SIM card. Participants with inconsistent cell service at home were asked to bring the device with them into a region with more consistent cell service (e.g., when getting groceries in town) at least once a week so that the adherence data stored on the device could be transmitted. The daily text reminder feature of Wisepill was disabled to focus on use of the device itself and the
values intervention content (i.e., the online intervention which focused on values as motivation for AET adherence; for values intervention details see Arch et al., 2022).

**Measures**

**Screener**

Breast cancer survivors had to report missing 2 or more AET pills in the past month or at least one factor that made taking their medication moderately difficult to be eligible [19].

**Feasibility**

Patient feasibility was assessed by examining the number of participants who successfully used the Wisepill device over the 30-day baseline period and the entirety of the seven-month study period.

Wisepill signal lapses greater than 48 h (i.e., no adherence data transmitted over a 48-h period) were briefly investigated by a member of the research team via the Wisepill-generated online technical report. The research team could largely determine the cause of a signal lapse using the technical report and would follow up via telephone with the participant to resolve the technical difficulty. The nature of the technical issue and number of contacts needed to resolve it were recorded as a measure of technical feasibility.

**Patient Acceptability**

Breast cancer survivors rated on a 5-point Likert-type scale (1 not at all, 5 extremely) how helpful and convenient they found the Wisepill device, and how likely they were to recommend the device to another breast cancer survivor taking AET.

Qualitative information on patient acceptability of Wisepill was extracted from semi-structured phone exit interviews conducted with a subsample of participants (n = 38) by four post-baccalaureate interviewers trained as either clinical interviewers or clinical psychology doctoral students with several years of clinical experience. Prior to conducting the qualitative interviews, the interviewers received additional instruction in active listening techniques and reflexive interviewing. Prepared prompts were used to guide the interviews and interviewers were also trained to respond in-the-moment to the participant and elicit relevant information (please see the Supplementary materials, Wisepill Qualitative Interview Guide, for the full interview prompts).

To ensure that the full range of experiences was represented in the interviews, 23 participants were randomly selected within satisfied, neutral, and dissatisfied strata based on their quantitative and qualitative responses to questions about their overall study satisfaction. As the responses to the values-based intervention were overwhelmingly positive, this approach resulted in oversampling negative responses; thus, 15 additional participants were randomly selected from the entire sample using a random number generator.

Interviews were transcribed and coded for both a priori and emergent codes regarding patient acceptability of Wisepill and suggestions for future Wisepill use. Codes for the qualitative patient acceptability data were informed by the widely used Health Belief Model [20, 21] by assessing perceived benefits, barriers, and cues to action. The research team reviewed and revised the codes based on their clinical and research experience with breast cancer survivors taking AET. Example questions from the interviews include, “Did you experience any benefits in using the Wisepill box?” and “How convenient or inconvenient was it [Wisepill] to use?” Participants were also asked about how the monitoring function of the Wisepill may have affected their behavior and their recommendations for future use. All transcripts were coded in ATLAS.ti version 9.1 twice by 2 to 3 independent coders: once for broader themes and again for relevant sub-themes. After coding, the team met to establish consensus by resolving any conflicts through discussion.

**Results**

**Sample characteristics**

On average, participants were 58 years of age, 14 months from the end of primary treatment, and prescribed AET approximately 13 months prior to study entry (Table 1). Most participants were non-Latina white (92%) and prescribed aromatase inhibitors (63%). The average duration of the qualitative interviews was 36:57 (range = 17:30–55:09).

**Feasibility: completion**

All participants (100%) completed a 30-day Wisepill monitoring baseline, exceeding the study’s 95% completion goal, and 98.86% (87/88) completed the 6-month Wisepill monitoring follow-up period.

**Feasibility: technical difficulties**

Over the 7-month study, 13.64% of participants (n = 12) experienced technical difficulties using Wisepill which required a total of 38 contacts to resolve, including losing connectivity (n = 9, contacts = 25), not registering pillbox openings (n = 1, contacts = 6), charging cable not working (n = 1, contacts = 4), and needing to reset the battery (n = 1, contacts = 3). These contacts were almost exclusively initiated by the research team, specifically all of
those related to losing connectivity and not registering pill box openings were only research team initiated.

**Patient acceptability: quantitative ratings**

On a 5-point Likert-type scale, on average, participants found the Wisepill box to be moderately helpful (\(M = 3.15, SD = 1.31\)), moderately convenient (\(M = 3.66, SD = 1.36\)), and were somewhat likely (\(M = 3.40, SD = 1.49\)) to recommend the device to someone else taking AET. There were no statistically significant differences on any of the quantitative patient acceptability ratings by trial condition (\(p's > 0.190\)).

**Patient acceptability: qualitative interviews**

**Patient perceptions of convenience**

Women responded to open-ended prompts about the acceptability of Wisepill and offered suggestions for future use. Most breast cancer survivors found Wisepill convenient to use (\(n = 27\)). For example, when asked about the convenience of the Wisepill, one participant stated:

*It was not at all inconvenient. It's no different than a pill bottle to me in terms of use.* (1056, prescribed an AI)

**Patient perceptions of benefits**

Many women (\(n = 22\)) also found benefits in using the Wisepill. Breast cancer survivors found the real-time tracking features of the Wisepill to be a source of motivation, for example, one participant stated:

*I think the idea that someone was tracking you and that they were going to ask you about it...was a little more motivating to make sure I took it.* (1046, prescribed tamoxifen)

The mere presence of the device was a helpful reminder and benefit for others:

*It made me aware of every day that I was taking my medications. And it helped me keep track of them.* (1068, prescribed tamoxifen)

While others did not perceive any benefits from their use of Wisepill, they noted its ease of use:

*Did I experience any benefits in using it? No, [but] it was convenient to have. It was easy to open instead of opening a pill bottle, so that was kind of nice, you just kind of slid it, flipped it open.* (1073, prescribed an AI)

**Patient perceptions of device-influenced behavior change**

Many participants (\(n = 16\)) reported no changes in their behavior or motivation to take AET because their adherence was being monitored. For example, when asked whether knowing that her adherence data were being monitored had changed her behavior, one participant stated:

*I really don't think it affected it at all. Because yeah, I just don't think that that box motivated me in any way to take my medications. I take them because they're prescribed...* (1066, prescribed tamoxifen)

Other participants (\(n = 9\)) reported positively changing their adherence behavior or feeling more motivated or committed.
to taking AET because of the knowledge that Wisepill was remotely transmitting their adherence data. One participant stated:

*I think occasionally like I said, I don’t want to take it today. And then knowing that somebody was going to know whether I took it or not, okay fine I’ll take it.*

(1037, prescribed an AI)

Participants were also asked for their recommendations for future use of the Wisepill device. Suggestions included daily access to an online Wisepill medication log (n = 10), a device-initiated reminder (alarm, blinking light, text message) to take their medication (n = 9), and a 7-day medication divider insert to track their medication (n = 11; Table 2).

### Discussion

Findings demonstrate that real-time wireless monitoring of AET adherence among breast cancer survivors is generally acceptable to patients and technically feasible. That 100% of participants completed a 30-day Wisepill monitoring baseline, and 99% completed a 6-month monitoring follow-up period also provides strong evidence of feasibility. The most common technical issue, lost wireless connectivity, delayed the transmission of data but still allowed for adherence information to be transmitted once the device reconnected. Although technical components of the device must be monitored to ensure proper functioning, serious technical issues were rare. These findings converge with previous research on the technical feasibility of Wisepill among patients with HIV/AIDS [17, 22].

In addition, the devices were acceptable to patients, even with some of the more useful features, such as reminders, inactivated to focus on the use of the device itself. The device was rated as moderately helpful, convenient, and recommendable on quantitative measures. In qualitative exit interviews, many breast cancer survivors reported that the devices were convenient and beneficial for adherence. The accountability that comes from the devices being actively monitored by an outside team served as a cue to action for some participants, while others found the mere presence of the device to be a helpful reminder to take their medications. The ability of standard electronic adherence-monitoring devices to serve as a visual reminder has been noted as a facilitator of medication adherence among patients with HIV/AIDS [23]. While not all participants found benefits in the use of Wisepill as a reminder or otherwise, many still noted its convenience and ease of use.

The knowledge that their adherence was being tracked by others was cited as a facilitator for some participants, and may serve as a benefit in clinical settings, but lead to higher adherence rates in research settings. Implementing a

| Table 2: Patient suggestions from semi-structured exit interviews for Wisepill |
|---|
| **Suggestion for Future Use** | **Illustrative Quote** | **n** |
| Daily log | Participants wanted access to an online or app-based daily medication log that they could check themselves as often as they desired | 10 |
| Reminders | Participants wanted a reminder (e.g., alarm, blinking light, text message) from the Wisepill to cue them to take their medication | 9 |
| Pillbox divider | Participants wished that the Wisepill had a weekly divider with the days of the week separated to help them keep track of their medications | 11 |

*“I think sometimes for people taking prescriptions, it is helpful to have almost a Sunday, Monday, Tuesday, Wednesday, Thursday, Friday type container because at least for me it’s easy to forget once I’ve gotten up in the morning, to get involved with something and then forget whether or not I’ve taken my medication.”*
baseline period of monitoring to allow participants to adjust
to using the device as well as providing the device to all the
experimental groups, as was done in the present trial, may
mitigate the risk of inflated adherence.

While moderate difficulty taking their medication was an
eligibility criterion, many women had high adherence dur-
during the study time period [19]. On one hand, this renders it
notable that breast cancer survivors still found the device to
be moderately helpful, convenient, and recommendable even
if they adhered to AET throughout the study period. On the
other hand, high AET adherence rates may have inflated the
feasibility estimates that showed very high Wisepill device
use throughout the study period. Thus, future research
examining feasibility among less AET adherent samples is
essential.

Similar to studies in HIV/AIDS populations [24], the
full capabilities of the Wisepill device, namely the daily
reminder function, were not enabled in the present study,
in order to focus exclusively on the device itself (and val-
ues intervention content). It is notable that participants
still largely found the devices to be acceptable despite the
absence of the reminder function. Research has shown some
minimal benefit of electronic medication device reminders
alone for promoting adherence among patients with non-
cancer illnesses [25]. Thus, future research examining the
patient acceptability of real-time adherence devices with all
features activated is warranted.

For future use, patients had consistent and feasible recom-
endations that included a daily pill log, daily reminders,
and a 7-day pillbox divider, which could be incorporated
into future interventions or clinic policies to further pro-
mote adherence. Wisepill can be used with a 7-day pillbox
divider and as noted, already supports a reminder function,
as recommended by the current sample.

Despite variation with respect to socioeconomic status,
this sample lacked racial and ethnic diversity, which requires
cautions in generalizing the findings to diverse groups. AET
adherence differs among racial and ethnic groups, with lower
AET adherence among women of other racial and ethnic
groups compared to white women [26]. The response rate
to our mailing recruitment was high, nonetheless, recruitment
by mail tends to overselect for white participants and those
with stable housing situations [27]. Higher touch recruitment
methods such as clinic visits and partnering with community
members and organizations are important areas for devoting
resources to collect more representative samples [28].

Research has shown that AET non-adherence predicts
breast cancer recurrence and subsequent mortality [3, 4, 10,
29]. More accurate adherence monitoring, in combination
with the potential for early intervention for non-adherence,
would allow for prioritization of limited resources to pro-
mote adherence among breast cancer survivors at greatest
risk for poor AET adherence or discontinuation. The use of
wireless medication monitors that transmit real-time adher-
ence data is uniquely promising for maximizing the ben-
efits of AET by allowing for continuous tracking, ongoing
communication with oncologic or research teams, and early
intervention. Future research examining the long-term use of
such devices with all features activated among diverse popu-
lations is an important next step for furthering our under-
standing of their utility for women prescribed AET. The
present study is the first to our knowledge to demonstrate
the technical feasibility and patient acceptability of a real-
time wireless medication adherence monitor among breast
cancer survivors taking AET, thus establishing a foundation
for further use and investigation of these promising devices
in this population.

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Data availability Upon reasonable request, the quantitative data ana-
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Declarations

Conflict of interest The authors have no relevant financial or non-fi-
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Ethics approval University of Colorado Institutional Review Board
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