PSYCHO-SOCIAL DETERMINANTS AND STRATEGIES FOR FACILITATING ADHERENCE TO A COMPLEX MEDICATION REGIMEN IN CANCER TREATMENT

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ABSTRACT

PSYCHO-SOCIAL DETERMINANTS AND STRATEGIES FOR FACILITATING ADHERENCE TO A COMPLEX MEDICATION REGIMEN IN CANCER TREATMENT

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Medication adherence in individuals taking multiple medications has received little research attention, despite its importance in clinical treatment and its relevance to achieving optimal health outcomes. With the growth of the aging population and prevalence of chronic diseases, adherence to multiple medication regimens has become a critical issue. This project, consisting of three related studies, investigated medication adherence of cancer patients who received an allogeneic hematopoietic cell transplant (alloHCT) and whose conditions require adherence to complex, multiple medication regimens for prolonged periods of time.

The Information-Motivation-Behavioral Skills (IMB) model was the theoretical framework for the study. This model posits that well-informed, highly motivated individuals have better adherence behaviors. In addition to having optimal information and motivation, patients also need to develop the appropriate behavioral skills to maximize the value of information, motivation and aid adherence. Thus, within this framework, the link between information, motivation, and adherence is mediated by behavioral skills. Using the IMB model, the aim of this project was to examine different approaches to facilitating medication adherence after transplant. The first study used a mixed-methods approach to examine the feasibility of using an electronic pillbox for assessing adherence to multiple medications. The second study utilized patient interview data to assess the link between social support and adherence to multiple medications. The third study also used patient interview data to identify adherence determinants and strategies that patients used after transplant.

The results of the first study show that even though some features of the electronic pillbox need to be modified, it is feasible to use it to facilitate medication adherence for patients after transplant. The second study demonstrated the importance of social support from lay caregivers, such as spouse and family members, as well as healthcare providers, for adherence tasks after transplant. Lay caregivers provided emotional and practical support, whereas healthcare providers were the main source of informational and medical support. The third study identified various determinants that facilitated and hindered medication adherence. The study also suggests practical lessons for adherence to multiple medications. Collectively, the findings provide a foundation for developing intervention approaches for this particular patient population.

DEDICATION

For my family, Young Joon Song, Sun Hee Lee & Yae Sam Song

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INTRODUCTION

Medication adherence—taking medications in prescribed amounts and intervals—is important for any individual undergoing medical treatment. Despite the importance of taking medications, patients face challenges adhering, and about half of patients with chronic health conditions do not, resulting in poor health outcomes and greater healthcare costs (Bosworth et al., 2011; Brown & Bussell, 2011; Sabaté, 2003). It is found that adherence is especially challenging for patients with chronic diseases; though these patients have to persistently maintain adherence behavior, their rate of adherence drops dramatically after the first six months of treatment (Osterberg & Blaschke, 2005). Moreover, adherence is especially challenging for patients with multiple medications; studies show that adherence decreases as the number of pills taken increases (Claxton, Cramer, & Pierce, 2001; Pantuzza, Ceccato, Silveira, Junqueira, & Reis, 2017). Since taking multiple medications (more than five) has become more prevalent (Kantor, Rehm, Haas, Chan, & Giovannucci, 2015), it is all the more important to study adherence to multiple medications.

Patients who undergo allogeneic hematopoietic cell transplant (alloHCT) typically must take multiple medications over extended periods of time. Medication adherence is critical for this population, since most potential health risks after transplant, including morbidity, mortality, hospital readmissions, and healthcare costs, can be prevented with proper adherence (Bishop, Rodrigue, & Wingard, 2002; Hoodin, Harper, & Posluszny, 2010). However, due to the complexity of their medication regimens (that often involve dozens of medications) and the extended period of the treatment (especially critical for the first 100 days after hospital discharge), medication adherence is challenging for patients after alloHCT (Tomblyn et al., 2009). Adherence to medication in this patient population is understudied; a recent review of literature, which only covered five studies, found that the rate of adherence for cancer patients with hematopoietic stem cell transplant ranged from 33% to 95% and suggested the need for further research in this area (Morrison, Martsolf, Wehrkamp, Tehan, & Pai, 2017). Another study, examining task distribution between patient and caregiver, found that adherence varies between 19% to 100% depending on the task and who is responsible for completing it, indicating that there is significant variation and complexity in adherence tasks (Posluszny et al., 2018). Therefore, the dissertation research seeks to examine adherence of patients after alloHCT, who need to adhere to multiple medication regimens. The first study seeks to examine the feasibility of using an electronic pillbox for patients after alloHCT to manage and maintain adherence for multiple medications. The second study explores the sources and the role of social support in this sample. Finally, the third study investigates the determinants and practical strategies patients utilize to maintain their adherence.

Problem Statement

Despite the importance of adherence to multiple medications required by some patient populations, it is understudied and remains a challenge. In order to better understand and examine ways to improve adherence to multiple medications for leukemia and lymphoma patients after alloHCT, the following questions were addressed in this study: What is the feasibility of using digital technology for multiple medication regimens, what is the role of social support, and what are the psychosocial determinants and strategies of medication adherence for leukemia and lymphoma patients after receiving allogeneic hematopoietic cell transplant (alloHCT)?

Purpose of the Study

The purpose of this study was to provide a better understanding of adherence to multiple medications for patients with leukemia and lymphoma who received allogeneic hematopoietic cell transplant (alloHCT), and examine factors that are critical for the optimization of medication adherence for their survival.

Specific Aims

The specific aims of this study were to:

1. Conduct an observational study, which will identify the feasibility of using an electronic pillbox, as well as its benefits and limitations.
2. Examine the sources and the role of social support for adherence and the care of patients after transplant.
3. Identify effective strategies of medication adherence using qualitative data.

Theoretical Perspective

This study is based on the Information-Motivation-Behavioral Skills (IMB) model (see Figure 1.1), which is a comprehensive and validated health behavior change framework initially developed for patients undergoing highly active antiretroviral therapy (also known as HAART) (Fisher, Fisher, Amico, & Harman, 2006). According to the IMB model, information, motivation, and behavioral skills relevant to adherence are needed for optimal medication adherence. The adherence information and motivation can be demonstrated through behavioral skills and can influence adherence behavior and, eventually, health outcomes.

Although the IMB model was first designed for preventive health behavior changes in individuals with HIV, its concepts and framework can also be applied to patients with different chronic conditions requiring complex medications, such as diabetes (Mayberry & Osborn, 2014; Osborn & Egede, 2010). Thus, this model also seems to be suitable for explaining medication adherence for patients after alloHCT. Given that the some of the patients after alloHCT have to take at least 24 medications at different scheduled times every day, access to accurate information, positive motivation, and effective behavioral skills are critical predictors of medication intake. Having accurate information about the medication dosage, schedule, and side effects would provide patients with a sense of urgency and help them make more health-conscious decisions. Motivation, which includes having a positive attitude and beliefs and receiving social support,[1] would help them stay positive and maintain adherence behavior. Relevant

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[1] Social support is an especially strong predictor of medication adherence. Previous studies have shown a greater effect of social support on adherence for patients requiring more than one regimen (DiMatteo, 2004).

skills to manage and maintain medication adherence are needed in order to leverage adequate information and motivation in improving adherence.

Each of the three studies that comprise this dissertation focuses on different constructs in the IMB model. Study 1 examines ways to optimize adherence behavior as measured by an electronic monitoring system called the MedMinder (Maya, Massachusetts, USA). According to the IMB model, medication adherence, which is influenced by the three components (Information, Motivation, and Behavioral skills), can be measured by optimal adherence (an arbitrary threshold), proper dosing (taking the correct pills), and adherence levels over time (Fisher et al., 2006). Other studies have found that the use of an electronic pillbox provides the most objective measure of adherence, and that it also enhances adherence behavior (McGillicuddy et al., 2015; Ruddy, Mayer, & Partridge, 2009). Bringing these together, Study 1 examines adherence by observing the use of an electronic pillbox, which can help patients maintain optimal levels of adherence over time. We predict that a sizable subgroup of patients will be able to use the pillbox, and we will describe how many patients are willing to use the pillbox and how frequently and accurately they make use of an electronic pillbox.

Study 2 focuses on social motivation in the motivation component of the IMB model, which concerns perceptions of social support from others (Fisher et al., 2006). We predict that social support plays a significant role for individuals with multiple medications and that different types of support matter. We will describe the sources of support and the types of support received at length.

Finally, Study 3 examines each of the constructs in the IMB model to identify the determinants of and strategies for medication adherence. We will thus describe the determinants and strategies of medication adherence that patients developed and used, which could be also useful for other individuals in malignant health conditions prescribed with multiple medications.

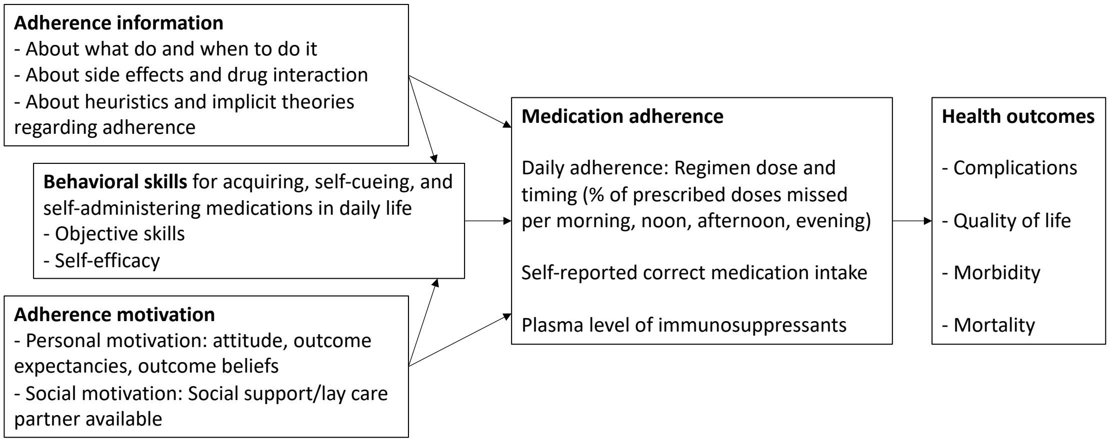

Figure 1.1. The Information-Motivation-Behavioral Skills (IMB) Model. Adherence Information, Motivation and Behavioral Skills determine the level of Medication Adherence and Health Outcomes. Information and Motivation also influence Behavioral Skills, which in turn influence Medication Adherence and Health Outcomes (Fisher et al., 2006)

Significance of the Study

Adherence to medication remains a significant challenge in the treatment and management of chronic diseases and is especially problematic for patients who must take multiple medications (Allegrante, Wells, & Peterson, 2019; Bosworth, 2010). Two secular trends have made this challenge even more salient for healthcare: 1) life expectancy has increased, and 2) more people with chronic conditions are now prescribed multiple medications (Cross, Elliott, & George, 2016; Kantor et al., 2015; Patton et al., 2017). Moreover, medication adherence of patients who receive alloHCT is understudied despite its widespread adoption among more than 8,000 patients who receive alloHCT in the United States alone for cancer treatment, and the number continues to increase (D'Souza, Pasquini, & Zhu, 2016). While the survival rate of patients after alloHCT has improved over time with technological and other treatment advances, patients are still exposed to high risks of late complications, including the graft-versus-host disease (GVHD) that can result in death. Thus, a deeper understanding of the transplant survivors is needed (Gooley et al., 2010; Hashmi, Carpenter, Khera, Tichelli, & Savani, 2015; Majhail et al., 2013). Adherence to their prescribed medications can help reduce the risks of potential complications and side effects, but the regimen becomes increasingly complex with multiple medications, usually managing at least 18 medications with 24 different types of pills (Tomblyn et al., 2009). Thus, a study of this particular patient population may offer useful insights into multiple medications adherence.

Definition of Terms

Allogeneic Hematopoietic Cell Transplant (alloHCT): A type of cell transplant, which is commonly used for patients with leukemia and lymphoma cancer, where the person receives new and healthy blood-forming stem cells from a donor, who is genetically non-identical, but very similar, such as brothers and sisters (American Cancer Society, 2017). There are higher chances of psychological distress, physical side effects and complication, such as graft-versus-host disease, and other infections after the transplant since the patient is receiving blood-forming stem cells from a foreign donor (Foster et al., 2005; Hoodin et al., 2010).

Medication Adherence: The extent to which patients follow provider recommendations about day-to-day treatment with respect to the timing, dosage, and frequency (Bosworth et al., 2011). According to the IMB model, medication adherence is influenced by the information, motivation, and behavioral skills that are relevant to adherence, and it can be measured by optimal adherence (95% or above), proper dosing (taking the correct pills), and adherence levels over time (Fisher et al., 2006).

MedMinder (Maya, Massachusetts, USA): Similar to the functions of microelectronic monitoring systems (MEMS), the MedMinder is also an electronic medication pillbox, which transmits real-time data of pillbox activities (in hour, minute and seconds), including cap opening times and date, directly to the MedMinder central system using cellular signals. Patients, caregivers, and healthcare providers can monitor the medication adherence activities. This is the more suitable device for patients with multiple medications because one MedMinder pillbox carries 28 separate compartments that are divided into four different times of a day (morning, afternoon, evening, and night) for seven days (Monday to Sunday). It has functions of sending notifications and alarms at the appropriate times of dosage.

Delimitations

The delimitations of the study included:

1. The data were solely collected at a hospital in an urban area and it was a small sample study. Therefore, it is not certain how generalizable the findings are to the overall population.
2. About half of the leukemia and lymphoma patients at the hospital came from a minority background, but only English and Spanish speaking participants are

included in the study. There is a possibility that some were excluded from the study due to language difficulties.

Use of Human Subjects and Ethical Considerations

All study materials and protocols were approved by the respective Institutional Review Board (IRB) at the institutions related to the study, including Teachers College, Columbia University. Relevant information regarding the study was shared with participants, and they were asked to sign a written informed consent prior to participation. Electronic data were stored in a secured computer with a passcode, and the other documented data were placed into individual research participant folders, which are stored in a locked file cabinet in the office of the study institution. Only study personnel had the access to the stored files (both paper and electronic). All folders and data used for data analysis for individual participants were identified with unique patient numbers. No personal identification information was or will be published or disclosed to third parties without prior written consent of the participant. Patients were informed that they could skip questions and that they could also withdraw from the study at any time.

The dissertation project presented no potential risks or harms or co-interventions for the participants; however, in cases of unexpected emergency, study staff were available throughout the study period to respond accordingly. Participation in the study was thought to benefit patient participants in several ways: facilitating easier intake of medications on time; becoming more knowledgeable and informed about the importance of medication adherence; and becoming more motivated to make changes in their adherence behavior.

Organization of the Dissertation

This chapter has provided an overview of the study and its significance in the effort to better understand adherence to multiple medications in patients who have undergone alloHCT. The next three chapters (Chapter II, III, and IV) will present the three different studies that comprise the dissertation. The first study (Chapter II) will examine the feasibility of using electronic monitoring systems for multiple and complex medication regimens. The second study (Chapter III) investigates the sources and the role of social support. And the third paper contained in Chapter IV examines the determinants and practical strategies of medication adherence that patients used. Finally, Chapter V concludes with a general discussion of the overall contribution these studies make to understanding medication adherence among patients who are taking multiple medications.

References

Allegrante, J. P., Wells, M. T., & Peterson, J. C. (2019). Interventions to support behavioral self-management of chronic diseases. *Annual Review of Public Health*, *40*(1), null. https://doi.org/10.1146/annurev-publhealth-040218-044008

American Cancer Society. (2017). Stem cell transplant for chronic myelomonocytic leukemia. Retrieved June 6, 2018, from https://www.cancer.org/cancer/chronic-myelomonocytic-leukemia/treating/stem-cell-transplant.html

Bishop, M. M., Rodrigue, J. R., & Wingard, J. R. (2002). Mismanaging the gift of life: Noncompliance in the context of adult stem cell transplantation. *Bone Marrow Transplantation*, *29*(11), 875. https://doi.org/10.1038/sj.bmt.1703523

Bosworth, H. B. (2010). Medication adherence. In *Improving patient treatment adherence* (pp. 68–94). Springer, New York, NY. https://doi.org/10.1007/978-1-4419-5866-2_4

Bosworth, H. B., Granger, B. B., Mendys, P., Brindis, R., Burkholder, R., Czajkowski, S. M., … Granger, C. B. (2011). Medication adherence: A call for action. *American Heart Journal*, *162*(3), 412–424. https://doi.org/10.1016/j.ahj.2011.06. 007

Brown, M. T., & Bussell, J. K. (2011). Medication adherence: WHO cares? *Mayo Clinic Proceedings*, *86*(4), 304–314. https://doi.org/10.4065/mcp.2010.0575

Claxton, A. J., Cramer, J., & Pierce, C. (2001). A systematic review of the associations between dose regimens and medication compliance. *Clinical Therapeutics*, *23*(8), 1296–1310. https://doi.org/10.1016/S0149-2918(01)80109-0

Cross, A. J., Elliott, R. A., & George, J. (2016). Interventions for improving medication-taking ability and adherence in older adults prescribed multiple medications. *Cochrane Database of Systematic Reviews, 10*. John Wiley & Sons, Ltd. https://doi.org/10.1002/14651858.CD012419

DiMatteo, M. R. (2004). Social support and patient adherence to medical treatment: A meta-analysis. *Health Psychology*, *23*(2), 207–218. https://doi.org/10.1037/0278-6133.23.2.207

D'Souza, A., Pasquini, M., & Zhu, X. (2016). CIBMTR summary slides - HCT trends and survival data. Retrieved January 26, 2018, from https://www.cibmtr.org/ReferenceCenter/SlidesReports/SummarySlides/Pages/index.aspx

Fisher, J. D., Fisher, W. A., Amico, K. R., & Harman, J. J. (2006). An information-motivation-behavioral skills model of adherence to antiretroviral therapy. *Health Psychology*, *25*(4), 462–473. https://doi.org/10.1037/0278-6133.25.4.462

Foster, L., Mclellan, L., A. Rybicki, L., A. Sassano, D., Hsu, A., & Bolwell, B. (2005). Survival of patients who have undergone allogeneic bone marrow transplantation. *Journal of Psychosocial Oncology, 22*(2), 1-20. https://doi.org/10.1300/J077v22n02_01

Gooley, T. A., Chien, J. W., Pergam, S. A., Hingorani, S., Sorror, M. L., Boeckh, M., … McDonald, G. B. (2010). Reduced mortality after allogeneic hematopoietic-cell transplantation. *New England Journal of Medicine*, *363*(22), 2091–2101. https://doi.org/10.1056/NEJMoa1004383

Hashmi, S., Carpenter, P., Khera, N., Tichelli, A., & Savani, B. N. (2015). Lost in transition: The essential need for long-term follow-up clinic for blood and marrow transplantation survivors. *Biology of Blood and Marrow Transplantation*, *21*(2), 225–232. https://doi.org/10.1016/j.bbmt.2014.06.035

Hoodin, F., Harper, F. W. K., & Posluszny, D. M. (2010). Psychological care of adult allogeneic transplant patients. In H. M. Lazarus & M. J. Laughlin (Eds.), *Allogeneic Stem Cell Transplantation* (pp. 619–656). Humana Press. https://doi.org/10.1007/978-1-59745-478-0_35

Kantor, E. D., Rehm, C. D., Haas, J. S., Chan, A. T., & Giovannucci, E. L. (2015). Trends in prescription drug use among adults in the United States from 1999-2012. *JAMA*, *314*(17), 1818–1830. https://doi.org/10.1001/jama.2015.13766

Majhail, N. S., Tao, L., Bredeson, C., Davies, S., Dehn, J., Gajewski, J. L., … Kuntz, K. M. (2013). Prevalence of hematopoietic cell transplant survivors in the United States. *Biology of Blood and Marrow Transplantation*, *19*(10), 1498–1501. https://doi.org/10.1016/j.bbmt.2013.07.020

Mayberry, L. S., & Osborn, C. Y. (2014). Empirical validation of the Information–Motivation–Behavioral Skills model of diabetes medication adherence: A framework for intervention. *Diabetes Care*, *37*(5), 1246–1253. https://doi.org/10.2337/dc13-1828

McGillicuddy, J. W., Taber, D. J., Mueller, M., Patel, S., Baliga, P. K., Chavin, K. D., … Treiber, F. A. (2015). Sustainability of improvements in medication adherence through a mobile health intervention. *Progress in Transplantation*, *25*(3), 217–223.

Morrison, C. F., Martsolf, D. M., Wehrkamp, N., Tehan, R., & Pai, A. L. (2017). Medication adherence in hematopoietic stem cell transplantation: A review of the literature. *Biology of Blood and Marrow Transplantation*, *23*(4), 562–568. https://doi.org/10.1016/j.bbmt.2017.01.008

Osborn, C. Y., & Egede, L. E. (2010). Validation of an Information–Motivation–Behavioral Skills model of diabetes self-care (IMB-DSC). *Patient Education and Counseling*, *79*(1), 49–54. https://doi.org/10.1016/j.pec.2009.07.016

Osterberg, L., & Blaschke, T. (2005). Adherence to medication. *New England Journal of Medicine*, *353*(5), 487–497. https://doi.org/10.1056/NEJMra050100

Pantuzza, L. L., Ceccato, M. das G. B., Silveira, M. R., Junqueira, L. M. R., & Reis, A. M. M. (2017). Association between medication regimen complexity and pharmacotherapy adherence: A systematic review. *European Journal of Clinical Pharmacology*, *73*(11), 1475–1489. https://doi.org/10.1007/s00228-017-2315-2

Patton, D. E., Cadogan, C. A., Ryan, C., Francis, J. J., Gormley, G. J., Passmore, P., … Hughes, C. M. (2017). Improving adherence to multiple medications in older people in primary care: Selecting intervention components to address patient-reported barriers and facilitators. *Health Expectations*, 1–11. https://doi.org/10.1111/hex.12595

Posluszny, D. M., Bovbjerg, D. H., Agha, M. E., Hou, J.-Z., Raptis, A., Boyiadzis, M. M., … Dew, M. A. (2018). Patient and family caregiver dyadic adherence to the allogeneic hematopoietic cell transplantation medical regimen. *Psycho-Oncology*, *27*(1), 354–358. https://doi.org/10.1002/pon.4393

Ruddy, K., Mayer, E., & Partridge, A. (2009). Patient adherence and persistence with oral anticancer treatment. *CA: A Cancer Journal for Clinicians*, *59*(1), 56–66. https://doi.org/10.3322/caac.20004

Sabaté, E. (2003). *Adherence to long-term therapies: Evidence for action*. Geneva: World Health Organization.

Tomblyn, M., Chiller, T., Einsele, H., Gress, R., Sepkowitz, K., Storek, J., … Boeckh, M. A. (2009). Guidelines for preventing infectious complications among hematopoietic cell transplantation recipients: a global perspective. *Biology of Blood and Marrow Transplantation*, *15*(10), 1143–1238.

Chapter II

ELECTRONIC MONITORING OF ADHERENCE TO MULTIPLE MEDICATIONS: PROMISES AND CHALLENGES

Abstract

Background: An electronic pillbox can serve as a tracking device for adherence to a complex medication regimen. Blood cancer patients receiving an allogeneic hematopoietic cell transplant (alloHCT), typically prescribed with multiple pills, can benefit from it. Their medication adherence plays a critical role in post-transplant survival, as it can help limit severe side effects and toxic drug interactions. However, existing studies report a wide range of adherence rates.

Objective: The objective of this mixed-methods study was to test the feasibility of using an electronic pillbox for tracking a multiple-medication regimen in the first 180 days at home following an alloHCT.

Methods: Patients after alloHCT (n = 33, 45.5% female, age: M = 54.18, 45.5% ethnic minority) received an electronic pillbox. Most patients (n = 28, 84.8%) used the pillbox for up to 180 days after the hospital discharge and their signal transmission rate was calculated. Data were lost for one patient, so total adherence was calculated for 27 individuals (81.8%). Patients (*n* = 28) were also interviewed about their experiences using the electronic pillbox.

Results: Most patients used their pillbox immediately after their discharge and continued using it beyond 180 days. The average adherence score was 55%, and there was large variability in signal transmission rates. Based on the interviews, patients reported ease of use and benefits of the electronic pillbox, but they also reported challenges, such as the size of the box and limited battery life. The paper discusses the promise associated with medication monitoring using an electronic pillbox.

Conclusion: It is feasible to use an electronic pillbox for patients taking multiple medications. Overall, patients had a positive experience using an electronic pillbox. However, a more user-friendly device would have great potential for real-time interventions to facilitate adherence to multiple medication regimens.

Keywords: allogeneic hematopoietic cell transplant; cancer; electronic medication monitoring; electronic pillbox; medication adherence; multiple medications.

Introduction

Adherence to multiple medications is an increasingly important issue for patient care due to aging populations and the higher prevalence of chronic conditions and multimorbidity (Buttorff, Ruder, & Bauman, 2017; Sabaté, 2003; van Oostrom et al., 2016; Wu & Green, 2000). A majority of adults in the US (59%) take at least one prescription medication, and 15% take five or more (Kantor, Rehm, Haas, Chan, & Giovannucci, 2015). However, adherence is problematic; patients take only to half of the medications as prescribed, and the rate of adherence for patients with chronic conditions varies (Costa et al., 2015; Osterberg & Blaschke, 2005; Sabaté, 2003). As a meta-analysis of 95 clinical trials found, 40% of the patients stopped taking the medication under study, undermining the validity of the trial results (Blaschke, Osterberg, Vrijens, & Urquhart, 2012).

Taking multiple medications remains an understudied challenge (Inauen et al., 2017; Pasina et al., 2014). The complexity of the medication regimen (as measured by the number of different medications taken daily and/or the number of doses per day) was associated with decreased adherence in several reviews (Costa et al., 2015; Ingersoll & Cohen, 2008; McDonald, Garg, & Haynes, 2002; Richter, Anton, Koch, & Dennett, 2003), including in patients with blood cancer (Hall et al., 2016). Patients with blood cancer receiving an allogeneic hematopoietic cell transplant (alloHCT) are a good test case for studying multiple medication intake. They are routinely prescribed at least 24 pills per day when they are discharged from the hospital (Freifeld et al., 2011; Neumann, Krause, Maschmeyer, Schiel, & von Lilienfeld-Toal, 2013; Tomblyn et al., 2009).

Medications must be taken at carefully timed intervals to avoid toxic drug interactions. Furthermore, medication adherence plays a critical role in post-transplant survival because the medications prevent transplant rejection and severe side effects. However, adherence among alloHCT patients has received scant attention: The few available studies found greatly varying medication adherence rates ranging from 33% to 95% which could explain some variation in alloHCT patients' survival (Morrison, Martsolf, Wehrkamp, Tehan, & Pai, 2017; Posluszny et al., 2018).

Assessment of adherence to multiple medication regimens is challenging (Inauen et al., 2017). Various ways to measure adherence include: self-reports, pill counts by healthcare providers, pharmacy records, serum/urine drug levels, and an electronic monitoring system (Farmer, 1999; Inauen et al., 2017; Williams, Amico, Bova, & Womack, 2013). Though not without disadvantages, an electronic monitoring system, such as an electronic pillbox, allows for a more objective and precise real-time assessment by transmitting data signals, and it can be easily integrated into a patient's daily life (Inauen et al., 2017; McGillicuddy et al., 2013). Only recently have studies integrated these devices into clinical care, e.g., for hypertension, HIV, kidney transplant, and diabetes (Davidson et al., 2015; Haberer et al., 2012; McGillicuddy et al., 2013; Welch, Balder, & Zagarins, 2015). This study sought to assess the feasibility of using an electronic pillbox to monitor adherence to multiple medications in patients after alloHCT in the first six months after hospital discharge. In addition, the study addresses the feasibility of recruiting and retaining patients and lowering barriers to the use of the electronic pillbox.

Methods

As part of a larger transplant study, individuals with leukemia and lymphoma cancers were followed for 180 days after their first hospital discharge. We tracked patients' electronic pillbox use through real-time data transfer and also conducted semi-structured interviews to learn about their experiences. The study was approved by the Institutional Review Board of Columbia University, including Teachers College, and the hospital from which the data were collected. All participants signed a written informed consent prior to participating in the study. The study referred to the reporting guidelines for qualitative studies and mixed methods (Creswell, Klassen, Plano, & Smith, 2011; O'Brien, Harris, Beckman, Reed, & Cook, 2014; Tong, Flemming, McInnes, Oliver, & Craig, 2012; Tong, Sainsbury, & Craig, 2007) and especially followed COREQ (see Appendix C for responses to all items of COREQ) for reporting the qualitative results (Tong et al., 2007).

Setting and Participants

The study was conducted at a renowned hospital located in an urban area. The location of the study site allowed diverse individuals to receive treatment. Eligible patients were adults with leukemia or lymphoma cancers who received an alloHCT at the hospital. Patients were eligible for the study if they were 18 years or older and spoke and read English, Spanish or Mandarin. Participation in the study was fully voluntary and was conducted only with eligible patients who had formally agreed through written informed consent to participate.

Measures

Medication monitoring using electronic pillbox. The electronic pillbox used in this study was a wireless device (MedMinder, Maya, Inc, Needham, MA) with an internal cellular modem. It contained 28 compartments, suitable for up to 4 doses per day for 7 days. Each compartment contained a removable cup. The pillbox transmitted a real-time signal to MedMinder's server when the cup was removed. The electronic pillbox had to be switched on in order to transmit data. Due to limited battery time (approximately 30 minutes), the device had to remain plugged into a regular 110V outlet for continuous signal transmission. As this was an observational study, the reminder functions of the system were not activated. Electronic monitoring system is known to be a novel and objective method of measuring adherence (Ruddy, Mayer, & Partridge, 2009).

Interviews. The interviews were developed in order to best capture patients' overall experience of taking multiple medications and their use of the pillbox using a narrative approach. A theory-driven interview guide was developed by the principal investigator, who is an expert in health psychology and has conducted many studies in this area. The interview guide covered different areas related to adherence after hospital discharge, including the use of electronic pillbox. The last section (Part 7) of the interview specifically asked about their experience using their pillbox. The exact wording of the questions is included in Appendix A. The interview guideline also contained probing questions to facilitate gathering of further information from the participant. To ensure the quality of the interviews, interviewers were trained by the principal investigator; the interview questions were pilot tested during role-play interviews prior to conducting actual interviews with patients, and interviewers were also allowed to shadow interviews before they conducted an actual one. There was no relationship between researchers and participants prior to the study. All interviewers were female, and they hold either a bachelor's or master's degree in social sciences, public health or health sciences.

Two independent coders analyzed seven randomly selected interviews (25% of the whole sample) using the NVivo to calculate inter-rater reliability (agreement between coders that each relevant theme had been mentioned across interviews). Kappa coefficient for pillbox benefits was 0.71, and the equivalent figure for pillbox challenges was 1.00, both exceeding 0.70, which indicates satisfactory inter-rater reliability.

Procedures

Patients were recruited during pre-transplant outpatient visits prior to admission for transplant or during the transplant hospitalization. Patients consenting to the study received an electronic pillbox pre-tested for functionality and were trained on its use as part of their discharge education plan. Per routine pre-discharge policy, all medications (dose, schedule, side effects, potential interactions) were reviewed with the patient by a pharmacist or a nurse. Electronic pillboxes were filled with medications and given to the patient at discharge. Patients were asked to use the electronic pillbox for 180 days and to keep the device plugged in at all times. The research team monitored pillbox signals remotely and approached patients at their routine hospital visits if their pillboxes were not working. If the pillbox remained plugged in but did not transmit a signal, the research team replaced the defective pillbox. Trained research assistants interviewed patients in pairs, one taking notes and recording, and the other conducting the interview, at 3 and/or 6 months after discharge from the hospital. Interviews were conducted face-to-face in the hospital while patients were waiting for their hospital appointments or through the phone if they were not able to make it to the hospital because of their physical condition. In some interviews, the caregivers were present with the participants as they accompanied the patients for hospital appointments. The interview lasted about 40 to 60 minutes. All interviews were audio recorded and transcribed, with personal identification information removed to protect the privacy of participants.

Data Analysis

Time to initiation of pillbox use. Signal transmission in the first 180 days after hospital discharge was analyzed, excluding days when the patient was readmitted to the hospital and medication was under clinical supervision.[1] The research team checked the pillbox status daily on the device manufacturer's website and coded days when at least one signal was transmitted. The initiation period of the pillbox was calculated from the first full day after the patient was discharged home to the first signal transmission.

Period and rate of pillbox signal transmission. The period of signal transmission, when the device was switched on, was calculated based on the number of days between first and last signal transmission date. Then we calculated signal transmission rates as percentages (the number of non-hospitalized days with signal transmission as a percentage of the total number of non-hospitalized days). Signal transmission period and the rate of signal transmission of each pillbox were monitored to examine whether the pillbox functioned well, and as well as whether patients kept the pillbox on and for how long.

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[1] For patients who returned the pillbox during the study, we limited the calculation until that day and for patients who passed away during the study, we limited the calculation until the day before they passed away.

Duration of pillbox cap opening. The duration of pillbox cap openings (number of days between first and last pillbox opening) were counted based on the days when there was a signal transmission. It was examined to see whether the pillbox was actually in use in real time when the pillbox was kept on. We also calculated adherence score based on this measure.

Adherence. Based on the assumption that patients open the pillbox to take their medications, we used pillbox cup openings to measure adherence. This is the most common method of measuring adherence using an electronic device. Adherence for non-hospitalized days during the study period was calculated from the initiation of pillbox use (first signal transmission), following recommendations by Vrijens and colleagues (2012). The prescribed multiple medication regimen specified at least four daily doses (e.g., 8 am, 2 pm, 8 pm, 10 pm). We calculated adherence for each patient based on the number of pillbox cap openings for up to 180 days after the initiation of treatment. Implementation was measured by first dividing each non-hospitalized day into two-hour windows, counting from 4:00 am to 3:59 am the next day to allow for late-night doses. We then checked each two-hour window to determine whether there was at least one cap opening. For each day, we counted the number of windows with at least on cap opening and divided it by 4 to calculate a daily adherence score.[2] The daily adherence scores across the study period were used to arrive at the average adherence score for each patient (the sum of daily adherence scores/the number of days in the study period).

Interviews. All transcripts were read carefully before pillbox-related quotes were extracted. The codebook that identified themes with definitions and examples was

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[2] We limited the number of windows with cap openings to 4, even though 21 patients exceeded this number at least once. We did so under the assumption that the number of doses prescribed to patients would realistically not exceed 4.

developed under the supervision of the principal investigator. For this study, coding was focusing on the two big themes: the benefits and challenges of using the electronic pillbox because we wanted to examine what participants found useful and challenging. Using content analysis, two independent coders categorized the extracted quotes into the two different themes: pillbox benefits and challenges. By further reviewing the quotes, the two coders categorize the quotes into different themes within benefits and challenges. Coding was initially done on excel, but also on NVivo 11 for more systematic analysis.

Results

Characteristics of Patients

Participants (*n* = 33, 45.5% female, age: *M* = 54.18) had different ethnic backgrounds, with almost half of the sample (45.5%) reporting an ethnic minority background (Hispanic: 18.2%, Asian: 15.2%, African-American: 9.1%, Other: 3.0%) and the other half Non-Hispanic White background (54.5%). Most patients who used the pillbox participated in the interviews (*n* = 28) with nearly identical sociodemographic makeup (46.4% female, age: *M* = 53.97; ethnic minority group members: 46.4%).

Feasibility of Using an Electronic Pillbox in Patients After AlloHCT

During the study period (08/15/2012 – 07/15/2014), 84 adult patients received an alloHCT at the study site, which has an established cell transplant program. Some patients (*n* = 7, 8.3%) were ineligible for participation because of language barriers (all materials were available in English, Spanish, and Mandarin). The recruitment rate was high: Of the eligible patients (*n* = 77, 91.7%), about half (*n* = 38, 49.4%) agreed to participate and signed consent. Of the consented patients (*n* = 38), five patients did not participate in the data collection: One patient died prior to discharge; one patient had a complicated recovery with repeated hospitalizations; and three patients withdrew from the study before discharge citing the size of the box and concerns about using it at home.

The remaining patients (*n* = 33, 86.8%) each received an electronic pillbox. Of these, we did not detect any signal transmission from five patients (one patient used the pillbox without plugging it in, one was quickly readmitted to the hospital and passed away, two patients found it too cumbersome and decided not to use it after they received a pillbox, and one patient did not state a reason but chose not to use it). Most patients (*n* = 28, 84.8%) used the pillbox as instructed and kept it plugged in to allow signal transmission. However, a technical problem resulted in loss of data for one patient, so the adherence rate was calculated based on 27 (81.8%) patients. The flowchart below illustrates the patient recruitment and data collection (see Figure 2.1).

Pillbox Use and Signal Transmission

The first pillbox signal for most patients (*n* = 25) was transmitted on the first day after patients took the pillbox home (initiation period: *M* = 0 days). The initiation period was calculated counting from the date of taking the pillbox home to the first signal transmission. A few patients (*n* = 3) took longer to start using the pillbox after they received it and took it home (*M* = 27 days). The period of pillbox signal transmission was calculated based on the number of days between the first and the last signal transmission date. The median number of days we received signals from patients was 196 with an interquartile range of 111 (IQR = 265 – 154). We received signal transmission from many patients beyond the study period. The average among these patients was 296 days (*n* = 18/28 with a total of 5,328 days). The maximum number of signal transmission days was 503.

The duration of actual pillbox use, which takes the difference between the first day of pillbox opening and the last day, was calculated to examine whether patients actively used the pillbox and for how long. The median number of days on which patients opened the pillbox was 180 with an interquartile range of 108 (IQR = 224 – 116). 12 of the 18 patients continued opening the pillbox beyond the 180 days (with a total of 2,829 days and an average of 236 days). The maximum number of pillbox cap opening days was 326. The box plot in Figure 2.2 provides an overview of the pillbox use, including the interquartile ranges of signal transmission and pillbox cap opening days. It also shows the overall distributions of the initiation period, period of signal transmission and the duration of pillbox use using box plots. For analyses of signal transmission and adherence, we capped discontinuation at 180 days after the first transmission.

Among the patients who used an electronic pillbox (*n* = 28), we found high variability in signal transmission rates ranging from 6-100% with an average of 68.1%. There were eight patients (28.6%) with transmission rates below 50% and 20 patients (71.4%) with higher than 50%. Among the patients who exceeded 50% of signal transmission rates, eleven of them (11 of 20) had high transmission rates between 90-100% (see Figure 2.3).

Adherence Rate

We calculated the adherence score (*n* = 27) based on the first 180 days after first pillbox use when signal transmission was active. The average adherence score was 2.2 (55%) out of 4 with a median of 2.44 (see Figure 2.4). This means that patients, with the option to open their pillbox caps at least four different times each day, actually did so 2.2 times on average. Figure 2.5 shows pillbox cap openings of two patients with high signal transmission rates. Both of them consistently used the pillbox, mostly in the morning and evening to night. There is an observable gap for P35 when the patient was readmitted to the hospital.

Patient-Reported Experiences with the Pillbox

Most of the patients who received the pillbox (*n* = 28 of 33) participated in the interview. Interviews from five patients were missing: three patients were deceased, one patient was unavailable, and the other was too ill to participate in the interview (see Figure 2.1). Patients described their experiences of using the pillbox. Although they described some difficulties, their experiences were positive overall. The major themes are summarized as benefits and challenges associated with an electronic pillbox.

Benefits of using an electronic pillbox. Common benefits discussed by patients were ease of use and integration into everyday life, pill organization and storage, memory facilitation, and reminders for refills and dosage.

Ease of use and integration into everyday life. Patients were asked about ease of use and integrating the pillbox into their daily lives. Some patients (*n* = 8/28, 28.6%) experienced no issues with the pillbox and found it easy to use. Patients appreciated the layout of 28 small containers, which reminded them to take medications four times a day for seven days. “I like the way it was broken up into times. Rather than just morning, evening, and night. That I liked.” (P40, age 57, male). Other patients (*n* = 4/28, 14.3%) explicitly mentioned that they liked the removable containers. Patients were able to take the container from the pillbox and turn it upside down so that medication fell into their palms, rather than reaching into the pillbox. With the little cup, they could carry their medications between rooms. For example, one patient reported: “You could take the container out. [It is] easy to take pills out.” (P01, age 66, male). Another patient reported: “I liked the canisters because I was able to take them out.” (P38, age 64, female). Moreover, though the others did not verbalize, some patients (*n* = 4/28, 14.3%) specifically mentioned they are content with the size of the removable cups.

Patients commonly reported keeping their pillbox in a central location at home, most frequently the kitchen (*n* = 11/28, 39.3%), bedroom (*n* = 8/28, 28.6%), or living room (*n* = 3/28, 10.7%). Some patients reported multiple locations for different doses (*n* = 6/28, 21.4%). Its design allowed patients to integrate the pillbox into their daily lives. One patient mentioned,

> (…) the pillbox design is pretty simple. It is elegant so…it doesn’t look like it’s a something that reminds you that it’s medication, so psychologically when you’re looking at it you wouldn’t mind having it on display. (P20, age 50, male)

Many patients (*n* = 13/28, 46.4%) reported refilling pillboxes once a week, typically on weekends (*n* = 7/28, 25.0%). For example, one patient reported,

> I’ve been pretty good about that because the weekly, putting [medications] in the pillbox every week gives me some structure, so I know which ones I’m going to run out of. (P35, age 65, female)

However, other patients may not have reported the frequency of refills accurately. For example, P08 (age 53, male), who was interviewed in the presence of his wife, reported: “Yes, I always refill my box on Sunday, and I always take my medicine.” His wife interrupted,

> No, you don’t. He fills the box too often. I tell him not to refill the box until the end of the week. If compartment is empty, then he [will] know [whether he took them or not]. [But] he will refill it right after he takes it and when he goes back then he will forget if he took them.

Pill organization and storage. Patients (*n* = 10/28, 35.7%) reported that they used the pillbox as a place to store medications. When the patients were discharged from the hospital, they were provided with 18 or more pill bottles, a list of medications, and daily schedules of dosage. The multiple-medication schedule in this population is complex, and it took most patients and caregivers time and effort to understand it. Having a pillbox that laid out the appropriate medication for the week eased patient burden, minimized potential for error, and allowed patients time for other activities. For example, one mentioned,

> It was nice to have the medication lined up for the whole week. I liked the layout of it and I knew that once I filled it each week I was getting my medication I wasn't making a mistake, so I found it very good for that. (P38, age 64, female)

Another reported,

> I like it, I think it helps me get organized. You know it's visual, so you can see things. It's yeah, it's good to be able to see everything spread out. (P35, age 65, female)

Memory facilitator. Patients (*n* = 10/28, 35.7%) found that the pillbox helped them remember to take their medication and provided them with information on whether or not they had taken their medications. One reported,

> That if I'm not sure every now and then and say did I take that or not? You know did I take that 2 o'clock magnesium tablet and if I have the pillbox and if I have everything set up for the week then I'd be able to look in the pillbox and see if it is empty or not. (P28, age 59, male)

Another reported,

> Even the little green light, you can't miss that. Like I say, honestly I don't forget to take my medication but sometime even if I neglect it so every time I come to the room and I see that light, I say okay that's something that have to do with medication. That help[s] me. (P22, age 35, female)

Recognizing the need for refills in time. Filling the pillbox with one week of medications helped patients recognize when refills were needed (*n* = 8/28, 28.6%). This task is important in managing multiple medications that run out at different times. For example, a patient, whose husband helped with managing her medications reported: "[My] husband orders pills. When some are low on Sundays, he calls the pharmacy and gets refills." (P07, age 56, female).

Potential for reminder systems. The current study was designed as an observational feasibility study rather than an intervention study, so the built-in reminder functions such as flashing lights, acoustic alarms, text messages and calls were not activated. Yet, patients (*n* = 6/28, 21.4%) commented that such features would be useful: "Oh I needed to have something (…) an alarm to remind me of the time." (P35, age 65, female).

Challenges of using an electronic pillbox. Patients also encountered several challenges, such as the pillbox's size, lack of personalization, and issues with the charging cord and wireless connection.

Size and portability of the pillbox. The large size of the pillbox was found to be a challenge (*n* = 9/28, 32.1%). A patient reported,

> It's hard to relocate my pillbox to where it used to be because other items have (…) cluttered [in] that space and I just haven't had time to organize. It just became a little difficult to use the pillbox. (P19, age 46, male)

Another patient mentioned: "(…) the pillbox is kind of big and heavy, so I wish they will have a smaller one." (P29, age 63, Female).

Portability was also mentioned as a challenge (*n* = 6/28, 21.4%).

> Sometimes I skip just because I'm not around, but not intentionally. Or sometimes I just forget or go past the time. I'm not always at home and everything, and this pillbox is pretty big and I can't bring it everywhere. (P20, age 50, male)

Another patient reported: "And it's too big to take anywhere with you, you know? I mean like if you're going anywhere." (P40, age 57, male). Frequent follow-up visits to the hospital are required for these patients after transplant to monitor their condition. Appointments may take several hours, often overlapping with medication doses. When patients were recovering and went back to work and travel, they found it difficult to use the pillbox. Only one patient (*n* = 1/28, 3.6%) mentioned that he carried the pillbox wherever he went, and many (*n* = 11/28, 39.3%) mentioned carrying the pills only, emphasizing the need for portability. We observed patients carrying the pillbox in large bags or plastic bags during clinic appointments. Other patients resorted to "pocket-dosing": "So in the morning I'll separate all of them, put it in the pillbox then I'll take the morning pills. Then I just shove it in my pocket and go about my day." (P40, age 57, male).

Number and size of cups for medication doses. Patients often requested a smaller pillbox, yet also enough space for their multiple-medication regimens. Although most patients found the removable cups to be generously sized, some found them to be too small (*n* = 4/28, 14.3%). The pillbox currently provides four cups per day, labeled as Morning, Noon, Afternoon, and Evening, but sometimes patients have to take more than four doses per day. Some (*n* = 5/28, 17.9%) patients commented that adding more cups would be useful for managing their medications. For example, one reported: "Pillbox is [too] small to fill it up, [it needs] more variety, [and] more slot[s]." (P11, age 71, female). Another reported changes in his medication regimen,

> My pills have fit in the compartments. The complication is that sometimes [members of my treatment team] add meds that don't fit in the 4 periods. Sometimes I have 6 periods. Pills that I can't fit in the pillbox. Late morning pills or late afternoon pills, if required, have to stay outside the pillbox. (P19, age 46, male)

One even suggested using two: "It would have been better to have two sets." (P25, age 66, male).

Medications that cannot be stored in the pillbox. The current device does not offer a system to accommodate medications that do not fit in the removable cups, such as liquid medications or other dosing regimens such as powder packets, making it more difficult for patients to remember those medications (*n* = 3/28, 10.7%). A patient reported: "I had 2 liquids, you can't put it in the box, but you have to be aware that you have to take it." (P13, age 67, male). Another reported: "I take [a liquid medication] but I couldn't really utilize it for the pillbox because it was in liquid form. So that's another thing about the pillbox that I didn't like." (P20, age 50, male).

Power source, battery life, and wireless signal. Connecting the pillbox to a constant power source and wireless signal proved to be a challenge for patients (*n* = 5/28, 17.9%). The device had a short battery life of 30 minutes, so constant charging was necessary. When a patient was asked what he did not like about the pillbox, he answered: "Battery stopped working." (P20, age 50, male). The short battery life limited the patients' ability to move the pillbox to locations where an electrical outlet was not available. "Yes with traveling [I had an issue with keeping the box plugged in]." (P10, age 48, Male). Some patients (*n* = 3/28, 10.7%) struggled to keep a constant Internet connection, as the pillbox did not detect wireless signals. "I think my signal wasn't good for everybody else. It seems like my signal kept going in and out." (P38, age 64, female).

Discussion

This study demonstrated the feasibility of using an electronic medication monitoring device with cancer patients taking multiple medications. The recruitment rate was high, with one in two eligible patients participating. Most of the consented participants used the pillbox as instructed, allowing for signal transmission and remote monitoring of adherence. However, the signal transmission rate varied greatly among patients, with only one in three participants showing high signal transmission rates that would be essential for developing real-time interventions to improve adherence.

The adherence rate of cancer patients after alloHCT (55%) is comparable to that reported by the WHO (Sabaté, 2003) for other patients with chronic conditions (50%) and also falls within the range of adherence (33% - 95%) observed in patients with hematopoietic cell transplant in a recent review (Morrison et al., 2017). Another recent study similarly found suboptimal adherence rates (71% for taking immunosuppressants and 71% for taking other pills) (Posluszny et al., 2018). These results suggest the need for more research into multiple mediations adherence among patients with chronic conditions.

This was the first study to examine cancer patients' adherence to multiple medications using an electronic monitoring system. Though not without some challenges, the reported experiences from 28 alloHCT patients who used the electronic pillbox were positive overall. Eighteen patients continued using the pillbox beyond the 180 days. This suggests that an electronic pillbox can be used to study multiple medication intake in cancer patients, even when the medication regimen is highly complex, and patients suffer from high morbidity. The study not only reports quantitative outcomes from the electronic pillbox, which is known to be a more objective measure (Ruddy, Mayer, &

Partridge, 2009), but also reports patients' lived experiences while using the electronic pillbox.

The study has a number of limitations. First, this study was conducted at an urban hospital with a limited number of patients. While there was good representation of male and female patients and the diverse age and ethnic background speak to the potential generalizability of the results to other urban areas, future research with larger samples drawn from other regions is needed. Second, the implicit organization system of the pillbox prevents it from being purely observational. The layout of the pillbox promotes planning for a whole day's doses and up to one week at a time. Therefore, the adherence rates in this study are likely an upper bound of the adherence rates we would find without this organizational system.

Theoretical and Practical Implications

The current study has theoretical and practical implications relevant to both researchers and clinical practitioners, showing that an electronic medication monitoring system is feasible to use for patients taking multiple medications. Regarding theory, we suggest the addition of technological support as a facilitator for adherence in addition to social support, an established facilitator (DiMatteo, 2004). For example, the Information-Motivation-Behavioral Skills model proposes that individuals with adequate adherence information, motivation (both personal and social), and behavioral skills demonstrate better adherence and more positive health outcomes (Fisher, Fisher, Amico, & Harman, 2006). The current study indicates that theoretical models should include technological support in addition to social support, which could be based on the data from an electronic pillbox. Technological support can enhance each of the three components of the IMB model, information, motivation, and behavioral skills, and facilitate adherence by delivering a timely intervention when adherence problems are occurring. At the same time, there is considerable room for improvement in the devices available. Patients and the research team encountered a number of challenges in using the electronic pillbox. Therefore, we delineated a set of criteria for an ideal electronic monitoring system for multiple medication regimens in clinical practice and research.

Pillbox Design Suggestions

An updated pillbox would come in several sizes to accommodate patients' varying number of medications (28 compartments were suitable for the complex medication regimen in our population). Each compartment would have a built-in sensor to detect opening and closing and an additional sensor for the lid to assess refills. Patients could also personalize the labels for each compartment and store prescription instructions in the lid. To store the medications that do not fit in the pillbox (e.g., liquids, powder packs), an updated device would come with an additional sensor-equipped box that communicates with the electronic pillbox. The updated pillbox would be light-weight yet sturdy with clear lids for the whole box and for each compartment. It could be locked to prevent children or family members from inadvertently taking medications. It would have a charger cable that connects securely.

Portability. The updated device would come with a carrying bag and a portable single-day supply that contains sensors and communicates with the pillbox; one possible design solution could be to have removable compartments within the pillbox (see Figure 2.6).

Facilitating the set-up at home. A plug-and-play design would be best, as it is easy to use and intuitive to set up. It is important for less digitally literate populations, such as older patients. The electronic pillbox would have a phone line to support set-up at home. An ideal electronic pillbox would have built-in real-time wireless data transmission to a cloud server, with the possibility to connect with a local wireless network if the wireless phone signal at home is not consistent (e.g., in rural areas and in homes with poor cell phone reception). Battery life should be 24+ hours.

Reminder system. The pillbox would have an optional reminder system (such as a sound or light signal) that reminds the patients or caregivers at the dosing time and responds when the medication is taken. If medication is not taken within the two-hour window of the prescribed dosing time, patients or caregivers would receive text, email, or phone reminders. We observed that many patients do not display a time-anchored adherence pattern but rather have flexible wake-up times that anchor the day's medication intake. Therefore, we would recommend integrating a mobile phone sensor that starts the day when patients wake up.

Data storage and visualization. There was data loss for a patient because the website did not retain the data. A cloud service that stores data for at least 12 months that is encrypted, and password protected would aid patients in monitoring their adherence over longer durations and sharing data with their healthcare providers. Data storage on the device or link with a cell phone application is another way of storing data. A smartphone application would allow patients to easily receive updates on medication schedule and minimize data loss in case of battery failure. It would connect with medical prescription systems so that updates are suggested automatically, and patients could accept and modify them after medical appointments. Moreover, it would facilitate data visualization for patients and caregivers by showing adherence patterns over days, weeks, and months, with missed doses clearly labeled.

Conclusion

Despite the challenges encountered, most patients attempted to use the pillbox and were able to use it satisfactorily. This suggests that an electronic pillbox is an acceptable means of tracking adherence to multiple medications and that there is great promise for sensor-based assessment for multiple medication regimens. Based on this study, it will be possible to develop a suitable pillbox for patients prescribed with multiple medications. Future work might explore this technology and its uses for other chronic conditions where complex medication regimens are prescribed. Additionally, studies may utilize the real-time transmission of the devices data to build real-time interventions.

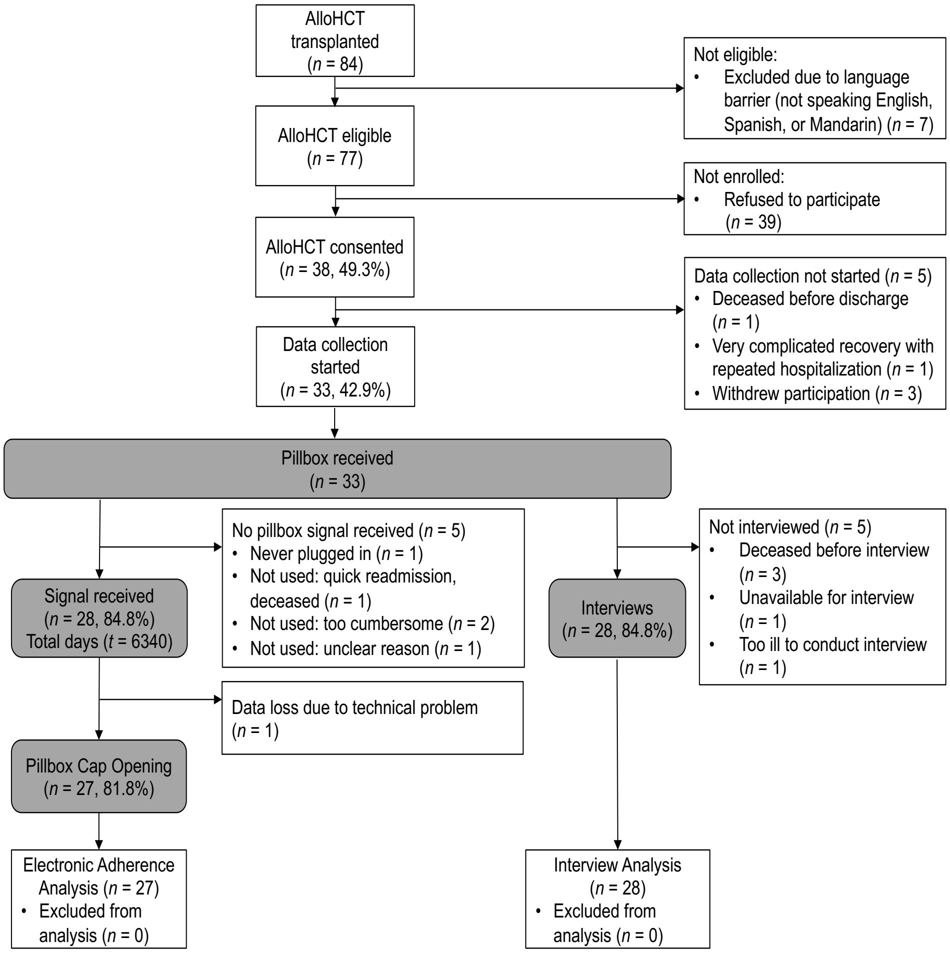


Figure 2.1. Flowchart of recruitment and data collection

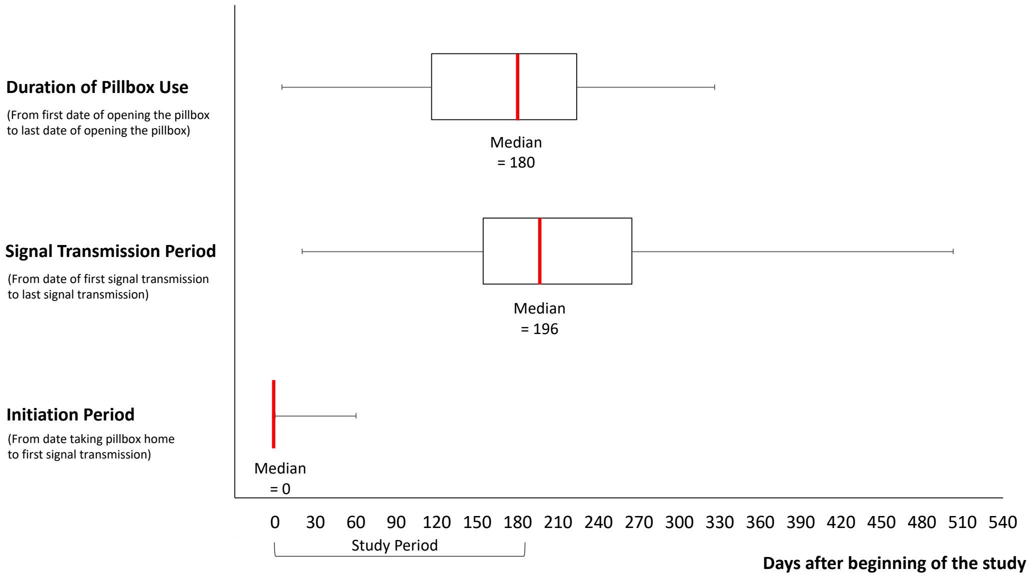


Figure 2.2. Overview of pillbox use: Time to initiation of pillbox use (number of days between first day at home after pillbox receipt and first signal transmission), period of pillbox signal transmission (number of days between first and last signal transmission date), and duration of pillbox use (number of days between first and last pillbox opening)

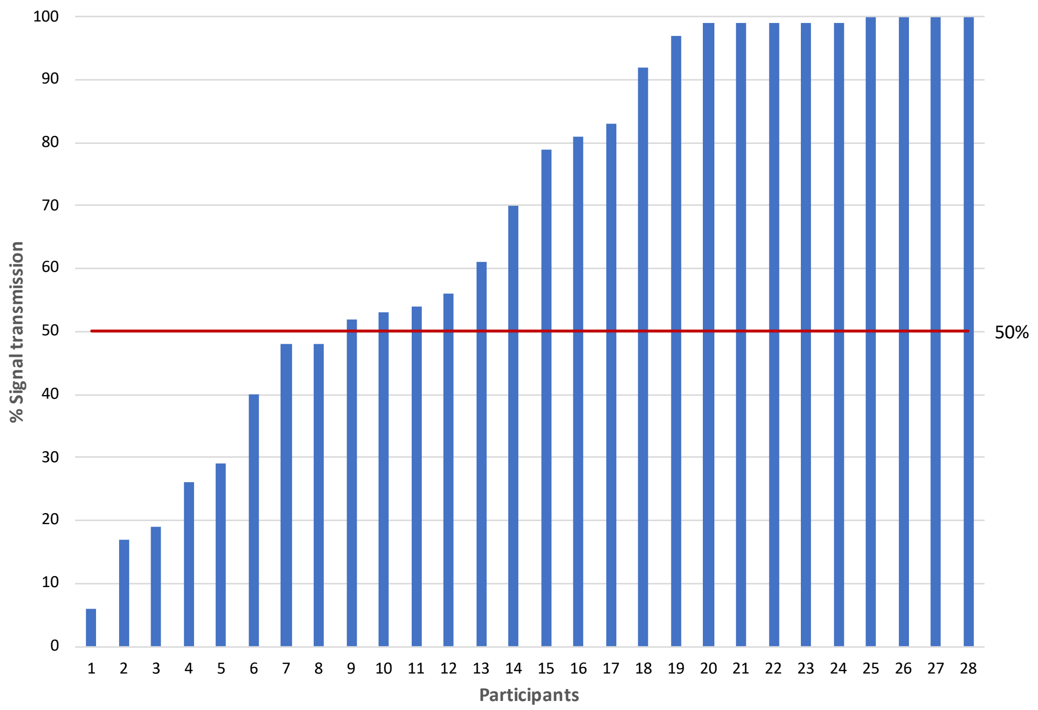


Figure 2.3. Signal transmission rates (% of non-hospitalized days during the first 180 days after hospital discharge) of alloHCT recipients (*n* = 28), with 50% signal transmission rate marked to identify participants with moderate and high transmission rates

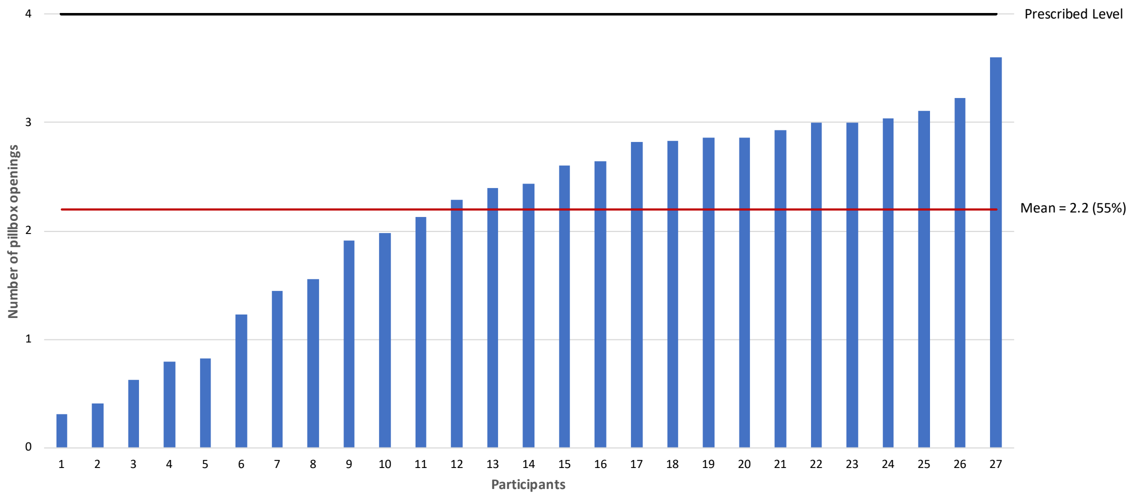
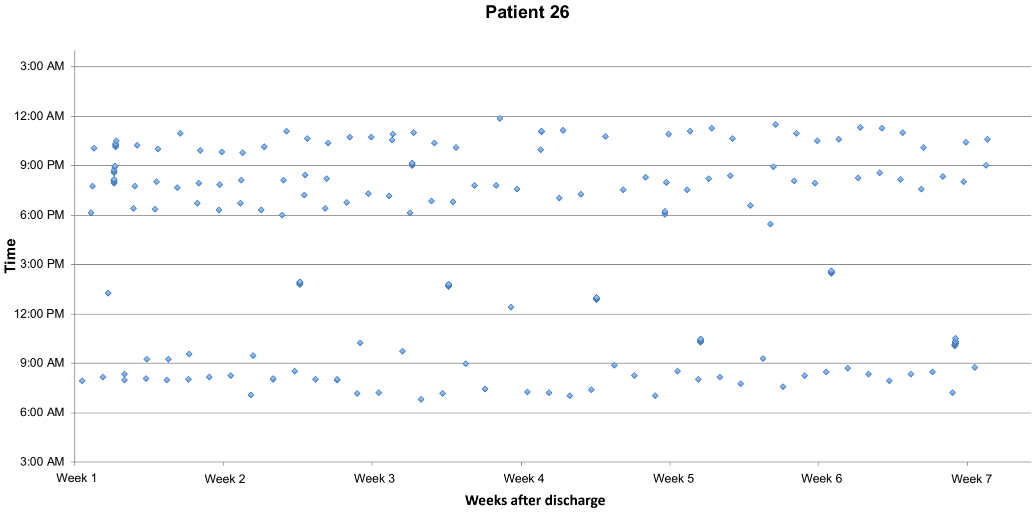


Figure 2.4. Adherence score of alloHCT recipients who used pillbox (*n* = 27; average number of daily pillbox cap openings out of a maximum of 4)



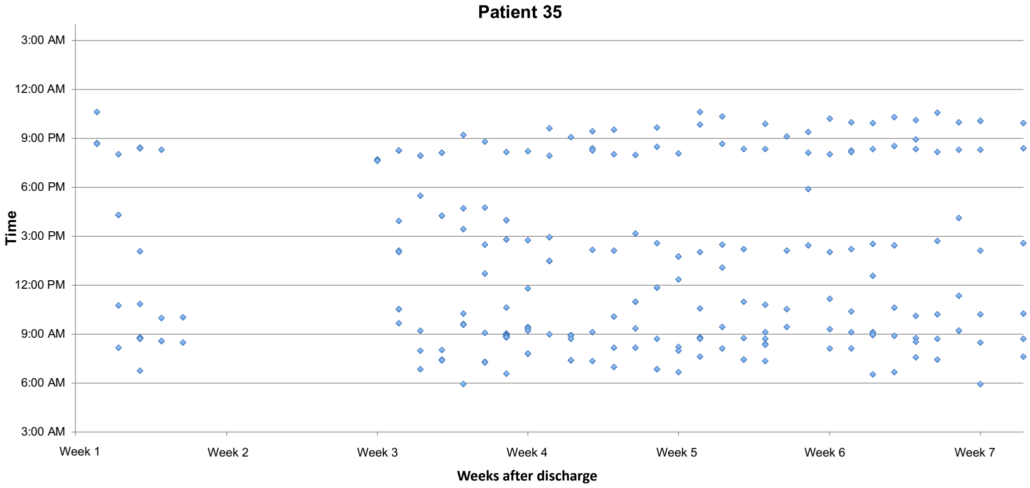
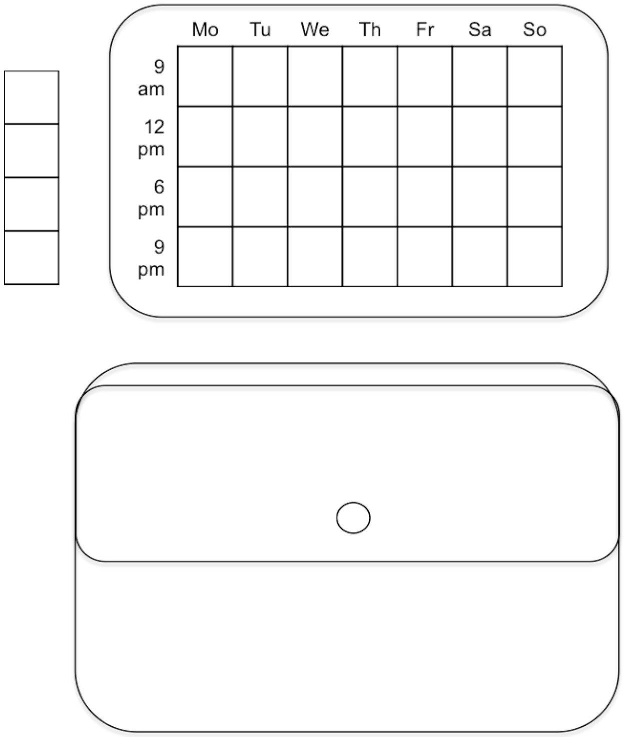


Figure 2.5. Examples of two patients with high signal transmission rates



Design. 28-compartment pillbox with 1-day portable supply

Portability. Carrying bag

Data. Built-in wireless and data storage, connected to cloud server and mobile phone app for data visualization

Power. Regular plug-in, built-in 24+ hour battery

Figure 2.6. Illustration of an updated electronic pillbox

References

Blaschke, T. F., Osterberg, L., Vrijens, B., & Urquhart, J. (2012). Adherence to medications: Insights arising from studies on the unreliable link between prescribed and actual drug dosing histories. *Annual Review of Pharmacology and Toxicology*, *52*(1), 275–301. https://doi.org/10.1146/annurev-pharmtox-011711-113247

Buttorff, C., Ruder, T., & Bauman, M. (2017). *Multiple Chronic Conditions in the United States*. Santa Monica, CA: RAND. https://doi.org/10.7249/TL221

Costa, E., Giardini, A., Savin, M., Menditto, E., Lehane, E., Laosa, O., … Marengoni, A. (2015). Interventional tools to improve medication adherence: review of literature. *Patient Preference and Adherence*, *9*, 1303–1314. https://doi.org/10.2147/PPA.S87551

Creswell, J., Klassen, A. C., Plano, V., & Smith, K. C. (2011). Best practices for mixed methods research in the health sciences. *Bethesda (Maryland): National Institutes of Health, 2013,* 541-545.

Davidson, T. M., McGillicuddy, J., Mueller, M., Brunner-Jackson, B., Favella, A., Anderson, A., … Treiber, F. A. (2015). Evaluation of an mHealth medication regimen self-management program for African American and Hispanic uncontrolled hypertensives. *Journal of Personalized Medicine*, *5*(4), 389–405. https://doi.org/10.3390/jpm5040389

DiMatteo, M. R. (2004). Social support and patient adherence to medical treatment: A meta-analysis. *Health Psychology*, *23*(2), 207–218. https://doi.org/10.1037/0278-6133.23.2.207

Farmer, K. C. (1999). Methods for measuring and monitoring medication regimen adherence in clinical trials and clinical practice. *Clinical Therapeutics*, *21*(6), 1074–1090. https://doi.org/10.1016/S0149-2918(99)80026-5

Fisher, J. D., Fisher, W. A., Amico, K. R., & Harman, J. J. (2006). An information-motivation-behavioral skills model of adherence to antiretroviral therapy. *Health Psychology*, *25*(4), 462–473. https://doi.org/10.1037/0278-6133.25.4.462

Freifeld, A. G., Bow, E. J., Sepkowitz, K. A., Boeckh, M. J., Ito, J. I., Mullen, C. A., … Wingard, J. R. (2011). Clinical practice guideline for the use of antimicrobial agents in neutropenic patients with cancer: 2010 update by the Infectious Diseases Society of America. *Clinical Infectious Diseases*, *52*(4), e56–e93. https://doi.org/10.1093/cid/cir073

Haberer, J. E., Robbins, G. K., Ybarra, M., Monk, A., Ragland, K., Weiser, S. D., … Bangsberg, D. R. (2012). Real-time electronic adherence monitoring is feasible, comparable to unannounced pill counts, and acceptable. *AIDS and Behavior*, *16*(2), 375–382. https://doi.org/10.1007/s10461-011-9933-y

Hall, A. E., Paul, C., Bryant, J., Lynagh, M. C., Rowlings, P., Enjeti, A., & Small, H. (2016). To adhere or not to adhere: Rates and reasons of medication adherence in hematological cancer patients. *Critical Reviews in Oncology/Hematology*, *97*, 247–262. https://doi.org/10.1016/j.critrevonc.2015.08.025

Inauen, J., Bierbauer, W., Lüscher, J., König, C., Tobias, R., Ihle, A., … Scholz, U. (2017). Assessing adherence to multiple medications and in daily life among patients with multimorbidity. *Psychology & Health*, *32*(10), 1233–1248. https://doi.org/10.1080/08870446.2016.1275632

Ingersoll, K. S., & Cohen, J. (2008). The impact of medication regimen factors on adherence to chronic treatment: A review of literature. *Journal of Behavioral Medicine*, *31*(3), 213–224. https://doi.org/10.1007/s10865-007-9147-y

Kantor, E. D., Rehm, C. D., Haas, J. S., Chan, A. T., & Giovannucci, E. L. (2015). Trends in prescription drug use among adults in the United States from 1999-2012. *JAMA*, *314*(17), 1818–1830. https://doi.org/10.1001/jama.2015.13766

McDonald, H. P., Garg, A. X., & Haynes, R. B. (2002). Interventions to enhance patient adherence to medication prescriptions: Scientific review. *JAMA*, *288*(22), 2868–2879. https://doi.org/10.1001/jama.288.22.2868

McGillicuddy, J. W., Gregoski, M. J., Weiland, A. K., Rock, R. A., Brunner-Jackson, B. M., Patel, S. K., … Treiber, F. A. (2013). Mobile health medication adherence and blood pressure control in renal transplant recipients: A proof-of-concept randomized controlled trial. *JMIR Research Protocols*, *2*(2). https://doi.org/10.2196/resprot.2633

Morrison, C. F., Martsolf, D. M., Wehrkamp, N., Tehan, R., & Pai, A. L. (2017). Medication adherence in hematopoietic stem cell transplantation: A review of the literature. *Biology of Blood and Marrow Transplantation*, *23*(4), 562–568. https://doi.org/10.1016/j.bbmt.2017.01.008

Neumann, S., Krause, S. W., Maschmeyer, G., Schiel, X., & von Lilienfeld-Toal, M. (2013). Primary prophylaxis of bacterial infections and Pneumocystis jirovecii pneumonia in patients with hematological malignancies and solid tumors. *Annals of Hematology*, *92*(4), 433–442. https://doi.org/10.1007/s00277-013-1698-0

O’Brien, B. C., Harris, I. B., Beckman, T. J., Reed, D. A., & Cook, D. A. (2014). Standards for reporting qualitative research: A synthesis of recommendations. *Academic Medicine*, *89*(9), 1245. https://doi.org/10.1097/ACM.0000000000000388

Osterberg, L., & Blaschke, T. (2005). Adherence to medication. *New England Journal of Medicine*, *353*(5), 487–497. https://doi.org/10.1056/NEJMra050100

Pasina, L., Brucato, A. L., Falcone, C., Cucchi, E., Bresciani, A., Sottocorno, M., … Nobili, A. (2014). Medication non-adherence among elderly patients newly discharged and receiving polypharmacy. *Drugs & Aging*, *31*(4), 283–289. https://doi.org/10.1007/s40266-014-0163-7

Posluszny, D. M., Bovbjerg, D. H., Agha, M. E., Hou, J.-Z., Raptis, A., Boyiadzis, M. M., … Dew, M. A. (2018). Patient and family caregiver dyadic adherence to the allogeneic hematopoietic cell transplantation medical regimen. *Psycho-Oncology*, *27*(1), 354–358. https://doi.org/10.1002/pon.4393

Richter, A., Anton, S. E., Koch, P., & Dennett, S. L. (2003). The impact of reducing dose frequency on health outcomes. *Clinical Therapeutics*, *25*(8), 2307–2335. https://doi.org/10.1016/S0149-2918(03)80222-9

Ruddy, K., Mayer, E., & Partridge, A. (2009). Patient adherence and persistence with oral anticancer treatment. *CA: A Cancer Journal for Clinicians*, *59*(1), 56–66. https://doi.org/10.3322/caac.20004

Sabaté, E. (2003). *Adherence to long-term therapies: Evidence for action*. Geneva: World Health Organization.

Tomblyn, M., Chiller, T., Einsele, H., Gress, R., Sepkowitz, K., Storek, J., … Boeckh, M. A. (2009). Guidelines for preventing infectious complications among hematopoietic cell transplantation recipients: A global perspective. *Biology of Blood and Marrow Transplantation*, *15*(10), 1143–1238.

Tong, A., Flemming, K., McInnes, E., Oliver, S., & Craig, J. (2012). Enhancing transparency in reporting the synthesis of qualitative research: ENTREQ. *BMC Medical Research Methodology*, *12*(1), 181. https://doi.org/10.1186/1471-2288-12-181

Tong, A., Sainsbury, P., & Craig, J. (2007). Consolidated criteria for reporting qualitative research (COREQ): A 32-item checklist for interviews and focus groups. *International Journal for Quality in Health Care*, *19*(6), 349–357. https://doi.org/10.1093/intqhc/mzm042

van Oostrom, S. H., Gijsen, R., Stirbu, I., Korevaar, J. C., Schellevis, F. G., Picavet, H. S. J., & Hoeymans, N. (2016). Time Trends in Prevalence of Chronic Diseases and Multimorbidity Not Only due to Aging: Data from General Practices and Health Surveys. *PLOS ONE*, *11*(8), e0160264. https://doi.org/10.1371/journal.pone.0160264

Vrijens, B., De Geest, S., Hughes, D. A., Przemyslaw, K., Demonceau, J., Ruppar, T., … Urquhart, J. (2012). A new taxonomy for describing and defining adherence to medications. *British Journal of Clinical Pharmacology*, *73*(5), 691–705. https://doi.org/10.1111/j.1365-2125.2012.04167.x

Welch, G., Balder, A., & Zagarins, S. (2015). Telehealth program for type 2 diabetes: Usability, satisfaction, and clinical usefulness in an urban community health center. *Telemedicine and E-Health*, *21*(5), 395–403. https://doi.org/10.1089/tmj.2014.0069

Williams, A. B., Amico, K. R., Bova, C., & Womack, J. A. (2013). A proposal for quality standards for measuring medication adherence in research. *AIDS and Behavior*, *17*(1), 284–297. https://doi.org/10.1007/s10461-012-0172-7

Wu, S. Y., & Green, A. (2000). *Projection of chronic illness prevalence and cost inflation.* Santa Monica, CA: RAND Health.

Chapter III

SOCIAL SUPPORT FOR ADHERENCE TO MULTIPLE MEDICATIONS: WHAT HEALTHCARE PROVIDERS AND CLOSE OTHERS DO TO HELP PATIENTS

Abstract

Background: Social support plays an important role in improving health outcomes, including medication adherence. However, social support for multiple medication regimens has been understudied despite the increasing prevalence of multiple medication regimens, advances in medicine, and longer life expectancy. Recipients of allogeneic hematopoietic cell transplant (alloHCT) are required to take multiple medications after transplant to prevent transplant rejections and complications.

Objective: The objective of this study was to examine the types of social support that are available to alloHCT patients from their caregivers and healthcare providers.

Methods: Through semi-structured in-depth interviews, 28 patients after alloHCT (46.4% female, age: *M* = 53.97, 46.4% ethnic minority) shared their experiences of taking multiple medications and managing adherence tasks. Coding categories for content analysis were developed based on the Information-Motivation-Behavioral Skills (IMB) model and prior research distinguishing practical, emotional and informational support.

Results: Individuals after transplant received support from both healthcare providers and a range of lay caregivers, most frequently spouses, partners and other family members. Having a relationship of trust with healthcare providers was important for patients after alloHCT; it encouraged and comforted patients to follow their instructions and medical decisions. Healthcare providers mainly fulfilled their medical need and provided informational support, while lay caregivers were the main source of emotional and practical support. The role of lay caregivers extends to different areas of patients' daily lives that are related to medication adherence, including support for attending doctor's appointments, managing medications, and sustaining a healthy diet. Furthermore, they were sources of financial support.

Conclusion: Support from healthcare providers is critical and the basis for patients' adherence at home. A dedicated lay caregiver is required for patients after alloHCT to follow their multiple medication regimens. The findings highlight the necessity for healthcare providers and lay caregivers to work in tandem to support patients' adherence to multiple medications.

Keywords: allogeneic hematopoietic cell transplant; cancer; caregiver support; healthcare providers; medication adherence; multiple medications; social support

Introduction

Adherence to multiple medications is a daily struggle for a growing number of people due to the increasing availability and complexity of oral medications for treating chronic conditions, such as cancer (National Center for Health Statistics (US), 2014; Sabaté, 2003). Individuals reporting the use of prescription drugs increased from 51% to 59%, while those reporting the use of five or more prescription drugs increased from 8.2% to 15% from 1999 to 2012 (Kantor, Rehm, Haas, Chan, & Giovannucci, 2015). But only about 50% of patients adhere to their prescribed medication regimens (Bosworth, 2010; Sabaté, 2003). For patients who are prescribed three or more daily medications, adherence may pose a particular challenge: Adherence declines as the number of daily doses increases (Claxton, Cramer, & Pierce, 2001; Pantuzza, Ceccato, Silveira, Junqueira, & Reis, 2017).

Social support has long been recognized as a key contributor to mental and physical health (Berkman, Glass, Brissette, & Seeman, 2000; Holt-Lunstad, Smith, & Layton, 2010; Uchino, 2006). It is associated with a higher quality of life—and even survival—in cancer (Aizer et al., 2013; Chou, Stewart, Wild, & Bloom, 2012; Luszczynska, Pawlowska, Cieslak, Knoll, & Scholz, 2013). A longitudinal study with a large sample found alloHCT patients who received pre-transplant emotional support had higher rates of post-transplant survival (Ehrlich et al., 2016). However, because it is a broad construct, there are different ways of measuring social support (Helgeson, 2003). Structural measure refers to the existence of social ties and networks (e.g., marital status, living with somebody or not, and having a family or not), whereas functional measure refers to the types of support, which usually include practical, emotional, and informational support (Helgeson, 2003; House, Kahn, McLeod, & Williams, 1985). Instrumental support refers to actual physical or material help; emotional support refers to love, care, value, empathy, and encouragement; informational support refers to factual knowledge, and certain types of support work more effectively in some situations than others (Cohen & McKay, 1984; Cutrona & Russell, 1990; Helgeson, 2003; Thoits, 2011).

Social support is also related to medication adherence. Reviews of the existing literature, which examined both structural as well as different functional support categories, found that social support, especially practical support provided by close others, is linked to better adherence (DiMatteo, 2004; Scheurer, Choudhry, Swanton, Matlin, & Shrank, 2012). Social support for medication adherence has also been studied in chronic conditions, such as HIV/AIDS, diabetes, and cardiovascular diseases (Berghoff et al., 2018; Kelly, Hartman, Graham, Kallen, & Giordano, 2014; Simoni, Frick, & Huang, 2006; Mayberry & Osborn, 2012; Zullig et al., 2015). These studies also reported a positive correlation between social support and adherence. A recent study of hematological cancer patients found that higher levels of social support were associated with higher rates of medication adherence (Hall et al., 2016). Moreover, the most recent study, which closely resembles the present study in its population of interest, examines adherence to a variety of post-transplant tasks as undertaken by patient-caregiver dyads, including medication adherence (Posluszny et al., 2018).

Since the 1990s, the number of individuals receiving alloHCT has increased, significantly improving the survival rate of patients (Hahn et al., 2013; Majhail et al., 2015). Nevertheless, even following a successful transplant, individuals experience high mortality due to potentially life-threatening complications, infections, graft-versus-host disease, and cancer recurrence (Holtan et al., 2015; Pasquini, Wang, & Schneider, 2009). The multiple medication regimen is prescribed to improve survival rates (Morrison, Martsolf, Wehrkamp, Tehan, & Pai, 2017). However, in part due to the complexity of this regimen and other personal and social factors, the rate of adherence has not been ideal. In a recent pilot study, 54.6% of alloHCT patients were found to be poorly adherent to their medication regimens (Lehrer et al., 2018). A 2014 study found that almost two-thirds of alloHCT patients were non-adherent in taking their immunosuppressants, the most essential of post-transplant medications (Kirsch et al., 2014).

Because receiving a hematopoietic transplant is a long, aggressive and exhausting process, many transplant programs require a caregiver for transplant eligibility, in line with national and international guidelines (National Marrow Donor Program, 2017; Tomblyn et al., 2009). Individuals often experience depression and fatigue after receiving an alloHCT (Jim et al., 2016). However, those who receive support from their caregivers tend to fare better psychologically and physically; studies on alloHCT patients specifically identify caregivers' support as a powerful factor of survival after transplant (Foster et al., 2005; McLellan et al., 2011; Rini et al., 2011). Moreover, a systematic literature review examined the relationship between social support and survival (Beattie, Lebel, & Tay, 2013). Of the six studies included in the review, five published studies found a link between social support and survival, while one unpublished dissertation with the largest sample size did not find any association between social support and survival (Beattie et al., 2013).

While these are suggestive findings, studies on the role of healthcare providers are limited (Hall et al., 2016), and the role of social support for adherence to a *multiple* medication regimen could also benefit from additional study. Thus, we sought to investigate how healthcare providers and lay caregivers help individuals after alloHCT adhere to a multiple medication regimen and what concrete actions they can take to enhance adherence.

Methods

This study was part of a larger transplant study that followed individuals with leukemia and lymphoma cancers for 180 days after their first discharge from the hospital. This study, based on directed content analysis (Hsieh & Shannon, 2005), uses a theory-informed qualitative approach to identify the types of support patients received. Individual semi-structured interviews were conducted between three to six months after hospital discharge. The use of human subjects was reviewed and approved by the Institutional Review Board of Columbia University, including Teachers College, and the hospital from which the data were collected. All participants provided written informed consent prior to participation. The study referred to the relevant standards for reporting qualitative results (Creswell, Klassen, Plano, & Smith, 2011; O'Brien, Harris, Beckman, Reed, & Cook, 2014; Tong, Flemming, McInnes, Oliver, & Craig, 2012; Tong, Sainsbury, & Craig, 2007) and followed COREQ (Tong et al., 2007) guideline closely (see Appendix C).

Setting and Participants

The study took place at a large urban teaching hospital, which provides a diverse population with access to healthcare, and is known to have a well-established hematology oncology and transplantation program. Eligible patients were invited by healthcare providers to participate in the interview during appointments. Individuals were eligible for the study if they were at least 18 years old and spoke English, Spanish or Mandarin. Two of the interviews were conducted in Spanish (7.1%), the rest in English (n = 26, 92.9%) and none in Mandarin. Participation was voluntary. All patients received allogeneic bone marrow transplants and were prescribed a multiple medication regimen.

Measures

Semi-structured in-depth interviews were conducted. Interviewers followed a structured interview guide listing questions and probed individuals for detailed answers about their medication adherence and social support. The interview guide was developed by the principal investigator, who is an expert in health psychology. The guide outlines in detail a theoretically-informed qualitative approach to interpreting patient interview data. Interview questions covered various domains related to individuals' overall medication adherence behaviors, including questions on social support (e.g., "Are there people in your life who support your taking medications?"). Part 2 and some elements of Part 6 specifically asked questions about social support and patients' relationships with caregiver and healthcare providers. The interview guide also contained probing questions to be used if the original question was not applicable to an individual. To ensure the quality of the interviews, interviewers were trained by the principal investigator; the interview questions were piloted tested during role-play interviews prior to conducting actual interviews with patients. All research assistants at the time had a bachelor's or master's degree in social sciences, public health or health sciences.

To assess inter-coder reliability, two coders selected seven interviews (25% of the sample) at random to code independently and calculated the Kappa coefficient in a binary fashion, assessing whether the coders agreed that the relevant theme had been mentioned in the randomly selected interviews. Kappa coefficients for support from lay caregivers and support from healthcare providers were calculated separately. The initial Kappa for lay caregivers' support was in perfect agreement ($\kappa = 1.00$) and that for lack of lay caregivers' support was 0.71, which is satisfactory inter-rater reliability. Initial Kappa for support from healthcare providers was 1.00, but that for lack of support from healthcare providers was 0.43. Discrepancies were discussed between the two coders until agreement was reached, especially the quotes on the lack of healthcare providers' support. After discussing and clarifying the discrepancies, Kappa for the lack of support from healthcare providers increased to 0.71. All interview transcripts and relevant quotes were carefully read again by one of the researchers to calculate the number of patients that had mentioned the theme at least once and its percentage.

Procedures

Participants who agreed to participate in the study and signed written informed consent forms were contacted in advance to schedule each interview. Interviews were conducted either in person before doctor's appointments and/or via telephone when participants could not manage hospital visits or simply preferred telephone interviews. In some cases, the caregiver also joined the interview when accompanying the participant to appointments. Interviews lasted from 40 to 60 minutes and participants could take a break if desired. All interviews were conducted by two interviewers, with one interviewer asking questions and the other taking notes and recording the interview. All the interviews were audio recorded and transcribed. Data were kept in a secure password protected drive. Every participant was aware of and agreed to being recorded. All confidential information in the interview transcripts was removed and replaced with generic titles (e.g., nurse Jane Doe with Nurse 1).

Data Analysis

Directed content analysis was used to analyze the data (Hsieh & Shannon, 2005). Social support, which also falls under "social motivation" in the Information-Motivation-Behavioral Skills (IMB) model (Fisher, Fisher, Amico, & Harman, 2006) and social support theory (Cohen & McKay, 1984; House et al., 1985; Thoits, 2011; Weiss, 1974), was the basis of the coding scheme. This study examined support received from both lay caregivers and healthcare providers, and the types of support, including emotional, instrumental, and informational support. A codebook was developed listing different themes, definitions, and examples (see Appendix B). Relevant quotes indicating support or the lack thereof were coded.

Among the 28 interviews analyzed, data on support from healthcare providers were missing for two of them because the participants felt too sick or could not finish the interview. Thus, percentages are calculated based on 26 interviews for that specific category. All interview transcripts were read carefully. Two independent coders manually extracted the quotes onto an excel spreadsheet to code, and the same procedure was repeated in NVivo version 11. This software allows the creation of categories and subcategories, comparing the coding between groups of people and calculating frequencies and discrepancies.

Results

Characteristics of Patients

In total, 28 individuals (46.4% female, age: *M* = 53.97) participated. The sample was ethnically diverse, with almost half of the participants coming from a minority background (*n* = 13, 46.4%), (Non-Hispanic White: 53.6%, African American: 7.1%, Asian: 17.9%, Hispanic: 17.9%, other: 3.6%).

Healthcare Providers

We found that all participants asked about healthcare providers (100% of 26 interviews) identified them as a source of support. Participants referred specifically to doctors and nurses when speaking about healthcare providers who provide medical care and treatment. At the hospital, clinical teams, including hematologists and nurse practitioners, worked closely together. Therefore, most individuals after transplant perceived them as a team (*n* = 22/26, 84.6%).

Nearly all individuals reported having a good relationship with their healthcare providers and evaluated the relationship as positive (*n* = 24/26, 92.3%). The quality of the patient-healthcare provider relationship influenced individuals' health behaviors, especially with regards to making medical decisions. When patients built trusting relationships with their healthcare providers, they felt confident following their healthcare providers' guidelines. One individual mentioned, "I'm a believer, I believe in him. First thing we do in any situation that you wanna get help you have to believe. I believe in him. So what he says is right." (P17, age 50, male). Another individual also mentioned,

> Very simply, they have my best intentions in mind, and they override what do you call it...they know what the right thing to do is, whether I like it or not. So they're not sticking me with bad tasting medications on purpose to make me feel bad. This is the right thing to take. They're the experts, they know the conditions, they know what's coming. (P13, age 66, male)

At the same time, one participant (*n* = 1/26, 3.8%), while mentioning he did receive some support from his healthcare providers, also expressed that he had received too little information at the discharge meeting and was therefore dissatisfied with the healthcare providers. He said,

> I ended up back in here [admitted to the hospital]. They didn't talk about hydration. (…) Hydration is likely a bigger deal than they tell you about. I was back in for 12 days. I was berserk about that. (P01, age 65, male)

Another patient was ambiguous in her response regarding the relationship with healthcare providers and did not quite perceive a relationship: "Well, I have not had problems with them. I don't care." (P12, age 53, female).

Types of Support from Healthcare Providers

Individuals after transplant perceived that their healthcare providers mostly provided informational support in line with their expertise. However, many individuals mentioned that they also received other types of support from the healthcare providers, including emotional support. We will present specific examples detailing the kinds of support provided and how they helped patients after transplant.

Informational support from healthcare providers. Individuals after transplant mostly received informational support from healthcare providers (*n* = 23/26, 88.5%). A wide spectrum of healthcare providers, including pharmacists, dietitians, hematologists and specialist nurses, provided informational support verbally and in writing. Patients received information on medications (*n* = 23/26, 88.5%) and nutrition, including hydration (*n* = 6/26, 23.1%).

One participant reported that the relationship with healthcare providers made it easier to take medications.

> Because they tell me exactly that I need to take them, why I need to take them, yeah always teaching. Always teaching, yup. Every single day, every single appointment. The nurse coming first goes over all of the medication and the doctor will do the same thing. (P22, age 34, female)

Support for medical needs. Many patients reported that their health providers met their medical needs, which required professional skills (*n* = 18/26, 69.2%). One individual mentioned, "They make sure that all my medical needs are met so I can recover and go back to a regular life." (P14, age 32, male). Another patient recalled the help she received when she forgot to refill her medications on time and needed an immediate supply. "I have run out of the Prograf and that is very important, but the doctors called in a four-day refill script to [name of pharmacy 6] and I picked it up." (P31, age 44, female). Often, support for medical needs was combined with emotional support, as a female participant reported in dealing with her difficult stage four graft-versus-host disease. She said,

> One of the reasons, I have to tell you, are the [name of hospital 1] nurses. They are angels. They packed me in ice at night. They looked at me, my skin was peeling, you couldn't touch me any place without me screaming because it hurt so much. It's very good to have nurses that are so kind. They actually stayed with me. They didn't have to do more than just come when I rang the bell. It's harder at night because everything is so quiet, and nothing can distract you from the pain. (P07, age 55, female)

Emotional support. Healthcare providers, usually nurses, encouraged individuals after transplant and showed care for their personal lives (*n* = 9/26, 34.6%). The attitude of healthcare providers and the way individuals after transplant perceived them influenced them in their recovery process.

> In the sense that they know things are important, they make me feel like my recovery is important, they make sure that all my medical needs are met so I can recover and go back to a regular life. (P14, age 32, male)

Another participant said,

> I think the best thing was speaking with all the nurses. Becoming friendly with them. (…) Yeah, and the day I left the hospital was my birthday and they brought me a birthday cake. I can't believe they did that! So that was nice, that brightened up my day. (P43, age 50, female)

Although emotional support might not have directly influenced patients' medication adherence, it contributed to a good and trusting relationship with healthcare providers, encouraging and helping individuals after transplant to recover.

Lay Caregivers

Lay caregivers, such as family members and friends, were the primary source of social support for transplant recipients. All participants reported receiving support from family members, friends, or acquaintances (*n* = 28/28, 100.0%). Moreover, about half of the participants reported to have at least one primary source of support, usually a spouse or partner, who was their main caretaker over the course of the transplant (*n* = 15/28, 53.6%, see Figure 3.1). For example, a participant mentioned that his wife supported him in taking his medications (P13, age 66, male). Another participant mentioned, "My husband does everything! He's actually on top of everything more than I am." (P07, age 55, female).

A considerable number of transplant recipients (*n* = 11/28, 39.3%) reported relying on several lay caregivers, such as the partner and other family members (*n* = 6/28, 21.4%), family members other than the partner (*n* = 4/28, 14.3%), or family members and friends (*n* = 1/28, 3.6%). One of the participants mentioned that his whole family ensures that he takes his medications regularly on time (P14, age 32, male). Another participant mentioned,

> Well, yes my mother, I talk to her every day, three times a day, again my son, my boyfriend, (...) so yes, I have a lot of people supporting me, asking me this, did I do this. (P31, age 44, female)

Additionally, in two cases, acquaintances or non-family members supported individuals after transplant as lay caregivers (*n* = 2/28, 7.1%). One of them mentioned,

> The helpers are mainly people from my [place of worship]. I have a woman who accompanies me to all my visits. Since my first transplant she has gone to every appointment with me. She brings lunch and meals and snacks. And uh, there's a team of persons who provide me what I need in terms of food and stuff like that. So they've been very helpful. Um…I have a staff. A secretary, a bookkeeper, a staff in the kitchen. They do parts just to make sure. To get my car moved, get my mail, someone to go to the bank. So they take care [of] all those things. (P19, age 46, male)

Regardless of the type of their connection to the patient, lay caregivers are essential for post-transplant recovery.

Types of Support from Lay Caregivers

Lay caregivers supported individuals after transplant in various ways, including instrumental, emotional, and informational support. We will present each type of support with examples.

Instrumental support. Lay caregivers had a wide range of tasks to help the patients with, including helping with taking medications or daily chores, such as cooking and cleaning.

> [My] husband does all the homework. He cooks, I don't. Doctor doesn't want me to have outside food. He reminds me to take the medication, he reminds me almost every time. (P11, age 71, female)

Instrumental support for medication intake. Individuals after transplant must take numerous medications even after a successful transplant and discharge from the hospital. Medication-related tasks are critical yet difficult for individuals after alloHCT due to the number and complexity of medications. Nearly all individuals in the sample (*n* = 26/28, 92.9%) mentioned that their lay caregivers helped with medication-related tasks, such as taking medications, reminding of doses, refilling, and picking up the medications.

> Every two three hours I have to take the medication. I have to be aware of the time and take and my husband reminds me. In 6 months, I have only missed one tablet. (P11, age 71, female)

She also mentioned that she was able to refill medications on time because of her partner's support: "[My] husband calls the pharmacy, they send us FedEx." (P11, age 71, female).

Instrumental support for daily living. Due to the necessity of immune suppression after alloHCT, individuals after transplant cannot be exposed to crowds, and must watch what they eat, drink, and touch while managing side effects and other physical complications (Beattie & Lebel, 2011). Therefore, instrumental support for daily living from lay caregivers is crucial, including driving, cooking, getting groceries, and fulfilling daily practical needs (*n* = 16/28, 57.1%).

One participant mentioned,

> Fortunately, my father helps me out with the transportation most of the time, so I don't have to rely on public transportation. So, I would be infection free or decrease the chances of infection. (P20, age 50, male)

Another participant said that his wife makes sure to provide food and drink that are nutritious and hydrating, yet very enjoyable and creative.

> My wife was coming up with creative things, too. I started running out of ideas. She found things at Whole Foods like chicken potpie and roasted vegetable pot pie. I had a lot of stuff like that. It was very flavorful. (P10, age 48, male)

His wife also provided him with different drinks to make sure he stayed hydrated. "I'm very aware of having to hydrate because of these drugs. It's also part because of my wife. She buys creative food things for recipes and different drinks." (P10, age 48, male).

One participant suffered from stomach issues that made her nauseous, and her husband cooked food that was easy to swallow and digest. She said,

> Husband does all the homework. He cooks, I don't. Doctor doesn't want me to have outside food. We eat together, every 2-3 hours I have to eat, unless I have a stomach problem. It's the time when I am going to eat. Some snack: rice cake, I am [Asian]. (…) Every 2 hours I ate rice cooked with lots of water. Don't have to chew; I was able to eat just a little bit, every 2 hours. (P11, age 71, female)

Instrumental support with financial matters. Hematopoietic cell transplant is expensive and requires an extensive treatment process over a long period of time, often creating financial hardship for individuals and their families after transplant (Khera et al., 2014; Kim et al., 2015). Instrumental support with financial matters helped individuals to ameliorate their financial burdens, as well as their emotional stress and anxiety, as explicitly mentioned by some (*n* = 4/28, 14.3%). One mentioned, "I don't even know where the bills are. I think he doesn't want me to know because he doesn't want me to worry." (P07, age 55, female). Moreover, lay caregivers needed to balance the need for financial support with caring for individuals after transplant.

> She has her own business, but she works from home. Financially we weren't fantastic but no, she didn't work a lot. She was kind of holding it all together. While I was at the hospital, she was not focusing on work at all. (P10, age 49, male)

Emotional support. Patients after alloHCT become physically and emotionally vulnerable (Rini et al., 2011). Therefore, emotional support, such as expressing encouragement, empathy and caring, plays a significant role in helping individuals after transplant. More than half of the participants reported receiving emotional support (*n* = 11/28, 39.3%). “As soon as I went into the hospital, my husband put up a website for me because everyone called. So many people wrote in, it was wonderful.” (P07, age 55, female). Internet and technology development have also facilitated emotional support. “I stay home, but I’m not alone a lot. I do have friends who drop in a lot. We have a lot of support. And I Skype a lot, everybody has that all over the world.” (P07, age 55, female).

For emotional support, individuals after transplant rely on a broader range of support sources than for instrumental support, including members of their extended family, friends, and acquaintances. In one case, an individual relied more on friends for emotional support than family members and distinguished the different types of support she received.

> They really support me in every way, my friends and my family. But for the medication, it’s my family, my husband and my little ones, they remind me all the time, but emotionally, my friends, they help me, like when I’m not feeling too up to it, or if I don’t have, like, enough energy they help me a lot. (P22, age 35, female)

Individuals after transplant also perceive the importance of receiving emotional support. An individual after transplant suggested to other patients,

> To be able to talk about your problems, talk with friends and family. I would [be] trying to get them involved in a support group. I am lucky to have a very supportive family and friends, so I didn’t have to go out of my shell. You want people to ask how you are doing. You need someone who is patient enough to listen. (P07, age 55, female)

Informational support. Healthcare providers were the primary source of informational support, and consequently informational support was not sought from lay caregivers (*n* = 0, 0%). Lay caregivers helped as memory facilitators and conveyers of information from the healthcare providers. In one interview the caregiver interrupted to provide the correct response when the patient was asked what medications he had to take on an empty stomach. The wife interrupted that "the only one that he takes on an empty stomach is Prilosec." (P25, age 66, male). This response indicates that she helped the patient to remember the information. One patient (*n* = 1/28, 3.6%) mentioned her "husband keeps asking doctors about [side effects of medications]" (P07, age 55, female). In this case, the patient's husband helped the patient by clarifying and reiterating the information received from the doctors and also asked further questions that the patient might have missed or forgotten to ask. All other participants sought information either by using online resources or directly asking their healthcare providers. One person mentioned, "most of the teaching [is through] the doctors, and the nurses. And I also go online sometimes and do my little own research." (P22, age 34, female).

Mixed feelings about support. Some support was not helpful to some individuals (*n* = 7/28, 25 %). These patients showed ambivalence about the support they received from others. One participant chose not to share his situation with the people around him at all, believing that it would only cause more trouble.

> I'm a public figure, I kept it secret for a long time, (…) Keeping it secret: if I told them they were going to worry. They would want me to take medication they know about. Take this, take that. I [had] not wanted to deal with all that advice. Listen, I have my doctors. You guys, just pray, don't try to be my doctors. (P19, age 46, male)

Four patients expressed that they did not like the feeling of being monitored by their lay caregivers. They sought independence and control over their situation, though to no avail. In these cases, less support may be better. They perceived actions of support not as helpful, but somewhat unpleasant and even troublesome. An individual mentioned,

> My wife asks me all the time whether I'm taking medications, whether I took the medications, but basically I just think she's asking too much because I'm just taking it. (P13, age 67, male)

One mentioned that he does not take medications when he is bothered by other people (P17, age 50, male). The degree of support received, and the quality of relationships varied among individuals.

In another case, the support from lay caregivers was ambiguously helpful. A participant mentioned the clothes she is accustomed to wearing.

> My sister doesn't want me to use that, she buys new clothes. I want the old clothes. She said I cannot use it any more. Where is it what I like. Even [the clothes] is old [in] our thinking, I will go to the dry cleaning, wash and dry clean. I don't know where the clothes are. She is hiding clothes away. I don't know where they are. The attic is kind of high. (P29, age 62, female)

Meaning in life. Some patients after transplant (*n* = 4/28, 14.3%) found new meaning in life, perceiving their life after transplant as another opportunity to love and be with loved ones. A participant mentioned,

> I have grown to love everything (…) I have taken advantage of time spent with my children, putting more attention to everything in life and being appreciative of God each and every day. (P23, age 59, female)

Discussion

This study explored the sources and functions of social support for adherence of individuals prescribed with multiple medications after alloHCT. They reported receiving social support from both healthcare providers and lay caregivers in taking their multiple medications. Our findings suggest that these support sources serve complementary functions. While medical needs and informational support are mostly provided by healthcare providers, emotional and instrumental support is largely within the domain of lay caregivers. Thus, individuals must coordinate support-seeking from both healthcare providers and lay caregivers to support multiple medication intake and improve long-term health outcomes and survival.

Based on the findings, a model was developed to show the process of social support and summarize the results of the study (see Figure 3.2). The figure represents the interactions among support sources, including healthcare providers, lay caregivers and patients, and the functions of social support from each source. Based on a strong foundation of trust, healthcare providers are mainly responsible for providing professional informational support about prescribed medications and medical needs, and effectively communicating this information to patients and lay caregivers. Lay caregivers provide more intimate, daily instrumental support, such as providing transportation, refilling and organizing medications, cooking, doing grocery shopping, and other household chores. They are also the major sources of emotional support, encouraging and comforting patients with kind words, which helped patients to maintain a positive and optimistic attitude towards their recovery.

The difficulties of recovery after transplant, often characterized by patients feeling unwell, fatigued, and socially limited due to their immunosuppressed state, make caregiver support essential for day-to-day living (Posluszny et al., 2018; Rini et al., 2011; So, Dodgson, & Tai, 2003; Wulff-Burchfield, Jagasia, & Savani, 2013). Although there were some cases in which individuals found support somewhat unpleasant and ambiguous, individuals mostly described support acts as helpful. Our culturally diverse sample showed a uniformly high reliance on social support, although ethnicity and cultural background played a role in providing appropriate concrete supportive acts (e.g., support for adequate nutrition and hydration with buying bread and soft drinks vs. cooking rice with lots of water). Furthermore, caregivers' presence often gave individuals after transplant reasons to live despite their difficult health conditions, supporting prior research (Krause, 2007). We assume that this mechanism is also true for lay caregivers themselves who were shouldering a high caregiver burden, meeting the considerable physical, financial, and emotional needs of individuals after transplant. The presence of their loved ones, despite their physical condition, may give meaning to their own lives and motivate them to overcome difficulties.

The effort made by healthcare providers to increase trust in their patient relationships was deeply appreciated by participants. Patient-centered care is shown to be effective in improving health outcomes (Kelley, Kraft-Todd, Schapira, Kossowsky, & Riess, 2014; Rathert, Wyrwich, & Boren, 2013; Robinson, Callister, Berry, & Dearing, 2008) and our findings reflect that. Although healthcare providers mainly provided informational support, they also made patients feel understood and cared for. This influenced patients' communication with their healthcare providers, their attitudes towards them and to follow their instructions.

This study makes contributions to the theory of social support for multiple medication adherence. Most adherence papers focus on methods for measuring adherence and how consistently an individual took medications. However, they do not highlight the support patients require in their daily lives, particularly as a factor that influences medication adherence. By contrast, this study reveals the types of support that is needed for adherence to such a complex medication regimen with additional dietary and hygienic requirements. The multiple medication regimens in some cases required multiple caregivers to ensure adherence. For example, individuals after transplant need their lay caregivers' help with transportation to attend doctor's appointments (see Figure 3.2). This study is unique because it offers a detailed description of daily essential supportive actions for medication adherence.

There are several limitations to the study. First, this study was conducted in a single treatment center in a large urban area, and the findings may not be generalized beyond this setting. Second, the treatment center we collaborated with requires nominating a dedicated support provider in order to receive an alloHCT, and the participants in the study all had access to health care. We were not able to study patients without such a support system to compare them with those who have a rigorous support system. However, during the study period, we received consent from two individuals after transplant whose lay caregiver support turned out to be very minimal, and both patients passed away before we could interview them. These two cases, in addition to our observations of the high support needs of our participants, indicate it is nearly impossible to maintain adherence to the multiple medication regimen and self-care recommendations without a rigorous support system, with severe consequences for survival. Third, there is a chance that individuals reported socially desirable responses during the interviews. However, some respondents attended or called in for interviews with their spouses or partners, who would correct them if they were giving responses that were not in line with the caregivers' perceptions. Moreover, participants were highly motivated and passionate about contributing to the study to improve care for future transplant recipients, so we believe that they gave us honest responses.

Despite these limitations, the study has several strengths. First, participants in the study were from diverse ethnic and social backgrounds. Moreover, our participants were highly motivated to participate in the study and to learn about the study results. Some participants would contribute more than we asked (e.g., send pictures of their numerous pill containers). Some even requested a copy of the paper once it is published. Therefore, we can assume that many participants responded with earnestness and sincerity despite their illness. Furthermore, the findings of this study emphasize the importance of integrating social support into daily life. Social support plays a critical role in adherence to multiple medications. Finally, to facilitate adherence to this complex multiple medication and self-care regimen, all three parties—the transplant recipient, lay caregivers, and the healthcare providers—must work together as a team. A prior systematic literature review showed that social support from family members increases medication adherence (DiMatteo, 2004), but does not focus on healthcare providers. Based on our findings, support from healthcare providers is critical in medication adherence and medication adherence should be taken as a team responsibility.

Adherence to multiple medications relies on a repeated process of actions, starting with attending appointments, refilling and organizing medications, preparing adequate intake of food and liquids, to correct and timely medication intake (see Figure 3.2). Social support from caregivers and healthcare providers is essential to enable adherence in patients after alloHCT who are prescribed multiple medications and are often fatigued and unwell (Rini et al., 2011; Wulff-Burchfield et al., 2013).

Based on our findings, we recommend the following practical measures to ensure adequate support for individuals after transplant. First, the initiation of a multiple medication regimen at home is a challenge. To ensure that patients and caregivers can follow the multiple medication regimen, healthcare providers need to devote time and attention to conveying all the details about the multiple medication regimen, including dietary and other treatment recommendations, to both patients and their caregivers. A scheduled dedicated prescription meeting delivered by a nurse or a pharmacist in the presence of both patient and caregiver was helpful to the participants in this study who received it. Methods to ensure adherence included a discussion of a printed medication list including the exact dose and time of intake, purpose and possible side effects; a supply of sufficient medications until the next appointment; provision of a pillbox to organize medications, color-coding of different medication bottles; and tips on how to remember medication doses (e.g., with cell phone reminders). Second, the requirement to nominate a dedicated lay caregiver after transplant seems to be warranted to ensure adherence to medical recommendations after transplant. Third, social support is essential for following a multiple medication regimen. If providers of social support cannot attend the prescription meetings, they should be informed about the patient's support needs via a phone call or at least by a written letter.

Conclusion

In conclusion, this study contributes to a more detailed theoretical and practical understanding of social support for a multiple medication regimen. To the best of our knowledge, this is the first in-depth investigation of multiple medication adherence and support in cancer patients. Moreover, the teamwork of patients, lay caregivers, and healthcare providers is the basis for adherence to a multiple medication regimen after transplant when patients are discharged home. Based on our findings, healthcare providers in health care settings and lay caregivers at home must work in tandem and are critical to promoting adherence to multiple medication regimens. The results of this study also suggest that there is a need to develop better organized patient education interventions for patients and their caregivers to facilitate multiple medication adherence.

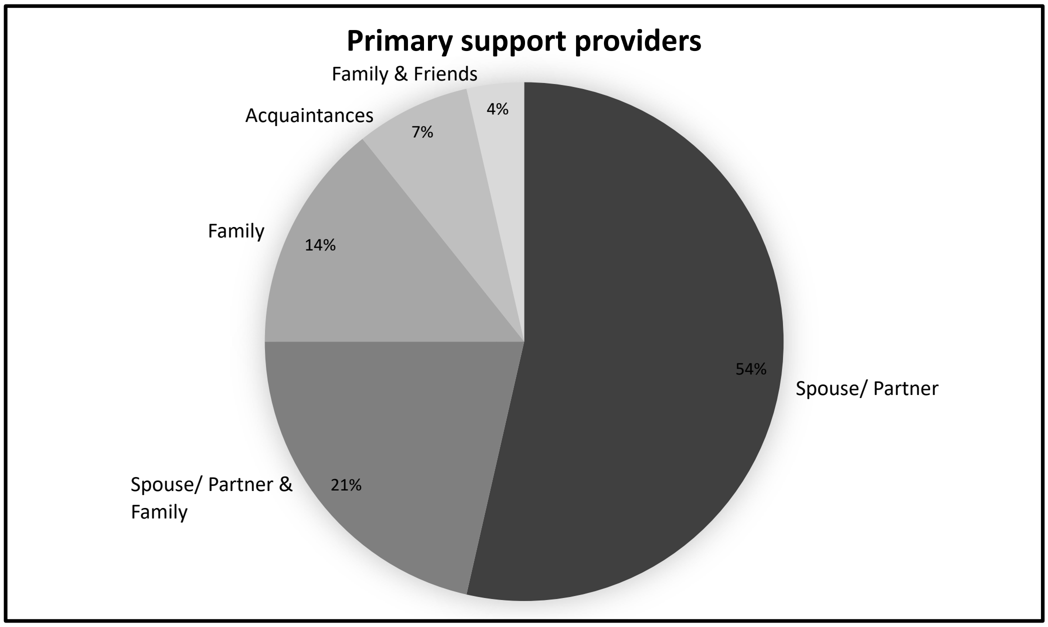


Figure 3.1. Primary support providers of alloHCT recipients (*n* = 28)

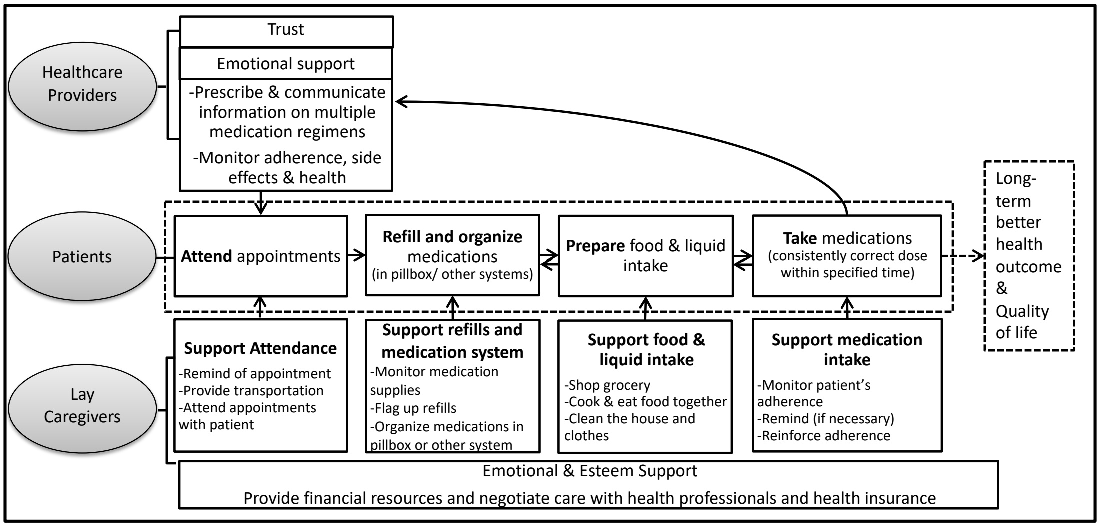


Figure 3.2. Process of social support tasks to ensure multiple medication adherence

References

Aizer, A. A., Chen, M. H., McCarthy, E. P., Mendu, M. L., Koo, S., Wilhite, T. J., … Nguyen, P. L. (2013). Marital status and survival in patients with cancer. *Journal of Clinical Oncology*, *31*(31), 3869–3876. https://doi.org/10.1200/JCO.2013.49.6489

Beattie, S., & Lebel, S. (2011). The experience of caregivers of hematological cancer patients undergoing a hematopoietic stem cell transplant: A comprehensive literature review. *Psycho-Oncology*, *20*(11), 1137–1150. https://doi.org/10.1002/pon.1962

Beattie, S., Lebel, S., & Tay, J. (2013). The influence of social support on hematopoietic stem cell transplantation survival: A systematic review of literature. *PLOS ONE*, *8*(4), e61586. https://doi.org/10.1371/journal.pone.0061586

Berghoff, C. R., Gratz, K. L., Portz, K. J., Pinkston, M., Naifeh, J. A., Evans, S. D., … Tull, M. T. (2018). The role of emotional avoidance, the patient–provider relationship, and other social support in ART adherence for HIV+ individuals. *AIDS and Behavior*, *22*(3), 929–938. https://doi.org/10.1007/s10461-017-1745-2

Berkman, L. F., Glass, T., Brissette, I., & Seeman, T. E. (2000). From social integration to health: Durkheim in the new millennium. *Social Science & Medicine*, *51*(6), 843–857. https://doi.org/10.1016/S0277-9536(00)00065-4

Bosworth, H. B. (2010). Medication adherence. In *Improving patient treatment adherence* (pp. 68–94). Springer, New York, NY. https://doi.org/10.1007/978-1-4419-5866-2_4

Chou, A. F., Stewart, S. L., Wild, R. C., & Bloom, J. R. (2012). Social support and survival in young women with breast carcinoma. *Psycho-Oncology*, *21*(2), 125–133. https://doi.org/10.1002/pon.1863

Claxton, A. J., Cramer, J., & Pierce, C. (2001). A systematic review of the associations between dose regimens and medication compliance. *Clinical Therapeutics*, *23*(8), 1296–1310. https://doi.org/10.1016/S0149-2918(01)80109-0

Cohen, S., & McKay, G. (1984). Social support, stress and the buffering hypothesis: A theoretical analysis. *Handbook of Psychology and Health*, *4*, 253–267.

Creswell, J., Klassen, A. C., Plano, V., & Smith, K. C. (2011). Best practices for mixed methods research in the health sciences. *Bethesda (Maryland): National Institutes of Health, 2013,* 541-545.

Cutrona, C. E., & Russell, D. W. (1990). Type of social support and specific stress: Toward a theory of optimal matching. In *Wiley Series on Personality Processes. Social support: An interactional view* (pp. 319–366). Oxford, England: John Wiley & Sons.

DiMatteo, M. R. (2004). Social support and patient adherence to medical treatment: A meta-analysis. *Health Psychology*, *23*(2), 207–218. https://doi.org/10.1037/0278-6133.23.2.207

Ehrlich, K. B., Miller, G. E., Scheide, T., Baveja, S., Weiland, R., Galvin, J., … Penedo, F. J. (2016). Pre-transplant emotional support is associated with longer survival after allogeneic hematopoietic stem cell transplantation. *Bone Marrow Transplantation*, *51*(12), 1594–1598. https://doi.org/10.1038/bmt.2016.191

Fisher, J. D., Fisher, W. A., Amico, K. R., & Harman, J. J. (2006). An information-motivation-behavioral skills model of adherence to antiretroviral therapy. *Health Psychology*, *25*(4), 462–473. https://doi.org/10.1037/0278-6133.25.4.462

Foster, L., Mclellan, L., A. Rybicki, L., A. Sassano, D., Hsu, A., & Bolwell, B. (2005). Survival of patients who have undergone allogeneic bone marrow transplantation. *Journal of Psychosocial Oncology, 22*(2), 1-20. https://doi.org/10.1300/J077v22n02_01

Hahn, T., McCarthy, P. L., Hassebroek, A., Bredeson, C., Gajewski, J. L., Hale, G. A., … Majhail, N. S. (2013). Significant improvement in survival after allogeneic hematopoietic cell transplantation during a period of significantly increased use, older recipient age, and use of unrelated donors. *Journal of Clinical Oncology*, *31*(19), 2437–2449. https://doi.org/10.1200/JCO.2012.46.6193

Hall, A. E., Paul, C., Bryant, J., Lynagh, M. C., Rowlings, P., Enjeti, A., & Small, H. (2016). To adhere or not to adhere: Rates and reasons of medication adherence in hematological cancer patients. *Critical Reviews in Oncology/Hematology*, *97*, 247–262. https://doi.org/10.1016/j.critrevonc.2015.08.025

Helgeson, V. S. (2003). Social support and quality of life. *Quality of Life Research*, *12*(1), 25–31. https://doi.org/10.1023/A:1023509117524

Holtan, S. G., DeFor, T. E., Lazaryan, A., Bejanyan, N., Arora, M., Brunstein, C. G., … Weisdorf, D. J. (2015). Composite end point of graft-versus-host disease-free, relapse-free survival after allogeneic hematopoietic cell transplantation. *Blood*, *125*(8), 1333–1338. https://doi.org/10.1182/blood-2014-10-609032

Holt-Lunstad, J., Smith, T. B., & Layton, J. B. (2010). Social relationships and mortality risk: A meta-analytic review. *PLoS Med*, *7*(7), e1000316.

House, J. S., Kahn, R. L., McLeod, J. D., & Williams, D. (1985). Measures and concepts of social support. In *Social support and health.* (pp. 83–108). San Diego, CA, US: Academic Press.

Hsieh, H. F., & Shannon, S. E. (2005). Three approaches to qualitative content analysis. *Qualitative Health Research*, *15*(9), 1277–1288. https://doi.org/10.1177/1049732305276687

Jim, H. S. L., Sutton, S. K., Jacobsen, P. B., Martin, P. J., Flowers, M. E., & Lee, S. J. (2016). Risk factors for depression and fatigue among survivors of hematopoietic cell transplantation. *Cancer, 122*(8), 1290–1297. https://doi.org/10.1002/cncr.29877

Kantor, E. D., Rehm, C. D., Haas, J. S., Chan, A. T., & Giovannucci, E. L. (2015). Trends in prescription drug use among adults in the United States from 1999-2012. *JAMA*, *314*(17), 1818–1830. https://doi.org/10.1001/jama.2015.13766

Kelley, J. M., Kraft-Todd, G., Schapira, L., Kossowsky, J., & Riess, H. (2014). The influence of the patient-clinician relationship on healthcare outcomes: A systematic review and meta-analysis of randomized controlled trials. *PLOS ONE*, *9*(4), e94207. https://doi.org/10.1371/journal.pone.0094207

Kelly, J. D., Hartman, C., Graham, J., Kallen, M. A., & Giordano, T. P. (2014). Social support as a predictor of early diagnosis, linkage, retention, and adherence to HIV care: Results from the steps study. *The Journal of the Association of Nurses in AIDS Care : JANAC*, *25*(5), 405–413. https://doi.org/10.1016/j.jana.2013.12.002

Khera, N., Chang, Y., Hashmi, S., Slack, J., Beebe, T., Roy, V., … Mikhael, J. (2014). Financial burden in recipients of allogeneic hematopoietic cell transplantation. *Biology of Blood and Marrow Transplantation*, *20*(9), 1375–1381. https://doi.org/10.1016/j.bbmt.2014.05.011

Kim, W., Mcnulty, J., Chang, Y. -h, Weise, M., Hashmi, S., Ailawadhi, S., & Khera, N. (2015). Financial burden after allogeneic hematopoietic cell transplantation: A qualitative analysis from the patient’s perspective. *Bone Marrow Transplantation; London*, *50*(9), 1259–1261. http://dx.doi.org/10.1038/bmt.2015.128

Kirsch, M., Götz, A., Halter, J. P., Schanz, U., Stussi, G., Dobbels, F., & De Geest, S. (2014). Differences in health behaviour between recipients of allogeneic haematopoietic SCT and the general population: A matched control study. *Bone Marrow Transplantation*, *49*(9), 1223–1230. https://doi.org/10.1038/bmt.2014.142

Krause, N. (2007). Longitudinal study of social support and meaning in life. *Psychology and Aging*, *22*(3), 456–469. https://doi.org/10.1037/0882-7974.22.3.456

Lehrer, J., Brissot, E., Ruggeri, A., Dulery, R., Vekhoff, A., Battipaglia, G., … Antignac, M. (2018). Medication adherence among allogeneic hematopoietic stem cell transplant recipients: A pilot single-center study. *Bone Marrow Transplantation*, *53*(2), 231–233. https://doi.org/10.1038/bmt.2017.233

Luszczynska, A., Pawlowska, I., Cieslak, R., Knoll, N., & Scholz, U. (2013). Social support and quality of life among lung cancer patients: A systematic review. *Psycho-Oncology*, *22*(10), 2160–2168. https://doi.org/10.1002/pon.3218

Majhail, N. S., Farnia, S. H., Carpenter, P. A., Champlin, R. E., Crawford, S., Marks, D. I., … LeMaistre, C. F. (2015). Indications for autologous and allogeneic hematopoietic cell transplantation: Guidelines from the American Society for Blood and Marrow Transplantation. *Biology of Blood and Marrow Transplantation*, *21*(11), 1863–1869. https://doi.org/10.1016/j.bbmt.2015.07.032

Mayberry, L. S., & Osborn, C. Y. (2012). Family support, medication adherence, and glycemic control among adults with type 2 diabetes. *Diabetes Care*, *35*(6), 1239–1245. https://doi.org/10.2337/dc11-2103

McLellan, L., Foster, L. W., Rybicki, L., Dabney, J., Cooper, M., & Bolwell, B. (2011). Optimal duration and frequency of in-hospital lay care-partner support for positive impact on patient survival in allogeneic BMT. *Biology of Blood and Marrow Transplantation*, *17*(2, Supplement), S243–S244. https://doi.org/10.1016/j.bbmt.2010.12.272

Morrison, C. F., Martsolf, D. M., Wehrkamp, N., Tehan, R., & Pai, A. L. (2017). Medication adherence in hematopoietic stem cell transplantation: A review of the literature. *Biology of Blood and Marrow Transplantation*, *23*(4), 562–568. https://doi.org/10.1016/j.bbmt.2017.01.008

National Center for Health Statistics (US). (2014). *Health, United States, 2013: With Special Feature on Prescription Drugs*. Retrieved from http://www.ncbi.nlm.nih.gov/books/NBK209224/

National Marrow Donor Program. (2017). After transplant guidelines for patients. Retrieved November 17, 2018, from https://bethematchclinical.org/resources-and-education/materials-catalog/after-transplant-guidelines-for-patients/

O’Brien, B. C., Harris, I. B., Beckman, T. J., Reed, D. A., & Cook, D. A. (2014). Standards for reporting qualitative research: A synthesis of recommendations. *Academic Medicine*, *89*(9), 1245. https://doi.org/10.1097/ACM.0000000000000388

Pantuzza, L. L., Ceccato, M. das G. B., Silveira, M. R., Junqueira, L. M. R., & Reis, A. M. M. (2017). Association between medication regimen complexity and pharmacotherapy adherence: A systematic review. *European Journal of Clinical Pharmacology*, *73*(11), 1475–1489. https://doi.org/10.1007/s00228-017-2315-2

Pasquini, M., Wang, Z., & Schneider, L. (2009). CIBMTR summary slides. *CIBMTR Newsletter*, 6–11.

Posluszny, D. M., Bovbjerg, D. H., Agha, M. E., Hou, J.-Z., Raptis, A., Boyiadzis, M. M., … Dew, M. A. (2018). Patient and family caregiver dyadic adherence to the allogeneic hematopoietic cell transplantation medical regimen. *Psycho-Oncology*, *27*(1), 354–358. https://doi.org/10.1002/pon.4393

Rathert, C., Wyrwich, M. D., & Boren, S. A. (2013). Patient-centered care and outcomes: A systematic review of the literature. *Medical Care Research and Review*, *70*(4), 351–379. https://doi.org/10.1177/1077558712465774

Rini, C., Redd, W. H., Austin, J., Mosher, C. E., Meschian, Y. M., Isola, L., … DuHamel, K. N. (2011). Effectiveness of partner social support predicts enduring psychological distress after hematopoietic stem cell transplantation. *Journal of Consulting and Clinical Psychology*, *79*(1), 64–74. https://doi.org/10.1037/a0022199

Robinson, J. H., Callister, L. C., Berry, J. A., & Dearing, K. A. (2008). Patient-centered care and adherence: Definitions and applications to improve outcomes. *Journal of the American Academy of Nurse Practitioners*, *20*(12), 600–607. https://doi.org/10.1111/j.1745-7599.2008.00360.x

Sabaté, E. (2003). *Adherence to long-term therapies: Evidence for action*. Geneva: World Health Organization.

Scheurer, D., Choudhry, N., Swanton, K. A., Matlin, O., & Shrank, W. (2012). Association between different types of social support and medication adherence. *The American Journal of Managed Care*, *18*(12), e461-7.

Simoni, J. M., Frick, P. A., & Huang, B. (2006). A longitudinal evaluation of a social support model of medication adherence among HIV-positive men and women on antiretroviral therapy. *Health Psychology: Official Journal of the Division of Health Psychology, American Psychological Association*, *25*(1), 74–81. https://doi.org/10.1037/0278-6133.25.1.74

So, W. K., Dodgson, J., & Tai, J. W. (2003). Fatigue and quality of life among Chinese patients with hematologic malignancy after bone marrow transplantation. *Cancer Nursing*, *26*(3), 211–219.

Thoits, P. A. (2011). Mechanisms linking social ties and support to physical and mental health. *Journal of Health and Social Behavior*, *52*(2), 145–161.

Tomblyn, M., Chiller, T., Einsele, H., Gress, R., Sepkowitz, K., Storek, J., … Boeckh, M. A. (2009). Guidelines for preventing infectious complications among hematopoietic cell transplantation recipients: A global perspective. *Biology of Blood and Marrow Transplantation*, *15*(10), 1143–1238.

Tong, A., Flemming, K., McInnes, E., Oliver, S., & Craig, J. (2012). Enhancing transparency in reporting the synthesis of qualitative research: ENTREQ. *BMC Medical Research Methodology*, *12*(1), 181. https://doi.org/10.1186/1471-2288-12-181

Tong, A., Sainsbury, P., & Craig, J. (2007). Consolidated criteria for reporting qualitative research (COREQ): A 32-item checklist for interviews and focus groups. *International Journal for Quality in Health Care*, *19*(6), 349–357. https://doi.org/10.1093/intqhc/mzm042

Uchino, B. N. (2006). Social support and health: A review of physiological processes potentially underlying links to disease outcomes. *Journal of Behavioral Medicine*, *29*(4), 377–387.

Weiss, R. (1974). The provisions of social relationships. In Z. Rubin (Ed.), *Doing unto Others: Joining, Molding, Comforming, Helping, Loving* (pp. 17-26). Englewood Cliffs, NJ: Prentice-Hall.

Wulff-Burchfield, E. M., Jagasia, M., & Savani, B. N. (2013). Long-term follow-up of informal caregivers after allo-SCT: A systematic review. *Bone Marrow Transplantation*, *48*(4), 469–473. https://doi.org/10.1038/bmt.2012.123

Zullig, L. L., Stechuchak, K. M., Goldstein, K. M., Olsen, M. K., McCant, F. M., Danus, S., … Bosworth, H. B. (2015). Patient-reported medication adherence barriers among patients with cardiovascular risk factors. *Journal of Managed Care & Specialty Pharmacy*, *21*(6), 479–485. https://doi.org/10.18553/jmcp.2015.21.6.479

Chapter IV

STRATEGIES FOR STRENGTHENING ADHERENCE TO MULTIPLE MEDICATIONS

Abstract

Background: Although patients face significant challenges adhering to multiple medication regimens on a daily basis, the subject remains understudied.

Objective: The objective of this study was to explore adherence strategies developed and adopted by patients prescribed with multiple medications for an extended period of time using the Information-Motivation-Behavioral Skills (IMB) model.

Methods: Semi-structured, in-depth interviews were conducted with 28 leukemia and lymphoma cancer patients (46.4% female, age: $M = 53.97$, 46.4% ethnic minority) who received an allogeneic hematopoietic cell transplant (alloHCT). Interviews covered different topics related to medication adherence, including questions on knowledge about the regimen, skills, and motivations. Interviews were transcribed, organized by themes, and coded using content analysis, with the IMB model (Fisher, Fisher, Amico, & Harman, 2006) as a guiding theoretical framework.

Results: Patients reported difficulties comprehending the information regarding their prescribed medications, although some patients knew the details of their regimens.

Patient interviews contained familiar themes of maintaining personal motivation (commonly having a positive attitude and beliefs about medications, and taking responsibility), receiving social support (commonly emotional and practical support from family members and friends, and support for medical needs from healthcare providers), and building behavioral skills relevant to taking medications (commonly having a fixed schedule and place, maintaining an adequate diet, and using prompts). However, there were also additional factors that have not been identified in the IMB model, like acceptance of patient role and general optimism.

Conclusion: The study offers practical suggestions for improving adherence to multiple medications and also builds a foundation to develop an intervention specific to this population by eliciting individuals' initial level of information, motivation, and behavioral skills regarding taking multiple medications. It also shows the need for mapping theoretical determinants of adherence and behavior change strategies for patients, lay caregivers, and health professionals to develop effective interventions to improve adherence to multiple medications.

Keywords: determinants; medication adherence; multiple medications; personal strategies

Introduction

As life expectancy increases, more people are living with multiple chronic conditions that require a number of different medications (Buttorff, Ruder, & Bauman, 2017; Kantor, Rehm, Haas, Chan, & Giovannucci, 2015; Kim & Parish, 2017; Sabaté, 2003), making adherence to multiple medications an increasingly important issue in healthcare (Cross, Elliott, & George, 2016; Patton, Cadogan, et al., 2017; Wu & Green, 2000). There has also been an increase in oral treatments for different health conditions, including cancer, and as patients and healthcare systems tend to prefer oral treatments, they are predicted to increase in the future (Banna et al., 2010; Mathes, Antoine, Pieper, & Eikermann, 2014; Ruddy, Mayer, & Partridge, 2009; Verbrugghe, Verhaeghe, Lauwaert, Beeckman, & Van Hecke, 2013). Consequently, patients assume a greater responsibility for their healthcare, as healthcare providers cannot directly supervise medication intake (Banna et al., 2010). However, medication adherence has been a struggle for many with chronic conditions, where only about half or less adhere (Sabaté, 2003).

Adherence to a multiple medication regimen is even more difficult than adherence to a single medication regimen (Claxton, Cramer, & Pierce, 2001; McDonald, Garg, & Haynes, 2002; Pantuzza, Ceccato, Silveira, Junqueira, & Reis, 2017). This holds true for patients after alloHCT, who are prescribed with multiple medications: the most recent observational study showed that more than half of the patients sampled poorly adhered to their medication regimens (Lehrer et al., 2018). A literature review found a wide range of adherence rates (33% to 95%) to multiple medications (Morrison, Martsolf, Wehrkamp, Tehan, & Pai, 2017). An additional study in this patient group also found a range of adherence rates for different tasks required after alloHCT, including taking immunosuppressants and other medications, as well as maintaining hygiene and exercise, even with assistance from family caregivers (Posluszny et al., 2018). Moreover, previous studies on organ transplants also found that long-term adherence is a challenge for patients; the longer the treatment period after transplant, the less adherent patients were, underscoring the need for healthcare providers to continually (re)educate their patients (Bishop, Rodrigue, & Wingard, 2002; Morrison et al., 2017; Siegal & Greenstein, 1999; Teichman, Burker, Weiner, & Egan, 2000).

Adherence interventions have had limited effectiveness, and vary greatly in terms of target patients, types, measures of adherence and health outcomes (Nieuwlaat et al., 2014). As such, better interventions for adherence to multiple medications could be developed. A recent systematic review and meta-analysis of 771 trials concluded that medication adherence interventions should focus on behavioral strategies rather than cognitive strategies (influencing patients' knowledge and beliefs) to improve adherence (Conn & Ruppar, 2017). Moreover, there is an unfortunate shortage of theory-based interventions for multiple medication adherence (Patton, Hughes, Cadogan, & Ryan, 2017). The Information-Motivation-Behavioral Skills (IMB) model (Fisher, Fisher, Amico, & Harman, 2006), a behavioral theory, addresses the underlying mechanisms of adherence and focuses on information, motivation, and behavioral skills as determinants of adherence. The study of these determinants could help predict better adherence behavior and eventually produce better health outcomes (Fisher et al., 2006). This model has predominantly been used for HIV/AIDS treatment, but it has also been used for other health conditions, such as diabetes and coronary artery diseases (Horvath, Smolenski, & Amico, 2014; Mayberry & Osborn, 2014; Zarani, Besharat, Sadeghian, & Sarami, 2010). Moreover, a review of 12 interventions based on the IMB model found that 10 of the interventions had significant behavior changes in different health conditions, indicating the promise of developing behavioral interventions using the IMB model (Chang, Choi, Kim, & Song, 2014).

This study, using the IMB model, aims to provide a theory-based overview of the strategies patients prescribed with multiple medications have developed for themselves. This is the first step towards developing theory- and evidence-based interventions for multiple medication adherence (Bartholomew Eldredge et al., 2016). Also, this study uses a technique called elicitation research, in which we receive information from participants, where there are no right or wrong answers, and identify the specific needs of the group (Fisher & Fisher, 1992). The questions concerned medication adherence, motivations, and behavioral skills. According to Fisher & Fisher (1992),

> Interventions that are based on elicitation research to assess group-specific needs, sensitivities, and intervention tactics are more apt to be successful than those that are based on the investigators' intuition because they are more apt to correspond to the needs and concerns of the target population. (p. 456).

By eliciting information from participants, this study aims to contribute to the development of a more effective intervention.

To study adherence strategies, we focus on individuals recovering from alloHCT (also known as bone marrow transplants) to treat leukemia or lymphoma. These individuals must adhere to a multiple medication regimen that is critical for their survival. Their multiple medication regimens typically include 18 medications with 24 or more pills per day in the first few months after transplant (Freifeld et al., 2011; Neumann, Krause, Maschmeyer, Schiel, & von Lilienfeld-Toal, 2013; Tomblyn et al., 2009). When patients are discharged from the hospital, they need to incorporate multiple medications into their daily lives, a task many struggle with (Morrison et al., 2017; Posluszny et al., 2018). Therefore, they are an appropriate population for studying multiple medication adherence.

By parsing the myriad adherence strategies developed by alloHCT patients over the course of three to six months, this application of the IMB model sheds new light on the determinants of adherence to a multiple medication regimen. Only a handful of studies have examined the adherence of alloHCT patients, yielding varying adherence levels and illustrating the challenges of home care after transplant (Gresch et al., 2017; Morrison et al., 2017; Posluszny et al., 2018). But none has identified the specific strategies patients spontaneously developed to maintain their adherence. Although there have been previous studies on the determinants of medication adherence for cancer patients (Kardas, Lewek, & Matyjaszczyk, 2013; Patton, Cadogan, et al., 2017), to our knowledge, this is the first study that seeks to identify medication adherence strategies of alloHCT patients. Therefore, we seek to provide a list of practicable strategies for adherence to multiple medications.

Methods

This study was part of a larger transplant study of individuals with leukemia and lymphoma cancers. Using theory-based semi-structured in-depth interviews, the determinants (i.e. facilitators and barriers) of multiple medication adherence after transplant were identified using directed content analysis (Hsieh & Shannon, 2005). The study was approved by the Institutional Review Board of all the related institutions, including Columbia University, Teachers College, and the hospital from which the data was collected. All participants provided written informed consent prior to participating. The study referred to the established standards for reporting qualitative results (Creswell, Klassen, Plano, & Smith, 2011; O'Brien, Harris, Beckman, Reed, & Cook, 2014; Tong, Flemming, McInnes, Oliver, & Craig, 2012; Tong, Sainsbury, & Craig, 2007), and especially followed COREQ (Tong et al., 2007) guideline (see Appendix C for more details).

Setting and Participants

Data were collected at a renowned hematology oncology department of a large urban area hospital. Individuals with leukemia and lymphoma cancers who received allogeneic bone marrow transplant HCT were asked if they were interested in participating in the study by their healthcare providers. Eligible participants included adults 18 years old or older, who spoke English, Spanish or Mandarin. Two interviews were in Spanish (7.1%), the rest in English (n = 26, 92.9%), and none in Mandarin. Participation was voluntary.

Measures

We chose a qualitative approach—theoretically-informed semi-structured in-depth interviews—in order to give patients after alloHCT an opportunity to fully express their experiences and share the strategies they found most useful. A previous study on hypertensive patients successfully used a qualitative approach to explore the experiences of patients (Ogedegbe, Harrison, Robbins, Mancuso, & Allegrante, 2004). Moreover, there is only one previous study that has examined the determinants of medication adherence for this particular patient group (Posluszny et al., 2018), so a qualitative approach, an elicitation research (as mentioned above), is sufficient to initiate the research and serve as a building block for developing an intervention (Creswell, 2013; Fisher & Fisher, 1992).

The principal investigator, who is an expert in health psychology, developed the interview guide. The interview covered various topics on adherence and home care, including questions on general medication adherence, knowledge of medications, skills, social motivation and successful (or unsuccessful) adherence strategies (see Appendix A for the interview guide). Some examples of the questions include: “Please tell me about the medication(s) that you take. What medication does your physician currently prescribe?”; “Do you know which of your medications is an antibiotic/ immunosuppressant/ antifungal/ antiviral medication? How did you find this out?”; “How well do you think the medications work in helping people after transplant? Or do you think medications might harm people after transplant?”

The inter-rater reliability for information (e.g. access to adequate information, lack of information, and flawed heuristics and implicit theory), motivation (e.g. positive attitudes, lack of positive attitudes, and social support from lay caregivers and from healthcare providers), and behavioral skills (e.g. strategies for dealing with difficult medications, fixed schedule, and diet) was calculated based on seven randomly selected interviews. We measured the similarity of coding between the two researchers using Cohen’s Kappa (κ), examining whether they agreed that a specific theme had been mentioned in a patient’s interview. The overall Kappa for information was initially 0.24, leading the two researchers to discussed coding strategies. They reconciled the differences in the next round of coding, increasing the figure to 0.81. Kappa coefficients for motivation, including personal motivation ($\kappa = 0.71$), healthcare providers' support ($\kappa = 0.86$), and lay caregivers' support, were similarly high ($\kappa = 0.86$). The overall coding agreement for behavioral skills was initially 0.60, so the discrepancies were communicated between the coders, and when it was coded again, the agreement came out to be 1.00.

Procedures

Those who agreed to participate in the study were scheduled for an interview between 3 to 6 months after their first hospital discharge. In person (during hospital visits) or phone interviews were conducted depending on the schedule and health of the participant. In some cases, when participants were accompanied by their caregivers to the appointment, the caregivers joined the interviews as well. Two interviewers conducted each interview in order to facilitate a conversational experience: One person took notes and recorded the interview, and the other continued the dialogue. The semi-structured interview lasted from 40 minutes to an hour. Interviewers used a prepared and previously piloted interview script as a guide. Interviewers asked additional probing questions for more details. The interview guide was developed under the supervision of the principal investigator and modified after a few pilot studies.

Interviews were audio recorded and transcribed later for analysis. All interviews were stored in a password secured drive and transcribed after the fact. For confidentiality, any identifying information was removed, and actual names were replaced by generic names post-transcription (e.g., Jane Doe with Physician 1).

Data Analysis

A codebook based on the Information-Motivation-Behavioral Skills model (Fisher et al., 2006) was developed prior to data analysis (see Appendix B). Themes were discussed and refined among the two researchers, and questions that could not be reconciled between them were discussed with the principal investigator. As outlined in the codebook, the interviews were coded according to the major themes of the Information-Motivation-Behavioral Skills Model using directed content analysis (Hsieh & Shannon, 2005). All interview transcripts were read repeatedly and manually coded by two coders using NVivo version 11. This software allows for the creation of categories and sub-categories, comparisons of coding by different researchers, and calculation of frequencies and discrepancies.

Results

Characteristics of Patients

We collected interview data from 28 individuals (46.4% female, age: *M* = 53.97). Individuals in the study came from different ethnic backgrounds, including Non-Hispanic White (*n* = 15, 53.6%), African American (*n* = 2, 7.1%), Asian (*n* = 5, 17.9%), Hispanic (*n* = 5, 17.9%), and other (*n* = 1, 3.5%). Of these, 26 individuals answered all interview questions. The remaining two answered some of the interview questions but not all: Patients 20 and 21 could not complete the section on healthcare providers. Most of them interviewed in English (*n* = 26, 92.9%) and a few in Spanish (*n* = 2, 7.1%).

Patients mentioned different strategies they had spontaneously developed for adherence to their medication regimens after transplant. Most themes that patients mentioned neatly fell into the categories of the IMB model, but there were also themes that did not.

Acceptance of Patient Role and General Optimism

This theme did not neatly fit into the IMB model, but it is an important theme to note as a catalyst that allows for other adherence strategies. Many individuals in our sample (*n* = 13/28, 46.4%) approached their life after transplant with optimism, although they perceived changes to their quality of life after receiving the transplant and had fears and worries. Patients found hope in the fact that they were still alive, and that their health had improved. “We have to leave on a lighter note! The problems are almost over. You have to take the lighter side!” (P13, age 67, male). “Don’t take the treatment lightly, it is important. Remain positive above all” (P23, age 59, female).

Moreover, some were able to find hope in the support they received from their close others and healthcare providers.

> So psychologically I am doing fairly well. (…) having a positive attitude was a big help. My family is very supportive. (…) So all in all I have no complaints. I’m happy to be alive (…) I keep everything in perspective. (P28, age 59, male)

Another mentioned, “I’ve been so fortunate in so many ways in this process. It’s a terrible situation, but it’s been as good as it can go. It could be a lot worse.” (P10, age 49, male). There was also one patient, who found a strong faith and positive beliefs to be helpful in taking medications and recovering after transplant. She mentioned, “If you don’t believe, how can you be cured? And then always pray.” (P29, age 63, female).

Concerns, Fears, and Worries

While many patients maintained their optimistic outlooks, others (*n* = 10, 35.7%) reported frustrations and anxieties, mainly due to uncertainties about their future, burdens on their families, health restrictions and side effects of treatment and medications.

> I had to get used to everything again, like eating. Also, it impacted my mental status. (…) I didn't recognize my son, and I didn't know where he lived. I didn't know what was going on, and it was scary. It's getting better now." (P09, age 49, female)

There were two cases where patients expressed frustrations about the consequences of their illness for family members. In one case, the patient had a daughter-in-law, who was pregnant. She had once lost her baby, and the patient was worried that she might lose her baby again, as she was "tense over things" (P38, age 64, female). In another case, every single family member struggled greatly after the patient became ill: his daughters struggled in school, and his wife became financially and mentally unstable (P10, age 49, male). The patient blamed himself for the plight of his family.

Half of these 10 individuals (*n* = 5/10, 50.0%) reported mixed feelings of both optimism and fears during the interview. For example, one patient mentioned, "I don't have cancer anymore. Because of the transplant and it makes everything better." But he also mentioned, "[I felt] stress because I had to be in the hospital, and kids are in school and you really worry about what's gonna happen next." (P14, age 32, male).

Information

According to the IMB model, having adequate information about the medication is necessary for adherence. By contrast, flawed heuristics and implicit theories about medications usually led to making inappropriate decisions.

Information about medications. For information regarding their medications, patients referred to the personalized list provided by their healthcare providers during hospital discharge and clinical visits, which provides information about their prescribed medication, including their dosage, schedule, functions, and side effects. Most of them had a very long list of about 24 medications and a number of them (*n* = 9/28, 32.1%) had comprehensive knowledge of their medications. A patient, for instance, recalled his entire medication regimen.

> Around 7 o'clock in the morning I take Mepron and the Phenadone I think it's called. Then at around 8 o'clock I would take the magnesium tablet, the Prograf and the Acyclovir. At 10 o'clock I'll take the Voriconazole. At 2 o'clock I'll take the magnesium tablet. At 6 o'clock I will take the Famotidine. 8 o'clock I would take the Prograf, the Tacrolimus, the Acyclovir and another magnesium tablet. And 10 o'clock I'd take the Voriconazole. (P28, age 59, male)

However, a greater number of patients had partial knowledge of their medications (*n* = 19/28, 67.9%). "I know they gave me prednisone [which] is steroid, and they gave me voriconazole, acyclovir, the other one I don't [remember]." (P32, age 46, female). Another mentioned,

> I have some pills that I take two times a day. I have another that I take once a day. I have another that I take three times a week, Monday, Wednesday and Friday. (…) oh the liquid medicine, that's three times a day. (P23, age 59, female)

Patients had difficulties comprehending and remembering their medication regimens due to the sheer number of medications and adjustments in their regimens.

> I'm not really sure. Not really sure, I mean there's so many to keep track of. I'm just taking it cause I was told to. (…) But they're lowering the immune-suppressant. (P21, age 29, male)

Another mentioned, "Immunosuppressants, I'm not sure. The antifungal I think is the uh…. let's see. No I don't know." (P13, age 67, male).

There were a number of cases (*n* = 11/28, 39.3%) in which caregivers were heavily involved in refilling and organizing medications (see section on caregiver support). In some of these cases, the patient had little knowledge regarding the prescribed medications.

> All are pills, cannot tell... All are pills. You do not know an antivirus. Pills all come in a box and I only take the pills in that box. My daughters will fill the box of pills. (P12, age 54, female)

Moreover, in two interviews, the spouses interrupted to provide additional information on medications: “Can I help him say it? I know them more than him.” (P20, age 50, male). Support from caregivers compensated for the patients’ lack of information, underscoring the benefits of adequately informing caregivers as well. Dedicated, well-informed caregivers can and sometimes must intervene if the patient cannot comprehend or retain information due to fatigue or cognitive problems.

Flawed heuristics and implicit theories. Some individuals developed heuristics and implicit theories with questionable validity (*n* = 6/28, 21.4%). One individual reported, “I took [a] break from [the] medications on purpose because I was feeling better.” (P40, age 57, male). Another mentioned, “too much medications would build immunity and will not be as effective” (P20, age 50, male). Two individuals mentioned that they would never take medications without food because it would be harmful, although some of their medications were prescribed to be taken without food. These heuristics and implicit theories suggest the importance of holding programmatic discharge meetings in which the prescribed medication regimens, including their functions and side effects, are explained in detail.

Personal Motivation

Personal motivation concerns individuals' attitudes towards taking medications and their evaluation and beliefs about health outcomes (Fisher et al., 2006). This includes taking responsibilities for and perceiving the importance of taking medications, as well as maintaining positive attitudes and beliefs about medications and health outcomes.

Taking responsibilities and perceiving the importance of taking medications. Our participants were highly motivated with a strong sense of commitment to and responsibility for their medication adherence. Almost everyone (*n* = 26/28, 92.9%) considered taking medications to be one's own responsibility and prioritized taking medications. "Sometimes (…) I don't want to take my medications. (…) I take them anyway, [laughs] I have no choice." (P43, age 51, male). Another mentioned,

> I have to take all the medication every day, weekend and weekday does not matter. (…) I took it every time, no matter what. Taking medications is very important to get better. (P11, age 71, female)

Positive attitudes and beliefs about medications and health outcomes. Many participants (*n* = 13/28, 46.4%) had positive attitudes and beliefs about medications.

> Some of them were not exactly very tasty and the repetition of taking all the medication all the time, but it's a minor thing compared to all the benefits of the pills. I'm around today because I've been doing this! (P13, age 67, male)

However, quite a number of individuals (*n* = 9/28, 32.1%) also expressed concerns and ambivalent opinions about their medications due to their side effects, though they remained generally positive about their prescribed medications.

> I hope that the medications are helpful and effective for my recovery. The medication can be helpful in one way and hurtful in another way. (…) But I think they are doing good by me. (P09, age 49, female)

Two participants were worried about the negative side effects after taking them: “I don’t want to take any more medications, every med has a side effect.” (P07, age 56, female). “I am concerned that the medicine may hurt my kidney, or my liver.” (P08, age 53, male).

Social Motivation

Social motivation refers to an individual’s perceived social support from others (Fisher et al., 2006). Healthcare providers are included in this domain, as well as family members and friends. Studies suggest that social support is a critical factor for post-transplant care and adherence (Ehrlich et al., 2016) (To learn more about the specific association between social support and adherence to multiple medications, please refer to the second paper of the dissertation).

Lay caregiver. All participants in our sample (*n* = 28/28, 100.0%) received some form of support from their family members and friends. The majority had a spouse or partner as a primary caregiver (*n* = 15/28, 53.6%), but many others received help from various family members and/or friends (*n* = 11/28, 39.3%), and others from non-family acquaintances (n=2, 7.1%).

Instrumental support. Lay caregivers mostly provided instrumental support related to medication adherence (*n* = 26/28, 92.9%). “My wife does bulk of it (reminding to take medications). (…) She’ll ask me if I have and she’s the one that makes sure I’m taking my medicine.” (P26, age 50, male). Lay caregivers also helped patients with daily tasks (*n* = 16/28, 57.1%), such as cooking, completing house chores, shopping for groceries, and driving them to destinations. “My partner did the cooking, he works from home, he did all of that.” (P16, age 46, male).

Caregivers also supported patients financially (*n* = 4/28, 14.3%). Financial support was a critical and sensitive topic because some patients felt indebted to their partners and frustrated about their financial situation (*n* = 8/28, 28.6%). It was more salient among male patients, as 6 of 8 male patients mentioned financial struggles that came after treatment, as opposed to 2 out of 8 female patients. It is possible that men felt a stronger sense of financial obligation to their family and felt guilty or indebted for being supported by their partners.

> It's been difficult financially. We have eaten into savings, into retirement. Because we were not producing income we needed it affected my wife's business and my business. (P10, age 49, male)

According to this participant, his wife was the sole income generator when he was in the hospital.

Emotional support. Lay caregivers also provided emotional support (*n* = 11/28, 39.3%). "With nobody, I could fall in depression and it would be a problem. Lonely. With support you do well." (P07, age 56, female). "How spectacularly kind, gentle, loving people are caring for me." (P41, age 65, female). Overall, lay caregivers can be encouraged to help individuals after transplant with medications by organizing and managing daily doses, picking up medication refills, and reminding patients to take medications. Lay caregivers are also crucial in helping patients complete daily tasks, such as cleaning and cooking, as well as providing financial support when needed. Moreover, sufficient emotional support can also motivate individuals to adhere to their regimens.

Healthcare provider support. There were two patients coded as missing for this part of the interview because they did not feel well during the interview and requested to stop. The results on the subject of healthcare provider support are thus based on 26 interviews. Healthcare providers, mainly referring to doctors and nurses, worked closely together and were perceived as a team by most participants (*n* = 22/26, 84.6%). While doctors and nurses were the main healthcare providers, pharmacists and dieticians also helped, especially when patients had questions about their medications or diet.

Informational support. Healthcare providers mainly provided patients with the appropriate information on the management of medications, as well as their functions and side effects (*n* = 23/26, 88.5%).

> Actually when I was getting discharged, they gave me list of medication and it's self-explanatory and two people came from the pharmacy, they told me everything and also the nurse who discharged me and also [name of nurse 3] from here so I had a lot of people who really talked to me about the medication. (P22, age 35, female)

Moreover, the healthcare providers informed patients about the appropriate diet and hydration (*n* = 6/26, 23.1%). "They gave me a chart of what I can eat and what I can't eat and went through." (P26, age 50, male). One patient complained about not receiving enough information at the discharge meeting and eventually being readmitted to the hospital. He claimed, "I ended up back in here (hospital). They didn't talk about hydration." (P01, age 65, male).

Providing medical needs. Healthcare providers were responsible for patients' medical needs, such as providing instructions about their medication intake (*n* = 18/26, 69.2%). Patients were satisfied with the medical teams and their treatment. "He is a very good professional. (…) My doctor understood my needs and the communication was clear and important." (P23, age 59, female). Another individual mentioned, "It was teams. Plural. They all helped. I couldn't have asked for better care." (P25, age 66, male).

Emotional support: Patients felt cared for, as well as encouraged and emotionally supported, by the healthcare providers (*n* = 9/26, 34.6%). “They are kind to me and help me.” (P11, age 71, female). Another individual mentioned,

> I think we (healthcare providers and self) have a good relationship. And they seem to really care. [W]hen I walked in after surviving that… ordeal during the summer, (…) they all started clapping and hugging me. It was nice. [Laughs] Made me happy to be there. Happy to be at the doctor’s. (P35, age 65, female)

This emotional support not only motivated them, but it also made them feel more comfortable with the treatment. “Knowing that he is a good doctor, for me, has been very important. And everything has been made way easier.” (P23, age 59, female).

Behavioral Skills

Behavioral skills can help well-informed and motivated individuals adhere to their medication regimens. It includes different personal self-regulation strategies, such as following dietary recommendations, placing the pillbox at a fixed place, and taking them at a fixed schedule. There are also other strategies patients personally developed to aid their adherence.

Fixed place. Participants mentioned different personal self-regulation strategies when organizing and managing their medication doses. First of all, almost all (*n* = 27/28, 96.4%) participants mentioned they have a fixed place to take or organize their medications. There were three common places where individuals placed their medications—the kitchen (*n* = 9/27, 33.3%), especially the kitchen counter, bedroom (*n* = 5/27, 18.5%) and living room (*n* = 3/27, 11.1%). Here are some examples: “Pillbox is in the kitchen (…) I (…) go to kitchen, take the first pill, then make coffee.” (P16, age 46, male). “I typically keep the pillbox in the living room area.” (P39, age 68, male). “I have my medications in a visible place, on top of my bed.” (P17, age 50, male).

Quite a few individuals kept medications in more than one place (*n* = 6/27, 22.2%), such as in the bedroom and kitchen. One mentioned, “I usually take the medications in the kitchen table and living room.” (P11, age 71, female). There was a case, where the patient took medications in the bathroom (n = 1/28, 3.7%), and another case, where she kept medications where she worked (n = 1/28, 3.7%): “I tend to wait until I come to the studio (to take medications).” (P41, age 65, female). There were two cases (n = 2/28, 7.4%), where patients did not specify the room location and rather specified a spot, e.g. “on a dresser” (P13, age 67, male), “by the sofa” (P20, age 50, male). It is helpful for individuals to keep their medications in a location they frequent to develop the habit of taking their medications.

Fixed schedule. Many individuals (*n* = 24/28, 85.7%) mentioned having a fixed schedule to manage and take their medications. “8 o’clock (AM), 10, 12 PM, 2, 8, 10 (PM) whatever the time on the sheet says.” (P08, age 53, male). Some gave more specific schedules,

> 8AM: Ursodiol and Magnesium. 2:00PM: Ursodiol and Magnesium. I take these two 3 times a day. After lunch – Mepron. If I cannot take it during the lunch hour I sometimes take it after dinner. 6-6:30 is two tablets. (Synthroid and Baraclude). 7-7:30: Prozac. 8:00: Acyclovir, Ursodiol, Magnesium. 11PM: Levaquin. Before bed: another Prozac and Colace. (P11, age 71, female)

There were individuals (*n* = 4/28, 14.3%), who were ambivalent in their responses and showed difficulties with having a fixed schedule.

> On a typical day I go by how I feel. Sometimes in the morning I have no energy. I go according to how I feel, I try not to abuse it by taking them all together, but sometimes I take them all together. It’s not uniform and according to schedule, but by night I take everything. (P17, age 50, male)

> If I sleep late I get all thrown off… if I sleep till 8 o'clock (…) I take my one pill that I'm supposed to take at 6 o'clock. And then I eat something and then I take the 5 or 6 pills that I'm supposed to take with food. Then I wait two hours to take the next pills. So I have specific times: 6, 8, 10, 8 and 10. But I haven't really been following it. (P35, age 65, female)

A patient particularly expressed difficulties with keeping a consistent schedule. "I'm actually having some trouble, based on my schedule. I just can't have a consistency of taking my pills daily on a set time when I'm supposed to take it." (P21, age 29, male). Although only one patient explicitly mentioned having trouble keeping a consistent schedule, the interviews suggest that others could also benefit from additional assistance taking their medications on time.

Prompts, tools, and reminders. Except for two patients, all others (*n* = 26/28, 92.9%) mentioned using different kinds of prompts, tools and reminders (including memory) to facilitate their medication adherence. About half of those who claimed to use prompts (*n* = 12/26, 46.2%) used objects, including a list of medications, phone alarm, time/clock and pillbox, as tools and prompts to take their medications on time.

> Well, I can manage on my own, I have the box sitting on the kitchen table, so it is right there that I don't forget about it. So I've been doing this so long now, it is just automatic. (P31, age 44, female)

For some (*n* = 6/26, 23.1%), taking medication became a routine, and even though they had a reminder, they remembered and did not have to depend on prompts: "Just basically the routine." (P40, age 57, male). Two individuals (n = 2/26, 7.7%) had situational cues that reminded them of taking medications, which included meal times and other events on their daily schedules.

> Yeah, that's like my little schedule so it kind of goes with eating the breakfast. Yeah, the one that I take after that is the breakfast. But definitely, after I finish

> eating that will remind me that I have to take the rest of the medication. (P22, age 35, female)

Quite a few individuals (*n* = 6/26, 23.1%) combined different types of prompts, such as tools, memory, human reminders, and situational cues together.

> My children downloaded Dosecast on my iPad and programmed the medication on it (…) Every afternoon I take my sugar, text it to my husband, he wants to know everything, and he texts back. (…) Using the timer and the phone (…) I have a cellphone, (…) I have to have it with me all the time. My children [and my husband] scream and shout [if they do not hear from me]. (P07, age 56, female)

There were only two patients (*n* = 2/28, 7.1%) who did not use any kind of prompts.

There was also a case (*n* = 1/28, 3.6%), where the patient stopped using reminders or prompts after their regimen became simpler. “I was using my cell phone alarm for a while. I have a much more simplified currently, drug routine, so I stopped using alarms.” (P41, age 65, female). This shows how critical it is to have an alarm system or prompt to facilitate medication adherence until patients are prescribed with a simpler regimen or form an adherence routine. Some individuals mentioned being confused at times as to whether they took and/or refilled medications. There was also a case where the patient (n = 1/28, 3.6%) refilled the pillbox too frequently. It is advisable to keep a journal or diary in order to prevent cases similar to this. One individual in the sample used a diary to keep track of taking medications. “I keep a diary of when I wake up and take it.” (P01, age 66, male). This is something that can be recommended to individuals. It might be difficult for some individuals after transplant, but it might help others reduce the confusion as to whether they took or refilled their medications.

Positive emotional self-reinforcement. Taking medications made very few participants (*n* = 3/28, 10.7%) feel better. This was not the main reason patients took medications on a regular basis, but it sometimes helped them to adhere. “Some medications. Pain medication, because when pain goes away you feel a lot better." (P14, age 32, male). "Not that I feel healthier but I feel content knowing that I took them." (P43, age 51, female). "Simply that one shouldn't give up so easily. That one should have more strength of character and of will and to continue on, nothing else." (P23, age 59, female).

Diet. Half of the patients experienced trouble eating due to a lack of appetite, smell and taste (*n* = 14/28, 50.0%). "The two main problems I have are the energy (fatigue) and no appetite, eating issues, I have to force myself to eat." (P01, age 66, male). Moreover, they were under a restricted diet, including a low microbial diet (*n* = 12/28, 42.9%), where certain foods were not allowed, including no raw foods, and everything had to be cooked thoroughly. They were also not allowed to have food from the outside (restaurants); instead, everything had to be cooked at home.

> I followed low microbial diet, no immunogenic food (…) I followed what they recommended, 95% of meals were home cooked. (…) [W]e went to restaurant that we knew (…) My partner did the cooking, he works from home, he did all of that (…) [the food was] pretty healthy and tasty. (P16, age 46, male)

Therefore, they even experienced frustration eating and drinking.

> I drink a lot of water during the day. As much as I can, which is hard. (…) I'm really not that hungry. A lot of times I eat even when I don't feel like it because I know I have to. And a lot of things I'm not really happy with. I'd rather have something else but I can't. (P39, age 68, male)

Fortunately, appetite improved for some individuals after they resumed a regular diet. In our sample, several individuals (*n* = 7/28, 25.0%) had a regular diet and had no dietary restrictions. One mentioned,

> [I] didn't want to eat food, look at food, [or] smell food [during low microbial diet]. [I am] no longer on [low] microbial diet, but on regular diet to gain back the weight I lost. (P25, age 66, male)

The role of caregivers was critical in terms of preparing nutritionally well-balanced food based on the patients' conditions. They had to consider many factors, including nutrition, taste, and ease of digestion. Moreover, culture also influenced their diet. "I'm from West Africa, you know I have to get my rice [laughs] (…) Rice, and I'll have different kind of sauce." (P22, age 35, female). Hydration was important regardless of dietary restrictions (low microbial or regular diet). Patients mostly drank water, Gatorade, lemonade and some fruit juices to stay hydrated.

Utilization of healthcare resources. Individuals were able to adhere to their prescribed doses through the effective use of healthcare resources, including the pharmacy and hospital. This is an area where individuals' behavioral skills work together with support from healthcare providers. Quite a number of individuals (*n* = 12/28, 42.9%) specifically mentioned how they utilized the healthcare resources available to them effectively. Most of them (*n* = 8/12, 66.7%) prepared and refilled medications ahead of time by using the hospital and pharmacy system (pick up or delivery). Individuals called in or visited the clinic and pharmacy to receive their refills on time. "I get my refills through the mail. It (refill) is not automatic. I phone it in." (P26, age 50, male). But the pharmacists also called to make sure. "Thanks due to God, pharmacist has called, they call and remind me." (P19, age 46, male).

At the same time, a few individuals (*n* = 5/28, 17.9%) mentioned both good and bad experiences with their healthcare systems. For example, a few individuals found themselves in a situation where the pharmacy did not have the specific medication they needed. In one case, the patient could not purchase an extra supply of medication because of insurance issues (P20, age 50, male). Another mentioned,

> Usually, the pharmacy, they remember. (…) But this time maybe they got busy, they didn't call me, so I was just going through the medication, both dapsone and acyclovir [were running out] one time. Just one time. (P22, age 35, female)

One patient developed a habit of ordering ahead of time because the pharmacy once made her wait a week to obtain her medication. "From then on, I always order 2 weeks ahead" (P29, age 63, female).

Moreover, there were a few individuals (*n* = 3/28, 10.7%), who experienced delivery problems and could not take their medications on time.

> The pharmacy claimed that they were going to deliver it, and then that the truck didn't finish his rounds, and the next day the truck broke down (…) and instead of Tuesday I got it on Saturday. (…) That was the worst one that I skipped really a lot. (P13, age 67, male)

In most cases, however, the healthcare providers promptly took action before patients ran out of pills. To prepare for the worst cases where the medication refill is delayed, it is important that each patient checks with healthcare providers and restocks the medications ahead of time.

Strategies to manage missed or late doses. Patients mentioned several reasons for missing or delaying a dose. The most frequently mentioned is forgetfulness; forgetting to take the medicine (*n* =21/28, 75.0%) or forgetting to refill (*n* =3/28, 10.7%). Other reasons include falling asleep/ sleeping through a dose (*n* = 9/28, 32.1%), being around other people (*n* = 2/28, 7.1%), being otherwise occupied (*n* = 7/28, 25.0%), and having difficulty managing changes in routines (*n* = 15/28 = 53.6%).

Many individuals said they skip (*n* = 18/28 = 64.3%) the missed dose. "[If I forget to take a pill] I take it the next day. I do not take it late. I wait till next day." (P09, age 49, female). Another mentioned, "[When I miss a dose] I skipped it and went on to the next." (P26, age 50, male). One person also mentioned that depending on the importance of the pill, the patient would decide whether to take it or not (P35, age 65, female). Patients also took the dose even a few hours later (*n* = 20/28, 71.4%). “Sometimes I forgot, then I take the pills an hour or two later than the scheduled time. When I am too busy then I forgot, mostly at work.” (P08, age 53, male). Two people (*n* = 2/28, 7.1%) mentioned adjusting the hours for the following doses: “The following doses I try to take them a little bit later.” (P14, age 32, male).

Quite a number of individuals (*n* = 12/28, 42.9%) mentioned both skipping and taking the medications later. In one interview, the wife interrupted and said*,* “he (patient) takes it as soon as he remembers, or as soon as we can, or if it’s too close to the next dose, then we miss a dose.” (P25, age 66, male).

> It depends when I forget, if it’s an hour later, I take it. If it’s supposed to be taken at 12 in the afternoon and it’s now 9 at night, or it’s something once a day and I’m not taking any other medications I may take it or skip it for the day. But for the most part, I haven’t skipped too many. I do recall once or twice that I did skip a pill. (P13, age 67, male)

Strategies not to miss a dose when being out/ traveling. A number of individuals (*n* = 12/28, 42.9%) mentioned they missed doses because they were out or traveling. In order to prevent missing doses when going out, one (*n* = 1/28, 3.6%) mentioned that she took the medications before going out (P11, age 71, female). The only time the individuals justifiably had to miss a dose was before the doctor’s appointment (*n* = 9/28, 32.1%): Patients would have to take an immunosuppressive drug, such as Prograf or Cyclosporine, after their blood was taken. Although there were cases in which individuals missed doses because they did not have enough pills in hand (*n* = 10/28, 35.7%), many patients brought their medications with them as they went out (*n* = 24/28, 85.7%). “If I go to a friend’s (…) then I make sure I take the medication with me. Maybe occurs once or twice a month.” (P13, age 67, male).

Strategies to deal with side effects. There were individuals who experienced difficulties in taking their medications due to side effects and sicknesses (*n* = 23/28, 82.1%), like nausea, upset stomach, graft-versus-host diseases, and more. Not all individuals shared how they handled the side effects, but some did, including: taking another medication to relieve the effects of the medication in question (*n* = 5/28, 17.9%), eating and drinking something (*n* = 2/28, 7.1%), stop taking (*n* = 3/28, 10.7 %), cutting down the dose (*n* = 1/28, 3.6%), spacing out doses (*n* = 1/28, 3.6%), going to the bathroom (*n* = 1/28, 3.6%), using stockings for swollen legs (*n* = 1/28, 3.6%), and putting on lip balms for dry lips (*n* = 1/28, 3.6%). Here are some examples: “Stomach condition, eat small things, that is common sense, that is a good thing to do.” (P11, age 71, female). “I stop taking the medication (if I feel I am having side effects) and wait for the result by waiting. I’m being patient.” (P17, age 50, male).

> I was taking Zofran in the beginning, you take it once a day that keeps you from getting an upset stomach, I would take one hour before getting the shots and I never threw up ever. The one day I didn’t take it I was throwing up. But the Zofran constipates you. I learned the side effects, now if I take it one day I can’t take it the second day. (P01, age 66, male)

A few individuals (*n* = 3/28, 10.7%) mentioned above used more than one strategy to deal with side effects. “Well I have the medicine [to deal with nausea] (…) I would just go into the bathroom and then you’re done, and you feel better.” (P31, age 44, female).

Strategies for taking medications that are difficult to swallow. Patients had trouble swallowing some of the medications due to taste and size (*n* = 17/28, 60.7%). Many of them (*n* = 13/17, 76.5%) shared how they managed medications that are difficult to swallow. Almost everyone (*n* = 12/13, 92.3%) mentioned they took their medications with food and/or drink. “They taste terrible, you have to drink more water and rinse it out.” (P07, age 56, female).

> Everything in the morning, with Gatorade Sub-zero (…) I can drink down 20 oz., it goes down so smooth (…) I cannot do that with a glass of water. (P01, age 66, male)

> Sweet things, soda, Gatorade, milk help, put the pill all the way (…) When I tried with water, big pill when you cut at the end of the tongue it melts, hard to swallow. I tried with sweet drink it is working, keep trying with milk. (…) I don’t know exactly if (…) the medication or the empty stomach that makes the nausea, I cannot figure it out. (P11, age 71, female)

Two patients used two strategies along with drinking water—closing their eyes or praying. “I closed my eyes and drink it and drink a lot of water.” (P22, age 35, female). Another mentioned, “I always take the medicine with water, swallow it and pray, that is all I am doing.” (P29, age 63, female). There was one person (*n* = 1/13, 7.7%), who held his breath to swallow the medications. “I hold my breath and then take it (medicine).” (P20, age 50, male).

Discussion

Individuals after transplant came up with numerous strategies for managing their multiple medications. In general, they maintained a positive attitude that underpinned the factors that the Information-Motivational-Behavioral Skills model (Fisher et al., 2006) delineates. We found that this framework is suitable for studying multiple medication adherence. Adequate information, personal and social motivation, and behavioral skills were central to maintaining adherence to multiple medication regimens. Many participants experienced challenges but were able to initiate and maintain their complex regimens by developing personal strategies, as well as seeking help from others.

Patients shared many of their lessons learned for taking multiple medications (see Table 4.1 for an overview). Patients reported that a positive attitude and optimism were helpful for adherence, so interventions should include strategies that affirm and encourage an optimistic attitude when faced with the challenge of multiple medications. Patients by and large were not able to remember the details of their regimen and relied on the printed information provided by their healthcare team. Therefore, interventions should ensure that healthcare providers offer patients adequate printed information when prescribing a multiple medication regimen, as well as include caregivers in explaining the multiple medications. The latter is essential because caregivers were frequently in charge of medication-related tasks. Taking multiple medications requires time and effort, and thus personal motivation. Patients reported taking personal responsibility (for example, treating it like a job) and adopting positive beliefs that each of the medications would lead to good health outcomes. Interventions could strengthen both responsibility-taking and positive beliefs. Social support, i.e., seeking emotional, instrumental, and informational support from close others and healthcare providers, was another important factor for maintaining multiple medication adherence, and caregivers were involved in all tasks, from medical appointments, refills, and reminders, as well as management of health insurances. Interventions should facilitate seeking and providing adequate support, as adherence tasks also multiply when patients need to manage multiple medications and health conditions. Patients with multiple medications needed to adjust their daily routines to adhere to the different intake times and instructions (e.g., on empty stomach, with vs.

without food). Therefore, they reported building a range of highly idiosyncratic behavioral skills to maintain optimal adherence and to manage late doses.

This study is the first to investigate adherence strategies cancer patients with a multiple medication regimen developed spontaneously. These strategies can form the basis for developing adherence interventions for multiple medication intake. The findings suggest that the Information-Motivation-Behavioral Skills model is a useful framework for multiple medication regimens. We found room for improvement for each of the model's adherence determinants in patients, who emphasized the role of caregivers that should therefore be included in adherence interventions for multiple medication intake. However, even with adequate information, motivation, and social support, patients and caregivers need to receive training in behavioral skills. For example, many patients reported using unreliable reminders, including visual cues such as leaving their pillbox on the kitchen table. But well-informed and motivated caregivers can remind patients or help them program reminders into their phones. Moreover, this study also suggested a modification to the IMB model by including general attitude and optimism. It is a new determinant that was not emphasized in the original IMB model, but this might be an especially significant factor for patients like those in our sample, who are required to manage treatment for a long period and are prescribed with multiple medications.

Strengths of the study are myriad. This study provides concrete strategies that patients obtained from their difficult experiences post-transplant. It is very practical and can be applied with due caution, addressing concrete needs of individuals after transplant. Moreover, a qualitative approach allowed us to capture all individuals' perspectives and their personal views on taking medications, as well as post-transplant treatment, making the points more applicable and concrete to other patients. This is only the second study to examine different medication adherence tasks of individuals after transplant. The first one was released last year (Posluszny et al., 2018). Lastly, the findings suggest the feasibility and the promise of developing an effective intervention.

Limitations

It is unclear whether this study can be generalized to another group of individuals prescribed with a multiple medication regimen because we obtained data from one institution in an urban area, and we collected data from patients with a very specific health condition. Moreover, we had a relatively small sample size, though it was ethnically diverse and covered a wide range of age groups (20 to 60 and older). Some patients experienced trouble with cognitive functioning, so it is possible that they lost some of their memories (even those of recent events). We conducted in-depth interviews with patients, which are rich in narratives, but we were not able to apply a strict standard with which to determine whether patients were adherent or not. For future research, it would be interesting to collect caregiver interview data on the strategies patients developed during home care. It would also be interesting to study the perspectives of the caregivers, as they play such a crucial role.

Conclusion

Answering the call for focusing on behavioral strategies (Conn & Ruppar, 2017), we have found a number of strategies that patients developed spontaneously over time. Some strategies, such as receiving reminders from close others, seem to be suboptimal, and could be supplemented with technological interventions, such as electronic reminders when the medication is not taken. Yet, the role of caregivers was significant in different areas of adherence, so caregivers must be included in training patients with adherence strategies. Moreover, some of the tasks can be divided and their responsibilities can be shared (Posluszny et al., 2018), so collaborative elements should be taken into consideration in developing the intervention. Patients took some time to develop these strategies. It would be ideal to train them on all adherence strategies on the prescription date to ensure adherence from Day 1. To this end, healthcare providers can ideally find ways to hold training sessions and prepare patients for discharge. Also, continually educating the patients over the course of the post-transplant treatment period seems important. Previous studies on organ transplants found that the longer the treatment period after transplant, the less adherent patients were, leading Bishop and colleagues to recommend educating patients repeatedly (Bishop, Rodrigue, & Wingard, 2002; Siegal & Greenstein, 1999; Teichman, Burker, Weiner, & Egan, 2000).

Most studies on adherence to multiple medications focus on the elderly population because this group is more susceptible to illness and takes more medications (Cross et al., 2016; George, Elliott, & Stewart, 2008), but the focus should be broadened as a more recent study shows that younger patients with alloHCT had lower adherence than older patients (Lehrer et al., 2018). It might be difficult for the elderly population to adhere as they experience declines in cognitive and physical abilities with age, but younger individuals with severe health conditions may also experience the same or even greater challenges in adherence.

Table 4.1. Major Determinants of Adherence and the Relevant Subgoals, Challenges, and Lessons Learned for Patients and Caregivers

Determinant and Subgoals	**Challenges**	**Lessons Learned**
General attitude		
Acceptance of health condition and patient role	Worry & fear	- Adopt an optimistic view while acknowledging the limitations and challenges of self-management: *“We have to leave on a lighter note! The problems are almost over. You have to take the lighter side!” (P13, age 67, male)*
		- Use affirmations for oneself and others: *“I’ve been so fortunate in so many ways in this process. It’s a terrible situation, but it’s been as good as it can go. It could be a lot worse.” (P10, age 49, male)*
Information		
Comprehensive knowledge of medication regimen	Complexity of a multiple medication regimen	- Request a personalized list of the multiple medication regimen, including medication name (and common generic names), doses per time of day, purpose, frequent side effects, and instructions for intake: *“[W]hen I was getting discharged, they gave me list of medication (...) and two people came from the pharmacy, they told me everything and also the nurse who discharged me and also [Nurse 3] from here so I had a lot of people who really talked to me about the medication.”(P22, age 35, female)*

		- Follow the list carefully: *"I always check with my medicine, I have a list of medicines prepared by nurse practitioner." (P29, age 63, female)* - Request an updated list whenever the regimen changes: *"They [healthcare providers] give me the information sheet every time they select prescription." (P28, age 59, male)*
	Partial knowledge	- Seek help from close others: *"Hard to distinguish the different pills [just at] 8 o' clock [I have] 10 pills. With my husband I learned it." (P11, age 71, female)*
		- Seek explanations of the consequences of non-adherence: *"They help you understand why you are taking the medication, the more you understand the easier it is." (P14, age 32, male)* - Do personal research, and also share questions and concerns about medications with healthcare provider: *"I do a lot of reading. Husband keeps asking doctors about it." (P07, age 56, female)*
Personal motivation Maintenance of personal motivation	Resistance to taking medications	- Acknowledge the importance of taking medications: *"Taking medications is very important to get better." (P11, age 71, female)*
Adoption of positive beliefs about health outcomes	Ambivalence, doubts, or negative beliefs due to side effects or slow recovery	- Remind oneself the benefits of transplant and medication adherence: *"I'm around*

		today because I've been doing this!" (P13, age 67, male) - Discuss doubts with healthcare provider: *"They (healthcare providers) are just so supportive and they've made everything so understandable for me (...) any questions that I've had they give me an answer to my liking where it hasn't hindered my feelings toward any type of medication." (P14, age 32, male)*
Social motivation Instrumental support from close others	Not enough or appropriate support from close others	- Provide support for taking medications: *"She's the one that makes sure I'm taking my medicine." (P26, age 50, male)* - Provide support with daily chores: *"My partner did the cooking, he works from home." (P16, age 46, male)* - Provide financial support: *"I don't even know where the bills are. I think he (husband) doesn't want me to know because he doesn't want me to worry." (P07, age 56, female)*

Emotional support from close others		- Stay with the patient and provide words of encouragement, comfort and peace: *"How spectacularly kind, gentle, loving people are caring for me." (P41, age 65, female)*
Support from healthcare providers	Obtaining adequate medical information and support, establishing trust with healthcare providers	- Provide adequate information about medications: *"They (healthcare providers) tell me, they teach me about the medications, how important they are, and what they do" (P22, age 35, female)*
		- Provide adequate information about diet and hydration; *"They gave me a chart of what I can eat and what I can't eat and went through." (P26, age 50, male)*
		- Support with medical needs; *"My doctor understood my needs and the communication was clear and important." (P23, age 59, female)*
		- Help patients feel cared for, encourage and build relationships of trust; *"Knowing that he is a good doctor, for me, has been very important. And everything has been made way easier." (P23, age 59, female)*

Behavioral skills development		
Facilitation of adherence	Missing a dose	- Choose a visible place to store medications/pillbox; *"I have my medications in a visible place, on top of my bed." (P17, age 50, male)*
		- Utilize cues, prompts, and reminders; *"I have the (pill)box sitting on the kitchen table so it is right there that I don't forget about it." (P31, age 44, female)*
	Trouble keeping a consistent schedule	- Follow the list obtained at the hospital discharge meeting and create a specific schedule for daily doses and weekly refills; "*8AM: Ursodiol and Magnesium. 2:00PM: Ursodiol and Magnesium (…)." (P11, age 71, female)*
	Too frequent or erratic intake	- Keep a diary log of medication adherence; *"I keep a diary of when I wake up and take it." (P01, age 66, male)*
		- Feel good about oneself after taking medications; *"Not that I feel healthier, but I feel content knowing that I took them." (P43, age 51, female)*
	Inadequate diet & dehydration	- Follow diet instructions provided by the hospital; *"I followed low microbial diet, no immunogenic food (…) I followed what they recommended, 95% of meals were home cooked." (P16, age 46, male)*
		- Have caregivers know about the patient's diet and cook for the patient; "*My partner did the cooking, he works*

		from home, he did all of that. 3% of time I cooked.” (P16, age 46, male)
		- Drink a lot of water or other beverages; “*I am drinking a lot of water, coconut juice, and Gatorade.”* (P29, age 63, female)
	Coordination with healthcare providers	- Prepare medications ahead of time by calling the pharmacy for refills; *“I get my refills through the mail. It (refill) is not automatic. I phone it in.”* (P26, age 50, male)
		- The pharmacy checks in with patients; *“Thanks due to God, pharmacist has called, they call and remind me.”* (P19, age 46, male)
	Delivery problem	- Stock medications ahead of time; *“I always order 2 weeks ahead”* (P29, age 63, female)
Management of doses when being out/ traveling	Not having pills in hand	- Always have the pills in hand; *“If I go to a friend’s or some people and I have to take medications (with me) because I’m going to be there for half a day, then I make sure I take the medication with me. Maybe occurs once or twice a month.”* (P13, age 67, male)
		- Take the pills before going out; *“When I go out then I take them early, before I go out.”* (P11, age 71, female).
Management of late doses	Forget, skip, sleep through doses; difficult to take medication when with other people; schedule changes	- Take medications within 1-2 hours of the scheduled dosing time; *“Sometimes I forgot, then I take the pills an hour or two*

		later than the scheduled time." (P08, age 53, male)
		- Resume adherence with the following doses; *"(when I miss a dose) I skipped it and went on to the next." (P26, age 50, male)*
		- Shift dosing hours of the following doses; *"The following doses I try to take them a little bit later." (P14, age 32, male)*
Management of side effects	Reactions from medications; side effects	- Take other medications; *"I'll take Carafate. I usually don't get an upset stomach. I was taking Zofran in the beginning, you take it once a day that keeps you from getting an upset stomach, I would take one hour before getting the shots and I never threw up ever." (P01, age 66, male)*
		- Eat something; *"Stomach condition, eat small things, that is common sense, that is a good thing to do." (P11, age 71, female)*
		- Stop taking; *"I stop taking the medication (if I feel I am having side effects) and wait for the result by waiting. I'm being patient." (P17, age 50, male)*
		- Space out the doses; *"Sometimes I'm supposed to take like two at a time so maybe I'll space it out so it's like one, one hour then wait" (P38, age 64, female)*
		- Go to the bathroom; *"I would just go into the bathroom and then you're done, and you feel better." (P31, age 44, female)*

		- Use other tools; *"I'm going nuts thinking there's something wrong with me, like my swollen legs. [Get] these stockings for your legs that don't let the water bunch up." (P01, age 66, male)*
Ease of intake	Large size and bad taste	- Take with food or drink: *"Take with rice milk, soup, apple sauce" (P21, age 29, male). "Drink soda after swallowing bad-tasting pill" (P01, age 66, male)*
		- Hold breath; *"I hold my breath and then take it (medicine)." (P20, age 50, male)*
		- Close eyes; *"I closed my eyes and drink it and dink a lot of water." (P22, age 35, female)*
		- Pray; *"I always pray. (...) I always take the medicine with water, swallow it and pray, that is all I am doing, I want to get better." (P29, age 63, female)*

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References

Banna, G. L., Collovà, E., Gebbia, V., Lipari, H., Giuffrida, P., Cavallaro, S., … Ferraù, F. (2010). Anticancer oral therapy: Emerging related issues. *Cancer Treatment Reviews*, *36*(8), 595–605. https://doi.org/10.1016/j.ctrv.2010.04.005

Bartholomew Eldredge, L. K., Markham, C. M., Ruiter, R. A., Fernández, M. E., Kok, G., & Parcel, G. S. (2016). *Planning health promotion programs: An intervention mapping approach (4th ed.)*. Hoboken, NJ: Wiley.

Bishop, M. M., Rodrigue, J. R., & Wingard, J. R. (2002). Mismanaging the gift of life: Noncompliance in the context of adult stem cell transplantation. *Bone Marrow Transplantation*, *29*(11), 875. https://doi.org/10.1038/sj.bmt.1703523

Buttorff, C., Ruder, T., & Bauman, M. (2017). *Multiple Chronic Conditions in the United States*. Santa Monica, CA: RAND. https://doi.org/10.7249/TL221

Chang, S. J., Choi, S., Kim, S.-A., & Song, M. (2014). Intervention strategies based on Information-Motivation-Behavioral Skills model for health behavior change: A systematic review. *Asian Nursing Research*, *8*(3), 172–181. https://doi.org/10.1016/j.anr.2014.08.002

Claxton, A. J., Cramer, J., & Pierce, C. (2001). A systematic review of the associations between dose regimens and medication compliance. *Clinical Therapeutics*, *23*(8), 1296–1310. https://doi.org/10.1016/S0149-2918(01)80109-0

Conn, V. S., & Ruppar, T. M. (2017). Medication adherence outcomes of 771 intervention trials: Systematic review and meta-analysis. *Preventive Medicine*, *99*, 269–276. https://doi.org/10.1016/j.ypmed.2017.03.008

Creswell, J., Klassen, A. C., Plano, V., & Smith, K. C. (2011). Best practices for mixed methods research in the health sciences. *Bethesda (Maryland): National Institutes of Health, 2013,* 541-545.

Creswell, J. W. (2013). *Research design: Qualitative, quantitative, and mixed methods approaches*. SAGE Publications.

Cross, A. J., Elliott, R. A., & George, J. (2016). Interventions for improving medication-taking ability and adherence in older adults prescribed multiple medications. *Cochrane Database of Systematic Reviews*. https://doi.org/10.1002/14651858.CD012419

Ehrlich, K. B., Miller, G. E., Scheide, T., Baveja, S., Weiland, R., Galvin, J., … Penedo, F. J. (2016). Pre-transplant emotional support is associated with longer survival after allogeneic hematopoietic stem cell transplantation. *Bone Marrow Transplantation*, *51*(12), 1594–1598. https://doi.org/10.1038/bmt.2016.191

Fisher, J. D., & Fisher, W. A. (1992). Changing AIDS-risk behavior. *Psychological Bulletin*, *111*(3), 455–474. https://doi.org/10.1037/0033-2909.111.3.455

Fisher, J. D., Fisher, W. A., Amico, K. R., & Harman, J. J. (2006). An information-motivation-behavioral skills model of adherence to antiretroviral therapy. *Health Psychology*, *25*(4), 462–473. https://doi.org/10.1037/0278-6133.25.4.462

Freifeld, A. G., Bow, E. J., Sepkowitz, K. A., Boeckh, M. J., Ito, J. I., Mullen, C. A., … Wingard, J. R. (2011). Clinical practice guideline for the use of antimicrobial agents in neutropenic patients with cancer: 2010 update by the Infectious Diseases Society of America. *Clinical Infectious Diseases*, *52*(4), e56–e93. https://doi.org/10.1093/cid/cir073

George, J., Elliott, R. A., & Stewart, D. C. (2008). A systematic review of interventions to improve medication taking in elderly patients prescribed multiple medications. *Drugs & Aging*, *25*(4), 307–324. https://doi.org/10.2165/00002512-200825040-00004

Gresch, B., Kirsch, M., Fierz, K., Halter, J. P., Nair, G., Denhaerynck, K., & De Geest, S. (2017). Medication nonadherence to immunosuppressants after adult allogeneic haematopoietic stem cell transplantation: A multicentre cross-sectional study. *Bone Marrow Transplantation*, *52*(2), 304–306. https://doi.org/10.1038/bmt.2016.262

Horvath, K. J., Smolenski, D., & Amico, K. R. (2014). An empirical test of the information-motivation-behavioral skills model of ART adherence in a sample of HIV-positive persons primarily in out-of-HIV-care settings. *AIDS Care*, *26*(2), 142–151. https://doi.org/10.1080/09540121.2013.802283

Hsieh, H. F., & Shannon, S. E. (2005). Three approaches to qualitative content analysis. *Qualitative Health Research*, *15*(9), 1277–1288. https://doi.org/10.1177/1049732305276687

Kantor, E. D., Rehm, C. D., Haas, J. S., Chan, A. T., & Giovannucci, E. L. (2015). Trends in prescription drug use among adults in the United States from 1999-2012. *JAMA*, *314*(17), 1818–1830. https://doi.org/10.1001/jama.2015.13766

Kardas, P., Lewek, P., & Matyjaszczyk, M. (2013). Determinants of patient adherence: A review of systematic reviews. *Frontiers in Pharmacology*, *4*. https://doi.org/10.3389/fphar.2013.00091

Kim, J., & Parish, A. L. (2017). Polypharmacy and medication management in older adults. *Nursing Clinics of North America*, *52*(3), 457–468. https://doi.org/10.1016/j.cnur.2017.04.007

Lehrer, J., Brissot, E., Ruggeri, A., Dulery, R., Vekhoff, A., Battipaglia, G., … Antignac, M. (2018). Medication adherence among allogeneic hematopoietic stem cell transplant recipients: A pilot single-center study. *Bone Marrow Transplantation*, *53*(2), 231–233. https://doi.org/10.1038/bmt.2017.233

Mathes, T., Antoine, S.-L., Pieper, D., & Eikermann, M. (2014). Adherence enhancing interventions for oral anticancer agents: A systematic review. *Cancer Treatment Reviews*, *40*(1), 102–108. https://doi.org/10.1016/j.ctrv.2013.07.004

Mayberry, L. S., & Osborn, C. Y. (2014). Empirical Validation of the Information–Motivation–Behavioral Skills model of diabetes medication adherence: A framework for intervention. *Diabetes Care*, *37*(5), 1246–1253. https://doi.org/10.2337/dc13-1828

McDonald, H. P., Garg, A. X., & Haynes, R. B. (2002). Interventions to enhance patient adherence to medication prescriptions: Scientific review. *JAMA*, *288*(22), 2868–2879. https://doi.org/10.1001/jama.288.22.2868

Morrison, C. F., Martsolf, D. M., Wehrkamp, N., Tehan, R., & Pai, A. L. (2017). Medication adherence in hematopoietic stem cell transplantation: A review of the literature. *Biology of Blood and Marrow Transplantation*, *23*(4), 562–568. https://doi.org/10.1016/j.bbmt.2017.01.008

Neumann, S., Krause, S. W., Maschmeyer, G., Schiel, X., & von Lilienfeld-Toal, M. (2013). Primary prophylaxis of bacterial infections and Pneumocystis jirovecii pneumonia in patients with hematological malignancies and solid tumors. *Annals of Hematology*, *92*(4), 433–442. https://doi.org/10.1007/s00277-013-1698-0

Nieuwlaat, R., Wilczynski, N., Navarro, T., Hobson, N., Jeffery, R., Keepanasseril, A., … Haynes, R. B. (2014). Interventions for enhancing medication adherence. *Cochrane Database of Systematic Reviews,* (11). https://doi.org/10.1002/14651858.CD000011.pub4

O'Brien, B. C., Harris, I. B., Beckman, T. J., Reed, D. A., & Cook, D. A. (2014). Standards for reporting qualitative research: A synthesis of recommendations. *Academic Medicine*, *89*(9), 1245. https://doi.org/10.1097/ACM.0000000000000388

Ogedegbe, G., Harrison, M., Robbins, L., Mancuso, C. A., & Allegrante, J. P. (2004). Barriers and facilitators of medication adherence in hypertensive African Americans: A qualitative study. *Ethn Dis*, *14*(1), 3–12. (15002917).

Pantuzza, L. L., Ceccato, M. das G. B., Silveira, M. R., Junqueira, L. M. R., & Reis, A. M. M. (2017). Association between medication regimen complexity and pharmacotherapy adherence: A systematic review. *European Journal of Clinical Pharmacology*, *73*(11), 1475–1489. https://doi.org/10.1007/s00228-017-2315-2

Patton, D. E., Cadogan, C. A., Ryan, C., Francis, J. J., Gormley, G. J., Passmore, P., … Hughes, C. M. (2017). Improving adherence to multiple medications in older people in primary care: Selecting intervention components to address patient-reported barriers and facilitators. *Health Expectations*, 1–11. https://doi.org/10.1111/hex.12595

Patton, D. E., Hughes, C. M., Cadogan, C. A., & Ryan, C. A. (2017). Theory-based interventions to improve medication adherence in older adults prescribed polypharmacy: A systematic review. *Drugs & Aging*, *34*(2), 97–113. https://doi.org/10.1007/s40266-016-0426-6

Posluszny, D. M., Bovbjerg, D. H., Agha, M. E., Hou, J.-Z., Raptis, A., Boyiadzis, M. M., … Dew, M. A. (2018). Patient and family caregiver dyadic adherence to the allogeneic hematopoietic cell transplantation medical regimen. *Psycho-Oncology*, *27*(1), 354–358. https://doi.org/10.1002/pon.4393

Ruddy, K., Mayer, E., & Partridge, A. (2009). Patient adherence and persistence with oral anticancer treatment. *CA: A Cancer Journal for Clinicians*, *59*(1), 56–66. https://doi.org/10.3322/caac.20004

Sabaté, E. (2003). *Adherence to long-term therapies: Evidence for action*. Geneva: World Health Organization.

Siegal, B., & Greenstein, S. (1999). Compliance and noncompliance in kidney transplant patients: Cues for transplant coordinators. *Journal of Transplant Coordination*, *9*(2), 104–108. https://doi.org/10.1177/090591999900900207

Teichman, B. J., Burker, E. J., Weiner, M., & Egan, T. M. (2000). Factors associated with adherence to treatment regimens after lung transplantation. *Progress in Transplantation*, *10*(2), 113–121. https://doi.org/10.1177/152692480001000208

Tomblyn, M., Chiller, T., Einsele, H., Gress, R., Sepkowitz, K., Storek, J., … Boeckh, M. A. (2009). Guidelines for preventing infectious complications among hematopoietic cell transplantation recipients: A global perspective. *Biology of Blood and Marrow Transplantation*, *15*(10), 1143–1238.

Tong, A., Flemming, K., McInnes, E., Oliver, S., & Craig, J. (2012). Enhancing transparency in reporting the synthesis of qualitative research: ENTREQ. *BMC Medical Research Methodology*, *12*(1), 181. https://doi.org/10.1186/1471-2288-12-181

Tong, A., Sainsbury, P., & Craig, J. (2007). Consolidated criteria for reporting qualitative research (COREQ): A 32-item checklist for interviews and focus groups. *International Journal for Quality in Health Care*, *19*(6), 349–357. https://doi.org/10.1093/intqhc/mzm042

Verbrugghe, M., Verhaeghe, S., Lauwaert, K., Beeckman, D., & Van Hecke, A. (2013). Determinants and associated factors influencing medication adherence and persistence to oral anticancer drugs: A systematic review. *Cancer Treatment Reviews*, *39*(6), 610–621. https://doi.org/10.1016/j.ctrv.2012.12.014

Wu, S. Y., & Green, A. (2000). *Projection of chronic illness prevalence and cost inflation.* Santa Monica, CA: RAND Health.

Zarani, F., Besharat, M. A., Sadeghian, S., & Sarami, G. (2010). The effectiveness of the Information-Motivation-Behavioral Skills model in promoting adherence in CABG patients. *Journal of Health Psychology*, *15*(6), 828–837. https://doi.org/10.1177/1359105309357092

Chapter V

SUMMARY, IMPLICATIONS, AND RECOMMENDATIONS

This dissertation sought to better understand the challenges patients face in managing multiple medications as part of a medical regiment following allogeneic hematopoietic cell transplant (alloHCT). The work consists of three related studies examining the feasibility of an electronic pillbox technology, the role of social support in facilitating adherence, and the psychosocial factors and strategies that enhance adherence for patients prescribed multiple medications after an allogeneic hematopoietic cell transplant. This chapter presents a summary of findings from each of the studies, discusses the implications of the work for theory and practice, and identifies both limitations and strengths and recommendations for future research.

Feasibility of Using Electronic Pillboxes

The first paper examined the feasibility of using an electronic pillbox for multiple medications. In line with previous studies of kidney transplant patients, which showed that the use of an electronic pillbox significantly improved medication adherence and supported the feasibility of using the technology (Davidson et al., 2015; McGillicuddy et al., 2013), our study finds that it is feasible to use an electronic pillbox to facilitate multiple medication adherence. The paper's main finding was the willingness of patients to use an electronic pillbox and the significant benefits they identified from doing so. For example, it provided storage for organizing medications and reminded patients to take and refill their doses. However, there were also several challenges to using the electronic pillbox, such as its limited portability and short battery life. Based on the recommendations from users, a more suitable electronic pillbox can be developed for individuals with multiple medications. Such a redesigned electronic pillbox could become the basis for a tailored, intensive longitudinal intervention for optimal adherence to multiple medications. This intervention would ideally not only be technology-based but also integrate social support for adherence as well.

The Role of Social Support

In the second paper, we examined the role of social support, specifically who helps patients after transplant and what kind of support patients receive given their very demanding self-care regimens and multiple medication regimens. In line with previous research, social support is a critical factor for adherence (DiMatteo, 2004). Both lay caregivers and healthcare providers provide ongoing support for patients after transplant. Patients predominantly mentioned doctors and nurses as healthcare providers giving support, but they also mentioned social workers, dieticians, and pharmacists. Lay caregivers were predominantly the patient's partner/spouse, and more rarely other family members and friends. Healthcare providers were most helpful with patients' medical needs and supplied information relevant to their medications and treatment. Although emotional support from healthcare providers occurred only rarely, some patients were nevertheless emotionally touched and encouraged by their emotional support.

Lay caregivers were the main source of emotional support for patients, using encouragement and empathy to address patients' emotional needs. Patients also received ongoing instrumental support, i.e., tangible help with daily chores and taking/ refilling medications. Many lay caregivers were very involved in caring for patients after transplant, including some who took significant time off work. Moreover, high costs for medications and treatments led to a need for substantial financial support. Caregivers were involved with financing the healthcare costs and keeping the household together as the patients were unable to work. Guidelines for admitting patients for transplant prescribe that patients have a 24 hour/7-day a week lay caregiver. Our findings provide evidence that the needs of patients after transplant justify this requirement. Due to the high involvement of caregivers after discharge from hospital, they should be included in all patient education about the multiple medication regimen and self-care. In an ideal situation, healthcare providers, patients and lay caregivers work as a close-knit triad to ensure adherence to the complex medication regimen and recommended self-care. For example, during hospital discharge, patients appreciated that the clinic provided with each supply of medication a printed information form, which patients consulted regularly. However, in some cases patients did not have a dedicated caregiver who could attend the meetings together. Our findings suggest that a highly structured discharge meeting with the patient and caregiver present would reduce stress and could improve adherence to the multiple medication regimen after transplant. As we suggest in the paper, the discharge meeting needs to prepare the patients and the lay caregivers for the cascade of adherence-related tasks, not only medication intake. The cascade model (Figure 3.2) specifies the ways in which lay caregivers can help patients accomplish an array of tasks pertaining to adherence, including attending appointments, refilling and organizing medications, preparing food and liquid intake, and taking medications. For example, to support the attendance of doctor's appointment, lay caregivers have to remind the patient of the appointment, provide transportation, and also accompany the patient to appointments. By doing so, the lay caregiver can receive at the discharge meeting all the relevant information necessary to support the patient in attending, refilling, preparing food and taking medications. Also, this discharge meeting should explain each medication's benefits, doses, side effects, and possible drug interactions, and help patients organize all medications into a pillbox.

Strategies to Manage Multiple Medications

In the third paper, we found that patients develop different strategies to manage their multiple medications. Consistent with the Information Motivation and Behavioral Skills (IMB) model (Fisher, Fisher, Amico, & Harman, 2006), patients needed adequate information about their medications, personal motivation (positive attitude about medications), and social motivation (social support) from lay caregivers and healthcare providers. Moreover, patients needed different behavioral skills to help them adhere and overcome barriers to adherence. Most interestingly, this paper suggests some factors that have not yet been identified in the IMB model, which include the role of general optimism, worries, fear and concerns. The different lessons patients learned and developed for themselves in taking multiple medications are also shared in the paper.

Based on some of the findings of the third paper, one could infer why we found (in the first paper) the adherence rate to be about half (55%), which is within the range of the reported average adherence rate among individuals with chronic diseases in developed countries (Sabaté, 2003). Many (*n* = 19/28, 67.9%) reported that they did not have comprehensive knowledge of their numerous medications because it was too complicated to keep track of, and the regimens tended to change. Also, although many (*n* = 13/28, 46.4%) had positive beliefs about their medications, a number of people (*n* = 9/28, 32.1%) expressed ambivalence and concerns about taking multiple medications and their side effects. Therefore, future interventions should carefully deliver detailed information about the prescribed medications, as well as emphasize their benefits.

Implications for Theory

Based on the findings of this study, the Information Motivation and Behavioral Skills model (Fisher et al., 2006) seems to be a suitable model for identifying factors of adherence to multiple medications. Having comprehensive information about medications and having positive motivations influence one's behavioral skills. The patient interviews reflect the links between the three factors of the IMB model to adherence. The IMB model emphasizes the importance of support from caregivers and healthcare providers. However, it might be even more useful to further specify the sources of support and how they help, such as identifying different types of support. For example, when a patient is unable to absorb all of the pertinent information regarding the post-transplant regimen, the caregiver can receive the information alongside the patient and help the patient develop suitable skills as a follow up. For this to work, the same medical information must be conveyed to both the patient and caregiver.

Overall, this study underscores the need for a more systematic understanding of caregivers, particularly their role in enhancing adherence by influencing information, motivation, and behavioral skills available to patients. One suggestion is to integrate the IMB model with the social support cascade model for multiple medication adherence, as each of the adherence cascades—such as attendance of doctor's appointment, refill and organization of medications, preparation for food and liquid intake, as well as taking of the medications—needs information, motivation, and skills.

This study also identified factors not mentioned or under-specified in the model. The importance of trust in the relationship between patient and healthcare provider is not adequately treated in the IMB model. However, based on our findings, trusting and believing in healthcare providers' decision-making in medical procedures influenced patients in their views and medication adherence. Moreover, meaning in life and spirituality, where individuals mentioned using prayers to maintain hope, were not identified in the model. They should be included as personal motivation factors, as general optimism and hope have been identified as important coping strategies for chronic diseases, including cancer (Duggleby et al., 2010; Raleigh, 1992).

Implications for Practice

There are several practical implications of the findings of these studies. First, some changes need to be made to the hospital discharge protocols. Both the patient and the caregivers need to be educated. For instance, the hospital needs to provide more comprehensive educational and practical training on medication adherence and other related behaviors, such as exercise and diet, which are as important as taking the medications.

Second, instead of giving the electronic pillbox already filled by the nurses, giving patients a chance to practice refilling it would also help them further familiarize themselves with using the pillbox. It can be overwhelming for the patient and the caregivers to absorb all the information in one hospital discharge meeting, so having several meetings would be more helpful for them to master the information. Many relied on using the information sheet they were given at the hospital discharge. Creating a comprehensive and detailed information sheet would help. The hospital also needs to have a system in place to ensure that the said information sheet is always up-to-date. Most importantly, the same massage has to be delivered to the lay caregivers in order to equip them to help the patients.

Third, in addition to delivering the technical matters related to medication adherence, such as gaining the information on their regimens, electronic pillbox and skills, sessions that can promote and help patients not to lose their hope might be needed. Hope seems to be a critical factor for the patients. Hospitals or healthcare centers can provide sessions on motivation and hope, which can encourage patients to stay optimistic, or create support groups so patients can encourage each other.

Fourth, although this study specifically examined individuals after alloHCT, the findings can be applied to individuals with comorbid conditions who have to take multiple medications. This would especially include the elderly, a population that has increased drastically over time and is projected to continue its increase in the future (United Nations, Department of Economics and Social Affairs, & Population Division, 2017). With advanced age, individuals are at increased risk for chronic diseases, and taking multiple medications represents a major challenge for this group (Nobili, Garattini,

& Mannucci, 2011; Pasina et al., 2014). Although the characteristics of individuals with leukemia or lymphoma after alloHCT do not exactly match those of other individuals with multimorbidity and an elderly individual, they face similar challenges. Thus, this study can offer practical suggestions for other populations where adherence to multiple medications is a problem.

Limitations and Strengths

The studies reported here present both limitations and strengths. First, the studies are based on a small study at a single cancer center in an urban area, so the findings may not be generalized to other conditions. In addition, this dissertation examined a very specific group of people who were in a difficult and life-or-death situation; they had no choice but taking the medications because otherwise they will die the next day. Adherence to multiple medications might look different in other patient populations and chronic conditions, who are in a less urgent situation. However, we assume that our findings that using an electronic pillbox is feasible, social support is required, and an array of adherence strategies is needed for ensuring adherence to multiple medications is likely to generalize to other populations who are prescribed multiple medications. A recent review of medication adherence interventions claims the need for improvement in interventions because the current state is that adherence interventions varied among different patient groups, treatments and health outcomes, and did not show significant improvement in clinical outcomes (Nieuwlaat et al., 2014). The current dissertation laid the groundwork for developing a longitudinal intervention by way of elicitation research, identifying potentially critical determinants for a specific population undergoing long-term treatment. This is a good starting point, as the sample, although small, was diverse because of the location of the cancer center. Moreover, this group of patients had been understudied, and this is one of the first studies that examined this population.

Second, the layout of the electronic pillbox, which promotes planning daily to weekly doses, might have influenced the nature of the purely observational study. Another limitation is that due to the nature of conducting an interview, there is a possibility that the patients have reported socially desirable responses.

Third, while we examined the role of social support for medication adherence of individuals after alloHCT, the actual relationship between the adherence rate and social support was not examined. It is possible that those who reported receiving more social support had higher adherence rates and vice versa because of the complexity of the regimen and their health conditions. But the study focused on reporting what healthcare providers and close others did to help patients. It would be the logical next step to examine the relationship between social support and the level of adherence for individuals in the study. Finally, there may also be potential biases in analyzing the data, but we tried to maintain a common standard of objectivity with inter-rater reliability checks.

Despite these limitations, the study had several notable strengths. First, this study is among the first to examine multiple medication adherence for patients after alloHCT. This is an understudied population, particularly in the context of multiple medication regimens. Based on the findings of this elicitation research, future interventions could be designed that address the needs of this specific population. Second, this study combines quantitative results of the electronic pillbox use with qualitative data. By combining an original metric of adherence with in-depth interviews, this study offers a systematic examination of adherence while allowing patients to fully express and convey their opinions and feelings. Finally, this study directly speaks to the existing theoretical literature by adopting the IMB model. It also suggests novel categories to improve the model's applicability, such as acceptance of patient role and general optimism.

Recommendations for Future Research

Based on the findings reported for these studies, several recommendations for future research are warranted. First, more suitable electronic pillboxes for patients with multiple medications should be designed based on the information obtained from patients and tested for their feasibility and efficacy. An intervention specific to a particular group of patients, such as those who have undergone alloHCT procedures, can be developed using the findings of this elicitation research (Fisher & Fisher, 1992). Moreover, technology can be harnessed in different ways to advance interventions for adherence to multiple medications. For example, text messaging or smart phone applications could be used to notify, reinforce and monitor adherence (Lester et al., 2009). This would facilitate adherence and capture real-time data for research that could lead to further quality-of-life improvements. Integrating technology in adherence interventions is still a relatively new area, and it is premature to conclude whether it can improve adherence (Granger & Bosworth, 2011; Nieuwlaat et al., 2014); however, we need more investigations and well-developed interventions.

Not only does this project draw on the well-established IMB model for rigorously studying adherence, but it also uncovers additional determinants of adherence that can inform new interventions by allowing patients to freely provide their opinions, hopes, and worries, as well as share some of the strategies they have developed for themselves. Future research should explore the relationship of these determinants to adherence and the implications for intervention approaches designed to facilitate patient behavior.

References

Davidson, T. M., McGillicuddy, J., Mueller, M., Brunner-Jackson, B., Favella, A., Anderson, A., … Treiber, F. A. (2015). Evaluation of an mHealth medication regimen self-management program for African American and Hispanic uncontrolled hypertensives. *Journal of Personalized Medicine*, *5*(4), 389–405. https://doi.org/10.3390/jpm5040389

DiMatteo, M. R. (2004). Social support and patient adherence to medical treatment: A meta-analysis. *Health Psychology*, *23*(2), 207–218. https://doi.org/10.1037/0278-6133.23.2.207

Duggleby, W., Holtslander, L., Kylma, J., Duncan, V., Hammond, C., & Williams, A. (2010). Metasynthesis of the hope experience of family caregivers of persons with chronic illness. *Qualitative Health Research*, *20*(2), 148–158. https://doi.org/10.1177/1049732309358329

Fisher, J. D., & Fisher, W. A. (1992). Changing AIDS-risk behavior. *Psychological Bulletin*, *111*(3), 455–474. https://doi.org/10.1037/0033-2909.111.3.455

Fisher, J. D., Fisher, W. A., Amico, K. R., & Harman, J. J. (2006). An information-motivation-behavioral skills model of adherence to antiretroviral therapy. *Health Psychology*, *25*(4), 462–473. https://doi.org/10.1037/0278-6133.25.4.462

Granger, B. B., & Bosworth, H. (2011). Medication adherence: Emerging use of technology. *Current Opinion in Cardiology*, *26*(4), 279–287. https://doi.org/10.1097/HCO.0b013e328347c150

Lester, R. T., Mills, E. J., Kariri, A., Ritvo, P., Chung, M., Jack, W., … Plummer, F. A. (2009). The HAART cell phone adherence trial (WelTel Kenya1): A randomized controlled trial protocol. *Trials*, *10*, 87. https://doi.org/10.1186/1745-6215-10-87

McGillicuddy, J. W., Gregoski, M. J., Weiland, A. K., Rock, R. A., Brunner-Jackson, B. M., Patel, S. K., … Treiber, F. A. (2013). Mobile health medication adherence and blood pressure control in renal transplant recipients: A proof-of-concept randomized controlled trial. *JMIR Research Protocols*, *2*(2). https://doi.org/10.2196/resprot.2633

Nieuwlaat, R., Wilczynski, N., Navarro, T., Hobson, N., Jeffery, R., Keepanasseril, A., … Haynes, R. B. (2014). Interventions for enhancing medication adherence. *Cochrane Database of Systematic Reviews,* (11). https://doi.org/10.1002/14651858.CD000011.pub4

Nobili, A., Garattini, S., & Mannucci, P. M. (2011). Multiple diseases and polypharmacy in the elderly: Challenges for the internist of the third millennium. *Journal of Comorbidity*, *1*, 28–44.

Pasina, L., Brucato, A. L., Falcone, C., Cucchi, E., Bresciani, A., Sottocorno, M., … Nobili, A. (2014). Medication non-adherence among elderly patients newly discharged and receiving polypharmacy. *Drugs & Aging*, *31*(4), 283–289. https://doi.org/10.1007/s40266-014-0163-7

Raleigh, E. D. (1992). Sources of hope in chronic illness. *Oncology Nursing Forum*, *19*(3), 443–448.

Sabaté, E. (2003). *Adherence to long-term therapies: Evidence for action*. Geneva: World Health Organization.

United Nations, Department of Economics and Social Affairs, & Population Division. (2017). *World population ageing, 2017: Highlights*. New York: United Nations; 2017.

BIBLIOGRAPHY

Aizer, A. A., Chen, M. H., McCarthy, E. P., Mendu, M. L., Koo, S., Wilhite, T. J., … Nguyen, P. L. (2013). Marital status and survival in patients with cancer. *Journal of Clinical Oncology*, *31*(31), 3869–3876. https://doi.org/10.1200/JCO.2013.49.6489

Allegrante, J. P., Wells, M. T., & Peterson, J. C. (2019). Interventions to support behavioral self-management of chronic diseases. *Annual Review of Public Health*, *40*(1), null. https://doi.org/10.1146/annurev-publhealth-040218-044008

American Cancer Society. (2017). Stem cell transplant for chronic myelomonocytic leukemia. Retrieved June 6, 2018, from https://www.cancer.org/cancer/chronic-myelomonocytic-leukemia/treating/stem-cell-transplant.html

Banna, G. L., Collovà, E., Gebbia, V., Lipari, H., Giuffrida, P., Cavallaro, S., … Ferraù, F. (2010). Anticancer oral therapy: Emerging related issues. *Cancer Treatment Reviews*, *36*(8), 595–605. https://doi.org/10.1016/j.ctrv.2010.04.005

Bartholomew Eldredge, L. K., Markham, C. M., Ruiter, R. A., Fernández, M. E., Kok, G., & Parcel, G. S. (2016). *Planning health promotion programs: An intervention mapping approach (4th ed.)*. Hoboken, NJ: Wiley.

Beattie, S., & Lebel, S. (2011). The experience of caregivers of hematological cancer patients undergoing a hematopoietic stem cell transplant: A comprehensive literature review. *Psycho-Oncology*, *20*(11), 1137–1150. https://doi.org/10.1002/pon.1962

Beattie, S., Lebel, S., & Tay, J. (2013). The influence of social support on hematopoietic stem cell transplantation survival: A systematic review of literature. *PLOS ONE*, *8*(4), e61586. https://doi.org/10.1371/journal.pone.0061586

Berghoff, C. R., Gratz, K. L., Portz, K. J., Pinkston, M., Naifeh, J. A., Evans, S. D., … Tull, M. T. (2018). The role of emotional avoidance, the patient–provider relationship, and other social support in ART adherence for HIV+ individuals. *AIDS and Behavior*, *22*(3), 929–938. https://doi.org/10.1007/s10461-017-1745-2

Berkman, L. F., Glass, T., Brissette, I., & Seeman, T. E. (2000). From social integration to health: Durkheim in the new millennium. *Social Science & Medicine*, *51*(6), 843–857. https://doi.org/10.1016/S0277-9536(00)00065-4

Bishop, M. M., Rodrigue, J. R., & Wingard, J. R. (2002). Mismanaging the gift of life: Noncompliance in the context of adult stem cell transplantation. *Bone Marrow Transplantation*, *29*(11), 875. https://doi.org/10.1038/sj.bmt.1703523

Blaschke, T. F., Osterberg, L., Vrijens, B., & Urquhart, J. (2012). Adherence to medications: Insights arising from studies on the unreliable link between prescribed and actual drug dosing histories. *Annual Review of Pharmacology and Toxicology*, *52*(1), 275–301. https://doi.org/10.1146/annurev-pharmtox-011711-113247

Bosworth, H. B. (2010). Medication adherence. In *Improving patient treatment adherence* (pp. 68–94). Springer, New York, NY. https://doi.org/10.1007/978-1-4419-5866-2_4

Bosworth, H. B., Granger, B. B., Mendys, P., Brindis, R., Burkholder, R., Czajkowski, S. M., … Granger, C. B. (2011). Medication adherence: A call for action. *American Heart Journal*, *162*(3), 412–424. https://doi.org/10.1016/j.ahj.2011.06. 007

Brown, M. T., & Bussell, J. K. (2011). Medication adherence: WHO cares? *Mayo Clinic Proceedings*, *86*(4), 304–314. https://doi.org/10.4065/mcp.2010.0575

Buttorff, C., Ruder, T., & Bauman, M. (2017). *Multiple Chronic Conditions in the United States*. Santa Monica, CA: RAND. https://doi.org/10.7249/TL221

Chang, S. J., Choi, S., Kim, S.-A., & Song, M. (2014). Intervention strategies based on Information-Motivation-Behavioral Skills model for health behavior change: A systematic review. *Asian Nursing Research*, *8*(3), 172–181. https://doi.org/ 10.1016/j.anr.2014.08.002

Chou, A. F., Stewart, S. L., Wild, R. C., & Bloom, J. R. (2012). Social support and survival in young women with breast carcinoma. *Psycho-Oncology*, *21*(2), 125–133. https://doi.org/10.1002/pon.1863

Claxton, A. J., Cramer, J., & Pierce, C. (2001). A systematic review of the associations between dose regimens and medication compliance. *Clinical Therapeutics*, *23*(8), 1296–1310. https://doi.org/10.1016/S0149-2918(01)80109-0

Cohen, S., & McKay, G. (1984). Social support, stress and the buffering hypothesis: A theoretical analysis. *Handbook of Psychology and Health*, *4*, 253–267.

Conn, V. S., & Ruppar, T. M. (2017). Medication adherence outcomes of 771 intervention trials: Systematic review and meta-analysis. *Preventive Medicine*, *99*, 269–276. https://doi.org/10.1016/j.ypmed.2017.03.008

Costa, E., Giardini, A., Savin, M., Menditto, E., Lehane, E., Laosa, O., … Marengoni, A. (2015). Interventional tools to improve medication adherence: review of literature. *Patient Preference and Adherence*, *9*, 1303–1314. https://doi.org/ 10.2147/PPA.S87551

Creswell, J., Klassen, A. C., Plano, V., & Smith, K. C. (2011). Best practices for mixed methods research in the health sciences. *Bethesda (Maryland): National Institutes of Health, 2013,* 541-545.

Creswell, J. W. (2013). *Research design: Qualitative, quantitative, and mixed methods approaches*. SAGE Publications.

Cross, A. J., Elliott, R. A., & George, J. (2016). Interventions for improving medication-taking ability and adherence in older adults prescribed multiple medications. *Cochrane Database of Systematic Reviews*. https://doi.org/10.1002/14651858.CD012419

Cutrona, C. E., & Russell, D. W. (1990). Type of social support and specific stress: Toward a theory of optimal matching. In *Wiley Series on Personality Processes. Social support: An interactional view* (pp. 319–366). Oxford, England: John Wiley & Sons.

D'Souza, A., Pasquini, M., & Zhu, X. (2016). CIBMTR summary slides - HCT trends and survival data. Retrieved January 26, 2018, from https://www.cibmtr.org/ReferenceCenter/SlidesReports/SummarySlides/Pages/index.aspx

Davidson, T. M., McGillicuddy, J., Mueller, M., Brunner-Jackson, B., Favella, A., Anderson, A., … Treiber, F. A. (2015). Evaluation of an mHealth medication regimen self-management program for African American and Hispanic uncontrolled hypertensives. *Journal of Personalized Medicine*, *5*(4), 389–405. https://doi.org/10.3390/jpm5040389

DiMatteo, M. R. (2004). Social support and patient adherence to medical treatment: A meta-analysis. *Health Psychology*, *23*(2), 207–218. https://doi.org/10.1037/0278-6133.23.2.207

Duggleby, W., Holtslander, L., Kylma, J., Duncan, V., Hammond, C., & Williams, A. (2010). Metasynthesis of the hope experience of family caregivers of persons with chronic illness. *Qualitative Health Research*, *20*(2), 148–158. https://doi.org/10.1177/1049732309358329

Ehrlich, K. B., Miller, G. E., Scheide, T., Baveja, S., Weiland, R., Galvin, J., … Penedo, F. J. (2016). Pre-transplant emotional support is associated with longer survival after allogeneic hematopoietic stem cell transplantation. *Bone Marrow Transplantation*, *51*(12), 1594–1598. https://doi.org/10.1038/bmt.2016.191

Farmer, K. C. (1999). Methods for measuring and monitoring medication regimen adherence in clinical trials and clinical practice. *Clinical Therapeutics*, *21*(6), 1074–1090. https://doi.org/10.1016/S0149-2918(99)80026-5

Fisher, J. D., & Fisher, W. A. (1992). Changing AIDS-risk behavior. *Psychological Bulletin*, *111*(3), 455–474. https://doi.org/10.1037/0033-2909.111.3.455

Fisher, J. D., Fisher, W. A., Amico, K. R., & Harman, J. J. (2006). An information-motivation-behavioral skills model of adherence to antiretroviral therapy. *Health Psychology*, *25*(4), 462–473. https://doi.org/10.1037/0278-6133.25.4.462

Foster, L., Mclellan, L., A. Rybicki, L., A. Sassano, D., Hsu, A., & Bolwell, B. (2005). Survival of patients who have undergone allogeneic bone marrow transplantation. *Journal of Psychosocial Oncology, 22*(2), 1-20. https://doi.org/10.1300/J077v22n02_01

Freifeld, A. G., Bow, E. J., Sepkowitz, K. A., Boeckh, M. J., Ito, J. I., Mullen, C. A., … Wingard, J. R. (2011). Clinical practice guideline for the use of antimicrobial agents in neutropenic patients with cancer: 2010 update by the Infectious Diseases Society of America. *Clinical Infectious Diseases*, *52*(4), e56–e93. https://doi.org/10.1093/cid/cir073

George, J., Elliott, R. A., & Stewart, D. C. (2008). A systematic review of interventions to improve medication taking in elderly patients prescribed multiple medications. *Drugs & Aging*, *25*(4), 307–324. https://doi.org/10.2165/00002512-200825040-00004

Gooley, T. A., Chien, J. W., Pergam, S. A., Hingorani, S., Sorror, M. L., Boeckh, M., … McDonald, G. B. (2010). Reduced mortality after allogeneic hematopoietic-cell transplantation. *New England Journal of Medicine*, *363*(22), 2091–2101. https://doi.org/10.1056/NEJMoa1004383

Granger, B. B., & Bosworth, H. (2011). Medication adherence: Emerging use of technology. *Current Opinion in Cardiology*, *26*(4), 279–287. https://doi.org/10.1097/HCO.0b013e328347c150

Gresch, B., Kirsch, M., Fierz, K., Halter, J. P., Nair, G., Denhaerynck, K., & De Geest, S. (2017). Medication nonadherence to immunosuppressants after adult allogeneic haematopoietic stem cell transplantation: A multicentre cross-sectional study. *Bone Marrow Transplantation*, *52*(2), 304–306. https://doi.org/10.1038/bmt.2016.262

Haberer, J. E., Robbins, G. K., Ybarra, M., Monk, A., Ragland, K., Weiser, S. D., … Bangsberg, D. R. (2012). Real-time electronic adherence monitoring is feasible, comparable to unannounced pill counts, and acceptable. *AIDS and Behavior*, *16*(2), 375–382. https://doi.org/10.1007/s10461-011-9933-y

Hahn, T., McCarthy, P. L., Hassebroek, A., Bredeson, C., Gajewski, J. L., Hale, G. A., … Majhail, N. S. (2013). Significant improvement in survival after allogeneic hematopoietic cell transplantation during a period of significantly increased use, older recipient age, and use of unrelated donors. *Journal of Clinical Oncology*, *31*(19), 2437–2449. https://doi.org/10.1200/JCO.2012.46.6193

Hall, A. E., Paul, C., Bryant, J., Lynagh, M. C., Rowlings, P., Enjeti, A., & Small, H. (2016). To adhere or not to adhere: Rates and reasons of medication adherence in hematological cancer patients. *Critical Reviews in Oncology/Hematology*, *97*, 247–262. https://doi.org/10.1016/j.critrevonc.2015.08.025

Hashmi, S., Carpenter, P., Khera, N., Tichelli, A., & Savani, B. N. (2015). Lost in transition: The essential need for long-term follow-up clinic for blood and marrow transplantation survivors. *Biology of Blood and Marrow Transplantation*, *21*(2), 225–232. https://doi.org/10.1016/j.bbmt.2014.06.035

Helgeson, V. S. (2003). Social support and quality of life. *Quality of Life Research*, *12*(1), 25–31. https://doi.org/10.1023/A:1023509117524

Holtan, S. G., DeFor, T. E., Lazaryan, A., Bejanyan, N., Arora, M., Brunstein, C. G., … Weisdorf, D. J. (2015). Composite end point of graft-versus-host disease-free, relapse-free survival after allogeneic hematopoietic cell transplantation. *Blood*, *125*(8), 1333–1338. https://doi.org/10.1182/blood-2014-10-609032

Holt-Lunstad, J., Smith, T. B., & Layton, J. B. (2010). Social relationships and mortality risk: A meta-analytic review. *PLoS Med*, *7*(7), e1000316.

Hoodin, F., Harper, F. W. K., & Posluszny, D. M. (2010). Psychological care of adult allogeneic transplant patients. In H. M. Lazarus & M. J. Laughlin (Eds.), *Allogeneic Stem Cell Transplantation* (pp. 619–656). Humana Press. https://doi.org/10.1007/978-1-59745-478-0_35

Horvath, K. J., Smolenski, D., & Amico, K. R. (2014). An empirical test of the information-motivation-behavioral skills model of ART adherence in a sample of HIV-positive persons primarily in out-of-HIV-care settings. *AIDS Care*, *26*(2), 142–151. https://doi.org/10.1080/09540121.2013.802283

House, J. S., Kahn, R. L., McLeod, J. D., & Williams, D. (1985). Measures and concepts of social support. In *Social support and health.* (pp. 83–108). San Diego, CA, US: Academic Press.

Hsieh, H. F., & Shannon, S. E. (2005). Three approaches to qualitative content analysis. *Qualitative Health Research*, *15*(9), 1277–1288. https://doi.org/10.1177/1049732305276687

Inauen, J., Bierbauer, W., Lüscher, J., König, C., Tobias, R., Ihle, A., … Scholz, U. (2017). Assessing adherence to multiple medications and in daily life among patients with multimorbidity. *Psychology & Health*, *32*(10), 1233–1248. https://doi.org/10.1080/08870446.2016.1275632

Ingersoll, K. S., & Cohen, J. (2008). The impact of medication regimen factors on adherence to chronic treatment: A review of literature. *Journal of Behavioral Medicine*, *31*(3), 213–224. https://doi.org/10.1007/s10865-007-9147-y

Jim, H. S. L., Sutton, S. K., Jacobsen, P. B., Martin, P. J., Flowers, M. E., & Lee, S. J. (2016). Risk factors for depression and fatigue among survivors of hematopoietic cell transplantation. *Cancer*, *122*(8), 1290–1297. https://doi.org/10.1002/cncr.29877

Kantor, E. D., Rehm, C. D., Haas, J. S., Chan, A. T., & Giovannucci, E. L. (2015). Trends in prescription drug use among adults in the United States from 1999-2012. *JAMA*, *314*(17), 1818–1830. https://doi.org/10.1001/jama.2015.13766

Kardas, P., Lewek, P., & Matyjaszczyk, M. (2013). Determinants of patient adherence: A review of systematic reviews. *Frontiers in Pharmacology*, *4*. https://doi.org/10.3389/fphar.2013.00091

Kelley, J. M., Kraft-Todd, G., Schapira, L., Kossowsky, J., & Riess, H. (2014). The influence of the patient-clinician relationship on healthcare outcomes: A systematic review and meta-analysis of randomized controlled trials. *PLOS ONE*, *9*(4), e94207. https://doi.org/10.1371/journal.pone.0094207

Kelly, J. D., Hartman, C., Graham, J., Kallen, M. A., & Giordano, T. P. (2014). Social support as a predictor of early diagnosis, linkage, retention, and adherence to HIV care: Results from the steps study. *The Journal of the Association of Nurses in AIDS Care : JANAC*, *25*(5), 405–413. https://doi.org/10.1016/j.jana.2013.12.002

Khera, N., Chang, Y., Hashmi, S., Slack, J., Beebe, T., Roy, V., … Mikhael, J. (2014). Financial burden in recipients of allogeneic hematopoietic cell transplantation. *Biology of Blood and Marrow Transplantation*, *20*(9), 1375–1381. https://doi.org/10.1016/j.bbmt.2014.05.011

Kim, J., & Parish, A. L. (2017). Polypharmacy and medication management in older adults. *Nursing Clinics of North America*, *52*(3), 457–468. https://doi.org/10.1016/j.cnur.2017.04.007

Kim, W., Mcnulty, J., Chang, Y. -h, Weise, M., Hashmi, S., Ailawadhi, S., & Khera, N. (2015). Financial burden after allogeneic hematopoietic cell transplantation: A qualitative analysis from the patient’s perspective. *Bone Marrow Transplantation; London*, *50*(9), 1259–1261. http://dx.doi.org/10.1038/bmt.2015.128

Kirsch, M., Götz, A., Halter, J. P., Schanz, U., Stussi, G., Dobbels, F., & De Geest, S. (2014). Differences in health behaviour between recipients of allogeneic haematopoietic SCT and the general population: A matched control study. *Bone Marrow Transplantation*, *49*(9), 1223–1230. https://doi.org/10.1038/bmt.2014.142

Krause, N. (2007). Longitudinal study of social support and meaning in life. *Psychology and Aging*, *22*(3), 456–469. https://doi.org/10.1037/0882-7974.22.3.456

Lehrer, J., Brissot, E., Ruggeri, A., Dulery, R., Vekhoff, A., Battipaglia, G., … Antignac, M. (2018). Medication adherence among allogeneic hematopoietic stem cell transplant recipients: A pilot single-center study. *Bone Marrow Transplantation*, *53*(2), 231–233. https://doi.org/10.1038/bmt.2017.233

Lester, R. T., Mills, E. J., Kariri, A., Ritvo, P., Chung, M., Jack, W., … Plummer, F. A. (2009). The HAART cell phone adherence trial (WelTel Kenya1): A randomized controlled trial protocol. *Trials*, *10*, 87. https://doi.org/10.1186/1745-6215-10-87

Luszczynska, A., Pawlowska, I., Cieslak, R., Knoll, N., & Scholz, U. (2013). Social support and quality of life among lung cancer patients: A systematic review. *Psycho-Oncology*, *22*(10), 2160–2168. https://doi.org/10.1002/pon.3218

Majhail, N. S., Farnia, S. H., Carpenter, P. A., Champlin, R. E., Crawford, S., Marks, D. I., … LeMaistre, C. F. (2015). Indications for autologous and allogeneic hematopoietic cell transplantation: Guidelines from the American Society for Blood and Marrow Transplantation. *Biology of Blood and Marrow Transplantation*, *21*(11), 1863–1869. https://doi.org/10.1016/j.bbmt.2015.07.032

Majhail, N. S., Tao, L., Bredeson, C., Davies, S., Dehn, J., Gajewski, J. L., … Kuntz, K. M. (2013). Prevalence of hematopoietic cell transplant survivors in the United States. *Biology of Blood and Marrow Transplantation*, *19*(10), 1498–1501. https://doi.org/10.1016/j.bbmt.2013.07.020

Mathes, T., Antoine, S.-L., Pieper, D., & Eikermann, M. (2014). Adherence enhancing interventions for oral anticancer agents: A systematic review. *Cancer Treatment Reviews*, *40*(1), 102–108. https://doi.org/10.1016/j.ctrv.2013.07.004

Mayberry, L. S., & Osborn, C. Y. (2012). Family support, medication adherence, and glycemic control among adults with type 2 diabetes. *Diabetes Care*, *35*(6), 1239–1245. https://doi.org/10.2337/dc11-2103

Mayberry, L. S., & Osborn, C. Y. (2014). Empirical Validation of the Information–Motivation–Behavioral Skills model of diabetes medication adherence: A framework for intervention. *Diabetes Care*, *37*(5), 1246–1253. https://doi.org/10.2337/dc13-1828

McDonald, H. P., Garg, A. X., & Haynes, R. B. (2002). Interventions to enhance patient adherence to medication prescriptions: Scientific review. *JAMA*, *288*(22), 2868–2879. https://doi.org/10.1001/jama.288.22.2868

McGillicuddy, J. W., Gregoski, M. J., Weiland, A. K., Rock, R. A., Brunner-Jackson, B. M., Patel, S. K., … Treiber, F. A. (2013). Mobile health medication adherence and blood pressure control in renal transplant recipients: A proof-of-concept randomized controlled trial. *JMIR Research Protocols*, *2*(2). https://doi.org/10.2196/resprot.2633

McGillicuddy, J. W., Taber, D. J., Mueller, M., Patel, S., Baliga, P. K., Chavin, K. D., … Treiber, F. A. (2015). Sustainability of improvements in medication adherence through a mobile health intervention. *Progress in Transplantation*, *25*(3), 217–223.

McLellan, L., Foster, L. W., Rybicki, L., Dabney, J., Cooper, M., & Bolwell, B. (2011). Optimal duration and frequency of in-hospital lay care-partner support for positive impact on patient survival in allogeneic BMT. *Biology of Blood and Marrow Transplantation*, *17*(2, Supplement), S243–S244. https://doi.org/10.1016/j.bbmt.2010.12.272

Morrison, C. F., Martsolf, D. M., Wehrkamp, N., Tehan, R., & Pai, A. L. (2017). Medication adherence in hematopoietic stem cell transplantation: A review of the literature. *Biology of Blood and Marrow Transplantation*, *23*(4), 562–568. https://doi.org/10.1016/j.bbmt.2017.01.008

National Center for Health Statistics (US). (2014). *Health, United States, 2013: With Special Feature on Prescription Drugs*. Retrieved from http://www.ncbi.nlm.nih.gov/books/NBK209224/

National Marrow Donor Program. (2017). After transplant guidelines for patients. Retrieved November 17, 2018, from https://bethematchclinical.org/resources-and-education/materials-catalog/after-transplant-guidelines-for-patients/

Neumann, S., Krause, S. W., Maschmeyer, G., Schiel, X., & von Lilienfeld-Toal, M. (2013). Primary prophylaxis of bacterial infections and Pneumocystis jirovecii pneumonia in patients with hematological malignancies and solid tumors. *Annals of Hematology*, *92*(4), 433–442. https://doi.org/10.1007/s00277-013-1698-0

Nieuwlaat, R., Wilczynski, N., Navarro, T., Hobson, N., Jeffery, R., Keepanasseril, A., … Haynes, R. B. (2014). Interventions for enhancing medication adherence. *Cochrane Database of Systematic Reviews,* (11). https://doi.org/10.1002/14651858.CD000011.pub4

Nobili, A., Garattini, S., & Mannucci, P. M. (2011). Multiple diseases and polypharmacy in the elderly: Challenges for the internist of the third millennium. *Journal of Comorbidity*, *1*, 28–44.

O'Brien, B. C., Harris, I. B., Beckman, T. J., Reed, D. A., & Cook, D. A. (2014). Standards for reporting qualitative research: A synthesis of recommendations. *Academic Medicine*, *89*(9), 1245. https://doi.org/10.1097/ACM.0000000000000388

Ogedegbe, G., Harrison, M., Robbins, L., Mancuso, C. A., & Allegrante, J. P. (2004). Barriers and facilitators of medication adherence in hypertensive African Americans: A qualitative study. *Ethn Dis*, *14*(1), 3–12. (15002917).

Osborn, C. Y., & Egede, L. E. (2010). Validation of an Information–Motivation–Behavioral Skills model of diabetes self-care (IMB-DSC). *Patient Education and Counseling*, *79*(1), 49–54. https://doi.org/10.1016/j.pec.2009.07.016

Osterberg, L., & Blaschke, T. (2005). Adherence to medication. *New England Journal of Medicine*, *353*(5), 487–497. https://doi.org/10.1056/NEJMra050100

Pantuzza, L. L., Ceccato, M. das G. B., Silveira, M. R., Junqueira, L. M. R., & Reis, A. M. M. (2017). Association between medication regimen complexity and pharmacotherapy adherence: A systematic review. *European Journal of Clinical Pharmacology*, *73*(11), 1475–1489. https://doi.org/10.1007/s00228-017-2315-2

Pasina, L., Brucato, A. L., Falcone, C., Cucchi, E., Bresciani, A., Sottocorno, M., … Nobili, A. (2014). Medication non-adherence among elderly patients newly discharged and receiving polypharmacy. *Drugs & Aging*, *31*(4), 283–289. https://doi.org/10.1007/s40266-014-0163-7

Pasquini, M., Wang, Z., & Schneider, L. (2009). CIBMTR summary slides. *CIBMTR Newsletter*, 6–11.

Patton, D. E., Cadogan, C. A., Ryan, C., Francis, J. J., Gormley, G. J., Passmore, P., … Hughes, C. M. (2017). Improving adherence to multiple medications in older people in primary care: Selecting intervention components to address patient-reported barriers and facilitators. *Health Expectations*, 1–11. https://doi.org/10.1111/hex.12595

Patton, D. E., Hughes, C. M., Cadogan, C. A., & Ryan, C. A. (2017). Theory-based interventions to improve medication adherence in older adults prescribed polypharmacy: A systematic review. *Drugs & Aging*, *34*(2), 97–113. https://doi.org/10.1007/s40266-016-0426-6

Posluszny, D. M., Bovbjerg, D. H., Agha, M. E., Hou, J.-Z., Raptis, A., Boyiadzis, M. M., … Dew, M. A. (2018). Patient and family caregiver dyadic adherence to the allogeneic hematopoietic cell transplantation medical regimen. *Psycho-Oncology*, *27*(1), 354–358. https://doi.org/10.1002/pon.4393

Raleigh, E. D. (1992). Sources of hope in chronic illness. *Oncology Nursing Forum*, *19*(3), 443–448.

Rathert, C., Wyrwich, M. D., & Boren, S. A. (2013). Patient-centered care and outcomes: A systematic review of the literature. *Medical Care Research and Review*, *70*(4), 351–379. https://doi.org/10.1177/1077558712465774

Richter, A., Anton, S. E., Koch, P., & Dennett, S. L. (2003). The impact of reducing dose frequency on health outcomes. *Clinical Therapeutics*, *25*(8), 2307–2335. https://doi.org/10.1016/S0149-2918(03)80222-9

Rini, C., Redd, W. H., Austin, J., Mosher, C. E., Meschian, Y. M., Isola, L., … DuHamel, K. N. (2011). Effectiveness of partner social support predicts enduring psychological distress after hematopoietic stem cell transplantation. *Journal of Consulting and Clinical Psychology*, *79*(1), 64–74. https://doi.org/10.1037/a0022199

Robinson, J. H., Callister, L. C., Berry, J. A., & Dearing, K. A. (2008). Patient-centered care and adherence: Definitions and applications to improve outcomes. *Journal of the American Academy of Nurse Practitioners*, *20*(12), 600–607. https://doi.org/10.1111/j.1745-7599.2008.00360.x

Ruddy, K., Mayer, E., & Partridge, A. (2009). Patient adherence and persistence with oral anticancer treatment. *CA: A Cancer Journal for Clinicians*, *59*(1), 56–66. https://doi.org/10.3322/caac.20004

Sabaté, E. (2003). *Adherence to long-term therapies: Evidence for action*. Geneva: World Health Organization.

Scheurer, D., Choudhry, N., Swanton, K. A., Matlin, O., & Shrank, W. (2012). Association between different types of social support and medication adherence. *The American Journal of Managed Care*, *18*(12), e461-7.

Siegal, B., & Greenstein, S. (1999). Compliance and noncompliance in kidney transplant patients: Cues for transplant coordinators. *Journal of Transplant Coordination*, *9*(2), 104–108. https://doi.org/10.1177/090591999900900207

Simoni, J. M., Frick, P. A., & Huang, B. (2006). A longitudinal evaluation of a social support model of medication adherence among HIV-positive men and women on antiretroviral therapy. *Health Psychology: Official Journal of the Division of Health Psychology, American Psychological Association*, *25*(1), 74–81. https://doi.org/10.1037/0278-6133.25.1.74

So, W. K., Dodgson, J., & Tai, J. W. (2003). Fatigue and quality of life among Chinese patients with hematologic malignancy after bone marrow transplantation. *Cancer Nursing*, *26*(3), 211–219.

Teichman, B. J., Burker, E. J., Weiner, M., & Egan, T. M. (2000). Factors associated with adherence to treatment regimens after lung transplantation. *Progress in Transplantation*, *10*(2), 113–121. https://doi.org/10.1177/152692480001000208

Thoits, P. A. (2011). Mechanisms linking social ties and support to physical and mental health. *Journal of Health and Social Behavior*, *52*(2), 145–161.

Tomblyn, M., Chiller, T., Einsele, H., Gress, R., Sepkowitz, K., Storek, J., … Boeckh, M. A. (2009). Guidelines for preventing infectious complications among hematopoietic cell transplantation recipients: A global perspective. *Biology of Blood and Marrow Transplantation*, *15*(10), 1143–1238.

Tong, A., Flemming, K., McInnes, E., Oliver, S., & Craig, J. (2012). Enhancing transparency in reporting the synthesis of qualitative research: ENTREQ. *BMC Medical Research Methodology*, *12*(1), 181. https://doi.org/10.1186/1471-2288-12-181

Tong, A., Sainsbury, P., & Craig, J. (2007). Consolidated criteria for reporting qualitative research (COREQ): A 32-item checklist for interviews and focus groups. *International Journal for Quality in Health Care*, *19*(6), 349–357. https://doi.org/10.1093/intqhc/mzm042

Uchino, B. N. (2006). Social support and health: A review of physiological processes potentially underlying links to disease outcomes. *Journal of Behavioral Medicine*, *29*(4), 377–387.

United Nations, Department of Economics and Social Affairs, & Population Division. (2017). *World population ageing, 2017: Highlights*. New York: United Nations; 2017.

van Oostrom, S. H., Gijsen, R., Stirbu, I., Korevaar, J. C., Schellevis, F. G., Picavet, H. S. J., & Hoeymans, N. (2016). Time Trends in Prevalence of Chronic Diseases and Multimorbidity Not Only due to Aging: Data from General Practices and Health Surveys. *PLOS ONE*, *11*(8), e0160264. https://doi.org/10.1371/journal.pone.0160264

Verbrugghe, M., Verhaeghe, S., Lauwaert, K., Beeckman, D., & Van Hecke, A. (2013). Determinants and associated factors influencing medication adherence and persistence to oral anticancer drugs: A systematic review. *Cancer Treatment Reviews*, *39*(6), 610–621. https://doi.org/10.1016/j.ctrv.2012.12.014

Vrijens, B., De Geest, S., Hughes, D. A., Przemyslaw, K., Demonceau, J., Ruppar, T., … Urquhart, J. (2012). A new taxonomy for describing and defining adherence to medications. *British Journal of Clinical Pharmacology*, *73*(5), 691–705. https://doi.org/10.1111/j.1365-2125.2012.04167.x

Weiss, R. (1974). The provisions of social relationships. In Z. Rubin (Ed.), *Doing unto Others: Joining, Molding, Comforming, Helping, Loving* (pp. 17-26). Englewood Cliffs, NJ: Prentice-Hall.

Welch, G., Balder, A., & Zagarins, S. (2015). Telehealth program for type 2 diabetes: Usability, satisfaction, and clinical usefulness in an urban community health center. *Telemedicine and E-Health*, *21*(5), 395–403. https://doi.org/10.1089/tmj.2014.0069

Williams, A. B., Amico, K. R., Bova, C., & Womack, J. A. (2013). A proposal for quality standards for measuring medication adherence in research. *AIDS and Behavior*, *17*(1), 284–297. https://doi.org/10.1007/s10461-012-0172-7

Wu, S. Y., & Green, A. (2000). *Projection of chronic illness prevalence and cost inflation.* Santa Monica, CA: RAND Health.

Wulff-Burchfield, E. M., Jagasia, M., & Savani, B. N. (2013). Long-term follow-up of informal caregivers after allo-SCT: A systematic review. *Bone Marrow Transplantation*, *48*(4), 469–473. https://doi.org/10.1038/bmt.2012.123

Zarani, F., Besharat, M. A., Sadeghian, S., & Sarami, G. (2010). The effectiveness of the Information-Motivation-Behavioral Skills model in promoting adherence in CABG patients. *Journal of Health Psychology*, *15*(6), 828–837. https://doi.org/10.1177/1359105309357092

Zullig, L. L., Stechuchak, K. M., Goldstein, K. M., Olsen, M. K., McCant, F. M., Danus, S., … Bosworth, H. B. (2015). Patient-reported medication adherence barriers among patients with cardiovascular risk factors. *Journal of Managed Care & Specialty Pharmacy*, *21*(6), 479–485. https://doi.org/10.18553/jmcp.2015.21.6.479

Appendix A

Qualitative Interview Guide

Multi-Method Study of Cancer Patients' Medication Adherence
After Allogeneic HSCT
Formative Research - In-Depth Interviews

Interviewer Note:
The goal of this interview is to get a description of the participants' overall medication adherence behaviors, with a focus on obtaining (1) specific information on situational cues related to adherence, (2) daily preparatory action, facilitator use and opportune situations, and (3) barriers and barrier management strategies employed. The interview also aims to elicit information on existing adherence strategies (i.e., specific plans for achieving adherence and anticipating barriers to it). The key is to identify strategies already employed and to explore the feasibility of using new adherence strategies. Careful attention should be paid to obtaining information on both structural and daily (i.e., fluctuating) barriers and facilitators, as well as relationships between the two.

Preparation:
Study coordinator schedules interview with patient at patient's convenience and hands out or emails interview material to patient (List of commonly prescribed medications for allogeneic HSCT patients).

Script:
Thank you for your time and for agreeing to participate in this project. We are interviewing allogeneic HSCT patients to learn about their experiences taking medications after transplant. Your participation is very important to us.

During the interview, my role is to learn about you and your experiences, feelings and behaviors related to taking your medications. There will be plenty of opportunity for you to describe them in your own words. To better understand you, I may ask for more details and fuller descriptions about the things you say. The focus of the interview will be on day-to-day barriers and facilitators to taking medication that you may experience.

If you wish not to answer a question, simply say so and we'll move on. If you wish to end the interview, let me know and we'll do so immediately. This will not affect your receiving the incentive we offered to you. If you need rest for a little bit, please let me know and we can take a break.

Everything you tell me will be completely confidential and will not be shared with anyone else outside the research team, including your healthcare providers. Your name will not

be used when anyone writes or speaks about the findings of the project and this interview. I may take some written notes as we talk in order for me to remember questions I want to ask you later. I will record the interview so that we can analyze later what was said. Do I have your permission to record this interview?
Do you have any questions before we begin?

PART 1: Background Information
1. Please tell me a little bit about yourself.
Probes:
a. Where are you from? Where do you live? How long have you lived in [New York City]?
b. How long have you been living with cancer?

2. Can you share with me a little bit about how life has changed for you since your transplant?
Probes:
a. What is the best thing and worst thing that has happened since transplant?
b. Has the transplant impacted your daily routines and/or behaviors? How so?
c. Do you ever feel like you have a hard time managing your cancer and the transplant treatment? Can you tell me more about that?

PART 2: Social Motivation and Support
1. Who in your life knows that you are taking medication? (Probe for partners and other family members, friends known in person and online/Facebook friends, religious community, coworkers, roommates, etc.)
a. Are there people in your life who support you taking your medications? Are there people who <u>do not</u> support you taking your medication?
b. Are there people in your life who help to make sure that you take your medication regularly/on time?
c. Are there people in your life who make it difficult for you to make sure that you take your medication regularly/on time?

PART 3: General Information about Medication Routines
1. Please tell me about the medication(s) that you take.
Probes:
a. What medication does your physician currently prescribe? (Interviewer asks participant to look at a list of common medications with a picture, brand name, and substance name on it, so participant can list all)
b. Do you know which of your medications is an antibiotic/immunosuppressant/antifungal/antiviral medication? How did you find this out? (e.g., from provider, participant looked it up, etc.)

2. Please tell me when and where you usually take your on a typical day?
Probes:

a. How many dosages do you take of your medication each day? That is, how often do you take your medication, and how many pills do you have to take each time you take them?
b. Do you have specific times to take your meds? Do you have any specific places in which you normally take them?
c. Are there moments of your day that represent good opportunities to take your medication? Tell me about those moments. What makes them good times to take your medication? How frequently/infrequently do you encounter them on a daily basis?
d. Does the time or process you use for taking your medication change during the week (such as on weekdays compared to the weekend)?
e. Which one(s) of your medications are you supposed to take with food? Which one of your medications should you NOT take with food?
f. Are you taking any other medications, herbal supplements, nonprescription medications, or recreational drugs aside from your medication? When do you take those?
g. Do you take them at the same time that you take your medication?
Do you smoke? Have your smoking habits changed because you are taking medications?

3. How often do you check for signs of infection? How often do you take your temperature?

4. How has your physical activity changed since the transplant? For example, what physical activities such as walking, bike riding, going to the gym, do you do regularly since the transplant?

PART 4: Behavioral Skills: Preparatory Actions/Using Facilitating Tools and Opportune Situations
Now I would like to ask you about things that you may do to help you take your medication when you are supposed to.
1. What do you do to help you take your medications? Do you place them in a visible place at home? Do you carry them with you?
2. What tools do you use to help you take your medicine? (Probe for: reminders on cell phone, pill boxes, websites/online tools, cell phone tools/apps/websites, watches and alarm clocks, computer apps/email systems, etc.)
Probes:
a. What is the (exact) name of the application (if P specified a phone application)?
b. Please describe how you use this tool.
c. How is this tool working for you?
d. How often/when do you use it?
e. Since when have you used this tool?
f. How did you find out about it?
g. Have you tried any other tools or ways to remember to take your medication?
h. What was your experience with those other tools? Why don’t you use them anymore?

3. When and where do you prepare for using these tools? (e.g., set reminders every morning or evening, set alarm clock when I take a nap)

4. What do you do when you face a situation in which taking your medication is a challenge? (May need to probe with examples participant gave in part 3.)
Probes:
a. What do you do when you forget to take a pill? What about when you forget to take a pill 1-2 hours within the timeframe you were supposed to?
b. How do you get back on track when you miss one or more dosages?

5. Has your day-to-day life had to change because you are taking medication? How so?
Probe:
a. What day-to-day changes have you had to make in order to facilitate taking your medication?

6. How have your eating and drinking habits changed since the transplant?
Probe:
a. What changes have you made in order to facilitate eating and drinking during the day?
b. What do you eat on a typical day – for breakfast? For lunch? For dinner? As snack? How often and how much do you eat?
c. What do you drink on a typical day? Do you like some beverages better than others (for example tap water vs carbonated drinks?) How often and how much do you drink? Do you drink alcohol? How often and how much? What types of alcohol?
d. Does feeling ill, such as nauseated, ever make it difficult to eat and/or drink during the day? How so? What have you done about it?

PART 5: Barriers to Medication Adherence and Barrier Management

1. How easy or difficult is it for you to take your medication when you are supposed to?
Probes:
a. How often do you miss a dose of your medications? (Daily, several times per week, once per week, once per month?)
b. Are there reasons that you can think of why you might miss taking a dose of your medication? Tell me more about that.
c. Tell me about that last time that you forgot to take a dose of your medication. What happened that time?
d. Tell me about day-to-day issues that you may encounter that can affect whether or not you take your medication (on time or at all). Are there certain times in your life when these issues arise more than other times?

2. How have weight changes affected you taking your medication?
Probe:
a. Have changes in appetite made it difficult to take your medications when you are supposed to?
b. Have you lost or gained weight since the transplant? How do you feel about this loss or gain of weight?

3. I am going to ask you about specific situations you may have experienced in which taking your medication (**on time or at all**) was difficult or challenging. Please tell me if you have experienced this situation and if so, what you did about it.

Probes:

a. Do you sometimes simply forget to take your medication? Why? (Busy with other things, sleeping through the dose)? What do you do about it?

b. Do you sometimes remember that you should take your medication but you cannot do it because you do not have the pills at hand (e.g., left the pills at home)? What do you do about it?

c. Do you sometimes forget to get your refill in time? (How do you get your refills?) What do you do about it?

d. Do you have difficulty taking your medication on the weekends? Why do you think this is so? What do you do about it?

e. Do you have difficulty taking your medication when you or close others are traveling? Why do you think this is so? What do you do about it?

f. Have you had difficulties when your daily routines changed (e.g., seasonal change, partner working longer hours)? What do you do about it?

g. Are there certain moods or emotions that you experience that make it harder for you to take your medication? (E.g., do you sometimes forget to take your meds when you are sad or down?) Can you tell me more about this? Why/how do you think this happens? What do you do about it?

h. Do you have difficulty taking your medication when you are with friends? Why is this so? What do you do about it?

i. Do you have difficulty taking your medication when you are with people that do not know about your transplant? Can you tell me more about that? What do you do about it?

j. Is it hard for you to take your medication when you meet someone new or are out with people who don't know you? What do you do about it?

k. Do other medications make it difficult to take your medication? What medications? How so? What do you do about it?

l. Do you have difficulty taking your medication when you are drinking alcohol? How so? How often does this happen? What do you do about it?

m. Do side effects impact taking your medication? Which ones? What do you do about it?

n. Does sickness impact you taking your medication? How so? What do you do about it?

o. Have you had trouble swallowing your medication and how does it taste? What do you do about it?

p. Have you ever taking a break from your medication on purpose (e.g., to avoid side effects)? What do you do about it?

q. Does a lack of money (i.e., end of a paycheck, periods of unemployment, a delayed government assistance check, lack of help from friends and family, etc.) ever make it difficult for you to take your medication? Can you tell me about this? What do you do about it?

r. Does facing a hardship in your life make it difficult for you to take your medication? Why or why not? What do you do about it?

4. Are there any other situations or times in which taking your medication is difficult or challenging for you that I haven't described? Please tell me about those situations/times and what you did.

a. Which of the situations that affect you taking your medication are the ones that you experience most of the time?

b. Which situations in which taking your medication is difficult do you experience least?

PART 6: Attitudes toward Healthcare Providers and Medications

Now I would like to ask you some question about your experiences receiving health care.
1. Tell me about your health care provider(s)?
Probes:
a. Who is the person who primarily treats you?
b. What is your relationship like with your care provider? Do you think your relationship with your care provider makes it easier or harder to take your medication? How so?
c. Do you feel like your care provider understands your needs? [for minority patients: What about as a Black, Latino/Latina, Asian man/woman?]?

2. What are your feelings about where your cancer came from?
Probes:
a. Do you feel that cancer is random or were there things that made you more vulnerable (lifestyle/smoking, stress)?
b. Do you feel that the government and scientists are doing all that they can to treat people living with cancer? Tell me more about that.

3. Do you know how your medications work to keep you recovering?
Probes:
a. Do you believe that the medications are helpful/effective for your recovery?
b. How well do you think the medications work in helping people after transplant? What about in helping you specifically?
c. Do you think medications might harm people after transplant?
d. How important is it for you personally to continue to take your medications on a regular basis, without missing doses? Why?
e. How important do you think it is for transplant patients in general to take their medications on a regular basis, without missing doses? Why?

4. How does taking your medications make you feel?
Probes:
a. Does it remind you of your disease status?
b. Do you feel healthier when take your medication, as you might after eating a piece of fruit or taking a vitamin?
c. Does the medications you take (or have taken) give you any side effects? Tell me more about this. What are the side effects? Does/has having side effects make you not want to take your medication?

PART 7: Electronic Pillbox

I would like to know a little more about how you use the electronic pillbox.

1. How would you describe the experience of using the electronic pillbox on a daily basis?
Probe:

a. Was it a good experience? Bad experience? Why?
b. Was it easy or hard to use the electronic pillbox?
c. What do you like about the pillbox? What do you not like about the pillbox?)

2. Did you have any problems using the electronic pillbox?
Probe:
a. How so? What did you do about the problems you encountered?
b. Were you able to keep it plugged in all the time? Did you have to use an extension cord?
c. Were there any other problems, for example, when you were traveling or leaving the home during the day?

3. Where do you typically keep the pillbox?

4. When do you typically refill the pillbox?

5. Does anyone help you with the pillbox? Who, specifically, helps you use the pillbox? How do they help you?
Probe:
a. Do they help you refill the box? Do they help you get medications out of the box?

6. Does anyone make it difficult for you to use the box? How so? What do you do about this?

7. Would you find it helpful to have reminders such as text message alerts or alarms on the pillbox that would prompt you to take your medication?

8. Is there anything else related to the pillbox that you would like to tell me?

Thank you for your participation and for sharing your experiences with me today. We are at the conclusion of the interview, is there anything else related to your experiences taking your medications that you would like to add?

Appendix B

Interview Coding Guide

Code	Definition	General guidelines and potential questions that target the code (but responses can be in elsewhere in the transcript)	Examples
General optimism	Accepting the health condition and patient role with optimism, perception of the situation with a positive attitude and hope.	Questions along these lines: A lot of them are in PART 1: *What is the **best** thing and worst thing that has happened since transplant? *Has the transplant impacted your daily routines and/or behaviors? How so? (Note: Might be in other sections in the interview).	"[I take] less than when I got discharged. It is going down, there is light at the end of the tunnel." (P07, age 56, female). "So psychologically I am doing fairly well. (…) having a positive attitude was a big help. My family is very supportive. (…) So all in all I have no complaints. I'm happy to be alive (…) I keep everything in perspective." (P28, age 59, male).

Concerns, worries, fears	Worries and fears about the situation, life and health condition, lack of positive attitude, frustration over the situation, and self-perceptions of limitations and inabilities after transplant.	Questions along these lines: A lot of them are in PART 1: *What is the best thing and **worst** thing that has happened since transplant? *Feeling depressed or down? *Possible harm of medications? *Can you share with me a little bit about how life has changed for you since your transplant? (Note: Multiple codes might apply/ overlap with Depression, side effects).	"I had to get used to everything again, like eating. Also, it impacted my mental status. (…) I didn't recognize my son, and I didn't know where he lived. I didn't know what was going on, and it was scary. It's getting better now." (P09, age 49, female).

Information-Adequate knowledge about medications	Patient having adequate and accurate information about medication; when and how to take them, adequate level of meds (how much), functions and potential drug interactions and side effects (including information provided from the list of medications). Usually asked in Part 3: general information about medication routines, Question 1 a & b.	**PART 3: General Information about Medication Routines** 1. Please tell me about the medication(s) that you take. a. What medication does your physician currently prescribe? (Interviewer asks participant to look at a list of common medications with a picture, brand name, and substance name on it, so participant can list all) b. Do you know which of your medications is an antibiotic/immunosuppressant/antifungal/antiviral medication? How did you find this out? (e.g., from provider, participant looked it up, etc.) 2. c. How many dosages do you take of your medication each day? That is, how often do you take your medication, and how many pills do you have to take each time you take them? d. Do you have specific times to take your meds? g. Which one(s) of your medications are you supposed to take with food? Which one of your medications should you NOT take with food? (Note: Any quotes on receiving information from health care providers or close others (informational support) should go into support section. The difference here is between possessing (adequate information) and receiving it (informational support)).	"Around 7 o'clock in the morning I take Mepron and the Fenadine (to treat fever symptoms) Phenadone syrup for respiratory disease, allergic conditions, arthritis) I think it's called. Then at around 8 o'clock I would take the um… magnesium tablet, the Prograf and the Acyclovir. At 10 o'clock I'll take the Voriconazole. At 2 o'clock I'll take the magnesium tablet. At 6 o'clock I will take the Famotidine. 8 o'clock I would take the Prograf, the Tacrolimus, the Acyclovir and another magnesium tablet. And 10 o'clock I'd take the Voriconazole." (P28, age 59, male). "Hopefully I can remember. Protozol that's the immune-suppressant, and I'm taking Dapsone, Acyclovir, I'm also taking magnesium it's a supplement. (…) I know Prograf that is so my body does not reject the bone marrow that I received from my little sister. And acyclovir that on is an anti-virus. (…) And Dapsone, I'm not sure exactly but I think Dapsone is um, is to protect my lungs from pneumonia." (P22, age 35, female).

Information-Inadequate knowledge about medications	Patient not knowing or partially knowing (knowledge with some ambiguity and unsureness) the information about his/her prescribed medications. Having inaccurate/incorrect or lacking information about medication / misinformed. Usually asked in Part 3: general information about medication routines, Question 1 a & b.	Same questions as INF-Adequate (Note: Same questions as INF-Adequate (but the patient response would be the opposite of INF-Adequate)).	I: “Do all your medications make it difficult to take your prescribed medications?” P: “Probably yes but I don’t know. I don’t know specific timing or specific medicine. So I cannot give you definite answer.” (P17, age 50, male)

Information- Flawed heuristics and implicit theories	Patient developed rules which permit automatic and cognitively effortless (that are often incorrect) decisions about whether or not to engage in a health behavior.	No specific question that targets this category	"I took [a] break from [the] medications on purpose because I was feeling better." (P40, age 57, male). "too much medications would build immunity and will not be as effective" (P20, age 50, male).
Personal Motivation - Taking responsibilities, importance of meds	Patients perceive the importance of taking medications, prioritize/demonstrate responsibility in taking them. Sense of commitment.	Questions along these lines: *How important is it for you personally to continue to take your medications on a regular basis, without missing doses? Why? *How important do you think it is for transplant patients in general to take their medications on a regular basis, without missing doses? Why? *Do side effects impact taking your medication? Which ones? What do you do about it? *Does sickness impact you taking your medication? How so? What do you do about it? (Responses with indication of perseverance, still taking the medications regardless the situation, taking medications is a priority, etc. would count as being responsible and prioritizing meds)	"I have to take all the medication every day, weekend and weekday does not matter. (…) I took it every time, no matter what. Taking medications is very important to get better." (P11, age 71, female). "Sometimes believe it or not I don't want to take my medications. (…) I take them anyway, [laughs] I have no choice." (P43, age 51, male).

Personal Motivation - Positive attitudes, beliefs about meds and health outcomes	Favorable beliefs and attitudes about taking medications, that it will do good to treat.	**PART 6: Attitudes toward Health Care Providers and Medications** Questions along these lines: 3. Do you know how your medications work to keep you recovering? a. Do you believe that the medications are helpful/effective for your recovery? b. How well do you think the medications work in helping people after transplant? What about in helping you specifically? c. Do you think medications might harm people after transplant? 4. How does taking your medications make you feel? b. Do you feel healthier when take your medication, as you might after eating a piece of fruit or taking a vitamin? (Did you feel or do you feel more healthy? When you took or when you keep making your medications? Do you believe that you progress each time you take your medications?)	“The best thing that has happened is that I did not have that many side effects from the medications itself, but Some of them were not exactly very tasty and the repetition of taking all the medication all the time, but it’s a minor thing compared to all the benefits of the pills. I’m around today because I’ve been doing this!” (P13, age 67, male).

Personal Motivation - Doubts about meds and health outcomes	Though patients do not have negative attitudes/beliefs about medications per se, they have doubts or ambivalent opinions. This is usually due to side effects and/or no progress in health outcomes.	**PART 6: Attitudes toward Health Care Providers and Medications** Questions along these lines, but the response would be the opposite: 3. Do you know how your medications work to keep you recovering? a. Do you believe that the medications are helpful/effective for your recovery? b. How well do you think the medications work in helping people after transplant? What about in helping you specifically? c. Do you think medications might harm people after transplant? 4. How does taking your medications make you feel? b. Do you feel healthier when taking your medication, as you might after eating a piece of fruit or taking a vitamin? (Did you feel or do you feel more healthy? When you took or when you keep making your medications? Do you believe that you progress each time you take your medications?) (Note: Responses would be opposite from Per Mot-Positive attitudes and beliefs about meds and health outcomes).	“I hope that the medications are helpful and effective for my recovery. The medication can be helpful in on way and hurtful in another way. (…) But I think they are doing good by me.” (P09, age 49, female).

Social Motivation - Healthcare provider-support: **1. practical,** **2. emotional,** **3. informational**	Health care providers attending to patients with medical needs (tangible, informational, and emotional support).	Healthcare provider related questions are the followings: 1. Tell me about your health care provider(s)? Probes: a. Who is the person who primarily treats you? b. What is your relationship like with your care provider? Do you think your relationship with your care provider makes it easier or harder to take your medication? How so? c. Do you feel like your care provider understands your needs? [for minority patients: What about as a Black, Latino/Latina, Asian man/woman?]?	"He is a very good professional. (…) My doctor understood my needs and the communication was clear and important." (P23, age 59, female) "It was teams. Plural. They all helped. I couldn't have asked for better care." (P25, age 66, male).

Social Motivation - Close others-General support: 1. practical, 2. emotional, 3. informational	Family members or friends provide tangible ("doing something physical/ beyond emotional level" (Cutrona)) support related to medication adherence and daily tasks, such as cooking, completing house chores, shopping for groceries, transportation, and financial support. Also includes family members of friends provide words of encouragement through verbal conversations or written communication.	Part 2: Social Motivation and Support: 1. Who in your life knows that you are taking medication? (Probe for partners and other family members, friends known in person and online/Facebook friends, religious community, coworkers, roommates, etc.) a. Are there people in your life who support you taking your medications? Are there people who do not support you taking your medication? b. Are there people in your life who help to make sure that you take your medication regularly/on time?	"My wife does bulk of it (reminding to take medications). (…) She'll ask me if I have and she's the one that makes sure I'm taking my medicine." (P26, age 50, male). "My partner did the cooking, he works from home, he did all of that." (P16, age 46, male)

Social Motivation - Ambiguity and unpleasant support from close others	Patient feeling confused or ambiguous about the received support from close others (lack of or insufficient support)	Part 2: Social Motivation and Support: 1. c. Are there people in your life who make it difficult for you to make sure that you take your medication regularly/on time?	“It depends, they watch me. I’m under observation.” (P17, age 50, male). “Keeping it secret: if I told them they were going to worry. They would want me to take medication they know about. Take this, take that. I not wanted to deal with all that advice. Listen, I have my doctors. You guys, just pray, don’t try to be my doctors. This remedy comes from the family. They send me home remedies. Well, they didn’t listen. Their kindness shows.” (P19, age 49, male)
Social Motivation - Lack of Health care providers' support	Patient complains about the health care providers' lack of clarity in communication and/or failure to deliver correct information	In Part 6: Attitudes toward Health Care Providers and Medications & some questions throughout the interview regarding medications	“What I discovered is they don’t do enough here telling people how to work out.” (P01, age 66, male). “First time, no, nurses did discharge from hospital with filled box, the nurse did not show, we had to figure it out ourselves.” (P11, age 71, female).

Behavioral Skills-Fixed place	Taking and organizing pills at a specific place	Part 3: General Information about Medication Routines: 2. Please tell me when and where you usually take your medications on a typical day? c. How many dosages do you take of your medication each day? That is, how often do you take your medication, and how many pills do you have to take each time you take them? d. second part of the question: Do you have any specific places in which you normally take them? Part 4: Behavioral Skills: Preparatory Actions/Using Facilitating Tools and Opportune Situations: 1. What do you do to help you take your medications? Do you place them in a visible place at home?	"Pillbox is in the kitchen (…) It is where I make coffee in the morning. (…) I (…) go to kitchen, take the first pill, then make coffee." (P16, age 46, male). "I typically keep the pillbox in the living room area" (P39, age 68, male). "I have my medications in a visible place, on top of my bed." (P17, age 50, male).

Behavioral Skills-Fixed schedule	Incorporating making refills and taking medications to daily life schedule. Having a specific time or time windows to follow the med regimens and manage medications	Part 3: General Information about Medication Routines: 2. Please tell me when and where you usually take your medications on a typical day? d. first part of the question: **Do you have specific times to take your meds?** Also includes questions like: are there moments of your day that represent good opportunities to take your medication? And how frequently or how infrequently do you encounter these good opportunities on a daily baseis Does the time or process you use for taking your medication change during the week? Do you have difficulty taking your medication on the weekends? Why do you think this is so? What do you do about it?	"8 o'clock, 10, 12 PM, 2, 8, 10 whatever the time on the sheet says." (P08, age 53, male). "8AM: Ursodiol and Magnesium. 2:00PM: Ursodiol and Magnesium. I take these two 3 times a day. After lunch – Mepron. If I cannot take it during the lunch hour I sometimes take it after dinner. 6-6:30 is two tablets. (Synthroid and Veracru). 7-7:30: Cryozac. 8:00: Acrovia, Ursodiol, Magnesium. 11PM: Levaquin. Before bed: another prylozac and Colase. Sometimes, once or twice is Quodimethol." (P11, age 71, female).
Barrier-Inconsistent schedule	Having no specific schedule to take medications or make refills (also includes when adherence is dependent on how patients were feeling on that day/ at the moment)	Same questions as Skills-Fixed schedule but the response would be the opposite (Note: Sometimes responses include INF-flawed heuristics and implicit theories).	"On a typical day I go by how I feel. Sometimes in the morning I have no energy. I go according to how I feel, I try not to abuse it by taking them all together, but sometimes I take them all together. it's not uniform and according to schedule, but by night I take everything." (P17, age 50, male). "I'm actually having some trouble, based on my schedule. I just can't have a consistency of taking my pills daily on a set time when I'm suppose to take it." (P21, age 29, male).

Behavioral Skills-Prompts, tools & reminders	Patients using different kinds of prompts, tools and reminders to facilitate their medication adherence, including alarms on phone, watch/clock, pillbox, ziplock bags, that allow them to take medications on time. Also, events during the day remind patients to take their medications, such as meal times.	Part 4: Behavioral Skills: Preparatory Actions/Using Facilitating Tools and Opportune Situations: 2. What tools do you use to help you take your medicine? (Probe for: reminders on cell phone, pill boxes, ziplock bags, websites/online tools, cell phone tools/apps/websites, watches and alarm clocks, computer apps/email systems, etc.)	"Well, I can manage on my own, I have the box sitting on the kitchen table so it is right there that I don't forget about it. So I've been doing this so long now, it is just automatic." (P31, age 44, female) "Yeah, that's like my little schedule so it kind of goes with eating the breakfast. Yeah, the one that I take after that is the breakfast. But definitely, after I finish eating that will remind me that I have to take the rest of the medication." (P22, age 35, female).

Behavioral Skills- Use mental note or memory, no prompts or reminders	Patient relying on their memory, making mental notes and just knowing when to take medications. Not using any kinds of reminders.	Same questions/ sections as Skills- Prompts, tools & reminders but patient responses would be using memory/ making mental notes, and/or not using any prompts/ tools/ reminders.	"I don't use any tools." (P09, age 49, female). "I don't. Just memory. It feels less important or serious now so it's not at the top of my mind. Before I was like I need to take these drugs today. I was fearful because I thought if I don't take this, I'll have a reaction. But now it doesn't feel that way. I've read up on what it does- it's good preventative bacteria but it never felt all that serious." (P10 age 49, male).

Behavioral Skills-Effectively utilizing healthcare resources	Patient effectively utilizing the healthcare resources, including pharmacy and hospital. Health care providers can help. This includes refilling medications ahead of time by effectively using the hospital and pharmacy system (pick up or delivery). Individuals have to call in to receive refill on time.	Questions like: *Do you sometimes forget to get your refill in time? (How do you get your refills?) What do you do about it? OR *Are there people in your life who support you taking your medications? Are there people who do not support you taking your medication? Are there people in your life who help to make sure that you take your medication regularly/on time?	“I get my refills through the mail. It (refill) is not automatic. I phone it in.” (P026, age 50, male). However, there were cases where the pharmacist called to make sure. “Thanks due to God, pharmacist has called, they call and remind me.” (P019, age 46, male)

Barrier- Poor navigation of or problem with healthcare resources	Poor navigation/ utilization of the healthcare resources, causing patients to miss doses, including delivery problems, insurance problems.	Questions along these lines: *Do you sometimes want to take your medication but cannot because you don't have the pills at hand? *Do you sometimes forget to get your refill on time? *How often do you miss a dose of your medications? (Daily, several times per week, once per week, once per month?) *Are there reasons that you can think of why you might miss taking a dose of your medication? Tell me more about that. *Which of the situations that affect you taking your medication are the ones that you experience most of the time?	"Well the pharmacy…gave me a certain number of pills because of insurance. So they give you just enough…but it's not really like you know, extra. So that's the situation." (P20, age 50, male) "Yeah but um that was acyclovir and dapsone [that I missed a couple of times]. Usually, the pharmacy, they remember. I guess they got busy. They will actually refill the medication and call me. I think I got used to that. Yeah, they refill and they will call me and even if there was nobody home, they do leave a message. But this time maybe they got busy, they didn't call me, so I was just going through the medication, both dapsone and acyclovir one time. Just one time." (P22, age 35, female). "The pharmacy claimed that they were going to deliver it, and then that the truck didn't finish his rounds, and the next day the truck broke down (…) and instead of Tuesday I got it on Saturday. (…) That was the worst one that I skipped really a lot." (P13, age 67, male).

Behavioral Skills- Diet	Any mentioning about what they eat and drink, including food restrictions. Low microbial diet. How they dealt with lack of appetite.	Questions from PART 4: Behavioral Skills: Preparatory Actions/Using Facilitating Tools and Opportune Situations: *How have your eating and drinking habits changed since the transplant? a. What changes have you made in order to facilitate eating and drinking during the day? b. What do you eat on a typical day – for breakfast? For lunch? For dinner? As snack? How often and how much do you eat? c. What do you drink on a typical day? Do you like some beverages better than others (for example tap water vs carbonated drinks?) How often and how much do you drink? Do you drink alcohol? How often and how much? What types of alcohol? d. Does feeling ill, such as nauseated, ever make it difficult to eat and/or drink during the day? How so? What have you done about it? *How is your appetite?	"I followed low microbial diet, no immunogenic food (…) I followed what they recommended, 95% of meals were home cooked. (…) We went to restaurant that we knew (…) My partner did the cooking, he works from home, he did all of that (…) [the food was] pretty healthy and tasty." (P16, age 46, male).

Barrier-Lack of appetite	Having no desire to eat, trouble with smelling and tasting the food. Feels even frustration about eating and drinking due to lack of appetite and restircted diet.	Questions from PART 5: Barriers to Medication Adherence and Barrier Management: How have weight changes affected you taking your medication? a. Have changes in appetite made it difficult to take your medications when you are supposed to? b. Have you lost or gained weight since the transplant? How do you feel about this loss or gain of weight?	"The two main problems I have are the energy (fatigue) and no appetite, eating issues, I have to force myself to eat." (P01, age 66, male). "I drink a lot of water during the day. As much as I can, which is hard. (…) I'm really not that hungry. A lot of times I eat even when I don't feel like it because I know I have to. And a lot of things I'm not really happy with. I'd rather have something else but I can't." (P39, age 68, male).
Behavioral Skills-Having pills when going out, traveling	Code whether patients missed doses because they were traveling or were out and how they dealt with not missing a dose when away from home, such as bringing and keeping pills with them.	PART 5: Barriers to Medication Adherence and Barrier Management: I am going to ask you about specific situations you may have experienced in which taking your medication (on time or at all) was difficult or challenging. Please tell me if you have experienced this situation and if so, what you did about it. *Do you have difficulty taking your medication when you or close others <u>are traveling</u>? Why do you think this is so? What do you do about it?	"If I go to a friend's (…) then I make sure I take the medication with me. Maybe occurs once or twice a month." (P13, age 67, male).

Barrier- Not having pills at hand	Patient missing a dose because they did not have pills at hand when they are going out.	Questions like: PART 5: Barriers to Medication Adherence and Barrier Management: I am going to ask you about specific situations you may have experienced in which taking your medication (on time or at all) was difficult or challenging. Please tell me if you have experienced this situation and if so, what you did about it. *How often do you miss a dose of your medications? (Daily, several times per week, once per week, once per month?) *Do you sometimes want to take your medication but cannot because you don't have the pills at hand?	"Once or twice a month. Because that would be because I got stuck in traffic or I ended up spending the night some place and I didn't have my medication with me." (P14, age 32, male)

Behavioral Skills-Managing missed doses	Strategies to manage late doses. Includes: 1. Skipping missed doses and getting back on track with the following doses. 2. Taking the missed dose even a few hours later (1-2 hours).	Questions from PART 4: Behavioral Skills: Preparatory Actions/Using Facilitating Tools and Opportune Situations: What do you do when you face a situation in which taking your medication is a challenge? (May need to probe with examples participant gave in part 3.) a. What do you do when you forget to take a pill? What about when you forget to take a pill 1-2 hours within the timeframe you were supposed to? b. How do you get back on track when you miss one or more dosages?	“(when I miss a dose) I skipped it and went on to the next.” (P26, age 50, male). “(If I forget to take a pill) I take it the next day. I do not take it late. I wait till next day.” (P09, age 49, female). “[I]t depends when I forget, if it’s an hour later, I take it. If its supposed to be taken at 12 in the afternoon and it’s now 9 at night, or its something once a day and I’m not taking any other medications I may take it, or skip it for the day. But for the most part, I haven’t skipped too many. I do recall once or twice that I did skip a pill.” (P13, age 67, male). “Sometimes I forgot, then I take the pills an hour or two later than the scheduled time. When I am too busy then I forgot, mostly at work.” (P08, age 53, male).

Behavioral Skills-Reasons to miss a dose	Missing a dose due to forgetting, busyness, sleeping (falling asleep and slept through a dose), being around with people, change in routines.	PART 5: Barriers to Medication Adherence and Barrier Management: I am going to ask you about specific situations you may have experienced in which taking your medication (on time or at all) was difficult or challenging. Please tell me if you have experienced this situation and if so, what you did about it. *Do you sometimes forget to take your medication on time?	"I forgot. Maybe stick-ems all over the place. Last time you forgot, last week. I took my night pills, morning pills were still there. Once it happens I become more cognizant." (P01, age 66, male) "I: Do you sometimes remember to take your medication, but can't do so because you do not have any of them? P: Well, yeah, of course it [pills] wasn't with me, I'll remember sometimes if I'm at—oh, I forgot it, that's…" (P38, age 64, female) "It's been a few times when I was uh late on getting refills. Not late but calling in. I always get them on time." (P39, age 68, male). "When I forgot to take one pill, it was prozac. That day I went to bed a little earlier. I was going to take a rest but I slept through the night. When I woke up in the morning I found that I missed one." (P11, age 71, female). "More than often it would be the sleeping over the time that you are supposed to be taken." (P14, age 32, male).

Behavioral Skills-Dealing with side effects	Different ways patients handled side effects. Includes: 1. Take another medication that will relieve the symptoms of sickness and side effects. 2. Eat something to relieve the symptoms of side effects. 3. Stop taking the medication that made patient feel sick. 4. Space out the dosing hours because of side effects/ feeling sick. 5.	PART 4: Does feeling ill, such as nauseated, ever make it difficult to eat and/or drink during the day? How so? What have you done about it? PART 5: Barriers to Medication Adherence and Barrier Management: *Do side effects impact taking your medication? Which ones? What do you do about it? *Does sickness impact you taking your medication? How so? What do you do about it?	"I stop taking the medication (if I feel I am having side effects) and wait for the result by waiting. I'm being patient." (P17, age 50, male).

Barrier- Side effects, sickness	Any mentioning about side effects, sickness. Missing a dose due to symptoms of side effects, physical pain and sickness. Also include having no side effects.	PART 4: Does feeling ill, such as nauseated, ever make it difficult to eat and/or drink during the day? How so? What have you done about it? PART 5: Barriers to Medication Adherence and Barrier Management: *Do <u>side effects</u> impact taking your medication? Which ones? What do you do about it? *Does sickness impact you taking your medication? How so? What do you do about it?	I: “The medicine you take (or have taken) gives any side effects? Tell me more about this. What are the side effects? The side effects have made him not want to take your medication?” P: “No pills cause me nausea or dizziness or any of these hoes. No side effects.” (P12, age 53, female). I: “Does the medications you take (or have taken) give you any side effects? Tell me more about this. What are the side effects? Does/has having side effects make you not want to take your medication?” P: “Yeah, there’s one fungus medication that I have to take at a different time from the Prograf. That’s the only one.” (P07, age 56, female).

Behavioral Skills-Dealing with difficult meds to swallow	Different ways patients handled to swallow pills that are difficult to swallow, including 1. taking medications with sweet drinks or with food to reduce the taste or to quickly swallow; 2. Holding breath as they swallowed pills; 3. Closing eyes; 4. Praying.	PART 5: Barriers to Medication Adherence and Barrier Management: Please tell me if you have experienced this situation and if so, what you did about it. Have you had trouble swallowing your medication and how does it taste? What do you do about it? (Note: Can combine different strategies (more than one) to deal with difficult medications).	“Everything in the morning, with Gatorade Sub-zero (…) I can drink down 20 oz., it goes down so smooth (…) I cannot do that with a glass of water.” (P01, age 66, male). “They taste terrible, you have to drink more water and rinse it out.” (P07, age 56, female). “Sweet things, soda, Gatorade, milk help, put the pill all the way (…) When I tried with water, big pill when you cut at the end of the tongue it melt, hard to swallow. I tried with sweet drink it is working, keep trying with milk. (…) I don’t know exactly if (…) the medication or the empty stomach that makes the nausea, I cannot figure it out.” (P011, age 71, female). “I hold my breath and then take it (medicine).” (P020, age 50, male). “I closed my eyes and drink it and drink a lot of water.” (P022, age 35, female). “I always pray, like the Signa, so far it went smoothly. I always take the medicine with water, swallow it and pray, that is all I am doing.” (P029, age 63, female).

Barrier- Size and taste of the med	Having trouble with taking meds due to the size and taste of medications	PART 5: Barriers to Medication Adherence and Barrier Management: Please tell me if you have experienced this situation and if so, what you did about it. Have you had trouble swallowing your medication and how does it taste? What do you do about it?	They taste terrible, you have to drink more water and rinse it out. (P07, age 56, female)
Pillbox- Benefits	perceived benefits of using pillbox	Section: PART 7: Electronic Pillbox	"You could take the container out. [It is] easy to take pills out." (P01, age 66, male).
Pillbox- Challenges	perceived challenges and difficulties of using pillbox	Section: PART 7: Electronic Pillbox	"I had 2 liquids, you can't put it in the box, but you have to be aware that you have to take it." (P13, age 67, male).

Appendix C

Consolidated Criteria for Reporting Qualitative Research

(COREQ) Checklist

1. Interviewer/ facilitator: Which author/s conducted the interview or focus group?
The authors, including YS, SC and the principal investigator (GS), and six other research assistants in the team conducted the interviews.

2. Credentials: What were the researcher's credentials? E.g. PhD, MD
The principal investigator holds a Ph.D. in psychology. Two authors (YS and SC) and six other research assistants were all female with either a bachelor’s or master’s degree in social sciences, public health or health sciences at the time of the study.

3. Occupation: What was their occupation at the time of the study?
The principal investigator was working as a research scientist at Columbia University, and the other members in the research team were either graduate students or recent graduates preparing for graduate schools.

4. Gender: Was the researcher male or female?
The interviewers were all female.

5. Experience and training: What experience or training did the researcher have?
The principal investigator is an expert in health psychology and has conducted several studies of frequent health behaviors with people living with and without chronic conditions. Interviewers were trained by the principal investigator with the interview guide and using role-play within the research team. Then interviewers shadowed interviews prior to conducting interviews with participants in the study.

6. Relationship established: Was a relationship established prior to study commencement?
There was no relationship between interviewers and participants prior to the study. Rather, relationships were built over the course of the study, beginning with recruitment and consenting by clinical staff, continuing with handing out the pillbox before or shortly after transplant in a research meeting before discharge home, and weekly contact after hospital discharge between research team and participants. By the time the interviews were conducted at 3 and 6 months after the first hospital discharge, participants had gotten to know the research team members well. Some participants sent us pictures of their table full of medications and also contacted the research team on their own via email and study phone with questions and for study logistics.

7. Participant knowledge of the interviewer: What did the participants know about the researchers?

Participants knew that all research team members were staff or students at Columbia University or Mount Sinai. Participants were aware that the research team included Spanish and also Mandarin speakers. Participants were also made aware that everything they shared with research team members would be kept confidential and would not affect their treatment.

8. Interviewer characteristics: What characteristics were reported about the interviewer/ facilitator?
The interviewers were an ethnically diverse group, with a nuanced understanding of different cultures. They were also fully aware of and trained in the ethics of conducting research, including maintaining strict confidentiality. Throughout the study, the interviewers tried not to be biased or look for specific results. Usually two interviewers conducted the interviews, with one interviewer mainly conducting the interview and the other audio recording and taking notes and helping to add probing questions and to keep the flow of the interview.

9. Methodological orientation and theory: What methodological orientation was stated to underpin the study? (e.g. grounded theory, discourse analysis, ethnography, phenomenology, content analysis)
Content analysis, more specifically directed content analysis, was utilized (Hsieh & Shannon, 2005).

10. Sampling: How were participants selected?
We used nonprobability sampling and participants were recruited from all patients undergoing alloHCT at a single urban treatment center from 08/15/2012 to 07/15/2014 due to the nature of the specific research objective (multiple medication adherence) and the particular characteristics of the population (leukemia and lymphoma patients after alloHCT).

11. Method of approach: How were participants approached?
Clinical staff members informed patients scheduled for alloHCT of the study, either during pre-transplant outpatient visits prior to admission for transplant or shortly after the transplant and obtained informed consent from interested eligible patients.

12. Sample size: How many participants were in the study?
In total, 28 individuals (46.4% female, age: $M = 53.97$) participated. The sample was ethnically diverse, with almost half of the participants coming from a minority background ($n = 13$, 46.4%), (Non-Hispanic White: 53.6%, African American: 7.1%, Asian: 17.9%, Hispanic: 17.9%, other: 3.6%). Two individuals answered some of the interview questions but not all: Patients 20 and 21 could not complete the section on healthcare providers due to time constraints and health conditions. Most of the interviews were conducted in English (n = 26, 92.9%), some in Spanish (n = 2, 7.1%), and none in Mandarin because some Chinese-American participants preferred English as their interview language.

13. Non-participation: How many people refused to participate or dropped out? Reasons?

Interviews from five patients were missing: Three patients were deceased, one patient was unavailable, and the other was too ill to participate in the interview.

14. Setting of data collection: Where was the data collected?
The study was conducted at a urban hospital. This hospital's department of hematology and medical oncology has a long history of treating hematological malignancies and cancer. The location of the study site allowed diverse individuals to receive treatment. Interviews were conducted face-to-face in the hospital while participants were waiting for their clinical appointments or through phone interview depending on participant preferences.

15. Presence of non-participants: Was anyone else present besides the participants and researchers?
In some interviews, the caregivers were present with the participant as they accompanied the participants for hospital appointments.

16. Description of sample: What are the important characteristics of the sample?
Eligible participants were adults with leukemia or lymphoma cancers who had received an alloHCT at the hospital. Participants were eligible for the study if they were 18 years or older and spoke and read English, Spanish or Mandarin.

17. Interview guide: Were questions, prompts, guides provided by the authors? Was it pilot tested?
A theory-driven interview guide (see Appendix A) was developed by the principal investigator, who is an expert in health psychology and has conducted many studies in this area. The interview covered various topics centered around adherence and home care, including questions on general medication adherence, knowledge of medications, skills, social motivation and adherence strategies, including use of an electronic pillbox. Interviewers were trained by the principal investigator; the interview questions were pilot tested within the research team meetings and also during role-play interviews prior to conducting actual interviews with patients, and interviewers were also allowed to shadow interviews before the interviewers conducted interviews themselves.

18. Repeat interviews: Were repeat interviews carried out? If yes, how many?
The research team conducted repeat interviews with 13 participants at 3 and 6 months after first hospital discharge, and single interviews for 15 participants, with 10 of these being interviewed at 3 months and 5 at 6 months after hospital discharge.

19. Audio/ visual recording: Did the research use audio or visual recording to collect the data?
All interviews were audio recorded.

20. Field notes: Were field notes made during and/or after the interview or focus group?
The research team took field notes for each contact with participants including during the interviews.

21. Duration: What was the duration of the interviews or focus group?
The interview lasted about 40 to 60 minutes.

22. Data saturation: Was data saturation discussed?
The research team discussed data saturation and decided to continue recruitment up to 30 patients to obtain enough data to reflect the multifaceted experiences in this diverse patient population.

23. Transcripts returned: Were transcripts returned to participants for comment and /or correction?
No, interviews were transcribed and given to the interviewers who had conducted the interviews for comment and correction, but not to participants.

24. Number of data coders: How many data coders coded the data?
Two individuals coded the data (YS and SC).

25. Description of the coding tree: Did authors provide a description of the coding tree?
A codebook, based on the relevant theoretical frameworks, including the Information-Motivation-Behavioral Skills model and classical social support theory, was developed under the supervision of the principal investigator. The researchers used both theory-driven and data-driven coding. For paper 1, it was mostly data-driven coding as the researchers extracted relevant quotes on pillbox use, then later identified and categorized the quotes in different themes. For paper 2 and 3 researchers started out with theory-driven coding, but we also applied data-driven coding along the way and identified additional emerging themes. Codes were modified and added as the researchers were reading through the transcripts. Over informed discussions between research assistants and the principal investigator, we refined the codebook with themes, definitions and examples (see Appendix B).

26. Derivation of themes: Were themes identified in advance of derivation from the data?
Yes, themes were identified based on the theoretical framework, but researchers also found some additional emerging themes from the interview that were not identified in the original theoretical model.

27. Software: what software, if applicable, was used to manage the data?
The coders (YS and SC) initially used Excel spreadsheet, and transferred all data into NVivo version 11 later to store, search and code the interviews in a more systematic way.

28. Participant checking reporting: did participants provide feedback on the findings?
No.

29. Quotations presented: Were participant quotations presented to illustrate the themes/findings? Was each quotation identified?
Yes, participant quotations were included throughout the manuscript with participant number, age and gender.

30. Data and findings consistent: Was there consistency between the data presented and the findings?
Several authors checked that the findings presented reflected the data with the intent to avoid drawing any unwarranted conclusions that are not supported by the data. Intercoder reliability scores are provided throughout the manuscript.

31. Clarity of major themes: Were major themes clearly presented in the findings?
The findings in the manuscript are reported based on the major themes from the data.

32. Clarity of minor themes: Is there a description of diverse cases or discussion of minor themes?
No.