**Leveraging Personal Values in an Endocrine Therapy Adherence-Promoting Trial for Breast Cancer Survivors: A Mixed-Methods Investigation**

**Abstract**

**Background:** Improving medication adherence represents one of the greatest behavioral challenges in medicine. Personal values are an under-examined source of motivation for adhering to medication. This secondary analysis leverages a mixed-method approach to understanding a novel, online, values-based intervention (‘REACH’) for promoting endocrine therapy (ET) adherence among breast cancer survivors, using data from a randomized trial.

**Methods:**Breast cancer survivors with challenges taking ET (*n*=88) were randomized 1:1 to ET Education+Values (REACH) or Education-only online interventions. This report focuses on the three values strategies used in REACH to promote ET adherence: affirming health-related values, using values-based perspective-taking to motivate adherence, and creating a personalized cue-to-action values sticker for participants’ ET pillbox. Immediate responses to these values strategies were analyzed using Linguistic Inquiry and Word Count (LIWC) and in both conditions, using repeated assessment of positive and negative affective states. Long-term responses to these strategies were evaluated using structured study exit interviews. Affective responses to REACH were used to predict objective ET adherence.

**Results:**Compared to Education, REACH led to less tense and sad. and more loving states in the immediate term. Convergently, during REACH values exercises, LIWC identified greater use of positive emotion words than negative emotion words. Thematic coding of exit interviews identified generally positive responses to values content in the longer-term with a small minority of negative responses.

**Conclusions**: Distinct approaches to linking domain-relevant values directly to ET adherence were associated with generally positive affective responses, informing theory and practice.

**Key words:** cancer; values; acceptance and commitment therapy; endocrine therapy; adherence

**Leveraging Values to Promote Adherence to Endocrine Therapy among Breast Cancer Survivors: A Mixed-Methods Investigation**

Promoting patient adherence to a prescribed medication regimen is one of the greatest behavioral challenges in medicine. Across medication type, only about half of patients follow their healthcare provider’s prescription in terms of the amount, frequency, and duration of medication (Brown & Bussell, 2011; Herk-Sukel et al., 2010). Two Cochrane reviews (Haynes et al., 2007; Nieuwlaat et al., 2014) identify an urgent need for innovation in interventions to promote medication adherence. The current study focuses on an innovative values-based intervention approach to promoting medication adherence among breast cancer survivors taking daily endocrine therapy (ET), also known as anti-hormonal or anti-estrogen medication. ET represents the most effective method of preventing recurrence of the most common form of breast cancer (estrogen receptor-positive; e.g., Early Breast Cancer Trialists' Collaborative Group, 2005), cutting recurrence rates by 40-50% (e.g., Early Breast Cancer Trialists' Collaborative Group, 1998) if taken once daily for the recommended 5 to 10 years after completing primary oncologic treatment (e.g., Burstein et al., 2010; Cardoso et al., 2019). However, only 50% to 60% of breast cancer survivors adhere to the recommended dose, duration, and frequency over that period (Hagen et al., 2019; Herk-Sukel et al., 2010; Murphy et al., 2012). The values intervention described herein, titled “REACH”, provides a novel, low-touch, remotely-delivered, individually tailored, brief intervention for promoting ET adherence among breast cancer survivors that aims to enhance motivation to take ET by connecting patients to their personal sources of value and meaning for taking the medication. The current study leverages a multi-method approach to elucidate women’s immediate and long-term experience of this values-based intervention, toward deepening the understanding of using values for ET adherence specifically and health promotion generally.

**Personal Values**

Affirming values (i.e., who and what are most important to a person) facilitates greater openness to health-promotion information (e.g., Epton & Harris, 2008) and reduces a sense of threat (Steele, 1988), and thus could enhance cancer survivors’ receptivity to information about the importance of ET adherence, and enhance adherence. Interventions that affirm personal values have successfully promoted behavior change in diverse areas outside of ET adherence (e.g., Chase et al., 2013). According to self-affirmation theory (Sherman & Cohen, 2006; Steele, 1988), values should be affirmed in domains that are distinct from the behavior of interest, as affirming values in relevant domains risks causing distress and avoidance (Blanton et al., 1997). Thus, from a self-affirmation theory perspective, in the context of medication adherence, individuals should be asked to affirm values *outside of* health. However, other values-based behavior change studies have drawn on Acceptance and Commitment Therapy (ACT; Hayes et al., 1999, 2012), a widely studied intervention that leverages freely-chosen personal values to motivate behavior change in personally meaningful directions. For example, an ACT online values intervention (plus goal-setting), but not goal-setting alone, improved university students’ grade point average (Chase et al., 2013). Among cancer survivors, an ACT telehealth intervention resulted in colorectal cancer survivors exercising more, losing more weight, and eating more vegetables over a 6 to 12 month period, relative to usual care (Hawkes et al., 2013). Thus, ACT values interventions have shown promise for supporting sustained behavior change.

Values also address known risk factors for ET non-adherence that are potentially modifiable. Our previous work demonstrated that breast cancer survivors with more negative affective associations and fewer positive affective associations with ET were at risk for poorer day-to-day adherence and quitting ET (Stanton et al., 2014). Convergently, a systematic review (Lin et al., 2017) found that among breast cancer survivors, one of the most consistent motivators for adherence to oral anti-cancer medications (including ET) was positive views and beliefs about the medication. By helping women associate the reasons for taking ET with their core values, the current approach aims to transform ET from an aversive medication predominantly associated with side effects and cancer to a more positively regarded medication linked with the capacity to live a longer life and fulfill one’s values (e.g., to be a loving parent, to do meaningful work). Personal values represent sustained, as opposed to transitory, sources of positive reinforcement (Hayes et al., 1999, 2012); thus, they offer the potential to support the sustained behavior change needed to adhere to ET for the recommended 5 to 10 years. That stated, self-affirmation theory posits that affirming domain-congruent values (i.e., values that are directly relevant in the domain of interest) and acknowledging direct links between values and behavior can cause feelings of distress and guilt because of resulting cognitive dissonance (Blanton et al., 1997; Sherman & Cohen, 2006), which in turn may promote avoidance and reduce health behavior change (e.g., Bright & Stanton, 2018). In contrast, ACT draws direct connections between values and behaviors of interest, theorizing that such direct links transform the motivation and experience of engaging in target behaviors. Thus, whether directly linking personal values to behavior in the context of ET adherence causes immediate or long-term distress (or not) remains an important unanswered question that the current study aims to address.

**The REACH Values-based Intervention**

The REACH intervention advances this prior values-based medication adherence work (Ogedegbe et al., 2012) in content, delivery, and assessment. First, in terms of content, REACH uses three distinct sets of values exercises to directly link personal values directly with ET adherence, including innovatively having participants design a personal values sticker to attach to their ET pillbox. The sticker *visually links* their values to their medication to create a personalized cue-to-action for ET adherence that aims to generate positive/meaningful associations with ET, thus addressing a core risk factor for ET non-adherence (Stanton et al., 2014). Second, in terms of delivery, REACH is brief and delivered entirely online and by post mail (for sticker delivery); it does not include provider or clinic contact. This approach reflects prior research suggesting that online/digital interventions are promising for medication adherence because they allow for individual tailoring while remaining scalable (Konstantinou et al., 2020). Third, in terms of assessment, the online REACH session includes repeated momentary assessment of positive and negative state affect to evaluate the differential effects of REACH’s three distinct values-focused strategies. Examining the state momentary affect measures also allows us to determine whether explicitly linking values to ET adherence increases negative affect, a form of psychological distress, as self-affirmation theory would predict (Blanton et al., 1997; Sherman & Cohen, 2006) among women struggling to take ET.

REACH also includes an education component that addresses two common reasons for ET nonadherence—experiencing ET-related side effects (Murphy et al., 2012) and not perceiving a need for ET (Stanton et al., 2014). Affective responses to REACH’s Values+Education content will thus be compared to a control intervention comprised of Education only.

**Study Aims**

This secondary analysis uses mixed methods to assess breast cancer survivors’ responses to the values-based exercises for promoting ET adherence that were completed during the intervention phase of the broader randomized trial. First, affective and written responses to the different values exercises in REACH were evaluated to elucidate momentary responses. Assessing momentary affective responses facilitated comparing between the three distinct values exercises in REACH and evaluating whether directly linking ET adherence with values (among breast cancer survivors who report difficulty taking ET) led to increases in negative affect and decreases in positive affect relative to baseline and relative to the Education control condition, which would be consistent with self-affirmation theory’s prediction of increased distress following domain-congruent values affirmation (Blanton et al., 1997; Sherman & Cohen, 2006), or not, as would be more consistent with ACT theory (Hayes et al., 1999, 2012). Consistent with ACT theory, we predicted that making connections between values and ET behavior would lead to more positive and less negative momentary affective responses relative to baseline, and relative to the Education session. We similarly predicted that positive responses in REACH would be reflected in women’s written responses to the values exercises. Second, to understand how REACH participants responded to the values exercises over the long-term, and to evaluate if more positive or negative responses to these exercises emerged over time, we conducted exit interviews with REACH participants six to ten months after the intervention and thematically coded their responses with regard to the longer-term positive and negative impact of the values exercises.

**Methods**

**Study Design**

Hormone-receptor positive breast cancer survivors (*n* = 88) were randomized 1:1 to the REACH intervention (*n* = 43) or Education only (control condition, *n* = 45), stratified by ET type (tamoxifen vs. aromatase inhibitors). Findings of the main trial are presented elsewhere (Arch et al., in press). To elucidate long-term responses to the values content in REACH, including their acceptability/feasibility, exit interviews were conducted with 38 REACH participants 6 or more months after completing the main REACH online session (range: 6.4 to 9.9 months). This report focuses on mixed methods assessment of momentary responses to the intervention, links to ET adherence, and long-term reflections on values content from the structured exit interviews.

**Participant Eligibility and Recruitment**

Study inclusion criteria were: (1) women [age 21+] diagnosed with hormone receptor-positive breast cancer stages 0-III who had finished primary breast cancer treatment; (2) prescribed ET (aromatase inhibitors [AI] or tamoxifen) in the past 2.5 years with at least 1 prescription year remaining; (3) difficulty taking ET as prescribed(see *Screener*);(4) internet access. There were no additional exclusion criteria. The University of Colorado Boulder Institutional Review Board (IRB) approved the study and served as the IRB of record.

Women were recruited through targeted mailings at the Pueblo, Colorado Springs, and Boulder clinics of Rocky Mountain Cancer Centers (RMCC), the largest network of community oncology practices in Colorado. (See Appendix for details.)

**Screener**

The *Screener* asked potential participants whether they had missed any ET pills in the past month, and whether any of 13 listed factors (drawn from the literature) made taking ET difficult (see Appendix). To be eligible, women had to either report missing at least two ET pills in the past month or report that at least one factor made taking ET at least moderately difficult.

**Interventions**

The online interventions were programmed into Qualtrics (*Qualtrics Software*, 2017) using interactive features. Images and examples with racially and age-diverse individuals were used throughout.

*Education Intervention*

The Education intervention consisted of a single online Qualtrics session lasting 15-20 minutes that provided information on the role of ET in preventing breast cancer recurrence, the importance of daily ET adherence, and suggestions for how to manage common side effects (Arch et al., in press). Education content was adapted from public resources (see Appendix) in collaboration with RMCC oncologists and pharmacists. Participants were asked which ET symptoms they had concerns about and wished to manage, triggering branching mechanisms that provided tips and suggestions for those specific side effects, including the recommendation to discuss them with their oncology care team. The session included mini-quizzes to check for understanding.

*REACH (Education+Values) Intervention*

*Main Session.*The main REACH session consisted of the Education content plus values exercises drawn from ACT and self-affirmation theory that culminated in the creation of a personal values sticker for participants to place on their ET Wisepill box (Arch et al., in press). Table 1 summarizes the content of the four-part session, which included three sets of values exercises (Parts 1, 3, and 4): (a) Part 1: a brief health-focused values affirmation, followed by Part 2: ET education, (b) Part 3: a series of values-based perspective-taking exercises, and (c) Part 4: the creation of the personalized values sticker. Part 1 and 2 are described in detail in Table 1 and in the *Education Intervention*, above. In Part 3, values perspective-taking exercises included four interactive exercises, three of which incorporated open-ended writing reflections. For example, one exercise involved selecting a value that most motivated taking ET and then reflecting in writing on: “How might this value motivate you (or continue to motivate you) to take your anti-hormonal therapy? Write down what about this value motivates you to take anti-hormonal therapy.” Additional perspective-taking exercises included “Looking from the future,” “Looking toward the future,” and “Looking from my loved one’s perspective” (see Appendix). Written responses were recorded in Qualtrics.

In Part 4, participants reflected on their main source of motivation for adhering to ET, uploaded a photo or phrase that captured this motivation, and then designed a sticker (online) with the text “I take these for:” at the top and their uploaded photo or phrase below (see Appendix Figure 1). Participants were encouraged to upload a photo, if possible (as opposed to writing a phrase), based on the assumption that images convey values more quickly and powerfully; all but 11 of the 88 women did so. The program projected participants’ chosen image or phrase onto an online sticker for viewing, and allowed them to customize the background color for the sticker. After the session, the study team printed each participant’s design onto an adhesive sticker and post mailed it to them. The participant placed the sticker on her ET pillbox, photographed the box with the sticker on it and emailed or texted it to the study team for confirmation. Participants in both conditions were sent a wireless medication box specifically for their ET pills that had a flat cover for sticker placement (see below and Appendix).

**Measures**

**Affective Response to the Intervention.** Participants’ negative and positive state affect were assessed in Qualtrics using items adapted from a previous study of negative and positive emotions about ET (Rosenberg et al., 2015). Based on pre-pilot user feedback, we limited the assessment to seven affective states, including four positive (happy, connected, enthusiastic, loving; current α’s = .90-.94) and three negative (tense, sad, guilty; current α’s = .64-.83) states assessed in response to “How are you doing *right now*? Feeling:” with each feeling state listed. Participants rated each state on a 0 to 100 scale in which 0 = not at all and 100 = completely. Affect was assessed five times during the main REACH online session, at baseline (T0) and after each of the four parts outlined in Table 1 (T1, T2, T3, T4). In the Education session, affect was assessed twice: at baseline (before ET education, paralleling T1 in the REACH session) and at the end (after ET education, paralleling T2 in the REACH session). For illustration, see Appendix Figures 2-3 and Tables 6-12.

**Written Responses to the Values Exercises**. The 43 REACH participants’ written responses to the four open-ended prompts about values and motivation to adhere to ET from Parts 1 and 3 (see Table 1) were analyzed using Linguistic Inquiry and Word Count (LIWC; Pennebaker et al., 2007). LIWC is a text analysis program which evaluates psychologically meaningful categories of words in written text or transcribed natural language (Tausczik & Pennebaker, 2010). The written reflections from Parts 1 and 3 were intended to be brief, and thus were combined and analyzed together as they were too brief to analyze separately. Proportions of positive and negative emotion words (of total word count) and emotional tone (how positive the affective tone is according to the words used) were calculated using LIWC.

**Thematically Coded REACH Exit Interviews.** Twenty-one exit interviews with REACH participants were conducted over the phone by four trained post-baccalaureate or doctoral student interviewers. The current analysis identified themes related to positive and negative experiences and with the values content in REACH and with the values sticker in particular (the most enduring part of the intervention). To select interviewees in a manner that ensured that the full range of their experiences was reflected, participants were stratified into predominantly negative, neutral, and positive feedback categories based on their quantitative and qualitative satisfaction survey responses; 5 participants (who embodied that strata in their responses) were then selected within each feedback strata. Given that most responses to REACH were positive, this approach resulted in oversampling negative responses. As we aimed to interview 21 participants (e.g., half of the *n* = 43 REACH sample), another 6 participants were randomly selected using a random number generator. Interviews were conducted using a structured interview guide and were transcribed and analyzed by three independent coders using thematic analysis; a preliminary codebook was developed *a priori* with broad categories, and emergent codes were later integrated (Hsieh & Shannon, 2005). To facilitate a consensual understanding of the complete codebook, the three coders initially independently coded four interviews and met weekly to ensure consensus throughout the coding process. The coders were trained by and met regularly with a qualitative data expert (K.A.) who oversaw the thematic identification and coding process. All transcripts were coded in ATLAS.ti version 9.1 twice by the independent coders: once for broader themes by the three independent coders and again by for sub-themes by two of the three coders.

**Analytic Approach and Power Calculations**

Participant characteristics in the two conditions were compared using independent *t* tests for continuous and tests for categorical variables. Affective responses were analyzed in Stata/SE 15.1 (StataCorp., 2017) using linear mixed models with fixed effects for session timepoint (categorical) and condition. The models included a random intercept for individual and an interaction between timepoint and condition to allow for condition differences in change over time. Separate models were fit for overall positive and negative affect and for individual affect items. Standardized effect sizes (*d*) were computed by refitting the models with standardized response variables, using the total sample’s standard deviation at baseline for standardization.

Power calculations for the longitudinal intervention trial (the main results of which will be reported elsewhere) used Optimal Design Software Version 3.01 (Spybrook et al., 2013) and indicated that a sample size of 32 per condition at 6-month follow-up would provide 80% power to detect a mean difference in slopes of 2.5 percentage points/month, which represents a medium effect size. Assuming 80% retention at 6-month follow up, we aimed to recruit 80 participants.

**Results**

See Table 2 for baseline participant characteristics.There were no significant differences between conditions on baseline characteristics (Table 2). All participants (88/88) across both conditions completed the main intervention session to which they were randomized.

**Values Motivating ET Adherence in REACH**

Per Appendix Table 1, in REACH, the most important values that participants identified as motivating their taking ET reflected themes related to “my family or children” (41.86%) or “self-love or vitality” (34.88%). Additionally, 74.42% (32/43) of participants uploaded a photo (the recommended option, see Appendix Figure 1 for examples) to use on their values sticker for their medication pillbox and 25.58% (11/43) uploaded a phrase (see Appendix Table 2).

**LIWC Analyses of Written Responses to the REACH Values Exercises**

REACH participants’ combined responses to the written values exercises included more positive emotion words (*M* = 7.53, *SD* = 3.97) than negative emotion words (*M =* 1.41, *SD* = 1.55), (*t* (42) = 8.35, *p* < .001, *d* = 4.81) see Table 4. In addition, the overall emotional tone was positive (*M* = 84.38, *SD* = 27.36), with numbers >50 reflecting more positive emotional content (Cohn et al., 2004). For specific negative emotions, written responses showed very low levels of anger, anxiety*,* or sadness (Table 4).

**Affective Responses to ET Education by Condition**

**Overall Positive and Negative State Affect.** Participants in both conditions completed the same ET education module. However, in REACH, participants first briefly identified and affirmed their core health-related values before completing the education module (see Table 1). To evaluate the effect of this health values affirmation, we compared state affect at baseline in each condition’s main session to affect reported immediately after finishing the ET education module. As Table 3 illustrates, the condition by time interaction (from baseline to T2) was not statistically significant for either overall negative affect (*b* = -3.12, *SE* = 2.55, *p* = .22, *d* = -.16) or overall positive affect (*b* = -.96, *SE* = 1.81, *p* = .60, *d* = -.04).

**Individual State Affects.** To gain a more granular view and generate future hypotheses, we explored the condition by time interactions (from baseline to T2, after ET education) separately for each affect item in the negative and positive affect scales (see Appendix Figures 2-3 and Appendix Tables 6-12). Condition by time interactions revealed greater increases in feeling loving (*b* = 7.49, *SE* = 3.11, *p* = .016, *d* = .32) and marginally greater decreases in sadness (*b* = -6.75, *SE* = 3.46, *p* = .051, *d* = -.24) in the REACH condition than in the Education condition. In contrast, the Education condition showed greater increases in feeling connected than REACH (*b* = -9.63, *SE* = 3.48, *p* = .006, *d* = -.41).

**Affective Responses to the Overall Session by Condition**

**Overall Positive and Negative State Affect.** As Table 3 presents, there were no significant condition differences in change in overall positive state affect from baseline through the end of each session (*b* = 2.28, *SE* = 1.81, *p* = .21, *d* = .11). However, REACH trended toward lower negative affect (*b* = -.4.88, *SE* = 2.55, *p* = .055, *d* = -.25).

**Individual State Affects.** On an exploratory basis, we evaluated condition differences in state affect responses from the start to the end of the sessions at the level of affect items (Appendix Table 6-12). For negative affect items, there was a marginal condition by time interaction in feeling tense (*b* = -7.83, *SE* = 4.02, *p* = .052, *d* = -.27; Appendix Table 10) such that tenseness dropped more during the REACH session than Education session. Similarly, there was a trend condition by time interaction in feeling sad (*b* = -6.36, *SE* = 3.46, *p* = .066, *d* = -.23; Appendix Table 11) such that sadness dropped significantly during the REACH session (*p* = .001) but not during the Education session (*p* = .47). From the start to the end of the sessions, these were no condition differences in guilt (*p* = .821, Appendix Table 12).

Across the entire session at the level of positive affect items (Appendix Tables 6-9), feeling loving dropped significantly for Education participants but showed a pattern of increasing for REACH participants, resulting in a significant condition by time interaction, *(b* = 11.56, *SE* = 3.11, *p* = <.0001, *d* = .49; Appendix Table 9). Conditions did not differ significantly on other positive affect items.

**Affective Responses During the REACH Session**

**Overall Positive and Negative State Affect.** As presented in Table 3 and Appendix Figures 2-3, during the REACH session, positive affect significantly increased after the Part 4 values sticker creation exercise *(b* = 2.60, *SE* = 1.31, *p* = .047, *d* = .12), relative to the Part 3 values perspective-taking exercise and negative affect significantly declined relative to baseline after each part of the REACH intervention session, *p*s < .05. Thus, the REACH session values exercises (Table 2) had the effect of reducing negative affect and, in the case of the values sticker exercise, increasing positive affect.

**Thematically Coded Responses to the REACH Values Content in the Exit Interviews:**

The following themes focus on the twenty-one interviewed REACH participants. Broader qualitative findings from the study are reported elsewhere (Arch et al., in press; Bright et al., in press)

**Positive Experiences with Reflecting on Values.** Most commonly, REACH participants (*n* = 12) described that reflecting on their values during the online intervention was a positive experience, noting it was “helpful,” “healthy,” and a “good reflective time.” For example, when asked what she thought about the online program and thinking through her values and motivations for taking the medication, one participant stated:

*That, to me, that was like the epiphany moment. I thought when we started to go into that I thought, wow this really is the key to having peace of mind about taking this medication. So, to me, that was the game changer.* (1050)

Others reported that reflecting on values validated their decision to take ET or provided additional support:

*And a lot of times your family doesn’t even think about you having to take this medication and having all these side effects. And it was nice to have that outside support and reminder that you are taking this for your family even though they don’t always thank you every day for it.* (1062)

Others shared that REACH helped them to reflect in new ways on their reasons for taking ET:

*It was kind of nice in the sense that I don’t do that, so I think it was a healthy exercise.* (1015)

**Positive Experiences with Reflecting on the Values Sticker.** REACH participants (*n* = 18) overwhelmingly described positive experiences with the values sticker specifically, stating that the sticker was sweet, cute, fun, worthwhile, brought them joy or pride, or made them smile or laugh:

*It was good. It was fun. It was a family picture, so it was just nice.* (1076)

*I was proud of myself. I was proud to see that sticker because I knew that was something that was meant for me, something that I needed to see every day and something that got me through every day.* (1033)

**The Importance of Personalizing the Sticker.** Some (*n* = 8) shared the importance of personalizing their sticker, noting that it was powerful to choose their image to give their pillbox meaning or make it theirs:

*It made it…personal that it was my medication, and I was doing the right thing.* (1048)

*It seems like a simple thing, but very powerful to have selected an image and have it on there…instead of you all just providing something that’s a reminder, it’s a personal reminder which made it a little more valid…so having it more personalized was more powerful than just some company generically saying, oh you should take this…it saves lives, or whatever their slogan would be.* (1046)

**The Values Sticker Serving as Motivation to Take ET.** Two thirds of REACH participants (*n* = 14) reported that the sticker was a helpful visual reminder that connected their values with their motivation for taking the medication.

*…It made me smile. Seeing my family and it makes you realize that…it’s not just about me, it’s about my kids and my husband and my siblings…my entire family. So it puts it right in front of your eyes, makes you remember why you’re taking your medication.* (1041)

Others reported that the sticker made them think more consciously and deliberately about taking their medication, as opposed to taking it out of routine or habit:

*You know how it is, you reach for something like that, it’s part of your routine, you’re not really thinking, you pick it up and you look and suddenly it’s like, oh it made me smile. So it was an added, it helped. You connect that with why did I pick that sticker, what does it mean, it means my values, and it’s just that constant reinforcement.* (1050)

**Negative Experiences with Values Intervention and Sticker.** Two participants described guilt or anger when thinking about their values and values sticker, either due to fear of recurrence or challenging ET side effects that led to nonadherence:

*I’m doing this for my family and for livelihood and all of that is sometimes a pretty emotional…thing and it triggers a lot of the fear part of it, of not being around…utilizing those things as emotional motivators is great but the flip side of that is if you do get rediagnosed or something like that then you’ve let all those people down.* (1072)

*At first I thought, oh yes okay this is good, but then as time went by and things got worse and worse for me [with ET side effects, which led to stopping ET], I kind of resented having the sticker there…and making me feel guilty for it not working, the medicine not working for me.* (1049)

Another participant reported a mixed experience with the values sticker due to her choice of image:

*I mean they were generally positive. My husband gave me a hard time about the picture that I chose…every time I would take out that darn pillbox he’d be like, his face, both of our faces, were on it. It wasn’t the kids or anything…I don’t know that that was very effective, honestly…But that’s just me. But everything else I thought was good information, helpful information, and maybe not so much with the picture. (1014)*

**Values Intervention and Values Sticker Not Impactful.** Three participants reported that reflecting on values during REACH was not significantly helpful, as they already had reflected on values or were committed to taking ET:

*I didn’t need those reminders because that’s how I basically have always operated anyway.* (1017)

*I guess it slightly helped…to be okay with taking the medication…but whether I [reflect on values] or not I’m still going to do it, so it didn’t really have a great impact.* (1066)

Similarly, more than a third of interviewed REACH participants (*n* = 9) reported that seeing the values sticker on their pillbox did not impact them or provide added value. Although many described the sticker positively, they reported that they were committed to taking ET regardless or that the rest of the REACH session content provided sufficient motivation and thus the sticker was unnecessary:

*…the pillbox alone was reminder enough and I had in my mind the information that you sent and my resolve to see it through.* (1032)

**Discussion**

This mixed-methods study evaluated positive and negative affective responses to the online REACH interventions at a granular level, distinguishing between responses to distinct values-based approaches to promoting medication adherence. As such, this study provides one of the first known evaluations of state affect during diverse values-based exercises. Additionally, the study used quantitative (e.g., LIWC) and qualitative (e.g., exit interviews) methods to further elucidate participants’ immediate and longer-term responses to linking personal values to ET adherence. At a conceptual level, this study evaluated whether directly and explicitly linking domain-relevant values to ET adherence, a health behavior, resulted in affective responses that were more consistent with the predictions of self-affirmation theory (Blanton et al., 1997; Sherman & Cohen, 2006; Steele, 1988) or ACT (Hayes et al., 1999, 2012).

**Affective Response Findings in Context**

Comparisons of state affect at the start and end of the main online session in each intervention revealed that relative to Education, the REACH session, which ended with creating the values sticker, led to patterns of decreased negative affect, driven by decreases in tension and sadness, as well as increases in loving feelings. In addition, comparing online ET education that was preceded or not by a health values affirmation showed that affirming health-related values in REACH prior to ET education led to less sadness and more loving feelings than Education alone, though Education alone led to more feelings of connection. Though greater feelings of connection in Education was unexpected, the bulk of the findings support the notion that the values exercises in REACH led to less distress and more loving feelings that Education alone. These findings are important given previous theory and evidence from self-affirmation theory that affirming domain-relevant values can increase cognitive dissonance and thus distress (e.g., Blanton et al., 1997). This prior research largely used samples of undergraduate students and domain-relevant values that were mandated rather than freely chosen. The current results show that when values are freely chosen, as in ACT, then multiple distinct approaches to affirming domain-relevant values (affirming health values, values-based perspective taking, and designing an ET values sticker) reduced distress (relative to baseline or to Education alone). These group-level findings challenge and expand previous theory and evidence and provide evidence that linking domain-relevant values directly to health behavior change was generally associated with decreases rather than increases in negative affect. Future ET studies should directly compare domain-relevant to domain-irrelevant values to evaluate differences in immediate and longer-term impacts on affect and behavior.

The state affect findings largely converge with the LIWC and qualitative findings on the REACH intervention. LIWC findings showed that the open-ended written reflections to the values exercises were generally positive in affective tone, with very low levels of negative affect and much lower use of negative affect words than positive affect words. This converges with the findings that the overall REACH session reduced specific negative affect and increased positive interpersonal affect relative to baseline (and relative to Education alone) and suggests that for most, reflecting on values and linking them to ET adherence was a positive experience. Because written responses to the values exercises were intended to be brief and thus were combined for analysis, we were unable to distinguish LIWC responses to the perspective-taking values exercises from the other values exercises, a limitation.

The qualitative interviews conducted 6 to 10 months after the online sessions similarly revealed that most REACH participants found that linking values to ET adherence was modestly to highly helpful, motivating, or pleasant. Participants appreciated being able to personalize their values sticker, and how it served as a helpful visual reminder to take their medication. However, two women in the exit interviews found the experience to be guilt-inducing and thus unhelpful; both had developed difficult ET side effects and stopped taking the medication as a result. Others, perhaps particularly those who did not have major issues taking ET to begin with, found that using the values sticker was unnecessary for their broader reflection on values or their motivation for taking the medication. The negative experience of this small minority of women is consistent with self-affirmation theory’s prediction that affirming domain-relevant values causes uncomfortable dissonance and related distress (Blanton et al., 1997). Thus, overall it appears that for most women, affirming domain-relevant values was a positive experience, consistent with ACT, but for a few, particularly those who struggled with significant ET side effects and with persisting to take ET, affirming domain-relevant values was associated with distress, consistent with self-affirmation theory. Thus, affirming domain-relevant values in the context of ET should be undertaken with sensitivity toward providing additional support for side effects (or other adherence barriers) particularly for women who most intensely experience them.

**Study Strengths and Limitations**

Study strengths include the repeated, granular assessment of positive and negative affect during the online interventions, and specific affects therein, and the use of mixed methods. Because the values content was delivered as part of an intervention, the order of the values components was fixed, a study limitation. However, the consistent pattern of positive affective responses to distinct values exercises that were not linearly related to their ordering in REACH suggest that order effects did not play a primary role in these responses. Analyses of the individual affects was exploratory but given the large number of tests, should be interpreted with caution pending replication. Finally, the lack of racial and ethnic diversity in the sample is a limitation that should be addressed in future studies through collaboration and outreach in underrepresented and underserved communities.

**Conclusions**

To our knowledge, this study represents the first evaluation of linking distinct values exercises directly to healthcare adherence among breast cancer survivors. The measurement of positive and negative state affect during the online intervention revealed that relative to baseline, the ET values exercises reduced negative affect and, upon designing a values sticker for one’s ET pillbox, increased positive affect. Qualitative and quantitative findings converged, revealing that a majority of breast cancer survivors responded positively to linking values to taking ET while two women with pronounced unmanaged ET side effects may have needed more support before continuing to engage in values. From a theoretical standpoint, the response of this minority was consistent with self-affirmation theory (Blanton et al., 1997; Sherman & Cohen, 2002; Steele, 1988) as women who stopped taking ET due to side effects did not wish to be reminded of the values at stake in taking ET. In contrast, the positive response of the majority of women was consistent with the ACT model (Hayes et al., 1999, 2012). The findings thus support the notion that directly linking values to medication adherence is helpful for many and could provide broader benefit by offering more support for addressing barriers to adherence.

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**Table 1.**

*Online REACH (Education+Values) Session Content*

|  |  |  |
| --- | --- | --- |
|  | **Content** | **Intended Function** |
| **Part 1.** Clarify and Affirm Values in Domain of Health and Self-Care | Participants identify values “that specifically motivate you to take care of yourself” using interactive content, and write freely about how the value is important to them, including examples of how it influenced what they did. | Clarify and affirm values prior to ET education, per studies showing more openness to health information after values affirmation (Epton & Harris, 2008; Sherman, 2000), but with a focus on health domain-specific (not general) values |
| **Part 2.** ET Education | Described in *Education Intervention*. | Educate participants about ET’s purpose, importance of adherence, and how to manage common side effects; Designed as an active control |
| **Part 3.** Values and Perspective Taking | Participants complete interactive, ACT-based exercises that draw on values and perspective-taking linked to motivation for ET adherence, including responding to 3 open-ended values writing prompts. | Link core personal values to the value of adhering to ET, thereby bolstering personal motivation for ET adherence |
| **Part 4.** Creating a Visual Reminder | Participants select the top value that motivates them to take ET, upload a photo or phrase that captures this value, and design a sticker that features it to place on their Wisepill box. | Visually reinforce the link between participants’ values and adhering to ET by creating a positive, affective “cue to action” in the form of a values sticker |

Note: ET = endocrine therapy

**Table 2.**

*Baseline sociodemographic and medical characteristics of randomized participants (n = 88)*

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
|  | *Total (n=88)*  *%(n)* | *REACH (n=43)*  *%(n)* | *Education (n=45)*  *%(n)* | Between Group | | | |
| *t or χ*2 | | *p* | |
| Female | 100.00% (88) | 100.00% (43) | 100.00% (45) |  | |  | |
| Age  (in years, Range: 31-81) | *M*=58.34(*SD*=10.37) | *M*=57.77(*SD*=11.22) | *M*=58.89(*SD*=9.58) | .51 | | .62 | |
| Race/Ethnicity1 | | | | | .21 | | .65 | |
| White/Caucasian & Non-Latina | 92.05% (81) | 90.70% (39) | 93.33% (42) |  | |  | |
| Hispanic/Latina | 3.41% (3) | 4.65% (2) | 2.22% (1) |
| Biracial | 1.14% (1) | 2.33% (1) | 0.00% (0) |
| Native American | 1.14% (1) | 2.33% (1) | 0.00% (0) |
| Black/African American | 0.00% (0) | 0.00% (0) | 0.00% (0) |
| Other | 2.27% (2) | 0.00% (0) | 4.44% (2) |
| Education (median) | Bachelor's degree | Associate degree | Bachelor’s degree | 1.45 | | .15 | |
| Household income (median) | $71,000 - $80,000 | $71,000 - $80,000 | $61,000 - $70,000 | -.13 | | .90 | |
| Married or partnered | 76.14% (67) | 79.07% (34) | 73.33% (33) | .40 | | .53 | |
| Children (1 or more) | 76.14% (67) | 81.40% (35) | 71.11% (32) | 1.28 | | .26 | |
| *Cancer treatment history* | |  |  |  | |  | |
| Months from end of treatment (Range 1–36) | *M*=13.83  (*SD*=8.54) | *M*=14.42  (*SD*=9.38) | *M*=13.33 (*SD*=7.64) | -.64 | | .52 | |
| % who received:   1. Surgery 2. Chemotherapy 3. Targeted Therapy 4. Radiation | 1) 100% (88)  2) 34.09% (30)  3) 10.23% (9)  4) 68.18% (60) | 1) 100% (43)  2) 39.53% (17)  3) 6.98% (3)  4) 69.77% (30) | 1) 100% (45)  2) 28.89% (13)  3) 13.33% (6)  4) 66.67% (30) | 2) 1.11  3) .97  4) .10 | | 2) .29  3) .33  4) .76 | |
| % BL ET Type:   1. Aromatase Inhibitors 2. Tamoxifen | 1) 62.50% (55)  2) 37.50% (33) | 1) 65.12% (28)  2) 34.88% (15) | 1) 60.00% (27)  2) 40.00% (18) | .25 | | .62 | |
| Months between ET Rx date and enrollment (Range 1–29) | *M*=13.11  (*SD*=8.29) | *M*=13.74  (*SD*=8.21) | *M*=12.51 (*SD*=8.41) | -.70 | | .49 | |
| *Cancer stage*2 | |  |  |  | |  | |
| 0 | 5.68% (5) | 6.98% (3) | 4.44% (2) | .39 | | .53 | |
| I | 71.59% (63) | 67.44% (29) | 75.56% (34) |
| II | 18.18% (16) | 25.58% (11) | 11.11% (5) |
| III | 4.55% (4) | 0.00% (0) | 8.88% (4) |

Note: BL = baseline; ET = endocrine therapy, Rx = prescription; 1The *χ*2 test compared the portion of White, non-Latinx participants to minority-identified participants; 2The *χ*2 test compared conditions on cancer stage categories of 0-I versus II-III. None had stage IV.

**Table 3.**

*Overall Positive and Negative Affective Responses to the Intervention by Condition: Mixed Model Findings*

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | **Positive affect** | | | **Negative affect** | | |
| **Session Timepoint**  **(T)** | Contrast (SE) | *p* value | *d* | Contrast (SE) | *p* value | *d* |
| **REACH: Change relative to baseline** | | | | | | |
| T1 minus T0 | 0.45 (1.31) | .731 | .02 (-.10, .14) | -4.37 (1.84) | **.040** | -.22 (-.41, -.04) |
| T2 minus T0 | -0.76 (1.31) | .564 | -.04 (-.15, .08) | -7.36 (1.84) | **.001** | -.38 (-.56, -.19) |
| T3 minus T0 | -0.13 (1.31) | .922 | -.01 (-.12, .11) | -8.03 (1.84)) | **.001** | -.41 (-.60, -.23) |
| T4 minus T0b | 2.48 (1.31) | .059 | .11 (.00, .23) | -9.12 (1.84) | **<.0001** | -.47 (-.65, -.28) |
| **REACH: Change relative to the previous assessment** | | | | | | |
| T2 minus T1 | -1.21 (1.31) | .357 | -.06 (-.17, .06) | -2.98 (1.84) | .105 | -.15 (-.34, .03) |
| T3 minus T2 | 0.63 (1.31) | .632 | .03 (-.09, .15) | -0.67 (1.84) | .714 | -.03 (-.22, .15) |
| T4 minus T3 | 2.60 (1.31) | **.047** | .12 (.002, .24) | -1.09 (1.84) | .554 | -.06 (-.24, .13) |
| **Education Only** | | | | | | |
| T2 minus T1a | 0.20 (1.24) | .872 | .01 (-.10, .12) | -4.24 (1.77) | **.017** | -.22 (-.40, -.04) |
| **Condition by Time Interactions** | | | | | | |
| T2 minus baselinea | -0.96 (1.81) | .597 | -.04 (-.21, .12) | -3.12 (2.55) | .221 | -.16 (-.42, .10) |
| Final minus baselineb | 2.28 (1.81) | .208 | .11 (-.06, .27) | -4.88 (2.55) | .055 | -.25 (-.51, .01) |

Note: In the main REACH session, state affect was assessed at baseline (T0) as well as *after* health values affirmation (T1), ET education (T2), values perspective-taking exercises (T3), and designing the values sticker (T4), i.e., after each part outlined in Table 1. In Education, state affect was assessed at baseline (T1) and after ET education (T2). Thus, the session baseline is labeled T0 in REACH and T1 in Education, see *Methods* and Appendix Tables 6-12*.*

a Difference of post-education timepoint (T2) minus their baseline timepoint

b Difference of final session timepoint (T4 in REACH, T2 in Education) minus their respective baseline timepoint

**Table 4.**

*LIWC emotion category responses in REACH*

|  |  |  |
| --- | --- | --- |
| LIWC Category | Mean (standard deviation) | Range |
| Word count | 83.05 (63.92) | 15-295 |
| Emotional tone | 84.38 (27.36) | 1-99 |
| Positive emotion | 7.53 (3.97) | 0-23.08 |
| Negative emotion | 1.41 (1.55) | 0-6.67 |
| Anger | 0.18 (0.51) | 0-2.27 |
| Anxiety | 0.42 (0.78) | 0-2.63 |
| Sadness | 0.44 (1.17) | 0-6.67 |

Note: All affective categories reflect percentages of total word count.