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Providers' Perspectives on Adherence to Hormonal Therapy in Breast Cancer Survivors. Is there a Role for the Digital Health Feedback System?

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Abstract

Objective: Despite the benefits of hormonal therapy (HT) adherence remains suboptimal in ER positive breast cancer patients. Medication adherence is challenging to assess and tends to be overestimated. The Digital Health Feedback System (DHFS) consists of an ingestible sensor attached to a pill that sends intake date and time to a smart phone or computer. Patients can share this information with health care providers and other persons. The DHFS can also send reminders. This mixed methods study examined providers' perceptions of HT medication adherence. The potential role of the DHFS in enhancing medication tracking and adherence was also explored.

Methods: We conducted semi-structured interviews with key informants (N=10). Questions examined perceptions about adherence barriers and facilitators, challenges tracking adherence, and views on the DHFS. Findings informed the development of a survey that was administered online (N=19).

Results: Providers emphasized the importance of fostering open and trustful communication around adherence. The most mentioned challenges to assessing adherence were the patient not disclosing discontinuation immediately (78.9%) and over-reporting adherence (57.9%). The perceived potential benefits of DHFS were the ability to track adherence better (94.7%) and reminders to take the medication (68.4%). Safety to ingest a sensor was as a major perceived barrier (84.2%).

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The authors declare that they have no conflicts of interest

Compliance with Ethical Standards

The study was approved by Georgetown University Institutional Review Board

Ethical Approval: All procedures in this study have been performed in accordance with the ethical standards as laid down in the 1964 Declaration of Helsinki and its later amendments or comparable standards.

Conclusion: Interventions that target providers and doctor-patient communication are warranted to enhance adherence and reduce communication delays around HT discontinuation.

Practice Implications: DHFS has the potential to enhance HT adherence by directly targeting barriers. Future studies should also examine the feasibility of adopting the DHFS with cancer patients.

Keywords

Patient-doctor communication; hormonal therapy adherence; Digital Health Feedback System

1. Introduction

Adjuvant hormonal therapy (HT) significantly reduces recurrence and mortality in women with hormone receptor positive breast cancer [1,2]. Five years of Tamoxifen reduces annual recurrence rates by half and mortality rates by one-third [3]. Five additional years result in bigger reductions in recurrence and mortality [1]. Adherence to the complete multi-year course (one pill daily for at least 5 years) is necessary to obtain full benefits [1,2]. Despite the benefits of HT, adherence significantly decreases from 79% to 68% at years one and five respectively. Non-persistence ranges from 13% at year one to 40% at year five [4]. Additionally, a substantial number of breast cancer patients experience interruptions in their daily medication intake that range from 60–180 days. The longer these gaps, the less likely patients are to continue therapy [5].

Potential reasons for low adherence are complex and involve an interplay of clinical, healthcare, demographic, and psychosocial factors [6]. Patient-doctor communication is one of the few modifiable psychosocial factors that has been consistently associated with HT adherence across studies [6]. Providers can have an important role in facilitating medication adherence via communication and helping to manage side effects [7,8]. Strategies to facilitate communication are necessary, yet little is known about providers' perspectives on managing adherence to HT [9].

Current methods of tracking adherence include self-report, obtaining pharmacy records or pill counting. These methods are not always effective, as they do not measure if the patient has actually ingested the medication [10]. Existing research has mostly focused on patients' perspectives on adherence [9]. Research on providers' perspectives has mostly focused on HIV and elderly patients with comorbidities [11,12]. In these studies, providers highlight the importance of trust in obtaining accurate adherence reports. However, they express concern that too much inquiry might come off as intrusive or paternalistic [11,12]. Research shows that tracking adherence by self-report can result in adherence overestimation [10]. Thus, accurate tracking of adherence is key for doctors to explore patients' barriers to adhere, help the patient manage side effects, and make changes in the treatment plan when appropriate.

The Digital Health Feedback System (DHFS), created by Proteus Biomedical Inc., can track adherence and share real-time information. The DHFS consists of a tiny sensor made from edible ingredients (similarly found in cashews and fish) that is attached to the pill. Acting like a battery, the stomach fluids activate the sensor once it is ingested. Then, the sensor

sends the pill's intake date and time as well as other physiological information to a disposable patch worn on the skin. The patch sends this information to a smartphone or computer through Bluetooth. The patient can choose with whom to share intake information (e.g., family and/or doctors). The DHFS includes mobile applications that can send reminders to take the medication and notify others (e.g. relatives) so that they may remind the patient. While pilot studies [13–15] support the safety and accuracy of the DHFS, to our knowledge none of has included cancer patients nor measured the DHFS as a comprehensive device for adherence.

The DHFS has the potential to address known barriers. By sending reminders and sharing intake information with caregivers the DHFS can decrease forgetfulness and has the potential to foster social support around adherence. Additionally, real-time monitoring may facilitate early detection of non-adherence and trigger communication about barriers. Further research is necessary to better understand the utility of using the DHFS for tracking and enhancing HT adherence [16]. The current mixed method study examined providers' perceptions of the barriers that breast cancer survivors may encounter adhering to HT. This study also identified providers' challenges in assessing adherence. Finally, it explores providers' reactions to the DHFS and its potential use as a pathway for tracking and enhancing HT adherence.

2. Methods

2.1 Key Informant Interviews

2.1.1 Participants and Procedures.—An oncologist from the research team provided contact information of key informants (e.g., oncologists and nurses). Additional key informants were recruited through snowball sampling. Key informants were eligible if they were healthcare providers who provide services to breast cancer survivors (e.g. oncologists, patient navigators) or researchers with relevant expertise on the intersection between health, communications, and technology. Participants (N=10) were interviewed in person and filled out a brief survey. They received a gift card. The study protocol was approved by Georgetown University's Institutional Review Board.

2.1.2 Measures

Semi-Structured Interview.: The interview initially focused on barriers and facilitators for adherence to hormonal therapy, and challenges assessing medication adherence. Participants subsequently watched two videos about the DHFS (produced by Proteus Biomedical). The first video provided an explanation of how the DHFS works. The second illustrated how the DHFS can be used to enhance communication and adherence (e.g., notifications about a missed dose). In the second part of the interview, participants expressed their perceptions of DHFS, identified potential benefits and challenges to adopting it, and identified patients who could benefit the most from it.

Survey.: Sociodemographic information and years of experience with cancer patients were captured.

2.1.3 Qualitative Analysis.—Interviews were recorded and transcribed. Using the Consensual Qualitative Research framework [17], each interview was independently coded by two coders. Consensus was reached when necessary. The final codes were analyzed using Dedoose qualitative software [18]. See Tables 1 and 2 for codes and exemplary quotes.

2.1.4 Results—Participants included oncologists (50%), nurses (20%) pharmacist (10%), and experts in communication and technology (20%). Most were females (80%) and were 51.60 years old on average ($SD=13.77$). Healthcare providers had a median of eight years of experience working with breast cancer patients ($Med=8.00$; $SD=11.29$).

Perceived Barriers and Facilitators for Adherence: Providers emphasized barriers for adherence and discussed different strategies they use to overcome them (see Table 1 for additional exemplary quotes).

Side Effects: Side effects (e.g., hot flashes) were identified as a common barrier for women taking hormonal therapy, especially when the disease is non-symptomatic as side effects become more salient: “I think the number one reason people stop it (HT) is because of side effects, such as hot flashes, aches in their joints.” Following up with patients and encouraging them to reach out as soon as they start experiencing side effects was deemed to be important.

Access: The cost of medication was also reported as one of the biggest barriers for adherence. Patients might struggle to pay medications if they are not covered by the health insurances or if they involve high co-pay. Solutions included referring patients to social workers, searching for programs that provide free drugs or samples, and finding cheaper pharmacies.

Forgetting: Patients may forget to take their HT medication. This is particularly problematic when there are comorbid conditions. To overcome this, providers recommended using reminders, developing compliance-prompting packaging, dosage simplification, and transitional care protocols.

Knowledge and Beliefs: Patients do not necessarily understand how to take the medication or why they are taking it. Some patients might decide to stop taking the medication because they feel well, and consider there is no need for additional therapy. Several providers acknowledged the importance of educating patients about how medications work, highlighting adherence as necessary to get full benefits. Additionally, some patients may prefer alternative medicine rather than HT. Providers stressed the need to be open-minded and encourage discussions about risks and benefits of alternative medicine with patients. Finally, an expert in medical communication stressed the importance of understanding patients’ experiences with breast cancer, treatment trajectories, and whether they identify as survivors. These factors influence perception of HT and medication intake behavior, “for women taking chemotherapy, who had to feel awful, lose their hair—just poison their body...now to take this tamoxifen, it’s nothing,” meaning that individuals differ on how they perceive HT in terms of side effects compared to their previous experience with chemotherapy. Similarly, tamoxifen could be a reminder of cancer diagnosis. For those who

do not want to have the label of a “sick person” or a “cancer survivor”, it could lead to avoidance and adherence lapses. Further, communicating about cancer as a chronic condition rather than an acute illness could help reframe HT attitudes.

Communication: Several providers reported that their patients concealed important adherence information (e.g., skipped doses), to not disappoint them. When patients disclose medication interruption, they usually wait until the in-person visit, creating time lags in communication. Participants’ suggestions to reduce the delay between discontinuation and disclosure emphasized more frequent contact between visits, but added that they lacked the resources to do so.

“I tend to hear is ‘I stopped that.’ Did you tell your oncologist? ‘I was going to tell him on my next visit.’ That could be three months from now.”

Another challenge in communication was asking the right questions. Strategies to obtain more accurate information included asking more precise questions (e.g., have you been taking the medication – every day/as prescribed), and building trust with patients. Participants also described the role of patient navigators, nurses, and pharmacists as crucial, because some patients are more likely to open up and share their concerns with them rather than the doctors.

“A lot of it is just human social interaction and you realize that getting to a patient on a person level and getting to trust me and understand that I am on their side and I want to hear anything that is going on”

Providers raised concerns that patients may be getting conflicting information about HT from different sources. They stressed the importance of coordinating healthcare teams so that the same message could be conveyed while reinforcing the importance of taking HT from the very beginning.

Perceived Barriers and Facilitators of the DHFS Use: After watching the DHFS videos, key informants discussed potential barriers and facilitators for implementing the DHFS in clinical practice (see Table 2 for additional exemplary quotes).

Accuracy: Although some participants questioned the accuracy of DHFS data, especially when taking multiple medications simultaneously, accuracy was perceived as one of the primary benefits of DHFS use. Tracking adherence with DHFS was considered by most participants an obvious improvement on current practices. Participants also praised the potential of the DHFS to reduce the uncertainty regarding whether patients are actually taking their medication.

“A positive would be data and getting a better grip on compliance. (...) I’m making sure the patient is adhering - assuming that the patient is taking everything inside of that blister, you can have confirmation of that.”

Additionally, providers commented on how the increased accuracy provided by the DHFS could also benefit patients as well.

“From a patient’s standpoint (...) patients get frustrated when the doctors don’t have that information: ‘why don’t you have it?’ So if you were able to get this sort of information, I think that would give the patient a sense of security: ‘my doctor know what’s going on with me.’ I like that.”

Logistics: Some participants noted that frequent and detailed information could be excessive for overworked healthcare providers. Excessive information about daily medication intake could also become a liability concern for providers who do not have time to be constantly checking on their patients.

“Sometimes the more information that we provide for them (doctors), the more work and liability we give them, right? So if they get so much information that becomes actionable but they are overwhelmed, now they would be obligated to do something with this patient, they are in a chain of distribution, a chain of liability.”

However, providers also saw the potential of the DHFS to easily assess adherence in a timely manner if the information was presented in a summarized “compact” way and the ability to facilitate the coordination between different healthcare providers responsible for patients taking HT.

“If it was in a form that was easily digestible—I don’t want to check anybody’s daily recordings, that’s just, I don’t have time for that. But compacted information—I see my patients every four months and I could see which ones that the patient didn’t take, so it’s kind of compact.”

Communication: Key informants commented on the potential positive and negative impact of the DHFS in patient’s communication with relatives and health care providers. Although sharing adherence information can foster support from relatives and other caregivers, it also has the potential of generating arguments around adherence.

In relation to the communication with providers, on one hand, the DHFS could avoid misrepresentations of patients’ adherence and help to open a discussion around adherence challenges: “I think it opens a discussion. I think sometimes patients don’t like to tell you that they are having trouble taking their medicines and they are.” On the other hand, the DHFS could decrease patient-provider communication as providers would take the information directly from reports instead of the patient.

“I think that a lot of these technologies move towards taking the personhood out – so now you could come into the office and, ‘are you on this program?’ ‘Yes, I am,’ (...) I don’t have to say ‘how are you feeling?’ So it could make less communication.”

Patient Barriers: Providers anticipated that patients could have several concerns including access, safety, and privacy concerns. First, DHFS may not be accessible to patients with lower socioeconomic status. Second, patients could be concerned about the safety of ingesting a sensor, especially those who are distrustful of technology: “patients have to be advised and make sure that the chip itself is not going to cause side effects and this is not harmful to their body- that this is not giving radiation”

Third, patients may have privacy concerns and may not feel comfortable being monitored so closely, especially if they already mistrust the medical system.

“Our patient population has the baseline suspicions, African Americans, have for the health care establishment, so introducing this kind of thing may cause anxiety. There has to be a lot of information like “why are we doing this” (...) “we are not trying to spy on you.”

Fourth, patients may struggle with the practicality of wearing the patch daily and the need to change it every week. Lastly, while DHFS may provide better tracking practices, it does not directly address the underlying problem of *why* patients are not taking their medications.

“If somebody is not compliant to a single medicine and we cannot figure out why that is, or if it’s their lifestyle that is not compliant, I think having objective data that has that, might not change that”

Ideal Patient for the DHFS: Patients with serious life-or-death conditions, adolescents, and any patient in a debilitated state were commonly identified as having the most potential for benefitting from the DHFS. Other ideal patients for the DHFS were those who have already demonstrated interest in using health apps. Overall, elderly patients were the most acknowledged and agreed upon ideal patient.

“People who are motivated are overwhelmed by what they need to do by the number of medicines or throw in the fact that they are a little bit older and a little bit more forgetful; I think that’s where people would benefit from this.”

2.2. Provider Surveys

2.2.1. Participants and Procedures.—The second component of this mixed method research involved a survey emailed to two lists of providers. One of the lists was provided by a software company, including 403 breast oncologists across the US. The second list included providers from the MedStar network. After a brief introduction of the study, participants followed a link to complete the consent form and the survey online. Participants received a gift card.

2.2.2. Materials.—The survey was informed by the findings from the interviews and the literature. The survey included multiple-choice and Likert-type response questions about prior experience working with breast cancer survivors and perceptions about patients’ HT adherence. Participants followed a link to the two DHFS videos. They were asked about familiarity with the DHFS, perceived benefits and challenges of using the DHFS, likelihood and degree of confidence in adopting the technology, and type of provider who would be most appropriate to handle adherence information.

2.2.3. Results—Nineteen providers completed the survey (one from the national list and 18 from the MedStar list). Participants were on average 45.79 years old ($SD=10.92$) and most were females (82.4%). Providers had worked with breast cancer survivors for a median of five years ($Med= 5.00$; $SD=8.69$). More than a third (36.8%) worked as medical oncologists. More than half of the providers (57.9%) estimated that between 0–20% of their

patients did not adhere to HT and 47.4 % of providers estimated that between 21–40% of patients discontinue HT before five years. Providers assessed HT discontinuation often ($M=5.79$, $SD=1.69$, range 1–7). More than half (63.2%) reported that medical oncologists were the most appropriate provider to handle adherence information. Most providers assessed adherence during their patients' regular in person check-ups (84.2%) and via patient self-report (78.9%). Assessing discontinuation was perceived to be moderately challenging ($M=3.74$, $SD=2.16$ -range 1–7). The most salient challenges providers reported to assessing adherence were patients' delay in informing about discontinuation (78.9%) and over-reporting adherence (57.9%). Most providers (47.4%) indicated that the time lag between discontinuation and disclosure of discontinuation was between one and three months. Perceived barriers to adherence included side effects of HT (84.2%), medication cost (36.8%), and forgetting to take their medication (31.6%). In respect to utilizing the DHFS, doctors reported the ability to track adherence better (94.7%) and having reminders about taking the medication (68.4%) as major benefits. A major barrier was patients' willingness to ingest a sensor (84.2%) (see Table 3).

3. Discussion

This study described the barriers and facilitators of patient adherence to HT as reported by providers, along with the challenges for assessing adherence. It also gathered providers' perspectives about DHFS as tool to enhance tracking and adherence. Findings from the interviews and the survey were complementary. The initial qualitative findings informed the development of the survey and provided details about provider perceptions and experiences. The survey allowed us to quantify responses. Providers identified several barriers for patients to adhere to HT including side effects, access, forgetfulness, knowledge and beliefs, and communication. Providers were aware that a significant percentage of patients do not adhere to medication but added that it is a challenge to accurately assess patients' adherence. Therefore, one of the most perceived potential benefits of using the DHFS was obtaining timely and accurate adherence information, as well as its potential capacity to address adherence through reminders and facilitated communication. The major anticipated barriers to DHFS use were concerns about safety, privacy, and systemic challenges for its implementation.

The most commonly endorsed barrier was side effects. This finding is consistent with the literature [19–24]. However, there is evidence that doctors' and patients' assessment might not always align. One study that compared doctors' and patients' perceptions about prevalence and distress caused by HT side effects found that doctors tend to underestimate the degree of distress that some of the side effects can cause patients [25]. Surprisingly, a recent meta-analysis found mixed evidence about the association between side effects and HT adherence. Among women reporting similar side-effects, some were adherent whereas others were non-adherent, which suggests that other factors need to be considered. For instance, results identified other psychosocial correlates of HT adherence including doctor-patient communication, social support, self-efficacy, and medication beliefs [6]. In this study, providers noted communication and medication beliefs as important aspects of HT adherence, but underreported social support and self-efficacy in the open-ended interviews. The absence of these types of responses indicates the need of increasing providers'

awareness about the importance of addressing other potentially modifiable psychosocial factors.

Doctor-patient communication was one of the main themes that emerged during the interviews. Providers highlighted the importance of building trust, checking how patients manage side effects, and understanding patient's knowledge and beliefs about HT. Several studies have documented the importance of patient-centered communication in adherence. Patients who feel more confident interacting with doctors, who have more frequent communication about HT, who receive information about side effects in advance, and who have the opportunity to ask questions and discuss barriers at the time of diagnosis, are more likely to adhere to HT [26–30]. Contrary to this ideal, a linguistic study that used direct observation of medical encounters found that doctors tend to provide general information about HT, rather than eliciting patients' perspectives on potential adherence barriers [31]. In another study only 44% of breast cancer survivors reported that doctors reinforced the importance of taking HT at every visit and a third stated that this discussion only happened once [32]. Thus, even though doctor-patient communication is recognized as a determining factor for adherence, it is often challenging to implement.

Research shows that tailoring physician-patient communication to individual preferences on information and involvement in decision-making can impact health outcomes [33]. Similar efforts should be considered in respect to adherence. Developing interventions that target doctors and doctor-patient communication is an essential step to enhance adherence. A recent systematic literature review [34] found five tested interventions to enhance hormonal therapy medications. Of the existing studies, all interventions targeted patients and predominantly focused on educational approaches. All were unsuccessful. Combined with recent research on increased medical costs due to poor adherence, the expansion of adherence based research is warranted [35]. Future efforts to develop educational interventions should inform doctors about patients' perceptions and experiences around HT (e.g., distress related to side effects, beliefs about HT, and concerns about identity) and provide skills to enhance patient-centered communication concerning HT.

Interventions are also needed to improve the accuracy and timeliness in the assessment of adherence. Providers typically assess adherence during in-person visits through patient self-report. Despite efforts in building trust and encouraging patients to reach out for help, most providers were still concerned about over-reporting of adherence and delays in disclosing discontinuation. Providers reported not having available tracking resources that could improve timely communication and were unsure about the best strategy to ask about adherence. Reducing the amount of time that passes since the patient discontinues medication and their disclosure to the doctor is a crucial step to address barriers in a timely manner. In turn, promptly addressing barriers may reduce discontinuation rates, as longer interruptions on medication intake are more likely to lead to discontinuation [5]. Moreover, low adherence and discontinuation of HT have been associated with loss of discounted life years and increased medical costs over time [2,35]. A recent study [36] showed that women who experienced a quick decline and those who had a moderate decline in HT use over a year had a 40% and 25% increased risk of death respectively. Thus, efforts to reduce communication delays have the potential to impact mortality rates. Emerging interventions

to tackle these problems are promising. For instance, a pilot that utilized bidirectional text messages was successful in assessing daily adherence, side effects, and connecting women who had low adherence or severe side effects to the provider team [37]. While this pilot is promising, it relied on self-reported adherence, which is not always accurate [10].

The DHFS can improve the accuracy of intake tracking as well as facilitating prompt detection of interruptions in medication if the patient chooses to share their data with their healthcare providers. The DHFS can also address forgetfulness and engage relatives for support. Future studies should examine the feasibility of incorporating the DHFS in real clinical settings and determine who would benefit the most. Forgetting has been documented as an adherence barrier in a variety of other medical contexts [38–40]. The current study suggests that patients who self-report as forgetful may form an initial target for future DHFS adherence research. Both quantitative and communication factors would be available, such as weekly number of missed doses or length of time before the oncologist contacts the patient. The results of this study also suggest that the elderly could potentially have greater benefits from DHFS use. The social aspect of the technology, evident in the ability to share adherence data with others beyond the healthcare team, provides a relevant opportunity for healthcare providers to begin capturing more information about what we describe as Collaborative Patient Care Networks (CPCN). This group would be interested and engaged in health outcomes for the patient, provide some concrete assistance in the medical care process, and could potentially increase the provision of support when equipped with additional information or guidance. Documenting membership in the CPCN for specific patients will be possible with DHFS data. With the elderly in particular, DHFS adherence data may provide a motivating opportunity for non-local adult children to check in with elderly parents via phone, text or email. Should DHFS have the secondary effect of building engagement of CPCN members in providing social support, the cost increase associated with the technology may be mitigated. Research on whether the technology as used with HT improves adherence to a full regimen of medication could also support a cost-benefit analysis and motivate adoption of the technology by Medicaid.

Finally, data from the existing study may support future research around interprofessional communication. Interrater reliability testing could be done when providing digital data to an oncologist and pharmacist from a particular healthcare team to explore what level of non-adherence warrants follow up calling from the medical care team. This type of physician / pharmacist exploratory study could build on existing research [41] that also focuses on the capacity of the pharmacy team to follow up with non-adherent patients. The current research found the oncology team member was cited as the one who should follow up with patients. However, relieving the task burden by engaging the pharmacy or primary care physician's team may be attractive to oncologists. Additionally, providers highlighted problems when patients receive conflicting messages about HT from different providers. This is consistent with recent findings on reduction in patient stress when concurrent messaging is given by both physician and pharmacist [42], as well as with broader calls for interprofessional collaboration to improve teamwork and care coordination [43]. More research is needed in this area to clarify the communication strategies deemed feasible and attractive for implementation.

The current study had certain limitations. Results are based on a small convenience sample of mostly female providers. Thus, they may not be generalizable. We did not have information about non-respondents so we could not examine potential participant bias. Despite the limitations, findings from this study contribute to the scarce literature on providers' perspectives about HT adherence. This is also one of the first studies to examine perceptions about the DHFS. The triangulation of qualitative and quantitative methods provided insights about potential intervention targets that have been understudied.

3.1. Conclusions

This mixed methods study examined providers' perspectives on HT medication adherence in breast cancer survivors and explored the potential of a new communication technology to improve adherence. While providers highlighted the importance of fostering trust and open communication around adherence, they felt they lacked resources and methods to accurately assess patient's adherence. Providers saw promise in the capacity of the DHFS to provide more precise and timely adherence information and the potential to enhance adherence through reminders. However, they also anticipated barriers for adopting this technology including patients' potential safety and privacy concerns and system level barriers such as doctors' liability.

To our knowledge there are no existing interventions to enhance HT medication adherence that target providers. Providers would benefit from interventions to increase awareness about patients' beliefs about HT and patients' adherence barriers. Interventions should also include information about the impact of other modifiable psychosocial factors such as self-efficacy and social support that were less commonly identified. Interventions to enhance communication skills around HT are warranted. Future studies should also examine the feasibility of adopting the DHFS in clinical settings and assess the impact of this communication technology in doctor-patient communication and in cancer patients' adherence.

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References

- [1]. Davies C, Pan H, Godwin J, Gray R, Arriagada R, Raina V, Abraham M, Medeiros Alencar VH, Badran A, Bonfill X, Bradbury J, Clarke M, Collins R, Davis SR, Delmestri A, Forbes JF, Haddad P, Hou MF, Inbar M, Khaled H, Kielanowska J, Kwan WH, Mathew BS, Mittra I, Muller B, Nicolucci A, Peralta O, Pernas F, Petruzella L, Pienkowski T, Radhika R, Rajan B, Rubach MT, Tort S, Urrutia G, Valentini M, Wang Y, Peto R, Adjuvant Tamoxifen: Longer Against Shorter (ATLAS) Collaborative Group. Long-term effects of continuing adjuvant tamoxifen to 10 years versus stopping at 5 years after diagnosis of oestrogen receptor-positive breast cancer: ATLAS, a randomised trial. *Lancet* 2013;381:805–816. [PubMed: 23219286]

- [2]. Hershman DL, Shao T, Kushi LH, Buono D, Tsai WY, Fehrenbacher L, Kwan M, Gomez SL, Neugut AI. Early discontinuation and non-adherence to adjuvant hormonal therapy are associated with increased mortality in women with breast cancer. *Breast Cancer Res.Treat.* 2011;126:529–537. [PubMed: 20803066]
- [3]. Early Breast Cancer Trialists' Collaborative Group, (EBCTCG). Effects of chemotherapy and hormonal therapy for early breast cancer on recurrence and 15-year survival: an overview of the randomised trials. *Lancet* 2005;365:1687–1717. [PubMed: 15894097]
- [4]. Huiart L, Ferdynus C, Giorgi R. A meta-regression analysis of the available data on adherence to adjuvant hormonal therapy in breast cancer: summarizing the data for clinicians. *Breast Cancer Res.Treat.* 2013;138:325–328. [PubMed: 23400580]
- [5]. Nekhlyudov L, Li L, Ross-Degnan D, Wagner A. Five-year patterns of adjuvant hormonal therapy use, persistence, and adherence among insured women with early-stage breast cancer. *Breast Cancer Res Treat* 2011;130:681–689. [PubMed: 21842245]
- [6]. Moon Z, Moss-Morris R, Hunter MS, Carlisle S, Hughes LD. Barriers and facilitators of adjuvant hormone therapy adherence and persistence in women with breast cancer: a systematic review. *Patient Preference and Adherence* 2017;11:305–322. [PubMed: 28260867]
- [7]. Ong LML, de Haes JCJM, Hoos AM, Lammes FB. Doctor-patient communication: A review of the literature. *Social Science & Medicine* 1995;40:903–918. [PubMed: 7792630]
- [8]. Kelly B, Haskard, Zolnieriek M, Robin DiMatteo. Physician Communication and Patient Adherence to Treatment: A Meta-Analysis. *Medical Care* 2009;47:826–834. [PubMed: 19584762]
- [9]. Wassermann J, Rosenberg SM. Treatment Decisions and Adherence to Adjuvant Endocrine Therapy in Breast Cancer. *Current Breast Cancer Reports* 2017;9:100–110.
- [10]. Farmer KC. Methods for measuring and monitoring medication regimen adherence in clinical trials and clinical practice. *Clinical Therapeutics* 1999;21:1074–1090. [PubMed: 10440628]
- [11]. Rivero-Mendez M, Dawson-Rose CS, Solis-Baez SS. A qualitative study of providers' perception of adherence of women living with HIV/AIDS in Puerto Rico. *The Qualitative Report* 2010;15:232. [PubMed: 21243076]
- [12]. Tarn DM, Mattimore TJ, Bell DS, Kravitz RL, Wenger NS. Provider Views About Responsibility for Medication Adherence and Content of Physician-Older Patient Discussions. *Journal of the American Geriatrics Society* 2012;60:1019–1026. [PubMed: 22646818]
- [13]. Eisenberger U, Wuthrich RP, Bock A, Ambuhl P, Steiger J, Intondi A, Kuranoff S, Maier T, Green D, DiCarlo L, Feutren G, De Geest S. Medication adherence assessment: high accuracy of the new Ingestible Sensor System in kidney transplants. *Transplantation* 2013;96:245–250. [PubMed: 23823651]
- [14]. Belknap R, Weis S, Brookens A, Au-Yeung KY, Moon G, DiCarlo L, Reves R. Feasibility of an ingestible sensor-based system for monitoring adherence to tuberculosis therapy. *PLoS One* 2013;8:e53373. [PubMed: 23308203]
- [15]. Kane JM, Perlis RH, DiCarlo LA, Au-Yeung K, Duong J, Petrides G. First experience with a wireless system incorporating physiologic assessments and direct confirmation of digital tablet ingestions in ambulatory patients with schizophrenia or bipolar disorder. *J.Clin.Psychiatry* 2013;74:533.
- [16]. Hurtado-de-Mendoza* A, Cabling* M, Sheppard VB. Rethinking agency and medical adherence technology: Applying Actor Network Theory to the case study of Digital Pills. *Nursing Inquiry* 2015;22:326–335. [PubMed: 25924851]
- [17]. Hill CE, Knox S, Thompson BJ, Williams EN, Hess SA, Ladany N. Consensual Qualitative Research. *Journal of Counseling Psychology* 2005;52:196–205.
- [18]. SocioCultural Research Consultants L. Dedoose Version 7.0.23, web application for managing, analyzing, and presenting qualitative and mixed method research data; 2016.
- [19]. Ayres LR, Baldoni ADO, De Sa Borges AP, Pereira LRL. Adherence and discontinuation of oral hormonal therapy in patients with hormone receptor positive breast cancer. *Int.J.Clin.Pharm.* 2014;36:45–54. [PubMed: 23934310]
- [20]. Cella D, Fallowfield LJ. Recognition and management of treatment-related side effects for breast cancer patients receiving adjuvant endocrine therapy. *Breast Cancer Res.Treat.* 2008;107:167–180. [PubMed: 17876703]

- [21]. Lash T, Fox M, Westrup J, Fink A, Silliman R. Adherence to tamoxifen over the five-year course. *Breast Cancer Res Treat* 2006;99:215–220. [PubMed: 16541307]
- [22]. Atkins L, Fallowfield L. Intentional and non-intentional non-adherence to medication amongst breast cancer patients. *European Journal of Cancer* 2006;42:2271–2276. [PubMed: 16644208]
- [23]. Grunfeld EA, Hunter MS, Sikka P, Mittal S. Adherence beliefs among breast cancer patients taking tamoxifen. *Patient Educ.Couns.* 2005;59:97–102. [PubMed: 16198223]
- [24]. Simon R, Latreille J, Matte C, Desjardins P, Bergeron E. Adherence to adjuvant endocrine therapy in estrogen receptor–positive breast cancer patients with regular follow-up. *Canadian Journal of Surgery* 2014;57:26.
- [25]. Leonard R, Lee L, Harrison ME. Impact of side-effects associated with endocrine treatment for advanced breast cancer: clinicians' and patients' perceptions. *Breast* 5, 259e269 1996.
- [26]. Jacob Arriola KR, Mason TA, Bannon KA, Holmes C, Powell CL, Horne K, O'Regan R. Modifiable risk factors for adherence to adjuvant endocrine therapy among breast cancer patients. *Patient education and counseling* 2014;95:98–103. [PubMed: 24492157]
- [27]. Liu Y, Malin JL, Diamant AL, Thind A, Maly RC. Adherence to adjuvant hormone therapy in low-income women with breast cancer: The role of provider-patient communication. *Breast Cancer Res.Treat.* 2013;137:829–836. [PubMed: 23263740]
- [28]. Neugut AI, Hillyer GC, Kushi LH, Lamerato L, Leoce N, Nathanson SD, Ambrosone CB, Bovbjerg DH, Mandelblatt JS, Magai C, Tsai WY, Jacobson JS, Hershman DL. Noninitiation of adjuvant chemotherapy in women with localized breast cancer: the breast cancer quality of care study (BQUAL). *Breast cancer research and treatment* 2012;134:419–428. [PubMed: 22527111]
- [29]. Kahn Katherine L., Schneider Eric C., Malin Jennifer L., Adams John L., Epstein Arnold M.. Patient Centered Experiences in Breast Cancer: Predicting Long-Term Adherence to Tamoxifen Use. *Medical Care* 2007;45:431–439. [PubMed: 17446829]
- [30]. Cluze C, Rey D, Huiart L, BenDiane MK, Bouhnik AD, Berenger C, Carrieri MP, Giorgi R. Adjuvant endocrine therapy with tamoxifen in young women with breast cancer: determinants of interruptions vary over time. *Ann.Oncol.* 2012;23:882–890. [PubMed: 21788360]
- [31]. Davidson B, Vogel V, Wickerham L. Oncologist-patient discussion of adjuvant hormonal therapy in breast cancer: results of a linguistic study focusing on adherence and persistence to therapy. *The journal of supportive oncology* 2007;5:139. [PubMed: 17410813]
- [32]. Kirk MC, Hudis CA. Insight into Barriers Against Optimal Adherence to Oral Hormonal Therapy in Women with Breast Cancer. *Clinical Breast Cancer* 2008;8:155–161. [PubMed: 18621612]
- [33]. Leighl Natasha, Gattellari Melina, Butow Phyllis, Brown Richard, Tattersall Martin H.N.. Discussing Adjuvant Cancer Therapy. *Journal of Clinical Oncology* 2001;19:1768–1778. [PubMed: 11251008]
- [34]. Hurtado-de-Mendoza A, Cabling ML, Lobo T, Dash C, Sheppard VB. Behavioral Interventions to Enhance Adherence to Hormone Therapy in Breast Cancer Survivors: A Systematic Literature Review. *Clinical breast cancer* 2016;16:247–255. [PubMed: 27133733]
- [35]. McCowan C, Wang S, Thompson AM, Makubate B, Petrie DJ. The value of high adherence to tamoxifen in women with breast cancer: a community-based cohort study. *Br. J. Cancer* 2013;109:1172–1180. [PubMed: 23949153]
- [36]. Winn AN, Dusetzina SB. The association between trajectories of endocrine therapy adherence and mortality among women with breast cancer. *Pharmacoepidemiology and Drug Safety* 2016;25:953–959. [PubMed: 27125337]
- [37]. Mougalian SS, Epstein LN, Jhaveri AP, Han G, Abu-Khalaf M, Hofstatter EW, DiGiovanna MP, Silber AL, Adelson K, Puztai L. Bidirectional Text Messaging to Monitor Endocrine Therapy Adherence and Patient-Reported Outcomes in Breast Cancer. *JCO Clinical Cancer Informatics* 2017;1:1–10.
- [38]. Varnell CD, Rich KL, Nichols M, Dahale D, Goebel JW, Pai ALH, Hooper DK, Modi AC. Assessing barriers to adherence in routine clinical care for pediatric kidney transplant patients. *Pediatr Transplant* 2017;21.
- [39]. Mehta P, Steinberg EA, Kelly SL, Buchanan C, Rawlinson AR. Medication adherence among adolescent solid-organ transplant recipients: A survey of healthcare providers. *Pediatr Transplant* 2017;21.

- [40]. Ramsey RR, Zhang N, Modi AC. The Stability and Influence of Barriers to Medication Adherence on Seizure Outcomes and Adherence in Children With Epilepsy Over 2 Years. *J Pediatr Psychol* 2017.
- [41]. Jordan TA, Hennenfent JA, Lewin JJ, Nesbit TW, Weber R, DP Elevating pharmacists' scope of practice through a health-system clinical privileging process. *Am J Health Syst Pharm* 2016;73:1395–1405. [PubMed: 27413142]
- [42]. Takaki H, Abe T, Hagihara A. Physicians' and pharmacists' information provision and patients' psychological distress. *J Interprof Care* 2017;31:575–582. [PubMed: 28753052]
- [43]. The Canadian Interprofessional Health Collaborative, (CIHC). A National Interprofessional Competency Framework 2010.

Table 1:

Perceived Barriers and Facilitators for Adherence

	Direct Quotes from Interviews
	Side Effects
Barriers	<ul style="list-style-type: none"> - "Side effects, which often times can be more annoying than the disease (...). "Adherence is a lot worse with non-symptomatic diseases. Research shows that things like high blood pressure, unless you are getting headaches or feeling faint or something, you don't notice the symptoms, but you do notice the fact that you have to go to the bathroom a lot of times." - "What I see more often is because side effects. Yes, on the Aromatase Inhibitors, it's very often, very frequent that you see patients stopping because of joint pain."
Facilitators	- "I tell my patients, whenever I start them on therapy, that they need to be a squeaky wheel and let me know how they're tolerating things because there are very few side effects that we can't manage or help manage to allow them to stay on therapy."
	Access
Barriers	- "The cost of the medication would cause some of my patients to stop."
Facilitators	- "I had to really change my questions and remember to ask "can you afford the medications? Because from a physicians' standpoint, we really never talk about costs to the patient."
	Forgetting
Barriers	<ul style="list-style-type: none"> - "People first of all miss doses because they forget." - "When we are dealing with multiple conditions, which is very typical now- (...). You know it's not unlikely for patients to be on 13 different medications. So juggling all these medications with your life is a real challenge."
Facilitators	- "So if we are able to somehow simplify that whole thing, (...) could we group some (medications) together, could we use some replacements that potentially would require the patient to take the medication less frequently than three times a day or four times a day; simplifying that."
	Knowledge and Beliefs
Barriers	<ul style="list-style-type: none"> - "People have cultural beliefs that we have to understand (...). Western medicine is not accepted in every culture despite its scientific base." - "Another part is how you feel: "There is nothing wrong with me, I feel fine, why do I need to take it" And that is a health literacy issue, it is a knowledge issue."
Facilitators	<ul style="list-style-type: none"> - "Educating the patient well and thoroughly in a level they can understand and makes sense to them, then the adherence is up there." - "I counsel them; I say that the 'efficacy of this drug is impaired if you don't take it every day and we don't know what's going to happen if you don't take it every day."
	Communication
Barriers	<ul style="list-style-type: none"> - "I'm wondering now whether I'm asking correctly. In the speed of the moment we ask "are you taking your medication? "Oh yeah, yeah, fine" (...) Probably just more specific questions I like to say I add but I don't add all the time." - "Tamoxifen is at the very end and it did not get reinforced at the beginning! That is another thing I have noticed, is that late in the game people would say "oh, no one said much about that."
Facilitators	<ul style="list-style-type: none"> - "I ask the patient who takes endocrine therapy every time "do you take the pill every day? I learned it the hard way. I used to ask "do you take your medicine" "Yes." Then, one patient asked a good question: Do you take it every day?" "No, I take it once a week" So now I ask "Do you take the pill every day." - "Now I think I'm a big fan of patients advocating for themselves, patients should speak up, let their providers know if they are having side effects or if something is or isn't working for them, or understanding what's going on better."

Table 2:

Perceived Barriers and Facilitators of using the DHFS

	Direct Quotes from Interviews
	Accuracy
Barriers	- “So how accurate is this stuff and data and are we using this data to make judgments and clinical decisions? (...) I would expect for those to be resistance points as we try to incorporate stuff like this.”
Facilitators	- “So some people have to go through this great big bag and then they find that they have refills for two (...) this removes the mystery out of taking your medicine. So that’s fascinating.” - “You know I think that’s as precise as you can be. You can’t cheat the system.”
	Logistics
Barriers	- “And we have to be realistic about this. Doctors want to automate things and help the population but they are also overwhelmed with the things that come to them.”
Facilitators	- “We could get more information quickly...as opposed to waiting three months when they bring in a whole thing and say, ‘oh well, I really miss the whole week,’ (...) I think the doctors would be receptive to it once they got used to it.” - “Even nurses—if this could be part of the chart—because they are always kind of the first line of defense. They always answer the phone and they always ask the patients, ‘are you taking the medication?’ and the first thing we ask the patient if they are having any problems is ‘are you taking your medications? Because if you are not taking it properly, that may be the reason why you are having these problems.’ So I think it would be good to be part of the chart.”
	Communication
Barriers	- “It may be ‘well I don’t want my kids knowing about this stuff.’ So for some people, it might work great and for other it may create an argument with their children or their caregivers.”
Facilitators	- “Now you are taking away the impression management of the doctor. So all along you were like ‘oh you know I work out.’ Everyone says they workout! So now, you know, ‘you really don’t. You’ve been saying that for the past five years that you are a walker but you don’t really walk. Like five minutes a day? That’s not walking.’ So all the impression management is taken away. Maybe that’s good.”
	Patient Barriers
	- “The patient may feel that it might be invading their privacy. Some patients want to be able to not tell you if they have taken it.” - “It sounds like we are dealing with more of a privileged group who can afford and want to pay, you know white glove, VIP, you know people who are willing to go for this.”

Table 3.**Providers' Perceptions of Medication Adherence and DHFS**

Provider Demographic Characteristics (n=19)	
Age – <i>M (SD)</i>	45.79(10.93)
Gender	
Female	16 (84.2)
Male	3 (15.8)
Experience working with BC survivors	
Years of working with BC survivors – <i>Md (SD)</i>	5 (8.69)
Provider Roles-N (%)	
Medical oncologist	7(36.8)
Nurse	7(36.8)
Surgeon	2(10.5)
Social worker	2(10.5)
Clinical Research Coordinator	1(5.3)
Estimated percentage of HT discontinuation -N (%)	
0–20%	8(42.1)
21–40%	9(47.4)
41–60%	1(5.3)
61–80%	0(0)
81–100%	1(5.3)
Estimated percentage of HT non-adherence - N (%)	
0–20%	11 (57.9)
21–40%	5(26.3)
41–60%	2(10.5)
61–80%	1(5.3)
81–100%	0(0)
Challenges assessing adherence - N (%)	
Patient not communicating immediately about discontinuation	15(78.9)
Patient over-reporting adherence	11(57.9)
Unsure how to assess adherence	5(26.3)
Lack of time	4(21.1)
High patient work load	3(15.8)
Other (does not come up as part of the discussion with me)	1(5.3)
Adherence Methods - N (%)	
Regular in person check ups	16(84.2)
Patient self-report	15(78.9)
Text messages/phone calls	1(5.3)
Other (refills from pharmacies)	1(5.3)
Surveys	0(0)
Time lag between discontinuation and reporting of discontinuation - N (%)	
Less than a month	4(21.1)

Provider Demographic Characteristics (n=19)	
1–3 months	9(47.4)
3–6 months	5(26.3)
6–12 months	1(5.3)
Patients' adherence barriers - N (%)	
Side-effects	16(84.2)
Medication cost	7(36.8)
Forgetting	6(31.6)
Communication with providers	3(15.8)
Lack social support	2(10.5)
Fertility concerns	1(5.3)
Other (patients feel good and do not see the need)	1(5.3)
Digital Health Feedback System (DHFS) - $M(SD)$, range 1–7	
DHFS as useful in monitoring adherence	4.95(1.9)
DHFS can help BC survivors adhere to HT	4.58(1.64)
Confident recommend/prescribe DHFS	4.26(1.82)
Likelihood of implementing/recommending DHFS	4.11(1.88)
Likelihood of other providers recommending DHFS	3.95(1.58)
Benefits to use DHFS for providers - N (%)	
Ability to track adherence better	18(94.7)
Patient having reminders	13(68.4)
Real time access to patient data	11(57.9)
Better connection to patient-social support	7(36.8)
Real time and automatic data storage	7(36.8)
Awareness of biometrics	2(10.5)
Other (real time)	1(5.3)
Barriers to adopt DHFS - N (%)	
Patients unwilling ingest a sensor	16(84.2)
Patients privacy concerns	15(78.9)
Providers overwhelmed with information flow	8(41.2)
Other (no smart phone, adhesive allergies)	2(10.5)
Provider most appropriate to handle adherence information - N (%)	
Medical oncologist	12(63.2)
Nurse	5(26.3)
PCP	1(5.3)
Other (depends on how much time is addressed/nurse navigator)	2(10.5)
Surgeon	0(0)
Social worker	0(0)
Interested in learning more about opportunities to learn the potential of DHFS to improve adherence - N (%)	10(52.6)