Self-Management by Adolescents and Young Adults Following a Stem Cell Transplant

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Abstract

Background: Stem cell transplant (SCT) is a major life event that affects not only the adolescents and young adults (AYA) receiving SCT but also the entire family. Patients are prescribed complex care regimens for disease treatment and to prevent life-threatening complications. AYA are particularly at risk for self-management difficulties as they are developmentally working to achieve independence from adults and may be more likely to act in ways that are contrary to the recommendations of healthcare providers.

Purpose: A grounded theory study was conducted to better understand the process AYA use to manage their care following a SCT. Specific aims included: 1) to explore self-management facilitators, barriers, processes and behaviors within individual, family, community and healthcare system domains using the pediatric self-management framework to develop initial interview guides; 2) to describe how AYA manage their care regimen post HSCT; and 3) to describe rates of oral medication adherence for AYA post HSCT and how they relate to patterns of self-management.

Methods: Semi-structured interviews were conducted with a sample of 17 AYA (13-25 years at SCT) and 13 of their caregivers after discharge following a SCT. Interviews were coded to consensus by the research team and analyzed using constant comparison methods. A subset of the sample (n=4) participated in electronic oral medication adherence monitoring.

Results: As data emerged the conceptualization of how adherence and self-management was viewed and experienced by AYA and caregivers was best characterized by the journey Dorothy took in the Wizard of Oz. Initially the patients and caregivers experienced a tornado of activities, information, and emotions but with the aid of family, friends and healthcare providers, families are empowered to manage their care, maintain a positive attitude and approach a

"normal" life as they travel the yellow brick road to recovery. Oral medication tracking showed near perfect adherence, but small rebellions in isolation precautions were self-reported.

Conclusion: Study participants were unable to disassociate self-management activities from the SCT experience. When working with AYA undergoing SCT on self-management, healthcare providers should take into account the patient experience and psychosocial needs. Nurses play an instrumental role in AYA self-management practices following SCT by providing information, education, and social support.

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CHAPTER 1: BACKGROUND AND SIGNIFICANCE

Hematopoietic stem cell transplantation (HSCT) is a relatively new treatment for a number of disease disorders such as cancer, primary immune disorders, hematologic disorders, bone marrow failures, and metabolic disorders. In 2012 more than 50,000 people received hematopoietic stem cell transplants worldwide (Worldwide Network for Blood and Marrow Transplantation [WBMT], 2013). The Health Resources and Services Administration (HRSA, 2015) reports 20,000 people are eligible for stem cell transplants each year in the United States, approximately 3,500 of which are children, adolescents and young adults (0-30 years). The Center for International Blood and Marrow Transplant Research (CIBMTR) reported during 2009-2013, more than 3,860 HSCTs were performed in Ohio (HRSA, 2015).

Since the first human transplants in the late 1960s, treatment protocols have advanced to improve survival rates (Whedon, 1995). Despite advances in chemotherapy, radiation therapy, immunotherapy, and prophylactic medications, patients continue to relapse or have treatment related mortality. Undergoing transplant is not an easy decision for patients or their families. Often HSCT is the only potentially life-saving treatment available.

There are several types of transplant a patient can undergo depending on the source or location and donor of the cells. Cell sources include cord blood, bone marrow, or peripheral blood. Types of cell donors are umbilical cord, autologous (self), related allogeneic (sibling or parent), or unrelated allogeneic (National Cancer Institute [NCI], 2013). Cord blood stem cells are obtained from cord blood banks. Patients and donors are matched genetically on several alleles using human leukocyte antigens (HLA) for the best possible outcomes and to prevent graft versus host disease (GVHD), graft loss or rejection (NCI, 2013). If a patient is a candidate for HSCT, genetic testing is completed in order to search for potential cell donors. All

consenting family members are tested first since full genetically matched sibling grafts have better outcomes than transplants from matched unrelated donors (Pasquini & Wang, 2013). If a family member is not an HLA match, stem cell donor registries, such as the National Marrow Donor Program, are consulted to find a suitable donor.

HSCT involves a complex treatment protocol that combines a preparative regimen of chemotherapy, GVHD prophylaxis, and/or radiation in order to remove diseased or dysfunctional hematopoietic stem cells from the bone marrow space, make room in the bone marrow space for new healthy donor cells to engraft, and suppress the host immune system to minimize the risks of graft rejection (NCI, 2013). The preparative regimen combined with immunosuppressive agents and medications for prophylaxis against infection allows the donor cells to engraft in the bone marrow space while protecting the patient during the period of immunosuppression following the preparative regimen prior to engraftment (NCI, 2013). Patients receiving treatment become very ill and require frequent blood product transfusions, nutrition therapy, anti-emetics, blood pressure control, pain management, and strict infection control in addition to immunosuppressant and prophylactic medications (NCI, 2013).

The most common and potentially life-threatening complications that occur during and following transplantation are primary disease relapse, infection, and GVHD (Pasquini & Zhu, 2015). Pasquini and Zhu (2015) reported the Center for International Blood and Marrow Transplant Research (CIBMTR) multicenter outcomes for 2003-2013 which showed that 74-79% of HSCT mortality was attributed to these three complications. Medication protocols are in place for each transplant patient to help prevent complications. Stem cell transplant medication protocols include immunosuppressant medications, prophylactic antibacterial medications, antifungal agents and oral care. These medications need to be taken consistently in order to

maintain therapeutic drug levels. As patients recover, many of these medications and therapies continue after discharge at home and in an outpatient setting.

Discharge after HSCT

U.S. News and World Report (2014) ranked Cincinnati Children's Hospital Medical Center (CCHMC) in the top 3 for pediatric hospitals and cancer care for 2014-2015. Guidelines have been established for discharge from the HSCT unit at CCHMC. The criteria for discharge include the patient having an adequate absolute neutrophil count (ANC), being stable on home medication regimen, stable on home nutrition therapy (oral feeding, enteral feeding, or total parenteral nutrition), the caregiver has received discharge and device management teaching, and no evidence of acute illness such as fever. Patients are expected to remain in close proximity to the medical facility in case of a medical emergency such as septic shock. Patients are also expected to remain isolated from public areas to prevent exposure to infectious agents while their immune system is recovering. Home care nurses, pharmacists, care coordinators, and bedside nurses give instructions during discharge teaching on follow-up appointments, home medication schedule, and when to call the physician. Inpatient nurse care managers facilitate discharge and arrange home health care and outpatient visits (personal communication, D. Maas, August 12, 2014).

Once the patient is discharged, care is continued on an outpatient basis. Outpatient clinic appointments are scheduled at a minimum of twice a week after initial discharge and often more frequently. Clinic appointments consist of physical and mental health assessments, symptom assessments, medication reviews and drug levels, labs, scheduled therapeutic infusions, and blood product transfusions as necessary. If the patient is experiencing complications, such as

GVHD or infection, the patient may be admitted to the inpatient unit or additional clinic appointments are added and follow-up care becomes more intense and time consuming.

Adolescent and Young Adult Development

Adolescence is characterized by a series of psychosocial developmental tasks: achieving independence from parents, adopting peer codes and lifestyles, acceptance of one's body image, and establishing sexual, ego, vocational, and moral identities (Coupey, 2008; Radzik, Sherer, & Neinstein, 2008). All of these tasks are interrupted by the experience of hematopoietic stem cell transplant. In their systematic review, Manning, Hemingway, and Redsell (2013) found that adolescent and young adult (AYA) survivors of critical illnesses were socially isolated, suffered loss of identity, mediated between independence and dependence on a caregiver, transitions and transformations in self-identity, and a new normal. Similar findings were reported in adult HSCT survivors (Adelstein, Anderson & Taylor, 2014). HSCT results in a change in body image due to side effects from chemotherapy and immune suppression medications and potentially GVHD, social isolation from peer group and extended support system during extended hospitalization, and dependence on caregivers for support as patients battle treatment-related fatigue and potential cognitive changes (Ahles & Shed, 1991; Taylor, Pearce, Gibson, Fern & Whelan, 2013).

Adolescents and young adults are developmentally at increased risk for mental health disorders such as depression and anxiety; this risk is compounded by critical and chronic illness such as cancer (Kutcher & Chehil, 2008; Zebrack et al., 2014). This has also been found to be true in adult HSCT survivors (Adelstein et al., 2014). Zebrack et al. (2014) found that 27% of cancer survivors suffered from clinically significant distress at one year following diagnosis, which is nine times the national average.

Adherence

The World Health Organization (WHO) defines adherence as: "the extent to which a person's behavior – taking medication, following a diet, and/or executing lifestyle changes, corresponds with agreed recommendations from a health care provider" (Sabaté, 2003, pp.3). Nonadherence has been identified as having modifiable influencers and health behaviors (Modi et al., 2012). The WHO has made adherence an international goal and provided guidelines and criteria for a variety of conditions including cancer care (Sabaté, 2003). DiMatteo (2004) estimated an overall nonadherence prevalence of 24.8% in the United States. Average adherence in cancer studies and pediatric studies was 79.1% and 70.6% respectively (DiMatteo, 2004). Bhatia et al. (2012) found that pediatric oncology patients with less than 95% adherence to their chemotherapy protocols were 2.5 times more likely to suffer disease relapse. It is estimated that over 188 million medical visits result in patient nonadherence to medical advice, 4.5 million in cancer care visits (DiMatteo, 2004). The estimated monetary waste of nonadherence to the U.S. healthcare system is $300 billion dollars a year (DiMatteo, 2004).

Adolescents are known to have difficulties with adherence to medication and treatment protocols (DiMatteo, 2004; McGrady, Williams, Davies, & Pai, 2014; Phipps & Decuir-Whalley, 1990; Shaw, 2001). Shaw (2001) estimated that the average adolescent adherence to treatment protocols is 50% over a variety of conditions such as diabetes, infectious diseases, renal transplant, and asthma. Barriers that are unique in this population include developmental stages that conflict with adherence to medical protocols, unclear delineation of responsibility between the AYA and caregivers, and psychiatric co-morbidities (Shaw, 2001).

To date three research articles have been published that address adolescent and young adult adherence to HSCT medication protocols. Phipps and Decuir-Whalley (1990) found 52%

of pediatric participants (n=54) had adherence difficulties while hospitalized; 40% in participants over the age of twelve (n=20). Martin et al. (2012) tested the effectiveness of oral beclomethasone dipropionate (BDP) on preventing acute GVHD (aGVHD). Although, the hypothesis that BDP would prevent aGVHD was not supported, BDP did reduce the severity of mucositis with an adherence rate greater or equal to 90%, which 53-57% of the study sample (intervention and placebo groups) met (Martin et al., 2012). McGrady et al. (2014) found adolescents (n=6) in the outpatient setting had an overall adherence to their medication schedule of 73% with an average monthly adherence of 40-91% that decreased over time. Phipps and Decuir-Whalley (1990) noted in their discussion that HSCT is a unique area for adherence in that it combines obstacles seen in both acute and chronic care that can potentially compromise adherence and care delivery.

Little is known about adolescent and young adult adherence to HSCT discharge care protocols and how they manage their day-to-day care following discharge from the HSCT unit. The research question for this study was: How do adolescents and young adults (13-25 years of age) manage their care after initial discharge from the HSCT unit?

The Study

The purpose of this study was to develop a framework to explain how AYA manage their care post- initial discharge after a HSCT by examining the following aims:

Aim 1: To explore self-management facilitators, barriers, processes and behaviors within individual, family, community and healthcare system domains using the pediatric self-management framework as an interview guide.

Aim 2: To describe how AYA manage their care regimen post HSCT.

Aim 3: To describe rates of oral medication adherence for AYA post HSCT and how they relate to patterns of self-management.

This study resulted in a better understanding of the dynamic process of AYA self-management and will inform intervention development, prescribers in managing medication and care regimens for AYA, healthcare workers who provide support to AYA and caregivers, and future research. Data from this study will serve as pilot data for a future studies on AYA self-management following HSCT.

Assumptions and Definitions

Assumptions

1. Adolescents and young adults have difficulties with adherence.
2. Social support plays a role in treatment adherence and wellbeing.
3. Adolescents and young adults develop routines/ processes to manage their day-to-day care and disruptions in these routines contribute to nonadherence.
4. There are modifiable and non-modifiable factors that influence self-management patterns and behaviors and using the Pediatric Self-management Framework to guide inquiry will elicit responses that allow the research team to discover influencing factors, behaviors, and self-management processes.
5. Participants will respond honestly and accurately when asked about managing their care.
6. Grounded theory methodology using individual semi-structured interviews will successfully elicit data that, combined with adherence data, can be used to explain the processes adolescents and young adults use to manage their care following a HSCT.

Definitions

For the purposes of this study, the following definitions were used:

Adherence: The World Health Organization defines adherence as: “the extent to which a person’s behavior – taking medication, following a diet, and/or executing lifestyle changes, corresponds with agreed recommendations from a health care provider” (Sabaté, 2003, pp.3)

Self-management: “The interaction of health behaviors and related processes that patients and families engage in to care for a chronic condition” (Modi et al., 2012, pp.e475)

Adolescent/ Young adult: (Radzik et al., 2008)

1. Early adolescence: approximate ages 10 to 13, or middle school years
2. Middle adolescence: approximate ages 14 to 17, or high school years
3. Late adolescence/ Young adult: approximate ages 17 to 25, or college or 4 years of work after high school.

Due to the limitations of illness on ability to work or attend school, and the potential for cognitive regression associated with HSCT, the ages included in this study will be 13-25.

CHAPTER 2: REVIEW OF THE LITERATURE

This study used grounded theory methodology to explore medication adherence and self-management in adolescents and young adults (AYA) following a hematopoietic stem cell transplant (HSCT). The purpose of this study was to develop a framework to explain how AYA manage their care following initial discharge after a HSCT. This chapter will provide an overview of HSCT, a literature review of AYA adherence, a literature review of AYA self-management, and an overview of the pediatric self-management framework (Modi et al., 2012).

Overview: Pediatric Hematopoietic Stem Cell Transplant

This section will cover HSCT as a treatment for various conditions, statistics related to HSCT treatment and survival, the complex care regimen associated with HSCT, and the patient and family experience of HSCT. Sources for this section include textbooks, national and international health and HSCT specialty organizations, and peer-reviewed articles.

HSCT: What is it?

Hematopoietic stem cell transplant is a treatment option for a variety of pediatric conditions including cancer and immune disorders. There are several types of transplant a patient can undergo depending on the source or location and donor of the cells. Cell sources include cord blood, bone marrow, or peripheral blood that can either be the patient's own cells (self) or another person (allogeneic). Types of cell donors are umbilical cord, autologous (self), related allogeneic (sibling or parent), or unrelated allogeneic (NCI, 2013). Cord blood stem cells are obtained from cord blood banks. Patients and donors are matched genetically on several alleles using human leukocyte antigens (HLA) for the best possible outcomes and to prevent graft versus host disease (GVHD), graft loss or rejection (NCI, 2013).

Candidacy for HSCT depends on disease and severity of illness. Alternative treatments such as chemotherapy are attempted first unless HSCT is front line treatment, such as in severe

combined immunodeficiency (SCID) and other immunodeficiencies (Filipovich, 2008). If a patient is a candidate for HSCT, genetic testing is completed in order to search for potential cell donors. All consenting family members are tested first since full genetically matched sibling grafts have better outcomes than transplants from matched unrelated donors (Pasquini & Wang, 2013). If a family member is not an HLA match, stem cell donor registries, such as the National Marrow Donor Program, are consulted to find a suitable donor.

HSCT involves a complex treatment protocol that combines a preparative regimen of chemotherapy, GVHD prophylaxis (immunosuppressants, discussion to follow), and/or radiation in order to remove diseased or dysfunctional hematopoietic stem cells from the bone marrow space, make room in the bone marrow space for new healthy donor cells to engraft, and suppress the host immune system to minimize the risks of graft rejection (NCI, 2013). The preparative regimen combined with immunosuppressive agents and medications for prophylaxis against infection allows the donor cells to engraft in the bone marrow space while protecting the patient during the period of immunosuppression following the preparative regimen prior to engraftment (NCI, 2013). Patients receiving treatment become very ill and require frequent blood product transfusions, nutrition therapy, anti-emetics, blood pressure control, pain management, and strict infection control in addition to immunosuppressant and prophylactic medications (NCI, 2013).

HSCT: Who gets it?

Hematopoietic stem cell transplantation is a relatively new treatment for a number of disease disorders such as cancer, primary immune disorders, hematologic disorders, bone marrow failures, and metabolic disorders. The first successful transplants were in the 1960s with bone marrow for patients with leukemias and primary immunodeficiencies (Whedon, 1995). In 2012 more than 50,000 people received hematopoietic stem cell transplants worldwide

(Worldwide Network for Blood and Marrow Transplantation [WBMT], 2013). The Health Resources and Services Administration (HRSA, 2015) reports 20,000 people are eligible for stem cell transplants each year in the United States, approximately 3,500 of which are children, adolescents and young adults (0-30 years). The Center for International Blood and Marrow Transplant Research (CIBMTR) reported during 2009-2013, more than 3,860 HSCTs were performed in Ohio (HRSA, 2015).

The most common pediatric cancers treated with HSCT are leukemias (acute lymphoblastic leukemia [ALL], acute myelogenous leukemia [AML], chronic myelogenous leukemia [CML]), Ewing sarcoma, neuroblastoma, medulloblastoma, Wilms' tumor, and myelodysplastic syndromes (MDS) (National Marrow Donor Program [NMDP], 2014). Wiskott-Aldrich syndrome (WAS), SCID, and other prematurely lethal X-lined immunodeficiencies account for 90% of primary immune deficiencies (PID) treated with HSCT (Filipovich, 2008). Hemophagocytic lymphohistiocytosis (HLH) is another potentially lethal immune deficiency treated with HSCT (Filipovich, 2008). Common hematologic disorders and bone marrow failure syndromes treated with HSCT include sickle cell disease, dyskeratosis congenital (DKC), severe aplastic anemia, and fanconi anemia (NMDP, 2014). Transplant is also available for select metabolic conditions such as Hurler's syndrome (NMDP, 2014).

Since the first human transplants in the late 1960s, treatment protocols have advanced to improve survival rates (Whedon, 1995). Despite advances in chemotherapy, radiation therapy, immunotherapy, and prophylactic medications, patients continue to relapse or have treatment related mortality. Undergoing transplant is not an easy decision for parents or patients. Often HSCT is the only potentially life-saving treatment available.

Outcomes Associated with HSCT

Lee et al. (2007) reported survival rates for unrelated National Marrow Donor Program (NMDP)-facilitated allogeneic transplants in patients with acute lymphoblastic leukemia (ALL), acute myelogenous leukemia (AML), chronic myeloblastic leukemia (CML), and myelodysplastic syndrome (MDS) based on data from the last two decades. The one-year survival rate for matched unrelated allogeneic transplant was 53% and mismatched unrelated allogeneic transplant was 43% (Lee et al., 2007). In 2011, the one-year survival rate for allogeneic transplant had risen to 60.3% (Pasquini & Wang, 2013). The five-year survival rates ranged from 10% for advanced disease at time of transplant to 50% for early disease stage at time of transplant (Lee et al., 2007). Survival for patients with PID ranges from 50-80% depending on clinical status at time of transplantation and donor source (Filipovich, 2008). The 5-year disease-free survival rates for HLH are 60-70% following HSCT (Filipovich, 2008).

The most common and potentially life-threatening complications that occur during and following transplantation are primary disease relapse, infection, and GVHD (Pasquini & Zhu, 2015). Pasquini and Zhu (2015) reported the CIBMTR multicenter outcomes for 2003-2013 which showed that 74-79% of HSCT mortality was attributed to these three complications. Medication protocols are in place for each transplant patient to help prevent complications that include immunosuppressant medications, prophylactic antibacterial medications, antifungal agents and oral care (NCI, 2013). These medications need to be taken consistently in order to maintain therapeutic drug levels. As patients recover, many of these medications and therapies continue at home after discharge and in an outpatient setting.

Care Regimens in HSCT

Care regimens in HSCT are complex and can be difficult for patients and caregivers to manage. Medications must be taken as prescribed in order to have a therapeutic effect, but often

medications prescribed for HSCT have side effects that can impact quality of life and require close monitoring (Phipps & DeCuir-Whalley, 1990). Table 1 lists common medications in the HSCT care regimen and potential common side effects. Typically, patients are on corticosteroids and at least one additional immunosuppressant medication (NMDP, 2014). In addition to immunosuppressants, prophylactic medications are prescribed to prevent infections such as *pneumocystis carinii pneumonia* (PCP) and other viral, bacterial, or fungal infections. Medications, such as vitamin or mineral replacements, antibacterial and antifungal mouth care (nystatin, clotrimazole, chlorhexidine gluconate, biotene), anti-hypertensives, and ursodiol for liver protection are also common medications administered 2-3 times daily. Medication regimens are frequently changing as the patient's condition changes, which can lead to confusion, medication errors, and adherence problems (Kondryn, Edmondson, Hill, Eden, 2011; Phipps & DeCuir-Whalley, 1990).

Table 1. Common home medications in the HSCT care regimen and adverse effects.

Medication	Adverse Effects	Administration	Dosing Schedule
Immunosuppressants			
Corticosteroids (methylprednisolone, prednisone)	Hypertension Sodium and fluid retention Psychosis, emotional instability Delayed growth, amenorrhea Osteopenia, avascular necrosis Muscle weakness (myopathy) Glaucoma, cataracts Cushingoid appearance Glucose intolerance, hyperlipidemia Ecchymosis, petechiae,	Intravenous/ Oral	Twice daily Every 12 hours IV push (IVP)

	increased sweating		
Cyclosporine	Nephrotoxicity Hypertension Neurotoxicity (tremor, paraesthesias, headache) Post-transplant diabetes mellitus Hyperuricemia, hyperkalemia, hyperlipidemia Excess hair growth, gum hyperplasia	Intravenous/ Oral	Twice daily Every 12 hours IV: over 1-2 hours
Mycophenolate mofetil (CellCept)	Bone marrow suppression: leukopenia, anemia, thrombocytopenia Gastritis, diarrhea	Intravenous/ Oral	Two-three times daily Every 8-12 hours IV: over 2 hours
Tacrolimus	Nephrotoxicity Hypertension Post-transplant diabetes mellitus Hyperkalemia, hypomagnesemia	Oral	Twice daily Every 12 hours
Sirolimus	Bone marrow suppression: leukopenia, anemia, thrombocytopenia Delayed wound healing, lymphocele formation Bone pain Pneumonitis Hyperlipidemia Acne, mouth ulcers	Oral	Twice daily Every 12 hours
Prophylactics			
Trimethoprim/ sulfamethoxazole (Bactrim)	Red skin rash Abdominal discomfort, colitis, pancreatitis Nephrotoxicity Neurotoxicity: seizures, headache, depression, tinnitus, insomnia	Intravenous/ Oral	Oral: Twice daily for three consecutive days a week IV: over 1 hour Every 6-8 hours

	Jaundice, hepatic necrosis Bone marrow suppression: leukopenia, anemia, thrombocytopenia Myalgia, muscle weakness		
Acyclovir	Red skin rash Nephrotoxicity Neurotoxicity: confusion, agitation, behavior changes, seizures Thrombocytopenia, leukopenia Dizziness, fainting Abdominal discomfort	Intravenous/ Oral	Two-three times daily Every 8-12 hours IV: over 1 hour

(Doyle, Harold & Nale, 2006; Morrisey, Flynn & Lin, 2007; U.S. National Library of Medicine, 2014)

In addition to following a complex medication regimen, patients and caregivers must also attend clinic appointments several times each week for laboratory tests, infusions, and transfusions (McGrady, Williams, Davies, & Pai, 2014). Activity restrictions and seclusion from public places are also recommended to prevent infection and injury during the healing process (Lehrnbecher et al., 2008). Patients are expected to follow a special diet such as the neutropenic diet or standard food safety guidelines as recommended by the Food and Drug Administration (FDA) and the Centers for Disease Control (CDC) in order to ensure foods are cleaned properly and to decrease exposure to harmful bacteria (Moody, Finlay, Mancuso & Charlson, 2006). The entire transplant process and immune system reconstitution typically takes from 12-18 months (NCI, 2013). Psychological recovery and social reintegration can take years (Molassiotis, 1997).

Living Through HSCT

AYA Experience. Cooke, Chung, and Grant (2011) reported qualitative interview data with 18-25 year olds on their experience in the year following HSCT. Data were grouped according to the 4 domains of quality of life- physical, psychological, social, and spiritual. Issues identified by AYA in the physical domain were sexuality and fatigue (Cooke et al., 2011).

Adolescence and young adulthood is the normal timeframe for sexual development and exploration (Radzik et al., 2008), however, HSCT has lasting consequences that effect sexuality such as infertility, appearance changes, and physical changes to mucous membranes that can affect the ability to enjoy sexual encounters (Mosher, Redd, Rini, Burkhalter, & DuHamel, 2009). Complications affecting sexuality can impact future intimate encounters and the ability to experience intimacy with others (Cooke et al., 2011; Mosher et al., 2009).

Psychological issues identified by participants in the Cooke and colleagues study (2011) were depression and poor coping skills that led to risk-taking behaviors such as illegal drug use. Depression was also attributed to financial concerns such as loss of medical insurance (Cooke et al., 2011), which is also a risk factor for nonadherence. Other psychological issues AYA identified were nonadherence to isolation/ avoiding public areas and infection control prophylaxis, and dependency on a caregiver, primarily a mother, who was overprotective and limited ability to exert independence (Cooke et al., 2011). Social issues AYA identified were changes in roles and relationships with significant others, peers and family, concerns over education and cognitive deficits from treatment, isolation, financial issues, and family conflict (Cooke et al., 2011). Spiritual issues AYA experienced while undergoing and recovering from HSCT were the strengthening of faith through the process, fear of the future and uncertainty, and the meaning of life (Cooke et al., 2011).

Adelstein, Anderson, and Taylor (2014) conducted a meta-synthesis of meaning-making in patients undergoing HSCT and confirmed the themes of psychological issues such as anxiety and depression, fear and uncertainty of the future, discovering the meaning of life and post-traumatic growth, changes in social roles and relationships, dependency on caregivers, isolation, and strengthening of faith. Themes such as isolation, changes in relationships to peers and

significant others, dependence on caregivers, sexuality and fatigue, facing mortality, and emotional responses of fear, depression, and anxiety are also seen in AYA cancer survivors (Lewis, Jordens, Mooney-Somers, & Kerridge, 2013; Manning et al., 2013; Moody, Meyer, Mancuso, Charlson, & Robbins, 2006).

Family Experience. McDowell, Titman, and Davidson (2010) explored parental experience of their child's HSCT. Parents reported having to adjust and develop an "abnormal normal" to provide routine, stability, and life for both the ill child and their siblings (McDowell et al., 2010). Parents felt isolated while experiencing uncertainty of living with the child's illness, stress, and intense emotions (McDowell et al., 2010). Gender differences between parents and marital conflicts were common occurrences as a result of their experience (McDowell et al., 2010). Parents also reported trying to find positives within a negative experience and bonding with others in similar situations (McDowell et al., 2010).

In summary, patient and family experiences while undergoing treatment for HSCT have direct implications on AYA adherence such as: unclear role delineation, family conflict, psychological co-morbidities, the desire to be independent and "normal" while experiencing symptoms that require dependency on a caregiver and isolation from peer group, and financial and insurance concerns.

Treatment Adherence

It is very common to experience psychological, social, physical, and spiritual changes as a result of the HSCT treatment regimen and the treatment experience (Adelstein et al., 2014; Ferrell et al., 1992). As a result, nonadherence is likely to occur. Consequences for nonadherence are not well understood in the pediatric HSCT population.

Butow et al. (2010) presented potential consequences of nonadherence to various tasks related to treatment for cancer that may be applicable to the AYA HSCT population. Failure to attend clinic appointments can lead to delayed identification of disease effects and complications, or secondary cancers (Butow et al., 2010). Nonadherence to chemotherapy can reduce treatment efficacy, which increases the risk for relapse (Bhatia et al., 2012; Butow et al., 2010). Nonadherence leading to reduced treatment efficacy could be applied to immunosuppressant medications used in organ transplant. In Dobbels et al. (2010), a systematic review of pediatric renal transplant adherence to immunosuppressive medication protocols revealed the prevalence of nonadherence was 31.8% which resulted in 44% graft losses and 23% late acute rejection episodes. Nonadherence to isolation precautions and prophylactic antimicrobials while immunocompromised increases the risk of developing a life threatening infection. Regression, cognitive impairment, stress, and social isolation are also factors that AYA undergoing treatment for cancer and HSCT may experience that can negatively affect adherence to complex care regimens (Butow et al., 2010). Compounded with developmental issues of risk-taking behaviors and egocentrism that may lead to the inability to understand the consequences of nonadherence (Malbasa, Kodish, & Santacroce, 2007), AYA undergoing treatment for HSCT are at high risk for nonadherence. AYA nonadherence in clinical research can lead to a reduced ability to assess treatment efficacy, which can compromise generalization of results (Butow et al., 2010).

AYA Development and Adherence

Adolescence is characterized by a series of psychosocial developmental tasks: achieving independence from parents, adopting peer codes and lifestyles, acceptance of one's body image, and establishing sexual, ego, vocational, and moral identities (Coupey, 2008; Radzik et al.,

2008). All of these tasks are interrupted by the experience of hematopoietic stem cell transplant. In their systematic review, Manning, Hemingway, and Redsell (2013) found that AYA survivors of critical illnesses were socially isolated, suffered loss of identity, mediated between independence and dependence on a caregiver, transitions and transformations in self-identity, and a new normal. This was also found to be true in adult HSCT survivors (Adelstein et al., 2014). HSCT results in a change in body image due to side effects from chemotherapy and immune suppression medications and potentially GVHD, social isolation from peer group and extended support system during extended hospitalization, and dependence on caregivers for support as they battle treatment related fatigue and potential cognitive changes (Ahles & Shed, 1991; Taylor et al., 2013).

Adolescents and young adults are also at increased risk for mental health disorders such as depression and anxiety that is compounded by critical and chronic illness such as cancer (Kutcher & Chehil, 2008; Zebrack et al., 2014). This has also been found to be true in adult HSCT survivors (Adelstein et al., 2014). Zebrack et al. (2014) found that 27% of cancer survivors suffered from clinically significant distress at one year following diagnosis, which is nine times the national average. Kennard et al. (2004) found nonadherence in adolescent cancer patients was associated with depression and lower self-esteem. DiMatteo, Lepper, and Croghan, (2000) also found depression to be a risk factor for nonadherence.

Overview: Adolescent and Young Adult Treatment Adherence

Stem cell transplant is a life saving procedure, however it is complex, intense and potentially life threatening. There are many potential negative side effects that affect patients not only physically, but also emotionally, spiritually, and socially (Adelstein et al., 2014). Adolescents and young adults are especially vulnerable due to developmental changes that are

occurring at this time. A review of the state of the science for AYA medication adherence and self-management during the acute phase following HSCT was conducted and the results are as follows.

Definitions

Adherence. There are various definitions of adherence in the literature. For the purposes of this review and the proposed study the following definition will be used: "the extent to which a person's behavior – taking medication, following a diet, and/or executing lifestyle changes, corresponds with agreed recommendations from a health care provider" (Sabaté, 2003, pp.3). This definition is used by the World Health Organization (WHO), which identified adherence as an international goal and has provided criteria and guidelines for various conditions including cancer care. The majority of treatment adherence research is focused on medication regimen adherence.

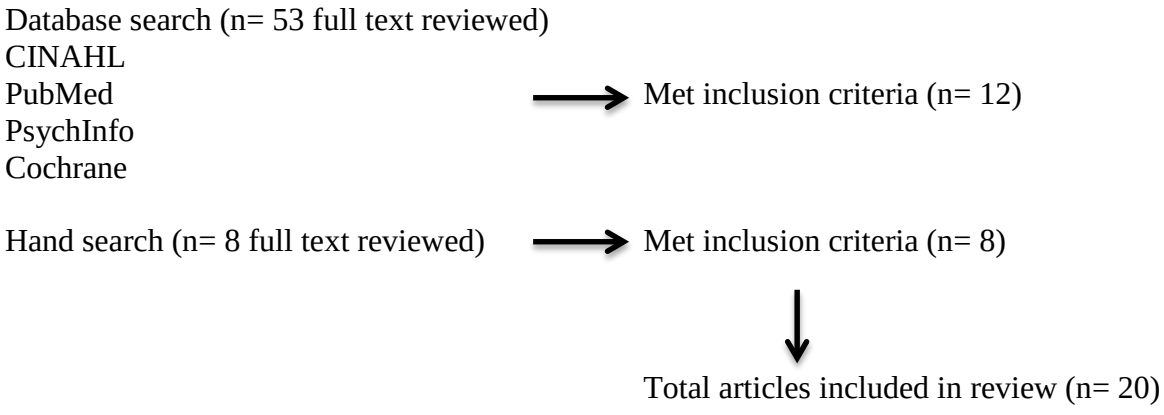
The State of the Science: Adherence in AYA HSCT and AYA Cancer Patients

A comprehensive literature search was conducted to discover the state of the science on adolescent and young adult HSCT patients' adherence to care regimens. A variety of databases were used to search the literature including: PsychInfo, CINAHL, Pubmed, Cochrane database, Medline, and Web of Science. A hand search of references and authors was also conducted to retrieve relevant sources. Search terms used for this review include: *hematopoietic stem cell transplant, bone marrow transplant, transplant, adolescent, young adult, pediatric, adherence, compliance, and cancer.* Terms were searched individually and in combination. National and international health organizations such as the National Institutes of Health (NIH), World Health Organization (WHO), National Marrow Donor Program (NMDP), Center for International Blood and Marrow Transplant Research (CIBMTR), and the Centers for Disease Control (CDC) were

also searched for relevant evidence-based information. The only search limitation was sources be published in English language.

Due to limited published research on pediatric or adolescent adherence during treatment within the first year of HSCT, the search was expanded to include adolescent and young adult adherence to cancer treatment regimens. A title search was performed on 732 sources, 78 abstracts were reviewed, and of these 53 articles were reviewed full text. A hand search was also performed, see figure 1 for more details. Twenty studies were included in this review; 3 articles with HSCT patients, and 17 with AYA cancer patients. Sources were included if they were original research, had adolescents and/or young adults as the population or stratified within the population, had medication adherence as an outcome measure. Articles were excluded if they were a review of the literature, a duplication of a research study, did not measure medication adherence, did not have adolescents or young adults as a population, had young adults but were either not stratified, had young adults but the majority of the subjects were older adults, examined compliance with survivor long-term follow-up guidelines, or only examined prescriber adherence to care guidelines.

Figure 1. Flow chart for adherence literature search.



The evidence table of the articles included in this chapter is located in Appendix A (table 2.). The objectives of this literature review are to provide the state of the science on medication regimen adherence for AYA who have experienced hematopoietic stem cell transplant (HSCT) and/or cancer. The gap in the literature on AYA adherence to medication regimens will be identified and how the proposed study will address the gap in current knowledge. The quality of the literature will be evaluated using the criteria presented in Jinks, Cotton, and Rylance (2011, pp.463) [see table 3. in Appendix B].

Treatment Adherence: AYA HSCT

Three researchers conducted studies in which they addressed medication regimen adherence in AYA HSCT patients (Martin et al., 2012; McGrady et al., 2014; Phipps & DeCuir-Whalley, 1990). Overall adherence to daily medication regimen ranged from 33% to 73%. Various methods were used to measure adherence. Martin et al. (2012) did not report the method of measuring adherence, Phipps and DeCuir-Whalley (1990) used chart review, and McGrady et al. (2014) used electronic pill bottle monitors and chart review.

Martin et al. (2012) examined the efficacy of oral beclomethasone dipropionate (BDP) in the prevention of acute GVHD. This was a double-blinded randomized control trial with placebo as the control. The final sample included 93 patients in the study arm and 47 in the placebo arm for a total sample size of 140 patients. Participant age ranged from 8 to 63 years old. Although the overall hypothesis that BDP would prevent aGVHD was not supported, the researchers found that > 90% adherence to BDP decreased the severity of mucositis patients experienced (Martin et al., 2012). Greater than 90% adherence during the first month of treatment was 53% for the BDP group and 57% for the placebo study group (Martin et al., 2012). The total prescribed course for

the study was 75 days. Adherence for the full course of treatment was 40% for the BDP group and 33% for the placebo group (Martin et al., 2012).

McGrady et al. (2014) published data from a subpopulation of a larger study of pediatric HSCT outpatients. Adherence data from AYA (ages 12-18) were analyzed over a 7-month timeframe following discharge from the inpatient HSCT unit. Six of the 8 eligible participants had sufficient data for analysis (McGrady et al., 2014). The overall adherence to the outpatient medication regimen was 73% for this sample of participants (McGrady et al., 2014). Overall results indicated that adherence decreased over time and all participants experienced at least 2 medication interruptions (periods >24 hours between doses) with an average of 4.2 interruptions over the 7-month study timeframe (McGrady et al., 2014). Perfect adherence occurred 56% of days and participants did not take any of their prescribed doses 13% of days (McGrady et al., 2014).

Phipps and DeCuir-Whalley (1990) examined treatment adherence while patients were inpatient on a pediatric HSCT unit. Fifty-four patients were included in this study, with 20 over the age of twelve (adolescents). Among the adolescents included in this study, 40% experienced adherence problems (Phipps & DeCuir-Whalley, 1990). Adherence to the oral antibiotic regimen was experienced by all participants classified as having adherence difficulties; 10.8% of participants had adherence difficulties with daily care activities such as daily bathing in addition to the oral antibiotic regimen (Phipps & DeCuir-Whalley, 1990).

The variability of adherence within each of these samples suggests that there are modifiable factors involved in treatment adherence that can inform intervention development specific to this population. Adherence to medication regimens decreased over time in all three studies. It has been suggested that nonadherence to immunosuppressant and oral antibiotic

medication regimens could increase the risk for developing GVHD, infection, or even disease relapse (McGrady et al., 2014; Phipps & DeCuir-Whalley, 1990), however no threshold has been established to define nonadherence. A better understanding of patterns of adherence and potential contributing and modifiable factors is needed for this population of patients. Longitudinal research is also needed with larger sample sizes to examine the effect of nonadherence on health and healthcare utilization outcomes such as infection, hospital readmissions, GVHD, disease relapse and mortality.

Treatment Adherence: AYA Cancer

Similar trends were seen in the AYA cancer treatment adherence literature as were seen in the AYA HSCT treatment adherence articles. Adherence is complex and multi-factorial.

Adherence typologies. Several authors reported 3 groups in AYA adherence to cancer medication regimens: adherent consistently, partially adherent, and nonadherent (Ellis et al., 1992; Rohan et al., 2013; Smith, Rosen, Trueworthy, & Lowman, 1979; Tebbi et al., 1986). This adherence typology was also reported in McGrady et al. (2014) with HSCT patients. Although three groups were identified in several studies, there were no descriptions or analyses between groups reported. Predictors of nonadherence seen in pediatric cancer adherence literature are inconsistent and often contradictory.

Adherence to chemotherapy regimen. The majority of researchers in studies with pediatric cancer patients examined adherence to 6-MP in patients with ALL. Several research teams examined steroid and other chemotherapy adherence in a variety of cancers such as leukemias, lymphomas, and solid tumors (Ellis et al., 1992; Festa, Tamaroff, Chasalow, & Lanzkowsky, 1992; Smith et al., 1979; Tebbi et al., 1986). Researchers in three studies examined prophylactic antibiotic adherence (Festa et al., 1992; Kennard et al., 2004;

Lehrnbecher et al., 2008). Malbasa et al. (2007) and Lehrnbecher et al. (2008) also examined adherence to other aspects of the cancer care regimen such as following a specialized diet for immunocompromised patients, wearing a mask in public, and avoiding crowds with adherence ranging from 50% to 90%. Diet had the highest adherence rates.

Adherence over time. Several studies followed patient adherence over time ranging from 1 month to 2 years. Adherence to medication regimens decreased over time in several studies. Tebbi et al. (1986) followed 46 pediatric and young adult patients, 2 to 23 years old, for a year to examine adherence to oral chemotherapy. Adherence was measured at 3 time points: 2 weeks, 20 weeks, and 50 weeks following diagnosis (Tebbi et al., 1986). Adherence decreased over time with the greatest noncompliance at 20 weeks and adolescents were less compliant than the pediatric patients in this sample (Tebbi et al., 1986). Hawwa et al. (2009) examined 19 pediatric patients' adherence to oral 6-MP for ALL and found an increase in self-report of nonadherence over the 6-month study period. Similarly, Rohan et al. (2013) found adherence decreased during the 1-month of data collection with 136 children with ALL and lymphoblastic lymphoma. In contrast, Festa et al. (1992) monitored at an initial time point and followed-up with the initial sample of patients classified as nonadherent and found nonadherence remained stable over time. However there was no follow-up with patients classified as adherent to see if they remained adherent over time.

Several factors may affect adherence including time of day. Lau, Matsui, Greenberg, and Koren (1998) followed 24 children with ALL for a mean of 44 days (range 15-94 days) and found variability in the time of day. One third of patients were adherent with their medication regimen. Five patients were more compliant with their medication regimen in the evening versus

in the morning (Lau et al., 1998). Two patients were 100% compliant in both the morning and the evening (Lau et al., 1998).

Another factor that may have a short term effect on adherence is patient education. Phillips, Richards, Boys, Hodgkin, and Kinsey (2011) had 4 time points over the 2 year treatment period for ALL. At time point 1, 28% of the sample was adherent to 6-MP based on pill count (Phillips et al., 2011). Information on the importance of adherence to the chemotherapy protocol on disease process of ALL was distributed to the study participants (Phillips et al., 2011). An initial increase in adherence to 78% was seen with a subsequent decline to 55% at the final study time point (Phillips et al., 2011). While distributing information was effective in the short term the effect was not sustained.

In summary, there is variability in adherence with relation to time. The time of day appears to have an impact on adherence as well as treatment adherence over time. Lau et al. (1998) reported evening medication doses were adhered to better than morning doses for a third of subjects. Adherence also appears to decrease over time. This study examined adherence over a 3-month period in a subset of participants with a device that electronically monitored the date and time the pill bottle was opened (Medication Event Monitoring Systems, MEMS^{TM}). This device allowed the research team to examine adherence over time, as well as, adherence patterns within a 24-hour time period. A self-report was also collected that includes the participant's knowledge of their medication regimen.

Methods of monitoring adherence. Adherence is thought to be under-reported leading researchers to search for objective measures for medication adherence such as bioassays (Davies, Lennard, & Lilleyman, 1993; Festa et al., 1992; Kennard et al., 2004; Pai, Drotar, & Kodish, 2008; Hawwa et al., 2009; Smith et al., 1979; Tebbi et al., 1986). The four adherence measures

used in these studies were bioassays, self-report, chart review, and electronic monitoring using Medication Event Monitoring Systems (MEMS^{TM}). Smith et al. (1979) examined the usefulness of hemoglobin and weight changes and urine assay of 17-ketogenic steroid as measures of adherence to prednisone in 52 children ages 6 months to 17 years old with ALL, AML, and non-Hodgkin lymphoma. Although hemoglobin and weight changes exhibited little change during the study timeframe, the urine bioassay was listed as a potential objective measure for prednisone adherence (Smith et al., 1979). Blood metabolites for 6-MP were monitored in pediatric patients with ALL and found to be an effective measure (Davies et al., 1993; de Oliveira, Viana, Zani, & Romanha, 2004; Hawwa et al., 2009; Pai et al., 2008).

Davies et al. (1993) examined serum bioassays for metabolites of 6-MP in 22 children and adolescents with ALL. Variable levels of metabolite were found in 6 patients (27%), 2 were adolescents who self-reported nonadherence (Davies et al., 1993). Thirty-nine children in the maintenance phase of treatment for ALL were examined for nonadherence to 6-MP by de Oliveira et al. (2004) using bioassays, chart review, and parent interviews. Almost 54% of the sample was nonadherent by at least one method; parental self-report only identified 6 patients (de Oliveira et al., 2004). Pai et al. (2008) examined adherence to 6-MP in 51 adolescents with ALL using bioassay and self-report. Forty-five percent of the sample was nonadherent by self-report, and 53% by bioassay (Pai et al., 2008). Adolescents reported missing doses on average 2 days in a 7 day period (Pai et al., 2008). Hawwa et al. (2009) used bioassay and the Morisky self-report measure to measure adherence to 6-MP in 19 children with ALL. Twenty-six percent (n=5) of the sample was nonadherent by bioassay, 2 of the 5 were confirmed on self-report (Hawwa et al., 2009). Across studies, 50-80% of the study sample were adherent.

Although a variety of adherence measures were used, variability in results by measures could indicate potential under-reporting of nonadherence and suggests it may be beneficial to use more than one measure of adherence when appropriate. This study electronically monitored adherence to an immunosuppressant medication and an oral prophylactic medication. Additionally data included a self-report of adherence, medication regimen knowledge, and delineation of medication administration tasks. The electronic medical record data also provided information on immunosuppressant drug levels when possible.

Reasons for nonadherence. Forgetfulness was the most common reason subjects gave for nonadherence across several studies (Ellis et al., 1992; Hawwa et al., 2009; Lehrnbecher et al., 2008; Mancini et al., 2012; Tebbi et al., 1986). Other predictors of nonadherence were adolescent age (Bhatia et al., 2012; Davies et al., 1993; Hawwa et al., 2009; Tebbi et al., 1986), single-mother household (Bhatia et al., 2012), adolescent developmental stage, previous experience with drug side effects, family conflict, psychological co-morbidities, and financial concerns (Ellis et al., 1992; Kennard et al., 2004; Malbasa et al., 2007).

Malbasa et al. (2007) held focus groups with AYA to explore adherence to oral 6-MP in patients with ALL. Normalcy, egocentrism, concrete thinking, and parental support were all found to have an impact on AYA adherence during cancer treatment (Malbasa et al., 2007). Normalcy involved being treated normally with family and peers, and being able to participate in activities with peers (Malbasa et al., 2007). Egocentrism was exhibited in risk-taking behavior and concrete thinking was evident when AYA were unable to connect nonadherence to long-term disease consequences such as disease relapse (Malbasa et al., 2007). Parental support was found to be a key to adherence, but unclear role delineation was a hindrance to treatment completion (Malbasa et al., 2007). Mancini et al. (2012) also found parental support to be a

facilitator for adherence in children and adolescents with ALL. All four themes directly relate to adolescent development suggesting the AYA population could benefit from interventions that are age appropriate and take into account developmental stage.

Consequences of nonadherence. Four out of the 17 articles reviewed presented overall medication adherence rates (Bhatia et al., 2012; Lau et al. 1998; Phillips et al., 2011; Rohan et al., 2013). One study used pill count (Phillips et al., 2011) and the remaining three studies used MEMS™ (Bhatia et al., 2012; Lau et al., 1998; Rohan et al., 2013) to measure adherence. Davies et al. (1993) estimated that 1 in 5 children with ALL were not taking 6-MP as prescribed. Bhatia et al. (2012) found that adherence rates below 95% for 6-MP increased the risk for relapse 2.5 times. Forty-two to 44% of patients fell below the 95% adherence rate for 6-MP across studies (Bhatia et al., 2012; Lau et al., 1998; Rohan et al., 2013). Taking this into account, nearly half the subjects were at high risk for relapse. Kennard et al. (2004) found 6-year survival to be lower for nonadherent patients in their study. In a meta-analysis by Simpson et al. (2006) adherence to medication regimens was compared to health outcomes and mortality. Adherence in both placebo and beneficial treatment groups was associated with positive health outcomes and improved mortality when compared to poor adherence group (pooled odds ratio of 0.55) suggesting that adherence may be a marker for overall healthy behavior (Simpson et al., 2006).

Overall, the consequences of nonadherence were found to be potentially life threatening. Risk factors discussed in the reviewed literature include forgetfulness, developmental factors, and socioeconomic factors. This study collected demographic information, reasons for nonadherence, facilitators and barriers of adherence to explore behaviors and adherence patterns for AYA following HSCT.

Process of adherence in sample of AYA with ALL. Landier et al. (2011) used grounded theory to study adherence to oral 6-MP in 17 Hispanic and Caucasian children and young adults ages 6-28 with ALL, and 21 of their caregivers. The process of adherence had three stages 1) recognizing the threat, 2) taking control, and 3) managing for the duration (Landier et al., 2011). The term used for the parent's role was doing our part, which referred to taking the ultimate responsibility of adherence to the medication as prescribed (Landier et al., 2011). Once the patient recognized the threat they could either make a connection or not. Making a connection led to a path of adherence, which included taking control and managing for the duration and ultimately more adherent behaviors (Landier et al., 2011). This process was moderated by parental support (Landier et al., 2011). By not making the connection, AYA were missing the connection, which led to low adherence behaviors. Five contextual factors influenced the process: 1) education, culture, and socioeconomic status; 2) religious beliefs; 3) young person's temperament, personality, and developmental stage; 4) family situation, structure, and dynamics; and 5) relationship with healthcare provider (Landier et al., 2011).

Although Landier et al. (2011) developed the process of adherence for a population of pediatric and young adult oncology patients, the sample was limited to patients with ALL and data were collected retrospectively. Also, it has been demonstrated that adolescents are less adherent than children and have different developmental factors that may affect adherence. The HSCT medication regimen differs from the regimen for pediatric ALL in intensity and complexity.

Summary of AYA HSCT and Cancer Adherence

Nonadherence was higher in adolescents when compared to pediatric patients within samples. Adherence decreased over time and varied throughout the day, which suggests

interventions need to address adherence at multiple time points in treatment and need to be developmentally specific. Overall adherence ranged from 50-80% for HSCT and cancer medication regimens. The main reason patients reported being nonadherent was forgetfulness. Predictors of nonadherence were depression, previous experience of treatment side effects, single-mother household, adolescent age, and Hispanic ethnicity. Two qualitative studies were included in this review, both with AYA receiving treatment with 6-MP for ALL (Landier et al., 2011; Malbasa et al., 2007). Both studies indicate that parents have a key role in AYA adherence to chemotherapy protocols and developmental stage has an impact on treatment decision-making (Landier et al., 2011; Malbasa et al., 2007). The quality of the literature rated fairly high with mostly 6.5-7 out of 8 on a quality scale adapted from Jinks et al. (2011), however most of the studies were descriptive in nature and lacked randomization due to small sample sizes. There were no studies that examined how AYAs and their caregivers manage their day-to-day care post HSCT.

Limitations of Adherence Literature

Small sample sizes in the majority of studies limit the ability to generalize results. However, the small prevalence of pediatric cancer and HSCT restricts the ability to do large sample randomized control trials at a single facility. The majority of studies included in this review were descriptive in nature with percent patients adhering to treatment protocol and initial attempts at identifying risk factors and influencers. Researchers in 2 studies in AYA HSCT medication adherence and 4 studies in AYA cancer medication adherence reported adherence rates, limiting the ability to determine levels of adherence and the relationship to health outcomes. Although several authors mentioned 3 groups of adherent patients, descriptions or profiles of each group are lacking. Two qualitative studies were included in this review, both

with AYA receiving treatment with 6-MP for ALL (Landier et al., 2011; Malbasa et al., 2007). Malbasa et al. (2007) explored psychosocial and developmental aspects of adherence, and Landier et al. (2011) explained the decision-making process AYA with ALL followed that lead to higher adherent or higher nonadherent behaviors.

The State of the Science: AYA Self-management of Care Regimens

Self-management is a concept that is inter-related to adherence and adherence-related behaviors (Kahana, Drotar, & Frazier, 2008). Self-management involves the methods of engaging, managing, and/ or controlling behaviors related to treatment, whereas, adherence is the extent the regimen is completed as prescribed (Kahana et al., 2008). For the purposes of this study the following definition of self-management will be used: "the interaction of health behaviors and related processes that patients and families engage in to care for a chronic condition" (Modi et al., 2012, pp.e475).

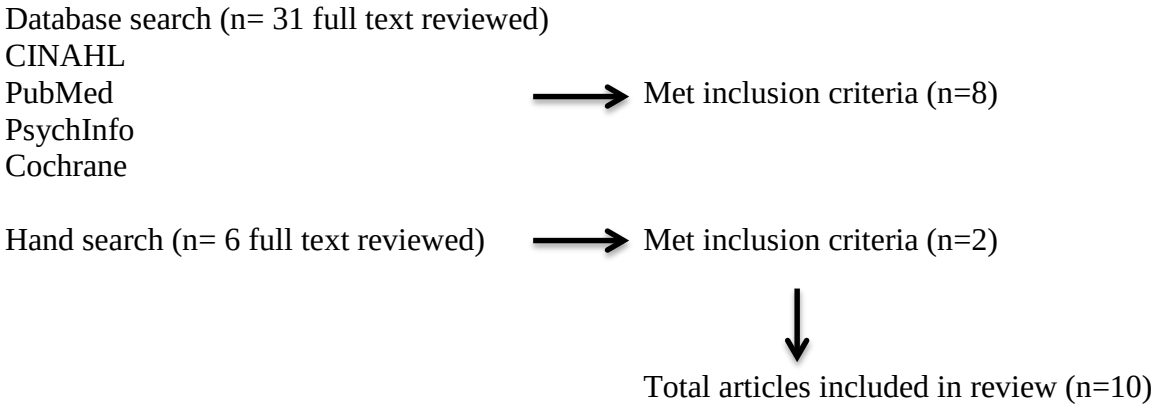
The Literature Search

A comprehensive literature search was conducted to discover the state of the science on adolescent and young adult HSCT patient's self-management of care regimens. A variety of databases were used to search the literature including: PsychInfo, CINAHL, Pubmed, Cochrane database, and Web of Science. A hand search of references and authors was also conducted to retrieve relevant sources. Search terms used for this review include: *hematopoietic stem cell transplant, bone marrow transplant, transplant, adolescent, young adult, pediatric, self-management, and cancer*. Terms were searched individually and in combination.

Due to limited published research on pediatric or adolescent adherence and self-management during treatment within the first year of HSCT the search was expanded to include adolescent and young adult self-management of cancer and chronic illness treatment regimens.

A title search was performed on 296 sources, 59 abstracts were reviewed, and 37 articles were reviewed full text. A hand search was also performed, see figure 2 for more details. Ten studies were included in this review; 3 articles on self-management with AYA cancer patients, and 7 with AYA chronically ill patients. Sources were included if they were original research, had adolescents and/or young adults as the population or included in the population, and had self-management as an outcome measure. Articles were excluded if they were a review of the literature, a duplication of a research study, did not measure self-management or a component of self-management, did not have adolescents or young adults as a population, had young adults but were not stratified, had young adults but the majority of the subjects were older adults, examined survivor long-term follow-up guidelines, young adults transitioning to adult care, or only examined prescriber management of care guidelines. There were 5 research studies that were excluded because they were the only studies on a single chronic condition, and therefore would make synthesis difficult.

Figure 2. Flow chart for self-management literature search.



AYA Self-management: Cancer Treatment

There were no articles on self-management during HSCT. One article with parents of children who had received a HSCT was excluded because it dealt exclusively with parental

involvement in care and others were excluded because they only addressed survivorship and /or transitioning from pediatric to adult care and assessing readiness. There were 3 articles that fit the review criteria for AYA self-management while undergoing treatment for cancer.

Mosher and Moore (1998) conducted a descriptive study in which they examined the relationship between self-concept and self-care using Orem's self-care deficit theory of nursing as a theoretical framework. The sample included 74 children ages 9-18 and 74 mothers. There were small significant correlations between self-concept and both self-care and dependent care practices (Mosher & Moore, 1998). Age was the only predictor as older children had lower self-concept (Mosher & Moore, 1998). Higher self-concept was related to higher self-care and dependent care provided by mothers (Mosher & Moore, 1998). The authors failed to provide a definition of self-concept, a major variable in this study. Nursing's influence on self-concept was examined in the review of the literature conducted by Mosher and Moore (1998) and the discussion of the literature. However, self-concept was not measured as a part of this study. Another limitation of this study was limiting dependent-care to mothers.

Moore and Beckwitt (2004) completed a qualitative study with 9 children with cancer and 18 parents (14 mothers and 4 fathers) on self-care and dependent-care practices using Orem's theory of self-care. Orem's definition of self-care involves meeting universal self-care, developmental self-care and health deviation requisites or needs (Moore & Beckwitt, 2004). Universal self-care requisites include air, water, food, elimination, rest and activity, solitude and social interaction, hazard elimination, and normalcy (Moore & Beckwitt, 2004). Developmental self-care requisites include provision of conditions that promote development, opportunities to engage in self-development, and handling interferences with development (Moore & Beckwitt, 2004). Health deviation includes the following requisites: securing medical assistance, being

aware of the effects of illness, carrying out prescribed measures, dealing with negative effects of therapy, modifying the self-concept, and learning to live with pathologic conditions (Moore & Beckwitt, 2004).

Parents cited food more than any other universal self-care requisite and children cited normalcy as the most important need (Moore & Beckwitt, 2004). Parental presence promoting development and support was cited by parents and children as the most important developmental self-care requisite (Moore & Beckwitt, 2004). Diagnosis overshadowed future care experiences and all participants discussed negative treatment effects but few discussed how they controlled negative effects (Moore & Beckwitt, 2004). None of the participants mentioned how they managed prescribed measures or performing medical procedures apart from IV line care (Moore & Beckwitt, 2004). Parental support and normalcy have both been found to be important in adherence literature with children with cancer (Landier et al., 2011; Malbasa et al, 2007).

Stinson et al. (2012) explored disease self-management in adolescents with cancer using a qualitative design. Interviews and focus groups were completed with 29 adolescents (ages 12-18), 30 parents, and 22 healthcare providers (Stinson et al., 2012). The four major themes of adolescents with cancer self-management needs are as follows: 1) disease knowledge and cancer care skills, 2) knowledge and skills to support effective transition to adult healthcare, 3) delivery of adolescents with cancer accessible healthcare services, and 4) supports for the adolescent with cancer (Stinson et al., 2012).

The literature on self-management by adolescents and young adults with cancer is difficult to synthesize due to the variety of research foci. Two studies used Orem's theory of self-care but examined different parts of the theory. One study examined self-concept (Mosher & Moore, 1998) and the other explored the universal, developmental and health deviation

requisites (Moore & Beckwitt, 2004). Researchers in the third study, included in this review, examined the self-management needs of adolescents with cancer (Stinson et al., 2012). Normalcy and parental support were both mentioned as factors affecting AYA medication adherence. Disease and medication regimen education were also shown to improve adherence temporarily. In short, adherence and self-management for AYA cancer patients is multi-factorial and includes developmental factors, social support, and an understanding of the needs of those involved with the treatment and care.

AYA Self-management of a Chronic Illness

The majority of articles in pediatric chronic illness self-management are in the specialties of asthma care and diabetes care. Three articles were accessed related to adolescent self-management for chronic illnesses in general, but only one met the inclusion criteria for this review. Five articles were excluded because they were the only article to examine self-management in a particular pediatric population and therefore made it difficult to synthesize. Most self-management articles accessed were in adult care and therefore excluded from this review. This review will be limited to general adolescent self-management of chronic conditions, asthma care and diabetes care.

Jedeloo, van Staa, Latour, and van Exel (2010) studied a sample of 31 adolescent and young adult (12-19 years) with chronic conditions and determined their preferences for self-management and healthcare using Q-methodology. Factor analysis was used to create profiles from participant responses. Four profiles emerged: 1) conscious and compliant, 2) backseat patient, 3) self-confident and autonomous, and 4) worried and insecure (Jedeloo et al., 2010). One third (11/31) of AYA fit the conscious and compliant profile. The backseat patient and worried and insecure profiles were comprised entirely of female participants. Participants with a

conscious and compliant profile preferred a high level of involvement in disease management, to be treated "normal", wanted to be treated like an adult, and often resented parental involvement (Jedeloo et al., 2010). Those with a backseat patient profile tended not to seek out information or resources, were apathetic to treatment, and tended to lean on others to gather information and manage care (Jedeloo et al., 2010). Participants with a self-confident and autonomous profile were characterized by a strong desire to be autonomous in decision-making and to be upfront about their condition (Jedeloo et al., 2010). Those with a worried and insecure profile were characterized by constant worrying and distress that led to denial about disease status and insecurities when dealing with healthcare providers (Jedeloo et al., 2010). The researchers concluded that understanding patient profiles can assist in information gathering and sharing as well as to potential approaches to self-management.

Asthma. The literature on asthma self-management primarily addressed medication adherence. Yang, Sylva and Lunt (2010) examined relationships between social support, healthy lifestyle, and asthma management in adolescent (ages 9-14) parent dyads. Healthy lifestyle had significant associations with medication levels, asthma-specific peer and parent support, and parent-reported peer acceptance (Yang et al., 2010). Riekert, Borrelli, Bilderback and Rand (2011) designed a motivational interviewing intervention and conducted feasibility testing with 37 African-American adolescents (ages 10-15) completed over the course of five home visits. Parental reported adherence to asthma medications increased from baseline from 46% to 62%, while adolescent adherence self-report decreased from 32% to 27% (Riekert et al., 2011). However, adolescent motivation to take medications and adherence readiness increased (Riekert et al., 2011). All subscales of quality of life increased for both parents and adolescents following the intervention (Riekert et al., 2011). Since adherence self-report was subjective and

varied based on source, it is unclear the impact of the intervention on self-management, but it appeared to improve motivation, readiness to adhere, and quality of life.

Guevara, Wolf, Grum, and Clark (2003) published a systematic review and meta-analysis on the effects of educational interventions on asthma self-management in children and adolescents. Analysis included 32 trials for a sample size of 3706 patients between 2 and18 years of age. Educational programs were found to improve lung function, feelings of self-control, reduce school absenteeism, reduce the number of days with restricted activity, and reduce number of emergency department visits (Guevara et al., 2003). The effect on morbidity was greatest when the programs included strategies based on peak flow, focused on the individual, and in participants with severe asthma (Guevara et al., 2003).

Diabetes. Researchers in most of the diabetes self-management studies examined maintaining a healthy lifestyle (eating and exercise habits and behaviors) and glycemic control. Stewart, Emslie, Klein, Haus, and White (2005) reported data from a longitudinal study on self-care and glycemic control in 111 adolescents ages 11-18 with type-1 diabetes. Adolescent self-report, parent self-report and glycemic control were all inter-correlated suggesting that self-report could be a useful indicator in this population (Stewart et al., 2005). Healthy self-care behaviors were loosely correlated to glycemic control (Stewart et al., 2005). The researchers suggested that this may potentially be due to the time lag between the behavior and expected results and the ability to compensate for unhealthy behaviors with regular blood testing and insulin administration (Stewart et al., 2005).

Rothman et al. (2008) examined self-management behaviors and glycemic control in 103 adolescents (ages 13-17) with type-2 diabetes. Eighty percent of the adolescents reported greater than 75% adherence to medication (Rothman et al., 2008). The main reasons for noncompliance

were lack of motivation and competing interests such as social engagement (Rothman et al., 2008). Adolescents also reported many perceived barriers and unhealthy behaviors (Rothman et al., 2008). Although adolescents in this study reported a relatively high adherence rate, many barriers and negative behaviors were also reported that could interfere with self-management such as poor diet and exercise habits, lack of motivation, and busyness (Rothman et al., 2008).

Karlsson, Arman, and Wikblad (2008) completed a phenomenological study with 32 adolescents in which they investigated the lived experience of the transition towards autonomy and self-management of type-1 diabetes. The over arching theme was hovering between individual actions and support of others (Karlsson et al., 2008). Teenagers were able to grow through individual self-reliance and confirmation of others (Karlsson et al., 2008). Incorporated into growth through individual self- reliance was self-determination as a developmental process of making one's own decisions, psychological maturity creating possibilities for increased responsibility and freedom, and motivation increasing successful self-management (Karlsson et al., 2008). Growing through confirmation of others included parental encouragement that increased the teenagers' certainty, peers' acceptance which facilitated incorporating self-management activities, and support form the diabetes team that strengthened self-esteem (Karlsson et al., 2008). Parental and peer support and motivation have been discussed previously as important factors in adherence and self-management.

In summary, AYA self-management includes self-care behaviors, support systems, and internal traits such as motivation and desire for autonomy. Self-management had direct consequences for adherence to treatment recommendations. Adolescent and young adult self-management to treatment recommendations immediately following HSCT has not been

investigated and must be understood in order to identify behavior, barriers and facilitators to adherence, and self-care that can be incorporated into interventions.

The Pediatric Self-management Framework

Modi et al. (2012) published the Pediatric Self-management Framework, which was used to develop the questions in the interview guide in the proposed study. The Pediatric Self-management Framework is the first pediatric model of adherence and links self-management behaviors to modifiable and nonmodifiable influences through four domains: individual, family, community, and healthcare system (Modi et al., 2012). Examples of nonmodifiable influences on pediatric adherence include age, gender, ethnicity, cognitive ability, single-parent family, socioeconomic status (SES), and health-related resources available in the community and within a healthcare system (Modi et al., 2012). Examples of modifiable influences on adherence include: social stigma, school-based accommodations for health related conditions, and patient-provider communication (Modi et al., 2012). The modifiable and nonmodifiable influences are located within one of the four domains and influence self-management processes and the resulting behaviors.

Modifiable influencers are ideal interventional targets with non-adherent individuals. In order to understand AYA self-management processes and behaviors we must understand the influencers they are experiencing. The individual, family, community and healthcare system domains provide information on the micro-, meso-, and macro-system levels of self-management that will inform individual and family counseling, policy development, and intervention and program development (Modi et al., 2012).

Conclusion

Adherence and self-management are multifactorial and interrelated. HSCT is a life-saving treatment that also has a high risk of mortality with an overall survival rate of fifty to sixty percent. The medication and care regimen that patients and families are prescribed is complex and can have negative consequences, such as infection or disease relapse, when not completed as prescribed. Adolescents and young adults are particularly at risk for nonadherence due to developmental tasks, such as achieving independence from parents, the importance of the peer group, and risk taking behaviors, that may conflict with medical recommendations. Depression has also been shown to be a risk factor for nonadherence in adolescent patients with cancer.

There is little evidence on adherence and self-management in AYA following HSCT. There is no evidence on how AYA manage their day-to-day care and the delineation of adherence tasks. Although there are several risk factors for nonadherence mentioned in the cancer literature, such as depression, unclear delineation of responsibility, single-mother households, the only risk factor that applied to HSCT were adolescent age and symptom experience. Three patterns of adherence were noted in several studies but there is a lack of description that could potentially allow for early intervention if non-adherers were able to be identified in a timely manner. In the self-management literature, adolescent and young adult developmental needs and parental support were the main determinants in adherence.

Based on the gaps in the literature, our research team explored AYA adherence and self-management following HSCT. Individual interviews with both AYA and caregivers gave us insight into how AYA care was managed. In addition to semi-structured individual interviews, AYA were also given a structured interview that explored their knowledge of their medication regimen, self-reported adherence to medication regimen, barriers and facilitators to adherence,

and medication administration task delineation. Electronically monitored adherence was collected to examine adherence over time and assist in developing self-management trajectories, and behaviors and patterns of adherence. This information was used to develop a self-management theoretical framework for AYA following HSCT.

CHAPTER 3: METHODOLOGY

The purpose of the study was to develop a theory explaining how adolescents and young adults (AYA) manage their care post-discharge following a hematopoietic stem cell transplant (HSCT). The study aims were as follows: 1) to explore self-management facilitators, barriers, processes and behaviors within individual, family, community and healthcare system domains using the pediatric self-management framework as an interview guide; 2) to describe how AYA manage their care regimen post HSCT; and 3) to describe rates of oral medication adherence for AYA post HSCT and how they relate to patterns of self-management. This chapter will include the philosophical background of grounded theory, grounded theory methodology, and a detailed description of the methods of the study.

Grounded Theory

Philosophical Underpinnings

Grounded theory is a qualitative methodology in which the end product is a theoretical framework derived from data collected from participants. Grounded theory spans several disciplines including philosophy, education, psychology, sociology and has its foundations in symbolic interactionism (Annells, 1996). Symbolic interactionism emerged in the 1960's from the thinking of social psychologist George Herbert Mead and his student Herbert Blumer who proposed the interactionist perspective. In these interactionist perspectives the self is defined through social roles and interactions, expectations, and the perspectives of society (Annells, 1996).

Grounded theory methodology evolved from the philosophy of symbolic interactionism and was developed by sociologists Barney Glaser and Anselm Strauss (Annells, 1996). In the 1990's, Strauss and Corbin shifted from Glaser's viewpoint and expanded the philosophy of

grounded theory to a more relativist ontology with an emphasis on perspective and the possibility that reality exists outside of social interaction (Annells, 1996). Glaser, Strauss, and Corbin all suggest that the researchers conducting the data analysis in grounded theory method use constant comparison in order to guard against bias. However, their procedures for analysis differed (Higginbottom & Lauridsen, 2014).

Glaser

Barney Glaser viewed grounded theory in a positivist empiricist lens and was considered a critical realist (Charmaz, 2006). Glaser's methodology is often termed classical grounded theory and is based on the scientific facts leading to theory generation with verification (Annells, 1996). He believed theory should be generated from data that are systematically collected and analyzed (Glaser & Strauss, 1967). The purpose of theory in social science to Glaser is to: 1) predict and explain behavior, 2) theoretically advance sociology, 3) be used in practical applications by practitioners, 4) provide perspective on behavior and data, and 5) guide and provide style for research on behavior (Glaser & Strauss, 1967). Glaser and Strauss (1967) also believed that both qualitative and quantitative data sources were valuable for theory generation and validation.

Strauss

Anselm Strauss took a pragmatic interpretivist stance in regards to grounded theory and was considered a constructivist because he allowed for multiple socially constructed realities and people being active agents in their social world (Charmaz, 2006; Higginbottom & Lauridsen, 2014). His approach uses more interactionism, and a focus on language and context (Charmaz, 2006). After Strauss split from Glaser, he partnered with Juliet Corbin to expand grounded theory methodology to incorporate multiple social realities and the use of a "conditional matrix"

that allows the researcher to address issues like gender, class, race and other critical phenomenon (Annells, 1996; Corbin & Strauss, 1990).

Charmaz

Charmaz (2006) approaches grounded theory from a constructivist viewpoint. According to Charmaz (2006), constructivists analyze how and why participants take action and the meanings in situations and assumes that people participate in and construct their own realities. In addition to Glaser and Strauss, she was influenced by Kuhn's work and the notions of scientific objectivity, reasoning and truth (Charmaz, 2006).

This study was approached philosophically from a constructivist viewpoint. Components of grounded theory research studies include: simultaneous data collection and analysis, developing codes directly from data, constant comparisons at each stage of data analysis, memo writing, initial and theoretical sampling towards theory development which occurs throughout the data collection and analysis process (Charmaz, 2006). Grounded theory incorporates different methods of data collection including but not exclusive to interviews, fieldnotes, records and reports and can use both quantitative and qualitative data as theory development requires (Charmaz, 2006; Glaser & Strauss, 1967).

Methods

Grounded theory is an ideal methodology for studying complex social and psychological actions and processes (Charmaz, 2006). Data gathered are rich and detailed including participants' views, actions, intentions, feelings, life structures and the context in which they are occurring (Charmaz, 2006). For this reason, grounded theory methodology was appropriate to answer a research question on the process of managing complex care and medication protocols following a hematopoietic stem cell transplant (HSCT) by adolescent and young adults (AYA)

and their caregivers. This qualitative study used grounded theory methodology with face-to-face interviews as the primary data source to investigate adolescents' and young adults' management of their care post hematopoietic stem cell transplant.

Setting

Cincinnati Children's Hospital Medical Center (CCHMC) has a 36-bed inpatient bone marrow transplant unit. Cincinnati Children's also has an outpatient clinic and infusion center, as well as, a late-effects clinic that follows patients who have received a HSCT or a cancer diagnosis throughout their lifetime. From January 2010 to December 2011, CCHMC completed 201 bone marrow transplants (National Marrow Donor Program [NMDP], 2013). This center averages between 100-150 transplants per year. Each patient is assigned a primary physician and care manager. There are 2 inpatient care managers, and 10 outpatient care managers. Cincinnati Children's bone marrow transplant unit attracts local, national and international patients.

Sampling Plan

Sample Characteristics

Based on 2009 NMDP registry data for CCHMC, 73% of the HSCT population was male and 81% was ≤12 years of age. The ethnic distribution was: 75% Caucasian, 12% African American, 3% Hispanic, 3% Asian, and 7% other. Thirty-nine percent of children were treated for malignant diseases (i.e. acute myeloid leukemia, acute lymphoid leukemia, Ewing's sarcoma) and 61% nonmalignant disease (i.e. Fanconi anemia, hemophagocytic lymphohistiocytosis). Twenty-four percent of children who underwent a HSCT were diagnosed with graft versus host disease (GVHD) within the first year following transplant in 2009.

Participants

Adolescents and young adults who underwent a hematopoietic stem cell transplant between the ages of 13 to 25 were the key participants in this study. In addition to AYA participants, caregivers of AYA who have undergone HSCT were also interviewed to gain a deeper understanding of context, participant relationships, participant behaviors, and how AYA care is managed post HSCT. Every attempt was made to have dyads of an AYA and at least one primary caregiver, however not having a primary caregiver was not an exclusion criterion.

Inclusion and Exclusion Criteria

The following inclusion and exclusion criteria were used in the recruitment of participants.

Inclusion criteria: AYA. Participants were included in the study if they: **1)** were between the ages of 13-25 at the time of transplant.

Inclusion criteria: Adult Caregivers. Participants were included in the study if they: **1)** were the caregiver of an adolescent/ young adult who had a HSCT between the ages of 13-25 years-old.

Exclusion criteria: AYA. Participants were ineligible if: **1)** the AYA participant did not assent/consent to participate, **2)** parental consent was unable to be obtained for AYA under the age of 18, **3)** participant did not speak or read English, **4)** their cognitive functioning prevented them from participating based on physician or nurse care manager reports, or **5)** if the participant was too ill to participate based on clinical status.

Exclusion criteria: Adult Caregiver. Participants were ineligible to participate if: **1)** they did not speak or read English, or **2)** their cognitive functioning prevented them from participating based on physician or nurse care manager reports.

Sample Size

We estimated that a sample size of 15-20 AYA participants and 15-20 adult caregivers would be sufficient to gain an understanding of the facilitators, barriers, behaviors and processes AYA experience while managing their care. Charmaz (2008) states that while ultimately sample size is determined by theoretical saturation, 25 interviews may be sufficient. Thomson (2011) analyzed 100 grounded theory research articles and found that grounded theory often requires around 30 interviews to reach saturation. This study expected to have 30-40 interviews to reach theoretical saturation. The first, second, and third levels of coding for the initial 5-7 participants' transcripts provided information and direction about the participants needed for theoretical sampling.

Theoretical sampling. Data collection and analysis occurred simultaneously in keeping with grounded theory methodology, so data that were analyzed from the first 5-7 participants in the study informed the researchers of potential theoretical concepts and relational statements, as well as which participants were needed to saturate the elements of the theory under development. The theoretical sample was purposefully selected based on the data collected in the initial interviews. Theoretical sampling for theory or framework development involves obtaining data from previously conducted interviews, additional interviews with current participants, new participants, observations in the field, and the literature to inform or confirm theoretical concepts and relationships (Charmaz, 2006). Data were collected until all theoretical concepts were saturated.

Recruitment

A written letter of support was obtained from the director of the bone marrow transplantation and immune deficiency program. After obtaining Institutional Review Board approval, the principal investigator used two recruitment methods: a) engaging staff assistance

for recruitment and b) principal investigator direct recruitment. The principal investigator presented an overview of the study at a staff meeting attended by inpatient and outpatient care managers, educators, managers, social workers and nursing directors who work with the AYA HSCT population at CCHMC. Inpatient and outpatient care managers and social workers were asked to identify eligible patients to be approached for inclusion in the study. Care managers are very familiar with their patients and their schedules. Care managers were given a flyer about the study and asked eligible patients if they agreed to talk to the principal investigator or a member of the research team while they were in the inpatient setting or during an outpatient appointment. The principal investigator was also familiar with this patient population, having had previous clinical experience in pediatric HSCT, and had permission to directly approach eligible patients and caregivers.

The principal investigator asked eligible AYA over the age of 18 or caregivers of AYA under the age of 18 for permission to approach and discuss the study. If the participant was inpatient at the time of recruitment, the principal investigator approached the participant and/or caregiver to discuss the study. Eligible participants who were already discharged were approached for enrollment at an outpatient appointment. Each participant was given a study flyer and consent form that included information on the study investigators, study purpose, procedures, methods, participant rights, protection of human subjects, and contact information for the study staff (See Appendix C and D).

Protection of Human Subjects

This study had Institutional Review Board (IRB) approval from the joint University of Cincinnati and Cincinnati Children's IRB. Participants 18 years and older were consented prior to data collection. Participants under the age of 18 were assented with parental consent.

Participants were ensured that they had the right to withdraw from the study at any time without any consequences. Participants were also asked for permission to re-contact for additional interviews or further research requests, this was optional and did not influence enrollment in the study. This was a minimal risk study and we did not have any emotional, psychological, or physical distress occurring due to study procedures. In the unlikely event that distress had occurred, Dr. Pai, the study mentor, a clinical psychologist at Cincinnati Children's Hospital Medical Center, was available at any time. All members of the research team with direct access to study participants had experience working with adolescents, young adults, and caregivers in the HSCT population.

Data Collection

If the caregiver and/or AYA patient agreed, parental consent and participant consent/assent was obtained for all participants under the age of 18 (see Appendix D for consent/assent forms). Demographics were collected using the demographic information sheet and information collected from the electronic medical record (i.e. transplant statistics, hospital readmissions, primary disease relapse).

If the participant agreed and was recently discharged from the inpatient unit, 2 Medication Event Monitoring Systems (MEMS^{TM}) were dispensed (1 immunosuppressant and 1 prophylactic medication). If participants were recruited at the time of initial discharge or within 6 months of initial discharge post HSCT and they agreed to use the MEMS^{TM} device, adherence data were collected for up to 3 months. Participants received a phone check-in at one week to check on the operation of the monitoring device. The MEMS^{TM} device was downloaded monthly at routine clinic visits. Downloads were completed by the principal investigator or a trained member of the research team, such as a research coordinator. After 3 months of oral medication

adherence electronic monitoring, the MEMS^{TM} data were downloaded and the devices were collected. MEMS^{TM} device data were not analyzed until the final 3-month data collection was complete.

If the AYA has been discharged for over a month, the semi-structured interview was completed at the participant's convenience. If recruited while inpatient or less than a month from discharge, the semi-structured face-to-face interview were scheduled at the 3-month data collection time point; the interview(s) occurred prior to MEMS^{TM} download and collection. AYA participants who used MEMS^{TM}, also completed the Medical Adherence Measure (MAM), a structured interview that includes questions on self-reported oral medication adherence. Each study participant received an incentive of $25 at the time of the semi-structured individual interview.

Interviews: Semi-structured interviews with AYA and caregiver participants occurred individually face-to-face or over-the-phone based on participant convenience. Face-to-face interviews took place in a private room at the study site to avoid interruptions or distractions. Caregivers were asked not to be present for AYA interviews. Interviews lasted between 15 minutes and 1.5 hours in length and were digitally recorded. Individual interviews were the primary data source for this study. All interviews were scheduled with the principal investigator (CM) according to participant availability.

Each semi-structured interview began with an initial open-ended question followed by questions from the inquiry guide. The same open-ended question began each AYA interview: You've been managing your care for ___ month(s), tell me what that's been like for you? The open-ended question that began each adult caregiver interview was as follows: You've been involved in managing your child's care for ___ month(s), tell me what that's been like for you?

There was an interview guide but the interviewer allowed the dialogue to evolve while eliciting reflections and stories that illustrated the participant's experience managing their care, asking clarifying questions when necessary in order to gain greater understanding of concepts and relationships. The framework for the interview guide was the Pediatric Self-Management Model (Modi et al., 2012) in which self-management behaviors are expressed and influenced within individual, family, community, and health care system domains (See Appendix E for the AYA and adult caregiver inquiry guides).

Demographics: Demographic data that were collected included age, ethnicity, relationship status, disease information, and education level (see Appendix F).

Healthcare Utilization: The electronic medical record (EMR) was accessed for additional demographic and disease-related data, transplant date and type, drug and laboratory levels, complications such as infections, graft versus host disease (GVHD) or primary disease relapse that occurred after discharge from the inpatient unit, and compliance with clinic appointments and lab draws (see Appendix G).

Self-reported Adherence: The MAM is a structured interview that assesses medication knowledge, self-reported adherence for each medication, perceived barriers to adherence, and oral medication regimen management. This tool has been used with adolescents and caregivers in the solid organ transplant population with an internal consistency of 0.88 in caregivers and 0.84 in adolescents (Simons & Blount, 2007). The MAM was administered to AYA participants at the conclusion of the semi-structured interview, for those who participated in oral medication tracking, in an effort to avoid influencing participant responses during the semi-structured interview. The MAM provides focused information that was useful for developing a theoretical framework that is translatable to healthcare provider practice (see Appendix H).

Electronically Monitored Adherence: MEMS™ are electronic monitoring devices that record the date and time the pill box or pill bottle are opened as a proxy for medication administration. Date and time are important factors that need to be monitored in medication protocol adherence. The data were used to understand patterns and potential barriers and facilitators an individual faces when managing their medication regimen and are more accurate than self-report (Pai, unpublished data). Participants were given the option of using a MEMS™ device such as a pill bottle and cap or a pill box. Two MEMS™ were distributed to each willing AYA participant at recruitment to collect 3 months of adherence data on oral immunosuppressant adherence and prophylactic antibiotic adherence. After 3 months of data collection, an appointment was made to download and collect the MEMS™ data (see Appendix I for manufacturer's information on MEMS™). Refusing to participate in adherence data collection was not an exclusion criterion, and many participants were no longer taking immunosuppressant or prophylactic medications at time of enrollment and were therefore ineligible for this part of the study.

Data Management

Qualitative Data. Interviews were digitally recorded with the participant's knowledge. Digital data are stored on a secure research drive accessible only to the researchers on this study. Digital recordings were transcribed verbatim. Any hard copies of data are kept secured in a locked file cabinet accessible only to the research staff in order to assure complete confidentiality. Participants were given assurance that the digital recorded sessions are also kept on a protected research server and are available only to members of the research team. Participant data were de-identified and coded as P1, P2, P3 to protect anonymity and confidentiality. Digital recordings will be destroyed once analyses of the data are complete.

Quantitative Data. All digital data are being stored on a secure research drive to which only members of the research team have access. Hard copies of the MAM were collected via verbal report with the interviewer writing the participant's answers and reading back. Hard copies of the MAM and Demographic information sheet were scanned and saved onto a secure research drive and the hard copy destroyed. MEMS^{TM} data were digitally downloaded and caps stored in a locked secure location until the study is concluded. The principal investigator and study mentors ran descriptive analyses on the demographic and adherence data.

Data Analysis

Qualitative

Charmaz's (2006) approach for data analysis was used to analyze semi-structured interview data. Data analysis in a grounded theory study is an iterative and continuous process. As theoretical concepts and relationships emerge, researchers cycle from data to theory development using constant comparisons. In this way the evolving theory is grounded in the data. Interviews were transcribed and coded as they were completed. Transcripts were read through several times for immersion and an understanding of the whole. Initial coding was line-by-line. The research team used second level coding to organize data into categories. Researchers convened weekly to discuss codes and memos generated to validate data, codes, and emerging theoretical concepts and relationships. NVivo qualitative software (QRS, 2013) was used to assist with the qualitative data analysis.

Latent content analysis was used to understand the meaning and context of the data and resulting codes. Field notes and memo writing were used continually to document observations from interviews, setting, context, data codes, categories, and as theoretical concepts and relationships emerged from the data. Memo writing occurred at all stages of data collection and

analysis to capture thoughts and aid in theory development and to provide an audit trail. Once theoretical concepts and relationships evolved from the initial data codes, a third level of coding was used to increase abstraction of the theoretical concepts and compare initial transcripts to the emerging theory. During later interviews the research team asked more focused questions based on the data coded from initial interviews from which the emerging theory was developed. The final level of coding and memo writing aided in diagramming concepts and relationships within the theory. All data were accounted for in the final theory.

Quantitative

Demographic and EMR data were analyzed using descriptive statistics such as means, averages, and percentages and provided a description of the sample. Adherence data from the MAM and MEMS^{TM} were also descriptive in nature (i.e. percentages, averages, adherence frequencies) and helped to explore relationships between adherence data and/or theoretical concepts or behavior patterns, refining the final theory.

Timeline

This study took 18 months to conduct with an additional 6 months for completion of data analysis, theoretical framework development and dissemination. See table 4 for detailed breakdown of study activities by month.

Table 4. Study activities by month.

Activity by Month	**1-3**	**4-6**	**7-9**	**10-12**	**13-15**	**16-18**	**19-21**	**22-24**
Weekly research team meetings								
IRB approval								
Team training on conducting an interview								

NVivo training for PI								
Participant recruitment and enrollment								
Distribute MEMS™								
Interviews + MAM data collection								
Qualitative analysis								
Theoretical sampling								
MEMS™ data collection								
Quantitative data analysis								
Integrating Qualitative and Quantitative data sources								
Develop theoretical framework								
Writing and Dissemination								

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CHAPTER 4: MANUSCRIPT 1

Medication Adherence in Hematopoietic Stem Cell Transplant: A Review of the Literature

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Abstract

Adherence to oral medications has been repeatedly shown to fall below the recommended 80-95% in pediatric and adult cancer populations. The purpose of this review is to report the state of the science about oral medication adherence during the acute phase of hematopoietic stem cell transplant across the lifespan. An exhaustive search of the literature yielded five records for inclusion in the review. Two studies examined adherence in pediatrics, two in adults, and one included both pediatric and adult patients. Three studies were descriptive, and two were interventional in design. The rate or adherence to oral medications ranged from 33% to 94.7%. Adherence decreased over time in all studies except one pharmacist-led intervention study. Different methods were used to measure adherence, but most relied on self-report. Further research is needed in medication adherence in hematopoietic stem cell transplant to better understand facilitators, barriers, and relationships to health outcomes.

Keywords: medication, adherence, hematopoietic stem cell transplant, treatment, acute phase

About 20,000 hematopoietic stem cell transplants (HSCT) occur each year in the United States (Health Resources and Services Administration [HRSA], 2015). HSCT is a potentially lifesaving procedure for multiple patient conditions such as cancer, immune disorders, hematologic disorders and metabolic disorders. The multifaceted HSCT care regimens are intensive and often life threatening. Patients receiving treatment become very ill and require frequent blood product transfusions, nutrition therapy, symptom management, and strict infection control in addition to a complex medication schedule (National Cancer Institute [NCI], 2016). Patients and families bear the burden of managing the majority of these care activities. Effective management and delivery of the highly complex treatment regimens is essential for optimizing the health outcomes of patients undergoing HSCT. Uncertainty associated with HSCT treatment and outcomes, along with the complexity of the care regimen (Chieng et al., 2013; Kondryn, Edmondson, Hill, Eden, 2011; Phipps & DeCuir-Whalley, 1990), frequently in the absence of social support (Lehrnbecher et al., 2008) combine to create an environment with a high probability for nonadherence to occur.

DiMatteo (2004) estimated an overall nonadherence prevalence of 24.8% in the United States. This overall rate included adherence to a variety of care activities, such as attending scheduled clinic visits and following medication regimen as prescribed, across a multitude of disease conditions. Average adherence in cancer studies was 79.1 percent (DiMatteo, 2004). It is estimated that over 188 million medical visits across various disease conditions result in patient non-adherence to medical advice; 4.5 million of these are cancer care visits (DiMatteo, 2004). The estimated monetary waste attributed to nonadherence in the U.S. healthcare system is $300 billion dollars a year (DiMatteo, 2004).

Adherence has been recognized at the national and international levels by the Centers for Disease Control (CDC, 2013), the National Institutes for Health (NIH, n.d.), and the World Health Organization (WHO, 2003) as a target for research and intervention. The World Health Organization made adherence an international goal and provided guidelines and criteria for a variety of conditions including cancer care (Sabaté, 2003). Despite guidelines and organizational support, very little is known about adherence in HSCT. This paper will present results of a review of the state of the science about oral medication adherence during the acute phase of HSCT across the age continuum in order to determine future research directions and potential avenues for intervention.

Background

The acute phase of HSCT is generally defined as the first 100 days post stem cell transplant and is characterized by severe immunosuppression, treatment side effects, complex medication regimens, frequent clinic visits and potentially long inpatient stays if complications develop. Patients are at high risk for life threatening complications such as infections and thrombotic events (Graf & Stern, 2012). Patients and caregivers are also faced with psychosocial symptoms such as uncertainty and distress (Phipps, Dunavant, Garvie, Lensing, & Rai, 2002) that can also impact self-management and recovery (Dunn, Arber, & Gallagher, 2016). The medication regimens during this time vary depending on illness severity, type of transplant and preparation received, co-morbidities, pharmacogenomics, and individual factors such as medication side effects and symptom experience. All of these factors can be overwhelming to patients and caregivers (Dunn et al., 2016) and potentially lead to non-adherence.

The World Health Organization defines adherence as: “the extent to which a person’s behavior – taking medication, following a diet, and/or executing lifestyle changes, corresponds

with agreed recommendations from a health care provider" (Sabaté, 2003, p. 3). Conversely nonadherence is the extent to which a person's behavior does not follow healthcare provider recommendations. Nonadherence has many influencers including individual, family, and healthcare system factors (Hugtenburg, Timmers, Elders, Vervloet, & van Dijk, 2013; McGrady, Brown, & Pai, 2016). Butow et al. (2010) presented potential consequences of nonadherence to various tasks related to treatment for cancer that may be applicable to the stem cell transplant population. Failure to attend clinic appointments can lead to delayed identification of disease effects and complications, or secondary cancers (Butow et al., 2010). Nonadherence to chemotherapy can reduce treatment efficacy, which increases the risk for relapse (Bhatia et al., 2012; Butow et al., 2010).

In Dobbels et al. (2010), a systematic review of pediatric renal transplant adherence to immunosuppressive medication protocols revealed the prevalence of nonadherence was 31.8% which resulted in 44% graft losses and 23% late acute rejection episodes. Nonadherence to immunosuppressants in HSCT may lead to similar reduced treatment efficacy and graft failures as seen in renal transplant. Nonadherence to isolation precautions and prophylactic antimicrobials while immunocompromised increases the risk of developing a life threatening infection. Regression, cognitive impairment, stress, and social isolation are also factors that those undergoing treatment for cancer and HSCT may experience that can negatively affect adherence to complex care regimens (Butow et al., 2010).

In pediatric cancer patients, Davies et al. (1993) estimated that 1 in 5 children with acute lymphoblastic leukemia (ALL) were not taking Mercaptopurine (6-MP), an oral chemotherapy, as prescribed. Bhatia et al. (2012) found that adherence rates below 95%, meaning patients were taking less than 95% of prescribed doses, for 6-MP increased the risk for relapse 2.5 times.

Between 42 and 44% of patients fell below the 95% adherence rate for 6-MP across studies (Bhatia et al., 2012; Lau, Matsui, Greenberg, & Koren, 1998; Rohan et al., 2013). Taking this into account, nearly half the subjects were at high risk for relapse. Kennard et al. (2004) found 6-year survival to be lower for nonadherent patients.

In adult cancer patients, similar adherence rates and patterns are seen. In their review of adherence to oral chemotherapy Bassan et al. (2014) reported adherence rates between 40% and 100%. Electronic tracking also indicated timing (taking medication at times prescribed) and time intervals between doses could be problematic for patients (Bassan et al., 2014). Anderson et al. (2015) found only 69.4% of patients were adherent to tyrosine kinase inhibitors for chronic myeloid leukemia. In Ganesan et al. (2011), nearly one third of patients were nonadherent (at least one week off treatment) at some point during their treatment period for chronic myeloid leukemia. Nonadherence was also associated with a significant difference in five-year event free survival (EFS), with nonadherent patients having an estimated EFS of 59.8% versus 76.7% in adherent patients (Ganesan et al., 2011). In summary, adherence to oral medications has been repeatedly shown to fall below the recommended 80-95% in pediatric and adult cancer populations.

Methods

A literature review was conducted to understand the state of the science on medication adherence during the acute phase of HSCT, including methods of measurement of adherence to oral medications, interventions and their effectiveness and rates of medication adherence for this population.

Search Strategy

A literature search was conducted from January 2016-February 2016 of the following databases: CINAHL, Evidence-Based Medical Reviews, Embase, PubMed, PsychINFO, and Scopus. Adherence, patient, compliance, bone marrow transplantation, hematopoietic stem cell transplantation, medication compliance, medication or pharmaceutical, and regimen were the search terms used to complete the literature search. Limitations were English language and human (not animal) subject research.

Criteria for inclusion in the review were: a) original research, b) medication adherence was measured, c) subjects were in treatment for stem cell transplant, and d) adherence was measured during treatment or/and the acute phase following treatment. Criteria for exclusion from the review were as follows: a) the adherence measured was not medication related, b) adherence was measured but not reported, or c) if multiple articles were published using the same dataset, the study was counted only one time.

In addition to the database review, a hand search was also conducted. The database search yielded 945 records, once duplicates were removed, and the hand search resulted in four additional records for a total of 949 records reviewed. The PRISMA flow diagram (Moher et al., 2009) in figure 1 provides more information on record selection. Five articles were included in the final review, which included one dissertation. Table 1 presents study details for each of the included articles.

Quality Assessment

Quality was assessed using criteria outlined in Jinks, Cotton and Rylance (2011) and include clearly stated and appropriate research question and study aims, clear methods and appropriate outcome measures, sample size, randomization, rigorous and adequately described analysis, outcomes clearly described, and ethical issues suitably addressed. Each criterion is

scored as zero for not present and one for present, with a maximum quality score of eight. Half-points were awarded for partial presence. Quality was assessed by two reviewers, any disagreements were discussed until consensus was reached. Threats to validity were assessed using criteria and definitions provided in Shadish, Cook and Campbell (2002). Table 2 presents the quality scores of the records included in the review.

Results

Five articles met criteria for inclusion in the final review, which included one dissertation. Table 1 presents study details for each of the included articles.

Settings and Samples

Setting. Five studies examined medication regimen adherence during the acute phase of HSCT patients (Chieng et al., 2013; Hoodin, 1993; Martin et al., 2012; McGrady et al., 2014; Phipps & DeCuir-Whalley, 1990). All studies took place in the United States except the study conducted by Chieng et al. (2013), which took place in an Australian hospital. Studies were conducted at a single metropolitan site, with the exception of Martin et al. (2012), which was conducted at two metropolitan sites. Phipps and DeCuir-Whalley (1990) was conducted on an inpatient unit. Two studies followed patients both inpatient and outpatient (Hoodin, 1993; Martin et al., 2012), and two outpatient settings only (Chieng et al., 2013; McGrady et al., 2014).

Sample. Sample size varied across studies from six in McGrady et al. (2014) to 138 in Martin et al. (2012). Two investigators examined adherence in pediatrics (McGrady et al., 2014; Phipps & DeCuir-Whalley, 1990). In Phipps and DeCuir-Whalley (1990), age ranged from one month to 20 years old. McGrady et al. (2014) examined adherence in teens 12 to 18. Two research teams looked exclusively at adult HSCT patients ages 18 and older (Chieng et al., 2013; Hoodin, 1993). Martin et al. (2012) conducted a drug study across the lifespan (8-63 years old).

Samples were primarily Caucasian Non-Hispanic and evenly distributed between males and females. Chieng et al. (2013) and Martin et al. (2012) enrolled only patients who had allogeneic transplants. In the three remaining studies, patients who had allogeneic transplants accounted for 60 to 73.2% of enrollment (Hoodin, 1993; McGrady et al., 2014; Phipps & DeCuir-Whalley, 1990).

Measures

Each study used different measures to assess medication adherence. Martin et al. (2012) did not report how adherence was assessed, only medication adherence percentiles. The majority of studies only used one measure to assess adherence, most often self-report. Chieng et al. (2013) and Hoodin (1993) used self-reported adherence. Hoodin (1993) used pill count in addition to self-report, and was the only researcher to use more than one measure to assess adherence. Phipps and DeCuir-Whalley (1990) conducted a retrospective chart review and used a nursing diagnosis of noncompliance as a measure of adherence difficulties. McGrady et al. (2014) used electronic monitors that date and time stamp each pill bottle opening to measure adherence.

Chieng et al. (2013) identified potential drug-related problems using standards developed by the Society of Hospital Pharmacists of Australia. In addition to oral medication adherence, Phipps and DeCuir-Whalley (1990) and Hoodin (1993) also examined adherence to hygiene protocols. Hoodin (1993) also collected additional psychosocial and disease-related measures to examine the influence of behavioral and psychological variables on adherence. Martin et al. (2012) measured drug adherence to determine the drug's effectiveness on acute graft versus host disease (aGVHD). The research team collected several indicators of aGVHD by chart review (Martin et al, 2012).

Study Design

Three studies included in the review used descriptive designs (Hoodin, 1993; McGrady et al., 2014; Phipps & DeCuir-Whalley, 1990), and two interventional designs (Chieng et al., 2013; Martin et al., 2012). No authors reported using theoretical frameworks to guide their work. Only Chieng et al. (2013) tested an adherence-promoting intervention. Two research teams attempted to find a relationship between medication adherence and clinical outcomes (Hoodin (1993; Martin et al., 2012).

Descriptive. Three of the five studies used descriptive designs; one was retrospective (Phipps & DeCuir-Whalley, 1990) and two prospective (McGrady et al., 2014; Hoodin, 1993).

Study characteristics. Phipps and DeCuir-Whalley (1990) identified retrospectively patients with nursing diagnoses or diagnostic category of non-compliance while inpatient. Each nursing diagnosis of noncompliance included specific problem behaviors. Each problem behavior was associated with a nursing intervention in the nursing care plan to address problem behavior. Examples of nursing interventions documented were age-appropriate education on treatment, cueing or medication reminders, operant conditioning, desensitization to aversions, modeling or role play, changing the medication dose or schedule, giving the patient choices in methods of medication administration, and if necessary threat or force (Phipps & DeCuir-Whalley, 1990). There were inconsistencies in charting intervention completion and outcomes. Of the 54 patient charts reviewed, 28 patients (52%) had at least one documented noncompliance diagnosis (Phipps & DeCuir-Whalley, 1990). Four (18%) patients showed documented improvement with nursing interventions over time (Phipps & DeCuir-Whalley, 1990). Nursing interventions used with the four patients who showed improvement were not reported. Of interest, adherence problems were greatest in children (ages 2 to 12), accounting for 71% of reported noncompliance diagnoses (Phipps & DeCuir-Whalley, 1990).

McGrady et al. (2014) examined adherence over a nine-month period, using electronic monitors, in a subset of adolescents and young adults from a larger longitudinal prospective pediatric dataset. Although limited by small sample size, adherence rates and patterns were documented for six patients. Adherence rates and patterns were equivalent to other studies in pediatric cancer. Individual adherence rates ranged from 58 to 92%, with an overall 73% of prescribed doses taken as prescribed (McGrady et al., 2014). Adherence rates decreased over time. Three patterns in adherence were noted from electronic monitoring: high-sustained adherence, variable adherence, and delayed nonadherence (McGrady et al., 2014).

Hoodin (1993) used a prospective correlational design to examine adherence and its behavioral and psychological influencers in adult HSCT patients. Although 88 patients were enrolled, only 56 completed the study primarily due to medical complications or mortality. Participants were monitored from admission pre-HSCT to day 100 after HSCT. An extensive battery of measures was used to identify variables that influence adherence. Only autologous transplantation was a predictor for poor oral medication adherence. Hoodin (1993) reported an overall medication adherence rate, by self-report, of almost 95%. More than half (57%) of the sample self-reported perfect adherence. The corroboration in adherence rates between self-report and pill count was 50%, which suggests inflation in self-reported adherence rates.

Intervention. Two studies included in the review used intervention designs (Chieng et al., 2013; Martin et al. 2012).

Study Characteristics. Martin et al. (2012) conducted a randomized, double-blind control trial testing the effectiveness of beclomethasone dipropionate, a steroid, in preventing aGVHD. This study consisted of a drug arm and a placebo arm. Medication was started at the start of conditioning and continued through day 75 after HSCT (Martin et al., 2012). Medication

adherence and occurrence of aGVHD were measured, however, the method of assessing adherence was not reported. Patients not able to ingest medication due to the presence of mucositis continued to participant in the study (Martin et al., 2012). It is not clear if missing medication doses due to mucositis was documented as nonadherence. Only 40% of the study arm, and 33% of the placebo arm, took the full dose of medication (Martin et al., 2012). Although the researchers did not see anticipated effects on aGVHD, they did note that beclomethasone dipropionate was associated with less severe mucositis with 90% adherence to the drug (Martin et al., 2012).

Chieng et al. (2013) reported on a pharmacist-led intervention to improve medication adherence. Patients participated in a 20-minute consultation with a pharmacist starting the second week after discharge. Patients had consultations every 7 to 10 days for six total sessions. At each consultation, participants reported drug-related problems, as defined by the standards of the Society of Hospital Pharmacists of Australia (Chieng et al., 2013). Drug-related problems were selected for individual intervention by the research team according to risk of potential consequences and chance of recurrence (Chieng et al., 2013). All patients received a medication administration aid (pillbox). Examples of medication problems targeted for intervention include therapeutic drug monitoring (immunosuppressants and antifungals), wrong medication dose, omitted medications, and unnecessary medications (Chieng et al., 2013). Self-reported adherence, using a modified Morisky questionnaire (scores of 0, high adherence, to 4, low adherence), was measured at each visit (Chieng et al., 2013). Chieng et al. (2013) reported significant attrition (27%), but Morisky scores for those who completed the study (n=17) decreased over the six clinic visits by 1.53 (95% CI 1.12-1.94, p=.0001).

Quality Assessment

Using criteria in Jinks et al. (2011) each report was assessed for quality. Four out of the five records included in the review scored seven out of a possible eight for quality, due to convenience sampling and lack of randomization. Martin et al. (2012) was deducted a half-point for not reporting the method of assessing adherence.

Threats to validity. All the studies included in the review had small sample sizes and lacked adequate power for causal inference. All studies had attrition and/or missing data that also contributed to small sample sizes and limited analyses. Martin et al. (2012) did not report the method used to assess adherence. All authors, with the exception of Hoodin (1993), only used one method of assessing medication adherence, primarily self-report. There is also concern for the reliability of self-report as a measure of adherence. Using one method of adherence measurement could lead to threats of mono-operation bias and mono-method bias. Defining the concept of adherence, using multiple methods of measurement, and collecting both quantitative and qualitative data could help alleviate this bias. It is also possible when using subjective measures of adherence to have the bias of reactivity to experimental situation (i.e. Hawthorne effect). Only Martin et al. (2012) had a control group, but only 40% of patients took the full dose of the medication, which hindered the ability to draw conclusions about drug effectiveness. The threat of ambiguous temporal precedence could apply to Martin's et al. (2012) finding of the potential effect of beclomethasone dipropionate on severity of mucositis. Martin et al. (2012) speculated that adherence to beclomethasone dipropionate could be related to reduced severity of mucositis; however, it is possible that those with severe mucositis who could not ingest the medication were considered nonadherent by the researchers. Threats of history and maturation are possible threats to the validity of all studies and could be mitigated by using a control.

Discussion

Overall adherence to daily medication regimen ranged from 33% to 94.7% across studies. The five studies examining adherence in HSCT demonstrated substantial variability in design, method of assessing medication adherence, and types of medications being measured, which hinders synthesis of the literature. The lack of measurement of morbidity and mortality outcomes severely limits the ability to make comparisons or research and clinical recommendations. Only Hoodin (1993) attempted to examine predictors of nonadherence, and no study offered rationale for nonadherence from the patient perspective. Hoodin (1993) was also the only investigator who used more than one measure of adherence to assess patient behavior.

No researcher reported a theoretical framework guiding their study. Lehane and McCarthy (2007) suggest that comprehensive models like the model proposed by the World Health Organization (Sabaté, 2003) could be used to conceptualize and guide research in adherence. The Pediatric Self-Management Model by Modi et al. (2002), or explanatory adherence models could also be useful in clinical practice, health services administration and research.

The variety of methods used to assess adherence impedes the ability to compare adherence across samples. Only Hoodin (1993), Martin et al. (2012) and McGrady et al. (2014) reported adherence rates. Hoodin (1993) reported an adherence rate of 94.7% by self-report. Martin et al. (2012) reported by adherence percentiles; 62% (drug) and 72% (placebo) of the sample maintained above an 80% adherence rate. McGrady et al. (2014) found that adolescents and young adults had a 73% adherence rate by electronic monitor. Although Hoodin (1993) reported a 94.7% adherence rate by self-report, pill count only corroborated 50% of the adherence. Although there is mixed evidence on the reliability of self-report, in general it is

recommended to use self-report in combination with other methods of measuring adherence (Dunbar-Jacob & Mortimer-Stephens, 2001).

Electronic monitoring as a method for assessing adherence has the advantage of documenting patterns of medication taking over time that could be useful for tailored interventions. Researchers working in pediatric adherence may also want to consider the role of the parent in patient adherence when considering measurement and intervention design, since it is more than likely that parents have a significant role in the medication administration and other self-management processes both inpatient and outpatient. Insight in the patient and family perspective, with facilitators and barriers to adherence for the HSCT population would also be useful in intervention design and clinical practice.

HSCT mortality rates remain high at 50 to 60% (Pasquini & Zhu, 2015). Future research should include larger sample sizes that take into account patient mortality and attrition when determining recruitment goals and power, particularly in longitudinal studies. This will likely require multi-site studies for the HSCT population. Multiple methods of measuring adherence should be considered to gain a better understanding of actual patient adherence and to reduce potential bias. Quantitative and qualitative data should be collected to assess adherence behaviors, predictors, and to gain a better understanding of the patient perspective. Longitudinal data associating nonadherence patterns and behaviors to clinical outcomes, such as infection, hospital readmissions, graft versus host disease, disease relapse and mortality, would also be beneficial to clinical decision-making.

Three out of the five research studies reviewed were written by psychologists, one by a medical doctor, and one by a pharmacist. The voice of the patient and nursing's perspective were clearly lacking. Phipps and DeCuir-Whalley (1990) used nursing diagnoses to identify

nonadherence behaviors, but psychologists conducted this study with an advanced practice nurse as a member of the research team. Gaining a better understanding of the patient experience, self-management processes and healthcare system factors would give critical information that would aid in future research and intervention development. Interventions also need to be developed and tested with randomized control trials specific to this patient population and take into account not only the disease processes, but also psychosocial factors like depression or isolation that may affect medication adherence (Kondryn et al., 2011; Lehrnbecher et al., 2008).

Clinical Implications

The variability of adherence rates within each of these samples suggests that there are modifiable factors involved in treatment adherence that can inform intervention development specific to the stem cell transplant population. Adherence to medication regimens decreased over time in the majority of the studies. A better understanding of patterns of adherence and potential contributing and modifiable factors is needed for this population of patients.

It has been suggested that nonadherence to immunosuppressant and oral antibiotic medication regimens could increase the risk for developing GVHD, infection, or even disease relapse (McGrady et al., 2014; Phipps & DeCuir-Whalley, 1990), however no threshold has been established to define when nonadherence increases the risk for developing negative health outcomes. Although 80% adherence is generally used as a threshold to indicate good adherence (Modi et al., 2012), this number is arbitrary, without clinical evidence, and may be inadequate to maintain therapeutic drug levels, prevent complications, and patient mortality.

Nurses are integrated into all levels of HSCT care, including medication reconciliation and patient education at the bedside, patient assessment, ordering refills, managing insurance considerations and other financial concerns, and behavioral and psychosocial intervention.

Therefore, nurses are in a unique position to understand factors affecting adherence for the stem cell transplant population. In order to expand knowledge about adherence in HSCT, nurse researchers should be part of any team examining adherence no matter the patient population.

Clinical Resources

Recognizing that nonadherence is a treatment problem in many cancer populations, several resources and interventions have been designed for use in the clinical environment. The Oncology Nursing Society (ONS, 2009) has published an evidence-based toolkit for oral agent adherence. The toolkit includes information on a select few cancer therapy regimens, financial resources, barriers to medication adherence documented in the oncology literature (many applicable to stem cell transplant), techniques for measuring adherence, tips for dialogue between patients and providers, and theories or models of behavior change using adherence as an example behavior (ONS, 2009).

Assessing medication adherence in pediatric oncology was a strong clinical recommendation as a standard of care by Pai and McGrady (2015) based on their critical appraisal of the literature. Pai and McGrady (2015) recommended routine standardized self-reported assessments of adherence by patients and families. In addition to standardized assessments, these researchers recommended creating developmentally appropriate educational materials for medications including information about the drug, possible side effects, the importance of adhering to the medication and possible consequences of nonadherence (Pai & McGrady, 2015). Barriers to taking medications, previous medication experiences, and strategies to improve medication adherence should be discussed using anticipatory guidance prior to starting a medication and with medication changes (Pai & McGrady, 2015). Pai and

McGrady (2015) provided examples from the literature and example scripts to aid clinicians in adherence-related discussions with patients and families.

Spoelstra and Sansoucie (2015) published evidence-based nursing interventions to improve adherence to oral medications. One recommendation included monitoring patients and gaining their feedback whether they are taking their medications and how they are managing (Spoelstra & Sansoucie, 2015). They also recommended multi-component interventions, combining education, counseling and alternative interventions such as reminders or healthcare professional feedback, to test for effectiveness in improving adherence and sustainability over time (Spoelstra & Sansoucie, 2015). Although these resources and recommendations are for the cancer population, there is sufficient overlap with HSCT in illness course and types of treatment to make these recommendations relevant to the HSCT population.

CONCLUSIONS

Adherence continues to be a critical area of need in terms of intervention development, measurement, clinical integration, and research for the stem cell transplant population. Larger studies are needed to understand adherence patterns, barriers, predictors, modifiable factors, and relationships to health outcomes. Research in pediatric stem cell transplant is needed particularly taking into account the patient and caregiver perspectives, developmental factors, and psychosocial factors that could contribute to nonadherence. Research is needed across the lifespan in stem cell transplant to better understand the relationship between adherence and health outcomes such as infection, relapse, graft versus host disease and mortality for this patient population.

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Figure 1. PRISMA flow diagram.

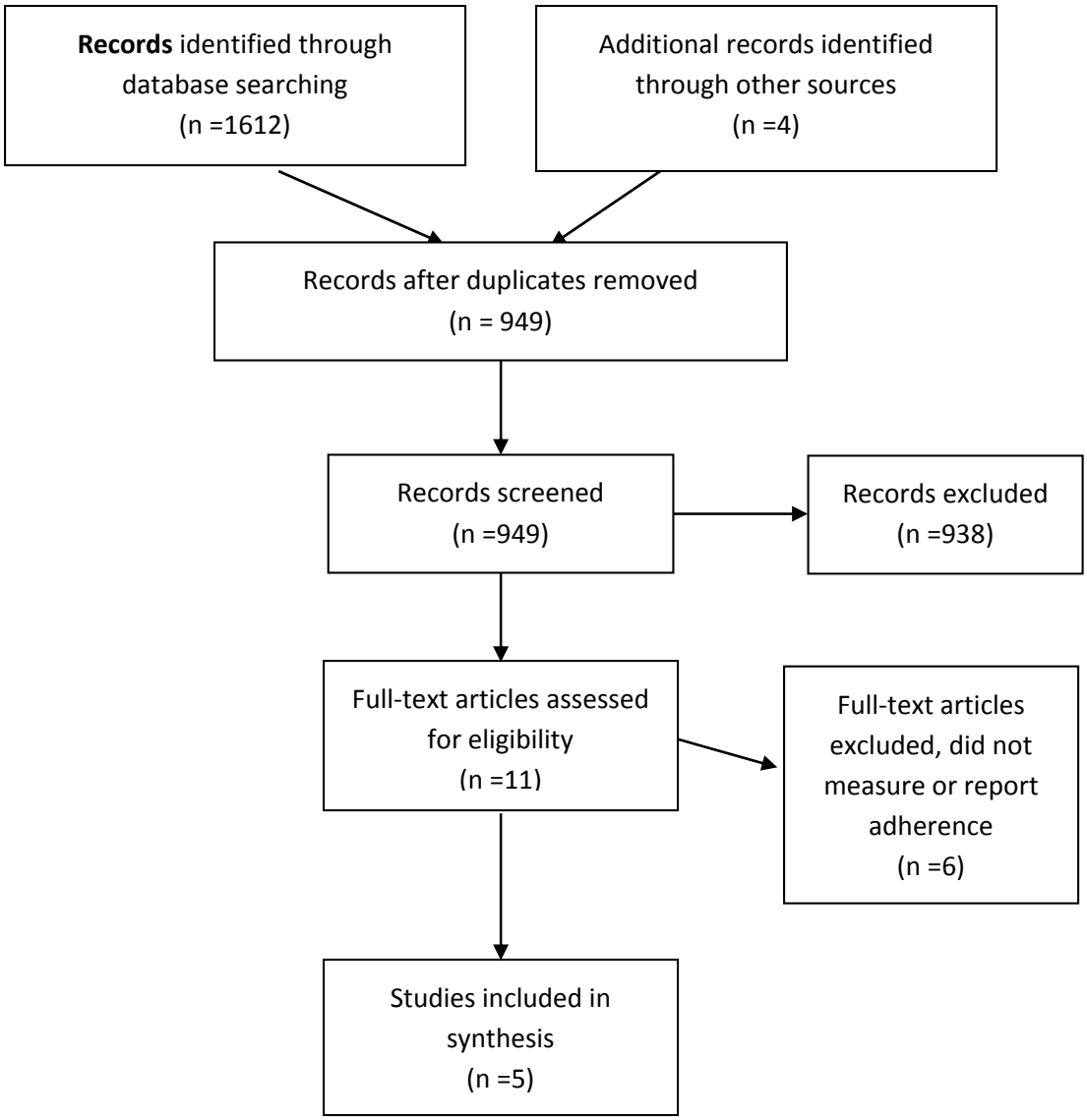

Table 1. Details of studies included in the review.

Author (year)	Design	Sample (N)	Setting	Adherence Measure	Adherence Findings
Chieng et al., (2013)	Prospective cohort study	N= 23 Adult 18-63 yrs	Outpatient Metropolitan Australia	Morisky questionnaire (0 high, 3-4 low adherence)	Scores decreased over 6 visits by 1.53 (95% CI 1.12-1.94), p=.0001. All scored 0 on 6th visit.
Hoodin, (1993)	Prospective correlational study	N= 56 Adult 18-60 yrs	Inpatient/ Outpatient Midwest USA	Self-report Pill count	Overall 94.7% 57% perfect adherence Auto SCT predicted lower adherence
Martin et al., (2012)	Phase II double-blind placebo-RCT	N=138 D (n=92) P (n=46) 8-63 yrs	Inpatient/ Outpatient Metropolitan USA	Not reported	90% drug adherence: D= 53%, P= 57% Took full course: D= 40%, P= 33%
McGrady et al., (2014)	Case study of Longitudinal prospective dataset	N= 6 Pediatric 12-16 yrs	Outpatient Metropolitan Midwest USA	Electronic pill cap monitors (MEMS™)	Overall 73% Decreased over time 1 mo= 91%, 3 mo= 80%, 6 mo < 60%
Phipps, & DeCuir-Whalley, (1990)	Retrospective cohort study	N= 54 Pediatric 1 mo-20 yrs	Inpatient West Coast USA	Nursing diagnosis of Nonadherence	52% adherence difficulties with oral antibiotics Decreased over time

Note. Abbreviations: D= drug, P= placebo, mo= months, yrs= years, RCT= randomized control trial, Auto= autologous

Table 2. Quality assessment of literature.

Author(s) & year	Purpose, hypothesis clear & appropriate	Methods clear & appropriate measures	Sample size is given	Randomization used	Attrition rate recorded	Data analysis described & rigorous	Outcomes of intervention clearly described	Ethical issues suitably addressed	Total Score (max 8)
Chieng et al., (2013)	1	1	1	0	1	1	1	1	7
Hoodin, (1993)	1	1	1	0	1	1	1	1	7
Martin et al. (2012)	1	0.5	1	1	1	1	1	1	7.5
McGrady et al., (2014)	1	1	1	0	1	1	1	1	7
Phipps, & DeCuir-Whalley, (1990)	1	1	1	0	1	1	1	1	7

CHAPTER 5: MANUSCRIPT 2

Follow the Yellow Brick Road: Self-management by Adolescents and Young Adults Following a Stem Cell Transplant

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Abstract

Stem cell transplant (SCT) is a major life event that affects not only the adolescents and young adults (AYA) but also the entire family. A grounded theory study was conducted to better understand the process AYA use to manage their care following a SCT. A sample of 17 AYA (13-25 years at transplant) and 13 caregivers were interviewed after discharge following a SCT. Interviews were coded to consensus by the research team and analyzed using constant comparison methods. Initially the patients and caregivers experienced a tornado of activities, information, and emotions but with the aid of family, friends and healthcare providers, families are empowered to manage their care, maintain a positive attitude and approach a "normal" life as they travel the yellow brick road to recovery. Oral medication tracking showed near perfect adherence, but small rebellions in isolation precautions were self-reported. Monotony and social isolation were the hardest obstacles for most of the AYA throughout the process. Nurses play an instrumental role in AYA self-management practices following SCT by providing information, education, and social support.

Keywords: stem cell transplant, adolescents and young adults, self-management, adherence

Undergoing stem cell transplant (SCT) is not an easy decision for adolescents and young adults (AYA) or their families. Often transplant is the only potentially life-saving treatment available. SCT is an intense treatment for a number of disease disorders such as cancer, primary immune disorders, hematologic disorders, bone marrow failures, and metabolic disorders. In 2012 more than 50,000 people received SCTs worldwide (Worldwide Network for Blood and Marrow Transplantation [WBMT], 2013), and 20,000 people are eligible for SCT in the United States (Health Resources and Services Administration [HRSA], 2015). In 2013, the Center for International Blood and Marrow Transplant Research (CIBMTR) reported more than 3,500 pediatric and young adult (birth to 30 years old) transplants (HRSA, 2015).

Despite advances in chemotherapy, radiation therapy, immunotherapy, and prophylactic medications, patients who receive a SCT continue to relapse or have treatment-related mortality. The 3-year survival rate for those needing SCT under the age of 20, ranges from 25-89% depending on disease, severity, and type of transplant (Pasquini & Zhu, 2015). The most common and potentially life-threatening complications that occur during the acute phase of transplantation are a) primary disease relapse, b) infection, and c) graft versus host disease (GVHD) (Pasquini & Zhu, 2015). Pasquini and Zhu (2015) reported CIBMTR multicenter outcomes for 2003-2013 which showed that 74-79% of SCT mortality was attributed to these three complications.

SCT involves a complex treatment protocol that combines a preparative regimen of chemotherapy, GVHD prophylaxis, and/or radiation in order to remove diseased or dysfunctional hematopoietic stem cells from the bone marrow space, make room in the bone marrow space for new healthy donor cells to engraft, and suppress the host immune system to minimize the risks of graft rejection (NCI, 2013). The preparative regimen combined with immunosuppressive agents

and medications for prophylaxis against infection allows the donor cells to engraft in the bone marrow space while protecting the patient during the period of immunosuppression following the preparative regimen prior to engraftment (NCI, 2013). Patients receiving treatment become very ill and require frequent blood product transfusions, nutrition therapy, anti-emetics, blood pressure control, pain management, and strict infection control in addition to immunosuppressant and prophylactic medications (NCI, 2013). Standards of care have been established in oncology and SCT to prevent potential sources of morbidity and mortality. Among these are infection control protocols, diet restrictions, and hygiene practices (Maziarz & Slater, 2015).

During treatment, patients are hospitalized for long periods of time where they are isolated from their friends and families (Jones, Parker-Raley, & Barczyk, 2011; Lewis, Jordens, Mooney-Somers, & Kerridge, 2013; Manning, Hemingway, & Redsell, 2013; Moody, Meyer, Mancuso, Charlson, & Robbins, 2006). Extended isolation, coupled with other stressors experienced when a child or family member requires treatment with a SCT, can have long-term psychosocial consequences for the entire family (McDowell, Titman, & Davidson, 2010). In AYA, these psychosocial consequences are compounded by their developmental drive for independence, immediate rewards, and risk-taking behaviors, which can influence self-management behavior and health outcomes (Kutcher & Chehil, 2008: Zebrack et al., 2014).

Research on self-management practices of children, adolescents, and young adults who have had a SCT focuses primarily on adherence to long-term follow-up guidelines, such as adherence to re-immunization schedules (Lerchenfeldt, Cronin, & Chandrasekar, 2013). This paper will report the results of a grounded theory study on the psychosocial processes AYA use to manage their care for a SCT.

BACKGROUND

SCT Experience

The SCT experience starts with diagnosis and the need for transplant. Donor searches are completed starting with family and extending to a donor registry when needed. Once a donor is found, the patient receives a preparative regimen that depletes the patient's immune system, removes dysfunctional cells, and makes room for the donor stem cells. During the inpatient period, patients receive infusion, transfusion and nutritional support while being closely monitored. When the patient is stable enough, patients and caregivers are educated for discharge.

Once the patient is discharged, care is continued on an outpatient basis. Outpatient clinic appointments are scheduled at a minimum of twice a week after initial discharge and often more frequently. Clinic appointments consist of physical and mental health assessments, symptom assessments, medication reviews and drug levels, labs, scheduled therapeutic infusions, and blood product transfusions as necessary. If the patient is experiencing complications, such as GVHD or infection, the patient may be admitted to the inpatient unit or have additional clinic appointments; follow-up care then becomes more intense and time consuming.

AYA Development

SCT impacts not only daily living and family functioning, but also AYA development. Adolescence and young adulthood are characterized by a series of psychosocial developmental tasks: achieving independence from parents, adopting peer codes and lifestyles, acceptance of one's body image, and establishing sexual, ego, vocational, and moral identities (Coupey, 2008; Radzik, Sherer, & Neinstein, 2008). All of these tasks are interrupted by the experience of SCT.

In the year following SCT, AYA have reported experiencing difficulties in all four domains of quality of life: physical, psychological, social, and spiritual (Cooke, Chung, and Grant, 2011). AYA experience physical issues related to SCT treatment such as sexuality,

fatigue (Cooke et al., 2011), appearance changes, and physical changes to mucous membranes (Mosher, Redd, Rini, Burkhalter, & DuHamel, 2009). AYA were also at risk for experiencing psychosocial issues due to SCT. AYA may experience fear of the future, uncertainty, and question the meaning of life while undergoing a SCT (Adelstein, Anderson & Taylor, 2014; Cooke et al., 2011). Zebrack et al. (2014) found that 27% of cancer survivors suffered from clinically significant distress at one year following diagnosis, which is nine times the national average.

Treatment-related experiences combined with AYA development have direct implications on AYA self-management. Issues such as unclear role delineation, family conflict, psychological co-morbidities, the desire to be independent and "normal" while experiencing symptoms that require dependency on a caregiver, isolation from peer group, financial and insurance concerns (Cooke et al., 2011) have the potential to affect patients and caregivers abilities to manage care.

Self-Management

Self-management involves the methods of engaging, managing, and/ or controlling behaviors related to treatment (Kahana, Drotar, & Frazier, 2008). For the purposes of this study the following definition of self-management will be used: "the interaction of health behaviors and related processes that patients and families engage in to care for a chronic condition" (Modi et al., 2012, p. e475). Adherence, or "the extent to which a person's behavior coincides with medical or health advice" (Haynes, 1979, p. 2), and adherence-related behaviors such as taking medications as prescribed, and following infection control protocols, are inter-related with the concept of self-management (Kahana, Drotar, & Frazier, 2008).

Existing research on self-management in AYA with cancer is difficult to synthesize due to the variety of research foci (Moore & Beckwitt, 2004; Mosher & Moore, 1998; Stinson et al., 2012). Two studies used Orem's theory of self-care but examined different parts of the theory (Moore & Beckwitt, 2004; Mosher & Moore, 1998). Researchers in a third study examined the self-management needs of adolescents with cancer (Stinson et al., 2012). Normalcy and parental support were both mentioned as factors affecting AYA medication adherence (Stinson et al., 2012). Disease and medication regimen education were also shown to improve adherence temporarily (Stinson et al., 2012). Adherence and self-management for AYA cancer patients is multi-factorial and includes developmental factors, social support, and an understanding of the needs of those involved with the treatment and care. These same factors are present in SCT treatment with the potential for serious complications and patient mortality when nonadherence to self-management protocols occurs.

The Pediatric Self-Management Framework is the first pediatric model of adherence and links self-management behaviors to modifiable and non-modifiable influences through four domains: individual, family, community, and healthcare system (Modi et al., 2012). The goal of the study was to develop a theory or framework that described the processes AYA use to manage their care. The research question for the study was: How do AYA (ages 13-25) manage their care after discharge from the SCT unit? The study had the following three aims: 1) to explore To explore self-management facilitators, barriers, processes and behaviors within individual, family, community and healthcare system domains, 2) to describe how AYA manage their care regimen post-SCT, and 3) to describe rates of oral medication adherence for AYA post SCT and how they relate to patterns of self-management.

METHODS

To address this gap in knowledge in the area of AYA self-management following a SCT, a research study was conducted using grounded theory methods (Charmaz, 2006). Grounded theory allows for the use of both quantitative and qualitative data to inform framework development (Charmaz, 2006; Glaser & Strauss, 1967). In this study, adherence data were used as a method of triangulation for self-management behaviors and processes. Components of grounded theory research studies include: simultaneous data collection and analysis, developing codes directly from data, constant comparisons at each stage of data analysis, memo writing, initial and theoretical sampling towards theory development which occurs throughout the data collection and analysis process (Charmaz, 2006).

Sample

Adolescents and young adults who underwent a hematopoietic SCT between the ages of 13 to 25 were the key participants in this study. In addition to AYA participants, caregivers of AYA who have undergone SCT were also interviewed to gain a deeper understanding of context, participant relationships, participant behaviors, and how AYA care is managed post SCT. Every attempt was made to have dyads of an AYA and at least one primary caregiver; however not having a primary caregiver was not an exclusion criterion. Charmaz (2008) states that, while ultimately sample size is determined by theoretical saturation, 25 interviews may be sufficient. Thomson (2011) analyzed 100 grounded theory research articles and found that grounded theory often requires around 30 interviews to reach saturation. Data were collected until all theoretical concepts were saturated. We estimated a total of 15-20 AYA and 15-20 caregivers of AYA to reach theoretical saturation. AYA and their caregivers were included in the study if they were between the ages of 13-25 at the time of transplant. AYA were excluded from the study if: 1) the AYA participant did not assent/consent to participate, 2) parental consent was unable to be

obtained for AYA under the age of 18, 3) participant did not speak or read English, 4) their cognitive functioning prevented them from participating based on physician or nurse care manager reports, and 5) if the participant was too ill to participate based on clinical status. Adult caregivers were ineligible to participate if: 1) they did not speak or read English, or 2) their cognitive functioning prevented them from participating based on physician or nurse care manager reports.

Procedures

Following institutional review board approval, individual semi-structured interviews with caregivers and AYA were conducted using interview guides. In addition to interviews, participants recruited at discharge from the SCT inpatient unit (n=4) were asked to track adherence to oral medications for three months. Adherence was measured using self-report and Medication Event Monitors (MEMS^{TM}), a pill bottle with a chip in the cap that tracks each time the bottle is opened with a date and time stamp. MEMS^{TM} are a proxy for direct observation, but have been shown to be accurate in measuring individual adherence as well as patterns of adherence.

The Pediatric Self-Management Model (Modi et al., 2012) was used as a guide to develop initial interview questions. All interviews started with the same question: You have been managing your care for (number) of months, can you tell me what that's been like for you? Initial AYA and caregiver guides were similar but additional questions were added during theoretical sampling to better understand theoretical concepts and their relationships within the developing framework. For a sample of questions included in the AYA interview guide please see Table 1. Interviews were digitally recorded, transcribed verbatim, de-identified, and then

coded. Interviews ranged from 15-90 minutes in length and were conducted at a large children's hospital in the Midwest, either in person or over the phone by the same investigator (CM).

Members of the research team, which included one faculty, one doctoral and three undergraduate students, and two practicing SCT nurses, coded data to consensus. Data were analyzed using constant comparison methods (Charmaz, 2008). Initial transcripts were coded line-by-line until categories emerged. The remaining transcripts were coded categorically. Theoretical concepts and their relationships emerged from the coded data. All data were accounted for in the final framework.

RESULTS

Sample

Fifty-five AYA and their caregivers at a Midwest pediatric hospital were screened for eligibility, and 44 were approached for recruitment. Thirty-eight AYA (n=20) and caregivers (n=18) consented to participate for an 86.4% recruitment rate. Over the course of the study eight participants, three AYA and five caregivers withdrew from the study. One AYA/caregiver dyad was withdrawn due to patient death. Others withdrew due to lack of time or lost to follow-up. Interviews were conducted with 17 AYA and 13 caregivers for a total sample size of 30. Of the 17 AYA, four also participated in oral medication adherence measures. See tables 2 and 3 for AYA and caregiver demographics respectively.

The Framework

The Pediatric Self-Management Framework (Modi et al., 2012) was used initially to inform interview questions, but as the data emerged the conceptualization of how adherence and self-management were viewed and experienced by AYA and caregivers were better characterized by the journey Dorothy took in the Wizard of Oz (LeRoy & Fleming, 1939).

Concepts that will be used to describe the process of self-management by AYA include: the tornado, the yellow brick road, there's no place like home, friends along the way, flying monkeys and poppy fields, the Great and Powerful Oz, and waking from a dream. Figure 1 provides a visual depiction of the framework.

The Tornado

A tornado is defined as "a violent destructive storm in which powerful winds move around a central point" (Merriam-Webster, 2015, Tornado). The tornado signifies the destructive, overwhelming and pervasive nature of the transplant process. It starts with diagnosis and continues throughout the treatment process. Tornados are unpredictable and often leave a lasting impact on families affected by them. Families who experienced transplant described similar scenarios: the suddenness of diagnosis, initial fear and anxiety, being uprooted and displaced away from friends and family, and a focus on treatment to the exclusion of all other life activities.

Suddenness of diagnosis. Transplant was the only viable option for most families, with a select few having the alternative to be on medication for the rest of their life. Some AYA did not have any signs of illness at time of diagnosis and others were extremely ill and rushed into transplant. AYA participants stated it this way:

> "If I didn't end up having a transplant [the cancer] could just keep on coming back, and I could get different types of cancer, and so long as I would live I would just keep fighting cancer. So at that point, transplant was pretty much the only option." [A5]
>
> "There wasn't really a whole lot of choices for me to do. I mean it was either, it was like, we gotta get him going right now, you know. It was that bad. And there was no second guessing." [A20]

A caregiver stated:

> "One day you feel like you're completely fine, and he actually never felt ill, we just, we found out he had [diagnosis] totally by accident. So, that was a shock because he never felt ill... The options are, you can take the Solaris every two weeks forever, or you can have the transplant and be cured." [C13]

Initial Fear and Anxiety. The event of diagnosis and the need for transplant were described as "this huge thing" that was "shocking," "scary," a "burden," "tiring and exhausting," and "overwhelming." Families felt "at the mercy" of the disease and treatment which led to a wide range of emotional responses such as anger, guilt, shock, fear, anxiety, depression, and acceptance. Several caregivers remarked that watching their child in pain, especially during the mucositis phase following chemotherapy, was the most difficult part of the inpatient experience. One mother described that time as "the only time I really stayed there overnight was when he was actually in the really bad mucositis phase, which is pretty horrifying." [C19] A father put it this way, "probably the hardest thing to watch and what we had to go through, besides finding out, was the mucositis. Don't like the mucositis, too much." [C16]

One mother was diagnosed and receiving treatment for post-traumatic stress syndrome following her son's transplant.

> "I didn't deal with it while I was there, because it was like fight or flight you know, and occasionally I would go to the bathroom and cry but I was there. I slept in his room. And I ended up developing post-traumatic stress syndrome." [C9a]

Discharge was characterized by mixed feelings of happiness to be out of the hospital but also an intense fear of infection and re-hospitalization, and anxiety to have to do all the care without the 'safety net" of nurses and the medical team should something happen. This period

was characterized by a “hyperawareness” of the immunocompromised state and the chance for infection. A few families described being obsessive about cleaning:

> “I’m still germ-a-phobia a little. A little, a lot less now, like but before I had to wash my hands when I got home and I would walk like a surgeon through the house like they’re clean they’re dry and I’d pick up my fork or I picked up whatever I was eating and I just, yeah very, very, very particular. And if I had touched something, I’d have to go to the bathroom and re-wash my hands.” [A7]

> “Staying healthy we probably were a little over aggressive on that, especially when we found out she was going to be discharged we had the entire house cleaned. Dry cleaned, upholstery cleaned, vents cleaned, I have no idea if that did anything to help her or not but we probably helped our mental state uh more than it helped [patient]… Just know if you go back [in the hospital] it’s not a big deal, remember we’re not going to freak out. But I did freak out. Try to freak out without [patient], I mean you know, just over clean. I think, from that point that was a difficult first month.” [C1]

A few participants remarked that it was a traumatic experience but they didn’t realize it until after it was over and they were trying to recover.

> “Emotionally for [son] it was yeah it was really hard and we didn’t find out until he’d gone back to school. Then he had some issues, emotional issues, and I just think that those parts were difficult because it was hard to find help.... So, to me the whole process with the resources there and his emotional wellbeing was absolutely the worst part of it. Because I mean he was in some major depression and at some point at one point I just thought like worried that you know as a mom that maybe he would harm himself.” [C19]

Uprooted and displaced from family and friends. Some families travelled long-distance to the medical center to receive a SCT and were separated from family and friends. While alternate housing such as Hope Lodge through the American Cancer Society and Ronald McDonald House provided room and board, families felt the separation from their support system.

> "Because like the most of my family couldn't afford to come and see me and stuff like the whole time I was inpatient and then at the Ronald McDonald House, I got to see my mamaw and papaw one time. . . Just being away from family, because I'm a family man, being away from family that long, kind of put me in depression, depression state." [A14]

Focus on treatment to exclusion of life activities. Once the decision was made to have the transplant, families adopted a joint mental attitude of "getting it done." One mother said, "this is the way life was" and "you get in that fight mode and you're just, immediately you don't even think about it" [C19]. Caregivers talked about just focusing on the transplant and getting well to the exclusion of all other life activities: "you just gotta give into it and trust in the doctors, and the nurses, and God and go with it." [C11] Another caregiver said:

> "All that other stuff fell off. All that other running here and there, we have a birthday party to go to, we have this outing, we don't do any of that other stuff anymore. We will again, eventually. But for right now, it's only one thing." [C15]

The Yellow Brick Road

"Follow the yellow brick road" was the advice Dorothy received from the good witch. In SCT, families are given advice, instructions, and support in order to assist them to follow the yellow brick road of self-management protocols and care activities designed to protect them and get them through the transplant process. Several AYA and caregivers talked about "milestones"

that helped them mark progress along the road. The self-management behaviors of adherence to oral medications and isolation precautions will be used as exemplars for following the yellow brick road after a SCT.

Advice. Throughout the SCT process, families received advice from a variety of sources, but primarily from the medical team. Most families said they were told to stay away from the internet as a source of information or only visit approved sites to prevent misinformation. One caregiver shared, "[The doctor] said this is the only site you should go to because it's all legit if it's there." [C1] Another caregiver stated:

> "The first thing [the doctor] said to me was, 'Do not go on the web and I can tell you are one that needs information.' So they gave me a packet to read and they said 'Trust this because what you read out there is gonna freak you out without a doubt.' And so I did." [C11]

Other healthcare providers, such as home health nurses, shared advice and knowledge with patients and families. One young adult put it this way:

> "Homecare helped a lot. They gave me advice. Um, they would help me with like certain like foods to eat, like because I remember I had a lot of like constipation problems when I was sick. I would have stool softeners galore, but they would always give me recipes or like help me. And then they would give me advice on like organizing my med stuff at home." [A12]

SCT survivors also gave advice to patients and families. A caregiver shared advice given to her by another caregiver who had experienced the SCT process:

> "They were going to transplant right before us and so she was a person who I could talk to and, I didn't even know what it was gonna be like, like none of us knew what

transplant meant, you know. Are you gonna use machines and bloods gonna be coming out of you into the machine and getting cleaned? You just had no idea that it was basically just a bag hanging on an IV pole. And you're receiving the really bad, no turning back now, kind of chemo. And then you receive your transplant, and then it's just a waiting game sitting around looking at each other. So it was really good having her, uh, to kind of light the way for us." [C15]

Instructions. Caregivers in particular described the teaching they received in order to provide care after discharge. Since care regimens were complex, each family found their own way to follow the instructions and organize their daily medications and supplies. Although methods for organizing medications varied by family, all families used the discharge instruction medication list as a guide.

"They had printed and typed up what I had to take in the morning, what I had to take in the afternoon, and what I took at night. And I'd get my paper out, and I'd get a cup out, and I'd fill the cup with all my meds and I'd take those all from the sheet." [A7]

Support. Self-management support was received from outside sources such as home health care and within the family unit. Care roles and responsibilities were often shared between the caregiver and the AYA to varying degrees. Some AYA were proactive and took full responsibility for part or all of their care: "I wanted to take full responsibility for my care… I tried to do my best to memorize the medications and keep track of them." [A1] Other AYA gradually took responsibility either to personally relieve their caregiver or because of a caregiver necessity. For example, some caregivers needed to return to work. One caregiver stated, "[Son] was very independent with starting the TPN at night. He just kept the pump in his room. He

eased the burden on me of going back to work because he managed that." [C13] Very few AYA took no active role in their care.

Adolescents and young adults discussed feeling tired and weak, and requiring assistance to complete many daily life activities such as showering, cooking, and walking for any distance. AYA were usually dependent on a caregiver to support them through these tasks until their strength was regained. Three AYA shared their experiences with caregivers support when they were weak:

> "Having the family around just because if I needed help getting any kind of, when it came to being weakened initially. They didn't have a problem you know helping me do whatever I needed to do. Like if I was like standing up and I dropped something on the ground I couldn't even like bend over and pick it up, like I would potentially fall over and not be able to get myself off of the ground. So I would always have people like grabbing stuff and like or and I'd have like one of those grabber arms." [A4]
>
> "I would lay on the couch and I didn't want to get up, so I would be like '[sister], go get me a cup of water.' '[Boyfriend], go make me a shake.' And it was kind of like that, I didn't want to get up at all." [A7]
>
> "You want to be able to take care of yourself like all alone, but knowing that you can't like there's certain things you cannot do especially in terms of touching things and cleaning things and cooking things was really hard at first I would get dizzy standing up for that long." [A1]

Weakness and fatigue required major life adjustments for many AYA, especially those who were previously healthy. "It's still kind of really hard to like go from running like ten miles

a day to not being totally sure that you're going to make it walking from one part of campus to another." [A4]

Milestones. The road was marked with milestones that AYA along with their caregivers used to track their progress. For some it was motivation to continue following medication and infection control guidelines by providing a "light at the end of the tunnel."

> "Once I got past that stage, it was kind of a return to normalcy. I remember just looking forward to the next big, kind of, milestone. So for instance like, getting like my, uh, line taken out and not having to get that flushed every day. And now, and then after that, um, when I could get my port taken out or when I will be at this checkup point or when my hair would start really growing back to the point where I didn't need to wear hats all the time, or, you know, I had eyebrows again. So it was just kind of this checklist of waiting for that next big step." [A19]

Adherence. Adherence to oral medications was tracked for four participants. AYA self-reported high adherence to oral medication, which was corroborated with electronic monitors. Medications that were monitored include immunosuppressants (cyclosporine and hydrocortisone), antibiotics (Bactrim), antivirals (acyclovir, valacyclovir), antifungals (posaconazole, itraconazole and voriconazole), and anti-hypertensives (chlorothiazide). Of the four participants who were monitored, they exhibited near perfect adherence over the three months with an overall adherence rate of 95%. Individual adherence ranged from 92.2 to 97.5%. This was corroborated by high self-reported adherence, with only one participant admitting to hiding medications because the pill was too big to swallow. Caregivers and AYA served as reminders for each other if one forgot to set out or take a medication.

Although AYA had high adherence to oral medication, several participants talked about small rebellions in isolation precautions. These rebellions were well thought out and planned to be minimal risk. Participants admitted going to the movies or the mall.

> "I went to the movies, I went to the mall, I never got sick. I never, I didn't wear my mask, I didn't get sick. I mean, it's so true, I didn't. I mean I was really surprised but, yeah, counts were zero and I was walking around. I was, I um, I didn't like to follow rules." [A7]

> "I went out by myself and no mask and I went to a movie and I remember I told my mom about it and she was like, 'oh my god what are you doing!' And I was like 'I don't know! I really want to do something.' I remember I like specifically chose that time of day because it wasn't that popular still and I remember I picked the 10:30 in the morning, like who goes at 10:30 in the morning showing and there was like 2 people and me so I picked good and I sat away from everyone and I had hand wipes in my purse and I would like clean my hands and stuff" [A12]

A few AYA discussed going to friend's houses but being aware of germs and making sure no one was sick prior to the visit.

> "Allowing him to, like, go to his girlfriend's house for instance. But, you know, like I said I, I don't do that blindly. I'll talk to mom first, you know 'I'm Lysoling the house down,' okay then I'm cool with that- my husband not so much. He freaks out a little more." [C11]

There's No Place Like Home

The concept of "there's no place like home" incorporates being isolated from friends and family, feeling like life is passing you by, and yearning to return to normal. Participants felt

separated from their lives which caused feelings of distress and depression, but also served as a self-management motivator to get well and follow healthcare provider recommendations.

Isolated from Friends and Family. Several AYA said that isolation from family and friends was the biggest barrier to their self-management. The disconnection from their social support network sometimes led to withdrawal and depression. For example, one adolescent stated, "I really didn't have many friends come over to my house and visit to me while I was in transplant, and, for like the first 4 or 5 months that was really non-existent." [A15]

One young adult was married with a young daughter. While it was difficult to be away from her daughter, she also served as a motivator to get through SCT:

> "It was hard knowing that I was going to have leave my daughter. But thinking of her made me realize I had to do it because it was better to take the chance, and there be a chance I'd be there for her than for there not to be a chance at all." [A5]

Caregivers also felt the isolation from friends and families impacted their mental state, as one caregiver shared, it was "not the taking care of him taking care of [my son] that put me in the depression, it was being away from home, being away from our family for so long." [C14]

Feeling Like Life is Passing You by. Many AYA and caregivers remarked on life passing you by. As one teen said: "It's so hard to see all your friends go out and do other things and you just have to sit on the sidelines" [A11].

> "I came in my junior year and that was kind of hard having to miss school. To me, that's like bigger than your senior year cause junior year I felt like is when you really start to figure out what you want to do, and, I don't know, people change a lot during junior year I felt like. And I felt like I missed out a lot on my high school experience because of that." [A13]

Caregivers had mixed reactions to others being able to live a normal life. Some saw it as a sign of hope that things would eventually return to normal: "I like to hear that other people are still going through normal stuff." [C15] Others were resentful or angry that others took for granted normal life activities like their child going to prom or homecoming while her child was hospitalized, "they just couldn't understand." [C12]

Goal to Return to "Normal." AYA talked about returning to a normal life like they had before SCT as a goal and motivator.

> "I was very independent in that sense I lived alone in [state] and I did all my cooking and stuff by myself and all my chores and errands, all of that was completely on me and so coming back from the hospital I was really wanted to get back to that but not being able to as quickly as I wanted to was definitely a challenge." [A1]
>
> "Going, walking into a class, and not being, feeling, like when I was wearing a mask or losing all my hair, and I was very pale and like just kind of being able to do the normal things. I couldn't go out with a lot of friends, they're going to a movie or they're going out to a restaurant or to a bar, anywhere. I had to limit myself to a few visitors in my own apartment. So I think for me, I was looking forward to just going about in regular activities and being a normal college student." [A19]

Friends Along the Way

Just as Dorothy met friends and travel companions along the way to the Wizard, so too families who experienced SCT had several sources of social support to help them get through the self-management process. There were four main sources of support that participants described: family, friends, healthcare workers, and survivors of SCT. Pets also played a large role in

support and motivation for AYA. Several AYA even recommended that others get a pet before they go through transplant to help them get through.

Friends. Friends were dichotomous in that sometimes they were an integral source of social support, and sometimes they caused distress when they didn't accept the AYA or were not "true friends." As one adolescent put it: "A lot of my friends weren't really very good friends, I found that out about when I got sick." [A20] Another AYA had a good experience with friends and family helping with self-management: "It's been difficult to get the hang of everything to start with. But then as time went on, everything, things became to get easier. Especially family and friends that I've made along the way and old friends." [A14] Or another AYA found people wanted to be her friends due to the notoriety of being sick: "Well that's just people I didn't really know, they just acted like my friends when I didn't really know them." [A16] Significant others also provided the support needed to self-manage for a few AYA: "My girlfriend. She's there for me and she's always the one hanging out with me every weekend, yeah. She kind of keeps me going." [A11]

Family. Family, particularly caregivers, were essential to the self-management process. For some AYA this was evident in the way they distributed care activities, in others they were primarily a source of social support.

> **"**Oh my gosh my family is everything I don't know what I would've done without my parents. Jeez. Um, they um now they're my safety net but before they had to do everything for me. I mean they had to cook for me, they had to clean my sheets, they had to clean for me, I couldn't. I wasn't allowed to do any of that at first, and I was too tired to do a lot of that at first. And um, my dad quit his job for the fall just to stay home and take care of me, just to make sure that I got to my appointments because I couldn't drive,

like I don't know what I would've done without them. I can't imagine doing this when you're independent so they were definitely, definitely a rock" [A1]

Healthcare Providers. Healthcare providers were essential to the self-management process by providing information and education, but also served in other roles as well. Nurses in particular, occupied more of a social role for many participants. For an extended period of time, while participants were isolated, inpatient and home care nurses were often the only social contact aside from immediate family for AYA. "My nurse was my only person, maybe a few like, my grandparents, but besides that, that was really all I had socially." [A15]

"Like the nurses, when I was inpatient, I really liked them. They helped me a lot. Uh, just, they were more than nurses to me, they were kind of my friends at that point. Someone to talk to and tell jokes to and just, mm, I kind of miss them." [A13]

"But [the nurses] helped us, the nurses were sooo good, we loved every one of them. We wanted to take them home with us every one of them, that's how good they were. Couldn't ask for nobody better, that made the biggest difference I think, is the nurses." [C16]

Survivors. Some families sought out or met along the way, survivors who shared their experience in treatment and self-management with participants. Those who went before, helped families to understand what to expect, AYA to validate their experience as "normal," provided peer pressure to follow self-management recommendations, and hope that they will be able to get through it too.

"And I had a friend who had a bone marrow transplant in like 2011 or 12 here and she helped me. I would always remember it. I would IM her just while I was in the hospital

just asking her these questions like, did you have these symptoms? Why am I doing this? She would help me all the time." [A12]

A few participants, AYA and caregivers, were able to serve in this role to another who was going through the transplant process:

"There was a young lady there…who also had [diagnosis], who just had a transplant who was having a hard time. [A13] went over with [care manager] to talk to her to tell her, 'you know, there's an end to it, to just take it just take it one day at a time, eventually you're going to get there.' He said 'Just look at me. Two years ago I didn't think I would be where I am right now.'" [C13]

"A counselor at his school, her young son, who was just in pre-school, needed a transplant, and, uh, they found a donor. And I reached out, you know everybody's different, I reached out to her and said, if you need anything let me know and I left it at that. And she did email me with a slew of questions and I answered them." [C11]

Flying Monkeys and Poppy Fields

Flying monkeys and poppy fields were setbacks that side tracked Dorothy and her companions from their end goal to self-manage and return to normal. AYA and caregivers described setbacks and outside life events that took them off the path to recovery or caused added stress that at times required intervention. Some AYA described blocking out everything to escape the process.

Blocked It Out. Some participants, AYA more so than caregivers, blocked out the experience as a protective mechanism.

"We would try to schedule the transfusion around the Survivor so I could be kind of distracted from it. And it was only an hour transfusion, so it worked really well, honestly.

> And I would just, I would kind of be more calm about it, and I was, I wasn't really focused on it, I mean, I remember multiple times where I was like, oh, it's done. Like I didn't even remember seeing that it was going or something like that. And it was a good way to kind of block out what was actually going on." [A15]

Some caregivers blocked out the experience as well which sometimes had a negative impact on interpersonal relationships. "It has also put a huge strain on our marriage, we are actually separated now. . . [Husband] never really accepted it and just kind of avoided everything that was going on." [A5]

Setbacks. At times AYA experienced setbacks, like infections or complications that required further monitoring or hospitalization. One mother describes how experiencing setbacks affected her emotionally:

> "It was like that frightening feeling was back instantaneously. So along the way there were times that it would be like that, like all of a sudden we'd be right back in the, where we were in the beginning." [C15]

Outside Life Events. Many participants talked about extraneous life events that compounded the stress of going through transplant and managing their care. A few families had a parent lose a job prior to diagnosis, some had to give up jobs to stay with their child, while others had to go to work to keep insurance and financial support while their child was hospitalized. One mother broke out in shingles while her son was inpatient and described how difficult it was to be away during this time:

> "I could call the hospital to check on [son], which for me that was a really big relief, um but once I got better . . . and could come back I was really happy that I could go back and

see him, but like I told the doctors, I didn't want to put [son] or any other child that was in the hospital in any danger." [C14]

Another mother had just gotten married the month prior to her son's diagnosis, which put strains on the new marriage:

"Having a new person in the house and then having all of this going on with the illness, then having to spend all of that time in Cincinnati when you're just recently married, and 'Oh I'm gonna take off and be gone all during the week for the next four months.' It was not easy." [C13]

The Great and Powerful Oz

The Great and Powerful Oz was supposed to have all the answers on how to get home, but ultimately the power resided with Dorothy. In SCT, families are given advice, education and help to get through the process but the power to follow through with care management rests with the patients and their families. Participants described the power to get through SCT as having a fight mentality, a positive attitude, and setting goals or motivators.

Fight Mentality. All the participants in this study described the importance of a positive attitude and an "all in" mentality to getting though the transplant experience. One AYA put it this way: "Just don't stop fighting I guess, because when you stop fighting then it's over with, done. But if you keep fighting there's always a chance it could get better." [A11]

Positive Attitude. Positivity was important as a personal trait but also in those who supported AYA and caregivers during their journey on the yellow brick road. As one AYA said:

"Stay positive, that is so important, and it's going to be hard and that's where other people come in. When you can't, let them help you get positive, cause that's the only way you're going to get through this is if you're positive. And you look at things in the light.

> You know, don't step into the darkness and stay in fear and you know wallow in the shadows. You want to come out into the light, you want to let everyone know, you want to talk to people, you want to interact with as many people and as many supporters as you can because that's going to help you. And that's where the real healing comes from." [A20]

Setting Goals and Motivators. Although most families were initially shocked by the diagnosis and reliant on others to help them make decisions and take action, ultimately they realized that the power to "go home" and be "normal" resided within. Many AYA set goals and motivators to help themselves move forward on the yellow brick road of self-management. As one young adult put it: "I have a goal, and I want to reach that goal, and that's all that really matters to me right now." [A7] Another young adult shared:

> "It's really important to have things to come home to that motivate you. Cause I'm kind of a materialistic person, some people aren't like that, but I like my toys, and that was a big thing for me. I wanna go home and play." [A20]

Waking from a Dream

When Dorothy wakes from her dream she finds herself home but changed from her experience. Life has returned to normal but she has a new awareness of herself and the people around her. Participants described a similar phenomenon many called the "new normal." Some participants, particularly AYA, also described a change in life philosophy or lifestyle after treatment. For many this included a new appreciation for life and health they gained through managing their care.

"New Normal." The families described the process of returning to "normal." For the majority of AYA, normal consisted of returning to life activities such as school or work, being

with friends, and the ability to go outside without isolation precautions. A few AYA did not perceive much had changed from prior to transplant. As one participant said, "I might have had a little detour for a while, and I dealt with that, and thankfully I overcame it, and I feel like I'm kind of pressing the play button again on my life." [A15]

Other AYA felt they were normal but a "new normal," which was different from life previously or those in their peer group. "Me being normal and life now is not like normal for other people." [A20] "New normal" was characterized by some personal change either in physical health or life philosophy. For some this meant growing apart from friends or having different priorities from their peer group.

> "Um, it's hard to go out with my friends cause I can't drink and I had just turned 21, and that was like something I was looking forward to, like going out and being able to go to bars. Yeah, so I don't get to go out with them so I miss a lot of time hanging out with my friends. Cause I don't want to sit in a bar, I just want to have like a girls' night like we did in high school, but they don't want to do that they want to go to the bars." [A7]
>
> "So I found that it was really hard for friends to come up, like, on a Friday night and hang out with me, because they were so sucked up in the world of like, oh dude, no there's this going on tonight, or this concert or whatever, or this person was having a birthday, and so, I think it was less of me being able to relate to them, cause I mean, deep down, if nothing had ever happened to me, I would be right there with them. Um, but it definitely changed my perspective on me finding that important, and also I think, they struggled to get to where I was, where I was like, why don't we hang out this Friday night and watch this movie or something?" [A19]

Change in Life Philosophy. AYA discussed how the process changed them, most often for the better. “I think I’ve changed a lot since transplant just as my own self, which I think has changed how I communicate and talk to other people now. I think that has changed.” [A13] Another said, “I feel like I’m so much more different than I was before. I prefer this me than that me, it’s weird. Cause this whole experience really opens your eyes really, especially at this age.” [A12] For some AYA it also gave them a new appreciation for life:

> “Through everything I’ve been through, I wouldn’t change any of it because it’s brought my relationship with my family closer and then it’s brought mine and God’s relationship a whole lot closer.…Before I never really looked at what I had in life, and I took a lot of stuff for granted. And now I don’t take anything for granted! I take it day by day, and I live my life the way I want to live it, I don’t live to please others.” [A14]

DISCUSSION

In this sample of AYA and caregivers, self-management of the care regimen was indistinguishable from the treatment experience. The Pediatric Self-Management Framework (Modi et al., 2012) was initially used to develop interview questions with the assumption that patients and families would associate self-management with health behaviors, the complexity of the care regimen, and adherence to prescribed protocols. Although all AYA and caregivers discussed health behaviors, the care regimen and adhering to protocols, the psychosocial aspects of managing the care regimen emerged as a major factor for this population.

Isolation and being separated from family and friends was a theme that ran throughout the treatment process. AYA and caregivers indicated that self-management was difficult from hospitalization to going home because of isolation and separation. Having to avoid social activities, having goals of returning to school, and spending time with friends were challenges to

AYA self-management. Isolation was also associated with feelings of fear and anxiety when linked to the possibility of getting an infection or being re-hospitalized. Monotony was also associated with isolation and several AYA recommended having activities to occupy time such as movies, video games or schoolwork. Isolation has been a theme in all research into the lived experience of SCT, both pediatric and adult (Jones et al., 2011; Lewis et al., 2013; Manning et al., 2013; Moody et al., 2006). Future research and interventions with AYA going through SCT should incorporate components that address isolation and social support.

Every adolescent and young adult participant talked about having a positive attitude as necessary to get through the transplant process. Several AYA, as well as caregivers, mentioned the effect of SCT on mental health and the need for more mental health and social services, particularly those that address depression, fear, anxiety, stress, and distress. The majority of participants got social support in some form either from friends, family, or healthcare providers, particularly nurses, who they saw more as friends than healthcare workers. All of the male AYAs used video games such as Xbox live to connect with others "on the outside." Incorporating technology and gaming into interventions and future research could be useful for this population.

AYA and caregivers used milestones to mark progress and motivate themselves to continue self-management strategies. The removal of isolation restrictions was often a turning point or milestone, where they were able to look forward and start to think about moving towards "normal." Normal was often similar but changed from prior to transplant either because they were still managing some aspect of their care or because they were somehow changed from the process.

Each family had a unique established routine for organizing and administering medications and other care activities using the discharge instructions as a guide. Monitored

adherence rates for the small subpopulation of this study were also higher than most published literature for SCT and AYA. During interviews, the entire sample of AYA self-reported high adherence to the care regimen. While self-report often lacks reliability, the corroboration of patient and caregiver self-report in this study may have increased reliability. In fact, patients and caregivers in this sample often acted as back-ups or reminders for each other in medication adherence.

Limitations

There are several potential limitations for these findings. The study sample was small and purposeful, in concordance with grounded theory methodology, and taken from a single Midwest metropolitan pediatric cancer center. While findings may not be generalizable, the SCT experience and process of self-management may be transferable to other AYA receiving SCT at similar institutions. Participants were also asked to retrospectively reflect on their experience, which may lead to a recall bias. The sample size for oral medication adherence was small which limited statistical analysis. There is also a potential Hawthorne effect because patients knew that the research team was monitoring their medication taking behavior. Participants who participated in oral medication monitoring had an average 95% adherence which is higher than most existing literature with this population, with the exception of Hoodin (1993). Adult study participants in a previous study had an average adherence rate of 94.7% by self-report (Hoodin, 1993). McGrady, Williams, Davies and Pai (2014) electronically monitored oral medication adherence for AYA SCT patients and reported a 73% overall adherence rate. Due to variations and adherence rates for this population, more research is needed in self-management and adherence with larger samples, including both quantitative and qualitative research methods.

CONCLUSIONS AND IMPLICATIONS

This grounded theory study developed a framework of self-management for AYA following a SCT. Initially participants experience a tornado of activities, decisions, and emotions as they get diagnosed and move through the treatment process. Along the road adolescents and caregivers completed care regimen activities including medication management in a methodical way by sticking to the yellow brick road. Nurses were an integral part of the healthcare team and played an instrumental role in AYA self-management practices by providing information, education, and social support. Having an up-to-date medication list was also necessary for medication organization and administration. As participants recovered from their experience they found a "new normal" and often a change in life philosophy.

Informational support and education on the care regimen was important at all stages of the transplant process. The discharge summaries with medication administration information were used by all families for organization and medication management. Mental health services and treating the patient holistically were also noted by a subset of the sample as areas for clinical improvement. Nurses are involved in each of these care activities and have an opportunity to significantly improve care to AYA going through transplant.

Further research is needed on the applicability of the self-management framework to other AYA going through transplant, particularly more diverse populations. While families discussed managing their care regimen activities, they eventually developed routines that got easier with time. Adherence measures should be incorporated into clinical practice and future research to better understand how self-management and adherence to medications and protocols affects health outcomes. Psychosocial issues were more prominent in the self-management process and should be addressed in future research and interventions with adolescents, young adults and caregivers.

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Table 1. Sample adolescent and young adult interview guide questions

Individual
Can you describe a typical day since you have been discharged from the transplant unit?
What was your role during the transplant process?
Was there anything that helped you manage your care?
Family
What role did family have in your care management?
How did your relationships change as a result of going through the transplant process?
Healthcare System
What was the role of healthcare providers in your care management regimen?
What advice would you like to give healthcare providers based on your experience?
Community
Were there resources outside of the hospital environment did you use to manage your care and how did you find out about them?
Is there any advice you would like to give other adolescents and young adults who are going to go through transplant?

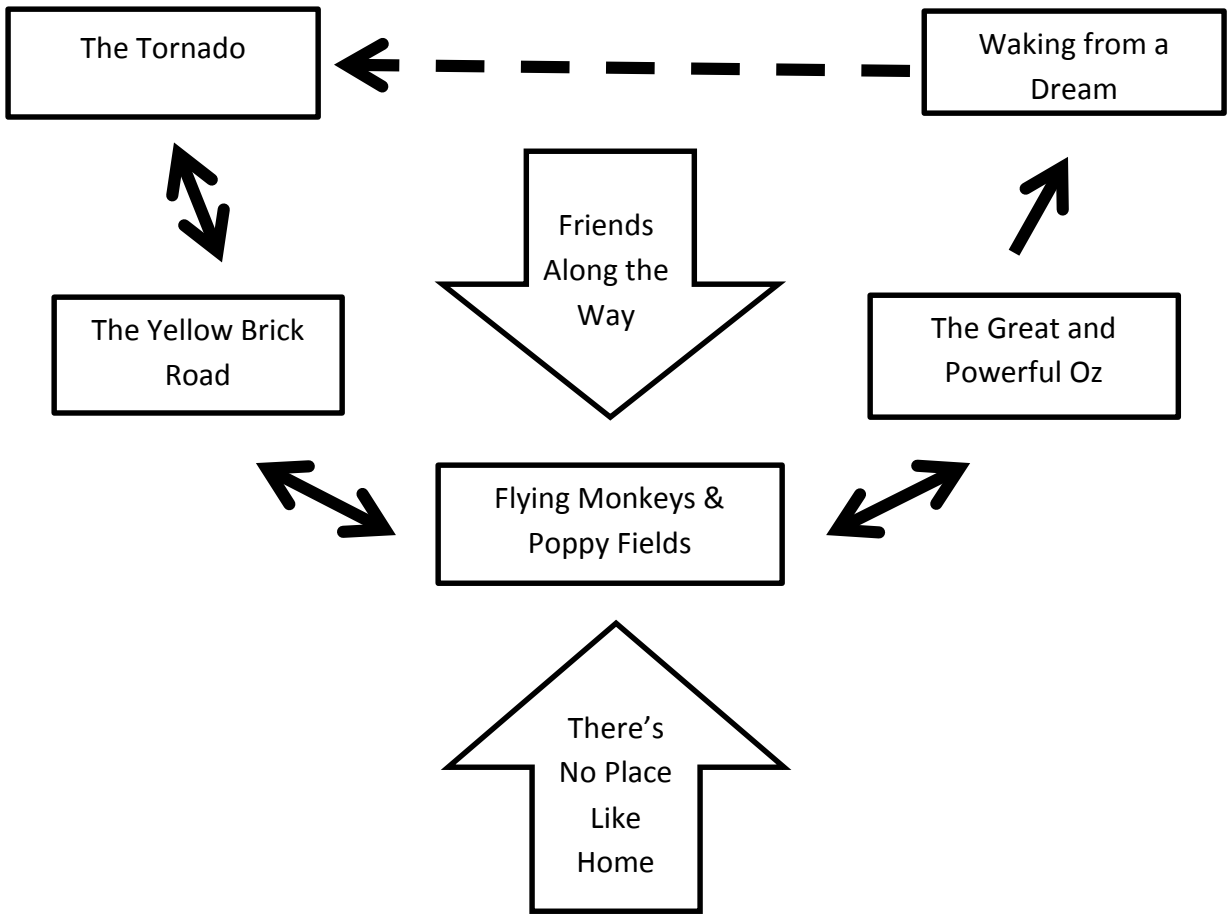
Table 2 Adolescent/young adult sample demographics.

Demographic Characteristic	AYA (n=17)
Female	35.3 (n=6)
Average Age at SCT	18.5
Range	(13.02-22.3)
Average Age at Interview	20.08
Range	(14.32-25.26)
Average time elapsed since SCT (years)	1.58
Range	(0.18-4.24)
Primary Diagnosis Receiving SCT	
Oncologic	58.8 (n=10)
Immunologic	17.6 (n=3)
Hematologic	23.5 (n=4)
Type SCT	
Autologous	35.3 (n=6)
Allogeneic: Matched Sibling Donor	29.4 (n=5)
Allogeneic: Matched Unrelated Donor	35.3 (n=6)

Table 3. Caregiver sample demographics

Demographic Characteristic	Caregiver (n=13)
Female (%)	69.2 (n=9)
Average Age at Interview	49.62
Range	(45-58)
Relationship status	
Single	7.7 (n=1)
Married	92.3 (n=12)
Highest level of education completed	
High School	7.7 (n=1)
Some College	15.4 (n=2)
Vocational	30.8 (n=4)
Graduated College	46.1 (n=6)

Figure 1. Framework for adolescent/young adult self-management following a stem cell transplant.



CHAPTER 6: MANUSCRIPT 3

Facilitators, Barriers and Recommendations for Practice on Adolescent and Young Adult Self-Management Following a Hematopoietic Stem Cell Transplant

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Abstract

Purpose/Objectives: Adolescents and young adults who experience hematopoietic stem cell transplant (HSCT) are at risk for self-management difficulties based on development, psychological co-morbidities, and the complexity of the care regimen. Recommendations for practice change were designed to address facilitators, barriers, and advice to healthcare providers on AYA self-management following HSCT.

Data Sources: Rossworm and Larrabee's Model for Practice Change was used to organize evidence based on participants' interviews (n=30) from a grounded theory research study into recommendations for practice change.

Data Synthesis: Participant responses were coded into categories, which were named with terms used by the participants. The number of participants who provided data per category was recorded.

Conclusions: Nursing practice should address ways to help with daily care regimen activities (like medication management), mental and emotional support, social support, and patient-provider communication.

Implications for Nursing: Self-management is generally characterized only in the ability to follow a prescribed care regimen. In this study, participants indicated mental and emotional experiences as a result of treatment were indistinguishable from self-management activities.

Nurses should assess and treat both the psychological aspects of treatment, as well as adherence to the prescribed regimen.

Keywords: hematopoietic stem cell transplant, adolescent and young adult, nursing, self-management

Every year at least 20,000 people in the United States are eligible for a hematopoietic stem cell transplant (HSCT), 1 in 5 are children, adolescents or young adults (Health Resources and Services Administration [HRSA], 2015). HSCT is a life-saving treatment that has a high risk of mortality with an overall survival rate of 50 to 60% (Pasquini & Zhu, 2015). The medication and care regimens that patients are prescribed are complex and, when not completed as prescribed, can have negative consequences, such as infection or disease relapse (Pasquini & Zhu, 2015).

Adolescents and young adults (AYA) are particularly at risk for nonadherence to treatment regimens due to normative developmental behaviors that may conflict with medical recommendations, such as achieving independence from parents, the importance of the peer group, and increased risk taking (Coupey, 2008; Radzik, Sherer, & Neinstein, 2008). AYA are also at increased risk for mental health disorders, such as depression and anxiety, which are compounded by illnesses like cancer (Kutcher & Chehil, 2008; Zebrack et al., 2014), and may interfere with self-management behaviors and adherence to the care regimen.

Although evidence of nonadherence and difficulties in self-management are documented in AYA cancer patients (Bhatia et al., 2012; Butow et al., 2010; Moore & Beckwitt, 2004; Mosher & Moore, 1998; Stinson et al., 2012), there is only emerging evidence on how AYA receiving a HSCT self-manage and adhere to prescribed medication and self-care regimens (McGrady, Williams, Davies, & Pai, 2014). This paper will address the knowledge gap by presenting facilitators of and barriers to AYA self-management following a HSCT, based on evidence from a grounded theory research study. Practice change recommendations will be made based on study findings using Rossworm and Larrabee's (1999) evidence-based practice model.

BACKGROUND

Model for Practice Change

Rossworm and Larrabee (1999) developed a model for evidence-based practice change. The model includes six steps: 1) assess the need for change in practice, 2) locate the best evidence, 3) critically analyze the evidence, 4) design practice change, 5) implement and evaluate change in practice, and 6) integrate and maintain change in practice (Larrabee, 2009). The steps are interconnected and allow for bi-directional movement as needs or new knowledge require re-evaluation.

Assess the Need for Change

Step one of the evidence-based practice process is to assess the need for change (Larrabee, 2009). Activities in this step include identifying stakeholders, collecting and comparing data on internal and external practices, and linking the problem to outcomes and practice changes (Larrabee, 2009). AYA have been shown to have difficulties with adherence to medication and isolation protocols following HSCT (McGrady, 2014; Phipps & DeCuir-Whalley, 1990). Adherence rates, meaning the number of times an activity is performed over the number of times prescribed (Modi et al., 2012), for this population range from 50 to 80% (McGrady et al., 2014; Phipps & DeCuir-Whalley, 1990). Bhatia et al. (2012) found that children with leukemia with oral chemotherapy adherence rates below 95% were twice as likely to relapse. Low adherence rates have been related to delayed treatment (Butow et al., 2010), disease relapse (Bhatia et al., 2012; Butow et al., 2010), graft failure (Dobbels et al., 2010), patient mortality (Ganesan et al., 2011; Kennard et al., 2004), and significant cost to the healthcare system (DiMatteo, 2004). Thus, the need for change in adherence rates and self-management by AYA after HSCT is crucial.

Locate and Critically Appraise the Best Evidence

The second and third steps in Larrabee's (2009) model are locating and critically appraising the evidence. Steps involved in these steps include identifying search criteria, conducting a systematic literature search, analyzing results, critically reviewing results, and creating a table of evidence (Larrabee, 2009). Literature reviews were conducted in AYA self-management and oral medication adherence during the acute phase of HSCT. The acute phase of treatment for HSCT includes treatment initiation and recovery, traditionally to day 100 post-transplant.

There is little evidence on adherence and self-management in AYA following HSCT. Although there are several risk factors for nonadherence mentioned in the cancer literature, such as depression (Kennard et al., 2004; Zebrack et al., 2014), unclear delineation of responsibility, and single-mother households (Malbasa, Kodish, & Santacroce, 2007), the only risk factors that applied to HSCT were adolescent age (McGrady et al., 2014) and symptom experience (Martin et al., 2012). In the self-management literature, AYA developmental needs and parental support were the main determinants in adherence (Karlsson, Arman, & Wikblad, 2008; Moore & Beckwitt, 2004; Stinson et al., 2012).

To address this gap in the literature, a grounded theory research study was undertaken to examine the process AYA use to manage their care following a HSCT. Following institutional review board approval, semi-structured interviews were conducted with 30 participants: 17 AYA who had a HSCT between the ages of 13 and 25, and 13 caregivers of AYA who had a HSCT (Morrison et al., unpublished data). During interviews participants were asked what was helpful or made it easier to manage their care (facilitators), what made managing care more difficult (barriers), and what advice they have for healthcare providers. Participant responses were coded into categories, which were named with terms used by the participants. The number of

participants who provided data in each category was recorded. The majority of participants responded with more than one facilitator, barrier and/or advice for healthcare providers. Tables 1, 2, and 3 display the percentage of participants and the number of responses for each facilitator, barrier and advice recommendation respectively.

Facilitators. Overall, facilitators fit into two categories: those that helped with the daily regimen activities, and those that helped mentally or emotionally. Facilitators of daily regimen activities were: a) organization of supplies and calendars, b) pillboxes to organize medications, c) education and supply delivery, d) baseline medical knowledge, e) AYA wanting to be involved in their own care, f) having good insurance, and g) access to the MyChart application. Facilitators that helped mentally or emotionally included: a) having a hobby, b) having a positive attitude, c) having a source of motivation, d) talking to a HSCT survivor, e) faith, f) acknowledging that you are not in control, and g) avoiding the internet for treatment information. Social support was also mentioned as assisting with both daily care regimen and psychological and emotional support.

Daily regimen facilitators. Organization of supplies, calendars, and medications were facilitators that helped with the daily self-management regimen for AYA following HSCT. Four participants specifically mentioned the pillbox as the major way in which they managed their medication regimen. Pillboxes were large, with multiple slots available for each day of the week, and filled weekly by adolescents or caregivers. Organizing supplies for procedures, such as central venous catheter care, helped families feel in control and prepared for managing their care. Supplies and medications were generally kept in one location throughout treatment.

Another facilitator that helped with the daily self-management regimen was the support that healthcare workers provided by educating patients and families on procedures and the care

regimen, and delivering supplies. Three AYA mentioned that healthcare workers who provided education and supply delivery were also a source of social support during their time in isolation. One caregiver was a nurse prior to HSCT, and felt having a baseline medical knowledge as well as an awareness of many of the medical procedures was helpful in managing her son's care. Another caregiver felt that having an AYA who was interested in being involved in his or her own care facilitated self-management of the daily regimen.

One caregiver mentioned the MyChart mobile application was helpful for getting updates on laboratory test results and outpatient clinic appointments. Having good insurance was also listed as a self-management facilitator by a caregiver. This caregiver defined good insurance as covering healthcare expenses and providing assistance navigating the healthcare system.

Mental and emotional facilitators. Having a positive attitude throughout the treatment process was a self-management facilitator. There were three main contributors to a positive attitude: a) making a personal decision to have a positive attitude, b) gaining positive attitude from family and friends, and c) gaining a positive attitude from healthcare providers. Several participants mentioned that having a positive attitude was not only a self-management facilitator but also aided in the healing process.

In addition to having a positive attitude, having a hobby to pass the time was mentioned by five participants as a self-management facilitator. Hobbies mentioned by AYA included video games, remote-controlled planes, shooting guns recreationally, playing musical instruments, and art projects. Motivators, both physical and mental, were also useful in keeping a positive attitude and looking towards the end of treatment. Physical motivators were usually gifts or rewards, and often had to do with hobbies. For example, one AYA received a remote-controlled airplane to fly in the park when he was able to go outside as a motivator and a reward for completing a phase in

treatment. Two AYA mentioned “keeping the eye on the prize,” or knowing continuing with treatment will only benefit them and to focus on treatment being a temporary but necessary phase of their life.

One caregiver said acknowledging that he was not in control and having faith in God were two facilitators that helped him mentally and emotionally so that he could care for his family. Before he gave up control, he felt stressed, overwhelmed, and experienced anger that prevented him from effectively participating in support and care activities. This same caregiver also mentioned avoiding the internet due to the overwhelming amount of information and not knowing what to trust. Instead, he relied on the healthcare team to provide information from trusted sources. One AYA mentioned that talking to an AYA HSCT survivor was helpful in confirming experiences as typical during the treatment process. The AYA survivor also provided encouragement and peer reinforcement to adhere to isolation guidelines.

Social support. Nearly half the sample viewed social support from friends and family as a self-management facilitator. The primary caregiver was an essential source of support for AYA participants. Social support from hometown communities was helpful and a stress reliever. Communities provided resources families needed to function such as meals, fundraisers or financial assistance, help with well-sibling activities, and encouragement in the form of cards and letters.

Barriers. Barriers to self-management fell into two categories: those that hindered daily regimen activities, and those that hindered mentally or emotionally from engaging in care activities. Barriers that hindered daily regimen activities included: a) experiencing physical symptoms, b) being essentially a single parent, c) difficulties with the medication regimen, d) bad experiences with home care, caregiver returning to work, and e) having little disease

information available to guide treatment and care delivery. Barriers that affected participants mentally or emotionally and hindered their participation in the care regimen included: a) extended isolation, b) monotony, c) experiencing psychological symptoms, and d) having a bad attitude.

Barriers to daily regimen. As a result of treatment, about one-third of the AYA in this study reported experiencing physical symptoms that affected their ability to manage their own care, at least initially. Physical symptoms AYA experienced included weakness, fatigue, pain, and nausea. Fatigue and weakness were considerable and affected the AYAs' energy levels and their ability to complete activities of daily living, such as bathing and walking, without assistance. Nausea affected the AYAs' ability to eat and take medications. Several AYA experienced pain, such as mucositis pain, that affected their ability to eat, or joint pain that prohibited certain physical activities.

Being the lone caregiver and essentially functioning as a single parent, was also a barrier to self-management. About one-third of caregivers shared experiences about difficulties they faced as the only caregiver. Experiences ranged from difficulty taking breaks to refresh, leaving a sick adolescent unattended to go to the grocery store since the child could not be in a crowded environment, and the strain of being responsible for all areas of care. One caregiver had to return to work after her son was discharged which required her to rely on her son to complete his own care activities. Not only did this hinder her ability to participate in the daily regimen but she also had to give up some control and trust her son to follow the care regimen.

Three participants listed difficulties with the medication regimen as barriers to self-management. Difficulties with medications included frequent changes in medications or dosing that were confusing and interrupted their system of organization, large pills that made

swallowing difficult, and resistance from the adolescent that affected timely medication administration. Two participants talked about bad experiences with home care. In both cases, participants indicated that home care nurses were not knowledgeable about a device or machine that left them with feelings of uncertainty and fear. Having a child diagnosed with a rare cancer meant there was little information available to make decisions and upon which to base the care regimen. Participants initially experienced feelings of uncertainty and fear, that led to trust in the healthcare team's knowledge and experience to prescribe effective treatments.

Mental or emotional barriers. Nine participants felt that going through HSCT affected their mental health in such a way that it became a barrier to self-management. Psychological symptoms participants experienced during treatment included depression, anxiety, fear, and post-traumatic stress syndrome. Two caregivers feared their son or daughter would harm themselves due to depression or distress. One caregiver was diagnosed with post-traumatic stress syndrome (Morrison, unpublished data). More than one-third of participants mentioned isolation from social support as a major mental and emotional barrier to self-management. One AYA felt he had a bad attitude as a result of being a teenager separated from his peers. Two AYA described the monotony of extended isolation as a barrier to self-management that contributed to isolation protocol nonadherence.

Advice to Healthcare Providers. Participants had advice for healthcare providers in three areas: a) effective communication, b) holistic health, and c) social support.

Effective communication. Effective communication incorporated interpersonal communication skills with how patients and families wanted information delivered. Seven participants wanted healthcare providers to be social and personable. These participants talked about needing more social support from healthcare providers since they were able to understand

what families were going through. Six participants said how important it was for healthcare providers to have a positive attitude when communicating to patients and families to keep spirits up and as a source of encouragement. Several AYA mentioned respect and treating them as adults and part of the team. One adolescent was suggested offering choices or options, such as type of central access device for treatment or if they want lidocaine prior to port access.

Participants also wanted healthcare providers to relay information in simple language, using age-appropriate materials, with consistency between providers. Two caregivers mentioned educational materials were age appropriate for parents with young children but did not have any tips for parents of teenagers who are testing boundaries. Another caregiver wanted an estimated rounding time for the healthcare team while inpatient to help her plan her day. One AYA felt her symptoms, particularly pain, could have been better managed with better communication between herself and the healthcare team.

Holistic health. Three participants specifically mentioned treating the patient holistically, acknowledging the body and the mind, medical treatment, and everyday life. As an extension of holistic health, five participants thought disease treatment was excellent but mental health treatment was lacking, and the stress and distress were not adequately addressed. Few participants received treatment beyond a prescription for an antidepressant. Anxiety, fear, distress, and depression was indistinguishable from self-management for both AYA and caregivers in this study (Morrison, unpublished data).

Social Support. Several participants discussed the need for more social services and support outside of healthcare providers. Participants felt social support services with peers or outside organizations would help to combat the isolation experienced during HSCT and would give families the opportunity to interact with others going through the same experience. One

AYA advised healthcare providers, particularly home health care, that assistance and advice in organizing supplies for would be welcome and helpful in planning self-management activities.

Design Practice Change

The fourth step in Larrabee's (2009) model is to design the change in practice. This is a planning step. A needs assessment, resource utilization, training, and sustainability plan should be incorporated into the design (Larrabee, 2009). Practice changes based on results from the study should maintain and encourage self-management facilitators, minimize self-management barriers and incorporate advice to healthcare providers.

Participants identified both facilitators and barriers in managing daily care regimen activities. Participants found it helpful to have a system of organization for supplies and medication, particularly a large pillbox. Frequently changing medication regimens and pill size were some challenges participants identified. Participants also identified education and information from healthcare providers as a facilitator. Interventions around medication management should incorporate education on the medication regimen, particularly when changes are being made. It would also be beneficial to do a check-in with patients to see if they are having any trouble with their regimen and offer suggestions on how to minimize identified problems. Establishing home health staff competency on patient care equipment would also be a meaningful intervention.

Interactions between healthcare providers and families should be respectful, positive, and informative. Families desired information to be presented in a way that was easily understood by laypersons, from a trusted source, and consistent across care providers. Information should also be available for different developmental levels. Practice changes that could be implemented are clustering care, developing educational materials for each developmental stage, and recognizing

that patients and families desire social interaction with healthcare providers. Families' desire to interact socially with healthcare providers may increase boundary crossings. Organizations should establish social media guidelines and train staff on appropriate social behaviors.

There were also facilitators and barriers in mental and emotional aspects of self-management for this population. Care should be holistic and take into account not only the patient's physical health and disease status but also mental health, social needs, and how medical care affects everyday life. A potential practice change participants identified includes incorporating mental health and psychological assessments and services into each patient's plan of care. Caregivers indicated this is an area where they struggle as well; consider having resources or services available to the entire family. The importance of a positive attitude both personally and in those providing support was evident in participant responses. It is important for healthcare providers to maintain a positive attitude while communicating with families and to find personalized sources of positivity and motivation for each patient.

Opportunities to socialize particularly with peers who have survived HSCT may be helpful for both AYA and caregivers. Isolation and monotony were identified as barriers and social support a facilitator to self-management. Finding ways to integrate socialization into care and activities particularly when patients are under isolation protocols could be helpful for patients and caregivers. Some suggestions include having Skype, Facetime or another social media outlet for socialization with family, friends, and school.

Implement, Evaluate, and Sustain

Steps five and six of the model involves implementing and evaluating the practice change and putting processes in place to sustain the change (Larrabee, 2009). These steps might involve pilot projects, cost projections, developing recommendations, disseminating findings, integrating

changes into standards of practice, monitoring fidelity to the practice change and outcome measurement (Larrabee, 2009). The literature on self-management practice and interventions for this population is minimal, so specific recommendations would be tentative and need further corroboration with future research.

Medication reconciliation has been identified as a National Patient Safety Goal (NPSG.03.06.01) by the Joint Commission (2015). Included in the National Patient Safety Goal organizations are to have an accurate record of medications the patient is taking and how they are taking them, the education the patient received about medication administration, and how this information is communicated between healthcare units and settings (The Joint Commission, 2015). As part of the medication reconciliation process nurses should not only ask what medications patients are taking and when their last dose was taken, but also if they think they have missed any doses in the last week and if so why (Pai & McGrady, 2015). These questions should be asked in an open and inviting way to encourage patient response. Honest feedback from patients is critical to finding a solution that works for each individual.

Research participants related how depression, anxiety, and fear drove their behaviors. AYA and caregivers in this study described being socially isolated and depressed which compounded symptom experiences of fatigue and generalized weakness. AYA are at an increased risk of having mental health co-morbidities while suffering from a chronic illness, which could affect daily functioning and their ability to manage their care regimen (Zebrack et al., 2014). For this reason, mental health screenings with both AYA and caregivers are essential to achieving early diagnosis and treatment (Kearney, Salley, & Muriel, 2015; Steele, Mullins, Mullins, & Muriel, 2015).

Evidence and practice changes should be presented to stakeholders, including staff involved at all levels of the practice change from leadership to bedside. Outcomes should be clearly defined and measured to understand intervention effectiveness on outcomes. Intervention fidelity should also be monitored to ensure outcome changes are due to the implemented intervention and not extraneous variables. Change agents or "super-users" may be helpful to assist staff in initial stages of implementation. The intervention should be cost-effective and sustainable over time, including adequate allocation of resources.

DISCUSSION

AYA and caregiver participants identified facilitators and barriers to self-management, and also advice to healthcare providers based on their personal experience. Based on these responses practice changes were suggested. The literature reinforces and expands upon many of the suggestions based on participant response. Nonadherence to care regimens has direct implications on nursing practice and organizational policy. Patient education, care coordination, bedside care, and initial triage and assessments are often included in the nurse's job role. Several of the proposed practice changes could lead to improved clinical practice, organizational policy change, and ultimately improved patient care.

Role modeling health behaviors to other healthcare professionals is seen as a hallmark of a good educator and mentor (Perry, 2009). Patients and families also rely on their healthcare providers to model healthy behaviors that they can reproduce in the home setting. Some of these behaviors are simple everyday activities that can be difficult for families to manage in the home setting, especially when caring for an adolescent or young adult. Examples include daily showers, reinforcing adequate nutritional intake, hand washing, and maintaining a clean

environment. Although these behaviors seem basic, they are the foundation of infection control practices.

Nurses can collaborate with patients and families in self-management by providing education throughout the care experience. Providing consistent easily understood information across disciplines, and repeating essential or pertinent information at each hospital encounter, helps to reinforce learning. Patient education can also lead to a short-term increase in medication adherence and improved health outcomes (Guevara, Wolf, Grum, & Clark, 2003; Phillips, Richards, Boys, Hodgkin, & Kinsey, 2011).

In addition to these suggestions, Roop and Wu (2014) suggested policies and procedures be developed to enable effective interdisciplinary communication. Communication between healthcare providers is essential to promote patient safety and coordinated care between providers. In order to ensure adequate time at the bedside for patients and family education, nurse-staffing models may need to be changed or developed.

IMPLICATIONS for NURSING

Changes in nursing practice were designed based on patient perspective and current literature. Self-management is generally characterized as the ability to follow a prescribed care regimen. In this study, participants indicated mental and emotional experiences as a result of treatment were indistinguishable from self-management activities. Nurses should assess and treat both the psychological aspects of treatment, as well as adherence to the prescribed regimen.

CONCLUSION

Recommendations for practice change were designed to address facilitators, barriers, and advice to healthcare providers on AYA self-management following HSCT. Evidence was based on participants' responses from a grounded theory research study. Practice changes designed to

address AYA self-management should integrate patient perspectives so they are applicable and relevant. All practice changes should be monitored for feasibility, fidelity, cost-effectiveness, and sustainability.

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Table 1. Self-Management Facilitators

Facilitator	% Participants (n=responses)
Helped with Daily Regimen	
Healthcare workers providing education and supply delivery	43.3 (n=13)
Pillbox	13.3 (n=4)
Organization	16.7 (n=5)
Baseline knowledge as a nurse	3.3 (n=1)
AYA wanted to be involved in care	3.3 (n=1)
Good insurance	3.3 (n=1)
MyChart	3.3 (n=1)
Helped Mentally or Emotionally	
Hobby/ Keeping busy	16.7 (n=5)
Positive attitude	10 (n=3)
Having a motivator	6.7 (n=2)
Talking to a survivor	3.3 (n=1)
Faith	3.3 (n=1)
Acknowledge not in control	3.3 (n=1)
Avoid internet for treatment Information	3.3 (n=1)
Social Support	
Friends and family	46.7 (n=14)

Table 2. Self-Management Barriers

Barrier	% Participants (n=responses)
Hindered Daily Regimen	
Physical symptoms	16.7 (n=5)
Nausea	
Fatigue	
Pain	
Single parenting	13.3 (n=4)
Difficulties with medication regimen	10 (n=3)
Bad home care experience	6.7 (n=2)
Caregiver returning to work	3.3 (n=1)
Rare cancer/ Lack of information	3.3 (n=1)
Hindered Mentally or Emotionally	
Isolation	36.7 (n=11)
Psychological symptoms	30 (n=9)
Post-traumatic stress syndrome	
Depression	
Anxiety	
Fear	
Monotony	6.7 (n=2)
Bad attitude	3.3 (n=1)

Table 3. Advice for Healthcare Providers

Advice	% Participants (n=responses)
Effective Communication	
Effective communication	63.3 (n=19)
Age appropriate materials	
Accessibility of HCP	
Treat patient with respect	
Consistency of information between HCP	
Offer options when possible	
HCP positive attitude	20 (n=6)
Estimated rounding times	3.3 (n=1)
Symptom management	3.3 (n=1)
Holistic Health	
Treat mental health	16.7 (n=5)
Treat patient holistically	10 (n=3)
Social Support	
Offer social support services	13.3 (n=4)
Assist organizing supplies/ Planning self-management activities	3.3 (n=1)

Note: Abbreviation. HCP= healthcare provider

Appendix A
Articles Included in the Literature Review

Table 3. Articles Included in the Literature Review

Citation	Methodology	Sample	Measures	Results	Implication
AYA HSCT Adherence					
Phipps, & DeCuir-Whalley, (1990).	Descriptive retrospective with chart reviews and case summaries	N=54 Ped HSCT-inpatient 1986-1988 1 month- 20 yrs (Average 9.1 yrs) 2/3 white, 1/3 Hispanic	Nursing diagnosis of noncompliance Chart review for evidence noncompliance behaviors	Significant adherence difficulties n= 28 (52%) 100% difficulties with oral antibiotics (abx) adherence 5 (10.8%) adherence difficulties with additional activities (baths) >2 yo at risk for non-compliance: overall 52% adherence problems ✓ 2-6 yo= 73% adherence problems ✓ 7-12yo= 82% adherence problems ✓ >12yo=40% adherence problems	New model for BMT that combines acute and chronic care issues Subjectivity in charting may have compromised data ✓ Unsure why >12 yo had lower compliance problems when typically this age is highest ✓ Parent's role in pediatric adherence
Martin et al., (2012)	Phase II randomized double-blind placebo-control study	N=138 Drug (n=92) Placebo (n=46) HSCT patients Age range: 8-63	Presence of acute graft versus host disease (aGVHD) by chart review Adherence measure not reported (NR)	Hypothesis that drug would decrease incidence aGVHD rejected >90% adherence associated with reduced mucositis severity Overall adherence started 94% and decreased to 65% over time	Symptom experience associated with chemo and mucositis accounted for some NA Adherence decreased over time

				40% of pts took study drug full course, 33% of placebo group took full course >90% adherence during 1st month following HSCT was seen in 53% of study arm, 57% placebo >80% adherence during 1st month following HSCT was seen in 62% of study arm, 72% placebo	
McGrady, Williams, Davies, & Pai, (2014).	Case study of Longitudinal prospective Time points 1-, 3-, 6-, and 9-months	N=6 Ped HSCT-outpatient Ages 12-18	Medication Event Monitors (MEMS™)-electronic pill bottles Immunosuppressant and oral antibiotics Chart review	Took 73% prescribed doses Ave #doses/month ranged 40-91% and decreased over time. 91% at 1-month to <60% at 6-months Mean average perfect adherence 56% Failed to take all doses 13% days Average days interrupted/ week= 3	Limitations: small sample size 3 patterns of adherence: high-sustained, variable, and delayed non-adherence Adherence patterns similar to other pediatric populations
AYA Cancer Adherence					
Smith, Rosen, Trueworthy, & Lowman, (1979)	Longitudinal prospective over 16 months	N=52 ALL, AML & non-Hodgkin's	Hemoglobin Weight change	59% of adolescents (over 11 yo) were NA to prednisone therapy, 18% under 11 yo were NA	3 levels of adherence: adherent, partially adherent, and non-adherent

		lymphoma Ages: 6 mos-17 yo	Urine assay of 17-ketogenic steroid	Small group (8/11) had lab value close to therapeutic and were classified partial compliers Hemoglobin and weight change poor NA prognostic value	Adolescents higher nonadherence than pediatric sample
Tebbi et al., (1986)	Longitudinal	N=46 pediatric & 40 parents ALL, Hodgkin disease, non-Hodgkin's lymphoma, other Age range 2.5-23	Self-report Blood bioassay	Adherence decreased over time (Range 18.8-39.5% overall NA) Adolescents less compliant than pediatric patients Forgetful, busy schedule, and not having medication available were reasons for NA	3 categories non-adherers: no misses, occasional misses, frequent misses.
Ellis et al., (1992)	Retrospective chart review	N=49 Cancer diagnosis Age range: 11.5-18 years	Chart review	21% overall NA 3 categories: adherent, delayed/ modified adherence, drop out/ refused Reasons for NA were drug side effects, social variables, or psychological variables	
Festa, Tamaroff, Chasalow & Lanzkowsky, (1992)	Cross-sectional descriptive	N=29 in prednisone adherence group Prednisone group Average age 15.6 (±2.2)	Prednisone: blood assay dehydro-epiandrosterone sulfate (DHEA-S) levels PCN: *Micrococcus luteus* urine bioassay	Prednisone adherence: 52% (11/21) nonadherent, 48% (10/21) adherent 14/21 patients available for evaluation 3-6 months following initial sampling and no change to nonadherence group	NA group remained NA over time Overall adherence 48-52% for this sample of patients Tamaroff, Festa,

		N=21 in Penicillin (PCN) adherence group PCN group Average age 19.1 (±4.1) ALL & Hodgkin disease outpatients		PCN adherence: 48% nonadherent (14/29), 52% adherent (15/29)	Adesman, & Walco (1992) examined psychological predictors and found realistic conceptualization of illness and vulnerability to illness were predictors of adherence for 34 AYA (12.9-25.6 yo) of original sample
Davies, Lennard, & Lilleyman, (1993)	Cross-sectional	N=22 ALL Children and adolescents (no ages given)	Blood bioassay Structured interview	6/22 variable blood metabolite levels- of 6, 2 reported NA in interview, both adolescents Estimated 1 in 5 children with ALL not taking 6-MP as prescribed	
Lau, Matsui, Greenberg & Koren, (1998)	Longitudinal	N= 24 youth, ALL maintenance phase 2.6-17.2 years (mean age 7.3 years)	MEMS^{TM} monitoring oral Mercaptopurine (6-MP)	≥95% adherence in 42% sample (10/24) ≤90% adherence in 33% (8/24) ≤80% adherence in 17% (4/24) 8/24 adherence variable morning vs. evening with 5/8 more adherent in evening	Time of day may be an influencer on adherence
de Oliveira, Viana, Zani & Romanha, (2004)	Cohort	N= 39 youth, 6 were ≥10 years ALL	Parent interview Medical chart review	53.8% (21/39) NA by at least one method Self report only identified 6	Self-report may not provide accurate adherence data

		maintenance	6-MP metabolite assays	In-depth medical history identified majority	
Kennard et al., (2004)	Cross-sectional	N=44 adolescent cancer patients Age range 12-17	Blood bioassay for trimethoprim/ sulfamethoxazole Self-report of parent and patient	27% no drug level on bioassay NA higher depression, lower self-esteem, higher parent-patient incongruence 6-year survival lower for NA group	NA has links to psychological co-morbidities Survival lower for NA group
Malbasa, Kodish & Santacroce, (2007)	Qualitative Focus group	N=6 ALL 16-23 years old, mean age 19.2	Focus group	<u>Themes:</u> *Normalcy* Child normal in home setting Medication made "not normal" among peer group Inability to participate in activities made "not normal" but desire to fit in with peers Some saw treatment as a temporary normal *Egocentrism* Engaging in risk-taking behavior negatively affected adherence Isolation from peer group increased egocentrism *Concrete thinking* Did not connect long-term consequences of NA Did not see immediate effect of	Adolescent development played a large role in AYA adherence especially in cognitive/ decision making skills and egocentrism and inability to see consequences for behavior

				NA in labs or health *Parental support* Key to adherence, especially mothers Unclear delineation of roles- most parent prepare and/or administer pills but some transitioning care to adolescent	
Lehrnbecher et al., (2008)	Prospective cohort	N=216 Leukemia/ lymphoma (148), solid tumor (63), no disease info given (5) Age range 1 month- 27 years (mean 8 years old)	Questionnaire with self-rated adherence and 6 factors that may affect adherence such as education available Adherence rated using Morisky self-report measure on diet, face mask in public, mouth care, antibiotics, PCP prophylaxis, systemic antifungals	Adherence rates: Diet (89.3%) Mouth care (88.2%) Use of PCP prophy (86.6%) Antifungals (73.9%) Reasons for NA: Forgetfulness (25.9%) Refused medication (25.5%) Previously experienced adverse effects (11.1%)	Overall compliance correlated significantly with younger age and belief in efficacy of recommended measures
Pai, Drotar, & Kodish, (2008)	Longitudinal	N=51 ALL Age range 12-19 (mean 15)	Blood bioassay for 6-MP metabolites Self-report	45% NA by self-report Reported missing doses average 2 days/ week 53% NA by bioassay	Self-report related to bioassay results
Hawwa et al., (2009)	Cohort	N=19 ALL receiving 6-MP	Blood bioassay Morisky self-report measure	<u>Self Report</u> Adherence decreased over time 26.3% of patients had at least one aspect of NA	Adherence decreased over time While bioassay did confirm NA in several

		Age range 3-17 (mean 10)		15.8% classified NA Reasons for not taking medications were: "careless at times about taking medication" (80%) and "forgetfulness" (60%) Higher age was correlated with NA <u>Bioassay</u> 5 (26.3%) classified NA by bioassay, 2 of which were also classified by self-report	patients, it can be costly and time consuming. In assessing adherence, self-report may be a cheaper and effective measure unless bioassay is needed clinically
Landier et al., (2011)	Grounded theory	N=17 patients, 21 caregivers Age range 6-28 at time of study	38 semi-structured interviews 4 focus groups	3 stages in process of adherence: a) *recognizing the threat*, b) *taking control*, c) *managing for the duration.* Parents making sure medications were taken as prescribed- *Doing our part.* Mediating adherence behaviors was *Making the connection*- understanding how adherence to medication affects curing leukemia	Making cognitive connection between medication and long term disease consequences mediated adherence The process involves recognition and taking action with commitment Each of these are developmental barriers to adherence seen in other studies
Phillips,	Cross-	N=50	Pill count 6-MP	Adherence for 4 time points:	Initial increase in

Richards, Boys, Hodgkin, & Kinsey, (2011)	sectional over 2 years	ALL Age range 1-17		Time 1: 28%- education sent out on 6-MP and importance to adhere to prescription Time 2: 45% Time 3: 78% Time 4: 55%	adherence with information on importance to take as prescribed but decreased over time
Bhatia et al., (2012)	Longitudinal prospective	N= 327 ALL N=169 Hispanic, 158 non-Hispanic Age range: 1-19 years old	MEMS^{TM} monitoring oral 6-MP for 6 months	Adherence >95% was 2.5 times more likely to relapse 44% non-adherence Risk factors for NA were Hispanic ethnicity, age ≥12, single-mother household	Adolescents (≥12) were more NA than pediatric patients Relationship between adherence to 6-MP and risk of relapse established
Mancini et al., (2012)	Mixed methods	Interviews: N=31 parents children (<11) N=12 parents adolescents N=12 adolescents (11-17) N=9 adult patients (>17) ALL	Interviews Self-report questionnaires Physician evaluation of adherence	Nonadherence increased with age: Children (13%), adolescents (33%), and adults (44%) Often was not found by physician evaluation (15%) Intentional NA in 8% 12 adolescent-parent pairs had matching self-reported scores Forgetfulness and not feeling ill were 2 main reasons adolescents were NA	Adolescents and young adults higher NA rates Adolescent development attributed for some NA Parental support and management for children and adolescents was also noted as a facilitator for adherence

				Adults main reasons were forgetfulness and symptom experience	
Rohan et al., (2013)	Objective observational method, multisite	N=136 ALL & lymphoblastic lymphoma (LBL) Age range 7-19	MEMS^{TM} monitoring oral 6-MP for 1 month	Overall adherence 86.5% Medication gaps (>24 hours between doses): mean 3 days (range 0-31 days) 44.3% had adherence rates below 95% Adherence decreased over time	Adherence decreased over time 3 groups: optimal adherence, deteriorating adherence, chronic nonadherence
AYA Cancer Self-management					
Mosher & Moore, (1998)	Descriptive correlational	N= 74 children with cancer and their mothers	The Children's Self-Care Performance Questionnaire The Dependent Care Agent Performance Questionnaire The Piers-Harris Children's Self-Concept Scale Cosmetic and Functional Impairment Ratings Demographic Data Form	Small significant correlations between self-concept and both self-care and dependent care practices Age was only predictor: Older children had lower self-concept Higher self-concept had more self-care and dependent care provided by mothers	Self-concept is positively related to self-care
Moore & Beckwitt,	Qualitative using Orem's	N=9 children and 18 parents (14	Self-reported self-care practices according to	**Universal self-care requisites:** Parents cited food more than any	**Universal self-care requisites:** air, water,

(2004)	theory of self-care	mothers, 4 fathers)	Orem's self-care requisites	other requisite, the children sited normalcy the most **Developmental self-care requisites:** Parental presence promoting development and support was cited most by parents and children **Health deviation:** Diagnosis overshadowed future experiences, all participants discussed negative treatment effects but few how they controlled them, none mentioned how they managed prescribed measures or performing medical procedures apart from IV line care.	food, elimination, rest and activity, solitude and social interaction, hazards, and normalcy. **Developmental self-care requisites:** provision of conditions that promote development, opportunities to engage in self-development, and handling interferences with development **Health deviation:** securing medical assistance, being aware of the effects of illness, carrying out prescribed measures, dealing with negative effects of therapy, modifying the self-concept, and learning to live with pathologic conditions
Stinson et al., (2012)	Qualitative to determine needs of adolescents in disease self-management for program development	N=29 adolescents 12-18 years, N=30 parents, N=22 healthcare providers	Individual interviews Focus groups	<u>Themes</u> Disease knowledge and cancer care skills Knowledge and skills to support effective transition to adult healthcare	Incorporate into program development

				Delivery of adolescents with cancer-accessible healthcare services Supports for the adolescent with cancer	
AYA Chronic Illness Self-management					
Guevara, Wolf, Grum, & Clark (2003)	Meta-analysis of randomized or controlled trials	32 studies included N=3706 patients (2-18 years) asthma	Analysis included 32 trials for a sample size of 3706 patients between 2 and18 years old.	Educational programs were found to improve lung function, feelings of self-control, reduce school absenteeism, reduce the number of days with restricted activity, and reduce number of emergency department visits The effect on morbidity was greatest when the programs included strategies based on peak flow, focused on the individual, and in participants with severe asthma	Education programs are effective in improving disease management in children with asthma
Jedeloo, van Staa, Latour, & van Exel, (2010)	Q-methodology	31 adolescents (12-19 years) 16 male, 15 female 74% diagnosed chronic condition within first 5 years of life Netherlands	Semi-structured interviews and factor analysis of rank order of 37 opinion statements	4 profiles for healthcare delivery preference and self-management **Conscious & Compliant** (11/31, 7 male) High level of involvement in disease management Prefer to be treated "normal" Want to be treated like an adult and can resent parental involvement **Backseat Patient** (4/31, all female)	1/3 sample conscious and compliant profile In this sample the 2 less assertive or less involved profiles were composed of all female participants

				Less mature, lean more on parents to talk and manage care Not information or resource seeking Apathetic **Self-confident & Autonomous** (4/31, 2 male) No hiding behind disease, live with it Enjoying life now more important than adherence Do not require help from anyone, independent but may take advice under consideration Only profile that would change treatment if felt necessary **Worried & Insecure** (3/31, all female) Worried about disease Prefer to pretend nothing is wrong to prevent worrying Insecure, welcome information especially on sensitive topics Not opposed to support on disease management Do not want a say in transition to adult care Appreciate parental support	
Yang, Sylva, & Lunt, (2010)	Descriptive exploratory	N=86 adolescent (ages 9-14) and parent dyads asthma	Healthy Lifestyle for Asthma Management Specific Social Support: Asthma-	Healthy lifestyle associated significantly with medication level, asthma-specific peer support, asthma-specific parent support, and parent-reported	Social support plays a role in healthy lifestyle that is developmentally appropriate for AYA and important for

			Specific Peer Support and Parent Support Peer Acceptance Socioeconomic Variables and Medication level	peer acceptance	disease management
Riekert, Borrelli, Bilderback, & Rand, (2011)	Pilot feasibility of self-management program using motivational interviewing	N=37 African American adolescents (10-15 years) and their caregivers asthma	5 home visits with pre-post program <u>evaluation & surveys:</u> Self-reported adherence and knowledge of medication Adolescents asked motivation to take medication daily Readiness to change Questionnaire Child Asthma Self Efficacy Scale Asthma Responsibility Interview Pediatric Asthma Quality of Life Questionnaire	Baseline: 32% adolescents/ 46% caregivers report 100% adherence Post-intervention: 27% adolescents/ 62% caregivers report 100% adherence Medication knowledge stayed high and stable among both adolescents and caregivers Motivation and readiness to change increase statistically significant following intervention Self-efficacy increased but not statistically significant No significant pre-post differences in responsibility for treatment, but caregivers less likely to administer and adolescents more likely to	Adolescents reported increased motivation and adherence readiness Caregivers more likely to report 100% adherence and adolescents increased responsibility in their care at program completion than before

			Pediatric Asthma Caregiver's Quality of Life Questionnaire Symptom-free days	remember to take medications following intervention Adolescent and caregiver statistically significant improvement in QoL on all subscales 89% caregivers/ 76% adolescents recommended program to others	
Stewart, Emslie, Klein, Haus, & White, (2005)	Data from larger longitudinal study on adolescent adherence	N=111 adolescents (11-18 years) Type-1 diabetes	Self-report adherence Metabolic control was measured by HgbA1C	Parent and adolescent self-reported adherence were correlated to each other and HgbA1C levels Weak correlations between HgbA1C levels and healthy self-care behaviors such as exercise and healthy diet	Weak correlations between glycemic control and healthy behaviors may be due to time it takes to see results and potential to compensate negative behaviors by blood testing and insulin administration- may not see consequences for behavior in short-term
Karlsson, Arman, & Wikblad, (2008)	Phenomenology	N=32 adolescents (13-17 years) Type-1 diabetes Sweden	Interviews	Over all was **Hovering between individual actions and support of others** Under **Growth through individual self-reliance** was self-determination as a developmental process, psychological maturity creates	Autonomy and social support were important to self-management and transition of care

				possibilities for increased responsibility and freedom, and motivation increases with successful self-management Under **Growth through confirmation of others** was parental encouragement and understanding increases certainty of teenagers' standpoints, peers' acceptance facilitates incorporation in daily self-management activities, and support form diabetes team strengthens self-esteem.	
Rothman et al., (2008)	Cross-sectional survey	N=103 (ages 13-17) Type-2 diabetes	Chart review Semi-structured interviews with 2 previously validated subscales- perceived barriers to eating healthy and exercise	Mean A1C 7.7% and duration of Type 2 diabetes 2 years 37% following healthy diet and exercise recommendations most challenging aspect of care 31% perceived medication adherence most challenging ≥75% adherence was self-reported by 80% of sample and 59% of sample monitored blood glucose >2 times daily Reasons for noncompliance were lack of motivation and competing interests	Although reported good adherence, also reported many perceived barriers and negative behaviors

Appendix B
Quality Scores of Articles Included in the Literature Review

Table 4. Quality Assessment of Literature

Author(s) & year	Research question/ objectives/ hypothesis/ aims clear and appropriate	Clear overview of methods/ intervention and appropriate outcome measures	Sample size is given	Randomization used (quant)/ Recruit-ment adequately described (qual)	Attrition rate recorded	Data analysis adequately described and rigorous	Outcomes of intervention clearly described	Ethical issues suitably addressed	Total Score (max 8)
AYA HSCT Adherence									
Phipps, & DeCuir-Whalley, (1990).	1	1	1	0	1	1	1	1	7
Martin et al. (2012)	1	0.5	1	1	1	1	1	1	7.5
McGrady, Williams, Davies, & Pai, (2014).	1	1	1	0	1	1	1	1	7
AYA Cancer Adherence									
Smith, Rosen, Trueworthy, & Lowman, (1979)	1	1	1	0	1	1	1	1	7
Tebbi et al. (1986)	1	1	1	0	1	1	1	1	7
Ellis et al., (1992)	1	1	1	0	1	1	1	1	7

Festa, Tamaroff, Chasalow & Lanzkowsky, (1992)	1	1	1	0	1	1	1	1	7
Davies, lennard, & Lilleyman, (1993)	1	1	1	0	1	1	1	1	7
Lau, Matsui, Greenberg & Koren, (1998)	1	1	1	0	1	1	1	1	7
de Oliveira, Viana, Zani & Romanha, (2004)	1	1	1	0	1	1	1	1	7
Kennard et al., (2004)	1	1	1	0	1	1	1	1	7
Malbasa, Kodish & Santacroce, (2007)	1	1	1	1	1	1	1	1	8
Lehrnbecher et al., (2008)	1	0.5	1	0	1	1	1	1	6.5
Pai, Drotar, & Kodish, (2008)	1	1	1	0	1	1	1	1	7
Hawwa et al., (2009)	1	1	1	0	1	1	1	1	7
Landier et al., (2011)	1	1	1	1	1	1	1	1	8
Phillips,	1	1	1	0	1	1	1	1	7

Richards, Boys, Hodgkin, & Kinsey, (2011)									
Bhatia et al., (2012)	1	1	1	0	1	1	1	1	7
Mancini et al., (2012)	1	1	1	0	1	1	1	1	7
Rohan et al., (2013)	1	1	1	0	1	1	1	1	7
AYA Cancer Self-management									
Mosher & Moore, (1998)	1	0.5	0.5	0	1	1	0.5	1	5.5
Moore & Beckwitt, (2004)	0.5	0.5	1	0.5	1	0.5	1	1	6
Stinson et al., (2012)	0.5	0.5	1	1	1	1	1	1	7
AYA Chronic Illness Self-management									
Guevara, Wolf, Grum, & Clark (2003)	1	1	1	1	1	1	1	1	8
Jedeloo, van Staa, Latour, & van Exel, (2010)	1	1	1	0	1	1	1	1	7
Yang, Sylva, & Lunt, (2010)	1	1	1	0	1	1	1	1	7
Riekert,	1	1	1	0	1	1	1	1	7

Borrelli, Bilderback, & Rand, (2011)									
Stewart, Emslie, Klein, Haus, & White, (2005)	1	1	1	0	1	1	0.5	1	6.5
Karlsson, Arman, & Wikblad, (2008)	1	1	1	1	1	1	1	1	8
Rothman et al., (2008)	1	1	1	0	1	1	1	1	7

Note: Quality criteria adapted from Jinks, Cotton, & Rylance, 2011 (Scoring: 1= present, 0= absent, 0.5 partially present)

Appendix C

Study Flyer

The AMOC Study

ADOLESCENT AND YOUNG ADULT MANAGEMENT OF CARE

Who is eligible?

- Adolescents and young adults ages who experienced a stem cell transplant between the ages of 13-25.
- Caregivers of an adolescent or young adult who received a stem cell transplant between the ages of 13-25.

Why are we asking for your help?

We want to understand how adolescents and young adults who have received a stem cell transplant manage things like medications and clinic appointments after returning home from the hospital.

What is involved?

This is an interview based study. The interview will occur individually at least 1 month after discharge from the inpatient unit and will require 1-2 hours. We would also like to understand how you are managing your medications which may require 2-3 additional study visits that should take about 15 minutes each and can occur during regularly scheduled hospital visits.

Additional Information:

Patients and their parents have the right to refuse to participate or answer any question or withdraw from the study at any time without it affecting the care they receive at Cincinnati Children's.

To thank families for their important contribution, participants will be compensated for their time.

To participate or for questions/concerns please contact:
Caroline Morrison, Principal Investigator
AMOCTeam@cchmc.org, Office: (513) XXX-XXXX, Cell: (513) XXX-XXXX

Appendix D
Consent Documents

STUDY TITLE: ADOLESCENT AND YOUNG ADULT MANAGEMENT OF CARE REGIMEN POST STEM CELL TRANSPLANT

STUDY NUMBER: 2014-4754

FUNDING ORGANIZATION: DAISY Foundation

Caroline Morrison MSN, RN
Name of Principal Investigator

513-803-5165
Telephone Number

INTRODUCTION

We are asking you to be in a research study so that we can learn new information that may help others. If you decide not to be in this study, we will still take good care of you. If you decide to be in this study, you may change your mind at any time during the study and you can stop being in the study. Take all the time you need to make your choice. Ask us any questions you have. It is also okay to ask more questions after you decide to be in the study. You can ask questions at any time.

WHY ARE WE DOING THIS RESEARCH?

In this research study we want to learn more about children and young adults who have had a transplant and their caregivers manage doing specific things like taking medication and coming to clinic appointments.

We are asking you, other people who have had a transplant and their caregivers to be in the research, because we would like to better understand how children, young adults, and parents manage their care activities.

WHO IS IN CHARGE OF THE RESEARCH?

Caroline Morrison is the researcher at Cincinnati Children's Hospital Medical Center (CCHMC) that is in charge of this study.

WHO SHOULD NOT BE IN THE STUDY

You cannot be in this study if you have any of the following:

1. **You do not speak or read English**
2. **You or your child have not had a transplant between the ages of 13 and 25 (there is no age limitation for caregiver participants).**
3. **Your medical status or condition will not allow you to participate as determined by the medical team.**

WHAT WILL HAPPEN IN THE STUDY?

The research staff will explain each visit to you and may give you a handout that explains each visit in

more detail. You will be able to ask questions to make sure that you understand what will happen.

If you qualify and decide you want to be in the study, you will potentially have 4 study visits over the next 3 months.

These are the things that will happen to you while you are in the study:

You will participate in an interview. Patients and caregivers will be interviewed separately. Each interview will last 1-2 hours. After the interview if the young adult participant is on oral medication, they will be asked questions on what they know about their medications and their schedule.
If the young adult participant is on oral medications, at the first visit you will receive 2 pill bottles with caps called MEMS that will record when they are opened. You will use the bottles for 2 of your medications. The cap can be downloaded into a computer. The download will happen once a month and last about 15 minutes. After 3 months the pill bottle and cap will be collected.

WHAT ARE THE GOOD THINGS THAT CAN HAPPEN FROM THIS RESEARCH?

Being in this study may not help you right now. When we finish the study, we hope that we will know more about how children, young adults, and their caregivers manage their care activities after transplant and how medical professionals can provide better care. This may help other people who have had a stem cell transplant later on.

WHAT ARE THE BAD THINGS THAT CAN HAPPEN FROM THIS RESEARCH?

There is little chance that bad things will happen if you participate in this research.

You may be asked questions that make you uncomfortable or cause you to remember situations that were upsetting to you. You do not need to answer any questions that you do not wish to answer and you can stop at any time. If you become very upset at any time, we will end the testing. We will also offer to have you speak to someone about what you are feeling.

WHAT OTHER CHOICES ARE THERE?

Instead of being in this study, you can choose not to be in it and it will not affect your medical care.

HOW WILL INFORMATION ABOUT YOU BE KEPT PRIVATE?

Making sure that information about you remains private is important to us. To protect your privacy in this research study we will:
Instead of your name, each participant will receive a number such as P1, P2, P3… that will be placed on all research materials to protect identity and confidentiality. Consent and assent forms will be the only materials that have both the name and number and these will be kept secure in a locked cabinet in the researcher's office space. Only research staff will have access to study materials. All digital forms and interviews will be kept on a secure password protected research drive that only research staff will have access to and is backed-up each day.
Each interview will take place individually and in a private room. What's said in the interview will be

kept confidential and will not be shared unless there is a danger to self or others.

WHAT IF WE LEARN NEW INFORMATION DURING THE RESEARCH?

The study doctor will tell you if they find out about new information from this or other studies that may affect your health, safety or willingness to stay in this study. If you share any unreported abuse or potential harm to yourself or others, it is mandatory for the study staff to report these.

WILL IT COST YOU ANYTHING EXTRA TO BE IN THE RESEARCH STUDY?

There are no costs for you or your child to participate in this research study. You will continue to be responsible for the usual costs of your medical care. However, no additional costs will be charged to you or your child for participating in this study.

WILL YOU BE PAID TO BE IN THIS RESEARCH STUDY?

You will be reimbursed for your time, effort and travel while you are in this research study.

You will be paid $25 at the completion of the interview as reimbursement for your time and effort.

WHO DO YOU CALL IF YOU HAVE QUESTIONS OR PROBLEMS?

For questions, concerns, or complaints about this research study you can contact the study person listed on page 1 of this document.
If you would like to talk to someone that is not part of the research staff or if you have general questions about your research study rights or questions, concerns, or complaints about the research, you can call the CCHMC Institutional Review Board at 513-636-8039.

AUTHORIZATION FOR USE/DISCLOSURE OF HEALTH INFORMATION FOR RESEARCH

AUTHORIZATION FOR USE/DISCLOSURE OF HEALTH INFORMATION FOR RESEARCH

To be in this research study you must also give your permission (or authorization) to use and disclose (or share) your “protected health information” (called PHI for short).

What protected health information will be used and shared during this study?
CCHMC will need to use and share your PHI as part of this study. This PHI will come from:

- Your CCHMC medical records
- Your research records

The types of information that will be used and shared from these records include:

- Laboratory test results, diagnosis, and medications
- Reports and notes from clinical and research observations
- Imaging (like CT scans, MRI scans, x-rays, etc.) studies and reports
- If applicable, information concerning HIV testing or the treatment of AIDS or AIDS-related conditions, drug or alcohol abuse, drug-related conditions, alcoholism, and/or psychiatric/psychological conditions (but not psychotherapy notes).

Who will share, receive and/or use your protected health information in this study?

- Staff at all the research study sites (including CCHMC)
- Personnel who provide services to you as part of this study
- Other individuals and organizations that need to use your PHI in connection with the research, including people at the sponsor and organizations that the sponsor may use to oversee or conduct the study.
- The members of the CCHMC Institutional Review Board and staff of the Office of Research Compliance and Regulatory Affairs.

How will you know that your PHI is not misused?

People that receive your PHI as part of the research are generally limited in how they can use your PHI. In addition, most people who receive your PHI are also required by federal privacy laws to protect your PHI. However, some people that may receive your PHI may not be required to protect it and may share the information with others without your permission, if permitted by the laws that apply to them.

Can you change your mind?

You may choose to withdraw your permission at any time. A withdrawal of your permission to use and share your PHI would also include a withdrawal from participation in the research study. If you wish to withdraw your permission to use and share PHI you need to notify the study doctor, listed on the first page of this document, in writing. Your request will be effective immediately and no new PHI about you will be used or shared. The only exceptions are (1) any use or sharing of PHI that has already occurred or was in process prior to you withdrawing your permission and (2) any use or sharing that is needed to maintain the integrity of the research.

Will this permission expire?

Your permission will expire at the end of the study. If the study involves the creation or maintenance of a research database repository, this authorization will not expire.

Will your other medical care be impacted?

By signing this document you are agree to participate in this research study and give permission to CCHMC to use and share your PHI for the purpose of this research study. If you refuse to sign this document you will not be able to participate in the study. However, your rights concerning treatment not related to this study, payment for services, enrollment in a health plan or eligibility of benefits will not be affected.

SIGNATURES

The research team has discussed this study with you and answered all of your questions. Like any research, the researchers cannot predict exactly what will happen. Once you have had enough time to consider whether you should participate in this research you will document your consent by signature below.

You will receive a copy of this signed document for your records.

_____
Printed Name of Research Participant

_____ _____
Signature of Research Participant Indicating Consent Date

_____ _____
Signature of Legally Authorized Representative* Date

_____
* If signed by a legally authorized representative, a description of such representative's authority must be provided

_____ _____
Signature of Individual Obtaining Consent Date

STUDY TITLE: ADOLESCENT AND YOUNG ADULT MANAGEMENT OF CARE REGIMEN POST STEM CELL TRANSPLANT

Caroline Morrison, MSN, RN
Name of Principal Investigator (study doctor)

513-652-3555
Telephone Number

INTRODUCTION

We want to tell you about a research study we are doing. A research study is a way to learn more about something. We would like to find out more about how children who have had a transplant and their parents manage doing specific things like taking their medication and coming to clinic. You are being asked to join the study because you had a transplant between the ages of 13 and 25.

WHAT WILL HAPPEN IN THE STUDY?

We would like to interview you and asked you questions about how you manage doing things like take your medication and if anyone helps you, what medications you take and how often you have missed taking your medication. You will also be asked to use a special pill bottle that records when it is opened, called a MEMS, for 2 of you medicines for up to 3 months. You will also have to bring the bottles to clinic every month for the research team to download the MEMS into a computer. We will also be looking at your electronic medical chart to see if you have had events like infections or being admitted into the hospital while you are in the study.

WHAT ARE THE GOOD THINGS THAT CAN HAPPEN FROM THIS RESEARCH?

We do not know if being in this study will help you. We may learn something that will help other children who have had a stem cell transplant someday.

WHAT ARE THE BAD THINGS THAT CAN HAPPEN FROM THIS RESEARCH?

There is little chance that bad things will happen to children or adults who participate in this research. There may be other risks that we do not know about yet.

WHAT OTHER CHOICES ARE THERE?

Instead of being in this study, you can choose not to be in it. Take all the time you need to make your choice. Ask us any questions you have at any time.

SIGNATURES

After you have read this form and talked about this research with your parents and the doctors or nurses you need to decide if you want to be in this research.

If you want to be in this research you should sign or write your name below.

_____	_____
Child's Assent	Date
_____	_____
Signature of Person Obtaining Assent	Date

STUDY TITLE: ADOLESCENT AND YOUNG ADULT MANAGEMENT OF CARE REGIMEN POST STEM CELL TRANSPLANT

STUDY NUMBER: 2014-4754

FUNDING ORGANIZATION: DAISY Foundation

Caroline Morrison MSN, RN
Name of Principal Investigator

513-652-3555
Telephone Number

INTRODUCTION

We are asking for your permission for your child to be in a research study so that we can learn new information that may help others. If you decide not to give your permission for your child to be in this study, we will still take good care of him/her. If you decide to allow your child to be in this study, you may change your mind at any time during the study and your child can stop being in the study. Take all the time you need to make your choice. Ask us any questions you have. It is also okay to ask more questions after you decide to allow your child to be in the study. You can ask questions at any time.

WHY ARE WE DOING THIS RESEARCH?

In this research study we want to learn more about how children who have had a transplant and their parents manage doing specific things like taking medication and coming to clinic appointments.

We are asking your child and other children who have had a stem cell transplant to be in the research, because we would like to better understand how children and parents manage their care activities.

WHO IS IN CHARGE OF THE RESEARCH?

Caroline Morrison is the researcher at Cincinnati Children's Hospital Medical Center (CCHMC) that is in charge of this study.

WHO SHOULD NOT BE IN THE STUDY

Your child cannot be in this study if he/she has any of the following:

1. Your child does not speak English
2. Your child was above the age of 25 at the time of transplant
3. Your child was below the age of 13 at the time of transplant
4. Your child has not had a stem cell transplant
5. Your child's medical status or condition will not allow them to participate as determined by the medical team or their caregiver.

WHAT WILL HAPPEN IN THE STUDY?

The research staff will explain each visit to you and may give you a handout that explains each visit in more detail. You will be able to ask questions to make sure that you understand what will happen to your child.

If your child qualifies and decide you want your child to be in the study, your child will have up to 4 study visits over the next 3 months.

These are the things that will happen to your child while in the study:
This is an interview based study. You and your child will be interviewed separately. Each interview will last 1-2 hours. After the interview, your child will be asked questions on what they know about their medications and their schedule. If your child is on oral medications, you will be asked to use 2 pill bottles with caps called MEMS that will record when they are opened. You will use the bottles for 2 of your medications. The cap can be downloaded into a computer. The download will happen once a month and last about 15 minutes. After 3 months the pill bottle and cap will be collected.

WHAT ARE THE GOOD THINGS THAT CAN HAPPEN FROM THIS RESEARCH?

Being in this study may not help your child right now. When we finish the study, we hope that we will know more about how children and their caregivers manage their care activities after transplant and how medical professionals can provide better care. This may help other children who have had a transplant later on.

WHAT ARE THE BAD THINGS THAT CAN HAPPEN FROM THIS RESEARCH?

There is little chance that bad things will happen to children or adults who participate in this research. Others have used the pill bottles and been interviewed with no bad things happening.

Children who participate may be asked questions that make them uncomfortable or cause them to remember situations that were upsetting to them. They will be told at the beginning of the testing and reminded during the

testing that they do not need to answer any questions that they do not wish to answer and that they can stop the testing at anytime. If your child becomes very upset during the testing at anytime, we will end the testing. We will also offer to have your child speak to someone about what they are feeling. We will also tell you about any problems.

There may be other risks that we do not know about yet.

WHAT OTHER CHOICES ARE THERE?

Instead of being in this study, you can choose not to have your child be in it and it will not affect your medical care.

HOW WILL INFORMATION ABOUT YOUR CHILD BE KEPT PRIVATE?

Making sure that information about your child remains private is important to us. To protect your child's privacy in this research study we will:
Instead of their name, each participant will receive a number such as P1, P2, P3… that will be placed on all research materials to protect identity and confidentiality. Consent and assent forms will be the only materials that have both the name and number and these will be kept secure in a locked cabinet in the researcher's office space. Only research staff will have access to study materials. All digital forms and interviews will be kept on a secure password protected research drive that only research staff will have access to and is backed-up each day.
Each interview will take place individually and in a private room. What's said in the interview will be kept confidential and will not be shared unless there is a danger to self or others.

WHAT IF WE LEARN NEW INFORMATION DURING THE RESEARCH?

The study doctor will tell you if they find out about new information from this or other studies that may affect your child's health, safety or your willingness for your child to stay in this study. If you or your child share any unreported abuse or potential harm to self or others, it is mandatory for the study staff to report these.

WILL IT COST YOU ANYTHING EXTRA FOR YOUR CHILD TO BE IN THE RESEARCH STUDY?

There are no costs for you or your child to participate in this research study. You will continue to be responsible for the usual costs of your medical care. However, no additional costs will be charged to you or your child for participating in this study.

WILL YOU/YOUR CHILD BE PAID TO BE IN THIS RESEARCH STUDY?

You (your child) will be reimbursed for your time, effort and travel while you are in this research study.

You (your child) will be paid $25 at the completion of the interview as reimbursement for your time and effort.

WHO DO YOU CALL IF YOU HAVE QUESTIONS OR PROBLEMS?

For questions, concerns, or complaints about this research study you can contact the study person listed on page 1 of this document.
If you would like to talk to someone that is not part of the research staff or if you have general questions about your research study rights or questions, concerns, or complaints about the research, you can call the CCHMC Institutional Review Board at 513-636-8039.

AUTHORIZATION FOR USE/DISCLOSURE OF HEALTH INFORMATION FOR RESEARCH

To be in this research study you must also give your permission (or authorization) to use and disclose (or share) your child's "protected health information" (called PHI for short).

What protected health information will be used and shared during this study?
CCHMC will need to use and share your child's PHI as part of this study. This PHI will come from:

- Your child's CCHMC medical records
- Your child's research records

The types of information that will be used and shared from these records include:

- Laboratory test results, diagnosis, and medications
- Reports and notes from clinical and research observations
- Imaging (like CT scans, MRI scans, x-rays, etc.) studies and reports
- If applicable, information concerning HIV testing or the treatment of AIDS or AIDS-related conditions, drug or alcohol abuse, drug-related conditions, alcoholism, and/or psychiatric/psychological conditions (but not psychotherapy notes).

Who will share, receive and/or use your child's protected health information in this study?

- Staff at all the research study sites (including CCHMC)
- Personnel who provide services to your child as part of this study
- Other individuals and organizations that need to use your child's PHI in connection with the research, including people at the sponsor and

organizations that the sponsor may use to oversee or conduct the study.
- The members of the CCHMC Institutional Review Board and staff of the Office of Research Compliance and Regulatory Affairs.

How will you know that your child's PHI is not misused?
People that receive your child's PHI as part of the research are generally limited in how they can use your child's PHI. In addition, most people who receive your child's PHI are also required by federal privacy laws to protect your child's PHI. However, some people that may receive your child's PHI may not be required to protect it and may share the information with others without your permission, if permitted by the laws that apply to them.

Can you change your mind?
You may choose to withdraw your permission at any time. A withdrawal of your permission to use and share your child's PHI would also include a withdrawal from participation in the research study. If you wish to withdraw your permission to use and share your child's PHI you need to notify Caroline Morrison, listed on the first page of this document, in writing. Your request will be effective immediately and no new PHI about your child will be used or shared. The only exceptions are (1) any use or sharing of PHI that has already occurred or was in process prior to you withdrawing your permission and (2) any use or sharing that is needed to maintain the integrity of the research.

Will this permission expire?
Your permission will expire at the end of the study. If the study involves the creation or maintenance of a research database repository, this authorization will not expire.

Will your child's other medical care be impacted?
By signing this document you agree for child to participate in this research study and give permission to CCHMC to use and share your child's PHI for the purpose of this research study. If you refuse to sign this document your child will not be able to participate in the study. However, your child's rights concerning treatment <u>not</u> related to this study, payment for services, enrollment in a health plan or eligibility of benefits will not be affected.

SIGNATURES

The research team has discussed this study with you and answered all of your questions. Like any research, the researchers cannot predict exactly what will happen. Once you have had enough time to consider whether your child should participate in this research you will document your permission by signature below.

You will receive a copy of this signed document for your records.

_____ Printed Name of Research Participant	
_____ Signature of Research Participant Indicating Consent or Assent	_____ Date
_____ Signature of Parent or Legally Authorized Representative*	_____ Date
_____ * If signed by a legally authorized representative, a description of such representative's authority must be provided	
_____ Signature of Individual Obtaining Consent	_____ Date

Appendix E

AYA Inquiry Guide

Opening question: You've been managing your care for ___ months, tell me what that's been like for you?

Individual

1. Can you describe a typical day since you have been discharged from the transplant unit?
2. Is this your first experience managing a medication regimen?
3. Can you describe what you saw your role as during the treatment process?
4. When you were first diagnosed what did you think your options were? How did you view them or feel about them?
5. Can you describe your mental attitude towards treatment? Your emotional journey?
6. Can you describe what normal looks like for you after transplant? How is this different from before transplant?
7. At this stage in treatment do you have any goals and if so what are they? How did you arrive at them and why are they so important? How will you know you reached them?
8. Was there anything that helped you manage your care?
9. Was there anything that made managing your care more difficult?

Family

1. What role did family have in your care management?
2. How have relationships within your family changed due to transplant?

Healthcare System

1. What is the role of healthcare providers in your care management regimen?
2. What advice would you like to give healthcare providers?

Community

1. How did your relationships with your friends change as a result of your transplant?
2. Were there resources you used to manage your care and how did you find out about them?
3. Did you use some form of media to communicate with family or friends during transplant?
4. Is there any advice you would like to give other adolescents or young adults going through transplant?

Adult Caregiver Inquiry Guide

Opening question: You've been involved in managing your child's care for ___ month(s), tell me what that's been like for you?

Individual

1. Can you describe a typical day since your child has been discharged from the transplant unit?
2. Is this your first experience managing a medication regimen?
3. Can you describe your son/daughter's role in their care? How were they involved in decision making?
4. After diagnosis what was your view or how did you feel about the options you had? Can you tell me a story about your options and making a treatment decision?
5. Can you describe your emotional journey through your child's transplant?
6. Was there anything that helped you manage your child's care?
7. Was there anything that made managing your child's care more difficult?
8. How would you have managed if you'd had less guidance at the hospital or with home health when you went home? What would you have done?

Family

1. What role did family have in your child's care management?
2. How has this experience changed relationships within your family? Can you share a story?

Healthcare System

1. What is the role of healthcare providers in your child's care management regimen?
2. What advice would you like to give healthcare providers?

Community

1. Were there resources you used to manage your child's care and how did you find out about them?
2. Did this experience change how you were able to relate to others who have not had a similar experience?
3. How did you keep in touch/ update friends and family?
4. Did you talk to another parent who had a child in transplant prior to your child going through transplant?
5. Is there any advice you would like to give other caregivers of adolescents or young adults going through transplant?

Appendix F

Demographic Information Sheet

Participant #: _____

Today's date: _____

Participant Date of Birth: _____

Gender: M F

Primary caregiver (if caregiver participant then relationship to AYA):

_____

Age primary caregiver: _____

Relationship status: Single Married Separated/Divorced Other_____

Primary diagnosis AYA receiving HSCT for: _____

Date diagnosis: _____

Date Day 0 HSCT: _____

Discharge Date for HSCT: _____

Ethnicity: Hispanic Asian White Black/ African American Other_____

Highest Education Completed:

Less than high school Grade_____ Graduated High School/ GED

Some college/ vocational school Graduated college/ vocational school

Some professional/ graduate school Graduated professional/ graduate school

Appendix G

Electronic Medical Record Data Sheet

Participant ID: _____ Today's date: _____

Name of person filling out this form: _____

Insurance: Private Limited coverage/ emergency Government No Insurance

Behavior or mental health diagnosis: _____ Date: _____

Type HSCT: _____

Chemo:_____ Radiation site: _____ ATG / Campath / MTX

Date day 0: _____

Immunosuppressant medications: _____ (attach drug levels since d/c)

Date initial discharge from HSCT unit: _____

New infections since date of discharge (list site, source, date diagnosed)

_____ _____ _____

_____ _____ _____

_____ _____ _____

_____ _____ _____

GVHD since discharge: Yes No Acute Chronic

If yes GVHD list site(s) and date(s) of diagnosis (indicate with an A or C if has had both acute and chronic GVHD):

_____ _____

_____ _____

_____ _____

Has primary disease relapse occurred? No Yes If yes, date: _____

Has secondary cancer developed? No Yes

If yes, date and diagnosis: _____

Readmissions since initial discharge (date and reason): _____

Missed clinic appointments (number): _____

Missed lab draws (number): _____

Appendix H

Date Administered: ___/___/_____ Date Completed: ___/____/_____
Person Administering: _____
Subject Number of the Patient(s): _____

MEDICAL ADHERENCE MEASURE (MAM)

Introduction: Patients who have a medical condition have to follow a complicated schedule that includes coming to clinic, getting labs, taking medications, and sometimes having to change the way they eat or how they exercise. As you know, this takes quite a bit of time and can be difficult to keep track of. Since not all patients follow the same schedule, we would like to understand how *you* manage your illness. Your answers will help us learn which parts are easy for you and which parts are more difficult. Please be honest because your answers can help us improve our program.

Date Administered: ___/___/_____ Date Completed: ___/____/_____
Person Administering: _____
Subject Number of the Patient(s): _____

I. MEDICATION MODULE

Interviewer should fill in the medication regimen (name and dosages) from the patient's medical record prior to the interview.
Directions: First, tell me all the medications that your doctor has prescribed. (Interviewer should check off the medications patient has *recalled.* Then ask patient if recognizes the rest of the medications on your list and check *prompted*). Now, I'm going to ask specific questions about *each* medication. Think about the last week when answering these questions so that would be since last _____ (count back 7 days). Do your best to answer these questions and if you're not sure we'll ask your mother (or any adult present) for help.

Was this a typical week for you? (a) yes (b) no Comments: _____

Before asking about each medication remind the patient, "In the past 7 days…."

	Medication Regimen *(record from patient's medical chart)*	**What kind of medicine is this?** *(circle one type per medicine)*	**How many times each day did you take this medication?**	**How much of this medication did you take each time?**	**What time of day did you take this medication?** *(circle all that apply)*	**How many times during this week did you miss taking this medication?**	**How many times during this week did you take this medication late?**
1	Name: _____ Dose: _____ Free Recall Patient only Prompted Parent help	Blood Pressure Immunosuppresants Anti-infectives Vitamins Binders Injections	0 1 2 3 4 5 w/ meals spaced apart _____ other _____	Liquids ml/cc ____ **OR** # of pills ____	Breakfast Lunch After school Dinner Bedtime	0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28	0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 N/A How late? ____
2	Name: _____ Dose: _____ Free Recall Patient only Prompted Parent help	Blood Pressure Immunosuppresants Anti-infectives Vitamins Binders Injections	0 1 2 3 4 5 w/ meals spaced apart _____ other _____	Liquids ml/cc ____ **OR** # of pills ____	Breakfast Lunch After school Dinner Bedtime	0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28	0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 N/A How late? ____
3	Name: _____ Dose: _____ Free Recall Patient only Prompted Parent help	Blood Pressure Immunosuppresants Anti-infectives Vitamins Binders Injections	0 1 2 3 4 5 w/ meals spaced apart _____ other _____	Liquids ml/cc ____ **OR** # of pills ____	Breakfast Lunch After school Dinner Bedtime	0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28	0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 N/A How late? ____
4	Name: _____ Dose: _____ Free Recall Patient only Prompted Parent help	Blood Pressure Immunosuppresants Anti-infectives Vitamins Binders Injections	0 1 2 3 4 5 w/ meals spaced apart _____ other _____	Liquids ml/cc ____ **OR** # of pills ____	Breakfast Lunch After school Dinner Bedtime	0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28	0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 N/A How late? ____

Date Administered: ___/___/_____ Date Completed: ___/____/_____
Person Administering: _____
Subject Number of the Patient(s): _____

Before asking about each medication remind the patient, "In the past 7 days…."

	Medication Regimen. ***(record from patient's medical chart)***	**What kind of medicine is this?** ***(circle one type per medicine)***	**How many times each day did you take this medication?**	**How much of this medication did you take each time?**	**What time of day did you take this medication?** ***(circle all that apply)***	**How many times during this week did you miss taking this medication?**	**How many times during this week did you take this medication late?**
5	Name: _____ Dose: _____ Free Recall Patient only Prompted Parent help	Blood Pressure Immunosuppresants Anti-infectives Vitamins Binders Injections	0 1 2 3 4 5 w/ meals spaced apart _____ other _____	Liquids ml/cc ____ **OR** ____ # of pills	Breakfast Lunch After school Dinner Bedtime	0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28	0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 N/A How late? ____
6	Name: _____ Dose: _____ Free Recall Patient only Prompted Parent help	Blood Pressure Immunosuppresants Anti-infectives Vitamins Binders Injections	0 1 2 3 4 5 w/ meals spaced apart _____ other _____	Liquids ml/cc ____ **OR** ____ # of pills	Breakfast Lunch After school Dinner Bedtime	0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28	0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 N/A How late? ____
7	Name: _____ Dose: _____ Free Recall Patient only Prompted Parent help	Blood Pressure Immunosuppresants Anti-infectives Vitamins Binders Injections	0 1 2 3 4 5 w/ meals spaced apart _____ other _____	Liquids ml/cc ____ **OR** ____ # of pills	Breakfast Lunch After school Dinner Bedtime	0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28	0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 N/A How late? ____
8	Name: _____ Dose: _____ Free Recall Patient only Prompted Parent help	Blood Pressure Immunosuppresants Anti-infectives Vitamins Binders Injections	0 1 2 3 4 5 w/ meals spaced apart _____ other _____	Liquids ml/cc ____ **OR** ____ # of pills	Breakfast Lunch After school Dinner Bedtime	0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28	0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 N/A How late? ____
9	Name: _____ Dose: _____ Free Recall Patient only Prompted Parent help	Blood Pressure Immunosuppresants Anti-infectives Vitamins Binders Injections	0 1 2 3 4 5 w/ meals spaced apart _____ other _____	Liquids ml/cc ____ **OR** ____ # of pills	Breakfast Lunch After school Dinner Bedtime	0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28	0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 N/A How late? ____
10	Name: _____ Dose: _____ Free Recall Patient only Prompted Parent help	Blood Pressure Immunosuppresants Anti-infectives Vitamins Binders Injections	0 1 2 3 4 5 w/ meals spaced apart _____ other _____	Liquids ml/cc ____ **OR** ____ # of pills	Breakfast Lunch After school Dinner Bedtime	0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28	0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 N/A How late? ____

Date Administered: ___/___/_____ Date Completed: ___/____/_____
Person Administering: _____
Subject Number of the Patient(s): _____

I. MEDICATION MODULE (CONTINUED)

1. Before this past week, when was the last time you missed any medications?
   (a) don't miss/NA (b) 1-2 weeks ago (c) last month (d) 3 months ago
   (e) 6 months ago (f) 1 year ago (g) >1year ago

2. What are some reasons you miss taking your medications? **(circle all that apply)**
   (a) don't miss/NA (b) interferes with activity (c) hard to swallow pills (d) hate the taste
   (e) just forget (f) not feeling well (g) don't like the side effects (h) wasn't home
   (i) ran out/didn't fill (j) refuse to/defiant (k) can't afford (l) don't think necessary
   (m) other _____

3. When do you tend to miss taking your medications most often? **(circle all that apply)**
   (a) don't miss/NA (b) morning (c) school/lunch (d) afternoon (e) dinner (f) bedtime

4. Who is in charge of making sure you have enough your medications and ordering more of them? **(circle all that apply)**
   (a) myself (b) mother (c) father (d) brother/sister (e) grandmother/grandfather (f) aunt/uncle

5. Where do you keep your medications organized? **(circle all that apply)**
   (a) no system (b) pill box (c) special shelf/cabinet (d) refrigerator (e) plastic bag (f) in my room

6. Who takes the primary responsibility over making sure that you take your medications? **(choose one)**
   (a) myself (b) mother (c) father (d) brother/sister (e) grandmother/grandfather (f) aunt/uncle

7. On a scale of 0 (hardly ever take my medications; usually miss) to 10 (always take my medications; rarely miss), how would you rate how well you take your medications, on average? **(enter a response for each one)**
   (a) patient ____ (b) mother ____ (c) father ____

II. CLINIC ATTENDANCE MODULE

1. How often are you supposed to come to clinic?
   (a) once/year (b) every 6 months (c) every 2-3 months (d) once/month (e) twice/month
   (f) once/week (g) twice/week (h) seen on dialysis, no regular clinic visits scheduled

2. Has there been a change as to how often you come to clinic?
   (a) no change, it's been this way for a while (b) yes, more frequent now (c) yes, less frequent now

3. How often do you miss your clinic appointments without calling or rescheduling?
   (a) never/NA (b) once/year (c) every 3 months (d) once/month (e) twice/month (f) once/week

4. In the past year, how many times have you rescheduled your appointment? _____

5. What are some reasons you miss your appointment? **(circle all that apply)**
   (a) always come/NA (b) just forget (c) can't take off work/school (d) interferes with sport/activity
   (e) not necessary to come that often (f) transportation problems (g) wasn't feeling well
   other _____

6. Who schedules/keeps track of your clinic appointments? **(circle all that apply)**
   (a) myself (b) mother (c) father (d) brother/sister (e) grandmother/grandfather (f) aunt/uncle

7. Who comes with you to your clinic appointment? **(circle all that apply)**

Date Administered: ___/___/_____ Date Completed: ___/____/_____
Person Administering: _____
Subject Number of the Patient(s): _____
(a) myself (b) mother (c) father (d) brother/sister (e) grandmother/grandfather (f) aunt/uncle

8. On a scale of 0 (hardly ever come to clinic; usually miss) to 10 (always come to clinic; never miss), how would you rate your attendance at scheduled clinic visits? **(enter a response for each one)**
(a) patient ____

MEMS® 6
Medication Event Monitoring System

	MEMS® 6 SmartCap (with LCD display)	MEMS® 6 TrackCap (without LCD display)
Housing type A		
Housing type B (child resistance capability)		

The monitor

MEMS 6 is an electronic monitoring system designed to compile the dosing histories of ambulatory patients prescribed oral medications. The system is comprised of two parts: a standard plastic vial with threaded opening and a closure for the vial that contains a micro-electronic circuit that registers dates and times when the closure is opened and when it is closed.

The results

Time-stamped medication events stored in the MEMS 6 can be transferred at any time through the MEMS Reader to a MS-Windows-based computer. MWV software analyzes and displays or prints in various formats the computed parameters of the patient's adherence. The results are now widely regarded as the gold standard measure of patient adherence to medications.

Key points

- Available in 38mm, 42mm and 45mm thread diameters
- Optional LCD display
- Optional child resistance functionality
- Battery expiration 36 months from initialization (18 months for LCD version)
- Water resistant
- Data transfer by patented wireless inductive coupling
- CE marked
- Non-volatile memory for data storage (maintains data integrity for years after loss of battery power)
- Optimal events detection technology

Technical specifications

Clock precision	**+/- 90 seconds per month**
Event resolution	**30 seconds**
Memory capacity	**> 3500 events**
Battery expiration date	**36 months (without LCD)** **18 months (with LCD)**
Thread	**38 mm – Neck Finish 38-400** **42 mm – Neck Finish 42-400** **45 mm – Neck Finish 45-400**
Vials	**Available in sizes from 60 cc to 1050 cc**
Material of the plunger and protection cap (see image below)	**High Density Polyethylene (HDPE) for Pharmaceutical/Medical applications** **Certificate of compliance is provided with MEMS 6 delivery**
Material of the external housing (see image below)	**Acrylonitrile Butadiene Styrene (ABS)**
Degree of permeation	**Water resistant (designed to resist but not entirely prevent the penetration of water)**
Identification	**Unique 6 digits serial number hard coded in the memory and printed on the bottom of the monitor**

LCD Display - optional

The number in the center of the LCD indicates the number of openings of the vial since 3 AM. It will be reinitialized every 24 hours (at 3 AM). After more than 9 daily openings, the digit "9" will blink. The 12 bars in a circle around the central number indicate the number of hours that have passed since the last opening. Each bar represents one hour. From the 13th hour, the corresponding bars will flash. After more than 24 hours, all 12 bars flash. They all disappear when the vial is next opened.

1 opening since the beginning of the day
4 hours passed since the last opening

1 opening since the beginning of the day
16 hours passed since the last opening

When the vial has not been opened for more than 168 hours (one week), the LCD display is automatically turned off, to conserve battery power. The display is reactivated, however, when the vial is next opened.

Child Resistance (CR) - optional

The MEMS 6 is available with child resistant closure based on "push down and turn" principle.

The MEMS 6 CR fulfill US C.F.R. Title 16, Part 1700 (child resistance and senior-friendliness). Tests have been performed by Perritt Laboratories Inc. in Hightstown, NJ.

Precautions

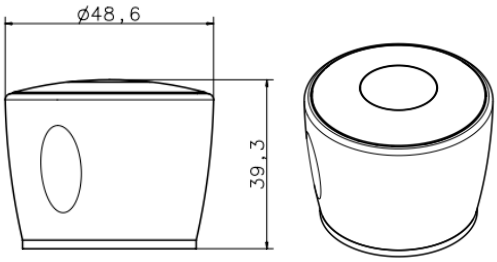
- Use with temperature between 4°C and 40°C
- Use with solid dosage forms
- Securely tighten the monitor onto the bottle
- Do not immerse in water or other liquids
- Do not use after the expiration date of the battery

Remarks

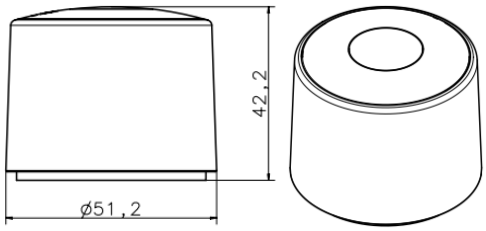
- The MEMS 6 monitor is intended to be used by only a single patient and a single drug
- The MEMS 6 monitor has been designed to withstand normal use in the home
- Improper use can result in the loss of data or product damage
- The MEMS 6 monitor is a sealed unit with no user serviceable or replacement parts

External housing dimension (in mm)

Housing type A



Housing type B



Product selection matrix

Desired features			Product order informations		Characteristics	
Thread	**Child resistance**	**LCD**	**Art. #**	**Art. Designation**	**Battery [months]**	**Housing type**
38mm Neck Finish 38-400	No	No	**1020-01**	**MEMS6 TrackCap 38mm**	36	A
		Yes	**1020-02**	**MEMS6 SmartCap 38mm**	18	
	Yes	No	**1021-01**	**MEMS6 TrackCap 38mm CR**	36	B
		Yes	**1021-02**	**MEMS6 SmartCap 38mm CR**	18	
42mm Neck Finish 42-400	No	No	**1022-01**	**MEMS6 TrackCap 42mm**	36	
		Yes	**1022-02**	**MEMS6 SmartCap 42mm**	18	
	Yes	No	**1023-01**	**MEMS6 TrackCap 42mm CR**	36	
		Yes	**1023-02**	**MEMS6 SmartCap 42mm CR**	18	
45mm Neck Finish 45-400	No	No	**1024-01**	**MEMS6 TrackCap 45mm**	36	
		Yes	**1024-02**	**MEMS6 SmartCap 45mm**	18	
	Yes	No	**1025-01**	**MEMS6 TrackCap 45mm CR**	36	
		Yes	**1025-02**	**MEMS6 SmartCap 45mm CR**	18	

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