Medication Adherence in Adolescent and Young Adult after Hematopoietic Stem Cell Transplant

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Abstract

Hematopoietic stem cell transplant is an effective treatment and curative therapy for many oncological, hematological, and immunological diseases. Following hematopoietic stem cell transplant, the management of the prescribed complex treatment regimen may be overwhelming for adolescents and young adults and their caregivers, resulting in non-adherence. In this patient population, adherence to the daily prescribed treatment regimen is estimated at 33 to 73%. Non-adherence to a prescribed medication regimen can lead to reduced treatment efficacy, resulting in suboptimal clinical outcomes and increased healthcare expenditure. The purpose of this evidence-based practice project was to determine if the implementation of adherence promoting interventions combined with the MedActionPlan PRO application and checklist over 12 weeks fosters treatment adherence and self-management of the prescribed medication regimen. Two adolescents and young adults, ages 12 -20 years, who underwent hematopoietic stem cell transplant were enrolled with their caregiver through convenience sampling from the bone marrow transplant unit in a tertiary care pediatric hospital in the Midwest. The intervention included a multicomponent intervention package and a MedActionPlan PRO checklist. The project demonstrated 100 % attendance for adherence-focused intervention sessions. Medication adherence through self-report from baseline to post-intervention remained unchanged. One participant showed acceptability for intervention sessions as indicated in self-report and endorsed that intervention sessions improved personal organization. Both participants reported feasibility and acceptability of the MedActionPlan PRO checklist.

Keywords: pediatric hematopoietic stem cell transplant, adolescents and young adults, non- adherence, adherence-focused interventions, MedActionPlan PRO checklist, and self-management.

Medication Adherence in Adolescent and Young Adult after

Hematopoietic Stem Cell Transplant

Hematopoietic stem cell transplantation (HSCT) has been an increasingly utilized therapy for many oncological, hematological, immunological diseases, as well as bone marrow failure (McGrady et al., 2014). The Worldwide Network for Blood and Marrow Transplantation (2013) reported that as of 2012 about 1 million people received hematopoietic stem cell transplants worldwide which is a significant increase since 2004. Each year approximately 20,000 people benefit from hematopoietic stem cell transplants in the United States which includes 3,500 children, adolescents, and young adults, ranging from infants to 30 years (Health Resources and Services Administration, 2015).

Significance

Hematopoietic stem cell transplantation is a complex process involving an intense and life-threatening treatment regimen (Ezzone, 2013) and carries potential complications such as primary disease relapse, infection, and graft versus host disease (Pasquini & Zhu, 2015) with overall survival of 50 to 60% (Morrison et al., 2017). Essentially, HSCT recipients require effective treatment management and monitoring to prevent potentially life-threatening complications. The treatment regimen mainly includes immunosuppressants, prophylactic antibacterial and antiviral and antifungal therapy, and electrolyte supplements. The HSCT recipients receive these therapies during their inpatient care and continue upon discharge. The therapies can become quite cumbersome for the patient and the caregiver, and often result in non-adherence (Morrison et al., 2017; Pai et al., 2017). In general, adolescents and young adults (AYAs) are known to be particularly vulnerable and have greater difficulties in adhering to treatment schedules due to normative developmental behaviors (Kondryn et al., 2011; Morrison et al., 2017). These behaviors are described as achieving independence from parents, adopting a

peer lifestyle, and risk-taking which are interrupted following HSCT (Kondryn et al., 2011; Morrison et al., 2017)

Given the negative ramification of medication adherence, the Center for Disease Control (CDC, 2013), the National Institutes for Health (NIH, n.d.), and the World Health Organization (WHO, 2003) have recognized adherence as a worldwide problem of striking magnitude, costing approximately $300 billion to the United States healthcare system (Pai et al., 2014). The National Institute of Health (NIH, 214) reported that the rate of non-adherence to treatment regimen increases over time, from 27% within the first month of discharge to 39 - 74% during the three months post-discharge. The non-adherence rate suggests that a substantial proportion of AYAs with special health care needs may be receiving sub-therapeutic doses of prescribed medications. Considering the prevalence of non-adherence in AYAs and the associated negative consequences, non-adherence is recognized as a target for research and intervention. Research suggests that multicomponent adherence interventions lead to the greatest improvements in medication adherence (Kahana, Drotar, & Frazier, 2008). Also, technology-based intervention results in improved adherence (Mistry et al., 2015).

Local Issue

According to the Center for International Blood and Marrow Transplant Research (CIBMTR) Transplant Activity Report from January 2014 – December 2015, participating centers in the Midwest include three pediatric hospitals. One of the pediatric hospitals performs about sixty-seven pediatric transplants annually, including fifty-two allogeneic and fifteen autologous transplants. Another hospital performs about eighteen transplants every year, including ten allogeneic and eight autologous transplants. The third pediatric hospital performs seventy transplants, and thirty-nine are allogeneic and thirty-one are autologous transplants. The CIBMTR from 2014 – 2015 for HSCT indicates that among unrelated donor allogeneic HSCT

within the first 100 days that mortality to infection, organ failure, and graft versus host disease account for 45% of the deaths. Among matched related sibling transplants within the first 100 days, the primary disease accounts for 27% of deaths, while infection and organ failure represent 36% of deaths.

Diversity Consideration

Over the past decade, one of the cities with a hospital that performs HSCT in the Midwest has experienced significant growth with an estimated population of 481,420 with 51.7% of the population as female while 48.2% is male (United States Census Bureau, 2010). The current increase in population makes this city the 37th largest city in the United States. Children over 5 to 18 years of age comprise 23.5% of the population (United States Census Bureau, 2010). The city is diverse, representing ethnicities of 60.1% Caucasian, 29.1% African American, and 10% Hispanic or Latino (United States Bureau, 2010). The median household income is approximately $47,489 with a poverty rate of 18.3% and 9.1% without health insurance (United States Census Bureau, 2010). The tertiary academic pediatric institution in this city was the site for the evidence-based project. According to a report from the pediatric hospital (2015), about 91.6% speak English as their primary language with 7.1% Spanish-speaking. The bone marrow transplant unit receives referrals from this patient demographic and performs about 35-40 HSCT yearly.

Problem and Purpose

In recent literature, suboptimal adherence to treatment regimens is defined as taking less than 80% of all prescribed medication (Rapoff, 2010) and is reported across ages, medical conditions and prescribed treatment regimen (Kondryn et al., 2010; Sitrratt et al., 2015; Wu et al., 2018). The highest incidence of non-adherence is reported among AYAs, resulting in morbidity and mortality, suboptimal clinical outcomes, and an increase in healthcare expenditure

(Kondryn et al., 2010; Sitrratt et al., 2015; Wu et al., 2018). Hematopoietic stem cell transplant is a relatively expensive and lifesaving treatment for many diseases (McGardy et al., 2014). During the past decade, there has been a significant increase in the incidence of HSCT recipients. Given the impact of HSCT on overall survival rates, the recipients must comply with the prescribed treatment regimen to achieve a therapeutic medication effect. Due to the complex nature of treatment adherence, the approach needs to be multifactorial (Pai & McGardy, 2015). Recent research suggests that incorporating adherence promoting interventions with technology-based intervention can substantially improve adherence to prescribed treatment. The purpose of this evidence-based practice project was to improve adherence and daily management of prescribed treatment in AYA by using an adherence promoting intervention combined with a MedActionPlan PRO application (app) with checklist.

Facilitators and Barriers

The facilitator for this project was a licensed psychologist at the project site and received her postdoctoral training in the Center for the Promotion of Treatment Adherence and Self-Management at Cincinnati Children's Hospital Medical Center. She has substantial experience in working with adolescents with chronic illnesses and has applied and tested a multicomponent intervention package (MIP) to improve adherence in youth with a chronic medical condition. As a facilitator, her ongoing support for this project was significant in the successful implementation of MIP in the study population. A barrier to this project was recruiting HSCT recipients ages 12 to 20 years within the limited timeframe of the study, given the complex process involved during pre and post-transplant. Before the transplant, the patients undergo pre-transplant screening. They are admitted for HSCT only when pre-transplant lab results are normal and they have achieved remission. After HSCT, their discharge is based on recovery and clinical condition which may take 3 -4 weeks or longer if they experience post HSCT complications.

Review of the Evidence

Inquiry

Does the delivery of a multicomponent intervention package and use of MedActionPlan PRO app with checklist improve adherence to prescribed medication in AYA hematopoietic stem cell recipients during three months at a bone marrow transplant outpatient clinic?

Literature Search

A variety of literature search methods were utilized in obtaining evidence-based research that supports adherence promoting interventions and technology-based interventions in adolescent and young adults with HSCT. The search used the databases of Cumulative Index to Nursing and Allied Health Literature (CINAHL), Ovid Medline, PubMed, and Cochrane. Search terms included *hematopoietic stem cell transplant, transplants, chronic health conditions, adolescents, young adults, non- adherence, adherence-focused interventions, technology-based interventions, and clinical outcome* (see Appendix A). Other sources included national and international health organizations such as National Institute of Health (NIH), World Health Organization (WHO), National Marrow Donor Program (NMDP), Center for International Blood and Marrow Transplant Research (CIBMTR), and the Center for Disease Control (CDC). The inclusion criteria for the studies derived from the databases were published in English from 2010 to current. Twenty studies provided evidence for this project. The search yielded nine articles with AYA transplant recipients, adherence barriers, and chronic health conditions including cancer. Eleven articles addressed adherence promoting interventions and technology-based interventions. Of these 20 studies, seven were systematic reviews, three were randomized control trials, seven were cohort studies, one was a longitudinal study, one was a single descriptive study, and one represented a consensus report. The level of evidence (Melnky & Overholt 2015)

included seven of level one, three of level two, seven of level four, one of level five, and one of level seven evidence (see Appendix B).

Synthesis of Evidence

Limited research is available on treatment adherence in the AYA who are HSCT recipients. Given the similar trend for medication adherence in AYA cancer and chronic health conditions, studies on chronic conditions were included in the synthesis of evidence. Three themes that support the inquiry are the a) impact of multicomponent intervention package (MIP) in promoting adherence in AYAs, b) utilization of technology-based intervention in enhancing treatment adherence in AYAs, and c) recognizing adherence barriers to maximize the impact of MIP (see Appendix C).

Multicomponent intervention package (MIP) to promote adherence. In a meta-analysis, Hood and colleagues (2010) studied the effects of adherence promoting interventions to improve glycemic control in youth less than 19 years old with diabetes type I. They found that improvement in glycemic control was significant in the treatment group compared to the no-treatment group. They reported that adherence promoting interventions focus on many facets, including treatment regimen and psychosocial aspect of patient and family by educating patients and caregivers throughout the process. These interventions enable patients and caregivers to sustain adherence to a treatment regimen for a longer duration. In another meta-analysis, Pai and McGardy (2014) studied youth with chronic health conditions and explored the efficacy of adherence enhancing interventions. They reviewed the impact of the implementation of both in-person and technology-mediated interventions. They concluded that future studies are needed to re-examine the effectiveness of these interventions which will dictate treatment adherence methodology and potential clinical outcomes in this crucial patient population.

Pai and McGardy (2014) conducted a systemic review and meta-analysis assessing medication adherence in pediatric oncology and established standard of care for enhancing treatment adherence in the study population. Based on their analysis of the literature, they recommended standardization of self-reported assessment of adherence by patients and families, routine assessment of adherence and education materials on medication, evaluation for medication side effects, and assessment for potential implications of non-adherence. They found ongoing education, using electronic pill bottles, self-report, and monitoring serum drug levels were effective measures for monitoring adherence; however, future studies are warranted for intervention effectiveness. Maddux and colleagues (2017) studied adolescents with inflammatory bowel disease and examined the effectiveness of a multicomponent intervention package on medication adherence. The intervention package was implemented in four weekly sessions, and adherence data was collected pre and post-intervention. The findings indicated that 100% attendance was achieved for the intervention sessions, and significantly higher adherence was observed from baseline to post-intervention. They concluded that the use of multicomponent interventions to enhance treatment adherence is both effective and feasible, particularly when the interventions are tailored to the adherence barrier identified by patients and their caregivers.

Utilization of technology-based intervention in enhancing treatment adherence. In a pilot study, Creary et al. (2014) studied children with sickle cell disease and examined the efficacy of *mobile electronic directly observed therapy (mDOT)* in improving compliance with oral hydroxyurea. The study participants were required to videotape their daily administration and ingestion of hydroxyurea. Throughout the study, each participant received electronic medication reminders and feedback from the project team member. The study authors reported that utilization of mDOT in enhancing compliance with hydroxyurea led to the improvement in clinical outcomes of participants. Mistry et al. (2015) conducted a systematic review of

randomized clinical trials (RTCs) assessing the effect of technology-mediated intervention (TMI) in enhancing patient adherence to prescribed medications and improving clinical outcomes. They grouped RTCs into education and counseling, self-monitoring and feedback, and electronic reminders. Half of all the studies showed improvement in treatment adherence with TMI and more than one-third of all the studies indicated improvement in clinical outcomes. They concluded that technology-mediated intervention remains promising for future application to improve treatment adherence.

Shellmer et al. (2016) developed and examined the Teen Pocket Path (TPP), a mobile health application, by conducting a prospective study. They used TPP application as an intervention to promote treatment adherence and improve adolescent and caregiver communication related to treatment management. The goal of the study was to motivate adolescents to self-manage their treatment regimen through the TPP approach. They concluded that the TPP application has the capability of keeping both the patient and the caregiver involved in the daily management of the treatment regimen by preventing non-compliance to the treatment schedule. They predicted that the TPP application could be broadly utilized as a future adherence tool.

Badawy and Kuhns (2016) conducted a systematic review to evaluate the cost-effectiveness of smartphone-based interventions used in improving treatment adherence in youth experiencing chronic illnesses. They suggested that because the technology-based interventions have shown beneficial evidence-based implications, they should be utilized to target adherence to treatment regimens. Given the increased usage of these technology tools in treatment management in adolescents with chronic illnesses, they suggested need for research to evaluate cost-effectiveness, sustainability, and benefits of smartphone-based tools.

In another prospective study, Wu et al. (2018) studied adolescents and young adults with cancer. They used a medication reminder smartphone application and examined the feasibility and acceptability. Each participant received four weeks of training about the usage of the smartphone application for medication reminders and was required to use this application for eight weeks as an adherence intervention. Also, each participant completed a weekly online self-report questionnaire that included questions about the usage of the application, and they received reminder prompts to take medication. The authors concluded that the smartphone application was easy to use and useful to promote medication adherence.

Recognizing adherence barriers to maximize impact of MIP. In a review, Prendergast and Gaston (2010) compared risk factors associated with non-adherence to immunosuppressants in young adult and older kidney transplant patients. They described a lack of education regarding treatment, health care coverage, social support, and complex treatment regimen as adherence barriers in young adults. They suggested that an adherence intervention must be multidimensional to have successful implication. They reported that non-adherence to immunosuppressive therapy is a major risk factor in post-renal transplant recipients that results in graft failure. Therefore, to ensure optimal clinical outcomes, emphasis must be geared towards ongoing education, focusing on the importance of adherence to immunosuppressive agents. In a meta-analysis, Shellmer et al. (2011) reviewed factors related to implications of nonadherence in organ transplant pediatric recipients. They reported that suboptimal family and child functioning as a potential risk factor for non-adherence to the treatment regimen. They recommended family-centered interventions that focus on improving family functioning and motivating adolescents to take ownership of the management of their treatment. They described that many studies found interventions to be effective when they are tailored to adherence barriers.

Kondryn et al. (2011) conducted a review of studies in teens and young adults ages 13-24 years with oncological diseases. They concluded that a knowledge gap exists in interventional studies focusing on medication adherence in AYAs with cancer. They described multifactorial strategies to foster optimal adherence, such as addressing problems with patients, family functioning, treatment regimen, and health professional support. McGrady et al. (2014) examined adherence patterns in adolescents ages 12-18 years with hematopoietic stem cell transplant and reported a rate of non-adherence of 27 to 63% among the transplant recipients. Given the inconsistency to treatment adherence across study participants, they recommended adherence promoting interventions involving the caregiver. They also suggested that adherence interventions can be implemented before discharge and after discharge based on patient needs. McCormick et al. (2016) studied association among emotional functioning, adherence barriers and treatment adherence in adolescents with solid organ transplants. They found that adolescents internalizing behaviors, such as depression and anxiety, and barriers to medication are interrelated and contribute to increasing non-adherence.

In a review of literature, Morrison et al. (2017) reported non-adherence in adolescents and young adults with oncological illnesses consistently remained below 80-95%. They suggested using multiple measures for monitoring adherence such as therapeutic drug levels, self-report, and adherence barriers of patient and caregiver. They concluded that researchers should utilize theoretical frameworks and models to guide adherence research that would aid in identifying variables, interventions, and outcomes. Pai et al. (2017) examined rates of non-adherence to prescribed oral medication in post-HSCT children for six months after discharge. They recruited fifty post-HSCT children ages 0 – 16 years with their caregiver. They measured adherence using an electronic pill bottle and found that average adherence percent decreased over six months from 63% at one-month post discharge to 57% at six months post discharge.

They found a decline in treatment adherence with the increased rates of infection across the six month post-transplant duration.

In a multicenter study, Danziger-Isakov et al. (2016) examined perceived adherence barriers in children and adolescents of solid organ recipients and their guardians. They found that caregivers of adolescents stated increased perceived adherence barriers versus caregivers of younger patients. They stated that patients reported more medication ingestion barriers and side effects than their caregivers. They recommended perceived barriers to medication adherence can be easily assessed in an outpatient setting and providers can focus their interventions accordingly to promote adherence. Foster and Pai (2014) reviewed studies conducted in kidney transplant adolescents and young adults. They reported three main elements that impact adherence, namely patient-related, social and economic, and therapy-related. There were two reported methods for measuring adherence, direct and indirect. The direct method is witnessing ingestion of medication and monitoring serum drug levels while the indirect method involves electronic monitoring, pill counts, pharmacy records, self-report, and caregiver and/or parent reports. They recommended program-level adherence intervention approaches in kidney transplant recipients if administered at a regular interval. By providing ongoing guidance and monitoring change, sustainable treatment compliance for long term graft survival may be accomplished through quality care.

Theory

The social cognitive theory (SCT) is influential for behavior modification and has been widely used in clinical practice. The SCT provides a framework for understanding human thought and behavior. The core determinants of SCT include personal, behavioral, and environmental factors that are interrelated to each other (Patton et al., 2017). The concept of social cognitive theory includes eight steps that provided an outline for the project (see Appendix

D). Observational learning is the first step where participants and their caregivers acquired knowledge through the MIP approach. They observed and learned skills during interactive education sessions. The next step is self-efficacy which is a key construct of this model. Self-efficacy is an important quality that participants and caregivers possess and that facilitated them to attain their goal of adherence to the medication regimen. Participants and caregivers were able to adopt behavior modification and organizational skills that enabled them to self-manage their treatment schedule (Patton et al., 2017). The internal and external environment ties participants and caregivers into a reciprocal relationship with the environment and behavior, resulting in behavior modification through learned skills (Patton et al., 2017). The final and most crucial step is long–term change that enabled participants and caregivers to sustain learned skills and carry out their tasks effectively (Patton et al., 2017). The goal of this project was to establish sustainability among participants through behavior modification that assisted them in achieving adherence to treatment management for a longer duration.

Methods

IRB Approval, Ethical Considerations, and Funding

The Institutional Review Board at a tertiary care pediatric hospital reviewed and approved the project as an evidence-based quality improvement (EBQI) project (see Appendix E). The privacy and confidentiality of the participants and the data were maintained. Before enrolling the participants, the author explained how the information would be used so that the process would facilitate their decision making. No ethical concerns or issues were raised by enrolled participants. The estimated cost for the project was approximately $500 (see Appendix F) and included handouts for education sessions for project team members and participants, as well as pillboxes for participants.

Setting and Participants

The evidence-based practice project was implemented at a tertiary care pediatric hospital in the Midwest. The project design was quasi-experimental with a prospective cohort. Two AYAs with hematopoietic stem cell transplant with their caregivers were enrolled after their discharge from the inpatient bone marrow transplant (BMT) unit of a tertiary care pediatric hospital. Participants who were clinically unstable, cognitively impaired, and younger than 11 years and older than 20 years were excluded from the intervention.

Evidence-based Intervention

The intervention applied was a multicomponent intervention package (MIP) and MedActionPlan PRO app with checklist. A month before the launch of the project, the project team, including the bone marrow transplant outpatient nurse practitioners (NPs) and pharmacists, attended two 180 minute training sessions led by the project clinical expert to ensure standardized implementation of the MIP. The HSCT recipient ranged from 12 – 20 years who were ready to be discharged from the inpatient unit along with their caregivers were approached by a project team member. During pre-intervention, the participants were required to complete the Adolescent Medication Barrier Scale (AMBS) and Parent Medication Barrier Scale (PMBS) at the initial outpatient visit. The content of each outpatient visit was based on standard BMT protocol including history and physical exam and routine lab draw. At each visit, the BMT pharmacists reviewed the medication list and asked if refills were needed for mediations. Following the initial visit, each enrolled participant was scheduled for four weekly MIP sessions, and these were incorporated into their regular outpatient visits to prevent multiple trips to the clinic after discharge. These follow up visits were comprehensive, lasting about 60 to 90 minutes. Consistent with the evidence on MIP, these weekly sessions included an educational and organizational intervention (week 1), behavior modification (week 2), guided problem-solving training (week 3), and family functioning (week 4). The participants also received

information and training based on their choice of MedActionPlan PRO app or checklist. Also, enrolled youth completed a weekly (week 1 through week 4) self-reported adherence behavior questionnaire.

At the 4-week session, the intervention was individualized based on the pre-intervention assessment using AMBS and PMBS findings. Upon completion of the MIP, at week 5, participants completed the post-treatment AMBS, PMBS, and adherence intervention satisfaction survey for youth and parents. Pre and post-intervention data from the AMBS, PMBS, and MedActionPlan PRO app or checklist smartphone application usage were compared to determine the impact of the intervention package on medication adherence (see Appendix G).

Change Process and Evidence-Based Model

The Change Curve Model was used in this project. This model supports basic assumptions for change and is useful in recognizing the stages of individual transition and organizational change (Melnyk & Fineout-Overholt, 2015). This five–stage process focuses on stagnation, preparation, implementation, determination, and fruition within the model (Melnyk & Fineout-Overholt, 2015). While developing this project, the author addressed stagnation and preparation stages of this change process (see Appendix H).

The Stetler Model of Evidence-Based Practice was used to guide the evidence implementation in this project. The model is comprised of five phases including preparation, validation, comparative evaluation/decision making, translation/application, and evaluation (Melnyk & Finout-Overholt, 2015). The author utilized this model in the development of the project by identifying a problem, locating and synthesizing evidence regarding the prevalence of non-adherence in AYAs with hematopoietic transplant recipients, and designing a practice change that was implemented through the project.

There is a high possibility of project sustainability after completion. The author plans to promote use of these intervention as standard of care for post-BMT outpatient follow up visits. The delivery of MIP with the app and checklist are effective interventions for promoting medication adherence. The AMBS and PMBS can continue to be utilized to assess adherence barriers, and education can be tailored accordingly. The use of the MedActionPlan PRO app with checklist can be encouraged to facilitate daily management of the treatment schedule. The utilization of these interventions can increase knowledge regarding adherence and self-management of the treatment regimen that ultimately improves adherence in this specific population.

Study Design

The project was a pilot, quality improvement initiative with a quasi-experimental, one cohort design. The impact of the MIP and MedActionPlan PRO app with checklist was measured by the change in adherence and self –management of the treatment schedule, designed to improve treatment efficacy. Medication adherence barriers were assessed using AMBS and PMBS pre and post-treatment sessions.

Validity

Given that the project was a pilot study with a small sample, there are potential threats to the internal and external validity or transferability of the quality improvement initiative to other similar sites. Also, the self-selection through convenience sampling is a threat to internal validity. Moreover, participant attrition or lack of adherence to the protocol may pose a threat to the internal validity and quality care if a participant chooses not to complete the MIP intervention or demonstrates inconsistency in using the MedActionPlan PRO app with checklist. However, the internal validity of the project is strengthened by using valid and reliable tools, namely PMBS and AMBS. The external validity of this proposed project is enhanced by the

diverse demographics of HSCT recipients at a tertiary care pediatric hospital. The internal and external validity was improved by using inclusion criteria during recruitment and an evidence-based intervention

Outcomes and Measurements Instruments

The outcome measures included optimizing adherence to medical treatment and self-management of the treatment schedule. The AMBS and PMBS assessment questionnaires evaluate perceived barriers to medication adherence. The PMBS consists of 16-items with a max score of 80 and has a Cronbach α of 0.87 which indicates strong internal consistency. The AMBS consists of 17-items with a max score of 85 and a Cronbach α of 0.86 which indicates strong internal consistency. The feasibility and acceptability of the MIP were assessed via participant attendance, attrition, and completion of the assigned task. The self-reported use of the MedActionPlan PRO app with checklist was assessed by usage and self-management of the treatment schedule. A self-reported adherence behavior questionnaire consisted of a 3-item measure to assess change in adherence behavior from baseline to post-intervention. The questionnaire addressed the percentage of medication taken, missed doses, and reason for missed doses of immunosuppressants, antiviral, and antifungal medications. Each enrolled youth completed the adherence behavior questionnaire from pre to post-intervention. The satisfaction survey for youth and parents consisted of a 12-item measure to assess enrolled youth and caregiver satisfaction with treatment sessions, including the content of educational sessions, perceived impact on adherence, and the likelihood of following through treatment recommendations. Responses were provided on a 4-point Likert scale (0 = Not at all, 1 = Somewhat, 2 = Very, and 3 = Extremely). This survey was administered to each patient and caregiver upon completion of interventions (see Appendix J)

Quality of Data

The measures chosen for this project were frequently used in studies focused on medication adherence in transplant and chronic health conditions. The PMBS and AMBS have been widely used in research, as well as in the clinical settings, to identify perceived barriers to medication. The interventions in MIP have been utilized in the research in optimizing adherence by tailoring and providing education to develop problem-solving and organizational skills through behavior modification. Technology-based interventions have been increasingly used over time to monitor adherence in individuals with chronic illness. A standard self-reported adherence behavior questionnaire was used to assess change in adherence. This evidence-based pratie was an initial approach in utilizing multicomponent intervention package for adolescents and young adults with post-HSCT who are potentially at risk of less than optimal self-management of a complex treatment regimen post-discharge. However, there is evidence for improved compliance with the administration of adherence intervention among youth and young adults with chronic illness. One study that evaluated the efficacy of MIP among youth with inflammatory bowel disease found substantial improvements in the study population including knowledge about their disease and treatment, self-reported adherence, and clinical outcomes (Maddux et al., 2017).

Analysis Plan

The AMBS and PMBS scores were evaluated to determine the decrease in the medication adherence barrier from baseline to post-intervention. Self-report adherence behavior responses were collected from baseline to post-intervention to evaluate the change in adherence from baseline to post-intervention. Similarly, the self-reported MedActionPlan PRO checklist was used to estimate the self-management of the treatment schedule. The intent of this evidence-based project was the delivery of MIP and use of MedActionPlan PRO app with checklist to

favorably impact medication adherence and self-management of treatment regimen in post-HSCT adolescents and young adults.

Results

Two participants, ages 12 – 20, were enrolled in the project, including one female with her mother (caregiver) and one male with his mother (caregiver). Both enrolled participants were Caucasian, diagnosed with Acute Lymphoblastic Leukemia, received HSCT for a malignant disease, and were on multiple prescribed oral medicine at the time of discharge.

The interventions used for this project included a multicomponent adherence promoting intervention package with a MedActionPlan PRO app with checklist, The MIP is comprised of four sessions including an educational and organizational intervention (session 1), behavioral modification (session 2), problem-solving skills and monitoring adherence (session 3) and family functioning. Each session occurred one week apart, lasted approximately 30 to 40 minutes, and took place at the patient BMT follow up outpatient visit. Both, enrolled participants choose to use the MedActionPlan PRO checklist instead of the MedActionPlan PRO app on their smartphone. The MedActionPlan PRO checklist was reviewed with each enrolled participant at each weekly visit, with a total time spent at each visit between 15 -2 0 minutes. The MedActionPlan PRO checklist review included time and dose of medication taken, missed medication dosing, and reasons for not taking medication at the prescribed time. At the session, each enrolled participant was provided with an updated current MedActionPlan PRO checklist for the coming week which was discussed with the enrolled participants until they voiced proper understanding of their current prescribed oral medication before their discharge from the clinic. Both of the enrolled youth attended all the sessions as scheduled and no participant withdrew from the project.

Each enrolled youth along with their caregiver completed the Adolescent Medication Barrier Scale (AMBS) and the Parent Medication Barrier Scale (PMBS) pre-intervention and post-intervention after receiving the four session MIP. The AMBS includes 3 subscales namely Disease Frustration/Adolescent Issue (AMBS -D), Regimen Adaptation/Cognitive (AMBS – R) and Ingestion Issues (AMBS – I). The PMBS includes four subscales, namely Disease Frustration/Adolescent Issue (PMS -D), Regimen Adaptation/Cognitive (PMBS- R), Ingestion Issue (PMBS -I), and Parent Reminder (PMBS-P). For both AMBS and PMBS, higher scores indicate a greater medication adherence barrier. Participant 1 indicated a decrease in AMBS-D, AMBS – R and AMBS -I scores from pre to post-intervention. Also, from pre to post intervention, participant 1 developed symptoms of skin graft versus host disease (GvHD) and another immunosuppressant medicine was added. This participant reported increased symptoms including pain, headache, nausea, vomiting, fatigue and weight gain. This youth's development of skin GvHD, ongoing systemic symptoms, and persistent minimal residual disease (MRD) post-transplant by molecular genetics resulted in increased disease frustration in the parent which were reported during clinic visits. This is believed to account for the parent's report of increased disease frustration on the PMBS from pre to post-intervention. Participant 1 showed an increased PMBS -D score, a decreased PMBS- R score, no change in PMBS-I score, and decreased PMBS – P score at post interventions.

Participant 2 showed an increased AMBS – D score, no change in AMBS – R score, and an increased AMBS – I score from pre to post intervention. Throughout the project, this youth experienced a reoccurrence of skin GvHD rash covering more than 50% of the body surface area despite being on two immunosuppressant agents. At this time, in the clinic, the youth received additional intravenous therapy weekly for his GvHD. Participant 2 completed the PMBS pre-treatment session, but the post-treatment PMBS was not completed. The caregiver of participant

2 did not attend any weekly intervention on medication adherence given that participant 2 is a young adult and capable of taking responsibility for his care. This youth attended all treatment sessions without the parent.

An adherence behavior questionnaire evaluated self-reported adherence, pertaining to the immunosuppressant, antiviral, and antifungal therapy. Each enrolled youth completed this questionnaire weekly for four weeks. Both participants reported 76 to 100% adherence to prescribed immunosuppressant, antiviral, and antifungal medications at both pre and post-intervention.

The other notable effort demonstrated from both of the youth was checking each medication on the MedActionPlan PRO checklist after ingestion. They brought the checklist with them at each visit and verbalized that the MedActionPlan PRO checklist assisted in tracking their medication time, frequency, and doses.

The MIP intervention feasibility was demonstrated by 100% attendance for all enrolled participants. Due to readmission, sessions were rescheduled for one participant within 2-3 days of the originally scheduled sessions. Youth and caregivers were provided a satisfaction survey at the post-treatment session. However, participant 1 did not complete the satisfaction Youth Survey but the mother completed the Parent Survey. She reported that the treatment sessions were “not at all helpful”; however, she acknowledged that the MedActionPlan PRO checklist was “somewhat helpful” and her likelihood of following through on treatment recommendations as “somewhat helpful.” When asked what this parent liked least about the intervention study, she answered that checking medication on the MedActionPlan PRO checklist was “more work” and was “somewhat helpful.” Participant 2 completed the satisfaction Youth Survey and endorsed that each treatment session was “somewhat helpful,” including the educational and organizational intervention, behavior modification, problem-solving, and adherence monitoring.

Participant 2 rated adherence since receiving the adherence intervention as “somewhat improved,” stress or worry about his adherence as “somewhat reduced,” and endorsed being “somewhat likely” to follow through on treatment recommendations. Furthermore, the participant rated that the project improved his organization.

Discussion

Based on the interventions delivered during the duration of the project, one of the primary findings pertains to youth participation in treatment sessions. Participants were engaged in discussions regarding their self-care and medication adherence and showed 100% attendance throughout the weekly educational sessions, indicating participant willingness to attend sessions and gain greater ownership for their care.

The project was implemented in a hematology, oncology, bone marrow transplant outpatient clinic setting at a tertiary care pediatric hospital. The outpatient clinic was an appropriate setting for the implementation of the project because the participants and their caregivers were familiar with the clinic culture and the staff. Each room in the clinic was quiet, spacious, and well lighted. The participants were scheduled for weekly sessions the same day of their BMT routine follow up, and no additional visits were necessary or expected from patients. Also, the BMT clinic staff were informed about the allocated rooms to conduct project sessions to avoid intermittent interruption during treatment sessions. The allocated rooms were prepared for sessions prior to the arrival of the participant. Each trained advanced practice nurse was provided with a folder containing treatment session handouts and questionnaires for each visit. The clinic manager and other clinic staff were also aware of the project including interventions to be conducted and duration of the visits.

The BMT outpatient advanced practice nurses and BMT pharmacist received training by a licensed psychologist at the project site for delivery of the MIP, while the BMT pharmacist

provided training for use of the MedActionPlan PRO application. The facilitated interactive intervention sessions with each youth and their caregiver included timely completion of weekly educational sessions, review of the medication checklist such as missed medicine doses, reasons for missed dose, and discussion of the updated medication checklist including missed medication doses and the revised medication checklist with changes in medication time, doses, and frequency. Clinic staff were kept informed of the project which aided in assigning clinic rooms and efficient clinic flow. A folder placed in the room before participant arrival assisted in the completion of the weekly self-report by the youth and questionnaire in a timely fashion. The project team received support from the BMT clinic staff that facilitated successful implementation.

The project examined the feasibility and impact of utilizing a MIP to increase medication adherence in AYAs with bone marrow transplant recipients. The enrolled participants demonstrated 100% attendance for weekly intervention sessions. This result supports previous studies showing a high level of attendance to adherence-focused MIP in youth with diabetes type 1 (Hood et al., 2010) and youth with inflammatory bowel disease (Maddux et al., 2017). Each enrolled participant and their caregiver opted for MedActionPlan PRO checklist for monitoring adherence instead of the application. Participants were required to check each medication on the checklist after ingestion. Both participants reported taking their oral prescribed medicine on time and reported no missed medication doses. They also completed the weekly MedActionPlan PRO checklist by placing checkmarks in the medication column.

Additionally, each youth completed a weekly self-report of adherence and stated 76% to 100% adherence. The use of self-reported measure of adherence is common practice in pediatrics (Pai & McGardy, 2015). Medication adherence barriers were evaluated for each enrolled youth and their caregiver, pre and post-intervention using the AMBS and the PMBS. In

the project, comparing scores on the AMBS and the PMBS from pre-intervention to post-interventions seems to reflect changes in medication adherence barriers with alteration in health status in AYAs with chronic conditions. The changes in health status resulted in changes in medication, which potentially impacted reports of medication adherence barriers.

Limitations

This project has many limitations. Both the enrolled youth endorsed 100% medication adherence via self-reported questionnaire and MedActionPlan PRO checklist from week 1 to week 4; therefore, no changes in the adherence were observed. A second limitation is a reliance on self -report of adherence via questionnaire and manual checking of each medication on the MedActionPlan PRO checklist which can overestimate adherence by the enrolled patients. The use of an objective measure of adherence, such as the smartphone app of MedActionPlan PRO or lab values for the drug level, would provide more accurate estimates of medication adherence. Another limitation is the actual measure of adherence which was developed for this project. The use of a validated tool is likely to detect more subtle variation in medication adherence among patients. The other notable limitation was the small sample size. This sample was primarily AYA bone marrow transplant recipients from a single institution within a given timeline which limits conclusions drawn regarding the impact of the intervention on medication adherence, generalizability to other patients, and transferability of the evidence-based intervention to other settings. .

During the project period, it was noticed that patients consistently checked their daily prescribed medicine on MedActionPlan PRO checklist that was provided to them on a weekly basis. This assisted them in knowing the name, dose, and frequency of the medications. The author is concerned about the possibility of losing or weakening of this gained attribute over time. The BMT advanced practice nurses and BMT pharmacist will continue to provide

medication checklists to patients at every outpatient BMT follow up visit and ensure use by checking with the patients at their clinic visit.

Throughout the project, efforts were made to minimize limitations by ensuring consistency in the delivery of intervention sessions such as highlighting the goals of each educational session, making it interactive, and finishing the session on time to maximize attendance. The BMT pharmacist reviewed each medication checklist with the patients and their caregivers at each visit to minimize errors in completing the checklist. Appointments for next visits were scheduled based on participant convenience. Data collection forms were reviewed with participants to lessen the possibility of error in completing the forms. Given the small sample size and reports of 76%- 100% adherence at baseline, a conclusion regarding the impact of the intervention on medication adherence and positive change in medication adherence in the project participant is not valid.

Interpretation

The outcome expected was that delivery of the intervention on medication adherence, combined with the smartphone medication reminder application, would improve treatment adherence in AYAs who are HSCT recipients. While the delivery of the intervention on medication adherence was achieved as expected, the impact of the MIP intervention was not demonstrated because of the small sample size. Additionally, project participants choose to use the MedActionPlan PRO checklist instead of the MedActionPlan PRO app on the smartphone to measure adherence. Due to this variation of intervention, project outcomes were affected. Given the complexity of treatments for HSCT recipients, as well as frequent changes in medication regimens in this patient population, relying on accurate patient self-reports of medication adherence cannot be expected and objective adherence measures should be used to validate improvement in adherence.

In the project, the project team expected the enrolled participants, including patients and their caregivers, to complete the study questionnaires, medication barrier scales, and satisfaction surveys, but this did not occur as expected. The caregiver of youth 2 completed the PMBS pre - treatment but did not complete the post-treatment PMBS. Similarly, participant 1 did not complete the youth satisfaction survey post- treatment session.

In conclusion, the implementation of this project provided an experience for both of the enrolled youth in knowing their medication name, dose and frequency. They came to the clinic with a list of medications to be refilled and they also voiced if a medication helped relieve their symptoms. Both patients were present for four weekly educational sessions and endorsed 100% medication adherence via self-report. Based on the targeted patient population in the project, the bone marrow outpatient clinic was an appropriate setting for the implementation of this project

The team suggests the use of a validated tool to detect more subtle variation in medication adherence among patients, such as technology-based tool which can potentially improve the accuracy of self-report. Because of the frequent changes to the treatment regimen and the potential for many side effects of the treatments, the intervention may need to expand in focus on education regarding adherence to include a more thorough description of side effects as well as anticipatory guidance regarding solutions to address side effects.

Because of the negative ramification of medication adherence, understanding and addressing adherence is imperative. Evidence-based interventions on medication adherence combined with technology-based intervention have been shown to result in improved adherence in AYAs with chronic illness. The impact of these interventions is substantial as non-adherence to medication in this population leads to frequent hospitalizations due to complications, increasing healthcare expenditure. We suggest there is a greater need for this study to be

replicated in a larger sample of patients following bone marrow transplant to fully evaluate the impact and effect of the interventions on medication adherence

The actual cost of the study was $500.00 and included handouts, questionnaires, and surveys for participants. The author calculated the cost of pillboxes; however, these were donated for participants by the hematology, oncology division at the project setting. The actual cost of the intervention for each enrolled youth was $ 10.00 – $15.00. The cost of the interventions was nominal and the likelihood of sustaining the intervention is possible because there is no potential economic burden to implement interventions.

Conclusion

Medication adherence is a multifaceted human behavior. Across the studies, medication non-adherence has been reported as a key public health issue resulting in suboptimal clinical outcomes and increased healthcare costs. Several factors contribute to medication non-adherence such as individuals, social, environmental, knowledge deficit of disease, inadequate self-efficacy, and beliefs about medications. Evidence shows that when adherence interventions are tailored specifically to perceived adherence barriers, AYA normative developmental behaviors, and psychosocial factors such as family functioning, then improvements in medication adherence are most significant. Major evidence exists in research that these interventions are feasible, applicable, and promising in promoting adherence in AYAs with chronic health conditions including transplant. With the negative consequences of poor adherence following HSCT and implications of patient outcomes, the application of adherence focused-intervention is promising in improving quality care.

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Appendix A: Definition of Terms

1. 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)

2. Adherence focused-interventions: intervention that are emphasize adherence

3. Adolescent/ Young adult: based on ages: a) Early adolescence: approximate ages 10 to 13, or middle school years; b) Middle adolescence: approximate ages 14 to 17, or high school years; and c) Late adolescence/ Young adult: approximate ages 17 to 25, or college or 4 years of work after high school.

4. Chronic illness: a health condition that lasts more the 3 months

5. Hematopoietic stem cell transplant: a procedure in which donor stem cell are infused intravenously in recipient

6. Technology-based interventions: A type pf electronic sent and received via mobile phone

Appendix B: Hierarchy of Evidence Table

Rating System for the Hierarchy of Evidence For an Interventional Inquiry (Modification by Dr. Lindholm for course N5613)	
Level I	Evidence from a systematic review or meta-analysis of all relevant RCTs. *Evidence-based clinical practice guidelines based on systematic reviews of RCTs).**
Level II	Evidence obtained from well-designed RCT. *Quantitative systematic review of well-designed controlled trial without randomization.*
Level III	Evidence obtained from well-designed controlled trial without randomization *(quasi-experimental).* *Quantitative systematic review of case-control, cohort, or correlational studies.*
Level IV	Evidence from well-designed case-control or cohort study *(or cross-sectional study)*
Level V	Evidence from systematic review of *quantitative* descriptive *(no relationships to examine)* or qualitative studies.
Level VI	Evidence from a single *quantitative* descriptive *(no relationships to examine in the study) or* qualitative study
Level VII	Evidence from the opinion of authorities and/or reports of expert committees

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Appendix C, Synthesis of Evidence

Inquiry: Among the adolescents and young adults who are recipients of hematopoietic stem cell transplant (HSCT), does implementation of a multicomponent intervention package (MIP) and smartphone medication reminder application improve adherence and self-management of treatment regimen, during a three-month period at a bone marrow transplant outpatient clinic?

Article	**Purpose of Study or Review**	**• Research Design • Evidence evel • Variables**	**• Sample • Population • Setting**	**Measurement of Variables**	**• Results • Data Analysis**	**• Findings Relevant to Project • Limitations**
Subtopic: Multicomponent intervention package (MIP) to promote adherence						
Pai et al. (2014) Systematic review and Meta-analysis of psychological Interventions to promote treatment adherence in children, adolescents and young adults with chronic illness	Examine the effectiveness of adherence-promoting interventions for youth with chronic health conditions	• Systematic review with meta-analysis of RTC • Level 2 • Adherence & health outcomes	• 23 studies • Children, adolescents and young adults with chronic illness	Bioassays, self-report, questionnaires, parent-report questionnaires, semi-structure interviews, prescription refill history, daily diaries & electronic monitoring device	• In-person and technology-based interventions were significant (p level < 0.02) • Cohen's *d* statistics & I^2 • Quality of the evidence base were evaluated using GRADE approach	• High or unclear risk of bias was due to difficulties in blinding participants involved in psychological interventions. • Small number of studies coupled w/ diversity of pediatric populations and adherence targets
Pai et al. (2015) Assessing medication adherence as a standard of care in pediatric oncology	Examining medication adherence among pediatric cancer patients and develop evidence-based guidelines for supporting med	• Review included prospective, cross-sectional, qualitative; RTC & guideline developed by experts • Level 7	• 14 studies • Children and adolescent oncology patients	• GRADE criteria used to assess quality of evidence	• Review concluded that there is moderate –quality evidence to support med adherence • Quality of the evidence base were evaluated	• Integration of routine adherence monitoring into standard of care in pediatric oncology could optimize treatment adherence and health outcomes

	adherence in clinical care	• Quality of evidence			using GRADE approach	
Hood at el. (2010) Interventions with adherence-promoting components in pediatric type I diabetes	Review interventions with adherence-promoting components and their impact on glycemic control via meta-analysis	• Meta-analysis of RTC • Level 2 • Adherence promoting intervention and glycemic control	• 15 studies • Youth < 19 years with type I diabetes	Mean effect size for pre- to post-treatment change for the intervention verses control group	• Analysis for pre to post-treatment effects for the intervention group was significant (P < 0.05) versus control group achieved P 0.01 – 0.23) • Weighted least square for effect size • Q statistic used to analyze studies included in meta-analysis	• Glycemic control will not improve if interventions focus on direct, behavioral process while neglecting emotional, social & family processes. • Few of studies targeted "high risk" youth who consistently demonstrate high A1C values and had fewer resources
Maddux et al. (2017) A pilot study evaluating the impact of an adherence-promoting intervention among non-adherent youth with inflammatory	Examine feasibility and impact of a multicomponent adherence intervention among youth with inflammatory bowel disease (IBD)	• Longitudinal, single-site, multiple base-line design (MBD) cohort study • Level 4 • Increased in adherence from baseline to post-intervention	• 12 IBD patients	• session attendance & completion of assigned behavioral tasks • Electronic pill boxes to measure adherence • Adherence to medication included baseline, post-	• Mean adherence increase 12% from baseline to post-intervention (p < 0.01) and 6% from baseline to 1 month post follow up (p < 0.025) • IBM's SPSS version 22	• Delivery of a multicomponent adherence interventions to poorly adherent youth with IBD can results in significant improvement in their adherence to oral medication

bowel disease (IBD)				intervention and 1-month follow up	statistics. Chi-square and General Linear Model were used	
Subtopic: Utilization of technology-based intervention in enhancing treatment adherence.						
Sheller et al.(2016) Development and field testing of Teen Pocket PATH (TPP), a mobile health application to improve medication adherence in adolescent solid organ recipients	Developed and tested the prototype of TPP – an mHealth application to promote medication adherence and enhance communication about medication management between adolescents and primary caregivers	• Prospective cohort study • Level 4 • Face to face usability sessions, 6 week field test of TPP and debriefing session at the end of field testing	• 7 adolescents 11 – 18 yrs with solid organ transplant who were >/= 1 yr post-transplant (included 4 liver-transplant, 2 heart transplant and 1 lung transplant) with caregivers • Transplant unit	Demographic questionnaires, level of electronic device/media use and TPP	• 100% participants expressed TPP effective for monitoring medications • PSSUQ-validated measure used in the development of technological application	• TPP found to be a promising mHealth adherence tool • Lack of ethnic diversity in study sample and TPP was tested in a single center – limiting generalizability
Badawy & Kuhns. (2016). Economic Evaluation of Text-Messaging and Smartphone-Based Interventions to Improve Medication Adherence in Adolescents with Chronic Health Conditions (CHC):	Conduct an economic evaluation of text-messaging and smartphone-based interventions that focus on improving medication adherence in adolescents with CHCs.	• Systematic Review of RTC • Level 2 • Technology-based intervention, adherence measures and rates, disease related outcomes and cost-	• 156 studies • 12 – 24 yrs children and adolescents with CHCs • Hem/Onc and adolescent medicine	• GRADE criteria used to assess quality of evidence	• Authors found no evidence to support the cost effectiveness of technology-based text messaging and smartphone app interventions • Quality of the evidence base were evaluated	• Technology-based interventions to support medication adherence are promising, but need to be tested and validated • Not all articles met pre-defined criteria.

A Systematic Review		effectiveness of technological intervention			using GRADE approach.	Smartphone app initiative have been piloted but data generated from these studies are limited. Efficacy, effectiveness and economic evaluation is warranted.

Story et al. (2016) Monitoring therapy adherence of Tuberculosis patients by using Video-enabled electronic device	Examine the effectiveness of video or virtually observed therapy (VOT) in improving tuberculosis (TB) patient outcomes	• Review of controlled trials • Level 3 • effectiveness of VOT	• Patients with TB on 6 months or 2 years therapy	N/A	• VOT is new and emerging technology with limited knowledge about its effectiveness and limitations	• VOT needs to be evaluated in more diverse conditions and settings • Synergies between digital health & traditional approaches to improve patient outcomes needs to be explored.
Creary et al. (2014) A pilot study of electronic directly observed therapy to improve hydroxyurea adherence in pediatric patients with sickle cell disease	Determine feasibility of electronic directly observed therapy (DOT) in improving hydroxyurea (HU) adherence	• Prospective cohort study • Level 4 • Feasibility and participants satisfaction with electronic DOT and HU adherence. Mean corpuscular volume (MCV), hemoglobin F % (HbF)	• 15 Sickle cell patients on HU therapy for >/= 6 months were enrolled but 14 completed the study • Pediatric Hem/Onc	• 8 dimension of telehealth obtrusiveness, 5-point Likert sacle survey to measure DOT's intrusiveness, usability and functionality.	• Participants medication possession ratio at study entry to the end of study improved from 0.75 to 0.91 (p = 0.02). HU adherence with DOT was 93.3%; MCV and HbF increased from 96.0 to 107.2 (p = 0.009) and 10.5 to 11.4 (p = 0.03), respectively.	• Study demonstrate electronic DOT is feasible, acceptable and can achieve high HU adherence • Single center pilot study. Need further study to confirm electronic DOT can improve HU adherence and impact clinical outcomes in children

					• Morisky medication adherence scale (MMAS – 4), medication possession ratio (MPR) and video observation	
Subtopic: Recognizing adherence barriers to maximize impact of MIP.						
Pai, et al. (2017). Poor adherence is associated with more infections after pediatric hematopoietic stem cell transplant	Examine rates of outpatient oral medication adherence in children after hematopoietic stem cell transplant (HSCT) and incidence of infections	• Controlled cohort study • Level 4 • Relationship to medication adherence with incidence of infection • Control variable includes age, medication dosing schedule, medication taste, swallowing difficulty, time since transplant and transplant type • Predetermine medication selected by research team using a priori	• 50 post-HSCT patients (aged 0-16 years) and their primary caregivers • Bone marrow transplant outpatient clinic (hospital-based)	• Medication Event Monitoring System (MEMS)	• Indicated no variables were significantly associated with GvHD within the model, including adherence (P > .05). • Older patient had significantly higher # of infections (P=.02) • lower adherence, associated with higher infections (P < .005) • Poisson Regression Analyses • Used 2 models 1 with graft vs host disease (GvHD) and 1 with infection outcome • Descriptive statistics were used to summarize	• Study results lend substantial support for the generalizability of the findings to larger pediatric HSCT population • Potential for Hawthorne effect with electronic pill bottles. • Exact medication monitored for the sample varied because of heterogeneity of the diseases treated and types of transplant

Prendergast & Gaston. (2010). Optimizing Medication Adherence: an Ongoing Opportunity To Improve Outcomes After Kidney Transplantation	• Identification of risk factors and measure that effectively address them improving clinical outcomes	• Mini-Review • Level IV • Medication monitoring, patient self-report, drug level	• Patients of renal allograft loss attributed to chronic rejection in recipients with functioning graft 6 months post-transplant	• Electronic medication monitoring, patient self-report, drug level monitoring • One study tested reliability of patient reporting and physician identification of non-adherence to electronic monitoring	• Use of repetitive teaching to promote adherence. •Combination of interventions via team approach improves adherence	• No study intervention was found to be superior as interventions to improve adherence needs to be multi-dimensional • Limitation includes: drug level do not provide information about adherence patterns, Biomarker/tracers were expensive and impractical; electronic pill box expensive and unattractive if participants using multi-dose pill box, self-report are poor recall and overestimate adherence measurement.
Foster & Ahna. (2014). Adherence in Adolescent and Young Adult Kidney Transplant Recipients	Review different ways in which adherence may be compromised and impact of poor adherence in adolescents	•Systematic Review • Level I • N/A	• Adolescent and Young Adult Kidney Transplant Recipients	• Direct methods included: observation, drug level and biomarker • Indirect methods included: electronic monitoring, pill count, pharmacy records & self-report	• Effective intervention for adherence included: education w/ combination of adherence monitoring, promotion of problem-solving, goal setting, development of routine and adherence support	

Danziger-Isakov et al. (2016) Perceived barriers to medication adherence in pediatric and adolescent solid organ transplantation	• Conduct comparison of perceived barriers to adherence in pediatrics and adolescent solid organ transplants	• Cross-sectional Cohort study • Level IV • Age, propensity score for age group, recipient and guardian perceptions of barriers to adherence and transplant type	• Pediatric and adolescent solid organ transplant patients (368 subject/their guardian enrolled) •Multicenter study	• Parent and adolescent medication barrier scale (PMBS and AMBS)	• Perceived barriers were more frequently reported by guardian of older recipients compared to guardian of younger recipients, related to medication scheduling and medication/disease frustration. Pre-adolescents & adolescents scores were not statistically different for any of 3 factors and there were no significant interaction between age group and organ for any AMBS factors ($p > 0.05$). • Primary analyses compared younger and older patients on each PMBS factors using linear regression models w/multiple imputation. The difference between older recipients and guardian perceptions of	• Lack of association between perceived barriers to adherence reported in the AMBS/PMBS; a single blood level of primary immunosuppressant demonstrated the limitation of adherence measure; study cross-sectional single snapshot design

					barrier to adherence were assessed using paired t-test on the participants PMBS & AMBS factor scores. Consistency between the matched PMBS & AMBS factor scores was assessed using intraclass correlation coefficients. Secondary analyses assessed the interaction between age group and transplant type on PMBS & AMBS factors using linear regression models Association of 3 identified PMBS factors and subject age was assessed. Secondary analyses assessed associations between PMBS, AMBS and patient demographic	

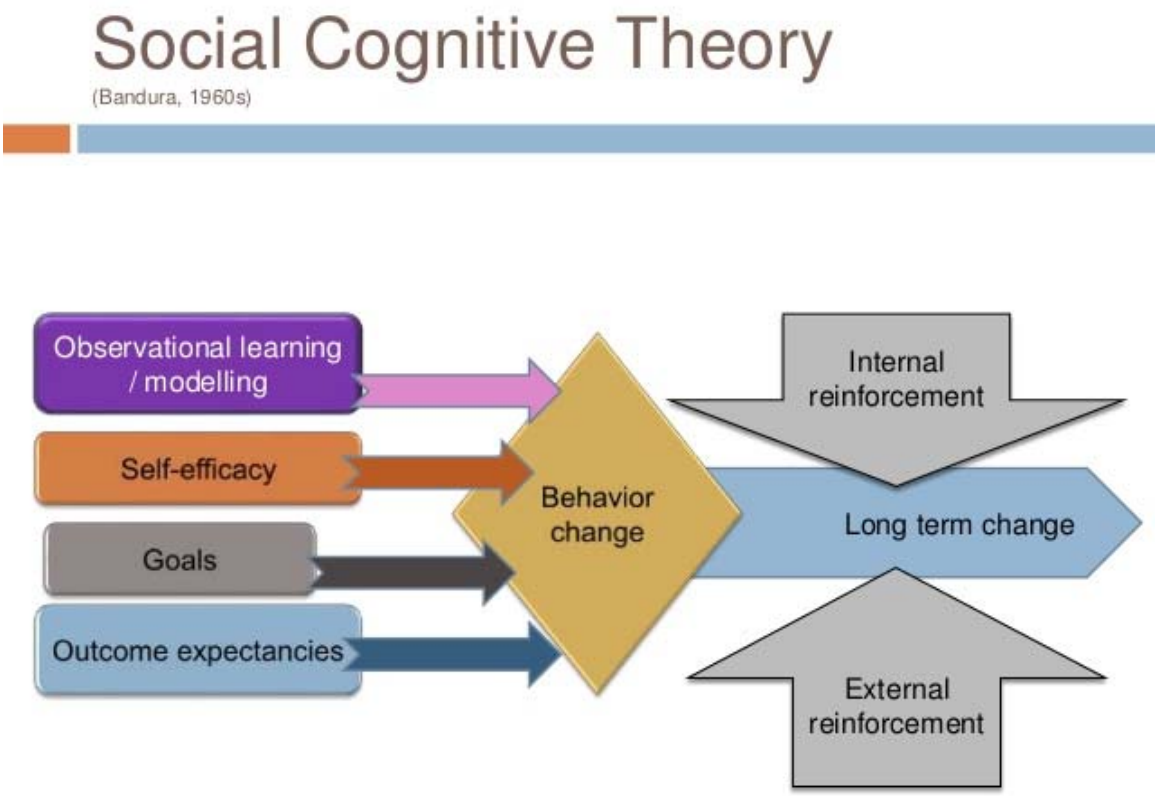
McCormick et al. (2013). Emotional Functioning, Barriers and medication Adherence in pediatric transplant recipients	• assessed relationship among internalizing symptoms, barriers to medication adherence and medication adherence in adolescents with solid organ transplants	• Controlled cohort Study • Level IV • Barriers to adherence; emotional functioning and medication adherence	• 72 adolescents with solid organ transplant at transplant unit	• AMBS that assessed adolescents, Adolescents emotional functioning was assessed by three domains of internalizing symptoms: depression, anxiety and posttraumatic stress. • Medication adherence measure (MAM) to assess prescribe medications • MAM has shown good convergent validity with a systematic review of adherence, reporting that higher rates of non-adherence on MAM were positively correlated with rates of non-adherence calculated with electronic monitoring	• Bivariate correlations revealed significant relationship between barriers and internalizing symptoms of depression, anxiety and posttraumatic stress. • Barriers indicative of adaptation to the med regimen were related to medication adherence and mediated the relationship between internalizing symptoms and med adherence • Multiple mediator models were tested via bootstrapping methods	• Due to the cross-sectional nature or research ability to draw conclusions about causality was limited. • findings were based on individual self-report, may pose the risk of inaccuracy due to poor recall or social desirability

Stirratt et al. (2015). Self-report measures of medication adherence behavior: recommendations on optimal use	• to review the current evidence-based behind self-report measures of medication adherence	• Level VII • N/A	• Patient with chronic illness Review included research report regarding one or more retrospective self-report measure of medication adherence behavior, published in English in the last 30 years that reported validation data relative to clinical outcome		• Rigorous development and testing of self-report measures of adherence should be a research priority. There is a need to better understand how to best assess adherence among patients taking multiple medications, most in patient with chronic conditions. Use of interactive voice device (IVR) or smart phone application is an important direction for future research	• Failure to use standardized and validated self-report measure is a common problem in health research and clinical practice

Mistry et al. (2015) Technology-mediated interventions (TMI) for enhancing medication adherence	• Assess the effects of TMI, intended to enhance patient adherence to prescribed medications on medication adherence and clinical outcomes	• Systematic Review of RTCs • Level I • RTCs grouped into 3 categories 1) education and/or counselling; 2) Self-monitoring and/or feedback; and 3) electronic reminders	• 38 studies met inclusion criteria • Children and adolescents with chronic illness	• Cochrane risk of bias tool	• All analyses were conducted using SPSS, version 20.0 • 50% (19/38) of studies found improvement in at least one measure of adherence and 39% (15/38) of studies found improvement in at least one clinical outcome measure whereas 36.8% (14/38) of studies finding improvement in both adherence and clinical outcome	• Review showed limited effective of TMI for improving patient adherence and clinical outcomes • Lack of high-quality studies. Need to future reviews including quasi-experimental study design in addition to RTCs • E-health and use of technology to improve medication adherence are in their infancy

Wu et.al. (2018) Use of smartphone application for prompting oral medication adherence among adolescents and young adults (AYAs) with cancer	• Explore the feasibility and acceptability of use of a smartphone medication reminder application to promote adherence to oral medication among AYAs	• Controlled cohort study • Level IV • Weekly self-report questionnaires. Usage of application by participants and Perceived ease of use and usefulness of application by participants	• 23 AYAs with cancer • Children's oncology group-affiliated children's hospital and National Cancer Institute – designated comprehensive cancer center in Salt Lake City, UT	• Pre/post-test, application usage was measure by 1) data download from cloud-based server; and 11) online self-report questionnaire completed by participants each week. Six item. Cronbach alpha for perceived ease of use of application and seven items, Cronbach alpha for perceived usefulness of application	• 95 participants (58%) indicated AYAs took medication ~ 76% - 100% of the time, whereas 33 participants ~ 20% indicated taking medication ~ 51% - 75% of the time. 15 (9%) of participant ignored medication reminders. 65% of participants endorsed that application was useful. • Descriptive statistics used for demographic characteristics. Feasibility frequencies and proportions calculated from Dosecast usage data downloaded and descriptive statistics used for acceptability including perceived ease of use and perceived usefulness of the application	• Results supports the use of electronically delivered health promotion interventions in pediatric and AYA population with cancer • Application usage data were downloaded directly from application server. Study sample size was small and was limited to single geographic area

Appendix D: Theory to Application Diagram



1. *Observational learning/modeling*- Participants with their caregiver received four weeks of educational session using multicomponent intervention package (MIP). The MIP consists of four components including educational and organizational intervention, behavioral modification, problem solving skills and monitoring adherence and family functioning. Each component of MIP will facilitate learning among participants and will aide to reduce adherence barriers
2. *Self-efficacy*- Is the key construct in this model. Each participant and caregiver belief about having ability and capacity to accomplish a task that would help them to perform behavior to ensure success.
3. *Goals:* improve adherence and self-management of treatment regimen
4. *Outcome expectancies*- improve adherence and self-management of treatment regimen.

5. *Behavior change*- learning behavior modification, problem solving and organizational skill and improving family functioning to help promote adherence. Participants and caregiver attended four weeks of education session and completed MedActionPlan PRO checklist daily after ingestion of medication.
6. *Internal reinforcement*- MIP education session provided knowledge and skill for self-management of treatment regimen
7. *Long-term change*- The goals of this project are to improve medication adherence and sustain compliance to self-management of their treatment regimen
8. *External reinforcement*- MIP education session, healthcare provider and caregiver were able inspire positive change, help patient to overcome barrier to change and provide ongoing support for emotional well-being.

Appendix E: Logic Model

Inquiry, PICOTS: Among the adolescents and young adults who are recipients of hematopoietic stem cell transplant (HSCT), does implementation of a multicomponent intervention package (MIP) and smartphone medication reminder application improve adherence and self-management of treatment regimen, during a three-month period at a bone marrow transplant outpatient clinic?

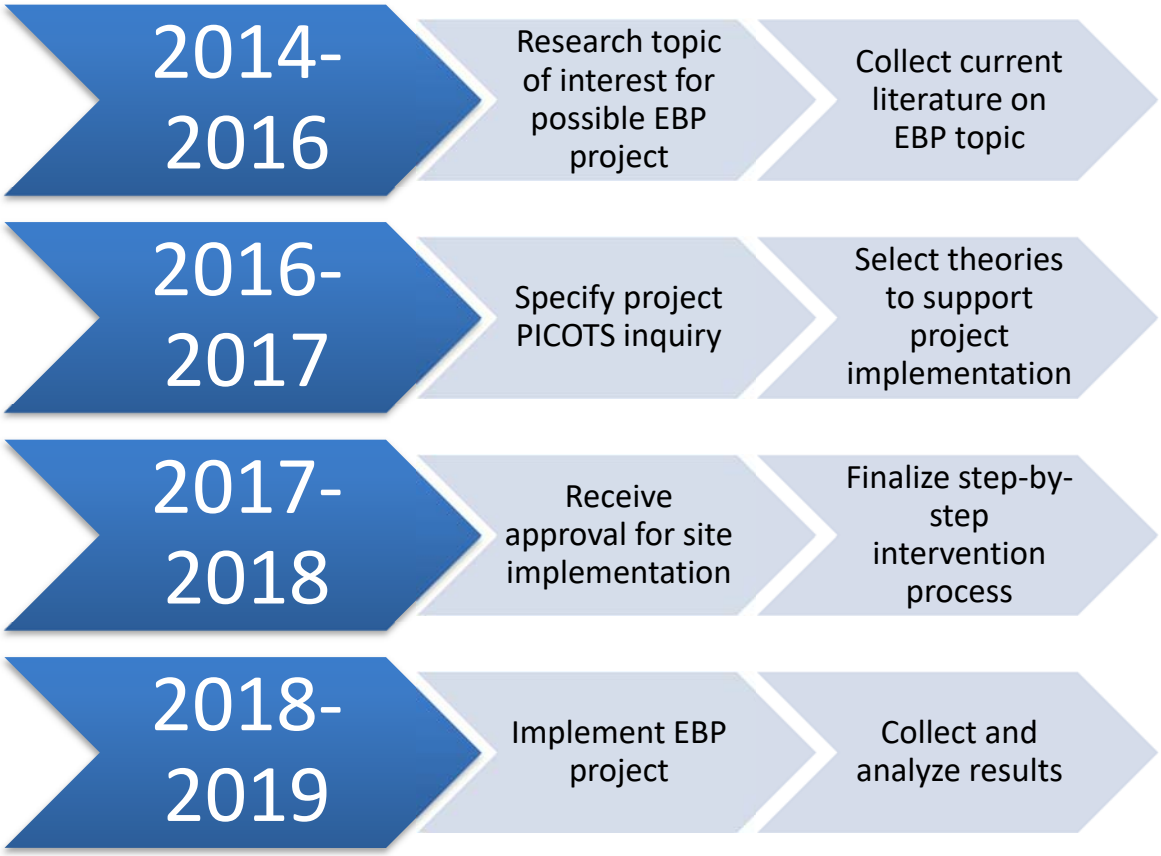
Inputs	Intervention(s) Outputs		Outcomes -- Impact		
	Activities	*Participation*	*Short*	*Medium*	*Long*
Evidence, sub-topics 1.Multicomponent adherence package (MIP) to promote adherence 2. Utilization of technology-based intervention in enhancing treatment adherence 3. Recognizing adherence barriers to maximize impact of MIP **Major Facilitators or Contributors** 1. Patient and caregiver readiness 2. BMT team support including midlevel providers, staff nurse and pharmacists 3. Mentor support **Major Barriers or Challenges** 1. Funding 2. Inadequate research staff support 3. Clinic time slot and room availability for education session 4. Inadequate IT support	**EBP Multicomponent Intervention Package (MIP) & smartphone medication reminder application for promoting adherence** - Participants and caregiver will receive ~ 4 weeks education session MIP. - Participants and caregiver will receive training for smartphone app usage - Participants and caregiver will complete self-report questionnaire – pre and post interventions **Major steps of the intervention (brief phrases)** 1. APRNs, pharmacist and will receive training to implement (MIP) 2. Schedule participants for clinic slot for FU 3. Install smartphone apps for MedActionPlan PRO	**The participants** Adolescents and young adults (12 – 20yr) with hematopoietic stem cell transplant and their caregivers **Site** Children's Mercy Hospital, outpatient clinic **Time Frame** October to January 2018 **Consent or assent:** Yes for participation in study **Other person(s) collecting data: NO** **Others directly involved in consent** Yes	**(Completed during DNP Project)** **Outcome(s) to be measured** Adherence from baseline to post-intervention and from baseline to 1 month follow up **Measurement tool** 1. PMBS/AMBS for pre- and post-interventions self-report questionnaire 2. Usage and responses of smartphone application **Statistical analysis to be used** 1. IBM's SPSS version 22 statistics. 2. A paired two tailed	**(after student DNP)** **Outcomes to be measured** Utilize MIP as standard of care to promote medication adherence in AYAs with	**(after student DNP)** **Outcomes that are potentials** Decrease in transplant related complication and improve quality of life

Rev. 7/09, 1/2015 http://www.uwex.edu/ces/lmcourse/interface/coop_M1_Overview.htm Logic-Model Worksheet content revisions by Lyla Lindholm, Applied to DNP EBP Project. Not to be placed on web for public used. For UMKC DNP coursework only

Appendix F: Cost Table

Student Investigator	Project Start Date- 01/2019	
Type of Grant-	None	
Item	**Cost**	**Note**
Rukhsana Rahmetulla- Student Investigator Salary	$0.00	Student Investigator- Uncompensated
BMT Outpatient NPs : 2	$0.00	Student Investigator- Uncompensated
BMT Pharmacist: 1	$0.00	Student Investigator- Uncompensated
Project clinical expert	$0.00	Student Investigator- Uncompensated
MedActionPlan PRO checklist	$0.00	Printed updated checklist was provided at each session
Supplies: MedActionPlan PRO checklist for participants Education handouts for project team and participants Pill boxes	 $0.00 $10 – 15/participants Received donation	 Provided by project team
Total	$ 20 – 30 for both participants	

Appendix G: Project Timeline Flow Graphic



Appendix H: Intervention Flow Diagram

Step 1: Study team training and recruitment

Outpatient bone marrow transplant (BMT) nurse practitioners and pharmacist received 2 sessions each 90 minutes by licensed psychologist (clinical expert) for Multicomponent Interventions Package (MIP) for standard implementation

Post-transplant recipients who are 12 – 20 years with their care giver were approached for project participation (BMT Outpatient APN and pharmacist), during parent care status ~ 3-4 days prior to their discharge from bone marrow transplant inpatient unit at local hospital.

↓

Step 2: Scheduling study participants with caregiver

Study participants and their care givers were scheduled for MIP (four weekly in person sessions) with regular outpatient clinic visits.

↓

Step 3: Baseline data collection

- Baseline assessment (pre-intervention) using Adolescents Medication Barrier Scale (AMBS) and Parent Medication Barrier Scale (PMBS)
- Med Rec (BMT Pharmacist/APN) using MedActionPlan PRO checklist and questionnaire self-report adherence behavior

↓

Step 4: Weekly Adherence assessment (Outpatient visit)

- Med Rec (BMT Pharmacist/APN) using MedActionPlan PRO checklist and questionnaire self-report adherence behavior

↓

Step 5: Education sessions and assessment

- MIP sessions every week x 4 weeks, using MedActionPlan PRO checklist with clinic visits, questionnaire self-report adherence behavior
- At 5th week participants to complete post-intervention Adolescents Medication Barrier Scale (AMBS), Parent Medication Barrier Scale (PMBS) as post intervention self-report and adherence intervention satisfaction survey (Parent/caregiver and patient)

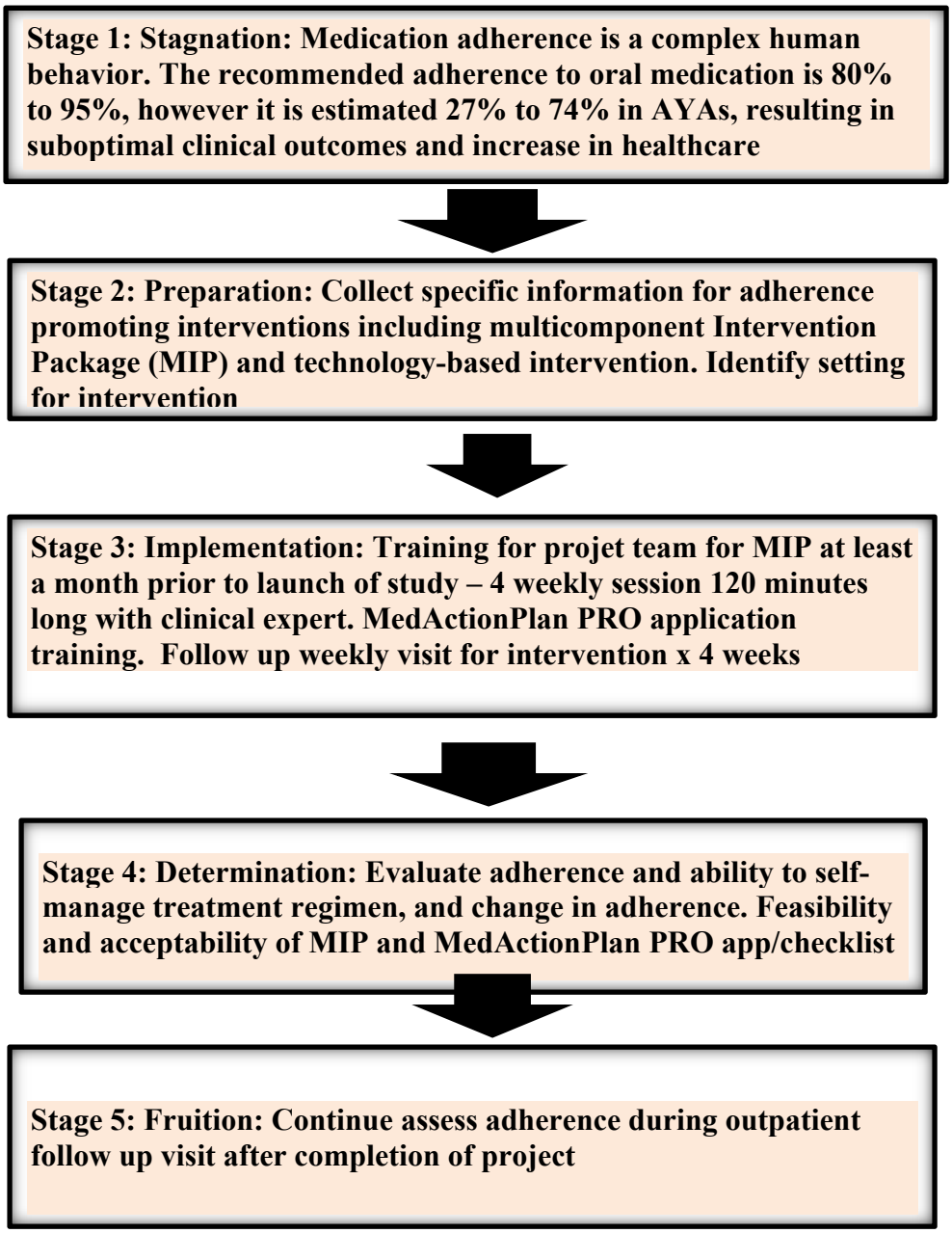
↓

Step 6: Data collection, analysis and evaluation

- Data Collection and analysis: Collect data from pre and post intervention using PMBA and AMBS average, usage of MedActionPlan PRO checklist with clinic visits, questionnaire self-report adherence behavior and adherence intervention satisfaction survey (Parent/caregiver and patient)

Appendix I: Theory to Application Diagram

Change Curve Model



Melnyk, D.M. & Fineout-Overholt, E. (2015). *Evidence-based practice in nursing and healthcare: a guide to best practice* (3rd ed). Philadelphia: Wolters Kluwer/Lippincott Williams & Wilkins.

Appendix J: Measurement Tool

Add the key reliability content to the body of the paper content.

Outcome	Instrument or Source	Validity	Reliability	Permission for Use
#1 (a) Barriers to adherence	AMBS & PMBS	PMBS is designed to assess adolescent and parent perceived barriers to their child's medication taking whereas AMBS assesses adolescent perceived barriers to their prescribed medication taking. Both are validated tools for assess barriers to medication adherence	PMBS consists 16 items with max score of 80. Cronbach α 0.87 indicates strong internal consistency. AMBS consists 17 items with a max score of 85. Cronbach α 0.86 indicates strong internal consistency.	Permission received via email
#2 MedActionPlan PRO application	MedActionPlan PRO checklist	N/A	N/A	N/A
# 3 Multicomponent adherence interventions	Intervention's impact	N/A	N/A	N/A
# 4 Self-Reported adherence behaviors	Questionnaire	N/A	N/A	N/A

Appendix K: Permission for Tool

Rukhsana,

Thanks for your interest!

Yes, you have permission to use! Attached are the measures and scoring directions.

Thanks!