2018 IEEE EMBS International Conference on Biomedical & Health Informatics (BHI)
4-7 March 2018
Las Vegas, Nevada, USA

A Social Cognitive Theory-based Framework for Monitoring Medication Adherence Applied to Endocrine Therapy in Breast Cancer Survivors

Mehdi Boukhechba[1]*, Sonia Baee[1]*, Alicia L. Nobles[1], Jiaqi Gong[2], Kristen Wells[3], Laura E. Barnes[1]

***Abstract*— Poor adherence to long-term therapies for chronic diseases, such as cancer, compromises effectiveness of treatment and increases the likelihood of disease progression, making medication adherence a critical issue in population health. While the field has documented many barriers to adherence to medication, it has also come up with few efficacious solutions to medication adherence, indicating that new and innovative approaches are needed. In this paper, we evaluate medication-taking behaviors based on social cognitive theory (SCT), presenting patterns of adherence stratified across SCT constructs in 33 breast cancer survivors over an 8-month period. Findings indicate that medication adherence is a very personal experience influenced by many simultaneously interacting factors, and a deeper contextual understanding is needed to understand and develop interventions targeting non-adherence.**

I. INTRODUCTION

By 2022, there will be nearly 4 million breast cancer survivors in the United States. Two thirds of women diagnosed with breast cancer have hormone receptor-positive breast cancer [1] and are prescribed long-term anti-hormonal medications (HMs) to reduce cancer recurrence and mortality [2]. Medication adherence, defined as whether patients take their medications as prescribed, is crucial to quality of life and survivorship. Despite the life-saving benefits of these medications, between 20% and 41% of women are not adherent to HMs during the first year of treatment [3], [4], [5].Compounding this, ethnic and racial minority women, women who lack health insurance, and women with low socioeconomic status are less likely to get optimal care following breast cancer treatment and have lower rates of survival from breast cancer than white women, women with health insurance, and women at higher socioeconomic levels [6].

Substantial research documents reasons why individuals do not adhere to prescribed medications, including HMs, with multiple predictors of medication adherence identified in cross-sectional and longitudinal studies. Using Social Cognitive Theory (SCT), personal, environmental, and behavioral factors are constantly interacting through a process called reciprocal determinism [7] to condition medication adherent behavior. Prior research indicates that personal factors that affect long-term adherence to medication include physiological, cognitive, and affective states. Environmental factors, including a person's social environment, physical environment, and the health system environment, influence whether or not an individual takes medication. Thus, sticking to a medication regimen is a conditioned process influenced by both personal and environmental factors, such as when a patient who has negative thoughts and feelings and experiences interpersonal conflict with their caregiver, who in turn avoids the patient and causes them to isolate themselves and therefore forget to take their medication multiple times. Medication taking is therefore a behavior that occurs in the context of other behaviors which can serve as a cue to action to initiate the behavior of interest [7]. Individuals who have a routine or schedule for medication taking are more likely to be adherent [8], [4], and may take their medication around other behaviors during the day, such as sleeping or eating [9]. Nevertheless, more work needs to be done to understand the varied personal, environmental, and behavioral factors involved in establishing a stable medication-taking routine.

Methods for assessing medication adherence include direct methods, such as measuring a biological marker in blood, or indirect methods, such as self-reports of adherence and pharmacy refills [10]. Although direct methods are considered more robust, they are often burdensome to both patients and the health care system. Indirect methods can be influenced by inaccurate reporting by the patient or reliant on a closed pharmacy system. A Medication Event Monitoring System (MEMS®) device can overcome these limitations. These devices consist of a standard prescription bottle that includes a larger lid containing a MEMS® monitoring cap, which records a timestamp for each time the bottle is opened. Assuming that each time a bottle is opened represents the patient taking medication, patterns of medication adherence can be passively monitored. Estimated pill counts from MEMS® are strongly correlated with adherence, and thus are used frequently to assess medication adherence in clinical trials.

In this work, we examined the relationship between personal and environmental factors and HM adherence behaviors of underserved women following breast cancer treatment using MEMS® devices. More specifically, we examined time series of MEMS® to identify unique patterns of medication-taking and compared to SCT constructs. These data were collected to evaluate a patient navigation intervention in collaboration with Sharp HealthCare in San Diego, California.

Our findings suggest that medication adherence is a very personal experience and that individuals have a unique pattern to taking medications. Additionally, we identified certain demographic characteristics of undeserved women, such as

*The two authors contributed equally
[1]Systems and Information Engineering, University of Virginia. mob3f/sb5ce/aln2dh/lb3dp@virginia.edu
[2]Department of Information Systems, University of Maryland Baltimore County. jgong@umbc.edu
[3]Department of Psychology, San Diego University. kwells@mail.sdsu.edu

age and stage of the disease, that are good discriminators of adherence patterns. For instance, older patients were found to be less adherent than younger patients and lower income patients appeared to be less adherent to medication than those with higher incomes. A deeper contextual understanding of reasons for medication adherence or nonadherence will aid developing evidence-based personalized interventions that are delivered at times when people most need them, ultimately improving mediation adherence.

II. Data Analysis and Results

To better understand patients medication-taking behaviors, we analyzed data assessing medication adherence of 33 patients using MEMS® over an 8-month period. The data were obtained from breast cancer survivors participating in a study to examine the efficacy of a patient navigation intervention for medically and historically underserved hormone-receptor positive breast cancer survivors. Participants were randomized to usual care plus written information or usual care plus patient navigation. Follow-up data were collected via surveys and medical record abstraction at 4- and 8-month follow-ups, and endocrine therapy adherence data are being collected continuously via MEMS®.

We first analyzed patients' medication-taking behavior over the study period as collected from the MEMS®. Figure 1 shows the average daily bottle opening (ADBO) and average medication intervals per day. Intervals are the time between each two bottle opening actions, and should ideally be be around 24 hours indicating the participant takes the medication at approximately the same time each day. On average, the intervals are less than 24 hours indicating that patients tend to take the medication earlier than expected. For some days, the intervals are well outside of 24 hours indicating that some patients did not take their medication for one or more days.

On the other hand, ADBO presented in Figure 1 estimated the average adherence of patients on daily basis, we notice that the global average was around 0.85 (i.e; each day, around 85% of patients took the medication). However, sometimes the average number of daily bottle opening exceeds one, indicating that some patients took their medication more than once a day or opened the bottle more than once per day. Finally, we recorded a drop in adherence in the last weeks of the study (starting from the day 240) where we can observe a decrease in the number of patients, average intervals, and average number of daily bottle openings.

After analyzing the fluctuation of medication-taking behavior over time, we explored the relationship between personal and environmental factors over the course of the study and their relationship to medication adherence. Figure 2 presents the relationship between medication adherence and demographic and temporal characteristics.

For each user, we calculate the average interval and the ADBO that represents the average daily medication taken over the course of the study (a patient having 0.7 ADBO means she missed 30% of her medication, thus the more ADBO is near one the more adherent the patient is). Figure

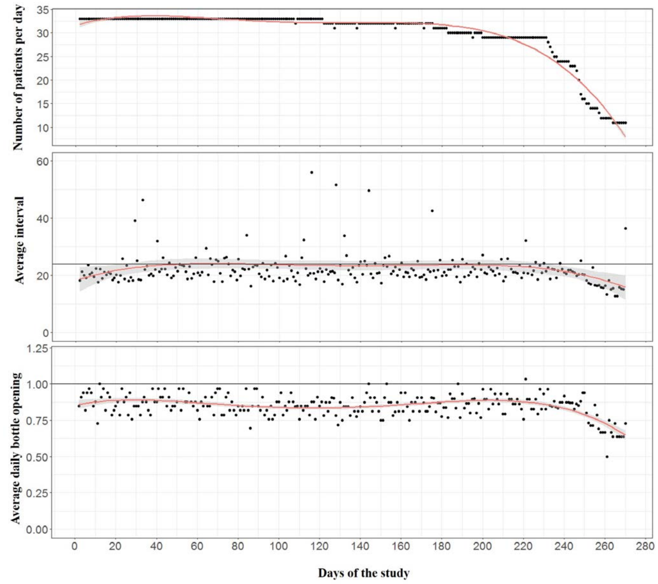

Fig. 1. The average daily bottle opening and average medication intervals over the 8-month study period. Intervals are represented in hours. The black horizontal lines represent the baseline for ideal adherence- for interval it is 24 hours while for ADBO it is one day (i.e., one bottle opening per day).

2 depicts the average and standard deviations of ADBO and interval using multiple metrics.

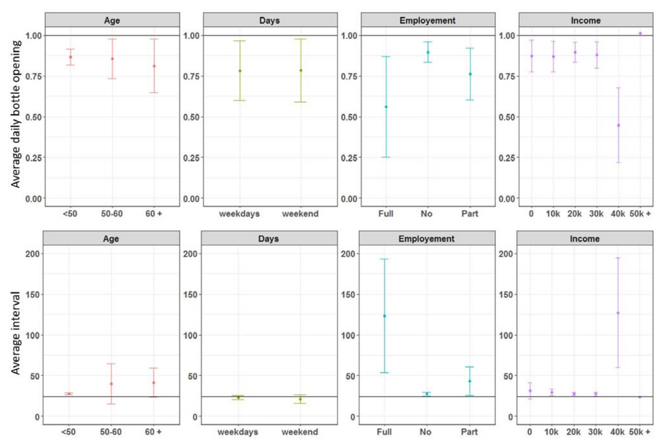

Fig. 2. The relationship between medication adherence and age, employment, income and the days of the week. Intervals are represented in hours. The black horizontal lines represent the ideal adherence- for interval it is 24 hours, while for ADBO it is 1 (i.e., one bottle opening per day). The error bars represent the standard deviation of intervals and ADBO of each group.

Younger patients (11/33) appear to have better adherence and more consistently take their medication than older patients. This is not surprising as older patients are prone to multiple comorbidities, and thus more likely to take multiple medications, and therefore may have a higher risk of nonadherence compared to younger patients [11]. We also found the average interval on weekends has more variation than weekdays. We hypothesize that this is because patient habits are more consistent on weekdays than weekends.

In order to study the impact of patients' socioeconomic levels on their medication adherence, we analyzed the medication taking behavior based on employment and income. Medication adherence appeared to vary across employment levels. We found that patients without jobs (26/33) showed higher ADBO and more regular intervals; thus, they appear then to be more adherent than employed patients (8/33). However, we did see a huge variation in adherence across annual household income levels, with the exception of the over $40,000 income group which only had two patients.

Over the course of the study, patients also reported other prescription and non-prescription medications they are taking at the same time as the HMs, their living situation (i.e., how many people they are living with), and stage of cancer at diagnosis. Figure 3 depicts the relationship between these variables and medication adherence. Patients taking more medications have a greater variation in both average ABDO and interval. Furthermore, we found that patients living alone or only with one person are more adherent than patients living with more than 2 people. Finally, the stage of cancer appears to have a strong relation with the medication adherence; patients in late stages showed high ADBO and stable intervals near 24 hours, thus indicating they are more adherent than patients in earlier stages.

In order to better understand the relationship between treatment length and adherence to medication, we calculated the Pearson correlation between each patients' ADBO and the number of days between the disease diagnosis and enrollment in the study, we found a correlation of around 0.64 which indicates that patients with longer treatment intervals are more adherent to their medications. We hypothesize that patients with later stage cancer and whose course of cancer treatment lasts longer have a greater fear of recurrence than patients at earlier stages.

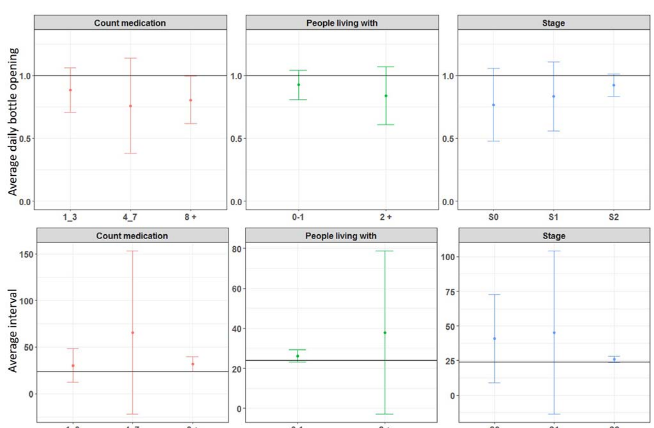

Fig. 3. The relationship between medication adherence and the count of different medications taken at the same time, the number of people living with, and the stage of the disease. Intervals are represented in hours. The black horizontal line represents the baseline for ideal adherence- for interval it is 24 hours while for ADBO it is one (i.e., one bottle opening per day). The error bars represent the standard deviation of intervals and ADBO of each group of patients.

Various SCT constructs have been measured at the beginning, the fourth month, and eighth month of the study via surveys and medical record abstraction. These constructs capture personal and environmental factors that may influence medication adherence such physical and social well being. Table I shows the correlation between these measures (for each measure we average the the baseline, fourth, and eighth months measures) and the adherence to medication estimated using the ADBO. The aim of this step is to analyze if these SCT measures have any relation with the medication adherence.

The Functional Assessment of Cancer Therapy-Breast Cancer measure (FACT-B) has been used to assess breast cancer-related quality of life, which may be tied to medication adherence [12]. The FACT-B also includes a Physical Well Being (PWB) domain, a Social/Family Well Being (SWB) domain, an Emotional Well Being (EWB) domain, and a Functional Well Being (FWB) domain. Higher scores on the FACT-B and its subscales indicates worse quality of life and more symptoms (i.e.; pain, fatigue, etc.). We found a negative correlation between these measures and medication adherence, indicating that the more symptoms patients are experiencing, the less adherent to medication. These results align with the literature that reports more side effects were associated with a significantly reduced likelihood of adherence [13].

The Perceived Stress Scale (PSS) is a widely used psychological instrument for measuring the perception of stress (see Table I), a Personal-Affective state [14]. Higher PSS scores can be associated with greater vulnerability to stressful life-event-elicited depressive symptoms. We found a negative correlation between PSS and adherence suggesting that the more patients are feeling stressed, the less they are adherent to HM.

The Medication Adherence Self-Efficacy Scale (MASES) and the General Belief about Medicine Questionnaire (BMQ-general) [15] have been used to measure patients' Personal-Cognitive state. MASES is a 40-item scale that is used to assess patients' confidence in their ability to take their medications in a variety of situations (e.g. while at work) [16]. Higher scores on the MASES implies low self-efficacy in adhering to prescribed medications. We found a negative correlation between ADBO and MASES which means that the more patients believe they can take their medication in different situations, the more adherent they are. A higher score on the BMQ-general measure [15] implies a good personal view about the medication. We found that the correlation between the BMQ-general and medication adherence was positive, so patients having good personal opinions about the medications tend to be more adherent to HM.

Finally, patients' social interactions have been studied using the the Krause and Borawski-Clark social support (SS) scale [17]. Higher score on the SS scale is associated with better personal perception about social support. Contrary to our expectations, results show a negative correlation between SS and adherence. This suggests that patients who report being provided with good social support were less adherent than patients who reported less support. This result

TABLE I

THE CORRELATION BETWEEN VARIOUS SCT CONSTRUCTS AND MEDICATION ADHERENCE. THESE MEASURES COVER BOTH PERSONAL AND ENVIRONMENTAL FACTORS THAT MAY IMPACT THE ADHERENCE.

Measurement of SCT construct	Correlation
Personal-Physiological	
Personal Well Being (PWB)	-0.19
Social Well Being (SWB)	-0.12
Emotional Well Being (EWB)	-0.2
Functional Well Being (FWB)	-0.16
Assessment Of Cancer Therapy (Fact-B)	-0.15
Personal-Affective	
Perceived Stress Scale (PSS)	-0.5
Personal-Cognitive	
Medication Adherence Efficacy (MASES)	-0.6
Belief about Medicine (BMQ-general)	0.22
Environmental	
Social Support (SS)	-0.4

is consistent with the result presented in Figure 3 where we found that patients living in big families (expected to have more social support) showed less adherence than patients living alone. This may be justified by the fact that while some research suggests that there is a positive relationship between SS and adherence, other researches [18] found that general support did not correlate with adherence but only medication-specific support did. Furthermore, high scores on the SS measure may indicate that patients have functional limitations requiring more support.

III. Conclusions and Future Work

Preliminary findings from our study indicate that personal and environmental SCT constructs are tightly linked to an individual's medication-taking behavior. However, the data are limited in that they cannot demonstrate a deeper contextual understanding of dynamic linkages between these constructs and medication-taking behavior. For example, medication-taking cannot be linked with other behavioral events (e.g., eating a meal, going to bed) or routines. Data also indicate some participants missed taking the medication for multiple days, which could have been caused my multiple factors, including a disruption in refilling their prescription, being unable to afford the prescription, experiencing side effects, or another disrupting event (e.g., vacation). Finally, it appears that certain patients took the medication more than once a day or took the medication at extremely random intervals (e.g., didn't take it some days and took it three times on other days). These data suggest that each individual's medication taking behavior is influenced by multiple interacting factors, and that more personalized interventions are needed to improve adherence in high-risk patient groups. In the future, tecnology-driven systems that leverage smartphone and wearable sensor technology will be developed to identify patterns of factors associated with medication-taking behavior and design personalized interventions to target non-adherence.

ACKNOWLEDGMENT

This research was supported by the National Institutes of Health under award number R21CA161077 and the Hobby Postdoctoral and Predoctoral Fellowships in Computational Science.

References

[1] E. P. Winer, C. Hudis, H. J. Burstein, A. C. Wolff, K. I. Pritchard, J. N. Ingle, R. T. Chlebowski, R. Gelber, S. B. Edge, J. Gralow *et al.*, "American society of clinical oncology technology assessment on the use of aromatase inhibitors as adjuvant therapy for postmenopausal women with hormone receptor–positive breast cancer: status report 2004," *Journal of clinical oncology*, vol. 23, no. 3, pp. 619–629, 2005.

[2] D. L. Hershman, L. H. Kushi, T. Shao, D. Buono, A. Kershenbaum, W. Y. Tsai, L. Fehrenbacher, S. L. Gomez, S. Miles, and A. I. Neugut, "Early discontinuation and nonadherence to adjuvant hormonal therapy in a cohort of 8,769 early- stage breast cancer patients," *J Clin Oncol*, vol. 28, no. 27, pp. 4120–8, 2010.

[3] T. I. Barron, R. Connolly, K. Bennett, J. Feely, and M. J. Kennedy, "Early discontinuation of tamoxifen: a lesson for oncologists," *Cancer*, vol. 109, no. 5, pp. 832–9, 2007.

[4] A. H. Partridge, A. LaFountain, E. Mayer, B. S. Taylor, E. Winer, and A. Asnis-Alibozek, "Adherence to initial adjuvant anastrozole therapy among women with early-stage breast cancer," *Journal of Clinical Oncology*, vol. 26, pp. 556–62, 2008.

[5] V. Ziller, M. Kalder, U. S. Albert, W. Holzhauer, M. Ziller, U. Wagner, and P. Hadji, "Adherence to adjuvant endocrine therapy in post-menopausal women with breast cancer," *Ann Oncol*, vol. 20, no. 3, pp. 431–6, 2009.

[6] P. Carcaise-Edinboro, C. J. Bradley, and B. Dahman, "Surveillance mammography for medicaid/medicare breast cancer patients," *Journal of Cancer Survivorship*, vol. 4, no. 1, pp. 59–66, 2010.

[7] A. Bandura, *Social foundations of thought and action: A social cognitive theory*, ser. Prentice-Hall series in social learning theory. Englewood Cliffs, NJ, US: Prentice-Hall, Inc, 1986.

[8] K. J. Wells, T. M. Pan, C. Vázquez-Otero, D. Ung, A. E. Ustjanauskas, D. Muñoz, C. Laronga, R. G. Roetzheim, M. Goldenstein, C. Carrizosa, S. Nuhaily, K. Johnson, M. Norton, E. Sims, and G. P. Quinn, "Barriers and facilitators to endocrine therapy adherence among underserved hormone-receptor-positive breast cancer survivors: a qualitative study," *Supportive Care in Cancer*, vol. 24, no. 10, pp. 4123–4130, 2016.

[9] E. A. Grunfeld, M. S. Hunter, P. Sikka, and S. Mittal, "Adherence beliefs among breast cancer patients taking tamoxifen," *Patient Educ Couns*, vol. 59, no. 1, pp. 97–102, 2005.

[10] P. M. Ho, C. L. Bryson, and J. S. Rumsfeld, "Medication adherence," *Circulation*, vol. 119, no. 23, pp. 3028–3035, 2009.

[11] A. F. Yap, T. Thirumoorthy, and Y. H. Kwan, "Medication adherence in the elderly," *Journal of Clinical Gerontology and Geriatrics*, vol. 7, no. 2, pp. 64 – 67, 2016.

[12] M. J. Brady, D. F. Cella, F. Mo, A. E. Bonomi, D. S. Tulsky, S. R. Lloyd, S. Deasy, M. Cobleigh, and G. Shiomoto, "Reliability and validity of the functional assessment of cancer therapy-breast quality-of-life instrument." *Journal of Clinical Oncology*, vol. 15, no. 3, pp. 974–986, mar 1997.

[13] C. C. Murphy, L. K. Bartholomew, M. Y. Carpentier, S. M. Bluethmann, and S. W. Vernon, "Adherence to adjuvant hormonal therapy among breast cancer survivors in clinical practice: a systematic review," *Breast Cancer Res Treat*, vol. 134, no. 2, pp. 459–78, 2012.

[14] S. Cohen, T. Kamarck, and R. Mermelstein, "A global measure of perceived stress," *J Health Soc Behav*, vol. 24, no. 4, pp. 385–96, 1983.

[15] R. Horne, J. Weinman, and M. Hankins, "The beliefs about medicines questionnaire: The development and evaluation of a new method for assessing the cognitive representation of medication," *Psychology & Health*, vol. 14, no. 1, pp. 1–24, 1999.

[16] G. Ogedegbe, C. A. Mancuso, J. P. Allegrante, and M. E. Charlson, "Development and evaluation of a medication adherence self-efficacy scale in hypertensive african-american patients," *Journal of Clinical Epidemiology*, vol. 56, no. 6, pp. 520–529, jun 2003.

[17] N. Krause and E. Borawski-Clark, "Social class differences in social support among older adults," *The Gerontologist*, vol. 35, no. 4, pp. 498–508, aug 1995.

[18] "Interactive effects of social support and social conflict on medication adherence in multimorbid older adults," *Social Science and Medicine*, vol. 87, pp. 23–30, 6 2013.