CULTURALLY INFORMED MOTIVATIONAL INTERVIEWING TO IMPROVE ORAL CHEMOTHERAPY ADHERENCE FOR PEDIATRIC ACUTE LYMPHOBLASTIC LEUKEMIAPATIENTS AND THEIR CAREGIVERS: A FEASIBILITY, ACCEPTABILITY, AND PRELIMINARY EFFICACY TRIAL

APPROVED BY SUPERVISORY COMMITTEE

Melissa A. Faith, Ph.D., ABPP

Sunita Stewart, Ph.D., ABPP

Julie Germann, Ph.D., ABPP

Naomi Winick, MD

Dailyn Acosta, Ph.D.

DEDICATION

"When a person really desires something, all the universe conspires

to help that person to realize his dream."

Paulo Coelho

To *mami*, *papi*, Farah, and Ben—thank you for conspiring to help me realize my dreams.

ACKNOWLEDGEMENTS

First and foremost, I would like to express my sincere appreciation and gratitude to my dissertation chair and primary mentor, Dr. Melissa Faith. Without her unwavering mentorship, knowledge, support, and encouragement throughout the past four years, this dissertation and research study would not have been possible. I am also grateful for Dr. Sunita Stewart, an inspiring and caring mentor. I truly admire the infectious passion she has for research and her ability to strike the delicate balance between providing guidance and fostering independence in her students. I also appreciate my other committee members, Dr. Naomi Winick, Dr. Julie Germann, and Dr. Dailyn Acosta; their expert suggestions and constant cheerleading were invaluable for my ability to complete this project. I am also grateful for Dr. Paul Nakonezny and Lucas Zullo's instrumental support with statistics and data analysis. Moreover, this study would not have come to fruition without my research partner-in-crime, Chelsea Pratt. Additionally, I am grateful for the support of our research team, as well as Children's Health Center for Cancer and Blood Disorders (CCBD) patients, families, and staff: Dr. Raul Montiel-Esparza, Maria Bisceglia, Leah Adix, Nancy Alvarez, Monica Garza Saenz, and Duc Lam.

I would also like to recognize my clinical supervisors at Children's Health: Dr. Celia Heppner, Dr. Jamie Becker, Dr. Betsy Kennard, Dr. Brittany Gresl, Dr. Kelli Triplett, Dr. Jasmine Ghannadpour, Dr. Andy McGarrahan, and Dr. Danette Beitra. Each of one of them has contributed greatly to my personal and professional growth as a clinician-researcher during the past four years. Similarly, this journey would not have been the same without the students, faculty, and staff at UT Southwestern's Clinical Psychology Department. To our Education Coordinator, Adrianna Harris—thank you for your endless patience and grace putting up with my tardiness on administrative deadlines during graduate school. Graduate school would not

have been as enjoyable without my classmates and friends: Jeanette Chong (best study buddy!), Sarah Dinkins, Cole Hague, Lucas Zullo, Savanna Duley, Natalie Benedetto, Jessica Wiblin, and Hunter Small. Similarly, many thanks to my colleagues and friends at UT Southwestern and Children's Health: Laura Frazee, Saba Masood, Tahnae Tarketon, Kelsey Rogers, Kristin Wolfe, Lexi Morehead, Sarita Patel, and Wade McDonald.

Last but not least, none of this would have been possible without my family: my parents Mohammed El-Behadli and Maria del Mar Gonzalez, my grandparents Eliseo Gonzalez and Maria de la Paz Vazquez, my sister Farah El-Behadli, and my husband Ben Lopez. My husband, Ben Lopez, deserves a special recognition for his constant support and encouragement each day of this long four-year journey—Ben, thank you for cooking me dinners, revising drafts, listening to presentations, and letting me vent; you deserve an honorary Ph.D! Finally, my sweet puppy Luna holds a special place in my heart for keeping me company on the couch during late nights devoted to writing this dissertation.

CULTURALLY INFORMED MOTIVATIONAL INTERVIEWING TO IMPROVE ORAL CHEMOTHERAPY ADHERENCE FOR PEDIATRIC ACUTE LYMPHOBLASTIC LEUKEMIAPATIENTS AND THEIR CAREGIVERS: A FEASIBILITY, ACCEPTABILITY, AND PRELIMINARY EFFICACY TRIAL

by

ANA F. EL-BEHADLI GONZALEZ, M.A.

DISSERTATION

Presented to the Faculty of the Graduate School of Biomedical Sciences

The University of Texas Southwestern Medical Center at Dallas

In Partial Fulfillment of the Requirements

for the Degree of

DOCTOR OF PHILOSOPHY

The University of Texas Southwestern Medical Center at Dallas

Dallas, Texas

August, 2019

.

CULTURALLY INFORMED MOTIVATIONAL INTERVIEWING TO IMPROVE ORAL CHEMOTHERAPY ADHERENCE FOR PEDIATRIC ACUTE LYMPHOBLASTIC LEUKEMIAPATIENTS AND THEIR CAREGIVERS: A FEASIBILITY, ACCEPTABILITY,AND PRELIMINARY EFFICACY TRIAL

Publication No._____

Ana F. El-Behadli Gonzalez, Ph.D.

The University of Texas Southwestern Medical Center at Dallas, 2019

Supervising Faculty, Project Mentor, and Co-Chair: Melissa A. Faith, PhD, ABPP
Dissertation Co-Chair: Sunita M. Stewart, PhD, ABPP

Background: Curative therapy for childhood acute lymphoblastic leukemia (ALL) mandates a two-to-three-year maintenance chemotherapy phase wherein patients must take daily oral 6-mercaptopurine (6-MP). 6-MP regimen adherence is challenging and failure to take medication has been associated with an increase in relapse risk. Accordingly, interventions that enhance 6-MP adherence during ALL maintenance chemotherapy may result in decreased morbidity and mortality for pediatric ALL patients. This study investigated the feasibility and acceptability of brief, English- and Spanish-delivered, culturally informed MI sessions during routine outpatient ALL maintenance therapy appointments. . Additionally, this study preliminarily explored MI efficacy, compared to an education-only control, for improving caregiver-reported 6-MP adherence, patients' TGN blood serum levels, and caregiver-perceived 6-MP adherence barriers. **Method:** Participants included 121 caregivers (Age *M*(*SD*) = 36.66(8.02), 80.7% mothers, 47.1% Hispanic, 23.1% Spanish-speaking) of pediatric ALL patients (Age *M*(*SD*) = 7.55(4.80), range = .9-24; 66.1% male; Medicaid = 54.2%; B- and T-ALL risk category: Standard = 50.9%, High/Very High = 49.1%) in maintenance ALL treatment. Eighty caregivers (66.12%) were randomized to receive MI and the remaining 42 caregivers (33.8%) were randomized to the education-only control group. For the purpose of analyses, participants were categorized based on their ethnicity and primary language as a proxy for potential cultural similarities. Cultural categories included: (1) Non-Hispanic, English-speaking caregivers (*N*=63, 52.07%); (2) Hispanic, English-speaking caregivers (N=30, 24.79%); and (3) Hispanic, Spanish-speaking caregivers (*N*=28, 23.14%). Participants completed self-report measures assessing demographics, 6-MP adherence, 6-MP knowledge, perceived medication adherence barriers, and intervention acceptability. We obtained biological data (i.e., TGN concentrations) via chart review. MI sessions were audio recorded and rated using the MITI 4.2.1. coding manual to ensure intervention fidelity. Primary analyses included Analysis of Covariance (ANCOVA). We also conducted exploratory post-hoc analyses. **Results:** Findings confirmed primary MI feasibility and acceptability hypotheses, supporting the possibility of delivering adherence-enhancing MI as part of routine oncological care. Additionally, although methodological limitations hindered adequate assessment of MI efficacy for improving caregiver-reported 6-MP adherence and patients' TGN concentration, post-hoc analyses

suggested MI was effective for reducing caregiver-perceived 6-MP adherence barriers.
Conclusions: MI may represent a deliverable, cost-effective, "no-risk" approach to improving adherence and represent an easily incorporated, low cost avenue for enhancing cure. Overall, study findings have the potential to inform a larger, future MI efficacy RCT by establishing the feasibility and acceptability of MI delivery during outpatient oncology clinic visits.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

LIST OF APPENDICES

CHAPTER ONE

Review of the Literature

ACUTE LYMPHOBLASTIC LEUKEMIA

Acute lymphoblastic leukemia (ALL), a malignancy involving aberrant lymphoblasts, is the most common pediatric cancer and the most frequent cause of cancer-related death for U.S. youth under age 20 years (Linabery & Ross, 2008; Smith et al., 2010; Hunger & Mullighan, 2015). United States oncologists diagnose approximately 6,000 new ALL cases annually, half of which are pediatric (Hunger & Mullighan, 2015) and with the peak incidence occurring between ages 3 and 5 years (Linet et al., 1999). Current U.S. incidence rates indicate that, of youth under age 20 years, 34 per million live with ALL (Siegel et al., 2017).

Although curative ALL treatments have improved dramatically in the past four decades, not all children have benefited equally. Racial and ethnic disparities in pediatric ALL incidence and treatment outcomes persist. Incidence rates vary by race and ethnic groups, ranging from 18.7 cases per million Black children to 42.9 cases per million Hispanic children. Incidence for White, Non-Hispanic children is 34.2 cases per million, falling between rates for Blacks and Hispanic children (Lim et al., 2014; Siegel et al., 2017). Moreover, Black and Hispanic children have strikingly worse treatment outcomes compared to White, Non-Hispanic children (Hunger et al., 2012). Early 2000s' rates suggest 87.6% of Hispanic and 87.8% of Black children attain five-year overall survival compared to 91.1% of White children (statistically significant differences $p < .01$; Hunger et al., 2012). Notably, even among patients with >90% chemotherapy adherence, Hispanic children fare worse because of both genetic and non-genetic factors (Yang et al., 2011; Bhatia et al., 2012). Because nearly all children achieve clinical remission regardless of race/ethnicity, treatment outcome differences result from differential relapse risk (Lim et al.,

2014). Therefore, because of racial and ethnic incidence and treatment outcome disparities, researchers have begun turning their attention to alarming statistics indicating Hispanic children have an elevated ALL risk and one of the lowest post-treatment survival rates (Lim et al., 2014).

Acute Lymphoblastic Leukemia Treatment

ALL results from malignant proliferation of immature white blood cells called lymphoblasts (Children's Oncology Group, 2011). Clinical symptoms include enlarged lymph nodes, bruising, fever, fatigue, bone pain, bleeding gums, and frequent infections (Children's Oncology Group, 2011). Childhood leukemia is treated with chemotherapy. This entails using multiple cytotoxic medications to kill cancerous cells (Morrison, 2010). Pediatric pathologist, Dr. Sidney Farber, the father of modern chemotherapy, conducted the first chemotherapy clinical trials for childhood leukemia in the early 1950s (Morrison, 2010). When Dr. Sidney Farber began his groundbreaking work, the majority of pediatric ALL patients typically died within one year following diagnosis (Seibel, 2008) and nearly 100% died within 5 years (Kersey, 1997). Since then, researchers have improved multiagent chemotherapy regimen efficacy and now stratify treatment intensity by patients' clinical features, response kinetics and the genetics of the lymphoblasts (Hunger & Mullighan, 2015). These improvements in risk stratification and therapy have increased patient survival rates from less than 10% to 90% in the 1960s and 2010s, respectively (Kersey, 1997; Hunger & Mullighan, 2015). The treatment goal is first, complete remission and then, remission maintenance, ultimately resulting in cure for most pediatric patients (Hunger & Mullighan, 2015). Continued chemotherapy beyond first documentation of complete remission, which includes a prolonged phase of "maintenance therapy," is critical to curative therapy (Lii, & Sallan, 1978; Children's Oncology Group, 2011). Although there is agreement on what constitutes remission, experts tend not to agree on an objective definition of

"cure" for children and adolescents with ALL. However, physicians usually define cure based on time since last identified cancer cells. Using these criteria, most physicians cite ALL cure 5 to 10 years post-remission.

Children with ALL undergo several discrete chemotherapy phases to achieve sustained remission. Though specific treatment protocols vary, basic treatment blocks usually proceed chronologically: induction, consolidation, interim maintenance, delayed intensification, and maintenance therapy (Hunger & Mullighan, 2015; Children's Oncology Group, 2011). Induction therapy spans four to six weeks and involves intensive multiagent chemotherapy designed to induce remission (Children's Oncology Group, 2011). At any point in therapy, but most often during induction, infections and other life-threatening complications can occur (Hunger & Mullighan, 2015). Thus, some institutions choose to deliver induction therapy in the inpatient setting (Children's Oncology Group, 2011). In addition to intensive chemotherapy, patients in induction phase generally require supportive care interventions to treat infections, bleeding, nausea, vomiting, and additional complications associated with bone marrow failure (Hunger & Mullighan, 2015; Children's Oncology Group, 2011). By the end of induction, around 95% of patients attain remission (Hunger & Mullighan, 2015); however, these patients require additional chemotherapy to prevent relapse (Hunger & Mullighan, 2015; Children's Oncology Group, 2011).

The next treatment phase, consolidation, is delivered over 4-8 weeks, based on the child or teens predicted risk of relapse. This phase of therapy deepens the marrow remission and prevents the development of central nervous system (CNS) leukemia (Hunger & Mullighan, 2015). Patients undergo multiple lumbar punctures with intrathecal chemotherapy delivered directly into the spinal fluid during all therapy phases therapy, but most frequently during

consolidation (Hunger & Mullighan, 2015; Children's Oncology Group, 2011). Following consolidation, patients enter an eight-week phase known as interim maintenance. Interim maintenance chemotherapy agents are commonly antimetabolites; these agents have a different mechanism of action compared to steroids and immunosuppressant agents used during induction and consolidation treatment (Children's Oncology Group, 2011). The absence of severe bone marrow suppression during interim maintenance allows for patients' significant recovery after induction and consolidation, prior to entering the delayed intensification treatment phase. Delayed intensification, or re-induction and re-consolidation treatment phase, includes chemotherapy agents similar, but not identical, to those delivered during induction and consolidation (Hunger & Mullighan, 2015; Children's Oncology Group, 2011). The goal of delayed intensification is to sustain remission and prevent leukemia from returning (Hunger & Mullighan, 2015). As determined by risk group stratification, patients may undergo a second interim maintenance phase after delayed intensification or proceed to the final and longest treatment phase, maintenance therapy. This phase involves less intensive but prolonged chemotherapy to lower post-remission relapse risk (Cooper & Brown, 2015; Hunger & Mullighan, 2015). In current Children's Oncology Group protocols, maintenance therapy continues for two years for girls and three years for boys, with boys receiving an additional therapy year in hopes of eliminating the differential outcome of boys and girls, favoring girls (Cooper & Brown, 2015; Hunger & Mullighan, 2015). During maintenance therapy, patients receive low-intensity "anti-metabolite-" based therapy. Primarily maintenance therapy consists of daily oral 6-mercaptopurine (6-MP), weekly oral methotrexate, monthly intravenous vincristine and oral steroid pulses, and quarterly intrathecal methotrexate (Schmiegelow et al., 2014).

6-MP and methotrexate are the backbone of maintenance therapy because of their synergistic activity in ALL and their relatively limited toxicity profile. More than half a century ago, Dr. Sidney Farber demonstrated 6-MP's efficacy in inducing temporary childhood leukemia remission (Cooper & Brown, 2015). Since then, 6-MP has remained an essential component of modern ALL treatment protocols. 6-MP, also known as Purinethol, is a thio-substituted purine analogue with immunosuppressive and cytostatic properties (Cooper & Brown, 2015). 6-MP is available in tablet and liquid form supporting daily, home-based, oral drug administration. Oncologists determine patients' 6-MP doses and schedule based on several factors. These factors include, but are not limited to, patients' weight, height, health status, genetic polymorphisms impacting 6-MP metabolism, and specific disease features (Schmiegelow, 2014). Patients receive oral 6-MP, in tablet or liquid form, and oncologists modify the dosage to maintain neutrophil counts between 500 and 1500/ml (Cooper & Brown, 2015; Children's Oncology Group, 2011). These low neutrophil counts, can put patients at increased risk of infection, anemia, and/or bleeding. Additionally, patients may experience unpleasant 6-MP side effects, including nausea, vomiting, poor appetite, and diarrhea (Schmiegelow et al., 2014). Nonetheless, patients in maintenance therapy generally spend significantly less time inpatient compared to previous phases, leaving adherence burden and monitoring largely with patients and their caregivers.

Because patients receive the majority of maintenance therapy medicines at home, patients and their caregivers undertake significant treatment management responsibilities. For the majority of patients, hospital visits decrease to monthly for blood-work, intravenous vincristine, and the initiation of five-day oral corticosteroid pulses (dexamethasone or prednisone). Additionally, most Children's Oncology Group (COG) protocols mandate quarterly (i.e., every

three months) lumbar punctures to deliver intrathecal methotrexate (Children's Oncology Group, 2011). Overall, decreased time spent at the hospital inevitably limits patients' access to supportive care provider- physician-driven adherence monitoring and encouragement.

Adherence during Maintenance Therapy

Adherence is the extent to which patient behavior coincides with prescribed medical advice (Kyngäs, Kroll, & Duffy, 2000; Kennard et al., 2004). Not surprisingly, adherence during maintenance therapy is often problematic because treatment requires prolonged, daily, home-administered oral medication (Bhatia et al., 2014). In particular, adherence rates are significantly lower for Hispanic patients (Lim et al., 2014), for whom there is already a higher relapse risk compared to White patients (Bhatia et al., 2002; Lim et al., 2014).

Psychosocial stressors relevant to oncological treatment may further complicate adherence. Although the majority of families affected by pediatric cancer adapt well to the treatment regimen (Kazak et al., 2004; Patenaude, & Kupst, 2005), a significant subset experience psychological problems (e.g., depressive symptoms, social maladaptation, poor self-esteem, denial) that can negatively impact adherence (Blotcky et al., 1985; Cromer & Tarnowski, 1989; LaGreca & Schuman, 1995; Lansky et al., 1983; Kennard et al., 2004). Furthermore, during maintenance therapy, families are likely to be fatigued and resources may be taxed from earlier, more intensive chemotherapy phases (Kristjanson & Ashcroft, 1994; Patenaude, & Kupst, 2005). Particularly for patients aged 12 to 18 years, unique adolescence developmental issues (e.g., gaining independence from caregivers) can further complicate adherence to prolonged anticancer medication oral self-administration (Kennard et al., 2004). Not surprisingly, adolescents are significantly less adherent than younger pediatric patients whose

caregivers closely manage 6-MP adherence (Smith et al., 1979; Tebbi, 1993; Lancaster, Lennard, & Lilleyman, 1997; Kyngäs, Kroll, & Duffy, 2000; Kennard et al., 2004).

Overall, during maintenance therapy, 20% of pediatric patients aged 0-18 years fail to take at least one 6-MP dose per 10 prescribed doses, with decreased adherence predicting greater relapse risk (Bhatia et al., 2014; Hunger & Mullighan, 2015). Relapse represents the main treatment failure cause, occurring in approximately 15% of ALL patients (Locatelli, Moretta, & Rutella, 2013). Unlike nonadherence to other chronic illness regimens, 6-MP nonadherence is not immediately linked to obvious clinical status changes; therefore, ALL patients may have greater nonadherence risk compared to other chronically ill youth. For example, diabetic patients who do not take prescribed insulin doses can experience life threatening, obvious clinical changes (e.g., rapid heartbeat, nausea, seizures) within hours or days of the missed doses. Conversely, ALL patients often feel better after they stop taking daily 6-MP doses. More concerning, whereas diabetic patients can experience clear and timely clinical improvements after resuming insulin doses, elevated ALL relapse risk does not remit when nonadherent patients resume oral 6-MP dosing (Bhatia et al., 2014; Hunger & Mullighan, 2015).

Notably, although poor adherence is just one of many factors contributing to relapse, non-adherent ALL patients have a progressively increasing relapse risk with increasing 6-MP non-adherence (Bhatia et al., 2012, 2014). Compared to patients who receive $\geq$ 95% of prescribed 6-MP, those who receive 90-94.9% of their 6-MP doses have a four-fold greater relapse risk (Bhatia et al., 2012). Those with < 85% adherence have a nearly six-fold increased relapse risk (Bhatia et al., 2012). Non-adherent patients who relapse must undergo even more aggressive chemotherapy, with a dramatic increase in morbidity and mortality risk, to achieve a second remission. Post-relapse outcomes vary, but fewer than half these patients survive five

years post-relapse (Locatelli, Moretta, & Rutella, 2013). Accordingly, 6-MP adherence-promotion intervention during ALL maintenance therapy may potentially to save lives.

Challenges Evaluating 6-MP Adherence

Biological assays, such as drug metabolites, are generally considered objective and direct measures helpful for verifying medication consumption (Rohan et al, 2017; Kenna et al., 2005). Using biological assays (e.g., drug metabolites) to assess adherence in a various pediatric chronic illness populations is extremely effective. For example, assessing immunosuppressant adherence in pediatric solid organ transplant patients via tacrolimus concentration provides an accurate reflection of patients' immunosuppressant adherence. Unfortunately, measuring 6-MP adherence via drug metabolites (e.g., 6-TGN/6-MMPN) has inconsistent support in the oncology literature, and cannot be used reliably to monitor and/or validate 6-MP adherence.

After ingestion, the body metabolizes 6-MP into two primary classes of metabolites: thioguanine nucleotides (TGN) and methylated mercaptopurine derivatives (MMPN; Rohan et al., 2016; Traore et al., 2006; Davies, Lennard, & Lilleyman, 1993). TGNs have cytotoxic properties that disrupt DNA structure and this disruption is largely responsible for 6-MP's therapeutic effect (Traore et al., 2006). Additionally, the enzyme thiopurine methyltransferase (TPMT) catalyzes 6-MP methylation, resulting in MMPN. A key difference between TGN and MMPN lies in MMPN's nature as a less active metabolite with respect to leukemia cell kill (Traore et al., 2006). Because 6-MP's therapeutic effect results from the drug's conversion to cytotoxic TGN metabolites, oncologists have historically assessed TGN blood serum concentrations as a rough indicator of 6-MP adherence (Bhatia et al., 2012), despite its limitations.

Although there is inconsistent evidence supporting the TGN's validity to measure 6-MP adherence, some researchers agree TGN variability likely results from 6-MP nonadherence, even after adjusting for intrinsic TPMT activity (Lennard, Welch, & Lilleyman, 1995; Bhatia et al., 2012). Proponents of using TGN levels as a 6-MP adherence measure suggest low TGN metabolite count, in addition to low MMNP, may indicate non-adherence and correlate with relapse (Bhatia et al., 2012). However, there is a lack of agreement regarding the specific TGN value, measured in pmol/8 $x10^8$ erythrocytes, suggestive of non-adherence and/or relapse risk. For example, Traore and colleagues (2006) propose TGN erythrocyte values <343 pmol/$8x10^8$, combined with an MMPN value of < 6,535 pmol/$8x10^8$, suggest 6-MP concentrations below the 75^{th} percentile. However, Traore and colleagues (2006) did not correlate this TGN value with any clinical outcomes (e.g., relapse). Conversely, Lennard and Lilleyman (1994) found a TGN value of 275 pmol/$8x10^8$ erythrocytes correlated with relapse. Consequently, insconsistences in the literature make it difficult to assess which specific TGN erythrocyte cut-off value may reflect 6-MP nonadherence or poor disease prognosis.

Despite this theoretical value of assaying TGN levels to assess 6-MP adherence, there remain numerous factors, other than patients' prescribed medical regimen adherence, contributing to high TGN variability (Alsous et al., 2017). These factors include, but are not limited to, prescribed 6-MP dosage, inherited variability in TPMT and other enzyme's activity, drug-drug interactions, absorption process, viruses, allopurinol treatment. Moreover, TGN concentrations are also reflect systemic 6-MP exposure over the past 30 days. Consequently, TGN levels cannot be used as a sole indicator of 6-MP adherence. It is and maybe misleading (Smith and O'Brien, 2015).

Although TGN concentration by itself, without MMPN levels, has limited value for assessing 6-MP adherence, some researchers are hopeful about TGN/MMPN metabolite profiles' utility for indicating 6-MP ingestion (Rohan et al., 2016; Hawwa et al., 2009; Traore et al., 2006). Researchers have suggested TGN and MMPN combined metabolite profiles may be promising as an objective and direct pharmacological 6MP adherence measure (Rohan et al., 2016; Hawwa et al., 2009; Traore et al., 2006). Notably, recent studies investigating 6-MP pharmacokinetics and therapeutic effects in pediatric ALL patients indicate that 6-MP metabolic profiles may be helpful for understanding medication adherence patterns (Rohan et al., 2016; Hawwa et al., 2009; Traore et al., 2006). Moreover, these studies have expanded on previous literature on 6-MP metabolic profiles by accounting for thiopurine methalytransferase (TPMT) activity and optimal versus suboptimal 6-MP dosing and its relative influence on metabolite profiles.

Specific to pediatric ALL patients, Rohan and colleagues (2017) conducted the first study to validate the prospective relationship between an indirect 6-MP behavioral adherence measure (i.e., electronic monitoring or the Medication Event Monitoring System (MEMS) SmartCap) and direct 6-MP pharmacological adherence measure (i.e., 6-MP metabolic profiles). Rohan and colleagues (2017) identified three metabolite profiles, consistent with those suggested by previous research (Hawwa et al., 2009; Traore et al., 2006). These three profiles correlated with 6-MP adherence patterns over the 15-month study period. In line with existing literature, the first identified metabolic profile described low TGN and MMPN metabolite levels (i.e., low TGN–low MMPN profile). The low TGN-low MMPN profile consistently predicted low behavioral adherence rates, as measured by the MEMS SmartCap, even after controlling for TPMT activity and 6-MP dosing. The other two metabolic profiles included (1) high TGN–low MMPN and (2)

low TGN–high MMPN, and demonstrated overall better behavioral adherence rates (i.e., adherence rates >85%) than the low TGN–low MMPN profile. There were no significant differences in adherence rates between the high TGN–low MMPN and low TGN–high MMPN metabolic profiles. Rohan and colleagues (2017) concluded that overall differences in adherence rates between the "high TGN–low MMPN" and "low TGN–high MMPN" profiles versus the "low TGN–low MMP" profile suggest medication-taking behaviors do impact metabolite levels. Consequently, TGN/MMPN metabolic profiles may indicate patients' 6-MP ingestion consistency (Rohan et al., 2016; Kenna et al., 2005). Nonetheless, one has to be skeptical about the ability of the TGN/MMPN profiles to differentiate among adherence levels rates (e.g., >85%) especially when it takes 6 weeks of constant dosing to reach steady state and there is so much variability in drug absorption and metabolism.

Lastly, an additional challenge to accurately assessing 6-MP adherence is that different measurement methods (e.g., electronic monitoring, self-report) often produce different results. Shi and colleagues (2010) conducted a meta-analysis examining correlations between MEMS SmartCap data and self-reported adherence rates and found correlations ranged from 0.24 (weak) to 0.87 (strong). The pooled correlation coefficient was 0.45, which suggests a weak to moderate correlation between MEMS SmartCap data and self-reported adherence rates.

THEORETICAL FRAMEWORKS FOR ADHERENCE PROMOTION

Accurately assessing adherence is not the only challenge providers and researchers face. Determining the most effective way to promote adherence is also a critical task. Treatment adherence is impacted by the interplay among several factors (e.g., individual factors, disease and regimen factors) across multiple contexts (e.g., family, healthcare system; Hommel et al., 2018; Roberts & Steele, 2010). The adherence literature describes many theoretical models to

predict medical adherence, such as the health belief model (Bush & Iannotti, 1990), social cognitive theory (Bandura, 2001), the theory of reasoned action/planned behavior (Ajzen, 1991), the pediatric self-management model (Modi et al., 2012), and the transtheoretical model (Prochaska & Velicer, 1997). Although many of these frameworks share theoretical domains, they also include unique variables. Interventionists often select domains to target in adherence interventions from one or multiple theoretical models (Prestwich et al., 2014). However, the numerous competing theoretical models can pose a challenge to researchers who wish to determine which intervention domains account for intervention efficacy (McGrady et al., 2015; Michie, 2005; Winstein, 1993). To address this barrier, health psychologist theorists have developed the theoretical domains framework (TDF; Cane, O'Connor, & Michie, 2012).

The TDF is an integrative theoretical framework that synthesizes 33 behavior change theories and 128 key theoretical constructs into 14 domains (Cane et al., 2012; see Figure 1). Cane and colleagues (2012) posit behavior change results from targeting one or more of the 14 TDF domains: emotions; goals; reinforcement; intentions; beliefs about consequences; beliefs about capabilities; social and professional role and identity; optimism; social influences; environmental context and resources; skills; knowledge; memory, attention, and decision making processes; and behavioral regulation. Each of the 14 domains is classified under one of three main umbrella components: (1) capability, (2) opportunity, (3) motivation (Cane et al., 2012). TDF developers (Cane et al., 2012) derived these three main umbrella components from a complementary theoretical approach developed by Michie and colleagues (2011): the Behavior Change Wheel (BCW). The BCW characterizes target behavior in terms of capability, opportunity, and motivation (Michie, van Stralen, & West, 2011). The BCW system provides basis for intervention design, allowing researchers to select the domains they want to investigate

and, hence, inform the intervention (see Figure 1. for a graphical representation of how the TDF domains map onto the BCW system).

The TDF lends itself to cross-disciplinary implementation by allowing researchers to adapt specific domain strategies to meet unique population needs (McGrady et al., 2015). For example, targeting *social influences* for pediatric ALL patients receiving maintenance therapy may include involving caregivers and siblings in treatment. Targeting *knowledge* and *skills* may involve instruction, such as teaching patients about the medication and how to take it. Similarly, interventionists may target *beliefs about capabilities* by focusing on the patient's past successes, prompting the patient to provide self-motivating statements describing his or her past adherence behavior.

Since its development, researchers have applied the TDF across various adult behavior change interventions. Recently, McGrady and colleagues (2015) expanded this work by elaborating on TDF utility for pediatric adherence-promotion. Specifically, McGrady and colleagues (2015) conducted a systematic literature review describing pediatric adherence-promotion interventions. Not surprisingly, McGrady and colleagues (2015) found pediatric adherence-promotion interventions draw from numerous health behavior theories and lack consistent language for describing targeted domains. These inconsistencies make it difficult to attribute differences in effect sizes across interventions to specific domains (Michie, 2005). Consequently, McGrady and colleagues (2015) have encouraged pediatric adherence researchers to utilize the TDF for characterizing intervention domains, elucidating the processes underlying intervention efficacy. By reducing variability in adherence intervention research and development, researchers can move closer to identifying the intervention processes and domains that improve adherence (McGrady, 2015).

MOTIVATIONAL INTERVIEWING

Motivational interviewing (MI) is a person-centered, goal-oriented psychotherapeutic intervention designed to enhance motivation for and commitment to a target behavior change (Miller & Rollnick, 2013). MI entails evoking patients' change talk, or explicit verbalizations about their desire, ability, reasons, need, commitment, activation, and steps taken related to a target behavior change. In addition to increasing patients' change talk, MI interventionists aim to diminish patients' sustain talk. Sustain talk involves patients' statements sustaining the behavior without change (e.g., preference for the status quo, behavior change barriers). MI researchers have consistently identified patient change talk as a key mechanism of change (Morgenstern et al., 2012; Lee et al., 2015). Thus, MI therapists promote patient change talk as much as possible. Promoting patient change talk is accomplished by reflecting and asking open-ended questions designed to aid exploration and affirm the patient's strengths, abilities, and efforts. When patients show change readiness, as evidenced by increased change talk, diminished sustain talk, and steps taken toward change, the MI therapist may aid the patient in developing a change plan.

MI's spirit encompasses four key interrelated elements: collaboration, acceptance, compassion, and evocation (Miller & Rollnick, 2013). First and foremost, MI involves *collaboration,* or partnership. MI is conducted "for" and "with" a patient as an active collaboration between experts (i.e., practitioner and patient; Miller & Rollnick, 2013). This collaborative conversation style differs from traditional cognitive-behavioral approaches, which follow a Socratic method designed to educate the patient (Clark & Egan, 2015). Keeping with MI's partnership spirit, MI focuses on a specific target behavior that the patient and MI interventionist collaboratively choose (Miller & Rollnick, 2013). The second MI spirit, *acceptance*, requires the MI interventionist to profoundly embrace and value what the patient

brings to the conversation. This acceptance has deep roots in Carl Rogers's person-centered, humanist treatment approach (Rogers, 1995; Miller & Rollnick, 2013) and involves prizing the patients' inherent worth and potential, understanding the person's internal reference frame, honoring and respecting the individual's autonomy, and seeking and acknowledging the patient's strengths and efforts (Miller & Rollnick, 2013). Next, a *compassionate* MI practitioner promotes the patient's welfare and prioritizes patient needs. For patients who are not ready to embrace behavior change, compassion involves "dancing with discord" (Miller & Rollnick, 2013). Miller and Rollnick (2013) framed "dancing with discord" as an interpersonal dynamic, an inherent process of working through a patient's behavior change ambivalence. The practitioner must use MI-specific techniques to work with the patient through discord toward effective behavior change. Finally, the *evocation* spirit entails eliciting and strengthening patients' pre-existing motivations for change (Miller & Rollnick, 2013). A skilled MI practitioner is selective about questions asked, statements reflected, and content summarized to evoke change talk and move the patient toward behavior change.

MI involves four primary processes or tasks, listed in emphasis order: engaging the patient, focusing on a specific behavior change, evoking the patient's change talk, and collaborating to create a change plan (Miller & Rollnick, 2013). *Engaging* is the process by which both the clinician and patient establish a helpful connection and working relationship (Miller & Rollnick, 2013). *Engaging* leads to *focusing* on a particular agenda or change behavior (Miller & Rollnick, 2013). With one change goal as a focus, *evoking* involves eliciting the patient's own motivation for change as opposed to the clinician suggesting motivators for change (Miller & Rollnick, 2013). Lastly, *planning* encompasses both developing commitment to change and formulating a specific action plan (Miller & Rollnick, 2013). Overall, MI is strength-

based, confirming the patient's autonomy and abilities while also providing collaboration and accurate empathy for the patient's ambivalence and/or change barriers (Miller & Rollnick, 2013). Although MI can be delivered in an "alternation model" integrating MI with other conversation styles (Hettema et al., 2005; Longabaugh et al., 2005; Miller, 2004) and in brief 10-15 minute applications (Bernstein et al., 2005; Soria et al., 2006), MI appears to be most effective when delivered in an exclusive, longer format (e.g., 30-50 minutes; Miller & Rollnick, 2013).

Motivational Interviewing Historical Context

Miller (1983) originally devised MI in the early 1980s to treat adult substance use disorders. Since its inception over three decades ago, MI has evolved substantially and researchers have shown its efficacy for facilitating change across various behaviors, settings, and age groups (Miller & Rollnick, 2013; Gayes & Steele, 2014). Early in MI's growth as a therapeutic strategy, researchers demonstrated MI's efficacy for treating adult substance abuse, including alcohol (Sellman et al., 2001; Juarez et al., 2006; Naar-King et al., 2006), marijuana (Grenard et al., 2007; Naar-King et al., 2006), tobacco (Ahluwalia et al., 2006), and polysubstance abuse problems (Carroll et al., 2005; Grenard et al., 2007). Given widespread MI effectiveness with substance use disorders, researchers began evaluating MI with other populations in the early 2000s. Additionally, Lundahl and colleagues (2010) conducted a meta-analysis and found statistically significant positive MI effects for improving parenting practices (Weinstein, Harrison, & Benton, 2004; Wilhelm et al., 2006), decreasing unsafe water consumption in under-resourced countries (Thevos et al., 2000), increasing treatment engagement (Carroll et al., 2006, Maltby & Tolin, 2005), increasing patients' intention to change in psychotherapy (Stotts et al., 2001, 2004; Steinberg et al., 2004), improving health behavior (e.g., diet, exercise; Sellman et al., 2001; Bennet et al., 2005; Brodie & Inoue, 2005; Channon et al., 2003, 2007; Kreman et al.,

2006), and reducing risky behavior (e.g., unsafe sex; Johnston et al., 2007). Unsurprisingly, researchers have also found MI effective for non-substance abuse-related addictive problems such as gambling (Hodgins, Currie, & El-Guebaly, 2001; Hodgins et al., 2004). Lundahl and colleagues (2010) suggest MI indirectly increases well-being, as MI is associated with positive gains in general well-being measures (e.g., lower stress and depression levels) post-behavior change.

Motivational Interviewing in Pediatric Health

Although MI has traditionally been applied and deemed effective across various adult populations, evidence supporting MI's efficacy has more recently expanded to other patient age groups including children and adolescents with various health behaviors (Gayes & Steele, 2014; Borrelli, Tooley, & Scott-Sheldon, 2015). Similarly to the adult literature, two systematic reviews and one meta-analysis suggested MI is effective with adolescent substance users (Tevyaw & Monti, 2004; Wachtel & Staniford, 2010; Jensen et al. 2011). Specifically, Jensen and colleagues (2011) found MI for adolescent substance use has a small but significant mean effect size ($d = 0.17$) that persists over time.

Outside adolescent substance use, researchers have also found MI to be efficacious for numerous pediatric health conditions, including diabetes, obesity, diet change, and dental care, among others (Erickson, Gerstle, & Feldstein, 2005; Suarez & Mullins, 2008; Gayes & Steele, 2014; Borrelli, Tooley, & Scott-Sheldon, 2015). Gayes and Steele (2014) conducted a meta-analysis of MI for pediatric behavior change and found MI had an overall effect size slightly higher than a small effect size ($g = 0.28$), which is somewhat higher than what the substance abuse literature typically reports. MI for behavior change related to type 1 diabetes, asthma, and calcium intake showed the largest effect sizes (Gayes & Steele, 2014). Nonetheless, researchers

have deemed MI helpful for changing and promoting adherence and other health behaviors related to various pediatric conditions, especially in light of the inexpensive, brief nature of the intervention (Gayes & Steele, 2014; Borrelli, Tooley, & Scott-Sheldon, 2015). Notably, although MI's effect size tends to be relatively small, the inexpensive, non-resource-intensive nature of MI makes MI an attractive intervention strategy in pediatric health settings.

Gayes and Steele (2014) found MI efficacy for pediatric health behavior change was moderated by practitioner background, health domain, and participating family member relationship to the patient. MI session number and follow-up length were not significant moderators (Gayes & Steele, 2014). MI tends to be most effective when both parent and child participate in sessions and when the practitioner's cultural background matches the family's cultural background (Gayes & Steele, 2014). In line with Gayes & Steele's (2014) findings, numerous studies investigating MI in pediatric health settings have identified caregivers as the intervention target (Doring et al., 2016; Mohammadi et al., 2015; Nyberg et al., 2016). Yet, recent studies have demonstrated MI efficacy when delivered directly to adolescents as well (Cushing et al., 2014). When MI has been delivered directly to adolescents, MI has been associated with adolescents' improved adherence to general medication regimens (Dean et al., 2016), psychotherapy recommendations (Hamrin & Iennaco, 2016), and specific adherence behaviors for pediatric asthma (Kolmodin-MacDonnel et al., 2016), obesity (Doring et al., 2016; Ige et al., 2016; Resnicow et al., 2016; Rifas-Shiman et al., 2016), diabetes (Gregory & Channon, 2009), and health-related risk-taking reduction efforts (Carter et al., 2016; Li et al., 2016; Sanci et al., 2015). Overall, findings indicate MI is an effective intervention for targeting health behavior change in pediatric medical settings.

Some researchers have specifically focused on investigating MI to improve treatment adherence for chronically ill youth (Erickson, Gerstle, & Feldstein, 2005). For example, Channon and colleagues (2007) conducted a multicenter, randomized control trial (RCT) of MI to improve glycemic control in adolescents with diabetes. Sixty-six adolescents (aged 14-17 years) with type 1 diabetes participated in this RCT; 38 patients received individual MI sessions and 28 control-group participants received support visits over a 12-month period. MI and support session numbers ranged between one and nine, averaging 4.7. Channon and colleagues (2007) found A1C serum levels significantly decreased for patients in the MI group compared to control participants ($p = 0.04$) after adjusting for baseline levels. This finding suggested patients improved their diabetes regimen adherence. Moreover, this intervention group difference in A1C serum levels was maintained ($p = 0.03$) at 24-month follow-up.

In addition to general treatment adherence and health-related lifestyle changes, researchers have begun to evaluate MI efficacy for improving medication adherence. Riekert and colleagues (2011) developed and evaluated a MI intervention to promote medication adherence among inner-city, African-American adolescents (ages 10-15 years) with asthma. Specifically, researchers followed adolescent asthma patients who had sought out emergency asthma treatment at an inner-city emergency department. Adolescents completed five home-based MI sessions (i.e., MI practitioner conducted home visits) to improve asthma controller medication adherence. Although there were no pre-post-differences in adolescent-reported medication adherence, the adolescents reported increased motivation and readiness to adhere to treatment. Additionally, caregivers reported a trend for adolescents taking greater responsibility for their asthma following MI sessions. Both adolescents and caregivers reported statistically significant increases in their asthma-related quality of life. Although there are MI efficacy data for various

pediatric chronic illnesses, researchers have yet to evaluate MI efficacy for improving medication adherence specific to pediatric oncology.

Culturally Adapted Motivational Interviewing

Although evidence suggests culturally un-adapted MI maintains efficacy with minority patients (Hettema, Steele, & Miller, 2005), the question of whether culturally adapting MI enhances its effect has not been extensively studied (Lee et al., 2011). Researchers theorize MI efficacy can be enhanced when used with racial, ethnic, and sexual minority populations by combining the intervention with practices that respect cultural values and traditions (Lee et al., 2011; Bloom, 2016). Recent studies suggest culturally sensitive, family-focused prevention programs are more successful than individual-focused programs when working with ethnic/racial minority patients (Bloom, 2016). Family-focused interventions' success is likely due to including cultural beliefs concerning the importance of family as the principal unit of function for many minority subgroups (Bloom, 2016).

Because MI was originally developed in the English language, exploring whether MI's change mechanisms are preserved when delivered in other languages is particularly important. Although MI "poetics," per se, are a central English-delivered MI focus (Carr & Smith, 2013), few researchers have investigated whether linguistic patterns essential to MI are preserved in languages other than English. For example, MI interventionists learn how to speak to clients in a simultaneously client-centered and directive way, in line with two longstanding American therapeutic traditions: "client-centered" and "directive" approaches (Carr & Smith, 2013). Moreover, MI interventionists learn elaborate Western communicative techniques, including how to punctuate ''open questions'' with sustained pauses, how to boost patients' relatively ordinary statements in ''reflections'' that move the patient towards change talk, and how to

control the stress and inflection of an ‘‘affirmation’’ (Carr & Smith, 2013). Given linguistic and cultural differences between English and other languages, it is perhaps not surprising that psychotherapy interventions for racial/ethnic minority patients are twice as effective in the patient's native language (Griner & Smith, 2006).

The potential for MI to be disseminated in Spanish is supported by preliminary evidence indicating positive response to Spanish-delivered MI with ethnically-matched providers and Latino patients (Field and Caetano, 2010; Lee et al., 2011). In particular, ethnically-matching Spanish-speaking providers and patients has been shown to increase brief MI cultural relevance (Field and Caetano, 2010). In their study, Field and Caetano (2010) randomized over 500 adult Latino patients with alcohol use problems to receive brief MI or treatment as usual. Although Field and Caetano (2010) did not ground their MI delivery in a particular culturally-sensitive conceptual framework, they manipulated the intervention by incorporating ethnic concordance between patients and providers. There was an ethnic match between participant and provider for 71% of the 259 participants who completed brief MI. Overall, Latino patients who received MI, as opposed to treatment as usual, showed a significant decrease in drinking behavior. Specifically, MI participants drank five or more alcoholic beverages per occasion significantly less frequently than control-group participants. Moreover, for Latino patients who received brief MI, an ethnic match between patient and provider resulted in enhanced MI efficacy ($p = 0.03$), with a significant reduction in alcohol volume consumed per week at 12-month follow-up (Field & Caetano, 2010). Ethnic-matching was especially beneficial for foreign-born and/or less acculturated Latinos (Field & Caetano, 2010). The authors argue ethnically-matched clinicians may be more likely to understand patients' culture-specific values, norms, and attitudes, thereby making the intervention more effective. Field & Caetano (2010) also hypothesized patient-

provider ethnic-matching may impact MI efficacy through several mechanisms including cultural scripts inclusion, ethnic-specific perceptions pertaining to the target behavior, and culturally-specific preferred communication channels. However, although ethnic- and language-matching may enhance MI efficacy for ethnic/racial minorities, these strategies may not be sufficient. To this end, Field and Caetano (2010) suggested that culturally adapting MI in more substantive ways may greatly increase MI effects by emphasizing cultural values and addressing cultural nuances that extend beyond linguistic differences.

Following from Field and Caetano's (2010) recommendations, Lee and colleagues (2011) moved beyond ethnic and language matching and developed a conceptual model guiding culturally adapted brief MI (CAMI). They conducted qualitative interviews with female and male adult Latino heavy drinkers to identify social and cultural processes related to alcohol drinking. Using interview data, Lee and colleagues (2011) created a model to guide culturally adapted MI for this population. Lee and colleagues' conceptual framework contends that social contextual factors (e.g., language barriers, discrimination) are essential to understanding racial/ethnic minorities' health behaviors. In their qualitative study, Lee and colleagues (2011) identified four acculturation-related social contextual factors that subsequently guided their MI adaptations. These four social stressors included: social context of immigration, changing family dynamics, diminished social support, and health literacy.

Regarding the social context of immigration, participants identified challenges (e.g., language barriers, lack of information and/or money, isolation) of adjusting to a new social context post-immigration. Qualitative interviews revealed that, particularly immediately following U.S. arrival, participants engaged in poorer health behaviors (e.g., increased alcohol use) compared to their pre-immigration behaviors. To account for social contextual barriers, Lee

and colleagues (2011) incorporated MI adaptations addressing the social context of immigration. Specifically, Lee and colleagues (2011) adapted MI structured strategies (e.g., adding the "Typical Day" exercise; Rollnick, Heather, & Bell, 1992) to enhance rapport and reduce stereotype-based biases when working with racial/ethnic minority patients. Adapted MI structured strategies, such as the Typical Day exercise (i.e., MI interventionist elicits from the participant a description of their average day, from the time they wake up in the morning until they go to bed), focus on exploring patient behavior within their daily routine (Lee et al., 2011). The MI focus is usually on the patient and his or her health behavior; however, Lee and colleagues' cultural adaptation involved exploring patients' contextual factors and their influence on patient's health behavior. To this end, MI interventionists who are performing Lee and colleagues' culturally-informed MI recommendations must explicitly ask patients about their social context as an influence on their health behaviors. For example, MI interventionists elicit discussions about stressors, such as discrimination, low status employment, and family back home, as influences on health behavior.

Next, participants identified changing family dynamics as an important social stressor. They lacked the strong family networks they left behind in their home countries and described the U.S. as more individualized with less family cohesion (Lee et al., 2006). Study participants also felt their children did not share their cultural and familial values. Following from this, Lee and colleagues' adaptation calls for the interventionist to highlight the discrepancy between what the patient values (e.g., being a stable provider and role model) and their health behavior. Eliciting this discrepancy may promote patient change talk via verbalized desires and/or need to change, thereby increasing intrinsic motivation to change. Lee and colleagues also culturally adapted MI to include the Elicit-Provide-Elicit strategy. When following the Elicit-Provide-Elicit

format, the MI interventionist asks the patient what they know about the topic and obtains permission to give feedback (Elicit). If the patient grants permission, the MI interventionists can give information (Provide). After providing information, the MI interventionist asks the participant what they think about the new information received (Elicit). Lee and colleagues' adaptation employs the Elicit-Provide-Elicit strategy to emphasize the health behavior's impact on the family and children, with emphasis on being a positive role model.

The third stressor that guided Lee and colleagues' cultural adaptation was social support. Participants reported having decreased contact with friends and family post-immigration, which resulted in losing social support. Lee and colleagues' adaptation focuses on the quality of social support in the patient's life and whether social support is relevant to the patient's health behavior. Interventionists elicit the importance of social and family support, people who are most important to the patient, and how these individuals influence the patient's health behavior.

Lastly, Lee and colleagues found participants in their study had poor health literacy, as evidenced by participants' limited awareness of their behavior's (i.e., alcohol drinking) negative health effects. However, poor health literacy was correlated to educational level, not just cultural background. Consequently, Lee and colleagues' adaptation uses the Elicit-Provide-Elicit approach to understand patients' views and knowledge about their target behavior. Similar to using the Elicit-Provide-Elicit format to emphasize the health behavior's impact on family members, interventionists can also use this strategy to provide information about the health behavior's negative consequences, thus improving patients' health literacy.

In summary, Lee and colleagues (2011) utilized qualitative research findings and a social contextual framework to culturally adapt MI for a heavy-drinking immigrant U.S. Latino population. Addressing social contextual factors within an MI intervention is a shift from the

traditional MI conceptual model. Conceptually, the traditional, non-adapted MI model focuses on the clinical interaction between provider and client, viewing social contextual factors, such as employment status, as potential treatment mediators or moderators (Miller & Rose, 2010). In contrast, Lee and colleagues' CAMI framework suggests social contextual factors are essential to understanding behavior change among racial/ethnic minorities. Traditional MI researchers have narrowly conceptualized social context as patient's interpersonal network, thus disregarding broader social contextual factors (e.g., discrimination) as primary influences on health behavior (Stanton, 2010). Alternatively, Lee and colleagues (2011) argue that acknowledging these social contextual factors to ethnic/racial minority patients can increase patients' sense of being understood by the MI therapist. In recent years, Lee and colleagues have begun presenting favorable data on participants' responses to CAMI (Lee et al., 2013, 2015, 2016). Although Lee and colleagues have advanced our understanding of culturally sensitive MI with adult patients, there is a dearth of research in this area with pediatric patients.

CHAPTER TWO

The Current Study

Researchers have applied MI to and deemed MI effective for numerous behavior problems for adults, including substance use, risky behaviors, poor health behaviors, and low medical and psychiatric treatment engagement (Lundahl et al., 2010). Because of demonstrated MI efficacy with various adult populations, researchers have also begun to evaluate MI's unique contribution to adherence and other health behaviors in pediatric illness groups. Studies have generally found MI to be effective when either or both the pediatric patient and/or caregiver participate in the MI intervention (Gayes & Steele, 2014); however, researchers have yet to evaluate MI efficacy in pediatric oncology populations. Specifically, despite strong efficacy in various pediatric health settings (Gayes & Steele, 2014; Borrelli, Tooley, & Scott-Sheldon, 2015), MI has yet to be evaluated for feasibility, acceptability, and efficacy in improving 6-MP adherence during pediatric ALL patients' maintenance therapy. Similarly, researchers have begun to study MI with racial/ethnic minority populations (Hettema, Steele, & Miller, 2005; Field and Caetano, 2010; Lee et al., 2011) but have yet to investigate MI feasibility, acceptability, and efficacy with racial/ethnic minority pediatric patients and their caregivers This study evaluated MI feasibility and acceptability, as well as preliminary efficacy to improve pediatric ALL patients' maintenance therapy 6-MP adherence. Specifically, I examined three culturally diverse groups of pediatric ALL patient-caregivers (i.e., Non-Hispanic and English-speaking, Hispanic and English-speaking, and Hispanic and Spanish-speaking caregivers). I was particularly interested in these three groups because of literature suggesting lower adherence rates among Hispanic patients compared to Non-Hispanic Caucasian patients (Bhatia et al., 2002; Lim et al., 2014) and because of potential linguistic implications of Spanish-delivered MI (Lee et

al., 2012). To this end, I conducted MI in both English and Spanish, per participant preference, and compared MI's efficacy to an education control intervention. Consistent with Lee and colleagues' (2011) recommendations, MI with Hispanic, Spanish-speaking caregivers acknowledged social contextual stressors related to minority status as well as culture-specific values, when possible. This approach, informed by Lee and colleagues' (2011) CAMI framework, is not only a notable intervention adaptation, but is a novel approach with caregivers of chronically ill pediatric patients.

AIMS AND HYPOTHESES

Study Aim 1

To test the feasibility of delivering MI during patients' routine clinic visits and the feasibility of our study design (to inform a larger, future RCT).

Hypothesis 1

Delivering MI or the education intervention to caregivers of pediatric ALL maintenance therapy patients, as an adjunct to patients' routine outpatient clinic visits, will be feasible as evidenced by enrollment and intervention completion for 79% of eligible caregivers during the study period.

Hypothesis 2

Given literature indicating U.S. minority populations associate greater stigma with mental health service compared to majority populations (De Luca et al., 2016), a greater percentage of non-Hispanic, English-speaking, caregivers/patients will agree to participate in our study compared to Hispanic, English- and Spanish-speaking caregivers.

Study Aim 2

To test MI acceptability as an adjunct to treatment as usual for pediatric ALL maintenance therapy patients and to evaluate whether MI acceptability differs among caregiver cultural groups (i.e., Non-Hispanic, English-speaking, Hispanic, English-speaking, and Hispanic, Spanish-speaking caregivers).

Hypothesis 3

Caregivers who receive MI will find the MI intervention acceptable, as evidenced by at least 75% of participants' MI session ratings corresponding with a mean AARP sum score ≥ 30 (Tarnowski & Simonian, 1992).

Hypothesis 4

If there are any differences in MI acceptability among caregiver cultural groups, the differences will be $d \leq 0.6$ (medium effect size).

Study Aim 3

Evaluate preliminary MI efficacy in improving (a) caregiver-reported 6-MP adherence and (b) patient TGN blood serum concentration, compared to an education control, from pre- to post-intervention.

Hypothesis 5

Caregiver-reported 6-MP adherence patient TGN blood serum concentration will improve from pre-intervention to one-month post-intervention follow-up more so for participants in the MI group than for participants in the education control. This finding will not be moderated by intervention language.

CHAPTER THREE

Methodology

ELIGIBILITY CRITERIA

Eligible participants included caregivers of pediatric ALL patients of any age, including adolescent and young adult (AYA) patients. For a caregiver to be eligible to participate in the study, their patient had to meet certain eligibility criteria. Patients had to be receiving maintenance therapy at Children's Health, Center for Cancer and Blood Disorders (CCBD). Patients were expected to remain in maintenance therapy as indicated by the medical record and/or the patient's primary oncologist for at least two additional months from caregiver recruitment. Eligible caregivers had to be adult caretakers with whom the patient lived at least 50% of the time, who identified himself or herself as providing the patient's primary home care (e.g., providing meals) at least 50% of the time, and who had legal authority to consent to the patient's participation in a research study. Caregivers had to speak and understand spoken and written English or Spanish to participate. Potential participants who had developmental (e.g., cognitive, speech production, hearing loss) problems that would preclude MI session and/or written measures completion were not eligible to participate in this study.

The larger, grant-funded study participants also included adolescent patients. Patients were able to complete self-report measures and participate in an individual MI session if the patient was at least 12 years of age; however, caregivers could participate even if the patient was under the age of 12 years. This criterion was selected because several studies document MI efficacy when used with adolescents as young as 12 years (Hamrin & Iennaco, 2016; Dean et al., 2016; Brown et al., 2015; Gold et al., 2016). AYA patients older than 18 years could participate

even if they did not have an adult caretaker and/or did not have a caretaker who chose to participate in this study.

PARTICIPANTS

Participants included 121 caregivers (Age *M*(*SD*) = 36.66(8.02), 80.72% mothers, 47.17% Hispanic, 23.14% Spanish-speaking) of pediatric ALL patients (Age *M*(*SD*) = 7.55(4.80), range = .9-24; 66.13% male; Medicaid = 54.26%; ALL risk category: Standard = 50.91%, High/Very High = 49.08%) in maintenance therapy. We used weighted randomization to randomize seventy-nine caregivers (65.29%) to the MI group and the remaining 42 caregivers (34.71%) to the education control group. Cultural categories included: (1) Non-Hispanic, English-speaking caregivers (*N*=63, 52.07%); (2) Hispanic, English-speaking caregivers (*N*=30, 24.79%); and (3) Hispanic, Spanish-speaking caregivers (*N*=28, 23.14%). For demographics and frequency statistics by intervention group and by cultural category, see Table 1.

Based on a priori power analyses, we required 74 caregivers receive the MI intervention. Because budgetary restrictions required a 2:1 randomization to MI:Education, the education control group needed 37 participants. Thus, this study required a minimum of 111 participants total. However, because the larger, grant-funded study remains ongoing for follow-up, the analytic sample available for this dissertation study included 103 participants (MI *N* = 66, education *N* = 37; see Figure 2. for CONSORT diagram).

MEASURES

Demographics Questionnaire and Medical Chart Review

Study investigators modified a demographics questionnaire developed by Faith and colleagues (2019) and created parallel English and Spanish demographic questionnaires to administer to caregivers. The questionnaires' content was identical and was based on

demographic measures regularly used in research protocols at Children's Health, Center for Cancer and Blood Disorders (CCBD). Items assessed basic family characteristics, including family living arrangements, patient treatment history, caregiver and patient education, caregiver occupation, and household income (see Appendices A and B for English and Spanish demographic forms). Research personnel also conducted medical chart reviews to obtain additional clinical variables of interest (e.g., insurance, NCI risk classification, TGN levels).

Thioguanine Nucleotide Concentration

Research personnel conducted medical chart reviews to obtain patients' TGN levels measured at their clinic visits as part of standard care. Research personnel documented TGN concentration as 'baseline TGN' if measurement was taken anytime 30 days prior to enrollment up to the intervention date. 'Post-intervention TGN' represented TGN concentration obtained 30 to 60 days after the intervention.

Parent and Adolescent Medication Barriers Scale

Simons and Blount (2007) developed the Parent Medication Barriers Scale (PMBS) and the Adolescent Medication Barriers Scale (AMBS) to assess perceived barriers to medication adherence in adolescent solid organ transplant patients and their caregivers, respectively (see Appendices C through F for PMBS-English, PMBS-Spanish, AMBS-English, and AMBS-Spanish forms). The PMBS and AMBS (Simons & Blount, 2007) contain 16 and 17 items, respectively, rated on a 5-point Likert-type scale (1 = Strongly Disagree, 2 = Disagree, 3 = Not Sure, 4 = Agree, 5 = Strongly Agree; see Appendix B). Items scored >3 on the 5-point Likert-type scale represent perceived medication barriers (Simons & Blount, 2007). Total scale score is composed by adding number of perceived medication barriers. The PMBS and AMBS

established cut-off scores for non-adherence risk in pediatric solid organ transplant are ≥ 2 and ≥ 3 barriers, respectively (Simons & Blount, 2007).

Twelve PMBS and AMBS items are parallel; thus, there are four and five additional unique PMBS and AMBS items, respectively (i.e., PMBS items # 8, 9, 13, 15; AMBS items # 5, 10, 15, 16, 17). For PMBS and AMBS parallel items, change in wording reflects the respondent (e.g., for caregivers, "My child has too many pills to take"; for patients, "I have too many pills to take"). Adolescent-only item examples include, "I don't want to take the medicine at school," "I sometimes just don't feel like taking the medicine," and "Sometimes I don't realize when I run out of pills." Parent-only items include, "My child relies on me to remind him or her to take his/her medication," "I am not always there to remind my child to take his/her medication," and "My child is tired of living with a medical condition." Additionally, there is a final open-ended question in both the PMBS and AMBS assessing any other medication adherence barriers not included in the previous items.

In the initial validation study with pediatric solid organ transplant patients, Cronbach's alphas for the PMBS and AMBS were .87 and .86, respectively (Simons & Blount, 2007). Simons and Blount (2007) also conducted a factor analysis that revealed four PMBS factors: (1) Disease Frustration/Adolescent Issues (7 items, α = .84), (2) Regimen Adaptation/Cognitive (5 items, α = .82), (3) Ingestion Issues (3 items, α = .69), and (4) Parent Reminder (1 item). Similarly, the AMBS contained the same first three factors (Disease Frustration/Adolescent Issues (8 items, α = .84); Regimen Adaptation/Cognitive (4 items, α = .76); Ingestion Issues (5 items, α = .70), but excluded the PMBS Parent Reminder factor (Simons & Blount, 2007)). As a native Spanish speaker, I forward- and backward-translated the PMBS and AMBS from English

into Spanish (and vice versa as an interpretation check). Additionally, native Spanish-speaking research personnel also reviewed the Spanish-translated measures.

Because the PMBS and AMBS had not been previously utilized in pediatric oncology, I conducted a Principal Components Analyses (PCA) using our caregiver study sample. Based on a requirement for items to load on a component ≥.30 and for any cross-component loadings' magnitude to exceed .40, I included 14 PMBS items in my analyses (see Exploratory Post-Hoc Analyses and Results sections for further information). Cronbach's alpha for the 14-item PMBS was α = .85, which suggests strong scale reliability. Moreover, scale reliability for each cultural group was also good (i.e., Non-Hispanic, English-speaking caregivers α = .833; Hispanic, English-speaking caregivers α = .824; Non-Hispanic, English-speaking caregivers α = .879). Lastly, AMBS scale reliability with our adolescent ALL patients was also good, as suggested by α = .818. I was unable to conduct a PCA with AMBS data because of the small adolescent sample size.

Medication Adherence to 6-Mercaptopurine

Because no published measures exist to assess 6-MP adherence, we developed the Medication Adherence to 6-Mercaptopurine (MA6-MP) for this study. We created the items based on input from one pediatric oncologist and two pediatric cancer psychologists. The MA6-MP questionnaire includes five multiple choice and four open-ended questions specific to 6-MP adherence (see Appendices G through J for Caregiver-English, Caregiver-Spanish, Patient-English, and Patient-Spanish MA6-MP versions). We assessed adherence by using a single MA6-MP item (i.e., How many time has your child completely missed a dose of 6-MP (not just late) in the past seven days?). Missing ≥1 6-MP dose(s) qualified as non-adherent behavior. Therefore, zero missed 6-MP doses represented adherent behavior. We modified the item

wording to reflect the respondent (e.g., for caregivers, "Over the past 7 days, how many times did your child take a dose of 6-MP more than two hours late;" for patients, "Over the past 7 days, how many times did you take a dose of 6-MP more than two hours late?"). The questionnaire also asked if the doctor had requested the patient stop taking 6-MP over the previous week. We included this question because the medical team, at times, has to temporarily discontinue therapy secondary to bone marrow suppression or illness. If 6-MP therapy had been temporarily discontinued, the participant still completed remaining questionnaire items, as appropriate. Lastly, as a native Spanish speaker, I forward and backward translated the MA6-MP questionnaire into Spanish (and vice versa as an interpretation check). Additionally, native Spanish-speaking research personnel also reviewed the Spanish-translated measure.

Mental Health Experiences Questionnaire

Because existing published measures of past experiences with mental health services are lengthy (e.g., Attkisson & Zwick, 1982), we developed the brief measure, the Mental Health Experiences Questionnaire (MHEQ), for the larger, grant-funded study. The MHEQ contains three multiple choice questions regarding mental health service use history (see Appendices K through N for Caregiver-English, Caregiver-Spanish, Patient-English, and Patient-Spanish MHEQ forms). We created the MHEQ with input from two pediatric psychologists. The first question, "Have you ever received counseling or other psychology/psychiatry services from a mental health professional?" is scored as a dichotomous variable (i.e., Yes, No). Participants who answer "Yes" to the first question will answer two follow-up items assessing their satisfaction with their previous mental health experiences (e.g., "How much did your previous mental health services help you with a problem?").

Abbreviated Acceptability Rating Profile

Tarnowski & Simonian (1992) developed the Abbreviated Acceptability Rating Profile (AARP) as an abbreviated version of the 15-item Intervention Rating Profile (Witt & Elliott, 1985). The AARP contains eight items rated on a 6-point Likert-type scale (1 = Strongly Disagree, 2 = Disagree, 3 = Somewhat Disagree, 4 = Somewhat Agree, 5 = Agree, 6 = Strongly Agree), with higher scores indicating greater intervention acceptability. Chronbach's alpha was .97 in the initial validation study (Tarnowski & Simonian, 1992). For this study, we added a brief questionnaire introductory statement identifying "medication-taking behavior" as the target behavior. Additionally, we modified the instructions' phrasing to reflect the respondent (e.g., for caregivers, "The treatment should be effective in changing the child's behavior;" for patients, "The treatment should be effective in changing my behavior"). Respondents were instructed to complete the AARP regarding their MI or education intervention. As a native Spanish speaker, I forward and backward translated all AARP versions from English to Spanish (and vice versa as an interpretation check). Additionally, native Spanish-speaking research personnel also reviewed the Spanish-translated measures. See Appendices O through R for Caregiver-English, Caregiver-Spanish, Patient-English, and Patient-Spanish AARP forms.

Cronbach's alpha for our study sample was $\alpha = .77$ reflecting acceptable scale reliability. Although removing Item 3 (i.e., "The child's behavior is severe enough to justify the use of this treatment") slightly increased Cronbach's alpha ($\alpha = .79$), reliability remained in the acceptable range, thus I did not remove this item for analyses. Similarly, ARRP reliability was acceptable for each intervention group (i.e., MI $\alpha = .77$; Education $\alpha = .76$).

Because of my interest in conducting analyses with cultural groups, I examined AARP reliability separately for Non-Hispanic, English-; Hispanic, English-; and Hispanic, Spanish-

speaking caregivers. In contrast to the study sample's acceptable Cronbach's alpha, AARP reliability for each cultural group was variable, ranging from poor to good (i.e., Non-Hispanic, English-speaking caregivers α = .78, acceptable; Hispanic, English-speaking caregivers α = .57, poor; Hispanic, Spanish-speaking caregivers α = .81). Again, removing Item 3 (i.e., "The child's behavior is severe enough to justify the use of this treatment") increased Cronbach's alpha for all cultural groups. However, there was only a notable increase in AARP scale reliability (α = .65) for Hispanic, English-speaking caregivers. Because AARP reliability remained questionable for Hispanic, English-speaking caregivers, I did not remove Item 3 to maintain AARP items consistent across cultural groups.

Finally, I also examined AARP scale reliability for adolescent to conduct exploratory analyses, if appropriate. AARP scale reliability for adolescent patients was poor α = .316. Similarly to AARP reliability with caregivers, Item 3 (i.e., "My behavior is severe enough to justify the use of this treatment") removal increased Cronbach's alpha α = .558. Nonetheless, reliability remained poor thus adolescent AARP was not included in exploratory analyses.

Motivational Interviewing Treatment Integrity

We audio-recorded and rated MI sessions for MI fidelity using the Motivational Interviewing Treatment Integrity Coding Manual (MITI version 4.2.1; Moyers, Manuel, & Ernst, 2014; see Appendix S). As stipulated in the MITI Coding Manual (MITI version 4.2.1; Moyers, Manuel, & Ernst, 2014), raters assigned a single, categorical behavioral code to each clinician utterance that warrants a code. Consistent with recommendations from Moyers, Manuel, and Ernst (2014), raters parsed and coded utterances at the same time within a single pass. Per MITI version 4.2.1, clinician behavior codes include several categories broadly categorized as MI-consistent (e.g., open questions, complex reflections), MI-inconsistent (e.g., confront, persuade

without permission), or MI-neutral (e.g., giving information). For this study, two bilingual raters and one English-only rater documented behavioral codes, session-level summary indices (e.g., % open questions), and global ratings (e.g., overall empathy for the entire session). Additionally, raters determined interventionist's competency as falling into one of three categories as set forth by MITI 4.2.1 recommendations: incompetence, basic competency, or expert level proficiency (e.g., 50% complex reflections for expert level, versus 40% complex reflections for basic level proficiency). If any sessions reflected less than expert-level proficiency, the interviewer met with the MI trainer to receive additional MI training, which only occurred in the early study stages.

Cultural Adaptation of Motivational Interviewing

Because of my particular interest in the linguistic and cultural adaptation of Spanish-delivered MI for Hispanic, Spanish-speaking caregivers, we developed a CAMI-informed manipulation check (see Appendix XX). The CAMI-informed manipulation check is a brief coding system based on Lee and colleagues' (2012) recommendations. For Spanish-delivered MI sessions, exclusively, MI raters noted (i.e., yes or no) whether the session content reflected (a) social contextual stressors related to minority status, and/or (b) culture-specific values (see Appendix T). The MI session was deemed CAMI-informed framework-adherent if either social contextual factors and/or culture-specific values were discussed.

PROCEDURES

This dissertation study is part of a larger, grant-funded study that has been approved by UT Southwestern Medical Center's Institutional Review Board (IRB# STU 082016-088). The larger, grant-funded study remains open for follow-up (for participant status, refer to Figure 2. depicting CONSORT diagram).

Recruitment, Consent, and Group Assignment

This study took place at Children's Health, Center for Cancer and Blood Disorders (CCBD). At any given time, CCBD cares for 80-100 children and adolescents with ALL who are in the maintenance phase of therapy. After screening the medical record for patient eligibility, study personnel met with eligible caregivers and/or adolescent patients for recruitment during the patient's CCBD outpatient clinic visit. Study personnel obtained written consent/assent and HIPAA acknowledgement from eligible caregivers and adolescent patients who agreed to participate in the study. We assigned consenting caregivers and assenting adolescent patients in alternation (2:1) to the MI group (N = 80) versus educational handout only group (N = 41). When the caregiver and adolescent both participated, we assigned the patient-caregiver dyad to either the MI or the education group. We performed weighted randomization (2:1) because of budgetary constraints precluding additional participant compensation.

Questionnaire Administration

Participants completed pre- and post-intervention self-report questionnaires (see Table 2 for questionnaire assignment by study time point). Study personnel administered pre- and post-intervention measures during the patient's clinic visit, so as not to place undue burden on participants. Specifically, we asked consenting caregivers and assenting adolescent patients to complete pre-intervention study questionnaires at enrollment. After participants completed pre-intervention questionnaires, study personnel informed participants whether they were assigned to the MI group or to the education group. For participants assigned to receive MI, study personnel scheduled the MI session for the patient's next CCBD clinic visit. If an adolescent-caregiver dyad agreed to participate and were assigned to the MI group, they each received individual MI sessions. Similarly, for participants assigned to the education control condition, study personnel

provided the adolescent patient and/or caregiver with the educational handout and AARP immediately after participants completed pre-intervention questionnaires.

Study personnel asked consenting caregivers and assenting patients to complete post-intervention measures assessing medical adherence barriers and patient- and/or caregiver-reported adherence ≥3 weeks following MI or educational handout administration, at the patient's next clinic visit. We established the post-intervention timepoint at ≥3 weeks following the intervention because most patients receiving maintenance therapy have monthly outpatient appointments. Additionally, we did not set a time limit for follow-up because we designed the study primarily as a feasibility trial. Study personnel administered post-intervention measures during the patient's clinic visit, so as not to place undue burden on participants. Months from enrollment and baseline measures administration to post-intervention follow-up were *M*(*SD*) = 4.12(1.57) and *M*(*SD*) = 3.63(1.09) for MI and education groups, respectively (independent samples t-test $t(104) = 1.75$, $p = .08$). Finally, we compensated study participants with $15 and $20 pre-loaded cards (i.e., ClinCard) for completing pre- and post-intervention measures, respectively.

STUDY INTERVENTIONS

Motivational Interviewing

The MI intervention condition consisted of a single 15-to-60-minute MI session, without education, focusing on enhancing and/or maintaining 6-MP adherence. We delivered MI in English or Spanish, depending on the participant's primary language. For Hispanic, Spanish-speaking participants, we assigned MI interventionists based on ethnicity and language match. MI interventionists included: two pediatric psychologists, one medical resident (Hispanic, native Spanish speaker), one doctoral-level clinical psychology student (Hispanic, native Spanish

speaker), one Master's level graduate student (Hispanic, native Spanish speaker), and one post-Master's research assistant. In preparation for this study, a licensed and board certified psychologist who had also been certified as an MI trainer trained the interventionists. Training included a basic four-hour MI workshop followed by small-group advanced didactic instruction and individualized feedback of audio-recorded mock MI sessions. MI training content and structure corresponded to the protocol described in Victor and colleagues' recently published MI training pilot study (Victor, et al., 2018). However, in our study, MI interventionists also received additional individualized instruction compared to the training described by Victor and colleagues (2018). Additional individualized didactic and practical training sessions continued until interventionists reached expert level proficiency as demonstrated by meeting criteria set forth by the MITI 4.2.1 (e.g., 50% complex reflections, 2:1 reflections to questions ratio, etc.; Moyers, Manuel, & Ernst, 2014) for at least two successive audio-recorded mock MI sessions. Prior to delivering MI in this study, each interventionist achieved expert-level proficiency. If MI study session coders found that any study interventionist's session performance failed to meet expert proficiency standards, that interventionist met with the MI trainer for additional training sessions.

Because there are no published training protocols for Spanish-speaking MI interventionists, I consulted with CAMI developer, Dr. Cristina S. Lee, to ensure we followed appropriate training procedures (C. Lee personal communication, June 14, 2017). All native Spanish-speaking interventionists qualified to deliver MI in both English and Spanish. Qualification was noted by the interventionist first reaching MI proficiency in English MI delivery. Then, a native-Spanish speaking psychologist, who had previously reached MI-expert proficiency (per training as part of Victor et al., 2018) and who was not a study investigator,

independently coded interventionists' Spanish-language mock MI sessions. Spanish-speaking interventionists demonstrated expert proficiency in English- and Spanish-language MI delivery before conducting interventions in this study. During the study, a certified MI trainer who was also a licensed and board certified pediatric psychologist conducted ongoing supervision for English-language MI sessions. Additionally, the bilingual MI rater who was not a study interventionist reviewed and coded Spanish-language MI sessions. These two psychologists and myself coded 39% of MI sessions conducted during this study to ensure adequate MI delivery. We established a minimum requirement to code ≥30% of sessions based on recommendations by Jelsma and colleagues (2015). Jelsma and colleagues (2015) evaluated published MI RCTs' methodology and found RCT investigators coded between 11–32% of total MI sessions per study. For future MI studies, Jelsma and colleagues (2015) specifically recommended coding ≥20% of MI sessions. Consequently, our criterion to code ≥30% of sessions exceeds minimum expert recommendations.

As the study progressed, interventionists continued delivering MI sessions as long as all recorded MI sessions surpassed basic level competency. If an interventionist's MITI-coded intervention session did not reach basic competency standards, the interventionist was suspended from delivering study interventions until he or she demonstrated expert level proficiency on two successive practice sessions. However, the study did not require implementing this measure.

CAMI-informed intervention manipulation. MI interventionist took into consideration Lee and colleagues' (2011) cultural adaptation of MI as guiding the intervention framework for all sessions. Consequently, the MI interventionist acknowledged patients' relevant social contextual factors (e.g., post-immigration stressors, changing family dynamics) as influences on behavior change, as well as considered patients' unique cultural values. However, because of the

scope of this dissertation study and my particular interest in MI with Hispanic, Spanish-speaking participants, I only coded Spanish-delivered MI sessions with the CAMI manipulation check.

Education Control

The control intervention consisted of an educational handout explaining the importance of remaining 6-MP adherent and providing adaptive medication adherence strategies (see Appendices U-X for Caregiver-English, Caregiver-Spanish, Patient-English, and Patient-Spanish handout versions). Research personnel delivered the handout to control participants during a clinic visit without providing additional psychoeducational material or engaging in problem-solving adherence strategies. We followed this education delivery method because it requires minimal clinic flow disruption. Prior to the study, we developed the educational handout with input from one pediatric oncologist and two licensed pediatric psychologists who specialize in pediatric oncology. We modified educational text to reflect the recipient (e.g., for caregivers, "Having a set schedule will help your child remember to always take the medicine;" for patients, "Having a set schedule will help you remember to always take the medicine"). Additionally, we utilized the Flesch–Kincaid (Flesch, 1948) readability formula available from Microsoft Word (Microsoft Corporation, 2010) to establish the handout reading level and compare it to recommended standards. Health literacy research suggests patient education material should be written at a sixth-grade or lower reading level, preferably including pictures, for optimal comprehension (Safeer & Keenan, 2005). In line with these recommendations, we revised our educational handout until it reached a Flesch-Kincaid 5th grade reading level (Flesh, 1948). As a native Spanish speaker, I forward and backward translated all handout versions from English to Spanish (and vice versa as an interpretation check). Additionally, native Spanish-speaking research personnel also reviewed the Spanish-translated measure.

DATA ANALYSES

Data Cleaning

Prior to primary analyses, I checked data for missing values. There were no missing data for demographic variables. Missing data rates for self-report questionnaire items and scores ranged from 0.83% to 13.22%. This higher proportion of missing data is secondary to ongoing study follow-up for some participants. As expected, missing data rates for TGN concentrations were higher (i.e., 38.02% at baseline and 47.93% post-intervention). We anticipated higher missing data rates for TGN concentrations because our study design precluded us from routinely collecting TGN blood serum levels for all study participants. Instead, we relied on TGN data collected for clinical care and available in the medical record. Overall, because missing data rates of 15% to 20% are common in educational and psychological research (Peugh & Enders, 2004; Schlomer, Bauman, & Card, 2010), I considered missing self-report data rates adequate for statistical analyses. Moreover, since missing data patterns were random (Little's MCAR test $p > .05$), I excluded cases pairwise to allow utilizing cases containing some missing data. Although I considered conducting data imputation procedures to address high rates of missing TGN data, missing data rates >10% are not appropriate for statistical imputation may be biased (Schafer & Olsen, 1998; Bennett, 2001). Consequently, I conducted TGN-related analyses with available data, without imputing missing values.

After identifying and managing missing values, I evaluated data to ensure data met statistical assumptions for parametric tests. I utilized histograms and box-plots to identify univariate outliers. I recoded extreme scores clearly resulting from participants misinterpreting questions, and thus were in fact invalid values. Specifically, there were outlier values ($N<5$) for MA6-MP item "How many times your child completely missed a dose of 6-MP in the past seven

days." A minority of caregivers (N<5) incorrectly reported seven missed doses over the previous week even though medical team had temporarily discontinued therapy secondary to bone marrow suppression or illness. It was clear caregivers misinterpreted this question because of their response to another MA6-MP item assessing therapy discontinuation (i.e., "Did the doctor tell your child to stop taking 6-MP in the last 7 days?"). Moreover, we also confirmed therapy discontinuation via medical chart review. Consequently, I recoded invalid scores to "0" (i.e., no missed doses). With the exception of these MA6-MP item outliers, additional self-report questionnaire scores did not have extreme outliers requiring recoding.

Next, I tested the normal distribution assumption by examining histograms showing frequency distributions, as well as skewness and kurtosis values. For data that were non-normally distributed, I corrected for non-normality by performing data transformations (i.e., square root transformation ($\sqrt{X_i}$) or logarithmic transformation ($\log(X_i)$; see Results section for further information regarding transformed data). Additionally, I examined the linearity assumption by evaluating scatterplots of the independent variables plotted against the dependent variables. Next, I ensured data met specific assumptions for performed analyses (e.g., ANCOVA, PCA). If data failed to meet statistical assumptions, and did not allow for statistical transformations, I submitted these variables to nonparametric tests (e.g., Fisher's exact test) replacing planned parametric analyses.

Prior to conducting analyses, I computed a new variable to create three caregiver cultural groups. Specifically, I categorized participants based on their ethnicity and primary language as a proxy for potential cultural variations. Cultural groups included (1) Non-Hispanic, English-speaking, (2) Hispanic, English-speaking, and (3) Hispanic, Spanish-speaking. I classified caregivers based on their demographic questionnaire responses or by reviewing the patient's

medical chart when the demographic questionnaire was unavailable. I coded family language dichotomously (Spanish-speaking vs. English-speaking), such that families classified as "Spanish speaking" if at least one family member (i.e., caregiver, patient) chose to participate in Spanish. When families did not provide study consent I classified them as "Spanish speaking" if the medical record indicated caregivers preferred Spanish over English communication in their child's care. I followed this protocol to be able to analyze potential differences between participants and nonconsenting families.

Descriptive and Group Analyses

I calculated sample demographics, descriptive statistics, bivariate correlations among variables of interest, and intervention fidelity statistics. I calculated descriptive statistics and frequencies for variables of interest, including: demographic data (e.g., patient age and sex), clinical data (e.g., diagnosis, NCI risk classification, TGN levels), participant self-reported data (e.g., 6-MP adherence, AARP), and treatment fidelity data (i.e., MITI). Subsequently, I performed group analyses to ensure no systematic group differences in participant characteristics (e.g., education, income, marital status, patient age) and questionnaire scores (e.g., PMBS) at baseline. Specifically, I conducted independent samples *t*-tests and Fisher's exact tests with Bonferroni correction to evaluate differences between the MI intervention group (N=80) and education control group (N=41).

I also conducted one-way ANOVAs and Fisher's exact tests to examine potential group differences in numerical and categorical variables, respectively, among cultural groups (i.e., (1) Non-Hispanic, English-speaking (52.5%); (2) Hispanic, English-speaking (25.0%); and (3) Hispanic, Spanish-speaking (22.5%). I chose to use Fisher's exact tests because data did not meet assumptions (i.e., minimum cell count ≥ 5) for chi-square difference tests.

Intervention Fidelity Analyses

MI raters reviewed 39% of total MI sessions (including English and Spanish sessions), following established a priori criteria to code ≥30% of sessions, to ensure MI fidelity per the MITI Coding Manual MITI version 4.2.1 (Moyers, Manuel, & Ernst, 2014; see Appendix X). Per stipulations provided in the MITI 4.2.1 manual, MI raters used session-level behavior code summary indices (e.g., % complex reflections, % open questions, % MI-inconsistent behaviors), and global ratings (e.g., cultivating change talk, empathy) to determine whether each MI session met criteria for incompetency basic competency, or expert-level proficiency (Moyers et al., 2014).

I examined MI intervention fidelity by calculating frequency of coded sessions that met incompetence, basic competence, or expert level proficiency as stipulated in the MITI Coding Manual (MITI version 4.2.1; Moyers, Manuel, & Ernst, 2014). I used an intent-to-treat approach for data inclusion in this study, meaning all MI sessions were included in analyses. After bilingual MI coders completed MITI 4.2.1 ratings, I evaluated MI session characteristics separately, by intervention language, for English- and Spanish-delivered MI. Furthermore, for Spanish-delivered MI sessions, I calculated frequency ratings of the number of sessions that addressed (a) social contextual stressors related to minority status, and/or (b) culture-specific values. Spanish language MI sessions conducted with Hispanic participants were included in analyses whether or not they met criteria for cultural adaptation. Finally, because I conducted numerous statistical tests, I controlled alpha by using a Bonferroni correction (Tabachnick & Fidell, 2012).

Primary Analyses

Study hypotheses and corresponding analyses were as follows:

Hypothesis 1

Delivering MI or the education intervention to caregivers of pediatric ALL maintenance therapy patients, as an adjunct to patients' routine outpatient clinic visits, will be feasible as evidenced by enrollment and intervention completion for 79% of eligible caregivers during the study period.

H1 data analysis. This dissertation study is part of a larger, grant-funded feasibility pilot study needed to prepare for a larger randomized controlled trial ("RCT"). The larger RCT will investigate MI efficacy as an adjunct to treatment as usual for improving pediatric ALL patient's adherence to oral chemotherapy regimens. Study investigators expect the larger RCT to enroll CCBD patients over a two-year study period. The CCBD, including both the Dallas and Legacy clinics, typically treats 90-100 ALL pediatric patients receiving maintenance therapy at any given time. The larger RCT will use Multivariate Analysis of Variance to determine whether MI participants differ from control participants in 6-MP adherence changes over. A priori power analysis conducted with G*Power 3.1.9.2 for MANOVA indicated a sample size of 142 will be needed in the larger RCT assuming effect size 0.25 and power = 0.95 at α error probability = 0.05 with three time point and *r* between repeated measures = .50. This means that, over two years of the larger RCT, 71 patients (79% of 90 patients total each year) must be enrolled to achieve adequate statistical power. Thus, the current dissertation study had to successfully enroll 79% of eligible families during the study period to demonstrate RCT feasibility.

Hypothesis 2

Given literature indicating U.S. minority populations associate greater stigma with mental health service compared to majority populations (De Luca et al., 2016), a greater percentage of

non-Hispanic, English-speaking, caregivers/patients will agree to participate in our study compared to Hispanic, English- and Spanish-speaking caregivers.

H2 data analysis. The original H2 data analytic plan involved using chi squares tests of independence; however, data did not meet assumptions for planned analyses. Consequently, I calculated *z* statistics to evaluate differences in study participation rates among Non-Hispanic, English-, Hispanic, English-, and Hispanic, Spanish-speaking caregiver. A priori power analysis conducted with G*Power 3.1.9.2 (Faul et al., 2007) for planned chi square tests of independence indicated a sample size of 74 caregivers who were approached to participate would be needed for planned analyses assuming, power = .80, one-tailed α error probability = .05, and ratio of English:Spanish speaking families as 1.5.

Hypothesis 3

Caregivers who receive MI will find the MI intervention acceptable, as evidenced by at least 75% of participants' MI session ratings corresponding with a mean AARP sum score $\geq$ 30 (Tarnowski & Simonian, 1992).

H3 data analysis. For each caregiver who completed an MI session, I computed the caregiver's AARP sum score. I then examined frequencies to determine what percentage of caregivers obtained AARP sum scores $\geq$ 30. There was no minimum sample size required for these analyses. I had planned parallel exploratory analyses with adolescents who participated in an MI session, if appropriate. However, adolescent AARP scale reliability was poor (α = .316), thus, I did not proceed with exploratory analyses.

Hypothesis 4

If there are any differences in MI acceptability among caregiver cultural groups, the differences will be $d \leq 0.6$ (medium effect size).

H4 data analysis. The original H4 data analytic plan involved using analysis of variance (ANOVA) to evaluate whether caregiver- reported MI acceptability differed among cultural groups. However, data was not appropriate for ANOVA, but rather required a non-parametric test. Therefore, I conducted Fisher's exact tests. Because Fisher's exact test requires categorical variables, I created a binary variable to reflect MI acceptability (i.e., unacceptable intervention = AARP total score <30; acceptable intervention = AARP total score ≥30). A priori power analysis conducted with G*Power 3.1.9.2 (Faul et al., 2007) for planned ANOVA indicated sample size of 30 Spanish-speaking and 44 English-speaking caregivers who complete the MI session would be needed for planned analyses assuming, power = .80, one-tailed α error probability = .05, and effect size of d = .60. I had planned parallel exploratory with adolescents who participated in an MI session, if appropriate. However, adolescent AARP scale reliability was poor (α = .316), thus, I did not proceed with exploratory analyses.

Hypothesis 5

Caregiver-reported 6-MP adherence and patient TGN blood serum concentrations will improve from pre-intervention to one-month post-intervention follow-up more so for participants in the MI group than for participants in the education control. This finding will not be moderated by intervention language.

H5 data analysis. The original H5 data analytic plan involved hirearchical linear regression models. However, consultation with a statistician revealed ANCOVA models to be more appropriate for evaluating intervention group differences. Consequently, I used two separate analyses of covariance (ANCOVA) to compare the efficacy of each intervention condition for improving (1) caregiver-reported adherence, and (2) TGN level. First, I conducted an ANCOVA to assess the efficacy of the MI and education interventions in improving

caregiver-reported 6-MP adherence (i.e., DV = post-intervention caregiver-reported number of missed 6MP doses over the previous week). The predictors were the 'intervention group' (i.e., MI, education control), 'caregiver language' (i.e., English, Spanish), and the interaction term 'intervention group x caregiver language'. I included baseline 6-MP adherence scores as a covariate to control for individual differences.

I assessed parametric and ANCOVA assumptions to ensure there was no violation of normality, linearity, homogeneity of variances, homogeneity of regression slopes, and reliable measure of the covariate. Data for 'caregiver-reported number of missed 6-MP doses over the previous week' violated the normality assumption, as data were highly positively skewed (skewness values were 4.722 and 2.401 for pre- and post-intervention scores, respectively). Consequently, I performed a logarithm data transformation to improve its distribution. However, skewness values did not improve (new skewness values were 4.211 and 2.123 for pre- and post-intervention scores, respectively), thus I conducted the ANCOVA using the original data.

Next, I conducted a second ANCOVA to assess the effect of the MI and education interventions on patients' TGN levels (i.e., DV = post-intervention TGN level). Data met parametric and ANCOVA assumptions of normality, linearity, homogeneity of variances, homogeneity of regression slopes, and reliable measure of the covariate. The predictors were the 'intervention group' (i.e., MI, education control), 'caregiver language' (i.e., English, Spanish), and the interaction term 'intervention group x caregiver language'. I included baseline TGN levels as a covariate to control for individual differences.

I calculated effect sizes by evaluating partial eta squared and converting them to Cohen's *d* statistics to improve findings interpretability (.20 = small effect; .50 = medium effect; .80 = large effect; Cohen, 1988). Additionally, I determined the variability proportion explained by the

model by examining partial eta squared statistics. A priori power analysis conducted with G*Power 3.1.9.2 (Faul et al., 2007) for planned regression models indicated a sample size of 77 would be needed for planned analyses assuming three predictors, power = .80, α error probability = .05, and medium effect size (f^2 = .15). I had planned parallel exploratory analysis with adolescents who participated in an MI session, if appropriate. However, small adolescent sample size was not appropriate for ANCOVA. Consultation with a statistician revealed no alternative non-parametric tests to replicate performed ANCOVAs with adolescent data. Finally, post-hoc power analysis for ANCOVA with caregiver self-reported adherence as dependent variable indicated observed power to detect intervention effect was .05, suggesting our study was powered to detect statistical significance only if we found a large effect size. Post-hoc power analysis for ANCOVA with TGN concentration as dependent variable indicated observed power to detect intervention effect was .30, suggesting our study was powered to detect statistical significance only if we found a large effect size.

Exploratory Post-Hoc Analyses

In addition to completing primary analyses, I conducted exploratory post-hoc analyses with PMBS data to evaluate whether caregiver-reported medication adherence barriers changed from pre- to post-intervention. Post-hoc hypotheses and corresponding analyses were as follows:

First, I was interested in examining PMBS descriptive statistics and potential differences in specific barrier endorsement rates among cultural groups. Consequently, I calculated PBMS data frequency distributions to examine endorsement rates for each specific adherence barrier. In addition to frequency distributions, I conducted Fisher's exact tests to examine differences in barrier endorsement by (1) cultural groups (i.e., Non-Hispanic, English-speakers; Hispanic, English-speakers; Hispanic, Spanish-speakers), (2) patient age groups (i.e., <12 y/o; ≥ 12 y/o,

based on typical age cutoff for adolescents), and (3) study groups (i.e., MI group; Education control). I chose to use Fisher's exact tests because data did not meet assumptions (i.e., minimum cell count ≥ 5) for chi-square difference tests. Moreover, I conducted Fisher's exact tests using Bonferroni correction to account for the numerous tests conducted.

Next, I was interested in evaluating the underlying structure of PMBS data in my study sample and whether it resembled the four-factor structure reported by Simons and Blount (2007; see previous Measures section for a review of original PMBS subscales). To this end, I conducted a Principal Components Analysis (PCA) with oblique rotation (i.e., Direct Oblimin) on the PMBS items. I examined factor analysis assumptions, including evaluating the Kaiser-Meyer-Olkin (KMO; required value >.6) statistic and Bartlett's test of sphericity (required $p <$ .05). Additionally, I evaluated the scree plot, component eigenvalues, and factor loadings. Lastly, I evaluated scale and subscale reliability coefficients by calculating Cronbach's alpha (i.e., <.7 = questionable/poor, ≥ .7–.8 = acceptable, ≥ .8 = good; Cronbach, 1951). The small adolescent patient sample precluded me from conducting parallel analyses with AMBS data.

Lastly, I sought to investigate whether caregiver-reported medication adherence barriers decreased from pre-intervention to post-intervention follow-up more so for participants in the MI group than for participants in the education control. I was also interested in exploring potential MI efficacy moderators (e.g., patient age, caregiver cultural group). Consequently, I conducted three separate ANCOVAs to assess the efficacy of the MI and education interventions in reducing (1) total PMBS score, (2) Regimen Adaptation subscale score, and (3) Disease Frustration subscale score, respectively. Prior to conducting ANCOVAs, I ensured data for variables included in the model met parametric and ANCOVA-specific assumptions. Regimen Adaptation scores violated the normality assumption, as data were highly positively skewed

(skewness values were 1.693 and 1.851 for pre- and post-intervention scores, respectively). Consequently, I performed a logarithm transformation of the Regimen Adaptation scores to improve the data distribution (new skewness values were .616 and .658 for pre- and post-intervention scores, respectively). Disease Frustration scores met all parametric assumptions.

Next, for each ANCOVA, the predictors were the 'intervention group' (i.e., MI, education control), 'patient age group' (i.e., <12 y.o., ≥ 12 y.o.), 'caregiver language' (i.e., English, Spanish), and the three-way interaction term 'intervention group x patient age group x caregiver language'. The ANCOVAs included this moderation term to evaluate a potential differential intervention effect for caregivers of young (i.e., <12 y.o.) and adolescent (i.e., ≥ 12 y.o.) patients, and Spanish- and English-speaking caregivers. I included baseline PMBS scores and subscale scores, in their respective models, as covariates to control for individual differences. Additionally, I calculated effect sizes by evaluating partial eta squared and converting them to Cohen's *d* statistics to imrpove findings interpretability (.10 = small effect; .30 = medium effect; .50 = large effect; Cohen, 1988). I also determined the variability proportion explained by the model by examining partial eta squared statistics. Unfortunately, AMBS data did not meet homogeneity of variance assumption for ANCOVA. Consequently, I did not proceed with parallel exploratory analyses with adolescent patients. Consultation with a statistician revealed no alternative non-parametric tests to replicate performed ANCOVAs with adolescent data. Finally, post-hoc power analysis for ANCOVA with total PMBS score as dependent variable indicated observed power to detect intervention effect was .53, suggesting our study was powered to detect statistical significance only if we found a medium effect size. Post-hoc power analyses for ANCOVA models using PMBS subscale scores as dependent variables revealed we had to obtain medium to large effect sizes to detect a statistically

significant intervention effect (i.e., Disease Frustration model observed power = .16 and Regimen Adaptation model observed power = was .58).

CHAPTER FOUR

Results

DESCRIPTIVE AND GROUP STATISTICS

I present frequency distributions for categorical variables, means with standard deviations for continuous variables, and bivariate correlations between demographic variables and primary measure indices in Tables 1 and 3. Additionally, I report descriptive statistics for outcome measures in Table 4.

Study Group Differences

First, Levene's test for homogeneity of variance indicated equal variances were assumed for all variables examined (i.e., patient age, caregiver age, number of children in the home, number of adults in the home, baseline TGN, and AARP score) with the exception of PMBS total score at baseline ($F = 4.063$, $p = .046$). Next, independent samples *t*-tests revealed a significant difference in TGN concentration means at baseline ($t(73) = -2.093$, $p = .040$) between study groups (MI intervention group $M(SD) = 350.20$ (215.29); Education control group $M(SD) = 453.12$ (175.98)). There were no significant differences in patient age, caregiver age, number of children in the home, number of adults in the home, AARP score, baseline self-reported adherence, and baseline PMBS score.

Fisher's exact test revealed significant differences in patient sex ($p = .015$) between the MI intervention group and the education control group. Post hoc tests indicated there were significantly more caregivers of male patients in the education control group (81.0%) compared to the MI intervention group (58.2%). There were no significant differences in caregiver type, caregiver race, caregiver ethnicity, caregiver language, caregiver relationship status, caregiver

education, caregiver employment, household income, caregiver past mental health experience, patient insurance, and patient ALL risk group.

Cultural Group Differences

Group analyses revealed statistical differences in demographic variables among cultural groups. Specifically, one-way ANOVA revealed significant differences in number of children in the home ($F(2,106) = 4.91$, $p = .009$) by cultural group. A Tukey post-hoc test revealed that Hispanic, Spanish-speaking caregivers reported having more children in the home ($M(SD) = 3.13$ (1.36), $p = .007$) compared to Hispanic, English-speaking caregivers ($M(SD) = 2.12$ (.971)). Tukey's post-hoc test also revealed a stastistically nonsignificant trend for Hispanic, Spanish-speaking caregivers reporting a greater number of children in the home ($M(SD) = 3.13$ (1.36)) compared to Non-Hispanic, English-speaking caregivers ($M(SD) = 2.52$ (1.10), $p = .072$). Additionally, a one-way ANOVA indicated the difference in adults in the home among cultural groups approached statistical significance ($p = .052$). Based on Tukey post-hoc test, Hispanic, Spanish-speaking caregivers reported a greater number of adults in the home ($M(SD) = 2.30$ (.993)) compared to Non-Hispanic, English-speaking caregivers ($M(SD) = 1.94$ (.435), $p = .066$) and Hispanic, English-speaking caregivers ($M(SD) = 1.90$ (.803), $p = .083$). Finally, one-way ANOVAs revealed no significant differences in patient age, caregiver age, baseline TGN level, AARP score, baseline self-reported adherence, and baseline PMBS score.

Fisher's exact tests with Bonferroni correction revealed significant differences among cultural groups in caregiver race ($p < .001$), caregiver education ($p < .001$), caregiver relationship status ($p = .001$), household income level ($p < .001$), and patient insurance type ($p < .001$). With regard to race, all Hispanic caregivers, regardless of primary language, identified their race as White. Although the majority of Non-Hispanic caregivers also reported White race (68.3%), a

portion of them (22.2%, $p < .001$) reported their race as Black. With regard to caregiver education, Non-Hispanic caregivers reported overall higher education levels compared to Hispanic caregivers ($p < .001$). Specifically, significantly more Non-Hispanic, English-speaking caregivers (38.1%) reported having obtained a Bachelor's degree compared to Hispanic, English-speaking caregivers (13.3%) and Hispanic, Spanish-speaking caregivers (3.7%). Additionally, cultural groups in our sample reported a significant difference in the proportion of caregivers who had not obtained a high school diploma; a tenth of Hispanic, Spanish-speaking caregivers (10.8%) reported not graduating high school, whereas only 2.5% and 3.3% of Non-Hispanic, English-speaking and Hispanic, English-speaking caregivers, respectively, reported not completing high school. Furthermore, about half (53.3%) of Hispanic, English-speaking caregivers reported their highest education level to be a high school degree, which significantly differed from the proportion of Non-Hispanic, English-speaking caregivers (23.8%) and Hispanic, Spanish-speaking caregivers (33.3%) who reported high school as their highest education level.

Next, cultural groups reported significantly different caregiver relationship statuses. Specifically, significantly more Non-Hispanic, English speaking (84.1%) and Hispanic, Spanish-speaking (80.8%) caregivers reported being in a relationship (i.e., married, remarried, cohabitating) compared to Hispanic, English-speaking caregivers (46.7%). Household income also significantly differed among cultural groups. Hispanic caregivers, regardless of primary language, reported significantly lower income levels than their Non-Hispanic counterparts ($p < .001$). Over half of Non-Hispanic, English-speaking caregivers (57.1%) reported an annual household income in the 80th percentile (i.e., ≥ $60,001) of household income statistics for the Dallas-Fort Worth area (U.S. Census Bureau, 2016), compared to only a quarter (25.0%) of

Hispanic, English-speaking caregivers and about a fifth (18.8%) of Hispanic, Spanish-speaking caregivers. Consistently, cultural groups also significantly differed at the lowest household income bracket. Roughly half of Hispanic caregivers (42.9% Hispanic, English-speaking and 52.4% Hispanic, Spanish-speaking) falling in the 20th household income percentile (i.e., < $20,000).

Finally, cultural groups also differed in patient insurance type ($p < .001$). Per medical chart review, the majority (88.5%) of Hispanic, Spanish-speaking caregivers' patients had Medicaid insurance, which was significantly higher than both Non-Hispanic, English-speaking (39.7%) and Hispanic, English-speaking (50.0%) caregivers' patients. There were no significant differences in patient sex, patient ALL risk category, caregiver type, caregiver employment, caregiver past mental health experience, and study group (i.e., MI vs. education control) assignment.

Intervention Fidelity Statistics

MI raters analyzed 32% of English-delivered sessions and 63% of Spanish-delivered sessions were coded. I purposefully coded more Spanish-delivered MI sessions to qualitatively explore CAMI-informed themes. MI interventionists reached expert-level proficiency for the majority of English-delivered MI sessions (94.12% expert-level proficiency, 5.88% basic competency, 0% incompetency). English-delivered MI session duration ranged from 11 minutes, 23 seconds to 25 minutes, 41 seconds (*M*=17-min, 32-sec; *Median*=18-min, 34-sec).

Compared to English-speaking MI interventionists, Spanish-speaking MI interventionists reached expert-level proficiency for 90% of the sessions and basic competency for 10% of the sessions (0% incompetency). With regard to intervention length, Spanish-delivered MI sessions ranged from 11 minutes, 56 seconds to 55 minutes, 35 seconds (*M*=27-min, 40-sec; median = 21-

min, 36-sec). An independent samples *t*-test revealed Spanish-delivered MI sessions lasted significantly longer than English-delivered MI sessions ($t(10.16) = -2.259$, $p = .047$). Furthermore, we used a CAMI-manipulation check to assess whether Spanish-delivered MI session content reflected (a) social contextual stressors related to minority status, and/or (b) culture-specific values. We coded these aforementioned content areas in Spanish-delivered MI session content by using a binary variable (i.e., theme present, theme not present). The CAMI-manipulation check indicated all Spanish-delivered MI sessions addressed at least one, if not both, of the two content areas. Specifically, 43% sessions addressed both content areas (i.e., social contextual stressors related to minority status and culture-specific values). The remaining sessions covered a single content area content, with 43% of sessions including discussion of culture-specific values and 14% of sessions addressing social contextual stressors related to minority status. All Spanish-delivered sessions covered at least one content area of the CAMI framework. Coders also identified qualitative content by identifying and recording broad themes via MI session audio review. Qualitatively, common social contextual stressors related to minority status included caregivers' perceptions of discrimination in the medical setting, deportation concerns, low health literacy, and lack of resources (e.g., pill boxes, transportation). MI session content also highlighted culture specific values such as familiaism (e.g., "cancer in the family"), respect for and perception of physicians as authority figures, sex roles within the family, emotional expression expectations, and strong faith-based beliefs.

PRIMARY ANALYSES RESULTS

Study Aim 1

To test the feasibility of delivering MI during patients' routine clinic visits and the feasibility of our study design (to inform a larger, future RCT).

Study Aim 1 Results

We actively enrolled study participants during a one-and-a-half-year period. We carried out the study in two CCBD clinics located in Children's Health's Dallas and Legacy campuses, respectively. In Dallas, study recruitment and enrollment occurred from June 14, 2017 through December 21, 2018. For the second outpatient clinic, located at the Legacy campus in Plano, study recruitment and enrollment occurred from May 2, 2018 through December 21, 2018. To establish participant eligibility and cultural group membership, we screened a CCBD-developed ALL patient list. This list included patients receiving maintenance therapy in either clinic location (i.e., Dallas campus, Legacy campus). Based medical chart review, we recorded diagnosis, treatment phase, ethnicity, and caregiver language for all eligible patients. The combined Dallas and Legacy eligible patient population included 137 patients. I confirmed the total number of eligible patients by conducting a second medical chart review in consultation with the Nurse Practitioner who manages care for CCBD ALL patients. Out of 137 eligible patients, we attempted to recruit 128 (93.43%) patients. We failed to approach nine eligible patients (6.57%) to participate in the study because of lack of research personnel's availability in clinic (i.e., Dallas, Legacy). Out of 137 eligible patients, we enrolled 121 (88.32%) patients. Only seven eligible patients who were recruited declined to participate in the study (for a detailed description of participant flow, refer to CONSORT diagram in Figure 2). Overall, we successfully enrolled 88.32% (N=121) of eligible patients. Furthermore, 87.5% of patients randomized to receive MI completed the intervention, demonstrating MI-delivery feasibility as adjunct to treatment as usual (see CONSORT diagram in Figure 2).

In addition to broadly assessing study feasibility, we were interested in evaluating study feasibility with culturally diverse caregivers. Slightly greater than half (*N*=71, 51.82%) of all 137

eligible patients had Non-Hispanic, English-speaking caregivers, whereas the remaining eligible patients had caregivers who identified as Hispanic. Among Hispanic caregivers, half (*N*=33, 24.09% of total eligible population) designated English and half (*N*=33, 24.09% of total eligible population) designated Spanish as their preferred language in the medical record. Research personnel approached 92.96% (*N*=66) of 71 eligible Non-Hispanic, English-speaking caregivers. Of those approached, 64 (96.97%) agreed to participate in the study and two (3.03%) declined participation. Similar recruitment and enrollment rates were seen for Hispanic, English- and Spanish-speaking caregivers. Research personnel approached 93.94% (*N*=31) of all eligible Hispanic, English-speaking caregivers to participate in the study. Only one Hispanic, English-speaking caregiver declined study participation, resulting in 96.77% of eligible caregivers in this cultural group completing study enrollment. Additionally, research personnel approached 90.91% of all eligible Hispanic, Spanish-speaking to participate in the study. Three (10%) out of all approached Spanish-speaking caregivers declined participation. Thus, 90% of all eligible Hispanic, Spanish-speaking caregivers enrolled in the study.

Per *z*-score examination, participation rates did not significantly differ for Non-Hispanic, English-speaking caregivers (96.97%), Hispanic, English-speaking caregivers (96.77%), and Hispanic, Spanish-speaking caregivers (90%). Group comparisons revealed the following *z*-statistics: (1) Non-Hispanic, English-speaking vs. Hispanic, English-speaking caregivers $z = -1.18$, $p = .24$; (2) Non-Hispanic, English-speaking vs. Hispanic, Spanish-speaking caregivers $z = 1.42$, $p = .16$; and (3) Hispanic, English-speaking vs. Hispanic, Spanish-speaking caregivers $z = 0.93$, $p = .35$.

Study Aim 2

To test MI acceptability as an adjunct to treatment as usual for pediatric ALL maintenance therapy patients and to evaluate whether MI acceptability differs among caregiver cultural groups (i.e., Non-Hispanic, English-speaking, Hispanic, English-speaking, and Hispanic, Spanish-speaking caregivers).

Study Aim 2 Results

MI AARP scores suggest 95.59% of caregivers who received MI rated the intervention above the acceptability threshold (i.e., ≥ 30 AARP score; (*M(SD)*=38.10(6.54), *Mdn*=38.82, range = 12-48). Furthermore, All Non-Hispanic, English-speaking and Hispanic, English-speaking caregivers rated the MI intervention as *acceptable* (AARP *M*(*SD*) =39.15(5.17), *Mdn*=39.22, range 30-48; AARP *M*(*SD*) =39.20(4.00), *Mdn*=39.50 range =32-46, respectively). Similarly, all but one Hispanic, Spanish-speaking caregiver rated MI as *acceptable (*AARP *M*(*SD*) =35.64 (9.38), *Mdn*=36.00, range= 14-44). Fisher's exact test revealed no significant differences (p = .16) in AARP ratings among caregiver cultural groups.

Study Aim 3

Evaluate preliminary MI efficacy in improving (a) caregiver-reported 6-MP adherence and (b) patient TGN blood serum concentration, compared to an education control, from pre- to post-intervention.

Study Aim 3 Results

I conducted two separate ANCOVA models to compare the efficacy of each intervention condition for improving follow-up caregiver-reported 6MP adherence and patient TGN levels. Results for each ANCOVA are below.

Change in caregiver-reported 6-MP adherence. After adjusting for baseline 6-MP adherence scores, the 'intervention group' main effect was not significant (F (1, 75) = .01, p = .92, partial $\eta 2$ < .001, d = .03), suggesting no difference in post-intervention number of missed 6-MP doses/week between the MI group (M = .18, SD = .07) and education control (M = .17, SD = .10). Similarly, the interaction 'intervention group x caregiver language' was not significant (F (1, 75) = .01, p = .94; see Table 5).

Because at face value descriptive statistics for baseline and follow-up caregiver-reported adherence (Table 4) appeared to indicate a pre- to post-intervention decline in adherence, I conducted paired-samples t-tests for each cultural and study group. Specifically, I conducted five paired-samples t-tests to compare caregiver-reported number of missed 6-MP doses over the past seven days at baseline and follow-up for each group (i.e., Non-Hispanic, English-speaking; Hispanic, English-speaking; Hispanic, Spanish-speaking; MI; Education). There were no statistically significant differences in caregiver-reported number of missed 6-MP doses over the past seven days at baseline and follow-up for any of the groups.

Change in patient TGN levels. After adjusting for baseline TGN levels, the main effect of 'intervention group' was not significant (F (1, 43) = 2.13, p = .15, partial $\eta 2$ = .05, d = .45), suggesting no difference in post-intervention TGN levels between the MI group (M = 417.54, SD = 48.09) and education control (M = 314.52, SD = 47.53). Similarly, the interaction 'intervention group x caregiver language' was not significant (F (1, 43) = 1.01, p = .32, partial $\eta 2$ = .02; see Table 6).

EXPLORATORY POST-HOC ANALYSES RESULTS

PMBS Descriptive Statistics

Based on the PMBS established cut-off score to determine non-adherence risk (i.e., ≥ 2 barriers), 84% of the study sample surpassed this non-adherence risk threshold. Out of 16 possible medication adherence barriers included in the PMBS, caregivers reported a mean of 4.21 barriers (SD=2.88, range 0-13). Table 7 summarizes frequencies for caregiver-reported barriers for the entire study sample, as well as by cultural and intervention groups. The top four medication adherence barriers, identified by at least half of caregivers, were: (1) My child relies on me to remind him/her to take his/her medication; (2) My child does not like how the medicine tastes; (3) My child is tired of taking medicine; and (4) My child is tired of living with a medical condition.

Based on Fisher's exact test findings, there were a few significant differences in specific medication adherence barrier endorsement rates between Hispanic, Spanish-speaking caregivers and Non-Hispanic, English-speaking caregivers (see Table 7). Specifically, three PBMS items were significantly more frequently identified as medication adherence barriers by Hispanic, Spanish-speaking caregivers compared to Non-Hispanic, English-speaking caregivers, These PMBS items included: (1) "My child has too many pills to take " (Item 2; endorsed by 48.0% Hispanic, Spanish-speaking caregivers *vs.* 14.8% Non-Hispanic, English-speaking caregivers; $p < .01$); (2) "My child is forgetful and doesn't remember to take his/her medication every time" (Item 5; endorsed by 36.0% Hispanic, Spanish-speaking caregivers *vs.* 11.7% Non-Hispanic, English-speaking caregivers; $p = .03$); and (3) "My child finds it hard to stick to a fixed medication schedule" (Item 10; endorsed by 15.4% Hispanic, Spanish-speaking caregivers *vs.* 1.6% Non-Hispanic, English-speaking caregivers; $p = .03$). We found no additional differences

in PMBS item endorsement rates between Hispanic, Spanish-speaking caregivers and Non-Hispanic, English-speaking caregivers.

Furthermore, Fisher's exact test findings revealed no differences in specific adherence barrier endorsement rates between Hispanic, English-speaking caregivers and Hispanic, Spanish-speaking caregivers. Similarly, we found no differences between Non-Hispanic, English-speaking caregivers and Hispanic, English-speaking caregivers. Finally, Fisher's exact test findings indicated no differences in specific adherence barrier endorsement rates between the MI group and the education control, as would be expected as a result of randomized group assignment.

PMBS Factor Structure

I conducted a Principal Components Analysis (PCA) with oblique rotation (i.e., Direct Oblimin) on the 16 PMBS items (See Table 8). The Kaiser-Meyer-Olkin measure verified the sample adequacy for the analysis, KMO = .74 ('acceptable' per Hutcheson & Sofroniou, 1999; Kaiser, 1970). Bartlett's test of sphericity X^2 (120) = 692.66, $p < .001$, indicated that correlations between items were sufficiently large for the factor analysis (Bartlett, 1954). I initially ran a PCA without limiting number of factors to explore eigenvalues for each component in the data. Four components had eigenvalues over Kaiser's criterion of 1 and in combination explained 59.54% of the variance. An inspection of the screeplot revealed a break after the second component; thus, using Cattell's (1966) scree test, I retained two components for further investigation.

The two-component solution explained 43.63% of the variance, component one (i.e., *Regimen Adaptation*) contributing 32.39% and component two (i.e., *Disease Frustration*) contributing 11.28%. The rotated solution, using Direct Oblimin rotation, showing strong factor

loadings, with 14 items loading substantially on only one component (See Table 8). Only two items did not load strongly on either component and thus were removed from the scale. There was a 'moderate to low' positive correlation (r = .40) between the two factors. These results support using *Regimen Adaptation* items and *Disease Frustration* items as separate scales. Furthermore, Cronbach's alpha reliability coefficients were r = .83 ('good') and r = .76 ('acceptable') for the *Regimen Adaptation* subscale and *Disease Frustration* subscale, respectively. Full-scale Cronbach's alpha for the newly PCA-reduced 14-item PMBS was α = .85, suggesting good scale reliability.

Pre- to Post-Intervention PMBS Scores Change

I conducted three separate ANCOVAs to assess the efficacy of the MI and education interventions in reducing (1) total PMBS score, (2) Regimen Adaptation subscale score, and (3) Disease Frustration subscale score. The ANCOVAs included a moderation analysis to evaluate a potential differential intervention effect for caregivers of young (i.e., <12 y.o.) and adolescent (i.e., ≥ 12 y.o.) patients, and Spanish- and English-speaking caregivers. Results for each ANCOVA are below.

Total PMBS Score Change

I conducted an ANCOVA with total post-intervention PMBS score as the dependent variable. The predictors were the 'intervention group' (i.e., MI, education control), 'patient age group' (i.e., <12 y.o., ≥ 12 y.o.), 'caregiver language' (i.e., English, Spanish), and the three-way interaction term 'intervention group x patient age group x caregiver language.' I included baseline PMBS scores as a covariate to control for individual differences. Table 4 summarizes baseline and follow-up PMBS means. Table 9 presents ANCOVA results. Figure 3 depicts a

graph representing pre- to post-intervention change in PMBS mean scores by (1) intervention group, (2) patient age group, (2) caregiver language).

I assessed parametric and ANCOVA assumptions to ensure there was no violation of normality, linearity, homogeneity of variances, homogeneity of regression slopes, and reliable measure of the covariate. After adjusting for baseline PMBS scores, the 'intervention group' main effect was significant (F (1, 85) = 4.18, p = .04, partial $\eta 2$ = .05, Cohen's d = 0.44, small-to-medium effect size), indicating caregivers who received MI reported less 6-MP adherence barriers (M = 3.01, SD = .41) following the intervention compared to caregivers in the education control group (M = 4.22, SD = .44). The variance in post-intervention PMBS scores explained by 'intervention group', after controlling for baseline score, was 47% based on partial $\eta 2$ = .05. Lastly, the interaction 'intervention group x patient age group x caregiver language' was not statistically significant (F (1, 85) = 1.72, p = .15, partial $\eta 2$ = .08).

PMBS Subscale Scores Change

In addition to evaluating the intervention effect on total PMBS score, I conducted two additional ANCOVAs with each PMBS subscale (i.e., Regimen Adaptation, Disease Frustration) as the dependent variable, respectively. Tables 10 and 11 present ANCOVA results. Figures 4 and 5 are graphs depicting pre- to post-intervention change in Disease Frustration and Regimen Adaptation mean scores by (1) intervention group, (2) patient age group, (2) caregiver language. After adjusting for baseline Regimen Adaptation scores, 'intervention group' main effect was significant (F (1, 85) = 4.77, p = .03, partial $\eta 2$ = .05, Cohen's d = .47, medium effect size), indicating caregivers who received MI reported less regimen adaptation barriers (M = .64, SD = .11) following the intervention compared to caregivers in the education control group (M = 1.32, SD = .12). The variance in post-intervention Regimen Adaptation scores explained by

'intervention group', after controlling for baseline score, was 5% based on partial $\eta 2 = .05$. The interaction 'intervention group x patient age group x caregiver language' was not statistically significant (F (1, 85) = 1.91, $p = .12$, partial $\eta 2 = .08$). Lastly, ANCOVA results for Disease Frustration were not significant; 'intervention group' had a small effect size per Cohen's $d = .21$.

CHAPTER FIVE

Discussion

Effective ALL relapse prevention requires adherence to a lengthy, complex maintenance chemotherapy course involving daily 6-MP. Unfortunately, 20% of pediatric ALL patients are 6-MP non-adherent (Bhatia et al., 2014; Hunger & Mullighan, 2015) even though missing ≤5% of prescribed 6-MP doses results in a four-fold increased relapse risk (Bhatia et al., 2012). Accordingly, culturally sensitive, evidence-based interventions aimed at improving 6-MP adherence may result in decreased morbidity and mortality for pediatric ALL patients. This dissertation study investigated the feasibility and acceptability of brief, English- and Spanish-delivered, culturally informed MI sessions during routine outpatient medical appointments for ALL maintenance therapy patients. Additionally, this study preliminarily explored MI efficacy, potentially moderated by ethnicity and language and compared to an education control condition, for improving caregiver-reported 6-MP adherence, patients' TGN blood serum levels, and caregiver-perceived 6-MP adherence barriers. Findings confirmed primary MI feasibility and acceptability hypotheses, supporting the possibility of universally delivering adherence-enhancing MI as part of routine oncological care. Additionally, although methodological limitations hindered adequate assessment of MI efficacy for improving caregiver-reported 6-MP adherence and patients' TGN blood serum levels, post-hoc analyses suggested MI was effective for reducing caregiver-perceived 6-MP adherence barriers. Overall, study findings have the potential to inform a larger, future MI efficacy RCT by highlighting opportunities for improved 6-MP adherence and optimized study design.

STUDY DESIGN AND MI FEASIBILITY

To our knowledge, this is the first study to examine MI feasibility as an adjunct to treatment as usual for pediatric ALL patients receiving maintenance chemotherapy. Regarding study design feasibility, we were able to successfully enroll and randomize the overwhelming majority (88.32%) of eligible patients, regardless of cultural background, across two clinic locations. These findings suggest study procedures and randomization were feasible and hence can be reasonably replicated in a future RCT. Further, to this date, 80.47% of study participants have successfully completed all study procedures and follow-up assessment, suggesting participant progression through the study is also attainable even in a busy outpatient setting (see Figure 2 CONSORT diagram for information about attrition and status of ongoing participants).

In addition to evaluating overall study design feasibility, I examined caregivers' willingness to participate in the study and, for those assigned to receive motivational interviewing, the intervention. There were no differences in study participation rates among cultural groups, disproving one of the study hypotheses. Specifically, we had hypothesized that because U.S. minority populations tend to associate greater stigma with mental health service compared to majority populations (De Luca et al., 2016), a greater percentage of non-Hispanic, English-speaking caregivers would agree to participate compared to Hispanic, English- and Spanish-speaking caregivers. However, results from this study demonstrate no differences in caregivers' willingness to participate. One potential explanation for caregivers' willingness to participate in the study is their likely perception of the target behavior (i.e., adherence to 6-MP) as a crucial part of their child's medical regimen. Regardless of cultural background, caregivers likely perceived 6-MP as key for preventing ALL leukemia relapse, which may have promoted inherent investment from caregivers to participate in this study. Another possibility is that the

nature of children's cancer treatment in an academic medical center may have decreased stigma around study participation for caregivers. Throughout treatment, patients and caregivers become familiar with oncology research protocols, likely making them more trusting of research and willing to participate in studies.

Findings supporting study design feasibility and caregivers' willingness to participate in the study are promising for future RCT development. More importantly, MI delivery was also feasible as evidenced by 87.5% (N=70) of patients randomized to receive MI (N=80) successfully receiving the intervention. Thus, our low-cost, non-time-intensive intervention may provide particularly efficient and feasible non-adherence prevention and/or adherence-promotion opportunities for pediatric ALL maintenance therapy patients.

We were not only able to deliver the intervention as planned, but did so while maintaining high intervention fidelity standards in both English (94.12% expert-level proficiency) and Spanish (90% expert-level proficiency). Thus, we promoted service access for traditionally underserved patients (i.e., Hispanic, Spanish-speaking). Moreover, the CAMI-manipulation check indicated all Spanish-delivered MI sessions addressed social contextual stressors related to minority status and/or culture-specific values. Therefore, we can conclude adherence to the CAMI-informed framework, during Spanish-delivered MI sessions, was also feasible. Strong intervention fidelity is important because MI treatment fidelity has predictive validity for patient behavior change post-intervention (Jelsma et al., 2015). Many MI research trials have failed to assess and report MI fidelity making it impossible to ascertain whether results can accurately be attributed to the MI intervention itself (Miller & Rollnick, 2014; Jelsma et al., 2015). Miller and Rollnick (2014) encourage MI researchers to assess and report MI fidelity allowing comparison across research trials.

Importantly, current findings add to the existing literature by demonstrating it is feasible to deliver MI *during* routine medical appointments in a busy pediatric oncology outpatient setting. Literature reviews on MI for health behavior change promotion, in both youth and adults, suggest MI has mostly been implemented as an adjunct intervention to routine medical care (Funderburk et al., 2018; Martins & McNeil, 2009; Gayes & Steele, 2014; Borrelli, Tooley, & Scott-Sheldon, 2015), rather than truly incorporated into ambulatory clinic visits. Although MI has been widely used in medical settings, a review of the literature suggests researchers studying MI across different health domains tend to recruit and enroll patients during routine clinic appointments, then schedule a separate additional appointment to conduct the MI intervention (e.g., Colby et al., 2005; Ogedegbe et al., 2008; Armit et al., 2009; Bakker et al., 2016; Resnicow et al., 2016; Wang et al., 2010). Consequently, although many previous researchers have conducted MI sessions within patients' regular medical clinics, the researchers asked patients to attend additional appointments likely requiring additional time, resources (e.g., transportation, childcare), and commitment from patients and caregivers. Moreover, the few studies evaluating MI during routine medical care, without requiring additional clinic appointments, involved using MI-informed techniques (e.g., discussing self-efficacy, problem-solving barriers) rather than delivering MI with high fidelity as a stand-alone intervention (e.g., Sims et al., 1999; Wierdsma et al., 2011).

By delivering brief MI sessions during routine ambulatory care for pediatric ALL patients, our findings support a more integrated patient-care model combining medical and behavioral interventions to promote 6-MP adherence during maintenance chemotherapy. Anecdotally, throughout the current study, oncologists' and nurse practitioners' informal feedback to the research team was in line with feasibility results. Providers reported that

integrating brief MI into routine outpatient appointments disrupted neither clinic flow nor the medical team's ability to care for patients. Moreover, universally delivering brief MI to caregivers of ALL patients receiving maintenance 6-MP was relatively inexpensive and time efficient, so the cost-benefit ratio is likely quite positive in light of strong acceptability and feasibility. The feasibility of integrating brief MI sessions during routine outpatient appointments may have important implications for improving medical adherence while containing healthcare costs and resources. Furthermore, brief MI sessions delivered during routine ambulatory care would likely be minimally burdensome, as the intervention itself requires minimal resources (e.g., time, cost) from patients, caregivers, and providers.

MI ACCEPTABILITY

Findings supported the study hypothesis that caregivers who received MI would find the intervention acceptable. Specifically, we hypothesized that at least 75% of participants' MI session ratings corresponding with a mean AARP sum score ≥30 (based on cut-off suggested by Tarnowski & Simonian, 1992). Findings exceeded study expectations, with all but one caregiver rating MI as an acceptable intervention for supporting 6-MP adherence during maintenance phase chemotherapy. Moreover, caregivers across all cultural groups regarded MI as a highly acceptable intervention and acceptability ratings did not vary by caregivers' demographic factors (e.g., ethnicity, language, SES, education).

These findings are consistent with past MI studies with ethnic minorities, in that minority caregivers (i.e., Hispanic, English- and Spanish-speaking caregivers) in our study reported strong intervention acceptability. Although most existing literature has focused on highlighting MI efficacy data with minority populations (for example, meta-analysis by Hettema, Steele, & Miller, 2004), a number of studies have also reported MI acceptability data. Specifically, Lee and

colleagues (2011) found adult Hispanic patients who completed culturally adapted brief MI to reduce substance use were strongly satisfied with MI treatment (M = 3.58 on a scale of 1–4, SD = .93) on a qualitative exit interview. Similarly, Gilder and colleagues (2011) studied MI to reduce underage drinking in Native American communities and found a substantial proportion of reservation youth were willing to accept MI for behavior change. Consequently, MI is not only an evidence-based intervention, but is also perceived as highly acceptable across cultural groups, creating buy-in from participants to engage in treatment.

MI's emphasis on empathy, partnership, and patient values may be especially appropriate for applications with ethnic minorities (Miller & Rollnick, 2002) because this approach provides a flexible framework for individualizing the intervention. Although there was already evidence suggesting culturally un-adapted MI maintains effectiveness with minority patients (Hettema, Steele, & Miller, 2005), our study findings add to the existing MI literature by demonstrating acceptability of culturally informed, brief MI targeting 6-MP adherence among caregivers of pediatric ALL patients receiving maintenance treatment. Overall, brief MI during routine medical appointments not only appears to be a viable intervention, but is also perceived by caregivers as an acceptable intervention promoting patients' 6-MP adherence. It is worth noting that, despite strong MI acceptability ratings across ethnic and language groups, the AARP presented with poor internal consistency for Hispanic, English-speaking caregivers. Thus, AARP findings for this cultural group should be interpreted with caution. Similarly, we also had a small Hispanic, Spanish-speaking caregiver sample, which rendered MI acceptability analyses exploratory for this group

Finally, the aforementioned MI feasibility and acceptability findings should be considered in the unique context of pediatric ALL treatment, which involves a long-lasting and

burdensome medical regimen requiring caregiver and patient adherence investment. Even in the context of a two-to-three-year, burdensome medical regimen, caregivers were willing to participate in MI sessions and rated MI sessions favorably as an intervention to improve their child's 6-MP adherence. High MI acceptability ratings among Hispanic caregivers are important to highlight, as racial and ethnic disparities in ALL incidence and treatment outcomes exist, with Hispanic children being disproportionally affected by ALL and at a higher relapse risk. As previously mentioned, one contributing factor to relapse risk is medication adherence, which is significantly lower among Hispanic patients. Consequently, this study suggests brief MI during routine ambulatory care is a viable and acceptable intervention for some of the most vulnerable pediatric ALL patient subgroups.

PRELIMINARY MI EFFICACY EVALUATION

In addition to evaluating MI feasibility and acceptability, a secondary aim of this study was exploring preliminary MI efficacy to improve 6-MP adherence. Unfortunately, our ability to evaluate MI efficacy to improve 6-MP adherence was constrained by study design limitations. Primarily, MI efficacy analyses were limited by the use of self-report and TGN concentrations as 6-MP adherence measures.

Evaluation of 6-MP Adherence Using Self-Report

Historically, many studies investigating 6-MP adherence have utilized parent-, patient-, and/or physician-report as a convenient and inexpensive medication intake measure. The current study replicated this widely use methodology—that is, using self-report as an adherence indicator; however, there are notable limitations of relying on self-report to assess medication adherence. Specifically, adherence researchers have consistently shown self-report is a subjective and unreliable medication intake indicator in various pediatric chronic illness populations

(Hommel et al., 2009; Modi et al., 2013; Farley et al., 2003; Bender et al., 2000), including pediatric ALL patients (Landier et al., 2017, Rohan et al., 2016). A robust body of literature in pediatric oncology and other chronic illness groups documents that self-report is subject to over-reporting adherence (Hommel et al., 2009; Landier et al., 2017) and potential biases (e.g., social desirability bias, recall bias; Landier et al., 2017; Marlowe & Crowne, 1961). Not surprisingly, caregivers in this study also reported markedly high rates (i.e., >93% at baseline) of 6-MP adherence. Because extant literature suggests that actual pediatric ALL maintenance therapy 6-MP adherence is poor for at least 20% of patients (Bhatia et al., 2014; Hunger & Mullighan, 2015), the markedly high adherence rate reported in our study is likely a result of over-report rather than an accurate representation of medication-taking behavior.

Unfortunately, elevated baseline adherence rates in our study created a ceiling effect that limited our ability to assess MI efficacy for improving self-reported 6-MP adherence. Notably, high self-reported adherence rates are not unique to this study, but rather consistent with the literature in other pediatric chronic illness populations reporting self-reported adherence rates that range from 80% to 100% (Hommel et al., 2009; Modi et al., 2013; Farley et al., 2003; Bender et al., 2000). To decrease potential demand characteristics for caregivers in our study, we ensured that caregivers were recruited and completed study procedures with study personnel who were unfamiliar to the caregiver. Nonetheless, inherent expectations in the medical setting (i.e. expectations for strong adherence) are ubiquitous and likely fueled social desirability bias, contributing to over-reporting adherence, as it is widespread in the adherence literature. Consequently, because of the limited utility of relying solely on self-report for assessing 6-MP adherence, a larger future RCT should employ more reliable and accurate alternatives.

Literature suggests medication electronic monitoring technology (i.e., Medication Event Monitoring System (MEMS) SmartCap) can be an asset for assessing pediatric ALL patients' medication adherence. The MEMS SmartCap is a computerized medication bottle that digitally tracks and records the date/time the bottle is opened. MEMS SmartCap technology has been used as a proxy for objectively tracking adherence in various pediatric populations (Ingerski et al., 2011), including ALL patients receiving maintenance chemotherapy (Rohan et al., 2016). Compared to using self-report, electronic monitoring more accurately captures data related to medication ingestion and, therefore, has been described as a "gold standard" method to track medication adherence (Osterberg & Blaschke, 2005; Riekert & Rand, 2002). Importantly, the MEMS SmartCap has enabled patients, caregivers, and providers to better assess medication adherence patterns and personalize interventions to address patient-specific medication-taking behaviors (Frias et al., 2017).

In a recent study, Landier and colleagues (2017) used the MEMS SmartCap, to objectively assess pediatric ALL patients' 6-MP adherence. Specifically, Landier and colleagues (2017) compared self-report to electronic monitoring of 6-MP intake during maintenance therapy and found that patients' self-report consistently overestimated their MEMS SmartCap-assessed 6-MP intake. Consistent with both previous literature and the findings from this dissertation study, Landier and colleagues (2017) found that most participants (92.6%) self-reported good 6-MP adherence, compared to 83.7% via electronic monitoring. More importantly, self-report overestimated electronically monitored 6-MP adherence at least some of the time (i.e., self-reported 6-MP intake exceeded MEMS records by ≥1 days in ≥1 study months) in most patients (84.4%; Landier et al., 2017). Only about one in 10 participants (12%) was a "perfect reporter" (i.e., self-report matched MEMS SmartCap records), while one quarter of participants (23.6%)

were classified as "over-reporters" (i.e., self-reported days of 6-MP intake exceeded MEMS SmartCap records by ≥5 days for at least half the study months). Furthermore, non-adherent patients were more likely to over-report 6-MP intake (47%) compared with adherent patients (8%). Specifically, non-adherent patients were 9.4 times more likely to over-report their 6-MP adherence compared to adherent patients (Landier et al., 2017). Consequently, these findings point to poor sensitivity, but high specificity, of self-report as a measure of 6-MP adherence. That is, patients who fail to self-report non-adherence may go unrecognized (i.e., 52.7% sensitivity), while patients who self-report not adhering to their medication are generally not taking them (i.e., 95.8% specificity). Therefore, combining self-report with objective medication intake assessments is crucial for identifying non-adherent patients and ensuring timely intervention.

Notably, although electronic monitoring (i.e., MEMS SmartCap) has been thought as the gold standard for objectively measuring adherence, growing literature suggests this method remains an indirect measure because it only presumes medication consumption but does not confirm the body's exposure to the drug. Consequently, when measuring adherence via electronic monitoring, it might also be beneficial to combine this method with additional adherence measures (e.g., self-report, 6-MP metabolite profiles; Rohan et al., 2016; Hoppmann et al., 2017; Landier et al., 2017; Traore et al., 2006).

Evaluation of 6-MP Adherence Using TGN Concentration

Because of the inherent limitations of self-report as a measure of adherence, accurate assessment of 6-MP adherence in pediatric patients with ALL requires using multiple adherence measures (Rohan et al., 2016; Hoppmann et al., 2017; Landier et al., 2017; Traore et al., 2006). Although there is inconsistent evidence supporting the utility of TGN levels as a 6-MP adherence

indicator, several previous studies have used TGN as a rough indicator of patients' 6-MP adherence behaviors (Bhatia et al., 2012). This study included TGN as an outcome variable per recommendations for multimodal 6-MP adherence assessment; however, TGN-related findings should be interpreted with caution in light of evidence questioning TGN's sensitivity to change.

Numerous past studies have examined TGN blood serum levels to evaluate ALL patients' 6-MP adherence; however, evidence varies as to the extent to which this 6-MP metabolite accurately characterize maintenance chemotherapy adherence (Relling et al., 1999; Chrzanowska et al., 1999; Harms et al., 2003; Lilleyman & Lennard, 1994; Schmiegelow et al., 1995). Several factors contribute to TGN concentrations' high variability and poor sensitivity to 6-MP intake. These factors include, but are not limited to, the characteristics of the assay used to measure TGNs, prescribed 6-MP dosage, inherited variability in TPMT and other enzyme's activity, drug-drug interactions, absorption process, viruses, allopurinol treatment (Alsous et al., 2017). Because of the unreliable nature of TGN levels as a 6-MP adherence indicator, TGN's poor change sensitivity could account for statistically non-significant findings. Not surprisingly, we found no change in patients' TGN levels pre-or post-MI and/or the educational control intervention.

Notably, methodological limitations prevented routine and reliable TGN data collection for all study participants. We relied on TGN levels that were recorded as standard care during routine medical clinic visits; however, not all physicians included TGN level assessment in routine care and slightly under half of patients were missing either a pre-intervention or post-intervention TGN value (i.e., 38.02% missing baseline TGN and 47.93% missing post-intervention TGN). Moreover, even if TGN levels had been reliably collected, some recently published studies have indicated that relying exclusively on TGN levels constitutes an

incomplete measure of 6-MP metabolite concentrations. In those recent studies, scholars have begun considering the value of assessing MMPN levels in conjunction with TGN levels to more comprehensively evaluate 6-MP-related metabolic activity (e.g., Rohan et al., 2016; Traore et al., 2006). In our study, study design limitations precluded collection of MMPN levels, in addition to TGN levels. During the development of the larger, grant-funded study, we did not consider the additive value of assessing MMPN levels. Therefore, we did not obtain IRB approval to collect MMPN data; however, this is a limitation that can easily be resolved to re-do analyses with 6-MP metabolic profiles. Because relying on one specific 6-MP adherence measure (e.g., TGN concentration) is unreliable, it will be important for the future RCT to include multiple adherence measures (i.e., MEMS Cap, self-report, 6-MP metabolite concentrations) with pediatric ALL patients.

Lessons Learned about Assessing 6-MP Adherence

In conclusion, current adherence assessment approaches (e.g., self-report, 6-MP metabolite profiles) pose inherent limitations for accurately measuring 6-MP adherence. The addition of electronic monitoring to assess 6-MP adherence would have strengthened the study design. Taken in aggregate, existing literature on 6-MP adherence in pediatric ALL and findings from this study provide strong evidence for the importance of combining self-report and 6-MP metabolite evaluation with more objective measures of 6-MP intake (e.g., electronic monitoring). Moreover, because of the increased risk of relapse associated with poor 6-MP adherence (Bhatia et al., 2012), retrospectively identifying patients who have failed to take 6-MP as prescribed is not adequate for decreasing morbidity and mortality. Consequently, Bhatia and colleagues (2016) have highlighted the need for developing alternative options to identify patients at-risk of 6-MP non-adherence. To this end, researchers in this field have begun to investigate methods,

mostly data analytic models, for identifying patients at-risk for treatment failure secondary to poor 6-MP adherence. Exploratory findings from the current dissertation study highlight the potential for screening patients at-risk for 6-MP non-adherence by assessing medication adherence barriers and 6-MP knowledge.

EXPLORATORY POST-HOC FINDINGS ABOUT ADHERENCE BARRIERS

PMBS Factor Structure

Because there were no psychometric data supporting PMBS use to specifically assess 6-MP adherence barriers in a pediatric ALL population, we conducted a PCA to better characterize the scale. The PCA resulted in a two-factor PMBS scale structure: (1) Disease Frustration Issues, and (2) Regimen Adaptation Issues. The two PMBS subscales, *Regimen Adaptation* and *Disease Frustration*, are fairly consistent with the original measure's four-factor structure (Simons and Blount, 2007). Similarly to this study, Simons and Blount (2007) found most items loaded onto the Disease Frustration and Regimen Adaptation subscales. The two remaining subscales, Ingestion Issues and Parent Reminder, only contained three items and one item, respectively. In my study sample, the three items from the original Ingestion Issues subscale loaded onto either the Disease Frustration or Regimen Adaptation subscale. The single item on the original Parent Reminder subscale did not load onto either the Disease Frustration or Regimen Adaptation subscale and was thus was removed from the scale. Because the two-factor PMBS structure obtained in this study closely resembles the two primary subscales of the original measure, I decided to retain the original names of these two subscales (i.e., Disease Frustration Issues, Regimen Adaptation Issues).

Pre- to Post-Intervention PMBS Scores Change

Caregivers who received MI reported fewer 6-MP adherence barriers, as measured by total PMBS score, following the MI intervention compared to caregivers in the education control group. Further, MI appeared to primarily impact caregivers' perceived regimen adaptation barriers (e.g., "My child finds it hard to stick to a fixed medication schedule) rather than disease frustration issues (e.g., "My child is tired of living with a medical condition"). On face value, regimen adaptation issues appear to be more behavioral in nature compared to the more emotion-focused issues encompassed in the Disease Frustration Issues subscale. Because MI is a goal-oriented psychotherapeutic intervention designed to enhance motivation for and commitment to a target behavior change (Miller & Rollnick, 2013), it seems fitting that MI would initially target more behavioral barriers as those in the Regimen Adaptation Issues. This is not to say MI cannot enhance motivation and commitment to overcome deeper internalized barriers such as disease frustration; however, the single-dose, brief nature of MI sessions delivered in this study might not affect immediate changes in internalized disease-related frustration.

Moreover, because 28% of study patients were aged 12 years or older, developmental factors unique to adolescence may impact our ability to accurately assess change in perceived barriers when using caregiver self-report, rather than adolescent self-report. This is particularly true for the PMBS, as items are worded so caregivers are mostly reporting on perceived barriers for their child, not for themselves (e.g., My child is tired of living with a medical condition). Specifically, disease frustration issues appear to involve patients' internalized emotions, as well as forward and retrospective cognitions about their illness and treatment. It is unknown if caregiver-perceived disease frustration barriers accurately reflect the internalized processes experienced by adolescent patients. Literature suggests caregiver and adolescent report of

emotional and/or internalizing problems often do not correlate, whereas adolescents and their caregivers seem to agree more on ratings of externalized problems (De Los Reyes, 2011, 2013; Achenbach, 2006). It is possible caregivers can more accurately report change in regimen adaptation barriers, as these are more externalized issues (e.g., difficulty sticking to a fixed medication schedule and/or swallowing pills), compared to more internalized disease frustration issues (e.g., being tired of living with a medical condition, disliking medication impact on appearance). Consequently, it is possible that MI efficacy for decreasing Disease Frustration Issues subscale scores was limited by caregivers' ability to accurately report changes in their patients' internalized experiences (e.g., perception of medication impact on appearance). Unfortunately, this study's small adolescent sample size precluded analysis of adolescent perceived barriers using AMBS data. Consequently, future studies should investigate AMBS factor structure and potential changes in AMBS total and subscale scores following MI.

In addition to evaluating the intervention effect on pre- to post-intervention PMBS score change, I explored main and moderation effects of caregiver language and patient age group (i.e., ≥12 years of age, <12 years of age). I included caregiver language in the interaction term because of my specific interest in the linguistic and cultural MI adaptation. Statistical and empirical reasons informed my decision to also include patient age group in the interaction term. Originally, I planned to include patient age group as a covariate; however, when ensuring data met ANCOVA statistical assumptions, I found patient age group violated the assumption of homogeneity of regression slopes. The assumption of homogeneity of regression slopes concerns the relationship between the covariate and the dependent variable and ensures there is no interaction between the covariate and the intervention. If data violates this assumption, as in the case of patient age group data, it suggests there might be interaction between the covariate and

the intervention. Consequently, I included patient age group as an interaction term rather than a covariate. Empirical reasons also supported the inclusion of patient age group as an interaction term. Mainly, adolescent patients aged ≥12 years were also eligible to receive the intervention themselves. Therefore, there were patient-caregiver dyads that arguably received higher intervention doses, compared to the caregivers who participated in the study without an adolescent patient.

Although the interaction 'intervention group x patient age group x caregiver language' was not statistically significant, the moderation term had a large effect size. The statistically nonsignificant trend was for MI to be most efficacious for Spanish-speaking caregivers of adolescent patients (i.e., aged ≥12 years; see Figures 3, 4, and 5). Specifically, for Spanish-speaking caregivers only, caregivers of adolescent patients (i.e., aged ≥12 years) benefited more strongly from MI than caregivers of younger patients (i.e., aged <12 years). For English-speaking caregivers, MI appeared beneficial regardless of patient age. These trends are consistent with previous research indicating observed MI effect sizes were larger with caregivers of patients over the age of 12 years and ethnic minority populations (Hettema, Steele, & Miller, 2004). Although not statistically significant, the moderation term's large effect size emphasizes group differences without confounding them with sample size. Specifically, the large effect size suggests caregivers benefited differently from the intervention, based on their primary language and patient age group. Post-hoc power analyses confirmed we were underpowered to detect a statistically significant difference. Consequently, attempting to replicate these findings with a larger sample size is a worthy research pursuit.

Lessons Learned from Exploratory Post-Hoc Analyses

The PMBS and AMBS are brief and psychometrically promising scales assessing caregiver- and adolescent patient-perceived adherence barriers for pediatric ALL patients during maintenance therapy. These scales may serve as brief screening tools to determine the most prominent medication adherence barriers for pediatric ALL patients and their caregivers. Further research is needed to better understand the relationship between perceived medication barriers and 6-MP adherence.

STUDY LIMITATIONS

Study Design Limitations

As previously discussed, the primary methodological limitation of this study was the lack of an objective 6-MP adherence measure, such as electronic monitoring, to supplement self-report. This study used multimodal adherence assessment by evaluating both caregiver self-report and TGN blood serum levels to measure adherence. However, these two methods may not provide a sensitive, accurate reflection of patients' true 6-MP adherence. Therefore, these measures likely prevented us from finding changes in 6-MP adherence. Additionally, several other limitations should be considered when interpreting MI efficacy findings and developing future research. First, there was likely a ceiling effect for assessing MI efficacy because the overwhelming majority of the sample reported high baseline adherence. One way to mitigate this limitation in a future RCT would be to utilize more objective measures of adherence (e.g., MEMS Cap), which would presumably identify approximately 20% of patients who are not strongly 6-MP adherent (Bhatia et al., 2014; Hunger & Mullighan, 2015).

Although this study had a repeated-measures design, it consisted of a single follow-up assessment (i.e., post-intervention). Patients were followed for a relatively short period of time ($M(SD)$ = 3.93(1.42) months) compared to the lengthy duration (i.e., two to three years) of

maintenance chemotherapy. Therefore, tracking adherence for a longer time period would improve future study designs. Additional follow-up assessments would allow documentation of longitudinal patterns of adherence after MI delivery. Similarly, future studies may evaluate the relative contributions of a single MI session versus repeated MI sessions over time.

Eligibility criteria allowed any patient receiving maintenance chemotherapy to participate in the study, without restricting eligibility to a specific period in maintenance therapy (e.g., early maintenance). Because some patients began the study late in their maintenance treatment, they completed ALL treatment prior to progressing through all study phases. Thus, these patients had to end their study participation contributing to the 7.77% study attrition rate. Moreover, it is possible non-adherent patients who might have benefited the most from participating in this study might have relapsed early in maintenance, which could perhaps be avoided by delivering MI early in maintenance therapy. Similarly, some patients might develop a pattern of non-adherence during maintenance. Strongly reinforced behavior patterns may be difficult to modify with MI, further supporting potential benefits of delivering MI early in maintenance therapy.

Next, our data collection was limited and/or incomplete in a number of instances. First, we were limited by the TGN data collected by providers in clinic, which was not available for all patients participating in the study. Specifically, we did not acquire IRB approval to collect TGN levels for patients who did not have a TGN order from their physician for clinical purposes. Consequently, we have missing TGN data for patients who did not already have TGN levels recorded in the medical chart as part of standard care. Relatedly, we did not have IRB approval to collect MMPN levels from medical chart reviews with enough time for those data to be included in this dissertation study.

Additionally, in retrospect, there were variables that might have added clarity to our findings. For example, it is unknown if unassessed cultural values (e.g., respect for authority figures, such as medical providers, acculturation) may have contributed to high rates intervention participation and acceptability rates. Assessing culture- and acculturation-related constructs assessment may help clarify if such values impact participation in and/or acceptaility of the MI intervention. Future RCTs can establish procedures to collect additional data, which would allow for a larger sample size, increasing statistical power to control for additional covariates.

Study Sample Limitations

For certain statistical analyses, our sample sizes, particularly of adolescent patients and Spanish-speaking caregivers, were not adequate for achieving statistical power. A priori power analysis indicated need for 111 caregivers ($N_{MI} = 74$, $N_{Education} = 37$); however, the final analytic sample was 103 caregivers ($N_{MI} = 66$, $N_{Education} = 37$). Post-hoc power analyses further confirmed we were statistically underpowered to detect intervention group main effect in primary ANCOVA models. Although we initially randomized 128 participants for the study, we had 7.77% study attrition rate secondary to multiple factors (e.g., relapse, therapy termination; see Figure 2 for CONSORT diagram). Thus, the study was limited by lack of adequate statistical power for efficacy analysis. For example, because of small adolescent and Spanish-speaking sample sizes, we did not have adequate statistical power to conduct adolescent analyses and/or include covariates (e.g., socioeconomic status, caregiver education level, perceived medication adherence barriers) in primary analyses. It is worth noting, the small samples of adolescent patients and Spanish-speaking caregivers were not due to lack of participation rates from eligible patients, but rather represented clinic demographics. Nonetheless, this limitation can be resolved in a future RCT by extending study timeline to enroll more participants.

Another potential limitation is that the unique study setting (i.e., pediatric oncology clinic in academic medical setting) may limit generazability of our findings. For example, in pediatric academic medical settings, families are accustomed to participating in research protocols/studies. Thus, caregivers' increased comfort level with research might have increased families' willingness to participate in our study. Moreover, families know the treatment team well; therefore, they might have been more likely to agree to research studies conducted in this setting. However, most pediatric oncology clinics in diverse academic medical settings likely share these similarities with our research setting.

Psychometric Limitations

Some of our study measures (i.e., AARP, 6-MPAQ, PMBS, AMBS) posed psychometric limitations in our study. First, poor AARP reliability for Hispanic, English-speaking caregivers and our small sample size of Hispanic, Spanish-speaking caregivers rendered MI acceptability analyses exploratory for these groups. Additional psychometric limitations include lack of previous validation studies for the 6-MP Adherence Questionnaire, developed for this study. Similarly, the PMBS and AMBS were originally validated with English-speaking pediatric solid organ transplant patients and their caregivers and these measures lack previous validity data for English- and Spanish-speaking pediatric ALL patients. Thus, psychometric validation of the PMBS and AMBS will be an important step to complete prior to the larger future RCT. Nonetheless, we chose to use these measures because they contain face-valid items for assessing medication adherence barriers in a variety of chronically ill pediatric populations, including ALL patients. Relatedly, as a native Spanish speaker, I translated and back-translated measures from English to Spanish and vice versa. However, the gold standard is for two different individuals to perform the translation and back-translation procedures.

Lastly, in relation to the factor analytic procedures with PMBS data, this study sample size is in the smaller end of acceptability for conducting a PCA (Osborne & Costello, 2004). Therefore, PCA findings are exploratory. Again, this limitation can be reasonably addressed in a future, larger RCT. It is worth noting, the PMBS factor structure may differ slightly if evaluated in a larger pediatric ALL sample.

Intervention Limitations

Limitations regarding MI training, delivery, and evaluation may also limit generalizability of our findings. Although MI itself is not a resource-intensive intervention, it requires a significant up-front investment in training. The ability of our interventionists to deliver MI with high fidelity, as a stand-alone intervention, resulted from rigorous, resource-intensive training. Interventionists received ≥20 hours of advanced MI training from an expert-level trained MI instructor and practitioner. Training for this study consisted of didactic instruction, guided MI observation, micro-skills practice with live feedback, as well as recorded mock-MI sessions with MITI 4.2.1 coding sheet review. Such rigorous MI training and intervention fidelity might be difficult to replicate in other institutions if the appropriate resources (e.g., expert-level trained MI instructor) are not readily available.

With regard to MI delivery, a minority of sessions lasted for approximately 15 minutes, with a few sessions interrupted even before then as a result of need to accommodate patient care. We expected MI sessions to be brief, with the goal of not disrupting ambulatory care. However, our goal was to deliver MI for at least 15 minutes because there is limited evidence for MI effectiveness when delivered in increments shorter than 15 minutes. Small (<15 minutes), single doses of MI may have limited intervention effectiveness. Therefore, future RCTs should develop procedures to find a balance between the need to deliver a strong-enough dose of MI and the

need to accommodate the intervention into a busy and fast-paced ambulatory clinic schedule.

Additionally, intervention fidelity ratings were limited by the lack of multiple trained MITI 4.2.1 coders at the study's institution. Although we had two bilingual trained coders in addition to the MI trainer in this study, coders were unable to double-code MI sessions because of time constraints. Double-coding sessions would have allowed for inter-rater reliability ratings of intervention fidelity statistics. However, this limitation can easily be addressed in the future. Lastly, our thematic analysis of MI session content was limited by the lack of rigorous qualitative methodology. Relatedly, the CAMI manipulation check would benefit from refinement and validation to enhance evaluation of (a) social contextual stressors related to minority status and (b) culture-specific values. Future studies should follow a sound methodological framework supporting qualitative data collection and analyses.

STUDY STRENGTHS

Despite methodological limitations and opportunities for future research, this study has numerous strengths supporting its contributions to the literature. First, to the best of our knowledge, the current study is the first to evaluate the feasibility of delivering and the acceptability of brief, English- and Spanish-MI delivered to caregivers of pediatric ALL patients during routine maintenance-phase ambulatory care. This study's primary contribution was establishing the feasibility of universally delivered, brief MI in an outpatient pediatric oncology setting, as well as demonstrating high intervention acceptability ratings, even among ethnically diverse, non-English-speaking caregivers. An important strength of this feasibility, acceptability, and preliminary efficacy trial was its design, which included participant randomization and an education control group.

Moreover, this is the first study to use the CAMI framework to inform MI delivery with English- and Spanish-speaking caregivers of pediatric patients. The inclusion of ethnically and linguistically diverse participants makes the study sample representative of the patient population seeking treatment at our specific pediatric oncology clinic. Although the current study focused on ethnicity (i.e., Hispanic, Non-Hispanic) and language (i.e., English, Spanish) as parameters for establishing caregiver cultural groups within the study sample, there are other cultural diversity variables (e.g., SES, rural vs. urban) that are likely important to consider when promoting medication adherence. Fortunately, utilizing the CAMI framework appears to be a promising and effective way to ensure MI is tailored to the specific needs of culturally diverse patients. Furthermore, because MI interventionists followed the CAMI-informed approach with all participants, sessions had the potential to address other diversity parameters (for example, those related to low-SES) during sessions.

An important goal of MI interventionists in this study was delivering MI with high fidelity. Thus, a key study strength is that culturally informed brief MI upheld treatment fidelity and retained the core mechanisms of action (i.e., increasing patient change talk, softening patient sustain talk) and spirits (i.e., collaboration, acceptance, compassion, and evocation) of MI. These findings have the potential to inform future studies evaluating MI with culturally diverse populations, such as Hispanic, Spanish-speaking patients and/or caregivers. Particularly, the training and intervention fidelity assessment model we followed seems appropriate for bilingual MI interventionists.

Importantly, current mental health services, particularly in the hospital setting, tend to depend on scarce psychology providers (cite). MI sessions in this study were conducted by interventionists with diverse clinical backgrounds (i.e., one Clinical Psychology doctoral student,

two Master's-level research assistants, and one medical resident), which could improve patients' access to needed mental health intervention in future clinical and research applications. Consistent with previous studies (e.g., Victor et al., 2018), MI delivery by diverse interventionists suggests a variety of pediatric providers can be trained on and deliver MI with pediatric ALL patients. Training a variety of pediatric providers to deliver MI can increase access to services during routine medical appointments for patients and their caregivers.

Additional study strengths include its repeated-measures design. We were able to recruit, intervene with, and follow-up participants in clinic throughout multiple clinic visits. The ability to implement this repeated-measures design speaks to the feasibility of assessing and/or intervening with patients and caregivers at multiple time-points throughout treatment, allowing longitudinal follow-up of 6-MP adherence patterns. Additionally, the 6-MP Adherence Questionnaire developed for the purpose of this study may be a helpful tool to evaluate 6-MP-related knowledge (e.g., purpose, dose, administration schedule) among caregivers of ALL patients during maintenance chemotherapy.

Finally, an important strength of this study is the clinical relevance of its findings. For example, data gathered as part of this study elucidated variability in caregivers' 6-MP knowledge and understanding of medication dosing schedules. These findings highlight opportunities for education initiatives with pediatric ALL patients and caregivers. MI delivery feasibility during routine medical appointments suggests providers may be able to also deliver brief education initiatives targeting 6-MP knowledge to supplement adherence-enhancing interventions, such as MI. Consequently, findings from this study highlight an opportunity for quality improvement in outpatient oncology clinics.

RECOMMENDATIONS FOR FUTURE RESEARCH

Lessons learned from the current study highlight multiple opportunities to continue advancing MI research with culturally diverse, pediatric ALL patients and their caregivers. Future research recommendations are below:

Study Design Recommendations for Future RCT

An RCT, with an adequate sample size to achieve acceptable statistical power, is required for determining MI efficacy in improving oral chemotherapy adherence. It will be important for this RCT to investigate MI's impact on longitudinal 6-MP adherence patterns using electronic monitoring (e.g., MEMS SmartCap), which is considered the gold standard for measuring medication adherence. Additionally, the MEMS SmartCap should be supplemented with additional adherence measures (e.g., parent, patient, and/or provider self-report; TGN and MMPN metabolite profiles), in line with recommendations to use multiple measures of 6-MP adherence (Rohan et al., 2016; Hoppmann et al., 2017; Landier et al., 2017; Traore et al., 2006). With regard to TGN and MMPN data, metabolite concentration means do not represent the best parameter to use, rather analyses should measure change in metabolite profile (i.e., from the low TGN–low MMPN profile to either high the TGN–low MMPN or the low TGN–high MMPN profiles).

Additionally, measurement of red cell 6-MP metabolite levels (i.e., TGN, MMPN) should attempt to control for a variety of factors that can affect how the body metabolizes 6-MP (e.g., TPMT activity, allopurinol treatment; Relling et al., 2011) and thus may impact patients' membership in metabolite profile groups (i.e., Rohan et al., 2016; Traore et al., 2006). Using multiple methods of measuring adherence would not only improve research endeavors, but could inform clinical care and identification of patients in need of targeted adherence interventions.

As part of the larger, grant-funded study that served as a parent study for this dissertation, we collected data on caregivers' and patients' 6-MP knowledge and perceived medication adherence barriers. Self-reported medication adherence barriers and 6-MP knowledge may be valuable data for clarifying factors that may impact 6-MP adherence. Thus, future studies should evaluate the validity and clinical significance of using these variables (i.e., self-reported medication adherence barriers and 6-MP knowledge) to identify patients at-risk of poor 6-MP adherence. Screening at-risk patients can shed light on those who might benefit from targeted interventions. Additionally, information about perceived medication adherence barriers and/or 6-MP knowledge can serve as complementary data to inform MI sessions, potentially increasing their efficacy.

Important methodological recommendations include psychometric validation of the PMBS and AMBS with English- and Spanish-speaking pediatric ALL patients and their caregivers. This will be will be a crucial step to complete prior to the larger future RCT. Similarly, MA6-MP refinement and validation will be important for improving 6-MP knowledge and adherence assessment. Moreover, all measures should be translated and back-translated by two different individuals.

Other future study recommendations include evaluating whether intervening during a specific time point in ALL treatment (e.g., induction, consolidation, early maintenance) has an effect on MI efficacy to improve adherence patterns. Additionally, future studies may consider including patients who have relapsed during maintenance phase chemotherapy. Presumably, 6-MP non-adherence may represent one of many factors contributing to relapse among some of these patients. In those cases, these patients would likely benefit from targeted adherence promotion interventions. It will be important for future studies to not only determine the optimal

time point to intervene, but also the most effective dose of MI (e.g., one 60-minute session vs. multiple, brief 15-minute sessions) for different patients (e.g., patients in induction vs. patients who have relapsed). Furthermore, future studies can expand MI session focus beyond promoting 6-MP adherence to enhancing adherence to other medications routinely prescribed throughout ALL treatment (e.g., steroids). Because of the lengthy nature of maintenance chemotherapy, future studies should track adherence patterns for a longer time period, beyond the two time points included in this study.

Recommendations for Expanding MI Targets in Pediatric ALL

Future studies should examine the relationship between perceived medication barriers and 6-MP adherence behavior with the goal of elucidating barriers that can be targeted with MI. Moreover, exploring how barriers might differ among cultural groups will be important to better target these barriers with culturally-informed MI. This recommendation stems from our findings suggesting caregivers from different cultural groups may perceive different factors (i.e., numbers of pills prescribed, forgetting to take the medication, sticking to a fixed medication schedule) as barriers to supporting their child's 6-MP adherence. Additionally, future research should evaluate MI targeting behavior change to overcome specific medication adherence barriers. Targeted MI sessions may explore and intervene on barriers (e.g., social contextual stressors related to minority status) specifically endorsed by different cultural groups, if also relevant for the individual patient and/or caregiver. Future research should also investigate whether targeting specific barriers to adherence (e.g., "My child is tired of taking medicine") may help reduce risk of non-adherence among ALL patients. In addition to further evaluating 6-MP adherence barriers, future studies should evaluate the impact of 6-MP knowledge on adherence. Findings from this study suggest that roughly a fifth of caregivers lack accurate 6-MP knowledge (i.e., no

knowledge reported on MA6-MP questionnaire); however, it is unknown how 6-MP knowledge may impact caregiver medication administration and/or adherence among patients.

Qualitative Analyses Recommendations

Furthermore, future studies should consider using qualitative and/or mixed methods study design to evaluate MI session content. Although the current study coded CAMI-informed themes for at least 30% of sessions, rigorous qualitative analyses of these themes were outside the scope of this study. Nonetheless, it is worth noting that, anecdotally, MI sessions with Spanish-speaking, Hispanic caregivers highlighted numerous experiences (e.g., perceived discrimination in the medical setting, language barriers, intergenerational cultural differences) that may pose unique adherence challenges for pediatric oncology patients. Qualitative findings have the potential to inform future cultural adaptations of MI while retaining the core mechanisms of action (e.g., increasing patient change talk, softening patient sustain talk) and spirits (i.e., collaboration, acceptance, compassion, evocation) of MI.

In addition to future qualitative analyses of MI content, future studies should add to this study's MI acceptability findings by qualitatively evaluating caregivers' perceptions of MI. For example, future studies might consider adding open-ended, follow-up questions to the AARP or conduct qualitative study exit interviews with researchers. Capitalizing on qualitative and/or mixed methods approaches may enhance our understanding of caregivers' MI acceptability perceptions.

Cultural Considerations for Future Studies

Future studies may also explore whether discussion of cultural considerations during MI sessions significantly impacts efficacy in improving oral chemotherapy adherence. Additionally, previous studies with children and their caregivers suggest MI seems to be most effective when

the cultural background of the practitioner matches the family (Gayes & Steele, 2014). Hence, ethnic-match between patient and MI interventionist may impact MI efficacy. Future studies should investigate the role of ethnic and cultural background match in MI effectiveness in the context of pediatric ALL treatment. Moreover, although this study included interventionist-participant ethnic matching for Hispanic, Spanish-speaking caregivers, the future RCT should expand ethnic matching to Hispanic participants even when they chose to receive MI in English.

Future studies should continue to prioritize inclusion of diverse samples and expand beyond English- and Spanish-speaking participants to evaluate MI in other languages. When conducting research with diverse samples, it will be crucial to consider appropriate study measures to best support data collection. For example, future studies might consider offering measures in both English and Spanish, as many Hispanic caregivers in our sample were bilingual and likely had different language proficiency skills in reading versus speaking. Although this study had measures available in both languages, we presented caregivers with either an English or Spanish questionnaire packet after they had stated their preferred language. This approach may have been problematic for caregivers with varying proficiency in reading and spoken language skills, which might explain poor AARP reliability in Hispanic, English-speaking caregivers.

Researchers should also consider including additional diversity variables, such as socioeconomic status (SES). Extensive evidence indicates ethnic differences in morbidity and mortality across various chronic health issues are tied to socioeconomic factors (e.g., limited education access, scarce monetary resources, lack of medical insurance; Crimmins, Hayward, & Seeman, 2004; Hayward et al., 2000). The disadvantaged socioeconomic status commons to

ethnic minorities contributes to medication adherence barriers such as low health literacy and lack of adherence-promoting resources (e.g., pill boxes).

In addition to assessing MI efficacy with ethnically and socioeconomically diverse samples, future studies might consider evaluating diverse methods of MI delivery. For example, using telehealth technology and/or phone calls may increase access to services. Additionally, research suggests non-mental health pediatric providers (e.g., physicians, nurses) can effectively acquire MI knowledge and skills with adequate training (Victor et al., 2018). Our study utilized diverse MI interventionists, including one doctoral clinical psychology student, one medical resident, and two Master's level clinicians. Future research should aim to replicate this approach, and potentially expand training to other pediatric providers (e.g., nurses, child life specialists, physicians). Employing diverse MI interventionists would allow evaluating MI efficacy to improve 6-MP adherence when delivered by a variety of pediatric providers. Future studies should also attempt to replicate MI feasibility and acceptability findings with caregivers of children with a variety of chronic health conditions, adding to the broader pediatric health literature. Finally, this study compared MI to an education control so researchers should expand the literature by comparing MI to other interventions (e.g., cognitive-behavioral therapy, acceptance and commitment therapy, problem-solving therapy) in the context of pediatric chronic health.

IMPLICATIONS FOR CLINICAL PRACTICE

By demonstrating MI feasibility during routine ambulatory care, study findings support implementing universal adherence intervention for pediatric ALL patients in maintenance therapy. Moreover, because adequate 6-MP adherence during maintenance ALL therapy is crucial for sustaining durable remission, the cost of not intervening with non-adherent patients is

high. Therefore, there is a need to develop an integrated, tiered system of universal non-adherence prevention services and targeted adherence interventions. Fortunately, MI lends itself well for this sort of intervention delivery approach.

Broadly, clinical interventions, such as those to improve medication adherence, can be classified as (1) universal, (2) targeted, or (3) indicated treatment, based on their aim and target patient population (Moore, 2008). Each service level differs in their aim and target population: (1) universal interventions focus on the whole patient population to prevent the development of a specific problem (e.g., non-adherence); (2) targeted interventions for at-risk patients can reduce problem incidence (e.g., non-adherence); and (3) treatment services target individuals with an established problem (e.g., non-adherence) to minimize the condition's negative impact. Although there is empirical evidence supporting the efficacy of each distinct level of service (i.e., universal, targeted, and treatment), each individual approach has its unique strengths and weaknesses (for a review of each service approach refer to Moore, 2008).

Our current healthcare system prioritizes treatment-oriented interventions (Prilleltensky & Nelson, 2000; Moore, 2008). Therefore, services are unable to respond to patients' emerging needs and problems, missing opportunities to reduce the number of children and families needing intensive interventions (Tolan & Dodge, 2005). Moreover, these distinct levels of intervention (i.e., universal, targeted, or treatment) can lead to inequities in patterns of service use, as many patients are unable to access the treatment-oriented interventions prioritized by the system (Sayal 2006). By the time a problem (e.g., non-adherence) is so serious that it warrants a treatment intervention, it becomes more difficult and costly to remediate. Thus, Moore (2008) proposes strengthening universal services by developing an efficient tiered system of universal and targeted services that would decrease over-reliance on targeted and/or treatment services.

MI is an evidence-based, inexpensive, not resource-intensive intervention that can be flexibly delivered within the universal prevention approach proposed by Moore (2008). Our current feasibility findings support MI delivery as a universal strategy to promote 6-MP adherence among pediatric ALL patients and their caregivers. Universally delivering MI can help reduce inequities in patterns of service use commonly seen when there is over-reliance on a single level of service (e.g., targeted intervention). In the context of pediatric ALL treatment, the need to invest in universal non-adherence prevention interventions is supported by three important factors: (1) high rates of 6-MP adherence, (2) challenges identifying non-adherent patients, and (3) costly consequences of non-adherence that result in increased morbidity and mortality. From a practical standpoint, to support this universal prevention approach, there needs to be an integrated tiered system of universal, targeted, and treatment services (Moore, 2008). MI lends itself well to this service delivery approach as there's evidence supporting MI efficacy when delivered in a variety of doses, from a single 15-minute session to multiple sessions varying in length (e.g., ranging from 15- to 60-minutes).

Moreover, the ability of universal services to address needs of the entire population of ALL patients will depend on two important factors: (1) training appropriate providers (e.g., nurses), and (2) integrating inclusive practices and strategies (Moore, 2008). Utilizing MI can address these two factors. First, to address the training needs of primary care providers, research suggests healthcare professionals with diverse expertise can gain valuable MI knowledge, confidence and desire to use MI through adequate training (Victor et al., 2018). Similarly, because MI follows a patient-centered approach, it addresses the need to use inclusive practices and strategies. Inclusive practices and strategies are crucial for engaging and retaining the most vulnerable families such as ethnically diverse, non-English-speaking families. Particularly, the

spirits of MI (i.e., collaboration, acceptance, compassion, evocation) inherently promote these practices. Moreover, CAMI-informed sessions can further address the specific need culturally diverse patients.

CONCLUSIONS

In conclusion, study findings provide strong feasibility and acceptability evidence for brief, culturally-informed MI to support 6-MP adherence in pediatric ALL patients receiving maintenance chemotherapy. This dissertation study meaningfully contributes to the literature on the use of MI with pediatric health populations, as well as the literature on adherence in pediatric oncology. Study findings have the potential to inform future research on MI efficacy to improve oral chemotherapy adherence. This is a worthwhile research endeavor because interventions that enhance 6-MP adherence during ALL maintenance treatment have the potential to save lives.

TABLES

Table 1.
Sample demographic and frequency statistics.

	Sample	Cultural Groups			Intervention Groups	
		NHES *N*=63	HES *N*=30	HSS *N*=28	MI *N*=66	Education *N*=37
Caregivers						
Age						
M(*SD*)	36.66(8.02)	37.35(7.68)	34.30(8.89)	37.33(7.73)	36.47(7.81)	37.02(8.60)
Range	21-60	21-60	23-58	21-52	21-60	22-58
Type (%)						
Mother	80.7	78.7	80.0	85.2	81.8	78.6
Father	15.1	16.4	13.3	14.8	14.3	16.7
Grandparent	4.2	4.9	6.7	–	3.9	4.8
Race (%)						
White	83.4	68.3	100	100	82.3	85.7
Black/African American	11.6	22.2	–	–	13.9	7.1
Asian	5.0	9.5	–	–	3.8	7.1
Ethnicity (%)						
Non-Hispanic	52.9	100	–	–	53.2	52.4
Hispanic	47.1	–	100	100	46.8	47.6
Language (%)						
English	76.9	100	100	–	79.7	71.4
Spanish	23.1	–	–	100	20.3	28.6
Education (%)						
No high school diploma	17.4	4.8	13.3	48.1	15.2	21.4
High school graduate	33.1	23.8	53.3	33.3	34.2	31.0
Associate or some college	19.0	20.6	20.0	14.8	22.8	11.9
Bachelor's degree	24.0	38.1	13.3	3.7	19.0	33.3
Graduate degree	6.6	12.7	–	–	8.9	2.5
Employment (%)						
Part- or full-time job	45.2	54.2	42.9	29.6	44.7	46.2
Full-time caregiver	54.8	45.8	57.1	70.4	55.3	53.8
Relationship Status (%)						
Partner/Spouse	74.2	84.1	46.7	80.8	73.4	75.6
Single	25.8	15.9	53.3	19.2	26.6	24.4

Table 1. *(continued)*

	Sample	Cultural Groups			Intervention Groups	
		NHES	HES	HSS	MI	Education
Adults in the home						
M(*SD*)	2.01(.70)	1.94(.44)	1.90(.80)	2.30(.99)	1.97(.68)	2.07(.75)
Range	1-5	1-3	1-4	1-5	1-5	1-4
Children in the home						
M(*SD*)	2.55(1.17)	2.52(1.10)	2.12(.97)	3.13(1.36)	2.58(1.12)	2.51(1.28)
Range	1-7	1-7	1-4	1-6	1-7	1-6
Household Income[a] (%)						
20th percentile	28.3	12.7	42.9	52.4	27.8	29.3
40th percentile	22.1	19.0	21.4	33.3	19.4	26.8
Median	4.4	4.8	3.6	4.8	4.2	4.9
60th percentile	6.2	6.3	7.1	4.8	8.3	2.4
80th percentile	38.9	57.1	25.0	4.8	40.3	36.6
Mental Health Services (%)						
No past history	67.9	62.1	67.9	80.0	70.7	62.2
Positive past experience	29.5	34.5	28.6	20.0	26.7	35.1
Negative past experience	2.7	3.4	3.6	–	2.7	2.7
Patients[b]						
Age (years)						
M(*SD*)	7.55(4.80)	7.55(4.92)	6.33(4.04)	8.67(5.07)	7.57(4.86)	7.52(4.74)
Range	.9-24	.9-24	2-16	2-18	.9-24	2-17
Sex (%)						
Female	33.9	38.1	30.0	29.6	41.8	19.0
Male	66.1	61.9	70.0	70.4	58.2	81.0
ALL Risk Category (%)						
Standard Risk	50.9	51.7	63.3	37.0	54.1	45.2
High/Very High Risk	49.1	48.3	36.7	63.0	45.9	54.8
Insurance (%)						
Medicaid	54.2	39.7	50.0	92.3	54.4	53.7
Private	45.8	60.3	50.0	7.7	45.6	46.3

Note. NHES = Non-Hispanic, English-speaking; HES = Hispanic, English-speaking; HSS = Hispanic, Spanish-speaking; MI = Motivational Interviewing. Patients represent full patient sample referenced in caregiver analyses.

[a]Household income percentiles calculated statistics for the Dallas-Fort Worth area (U.S. Census Bureau, 2016).

Table 2.
Administration of self-report measures.

Study Time Point	
Pre-intervention baseline	Demographics Questionnaire Mental Health Experiences Questionnaire Medication Adherence to 6-Mercaptopurine Parent and Adolescent Medication Barriers Scale[a]
Intervention	Abbreviated Acceptability Rating Profile[b]
Post-intervention follow-up	Medication Adherence to 6-Mercaptopurine Parent and Adolescent Medication Barriers Scale[a]

[a]Simons & Blount (2007)
[b]Tarnowski & Simonian (1992)

Table 3.

Correlations among demographic variables and measure indices for the Motivational Interviewing and education control groups.

Variable	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19
1. Caregiver type†	–	.50¶	.04	.13	.38	-.53¶	-.26	.39	.14	.07	.15	.30	-.17	.08	-.11	.25	.04	.36*	-.34*
2. Caregiver age	.15	–	.06	.20	-.06	-.30	-.23	.20	**.67**	.02	.37*	.13	-.27	-.16	.24	.16	.20	.51¶	-.11
3. Caregiver ethnicity†	.03	.14	–	**-.56**	.35	-.08	-.27	.55*	-.06	.27	.10	.18	-.22	-.47*	-.11	-.20	-.21	-.16	.31
4. Caregiver language†	-.13	-.03	**-.54**	–	.59¶	.17	-.22	.56*	.32*	-.10	.26	-.34*	-.02	.17	.20	.36	.18	.10	-.14
5. Caregiver education‡	.21	.35¶	**.64**	**.46**¶	–	-.05	-.07	**.63**	-.26	.00	-.05	**.53**	.21	.09	**-.65**	-.36	.05	.11	-.12
6. Caregiver employment†	-.40¶	.03	-.22	.21	-.24*	–	-.21	.26	-.19	-.34*	.04	-.31	.01	-.19	-.25	-.15	.13	-.21	.22
7. Caregiver relationship†	-.08	-.19	-.24*	-.02	-.38¶	-.12	–	.44	-.09	-.04	.27	-.09	.36*	.33	.32	-.12	-.01	.06	-.16
8. Household income‡	.28	.27*	.45¶	.43*	**.57**	.34	**.55**	–	-.19	-.02	.12	**.60**	-.14	-.15	-.55¶	-.34	-.20	-.10	.05
9. Patient age	-.04	.33¶	.06	.05	.03	-.03	.26*	-.08	–	.11	.15	-.12	-.01	-.01	.23	.16	.09	.49¶	.13
10. Patient sex†	-.04	-.14	-.23*	.11	-.11	.06	.10	-.19	.13	–	.32*	-.04	-.01	-.33	.28	.06	-.06	.09	.53*
11. ALL risk group‡	.00	.26*	.05	.11	.15	.06	-.23*	.26*	.14	.07	–	.28	-.01	-.08	.05	.00	-.05	-.05	-.29
12. Insurance†	.15	.09	.32¶	**-.41**	**.48**	-.28*	-.22	**.68**	-.13	-.18	.05	–	-.19	.08	-.52¶	-.37	-.07	.11	-.20
13. Baseline 6-MP missed§	.17	-.17	-.19	-.08	-.13	.16	-.09	-.13	-.07	.15	-.16	.00	–	.14	-.18	-.12	-.05	.04	.07
14. Follow-up 6-MP missed	-.15	.05	-.14	.14	-.03	.25	.12	-.32*	.09	.18	.11	-.31*	-.07	–	-.07	-.36	-.03	.13	-.13
15. Baseline TGN	-.11	.13	-.01	-.05	-.07	.10	-.04	-.02	.22	.10	-.17	-.18	-.06	-.07	–	.50	.33	.38	.15
16. Follow-up TGN	.06	.08	.19	-.24	.16	-.08	-.13	.05	.07	.06	-.13	-.14	-.02	.01	**.83**	–	.41	.37	.14
17. Baseline PMBS	-.06	.03	-.08	.23*	-.11	.17	.09	-.03	.28*	-.04	.12	-.15	.02	.12	.00	-.24	–	**.73**	-.15
18. Follow-up PMBS	.09	.12	-.01	.15	.03	.00	-.07	.07	.11	-.19	-.01	-.05	-.21	.02	.20	.11	**.59**	–	-.02
19. AARP	.11	.13	.13	-.28*	-.02	-.04	.16	-.05	.05	-.20	-.10	.12	.01	-.31*	.14	.07	.13	-.02	–

Note. Correlations for the education control group are in shaded area. * $p < .05$, ¶ $p < .01$, correlations $p < .001$ in bold. Pearson correlation coefficient (r) used for all continuous variables and associations between continuous and dichotomous variables. Spearman's Rho (ρ) non-parametric correlations used for ordinal level and ranked variables. Cramér's V (φ) non-parametric correlations calculated between ordinal and dichotomous variables. Phi (Φ) coefficient used for associations between two dichotomous variables. 6-MP = 6-Mercaptopurine; TGN = thioguanine nucleotides; PMBS = Parent Medication Barriers Scale (Simons & Blount, 2007); AARP = Abbreviated Acceptability Rating Profile (Tarnowski & Simonian, 1992).

†Indicates dichotomous variables.

‡Indicates ordinal level and ranked variables.

§Baseline and follow-up 6-MP non-adherence based on number of doses missed over the previous seven days.

Table 4.
Descriptive statistics and frequencies for outcome measures.

Scale	Sample	Cultural Groups			Intervention Groups	
		NHES *N*=63	HES *N*=30	HSS *N*=28	MI *N*=66	Education *N*=37
Baseline TGN[a]						
M	385.88	372.26	389.11	400.00	350.20	453.12
SD	207.26	211.57	218.25	180.41	215.29	175.96
Range	53-1203	53-1203	101-944	61-762	53-1203	210-944
Follow-up TGN[a]						
M	386.35	393.35	356.60	386.50	356.16	451.25
SD	244.67	230.24	249.04	313.63	226.62	274.44
Range	37-1172	106-1035	37-816	86-1172	86-1035	37-1172
Baseline caregiver-reported adherence[b]	93.34%	98.32%	84.60%	90.51%	95.72%	88.67%
Follow-up caregiver-reported adherence[b]	84.88%	95.45%	75.00%	72.22%	85.96%	82.76%
AARP[c]						
M(*SD*)	38.81(5.70)	39.78(5.28)	38.93(4.85)	36.17(6.93)	38.49(5.74)	39.37(5.67)
Median	38.89	39.20	39.40	35.83	38.91	38.86
Range	14-48	28-48	25-47	14-46	14-48	25-48
Baseline Total PMBS[d]						
M(*SD*)	4.21(2.88)	3.69(2.45)	4.30(2.91)	5.00(3.22)	3.90(2.56)	4.80(3.38)
Range	0-13	0-9	0-13	0-11	0-11	0-13
Non-adherence risk	84.0%	79.0%	93.3%	84.6%	82.1%	87.8%
Follow-up Total PMBS[d]						
M(*SD*)	4.13(2.69)	3.76(2.04)	4.25(3.42)	4.55(2.80)	3.74(2.52)	4.85(2.90)
Range	0-12	0-9	0-12	1-11	0-11	0-12
Non-adherence risk	85.1%	85.7%	75.0%	95.0%	80.3%	93.9%
Baseline PMBS Regimen Adaptation						
M(*SD*)	1.29(1.73)	1.00(1.37)	1.13(1.55)	1.88(2.08)	1.04(1.36)	1.76(2.21)
Range	0-8	0-5	0-6	0-7	0-6	0-8
Follow-up PMBS Regimen Adaptation						
M(*SD*)	1.15(1.57)	0.78(0.98)	1.21(1.61)	1.65(1.84)	0.95(1.27)	1.52(1.99)
Range	0-8	0-3	0-6	0-5	0-5	0-8
Baseline PMBS Disease Frustration						
M(*SD*)	2.09(1.57)	1.94(1.60)	2.20(1.49)	2.31(1.64)	2.06(1.66)	2.15(1.41)
Range	0-6	0-6	0-5	0-5	0-6	0-5

Table 4. *(continued)*

Scale	Sample	Cultural Groups			Intervention Groups	
		NHES	HES	HSS	MI	Education
Follow-up PMBS Disease Frustration						
M(*SD*)	2.20(1.63)	2.29(1.53)	2.13(1.90)	2.05(1.64)	2.07(1.67)	2.45(1.54)
Range	0-6	0-6	0-6	0-5	0-6	0-6

Note. Sample refers to study caregiver sample. NHES = Non-Hispanic, English-speaking; HES = Hispanic, English-speaking; HSS = Hispanic, Spanish-speaking; MI = Motivational Interviewing.

[a]TGN = thioguanine nucleotides; measured in pmol/8 $x10^8$ erythrocytes, interpretation: TGN erythrocyte values <343 pmol/$8x10^8$ suggest 6-MP concentrations <75^{th} percentile and may indicate 6-MP non-adherence (Traore et al., 2006).

[b]Adherence = missing zero 6-MP doses over the past seven days.

[c]AARP = Abbreviated Acceptability Rating Profile (Tarnowski & Simonian, 1992); interpretation: score ≥ 30 = acceptable intervention. AARP data by cultural groups include all caregivers, regardless of intervention group assignment. Therefore, scores differ from those reported in the Results section, which describe AARP data for the MI group only.

[d]PMBS = Parent Medication Barriers Scale (Simons & Blount, 2007); total PMBS score includes both Regimen Adaptation and Disease Frustration subscale scores; interpretation: ≥ 2 barriers indicate non-adherence risk.

Table 5.

Analysis of covariance predicting intervention effect on post-intervention number of 6-MP doses missed over the past seven days.

			Group Difference[a]						
	LSM(SE)	95% CI	LSM (SE)	95% CI	*F*	*p*	η_p^2	*d*	R_{adj}^2
Corrected Model					.14	.97	.01		-.05
Intervention			.13(.13)	[-.23, .26]	.01	.92	.00	.03	
MI	.18(.07)	[.03, .33]							
Education	.17(.10)	[-.03, .37]							
Caregiver language			-.08(.13)	[-.33, .17]	.40	.53	.01	.19	
English	.14(.05)	[.03, .24]							
Spanish	.21(.11)	[-.01, .44]							
Intervention x Caregiver language					.01	.94	.00		
MI, English	.14(.06)	[.02, .26]							
MI, Spanish	.23(.14)	[-.04, .49]							
Education, English	.13(.09)	[-.04, .31]							
Education, Spanish	.20(.18)	[-.16, .56]							

Note. η_p^2 = partial eta squared; *d* = Cohen's *d*, interpretation: .2 (small), .5 (medium), .8 (large); R_{adj}^2 = adjusted R squared; covariate was baseline number of 6-MP doses missed over the past seven days.

[a]Group differences calculated by subtracting MI LSM minus Education LSM and English LSM minus Spanish LSM

Table 6.
Analysis of covariance predicting intervention effect on post-intervention patient TGN blood serum level.

			Group Difference[a]						
	LSM(SE)	95% CI	LSM (SE)	95% CI	*F*	*p*	η_p^2	*d*	R_{adj}^2
Corrected Model					15.74	< .001	.59		.56
Intervention			102.95 (70.47)	[-39.17, 245.07]	2.13	.15	.05	.45	
MI	417.54 (48.01)	[320.56, 514.53]							
Education	314.59 (47.53)	[218.74, 410.45]							
Caregiver language			39.51 (64.60)	[-90.77, 169.79]	.37	.54	.01	.25	
English	385.82 (27.05)	[331.28, 440.37]							
Spanish	346.31 (58.68)	[227.97, 464.66]							
Intervention x Caregiver language					1.01	.32	.02		
MI, English	403.07 (28.16)	[346.28, 459.87]							
MI, Spanish	432.01 (91.28)	[247.94, 616.09]							
Education, English	368.57 (46.41)	[274.98, 462.16]							
Education, Spanish	260.61 (81.74)	[95.76, 425.45]							

Note. η_p^2 = partial eta squared; *d* = Cohen's *d*, interpretation: .2 (small), .5 (medium), .8 (large); R_{adj}^2 = adjusted R squared; covariate was baseline patient TGN blood serum level; TGN blood serum levels measured in pmol/8 x10^8 erythrocytes, interpretation: TGN erythrocyte values <343 pmol/8x10^8 suggest 6-MP concentrations below the 75th percentile and may indicate 6-MP non-adherence (Traore et al., 2006).
[a]Group differences calculated by subtracting MI LSM minus Education LSM and English LSM minus Spanish LSM

Table 7.

Frequencies (%) for caregiver-reported medication adherence barriers per Parent Medication Barriers Scale (PMBS).

PMBS Items	Sample[a]	Cultural Groups[b]			Intervention Groups[c]	
		NHES	HES	HSS	MI	Education
		N=63	*N*=30	*N*=28	*N*=66	*N*=37
	15.3	13.1	16.7	15.4	13.0	19.5
1. My child has a hard time swallowing the medicine.						
2. My child has too many pills to take.	21.4	14.8**	23.1	48.0**	21.1	22.0
3. My child does not like how the medicine tastes.	56.0‡	48.3	69.0	61.5	56.6	55.0
4. My child feels that it gets in the way of his/her activities.	16.4	9.8	20.7	28.0	17.1	15.0
5. My child is forgetful and doesn't remember to take his/her medication every time.	18.1	11.7*	13.3	36.0*	13.3	26.8
6. My child is not very organized about when and how he/she takes his/her medication.	14.7	8.3	13.3	28.0	10.7	22.0
7. My child does not want other people to notice him/her taking the medicine.	10.3	4.9	16.7	12.0	10.5	9.8
8. My child is very busy with other things that get in the way of taking the medication.	16.2	13.1	16.7	20.0	11.8	24.4
9. My child sometimes feels sick and can't take the medicine.	21.0	19.4	26.7	15.4	16.7	29.3
10. My child finds it hard to stick to a fixed medication schedule.	6.8	1.6*	6.9	15.4*	3.9	12.2
11. My child doesn't like what the medicine does to his/her appearance.	21.8	19.4	20.0	26.9	21.8	22.0
12. My child is tired of living with a medical condition.	49.6‡	54.1	50.0	40.0	48.1	52.5
13. I am not always there to remind my child to take his/her medication.	17.1	19.7	10.3	15.4	15.8	19.5
14. My child believes the medication has too many side effects.	16.8	14.5	10.0	26.9	19.2	12.2
15. My child relies on me to remind him/her to take his/her medication.	73.7‡	71.0	80.0	72.0	70.1	80.5
16. My child is tired of taking medicine.	51.7‡	50.8	53.3	50.0	46.8	61.0

Note. PMBS = Parent Medication Barriers Scale (Simons & Blount, 2007); PMBS items were coded dichotomously (i.e., yes/no barrier). Significant differences in specific medication adherence barrier endorsement rates based on Fisher's exact tests: * $p < .05$, ** $p < .01$

[a]Sample refers to study caregiver sample.

[b]NHES = Non-Hispanic, English-speaking; HES = Hispanic, English-speaking; HSS = Hispanic, Spanish-speaking.

[c]MI = Motivational Interviewing.

‡Indicates top barrier identified by at least half of caregivers.

Table 8.

Factor loadings, communalities, and reliability coefficients of the Parent Medication Barrier Scale (PMBS) two-factor solution based on Principal Components Analysis (PCA) with oblimin rotation.

	Factor Loadings			
PMBS Item	1	2	h^2	α
Regimen Adaptation				.829
My child finds it hard to stick to a fixed medication schedule	**.873**	.101	.702	
My child is forgetful and doesn't remember to take his/her medication every time	**.808**	.099	.598	
My child is not very organized about when/how he/she takes his/her medication	**.712**	.041	.532	
My child has too many pills to take	**.664**	.065	.480	
My child is very busy with other things that get in the way of taking medication	**.661**	.051	.467	
I'm not always there to remind my child to take his/her medication	**.582**	.141	.292	
My child sometimes feels sick and can't take the medication	**.530**	.148	.365	
My child has a hard time swallowing the medicine	**.439**	.228	.325	
Disease Frustration				.757
My child is tired of living with a medical condition	.220	**.875**	.659	
My child is tired of taking medication	.037	**.841**	.683	
My child feels that it gets in the way of his/her activities	.057	**.610**	.403	
My child believes the medicine has too many side effects	.290	**.549**	.514	
My child does not like how the medicine tastes	.049	**.511**	.284	
My child doesn't like what the medication does to his/her appearance	.212	**.448**	.322	
Items Removed				
My child does not want other people to notice him/her taking the medication	**.376**	.300	.323	
My child relies on me to remind him/her when to take the medication	.170	.024	.033	

Note. h^2 = item communalities; α = Cronbach's alpha reliability. Factor loadings > |.30| in bold. PMBS = Parent Medication Barriers Scale (Simons & Blount, 2007).

Table 9.

Analysis of covariance predicting intervention effect on post-intervention caregiver perceived 6-MP adherence barriers as measured by Parent Medication Barriers Scale (PMBS) total score.

			Group Difference[b]						
	LSM(SE)	95% CI	LSM(SE)	95% CI	*F*	*p*	η_p^2	*d*	R_{adj}^2
Corrected Model					10.33	< .001	.49		.45
Intervention			-1.22(.60)	[-2.40, -.03]	4.18	.04	.05	.44	
MI	3.01(.41)	[2.19, 3.83]							
Education	4.23(.44)	[3.35, 5.09]							
Caregiver language			.18(.60)	[-1.01, 1.37]	.10	.76	.00	.08	
English	3.71(.32)	[3.08, 4.33]							
Spanish	3.52(.51)	[2.50, 4.54]							
Patient age[a]			.85(.60)	[-.35, 2.04]	2.00	.16	.02	.36	
Patient ≥ 12 y.o.	4.04(.53)	[2.98, 5.10]							
Patient < 12 y.o.	3.19(.28)	[2.63, 3.75]							
Intervention x Caregiver language x Patient age					1.72	.15	.08		
MI, English, Patient ≥ 12 y.o.	2.84(.61)	[1.63, 4.06]							
MI, Spanish, Patient ≥ 12 y.o.	2.58(1.36)	[-.14, 5.29]							
MI, English, Patient < 12 y.o.	3.18(.31)	[2.56, 3.80]							
MI, Spanish, Patient < 12 y.o.	3.43(.61)	[2.21, 4.64]							
Education, English, Patient ≥ 12 y.o.	5.33(.97)	[3.40, 7.25]							
Education, Spanish, Patient ≥ 12 y.o.	5.41(1.12)	[3.19, 7.63]							
Education, English, Patient < 12 y.o.	3.48(.43)	[2.62, 4.33]							
Education, Spanish, Patient < 12 y.o.	2.68(.79)	[1.10, 4.25]							

Note. η_p^2 = partial eta squared; *d* = Cohen's *d*, interpretation: .2 (small), .5 (medium), .8 (large); R_{adj}^2 = adjusted R squared; caregiver-perceived 6-MP adherence barriers measured by PCA-refined 14-item PMBS; covariate was baseline 14-item PMBS score; original PMBS developed by Simons & Blount (2007); PMBS interpretation: ≥ 2 barriers indicate non-adherence risk.

[a]Patients ≥ 12 y.o. considered adolescent patients.

[b]Group differences calculated by subtracting MI LSM minus Education LSM, English LSM minus Spanish LSM, and Patient ≥ 12 y.o. LSM minus Patient < 12 y.o. LSM.

Table 10.

Analysis of covariance predicting intervention effect on post-intervention PMBS Regimen Adaptation subscale score.

			Group Difference[b]						
	LSM(SE)	95% CI	LSM(SE)	95% CI	*F*	*p*	η_p^2	*d*	R_{adj}^2
Corrected Model					6.37	< .001	.38		.32
Intervention			-.29(.17)	[-.48, -.03]	4.77	.03	.05	.47	
MI	.64(.11)	[.38, 1.04]							
Education	1.32(.12)	[.85, 1.92]							
Caregiver language			-.06(.17)	[-.31, .29]	.13	.72	.00	.09	
English	.90(.09)	[.61, 1.34]							
Spanish	1.01(.15)	[.54, 1.63]							
Patient age[a]			.33(.17)	[-.03, .82]	3.24	.08	.04	.46	
Patient ≥ 12 y.o.	1.25(.15)	[.71, 1.97]							
Patient < 12 y.o.	.69(.08)	[.46, .97]							
Intervention x Caregiver language x Patient age					1.91	.12	.08		
MI, English, Patient ≥ 12 y.o.	.71(.18)	[.23, 1.36]							
MI, Spanish, Patient ≥ 12 y.o.	.37(.43)	[-.33, 1.81]							
MI, English, Patient < 12 y.o.	.64(.09)	[.39, .94]							
MI, Spanish, Patient < 12 y.o.	.91(.17)	[.38, 1.64]							
Education, English, Patient ≥ 12 y.o.	1.85(.29)	[1.85, .29]							
Education, Spanish, Patient ≥ 12 y.o.	2.84(.34)	[2.84, .34]							
Education, English, Patient < 12 y.o.	.63(.12)	[.30, 1.04]							
Education, Spanish, Patient < 12 y.o.	.63(.24)	[.07, 1.47]							

Note. η_p^2 = partial eta squared; *d* = Cohen's *d*, interpretation: .2 (small), .5 (medium), .8 (large); R_{adj}^2 = adjusted R squared; outcome variable measured by PCA-refined PMBS Regimen Adaptation subscale; covariate was baseline PMBS Regimen Adaptation subscale score; original PMBS developed by Simons & Blount (2007); PMBS interpretation: ≥ 2 barriers indicate non-adherence risk.

[a]Patients ≥ 12 y.o. considered adolescent patients.

[b]Group differences calculated by subtracting MI LSM minus Education LSM, English LSM minus Spanish LSM, and Patient ≥ 12 y.o. LSM minus Patient < 12 y.o. LSM.

Table 11.

Analysis of covariance predicting intervention effect on post-intervention PMBS Disease Frustration subscale score.

			Group Difference[b]						
	LSM(SE)	95% CI	LSM(SE)	95% CI	*F*	*p*	η_p^2	*d*	R_{adj}^2
Corrected Model					9.79	< .001	.48		.43
Intervention			-.38(.38)	[-1.13, .38]	9.68	.33	.01	.21	
MI	2.04(.26)	[1.51, 2.56]							
Education	2.41(.28)	[1.86, 2.96]							
Caregiver language			.32(.38)	[-.44, 1.07]	.69	.41	.01	.21	
English	2.38(.20)	[1.98, 2.78]							
Spanish	2.07(.32)	[1.42, 2.71]							
Patient age[a]			.06(.39)	[-.70, .83]	.03	.87	.00	.04	
Patient ≥ 12 y.o.	2.25(.34)	[1.58, 2.93]							
Patient < 12 y.o.	2.19(.18)	[1.83, 2.55]							
Intervention x Caregiver language x Patient age					.30	.88	.01		
MI, English, Patient ≥ 12 y.o.	1.95(.39)	[1.18, 2.73]							
MI, Spanish, Patient ≥ 12 y.o.	2.04(.88)	[.32, 3.81]							
MI, English, Patient < 12 y.o.	2.07(.20)	[1.68, 2.46]							
MI, Spanish, Patient < 12 y.o.	2.06(.39)	[1.28, 2.83]							
Education, English, Patient ≥ 12 y.o.	2.91(.62)	[1.68, 4.14]							
Education, Spanish, Patient ≥ 12 y.o.	2.10(.71)	[.68, 3.51]							
Education, English, Patient < 12 y.o.	2.60(.28)	[2.05, 3.14]							
Education, Spanish, Patient < 12 y.o.	2.04(.50)	[1.04, 3.04]							

Note. η_p^2 = partial eta squared; *d* = Cohen's *d*, interpretation: .2 (small), .5 (medium), .8 (large); R_{adj}^2 = adjusted R squared; outcome variable measured by PCA-refined PMBS Disease Frustration subscale; covariate was baseline PMBS Disease Frustration subscale score; original PMBS developed by Simons & Blount (2007); PMBS interpretation: ≥ 2 barriers indicate non-adherence risk.

[a]Patients ≥ 12 y.o. considered adolescent patients.

[b]Group differences calculated by subtracting MI LSM minus Education LSM, English LSM minus Spanish LSM, and Patient ≥ 12 y.o. LSM minus Patient < 12 y.o. LSM.

FIGURES

Figure 1. Representation of the Theoretical Domains Framework (Cane et al., 2012) and the Behavior Change Wheel's COM-B system (Michie et al., 2011).

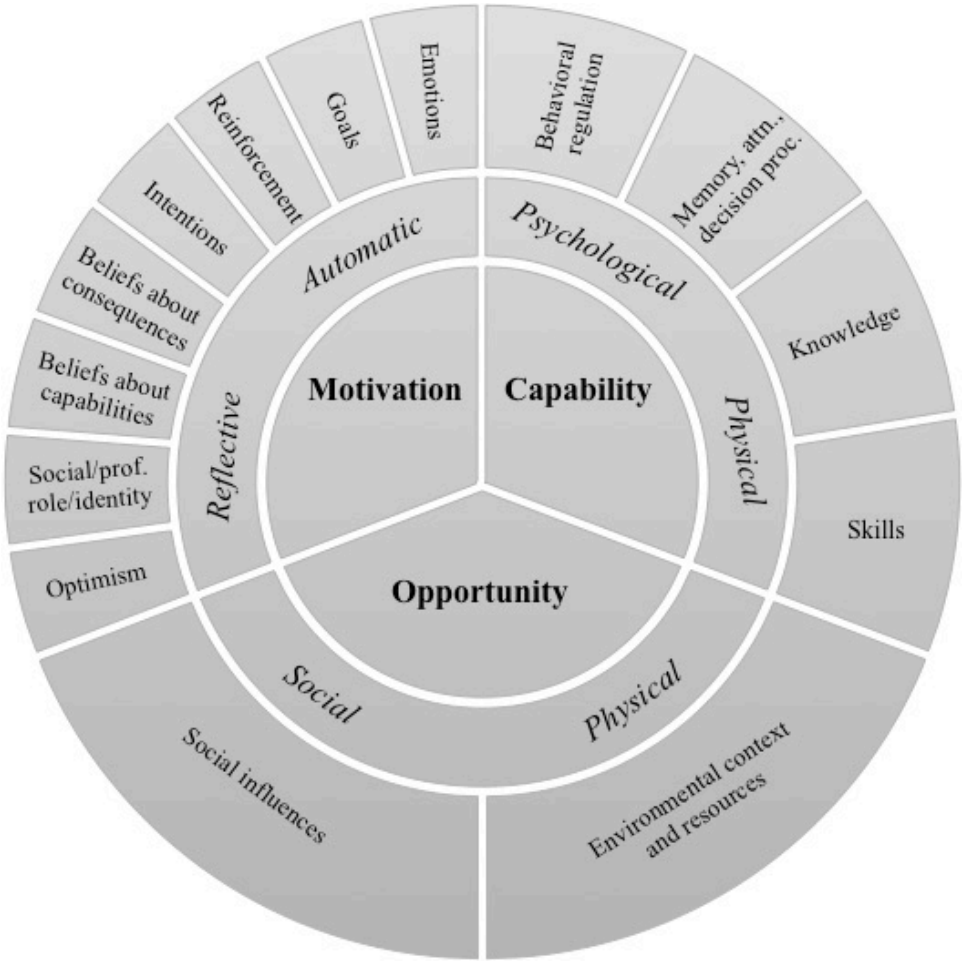


Figure 2. CONSORT diagram of participant flow.

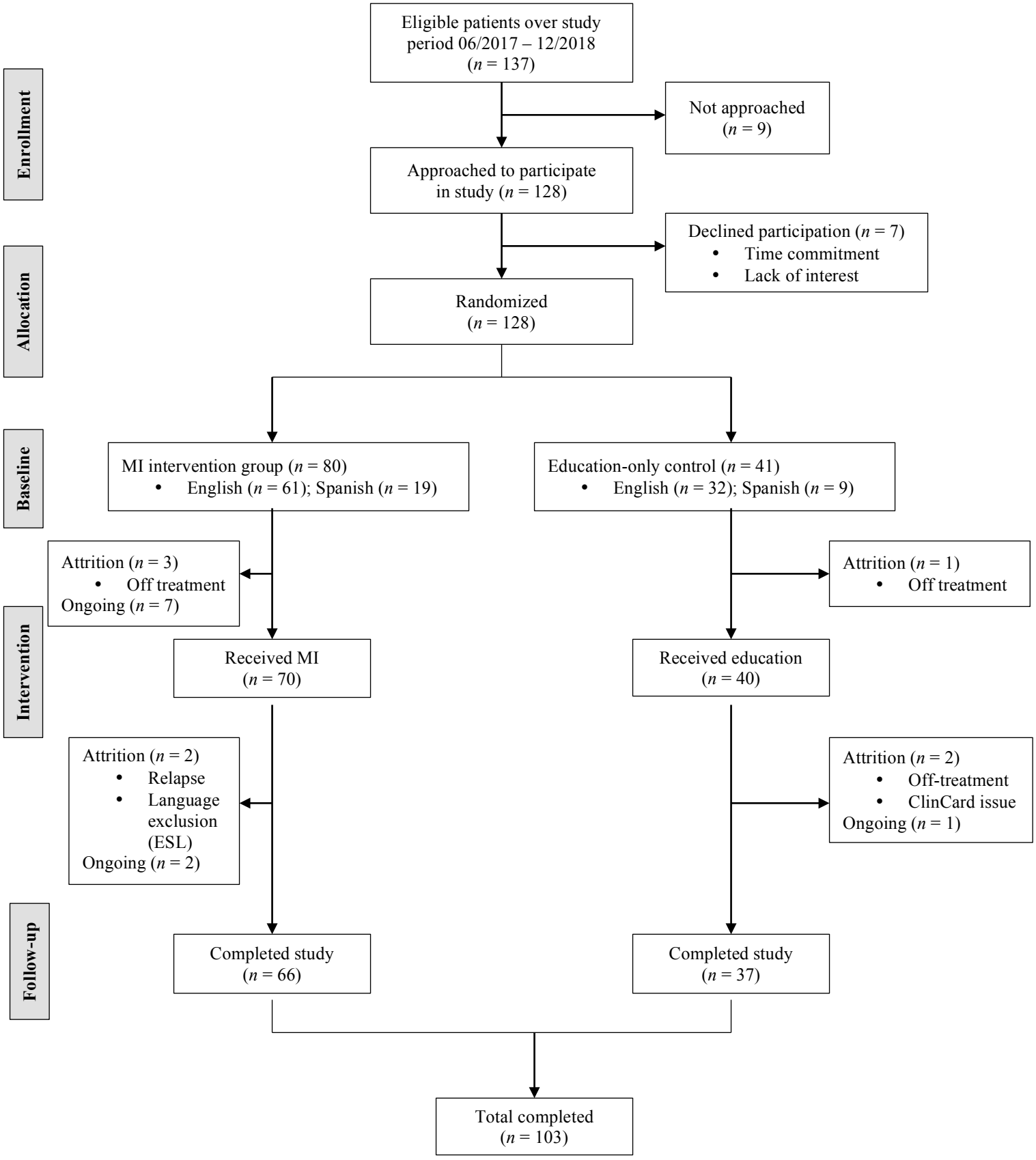
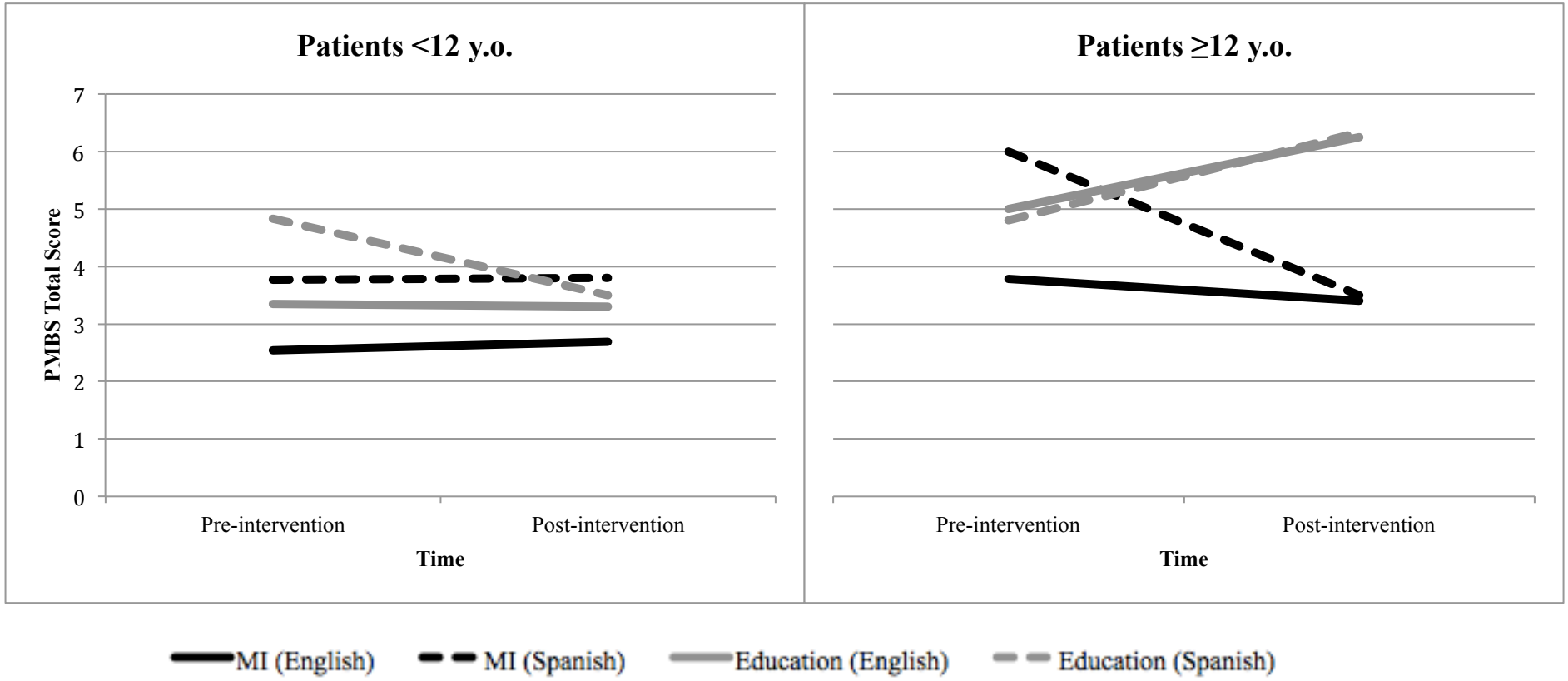
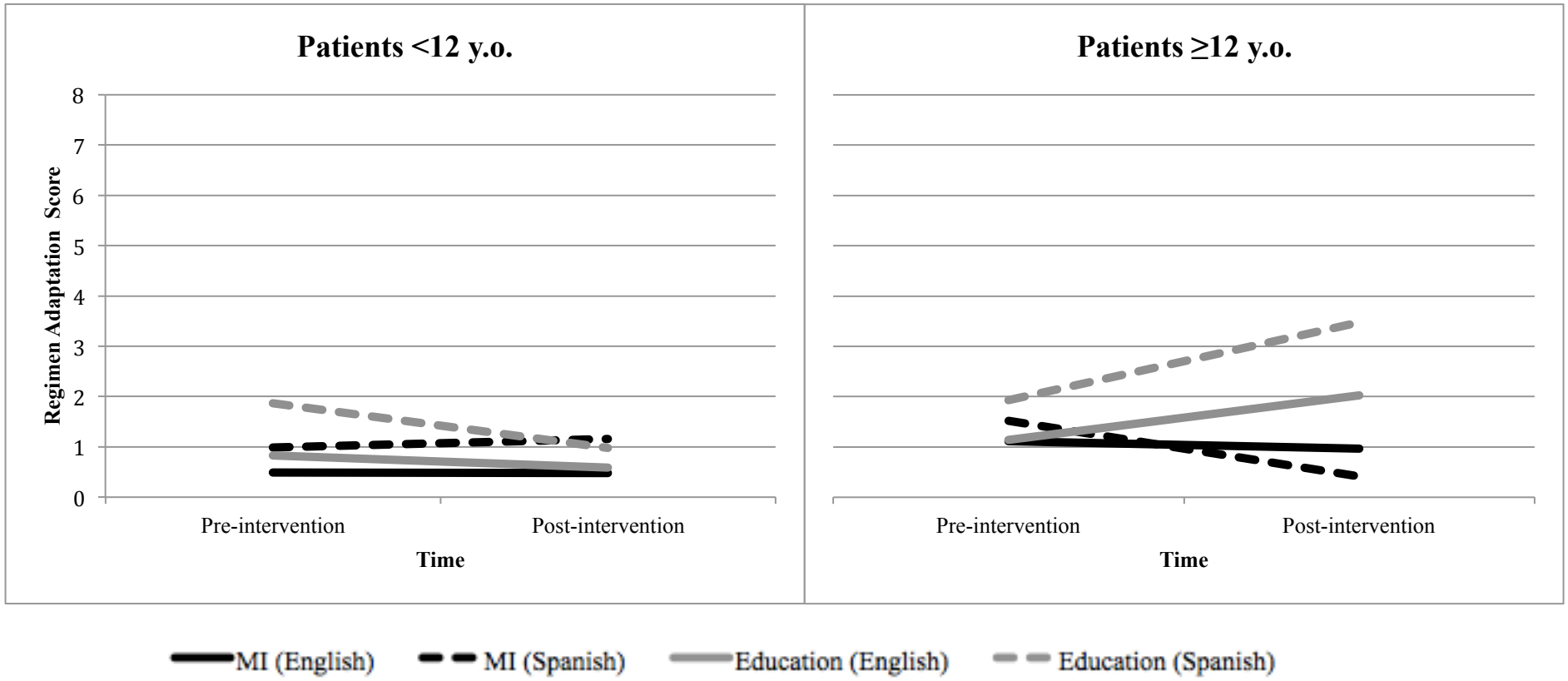


Figure 3. Pre- to post-intervention change in Parent Medication Barriers Scale (PMBS) total score.



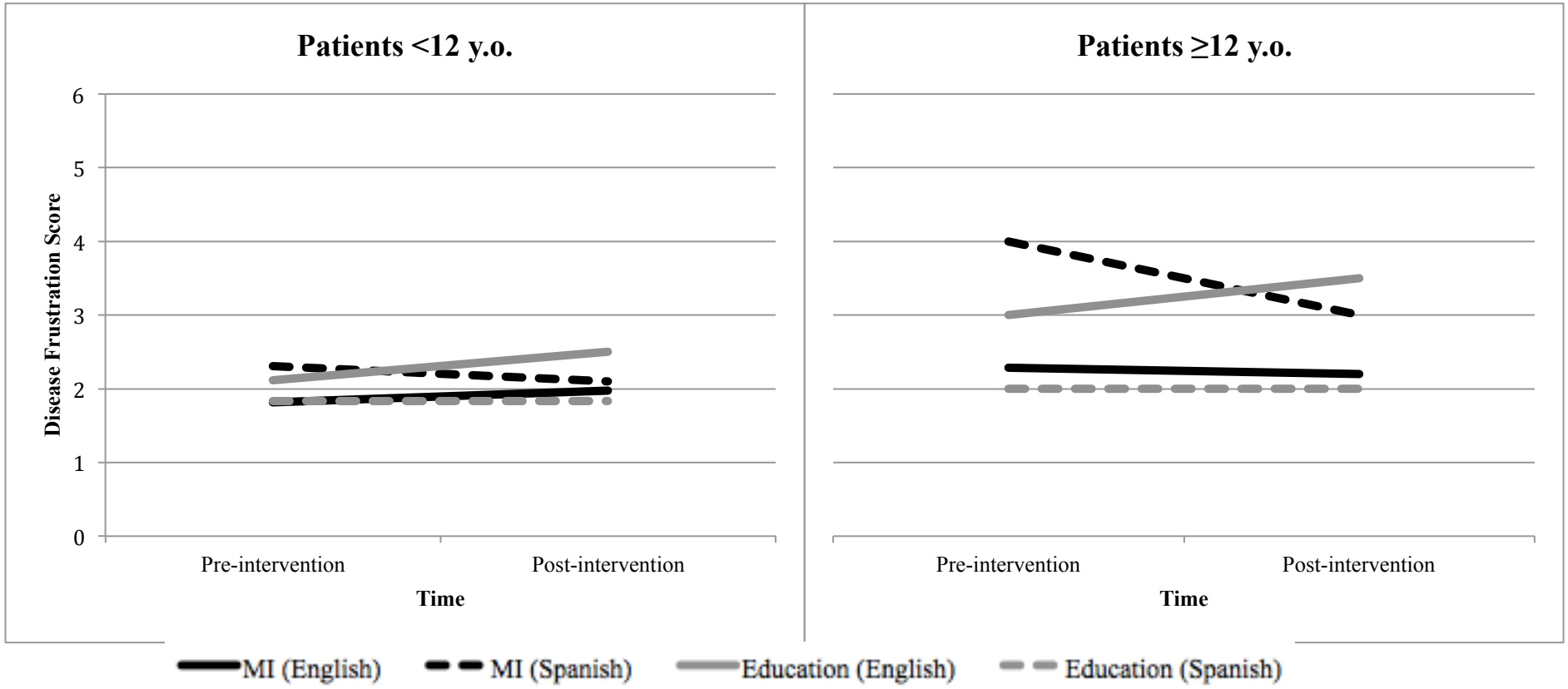
Note. PMBS = Parent Medication Barriers Scale (Simons & Blount, 2007); score computed using 14-item PMBS obtained from principal components analysis; y-axis shows 0-7 scale to improve graph readability; original PMBS scale is from 0-14.

Figure 4. Pre- to post-intervention change in Regimen Adaptation score from Parent Medication Barriers Scale (PMBS).



Note. PMBS = Parent Medication Barriers Scale (Simons & Blount, 2007); Regimen Adaptation subscale score ranges from 0-8, as represented in y-axis.

Figure 5. Pre- to post-intervention change in Disease Frustration score from Parent Medication Barriers Scale (PMBS).



Note. PMBS = Parent Medication Barriers Scale (Simons & Blount, 2007); Disease Frustration subscale score ranges from 0-6, as represented in y-axis.

APPENDICES

Appendix A

Demographic Questionnaire (English)

Subject ID: _____

About Us (Demographics Form, English Version)

1. How many children live **in your home**? _____
2. How old are the children who live in your home?
   a.
   b.
   c.
3. How many adults live **in your home**? _____
4. How are you related to your child who has leukemia? _____
5. Who is usually responsible for making sure your child takes his/her medicine (please check all that apply)?
   a. Me
      ☐ Rarely ☐ Sometimes ☐ Usually ☐ Always
   b. Another adult (my spouse, my parent, babysitter, etc.)
      ☐ Rarely ☐ Sometimes ☐ Usually ☐ Always
   c. My child
      ☐ Rarely ☐ Sometimes ☐ Usually ☐ Always
   d. One of my child's sisters or brothers
      ☐ Rarely ☐ Sometimes ☐ Usually ☐ Always
   e. Someone at my child's school or daycare (school nurse/daycare worker, etc.)
      ☐ Rarely ☐ Sometimes ☐ Usually ☐ Always
6. Other than your child who has leukemia, do any other people **in your home** have any major medical problems or disabilities that require your help? ☐ Yes ☐ No
7. How would you describe yourself (please check all that apply):
   ☐ White ☐ Asian
   ☐ Black/African American ☐ Native Hawaiian or Pacific Islander
   ☐ American Indian or Alaska Native
   a. Are you Hispanic/Latino?
      ☐ Yes ☐ No
8. What is the highest grade you completed in school? _____
9. How old are you? _____
10. What kind of work do you do now? Please check all that apply.
    ☐ Student ☐ Full-time job ☐ Part-time job ☐ Full-time caregiver (stay-at-home parent)
11. Are you:
    ☐ Single ☐ Divorced ☐ Remarried
    ☐ Married ☐ Widowed ☐ Cohabitating
12. What is your average household yearly income (please select one)?
    ☐ $0-$10,000 ☐ $30,001-$40,000 ☐ $60,001-$70,000
    ☐ $10,001-$20,000 ☐ $40,001-$50,000 ☐ $70,001-$80,000
    ☐ $20,001-$30,000 ☐ $50,001-$60,000 ☐ $80,001 or more

Appendix B

Demographic Questionnaire (Spanish)

Subject ID: _____

Sobre Nosotros (Demographics Form, Spanish Version)

1. ¿Cuántos niños viven **en su hogar**? _____
2. ¿Cuántos años tienes los niños(as) que viven en su hogar?
   a.
   b.
   c.
3. ¿Cuántos adultos viven **en su hogar**?_____
4. ¿Cuál es su relación a este niño(a) con leucemia (madre, padre, abuela, etc.)? _____
5. ¿Quién ha sido usualmente el/la responsable de recordarse de que su niño(a) tome su medicina (por favor marque todas las que apliquen)?
   a. Yo mismo(a)
      ☐ Casi nunca ☐ A veces ☐ Usualmente ☐ Siempre
   f. Otro adulto (mi esposo(a), mi madre/padre, niñera/cuidadora, etc.)
      ☐ Casi nunca ☐ A veces ☐ Usualmente ☐ Siempre
   g. Mi niño(a)
      ☐ Casi nunca ☐ A veces ☐ Usualmente ☐ Siempre
   h. El/la hermano(a) de mi niño(a)
      ☐ Casi nunca ☐ A veces ☐ Usualmente ☐ Siempre
   a. Alguien en la escuela o guardería de mi niño(a) (enfermera en la escuela, maestra, etc.)
      ☐ Casi nunca ☐ A veces ☐ Usualmente ☐ Siempre
6. A parte de su niño(a) que tiene leucemia, ¿hay alguna otra persona en su hogar que tiene algún problema medico grave o alguna discapacidad? ☐ Sí ☐ No
7. ¿Cómo se describiría usted? (por favor marque todas las que apliquen):
   ☐ Blanco/Caucásico ☐ Asiático
   ☐ Negro/Afroamericano ☐ Nativo de Hawai o Islas del Pacífico
   ☐ Indio/Nativo Americano/Nativo de Alaska
   b. ¿Usted es Hispano/Latino?
      ☐ Sí ☐ No
8. ¿Cuál es el grado más alto que usted completó en la escuela?_____
9. ¿Cuántos años tiene usted? _____
10. ¿ Qué tipo de trabajo hace usted? (por favor marque todas las que apliquen):
    ☐ Estudiante ☐ Trabajo tiempo complete ☐ Trabajo tiempo medio ☐ Cuidador(a) a tiempo completo (ama de casa)
11. Usted está:
    ☐ Soltero(a) ☐ Divorciado(a) ☐ Vuelto a Casarse
    ☐ Casado(a) ☐ Viudo(a) ☐ Conviviendo
13. ¿Cuál es el ingreso promedio anual de su hogar (por favor marque una)?
    ☐ $0-$10,000 ☐ $30,001-$40,000 ☐ $60,001-$70,000
    ☐ $10,001-$20,000 ☐ $40,001-$50,000 ☐ $70,001-$80,000
    ☐ $20,001-$30,000 ☐ $50,001-$60,000 ☐ $80,001 o más

Appendix C

Parent Medication Barriers Scale (English; adapted from Simons & Blount, 2007)

Subject ID: _____

Medication Adherence Barriers—Parent (English)

Taking medication daily for life is a difficult task. We would like to find ways to make this process easier for your child. Listed below are several reasons that families have told us make it difficult for their child to take their medications on schedule every day. Please read each statement carefully. Check the box that reflects how much you agree or disagree with each statement.

	Strongly Disagree	Disagree	Not Sure	Agree	Strongly Agree
My child has a hard time swallowing the medicine.					
My child has too many pills to take.					
My child does not like how the medicine tastes.					
My child feels that it gets in the way of his/her activities.					
My child is forgetful and doesn't remember to take his/her medication every time.					
My child is not very organized about when and how he/she takes his/her medication.					
My child does not want other people to notice him/her taking the medicine.					
My child is very busy with other things that get in the way of taking the medication.					
My child sometimes feels sick and can't take the medicine.					
My child finds it hard to stick to a fixed medication schedule.					
My child doesn't like what the medication does to his/her appearance.					
My child is tired of living with a medical condition.					
I am not always there to remind my child to take his/her medication.					
My child believes the medication has too many side effects.					
My child relies on me to remind him or her to take his/her medication.					
My child is tired of taking medicine.					

Is there anything else that we did not mention that makes it hard for your child to take his/her medication on schedule every day?

_____

_____

_____

Appendix D

Parent Medication Barriers Scale (Spanish; adapted from Simons & Blount, 2007)

Subject ID: _____

Medication Adherence Barriers—Parent (Spanish)

Tomar medicamentos diariamente por el resto de la vida es una tarea difícil. Nos gustaría encontrar maneras de hacer este proceso más fácil para su hijo(a). A continuación se enumeran varias razones, que las familias nos han dicho, hacen difícil para su niño(a) tomar sus medicamentos a tiempo todos los días. Por favor lea cada declaración cuidadosamente. Elija la respuesta que refleja qué tan de acuerdo o en desacuerdo está usted con cada declaración.

	Muy en desacuerdo	En desacuerdo	No estoy seguro(a)	De acuerdo	Muy de acuerdo
Mi hijo(a) tiene dificultades tragando el medicamento.					
Mi hijo(a) tiene demasiadas píldoras que tomar.					
A mi hijo(a) no le gusta el sabor de los medicamentos.					
Mi hijo(a) siente que interfiere con sus actividades.					
Mi hijo(a) es olvidadizo(a) y no se recuerda de tomar los medicamentos todas las veces.					
Mi hijo(a) no es muy organizado(a) acerca de cuando y cómo él/ella toma sus medicamentos.					
Mi hijo(a) no quiere que otras personas noten o se den cuenta que él/ella toma medicamentos.					
Mi hijo(a) está muy ocupado(a) con otras cosas que interfieren con tomarse los medicamentos.					
Mi hijo(a) a veces se siente enfermo(a) y no puedo tomar los medicamentos.					
A mi hijo(a) le resulta difícil seguir un horario de medicamentos fijo.					
A mi hijo(a) no le gusta lo que los medicamentos le hacen a su apariencia física.					
Mi hijo(a) está cansado(a) de vivir con una condición medica.					
Yo no estoy siempre ahí para recordarle a mi hijo(a) de tomar sus medicamentos.					
Mi hijo(a) cree que los medicamentos tienen demasiados efectos secundarios.					
Mi hijo(a) depende de mi para recordarle que tome sus medicamentos.					
Mi hijo(a) está cansado(a) de tomar medicamentos.					

¿Hay algo más que no mencionamos que hace difícil para su niño(a) tomar sus medicamentos a tiempo todos los días?

_____

_____

_____

Appendix E

Adolescent Medication Barriers Scale (English; adapted from Simons & Blount, 2007)

Subject ID: _____

Medication Adherence Barriers—Adolescent (English)

Taking medication daily for life is a difficult task. We would like to find ways to make this process easier for you. Listed below are several reasons that teens have told us make it difficult for them to take their medications on schedule every day. Please read each statement carefully. Check the box that reflects how much you agree or disagree with each statement.

	Strongly Disagree	Disagree	Not Sure	Agree	Strongly Agree
I believe that the medicine is hard to swallow.					
I believe that I have too many pills to take.					
I don't like how the medicine tastes.					
I believe this medicine has too many side effects.					
I don't want to take the medicine at school.					
I feel that it gets in the way of my activities.					
I am forgetful and I don't remember to take the medication every time.					
I am not very organized about when and how to take the medication.					
I do not want other people to notice me taking the medicine.					
I sometimes just don't feel like taking the medicine.					
I find it hard to stick to a fixed medication schedule.					
I don't like what the medication does to my appearance.					
I am tired of taking medicine.					
I am tired of living with a medical condition.					
Sometimes I don't realize when I run out of pills.					
I get confused about how the medicine should be taken (with/without food, with/without water, etc.).					
Sometimes it's hard to make it to the pharmacy to pick up the prescription before it runs out.					

Is there anything else that we did not mention that makes it hard for you to take your medication on schedule every day?

_____

_____

_____

Appendix F

Adolescent Medication Barriers Scale (Spanish; adapted from Simons & Blount, 2007)

Subject ID: _____

Medication Adherence Barriers—Adolescent (Spanish)

Tomar medicamentos diariamente por el resto de la vida es una tarea difícil. Nos gustaría encontrar maneras de hacer este proceso más fácil para ti. A continuación se enumeran varias razones, que los jóvenes nos han dicho, hacen difícil para ellos tomar sus medicamentos a tiempo todos los días. Por favor lea cada declaración cuidadosamente. Elija la respuesta que refleja qué tan de acuerdo o en desacuerdo está usted con cada declaración.

	Muy en desacuerdo	En desacuerdo	No estoy seguro(a)	De acuerdo	Muy de acuerdo
Yo creo que el medicamento es difícil de tragar.					
Yo creo que tengo demasiadas píldoras que tomar.					
A mí no me gusta el sabor de los medicamentos.					
Yo creo que los medicamentos tienen demasiados efectos secundarios.					
Yo no quiero tomar los medicamentos en la escuela.					
Yo siento que interfiere con mis actividades.					
Yo soy olvidadizo(a) y no me recuerdo de tomar los medicamentos todas las veces.					
Yo no soy muy organizado(a) acerca de cuando y cómo tomo mis medicamentos.					
Yo no quiero que otras personas noten o se den cuenta que tomo medicamentos.					
A veces no tengo ganas de tomar los medicamentos.					
A mí me resulta difícil seguir un horario de medicamentos fijo.					
A mí no me gusta lo que los medicamentos le hacen a mi apariencia física.					
Yo estoy cansado(a) de tomar medicamentos.					
Yo estoy cansado(a) de vivir con una condición medica.					
A veces no me doy cuenta cuando se me acaban las píldoras.					
Yo me confundo acerca de cómo debo tomar las píldoras (con/sin comida, con/sin agua, etc.)					
A veces es difícil ir a la farmacia a recoger la prescripción antes de que se me acaben.					

¿Hay algo más que no mencionamos que hace difícil para usted tomar sus medicamentos a tiempo todos los días?

_____

_____

_____

Appendix G

Medication Adherence to 6-MP Questionnaire (Caregiver version, English)

Subject ID: _____

Medication Adherence to 6MP—Parent (English)

1. Did the doctor tell your child to take the same number of 6MP pills every day for the past week? (Note: 6MP might be called Purinethol on the bottle)
    a. If 'Yes', how many pills was your child prescribed to take each day? _____
    b. If 'No', please describe your child's dosing schedule: (ex: "My child takes one pill Monday-Friday and two pills on Saturday and Sunday" or "My child takes two pills every day", etc.)
    _____
    _____
2. How many times has your child completely missed a dose of 6MP (not just late) in the past 7 days? _____
3. Did the doctor tell your child to stop taking 6MP in the last 7 days?
    a. Yes
    b. No
    c. I don't know
4. Over the past 7 days, how many times did your child take a dose of 6MP more than 2 hours late? _____
5. What is the purpose of 6MP (Note: 6MP might be called Purinithol on the bottle)?
    _____
    _____
6. Who was usually responsible for remembering your child's 6MP over the past 7 days?
    a. Myself
    b. My child
    c. Other family member (not parent or primary caregiver)
    d. Hospital nurse
    e. School nurse
    f. Home nurse
    g. Other person
7. Who is USUALLY responsible for remembering your child's 6MP? (not just over the past 7 days)
    a. Myself
    b. My child
    c. Other family member (not parent or primary caregiver)
    d. Hospital nurse
    e. School nurse
    f. Home nurse
    g. Other person
8. I wish I had more help remembering my child's 6MP.
    a. Yes
    b. No
9. How hard is it to remember to take your child's 6MP?
    a. Extremely hard
    b. Very hard
    c. Moderately hard
    d. A little hard
    e. Not hard at all

Appendix H

Medication Adherence to 6-MP Questionnaire (Caregiver version, Spanish)

Subject ID: _____

Medication Adherence to 6MP—Parent (Spanish)

1. ¿El doctor te dijo que su hijo(a) tomara el mismo número de píldoras 6MP cada día de la semana pasada? (Nota: Las píldoras de 6MP pueden tener el nombre Purinethol en el frasco o botella)
    a. Sí—¿Cuántas píldoras 6MP toma cada día? _____
    b. No—Por favor describa horario de dosis de su hijo(a): (por ejemplo, "MI hijo(a) toma una pastilla/píldora de lunes a viernes y dos píldoras el sábado y el domingo " o " mi hijo(a) toma dos pastillas/píldoras todos los días ", etc.)
    _____
    _____
2. ¿Cuántas veces ha dejado su hijo(a) de tomar por completo una dosis de 6MP (no sólo que la haya tomado tarde) en los últimos 7 días? _____
3. ¿El doctor le dijo a su hijo(a) que dejara de tomar tus píldoras de 6MP en los últimos 7 días?
    a. Sí
    b. No
    c. No sé
4. ¿En los últimos 7 días, cuántas veces tomó su hijo(a) una dosis de 6MP mas de dos horas tarde? _____
5. ¿Cuál es el propósito de las píldoras de 6MP? (Nota: Las píldoras de 6MP pueden tener el nombre Purinethol en el frasco o botella)
    _____
    _____
6. ¿Quién ha sido usualmente el/la responsable de recordarle a su hijo(a) de su 6MP en los últimos 7 días?
    a. Yo mismo(a)
    b. Mi hijo(a)
    c. Otro miembro de la familia (no madre/padre o guardián)
    d. Enfermera en el hospital
    e. Enfermera en la escuela
    f. Enfermera en el hogar
    g. Otra persona
7. ¿Quién es USUALMENTE el/la responsable de recordarse de tu 6MP? (no solo en los últimos 7 días)
    a. Yo mismo(a)
    b. Mi hijo(a)
    c. Otro miembro de la familia (no madre/padre o guardián)
    d. Enfermera en el hospital
    e. Enfermera en la escuela
    f. Enfermera en el hogar
    g. Otra persona
8. Me gustaría tener más ayuda para recordarme de que mi hijo(a) tome su 6MP .
    a. Sí
    b. No
9. ¿Qué tan difícil te es recordarte de las píldoras de 6MP de su hijo(a)?
    a. Extremadamente difícil
    b. Muy difícil
    c. Moderadamente difícil
    d. Un poco difícil
    e. No es difícil

Appendix I

Medication Adherence to 6-MP Questionnaire (Patient version, English)

Subject ID: _____

Medication Adherence to 6MP—Adolescent (English)

1. Did your doctor tell you to take the same number of 6MP pills every day for the past week? (Note: 6MP might be called Purinethol on the bottle)
    a. If 'Yes', how many pills were you prescribed to take each day? _____
    b. If 'No', please describe your dosing schedule: (ex: "I take one pill Monday-Friday and two pills on Saturday and Sunday" or "I take two pills every day", etc.)
    _____
    _____
2. How many times have you completely missed a dose of 6MP (not just late) in the past 7 days? _____
3. Did your doctor tell you to stop taking 6MP in the last 7 days?
    a. Yes
    b. No
    c. I don't know
4. Over the past 7 days, how many times did you take a dose of 6MP more than 2 hours late? _____
5. What is the purpose of 6MP (Note: 6MP might be called Purinithol on the bottle)?
    _____
    _____
6. Who was usually responsible for remembering your 6MP over the past 7 days?
    a. Myself
    b. Parent/caregiver
    c. Other family member (not parent or primary caregiver)
    d. Hospital nurse
    e. School nurse
    f. Home nurse
    g. Other person
7. Who is USUALLY responsible for remembering your 6MP? (not just over the past 7 days)
    a. Myself
    b. Parent/caregiver
    c. Other family member (not parent or primary caregiver)
    d. Hospital nurse
    e. School nurse
    f. Home nurse
    g. Other person
8. I wish I had more help remembering to take my 6MP.
    a. Yes
    b. No
9. How hard is it to remember to take your 6MP?
    a. Extremely hard
    b. Very hard
    c. Moderately hard
    d. A little hard
    e. Not hard at all

Appendix J

Medication Adherence to 6-MP Questionnaire (Patient version, Spanish)

Subject ID: _____

Medication Adherence to 6MP—Adolescent (Spanish)

1. ¿Tu doctor te dijo que tomaras el mismo número de píldoras 6MP cada día de la semana pasada? (Nota: Las píldoras de 6MP pueden tener el nombre Purinethol en el frasco o botella)
    a. Sí—¿Cuántas píldoras 6MP tomas cada día? _____
    b. No—Por favor describa su horario de dosis: (por ejemplo, "Tomo una pastilla/píldora de lunes a viernes y dos píldoras el sábado y el domingo " o " que tomo dos pastillas/píldoras todos los días ", etc.)
    _____
    _____
2. ¿Cuántas veces has dejado de tomar por completo una dosis de 6MP (no sólo que la hayas tomado tarde) en los últimos 7 días? _____
3. ¿Tu doctor te dijo que dejaras de tomar tus píldoras de 6MP en los últimos 7 días?
    a. Sí
    b. No
    c. No sé
4. ¿En los últimos 7 días, cuántas veces tomaste una dosis de 6MP mas de dos horas tarde? _____
5. ¿Cuál es el propósito de las píldoras de 6MP? (Nota: Las píldoras de 6MP pueden tener el nombre Purinethol en el frasco o botella)
    _____
    _____
6. ¿Quién ha sido usualmente el/la responsable de recordarse de tu 6MP en los últimos 7 días?
    a. Yo mismo(a)
    b. Madre/padre o guardian
    c. Otro miembro de la familia (no madre/padre o guardián)
    d. Enfermera en el hospital
    e. Enfermera en la escuela
    f. Enfermera en el hogar
    g. Otra persona
7. ¿Quién es USUALMENTE el/la responsable de recordarse de tu 6MP? (no solo en los últimos 7 días)
    a. Yo mismo(a)
    b. Madre/padre o guardian
    c. Otro miembro de la familia (no madre/padre o guardián)
    d. Enfermera en el hospital
    e. Enfermera en la escuela
    f. Enfermera en el hogar
    g. Otra persona
8. Me gustaría tener más ayuda para recordarme de tomar mi 6MP .
    a. Sí
    b. No
9. ¿Qué tan difícil te es recordarte de tomar tus píldoras de 6MP?
    a. Extremadamente difícil
    b. Muy difícil
    c. Moderadamente difícil
    d. Un poco difícil
    e. No es difícil

Appendix K

Mental Health Experiences Questionnaire (Caregiver version, English)

Subject ID: _____

Past Experience with Mental Health Services—Parent (English)

Please answer the following questions regarding your previous experience with mental health services.

1. Have you ever received counseling or other psychology/psychiatry services from a mental health professional?
    a. Yes
    b. No

2. How much did you like your previous mental health provider (e.g., how well did you get along with each other)?
    a. I didn't like him/her at all
    b. I liked him/her a little
    c. I really liked him/her

3. How much did your previous mental health services help you with a problem?
    a. Didn't help at all
    b. Helped a little
    c. Helped a lot

Appendix L

Mental Health Experiences Questionnaire (Caregiver version, Spanish)

Subject ID: _____

Past Experience with Mental Health Services—Parent (Spanish)

Por favor responda las siguientes preguntas sobre su experiencia con servicios de salud mental.

1. ¿Alguna vez ha recibido servicios de asesoramiento, psicología, y/o psiquiatría de parte de un profesional de salud mental?
    a. Sí
    b. No

2. ¿Qué tanto le gustó el profesional de salud mental con el que trabajó anteriormente (por ejemplo, ¿qué tan bien se llevo con el/ella?)
    a. No me gustó para nada
    b. Me gustó un poco
    c. Me gustó mucho

3. ¿Qué tanto lo ayudó los servicios de salud mental que recibió anteriormente?
    a. No me ayudó para nada
    b. Me ayudó un poco
    c. Me ayudó mucho

Appendix M

Mental Health Experiences Questionnaire (Patient version, English)

Subject ID: _____

Past Experience with Mental Health Services—Adolescent (English)

Please answer the following questions regarding your previous experience with mental health services.

1. Have you ever received counseling or other psychology/psychiatry services from a mental health professional?
    a. Yes
    b. No

2. How much did you like your previous mental health provider (e.g., how well did you get along with each other)?
    a. I didn't like him/her at all
    b. I liked him/her a little
    c. I really liked him/her

3. How much did your previous mental health services help you with a problem?
    a. Didn't help at all
    b. Helped a little
    c. Helped a lot

Appendix N

Mental Health Experiences Questionnaire (Patient version, Spanish)

Subject ID: _____

Past Experience with Mental Health Services—Adolescent (Spanish)

Por favor responda las siguientes preguntas sobre su experiencia con con servicios de salud mental.

1. ¿Alguna vez ha recibido servicios de asesoramiento, psicología, y/o psiquiatría de parte de un profesional de salud mental?
    a. Sí
    b. No

2. ¿Qué tanto le gustó el profesional de salud mental con el que trabajó anteriormente (por ejemplo, ¿qué tan bien se llevo con el/ella?)
    a. No me gustó para nada
    b. Me gustó un poco
    c. Me gustó mucho

3. ¿Qué tanto lo ayudó los servicios de salud mental que recibió anteriormente?
    a. No me ayudó para nada
    b. Me ayudó un poco
    c. Me ayudó mucho

Appendix O

Abbreviated Acceptability Rating Profile (Caregiver version, English)

(Adapted from Tarnowski & Simonian,1992)

Subject ID: _____

Abbreviated Acceptability Rating Profile, MI version—Parent (English)

Please answer the following questions regarding you session you had with the psychologist or doctor. In the following questions, the "behavior" or "problem" refers to medication-taking behavior.

	Strongly Disagree	**Disagree**	**Somewhat Disagree**	**Somewhat Agree**	**Agree**	**Strongly Agree**
This is an acceptable treatment for the child's behavior.						
The treatment should be effective in changing the child's behavior.						
The child's behavior is severe enough to justify the use of this treatment.						
I would be willing to use this treatment with my child.						
This treatment *would not* have bad side effects for the child.						
I liked the treatment.						
The treatment was a good way to handle the child's problem.						
Overall, the treatment would help the child.						

Appendix P

Abbreviated Acceptability Rating Profile (Caregiver version, Spanish)

(Adapted from Tarnowski & Simonian,1992)

Subject ID: _____

Abbreviated Acceptability Rating Profile, MI version—Parent (Spanish)

Por favor conteste las siguientes preguntas con respecto a la sesión que tuvo con el psicólogo o doctor. En las siguientes preguntas, el "comportamiento" o "problema" se refiere a tomar los medicamentos.

	Muy en Desacuerdo	En Desacuerdo	Algo en Desacuerdo	Algo De Acuerdo	De Acuerdo	Muy De Acuerdo
Este es un tratamiento aceptable para el comportamiento de mi niño(a).						
El tratamiento será eficaz para cambiar el comportamiento de niño(a) .						
El comportamiento de niño(a) es lo suficientemente grave como para justificar el uso de este tratamiento .						
Yo estaría dispuesto a utilizar este tratamiento para niño(a) .						
Este tratamiento no tendrá efectos secundarios negativos para mi niño(a)						
Me gustó el tratamiento.						
El tratamiento fue una buena manera de manejar el problema de niño(a).						
En general, el tratamiento podrá ayudar a mi niño(a)						

Appendix Q

Abbreviated Acceptability Rating Profile (Patient version, English)

(Adapted from Tarnowski & Simonian,1992)

Subject ID: _____

Abbreviated Acceptability Rating Profile, MI version—Adolescent (English)

Please answer the following questions regarding you session you had with the psychologist or doctor. In the following questions, the "behavior" or "problem" refers to medication-taking behavior.

	Strongly Disagree	Disagree	Somewhat Disagree	Somewhat Agree	Agree	Strongly Agree
This is an acceptable treatment for my behavior.						
The treatment should be effective in changing my behavior.						
My behavior is severe enough to justify the use of this treatment.						
I would be willing to use this treatment.						
This treatment *would not* have bad side effects for me.						
I liked the treatment.						
The treatment was a good way to handle the problem.						
Overall, the treatment would help me.						

Appendix R

Abbreviated Acceptability Rating Profile (Patient version, Spanish)

(Adapted from Tarnowski & Simonian,1992)

Subject ID: _____

Abbreviated Acceptability Rating Profile, MI version—Adolescent (Spanish)

Por favor conteste las siguientes preguntas con respecto a la sesión que tuvo con el psicólogo o doctor. En las siguientes preguntas, el "comportamiento" o "problema" se refiere a tomar los medicamentos.

	Muy en Desacuerdo	En Desacuerdo	Algo en Desacuerdo	Algo De Acuerdo	De Acuerdo	Muy De Acuerdo
Este es un tratamiento aceptable para mi comportamiento.						
El tratamiento será eficaz para cambiar mi comportamiento .						
Mi comportamiento es lo suficientemente grave como para justificar el uso de este tratamiento .						
Yo estaría dispuesto a utilizar este tratamiento .						
Este tratamiento no tendrá efectos secundarios negativos para mí.						
Me gustó el tratamiento.						
El tratamiento fue una buena manera de manejar el problema .						
En general, el tratamiento podrá ayudarme .						

Appendix S

Motivational Interviewing Treatment Integrity 4.2.1

(Moyers, Manuel, & Ernst, 2014)

Recording #:_____ Coder:_____ Date: ____/____/____

Global Ratings

Technical Components						
Cultivating Change Talk	1	2	3	4	5	Target Change:_____
Softening Sustain Talk	1	2	3	4	5	
Relational Components						
Partnership	1	2	3	4	5	
Empathy	1	2	3	4	5	

Behavior Counts

		Total
Giving Information (GI)		
Persuade (Persuade)		
Persuade with Permission (Persuade with)		
Question (Q)		
Simple Reflection (SR)		
Complex Reflection (CR)		
Affirm (AF)		
Seeking Collaboration (Seek)		
Emphasizing Autonomy (Emphasize)		
Confront (Confront)		

Start time and sentence:_____

End time and sentence:_____

Appendix T

Cultural Adaptation Manipulation Check

Study ID #: _____

Manipulation Check for Spanish-delivered MI Sessions

Date MI Session: ___ /___ /___

MI Provider: _____

Coder: _____

Manipulation	Present (Yes/No)	Themes Discussed
Social contextual stressors related to minority status		
Culture-specific values		

Appendix U

6-MP Adherence Educational Handout (Caregiver version, English)

A.L.L. MAINTENANCE

Your child has acute lymphoblastic leukemia or ALL and he or she is in the maintenance phase of therapy. This means your child has to take a medicine called 6-MP every day. Sadly, missing even a small number of the doses your child is supposed to take can make it easier for the leukemia to come back.

Here are some ideas to help your child remember to take his or her medication every day.

1. **Find a buddy!**		Your child's buddy can help him or her remember to take the 6MP. Ask the buddy to watch your child take the medicine so there's no doubt your child has accomplished the mission! Some good buddies might be you, another parent or caregiver, a grandparent, or a school nurse.
2. **Set an alarm or reminder for the same time every day.**		Having a set schedule will help your child remember to always take the medicine.
3. **If your child is not home**		Ask them to bring a water bottle and pillbox with the 6-MP so they can take the medicine on the go!
4. **Keep a calendar**		Sometimes it's hard for children to remember if they have taken the medicine. Keeping a calendar can help your child! Check off every time your child takes the medicine. You can also use a pillbox with the days of the week. If you need a calendar or a pillbox, ask a nurse at CCBD to give you one!
5. **Ask for help!**		Ask someone to call your child every day to make sure they took the medicine.
6. **Your child can eat or drink before or after they take the medicine.**		The most important thing is that they take it!
7. **If the medicine makes your child feel sick**		Give them Zofran or another anti-nausea medicine 20 minutes before they take the 6-MP.

[redacted]

The doctor may tell your child to stop taking 6-MP for medical reasons. Always talk to your doctor or nurse if you have any questions about your child's medication. Call us at (214) 456-2382 if your child has trouble taking the 6-MP. Do not wait until your next appointment!

Thank you!

Appendix V

6-MP Adherence Educational Handout (Caregiver version, Spanish)

A.L.L. MAINTENANCE

Su niño o niña tiene leucemia linfoblástica aguda o ALL y está en la fase de terapia de mantenimiento. Esto significa que tiene que tomar un medicamento llamado 6-MP todos los día. Lamentablemente, si falta un pequeño numero de dosis que tiene que tomar es más fácil que la leucemia vuelva.

Estas son algunas ideas para ayudarle a su niño o niña a acordarse de tomar su medicamento todos los días.

1. ¡Encuentre a un compañero! 	El compañero de su niño o niña puede recordarle que tome su 6MP. ¡Pídele a el compañero que vea a su niño o niña tomar su medicina para que no haya duda que ha cumplido su misión! Algunos compañeros buenos pueden ser usted u otro padre, un abuelo, o una enfermera de la escuela.
2. Coloque una alarma o recordatorio para la misma hora cada día	Tener un horario establecido le ayudará a su niño o niña a acordarse de tomar siempre el medicamento.
3. Si su niño o niña no va a estar en la casa	Traiga una botella de agua y una caja de píldoras con su 6-MP para que pueda tomar la medicina en la calle!
4. Calendario 	A veces es difícil recordarse si su niño o niña ya tomó su medicina. Tener un calendario puede ayudarle! Marque cada vez que su niño o niña se tome su medicina. También puede usar una caja de píldoras con los días de la semana. Si necesita un calendario o una caja de píldoras, pídale a una enfermera en el CCBD que le de uno!
5. Pida ayuda	Pídale a alguien que llame a si niño o niña todos los días para asegurarse de que haya tomado la medicina.
6. Su niño o niña puede comer o beber antes o después de tomar la medicina.	Lo más importante es que la tome!
7. Si la medicina hace que su niño o niña se sienta mal 	Dele Zofran o algún otro medicamento contra las Náuseas 20 minutos antes de que tome su 6-MP.

Su doctor puede indicarle a su niño o niña que deje de tomar 6-MP por razones médicas. Hable con su doctor o enfermera si tiene alguna duda sobre los medicamentos de su niño o niña. Llámenos al (214) 456-2382 si su niño o niña tiene problemas tomando su 6-MP. ¡No espere hasta la próxima cita!

¡Gracias!

Appendix W

6-MP Adherence Educational Handout (Patient version, English)

A.L.L. MAINTENANCE

You have acute lymphoblastic leukemia or ALL and you are in the maintenance phase of therapy. This means you have to take a medicine called 6-MP every day. Sadly, missing 18 or more days in a year can make it easier for the cancer to come back.

Here are some ideas to help you remember to take your medication every day.

1. **Find a buddy!**		Your buddy can help you remember to take your 6MP. Ask your buddy to watch you take your medicine so there's no doubt you've accomplished your mission! Some good buddies might be a parent, grandparent, or a school nurse.
2. **Set an alarm or reminder for the same time every day.**		Having a set schedule will help you remember to always take the medicine.
3. **If you are not home**		Bring a water bottle and pillbox with the 6-MP so you can take the medicine on the go!
4. **Keep a calendar**		Sometimes it's hard to remember if you already took your medicine. Keeping a calendar can help you! Check off every time you take your medicine. You can also use a pillbox with the days of the week. If you need a calendar or a pillbox, ask a nurse at CCBD to give you one!
5. **Ask for help!**		Ask someone to call you every day to make sure you took your medicine.
6. **You can eat or drink before or after you take the medicine.**		The most important thing is that you take it!
7. **If the medicine makes you feel sick**		Take Zofran or another anti-nausea medicine 20 minutes before you take the 6-MP.

The doctor may tell you to stop taking 6-MP for medical reasons. Always talk to your doctor or nurse if you have any questions about your medication. Call us at (214) 456-2382 if you have trouble taking the 6-MP. Do not wait until your next appointment!

Thank you!

Appendix X

6-MP Adherence Educational Handout (Patient version, Spanish)

A.L.L. MAINTENANCE

Tu tienes leucemia linfoblástica aguda o ALL y estás en la fase de terapia de mantenimiento. Esto significa que tienes que tomar un medicamento llamado 6-MP todos los dia. Lamentablemente, si faltas un pequeño numero de dosis que tienes que tomas es más fácil que la leucemia vuelva.

Estas son algunas ideas para ayudarte a acordar de tomar tu medicamento todos los días.

1. **¡Encuentra a un compañero!**		Tu compañero puede recordarte que tomes tu 6MP. ¡Pídele a tu compañero que te vea tomar tu medicina para que no haya duda que has cumplido tu misión! Algunos compañeros buenos pueden ser un padre, un abuelo, o una enfermera de la escuela.
2. **Coloca una alarma o recordatorio para la misma hora cada día**		Tener un horario establecido te ayudará a acordarte de tomar siempre el medicamento.
3. **Si no vas a estar en tu casa**		Trae una botella de agua y una caja de píldoras con tu 6-MP para que puedas tomar la medicina en la calle!
4. **Ten un calendario**		A veces es difícil recordarse si ya te tomaste tu medicina. Tener un calendario puede ayudarte! Marca cada vez que se tomas tu medicina. También puedes usar una caja de píldoras con los días de la semana. Si necesitas un calendario o una caja de píldoras, pídele a una enfermera en el CCBD que te de uno!
5. **Pide ayuda!**		Pídele a alguien que te llame todos los días para asegurarse de que te tomaste la medicina.
6. **Puedes comer o beber antes o después de tomar la medicina.**		Lo más importante es que la tomes!
7. **Si la medicina te hace sentir mal**		Toma Zofran o algún otro medicamento contra las náuseas 20 minutos antes de tomar tu 6-MP.

Tu doctor puede indicarte que dejes de tomar 6-MP por razones médicas. Habla con tu doctor o enfermera si tienes alguna duda sobre tus medicamentos. Llámanos al (214) 456-2382 si tienes problemas tomando tu 6-MP. ¡No esperes hasta tu próxima cita!

¡Gracias!

BIBLIOGRAPHY

Achenbach, T. M. (2006). As others see us: Clinical and research implications of cross-informant correlations for psychopathology. *Current directions in psychological science*, *15*(2), 94-98.

Ahluwalia, J. S., Okuyemi, K., Nollen, N., Choi, W. S., Kaur, H., Pulvers, K., et al. (2006). The /effects of nicotine gum and counseling among African American light smokers: A 2 x 2 factorial design. Addiction, 101, 883-891.

Ajzen, I. (1991). The theory of planned behavior. *Organizational behavior and human decision processes*, *50*(2), 179-211.

Alsous, M., Farha, R. A., Alefishat, E., Al Omar, S., Momani, D., Gharabli, A., ... & Rihani, R. (2017). Adherence to 6-Mercaptopurine in children and adolescents with Acute Lymphoblastic Leukemia. *PloS one*, *12*(9), e0183119.

Armit, C. M., Brown, W. J., Marshall, A. L., Ritchie, C. B., Trost, S. G., Green, A., & Bauman, A. E. (2009). Randomized trial of three strategies to promote physical activity in general practice. *Preventive medicine*, *48*(2), 156-163.

Attkisson, C. C., & Zwick, R. (1982). The Client Satisfaction Questionnaire: Psychometric properties and correlations with service utilization and psychotherapy outcome. *Evaluation and program planning*, *5*(3), 233-237.

Bandura, A. (2001). Social cognitive theory: An agentic perspective. *Annual review of psychology*, *52*(1), 1-26.

Bakker, J. P., Wang, R., Weng, J., Aloia, M. S., Toth, C., Morrical, M. G., ... & Ware, J. H. (2016). Motivational enhancement for increasing adherence to CPAP: a randomized controlled trial. *Chest*, *150*(2), 337-345.

Bartlett, M. S. (1954). A note on the multiplying factors for various χ 2 approximations. *Journal of the Royal Statistical Society. Series B (Methodological)*, 296-298.

Bender, B., Wamboldt, F., O'Connor, S. L., Rand, C., Szefler, S., Milgrom, H., & Wamboldt, M. Z. (2000). Measurement of children's asthma medication adherence by self report, mother report, canister weight, and Doser CT. *Annals of Allergy, Asthma & Immunology*, *85*(5), 416-421.

Bennett, D. A. (2001). How can I deal with missing data in my study?. *Australian and New Zealand journal of public health*, *25*(5), 464-469.

Bennett, J. A., Perrin, N. A., Hanson, G., Bennett, D., Gaynor, W., Flaherty-Robb, M., et al. (2005). Healthy aging demonstration project: Nurse coaching for behavior change in older adults. Research in Nursing and Health, 28, 187-197.

Bernstein, J., Bernstein, E., Tassiopoulos, K., et al. (2005). Brief motivational intervention at a clinic visit reduces cocaine and heroin use. *Drug and Alcohol Dependence, 77*(1), 49-59.

Bhatia, S., Landier, W., Hageman, L., Kim, H., Hanby, C., Nancy, K., ... & Mascarenhas, L. (2012). Nonadherence to Oral 6-Mercaptopurine (6MP) in a Multi-Ethnic Cohort of Children with Acute Lymphoblastic Leukemia (ALL) and Its Impact On Relapse–a Children's Oncology Group (COG) Study (AALL03N1).

Bhatia, S., Landier, W., Shangguan, M., Hageman, L., Schaible, A. N., Carter, A. R., ... & Mascarenhas, L. (2012). Nonadherence to oral mercaptopurine and risk of relapse in Hispanic and non-Hispanic white children with acute lymphoblastic leukemia: a report from the children's oncology group. *Journal of Clinical Oncology*, *30*(17), 2094-2101.

Bhatia, S., Landier, W., Hageman, L., Kim, H., Chen, Y., Crews, K. R., ... & Maloney, K. W. (2014). 6MP adherence in a multiracial cohort of children with acute lymphoblastic leukemia: a Children9s Oncology Group study. *Blood*, *124*(15), 2345-2353.

Bhatia, S., Sather, H. N., Heerema, N. A., Trigg, M. E., Gaynon, P. S., & Robison, L. L. (2002). Racial and ethnic differences in survival of children with acute lymphoblastic leukemia. *Blood*, *100*(6), 1957-1964.

Bloom, A. W. (2016). Advances in substance abuse prevention and treatment interventions among racial, ethnic, and sexual minority populations, *Alcohol Research, 38*(1), 47-54.

Blotcky, A. D., Cohen, D. G., Conatser, C., & Klopovich, P. (1985). Psychosocial characteristics of adolescents who refuse cancer treatment. *Journal of Consulting and Clinical Psychology*, *53*(5), 729.

Borrelli, B., Tooley, E. M., & Scott-Sheldon, L. A. (2015). Motivational interviewing for parent-child health interventions: a systematic review and meta-analysis. *Pediatric dentistry*, *37*(3), 254-265.

Brodie, D. A., & Inoue, A. (2005). Motivational interviewing to pro- mote physical activity for people with chronic heart failure. Journal of Advanced Nursing, 50, 518-527.

Brown, R. A., Abrantes, A. M., Minami, H., et al. (2015). Motivational interviewing to reduce substance use in adolescents with psychiatric comorbidity. *Journal of Substance Abuse Treatment, 59*, 20-29.

Bush, P. J., & Iannotti, R. J. (1990). A children's health belief model. *Medical care*.

Cane, J., O'Connor, D., & Michie, S. (2012). Validation of the theoretical domains framework for use in behaviour change and implementation research. *Implementation science*, *7*(1), 37.

Carr, E. S., & Smith, Y. (2014). The poetics of therapeutic practice: motivational interviewing and the powers of pause. *Culture, Medicine, and Psychiatry*, *38*(1), 83-114.

Carroll, K. M., Ball, S. A., Nich, C., Martino, S., Frankforter, T. L, Farentinos, C, et al. (2005). Motivational interviewing to improve treatment engagement and outcome in individuals seeking treatment for substance abuse: a multisite effectiveness study. Drug and Alcohol Dependence, 81, 301-312.

Carroll, K. M., Ball, S. A., Nich, C., Martino, S., Frankforter, T. L., Farentinos, C., ... & Polcin, D. (2006). Motivational interviewing to improve treatment engagement and outcome in individuals seeking treatment for substance abuse: A multisite effectiveness study. *Drug and alcohol dependence*, *81*(3), 301-312.

Carter, P. M., Walton, M. A., Zimmerman, M. A., et al. (2016). Efficacy of a universal brief intervention for violence among urban emergency department youth. *Academics in Emergency Medicine,* e-publication ahead of print.

Cattell, R. B. (1966). The scree test for the number of factors. *Multivariate behavioral research*, *1*(2), 245-276.

Channon, S., Smith, V. J., & Gregory, J. W. (2003). A pilot study of motivational interviewing in adolescents with diabetes. *Archives of disease in childhood*, *88*(8), 680-683.

Channon, S. J., Huws-Thomas, M. V., Rollnick, S., Hood, K., Can-nings-John, R. L., Rogers, C., et al. (2007). A multicenter randomized controlled trial of motivational interviewing in teenagers with diabetes. Diabetes Care, 30, 1390-1395.

Children's Oncology Group (2011). *Acute lymphoblastic leukemia*. Retrieved from https://www.childrensoncologygroup.org/index.php/acute-lymphoblastic-leukemia.

Chrzanowska, M., Kolecki, P., Duczmal-Cichocka, B., & Fiet, J. (1999). Metabolites of mercaptopurine in red blood cells: a relationship between 6-thioguanine nucleotides and 6-methylmercaptopurine metabolite concentrations in children with lymphoblastic leukemia. *European journal of pharmaceutical sciences*, *8*(4), 329-334.

Clark, G. I., & Egan, S. J. (2015). The Socratic method in cognitive behavioural therapy: A narrative review. *Cognitive Therapy and Research*, *39*(6), 863-879.

Cohen, J. (1988). Statistical power analysis for the behavioral sciences. Hillsdale, NJ: Lawrence Erlbaum Associates.

Colby, S. M., Monti, P. M., Tevyaw, T. O. L., Barnett, N. P., Spirito, A., Rohsenow, D. J., ... & Lewander, W. (2005). Brief motivational intervention for adolescent smokers in medical settings. *Addictive behaviors*, *30*(5), 865-874.

Cooper, S. L., & Brown, P. A. (2015). Treatment of pediatric acute lymphoblastic leukemia. *Pediatric clinics of North America*, *62*(1), 61.

Cromer, B. A., & Tarnowski, K. J. (1989). Noncompliance in adolescents: a review. *Journal of Developmental & Behavioral Pediatrics*, *10*(4), 207-215.

Cushing, C. C., Jensen, C. D., Miller, M. B., & Leffingwell, T. R. (2014). Meta-analysis of motivational interviewing for adolescent health behavior: Efficacy beyond substance use.

Davies, H. A., Lennard, L., & Lilleyman, J. S. (1993). Variable mercaptopurine metabolism in children with leukaemia: a problem of non-compliance?. *BMJ: British Medical Journal*, *306*(6887), 1239.

Dean, S., Britt, E., Bell, E., Stanley, J., & Collings, S. (2016). Motivational interviewing to enhance adolescent mental health treatment engagement: a randomized clinical trial. *Psychological medicine*, *46*(9), 1961-1969.

De Luca, S. M., Blosnich, J. R., Hentschel, E. A., King, E., & Amen, S. (2016). Mental health care utilization: How race, ethnicity and veteran status are associated with seeking help. *Journal of Community Mental Health, 52*(2), 174-179.

De Los Reyes, A. (2011). Introduction to the special section: More than measurement error: Discovering meaning behind informant discrepancies in clinical assessments of children and adolescents. *Journal of Clinical Child & Adolescent Psychology*, *40*(1), 1-9.

De Los Reyes, A. (2013). Strategic objectives for improving understanding of informant discrepancies in developmental psychopathology research. *Development and psychopathology*, *25*(3), 669-682.

Doring, N., Ghaderi, A., Bohman, B., et al. (2016). Motivational interviewing to prevent childhood obesity: A cluster RCT. *Pediatrics, 137*(5). Doi:10.1542/peds.2015-3104.

Erickson, S. J., Gerstle, M., & Feldstein, S. W. (2005). Brief interventions and motivational interviewing with children, adolescents, and their par- ents in pediatric health care settings. *Archives of Pediatric Adolescent Medicine, 159,* 1173–1180. doi:10.1001/archpedi.159.12.1173

Faith, M. A., El-Behadli, A. F., Frazee, L. A., Pratt, C. D., & Stromberg, S. (2019). Parents' emotion socialization beliefs moderate relations between parent and patient coping, but not sibling coping, with pediatric cancer. *Psycho-oncology*.

Farley, J., Hines, S., Musk, A., Ferrus, S., & Tepper, V. (2003). Assessment of adherence to antiviral therapy in HIV-infected children using the Medication Event Monitoring System, pharmacy refill, provider assessment, caregiver self-report, and appointment keeping. *Journal of acquired immune deficiency syndromes (1999)*, *33*(2), 211-218.

Faul, F., Erdfelder, E., Lang, A.-G., & Buchner, A. (2007). G*Power 3: A flexible statistical power analysis program for the social, behavioral, and biomedical sciences. *Behavior Research Methods*, *39*, 175-191

Field, C., & Caetano, R. (2010). The role of ethnic matching between patient and provider on the effectiveness of brief alcohol interventions with Hispanics. *Alcoholism: Clinical and Experimental Research*, *34*(2), 262-271.

Flesch, R. (1948). A new readability yardstick. *Journal of applied psychology*, *32*(3), 221.

Frias, J., Virdi, N., Raja, P., Kim, Y., Savage, G., & Osterberg, L. (2017). Effectiveness of digital medicines to improve clinical outcomes in patients with uncontrolled hypertension and type 2 diabetes: prospective, open-label, cluster-randomized pilot clinical trial. *Journal of medical Internet research*, *19*(7), e246.

Funderburk, J. S., Shepardson, R. L., Wray, J., Acker, J., Beehler, G. P., Possemato, K., ... & Maisto, S. A. (2018). Behavioral medicine interventions for adult primary care settings: A review. *Families, Systems, & Health*, *36*(3), 368.

Gayes, L. A., & Steele, R. G. (2014). A meta-analysis of motivational interviewing interventions for pediatric health behavior change.

Gold, M. A., Tzilos, G. K., Stein, L. A., et al. (2016). A randomized controlled trial to compare computer-assisted motivational intervention with didactic educational counseling to reduce unprotected sex in female adolescents. *Journal of Pediatric Adolescent Gynecology, 29*(1), 26-32.

Gregory, J. W. & Channon, S. (2009). Motivational interviewing to improve blood-glucose control in childhood diabetes. *Paediatrics and Child Health, 19*(7), 331-334.

Grenard, J. L., Ames, S. L., Wiers, R. W., Thush, C., Stacy, A.W., & Sussman, S. (2007). Brief intervention for substance use among at risk adolescents: A pilot study. Journal of Adolescent Health, 40, 188-191.

Griner, D., & Smith, T. B. (2006). Culturally adapted mental health intervention: A meta-analytic review.

Hamrin, V. & Iennaco, J. D. (2016). Evaluation of motivational interviewing to improve psychotropic medication adherence in adolescents. *Journal of Child and Adoelscent Psychopharmacology*, e-publication ahead of print.

Harms, D. O., Göbel, U., Spaar, H. J., Graubner, U. B., Jorch, N., Gutjahr, P., & Janka-Schaub, G. E. (2003). Thioguanine offers no advantage over mercaptopurine in maintenance treatment of childhood ALL: results of the randomized trial COALL-92. *Blood*, *102*(8), 2736-2740.

Hawwa, A. F., Millership, J. S., Collier, P. S., McCarthy, A., Dempsey, S., Cairns, C., & McElnay, J. C. (2009). The development of an objective methodology to measure medication adherence to oral thiopurines in paediatric patients with acute lymphoblastic leukaemia—an exploratory study. *European journal of clinical pharmacology*, *65*(11), 1105-1112.

Hayward, M. D., Miles, T. P., Crimmins, E. M., & Yang, Y. (2000). The significance of socioeconomic status in explaining the racial gap in chronic health conditions. *American sociological review*, 910-930.

Hettema, J., Steele, J., & Miller, W. R. (2005). Motivational interviewing. *Annual Review of Clinical Psychology, 1*, 91-111.Hunger, S. P., & Mullighan, C. G. (2015). Acute lymphoblastic leukemia in children. *New England Journal of Medicine*, *373*(16), 1541-1552.

Hodgins, D. C. Currie, S. R., & El-Guebaly, N. (2001). Motivational enhancement and self-help treatments for problem gambling. Jour- nal of Consulting and Clinical Psychology, 69, 50-57.

Hodgins, D. C., Currie, S. El-Guebaly, N., & Peden, N. (2004). Brief motivational treatment for problem gambling: A 24-month follow- up. Psychology of Addictive Behaviors, 18, 293-296.

Hunger, S. P., & Mullighan, C. G. (2015). Acute lymphoblastic leukemia in children. *New England Journal of Medicine*, *373*(16), 1541-1552.

Hunger, S. P., Lu, X., Devidas, M., Camitta, B. M., Gaynon, P. S., Winick, N. J., ... & Carroll, W. L. (2012). Improved survival for children and adolescents with acute lymphoblastic leukemia between 1990 and 2005: a report from the children's oncology group. *Journal of Clinical Oncology*, *30*(14), 1663.

Hutcheson, G. D., & Sofroniou, N. (1999). *The multivariate social scientist: Introductory statistics using generalized linear models*. Sage.

Ige, T. J., DeLeon, P., & Nabors, L. (2017). Motivational interviewing in an obesity prevention program for children. *Health promotion practice*, *18*(2), 263-274.

Ingerski, L. M., Hente, E. A., Modi, A. C., & Hommel, K. A. (2011). Electronic measurement of medication adherence in pediatric chronic illness: a review of measures. *The Journal of pediatrics*, *159*(4), 528-534.

Jelsma, J. G., Mertens, V. C., Forsberg, L., & Forsberg, L. (2015). How to measure motivational interviewing Fidelity in randomized controlled trials: practical recommendations. *Contemporary clinical trials*, *43*, 93-99.

Jensen, C. D., Cushing, C. C., Aylward, B. S., Craig, J. T., Sorell, D. M., & Steele, R. G. (2011). Effectiveness of motivational interviewing interventions for adolescent substance use

behavior change: a meta-analytic review. *Journal of consulting and clinical psychology*, *79*(4), 433.

Johnston, B. D., Rivara, F. P., Droesch, R. M., Dunn, C., & Copass, M. K. (2007). Behavior change counseling in the emer- gency department to reduce injury risk: A randomized controlled trial. Pediatrics, 110, 267-274.

Juarez, P., Walters, S. T., Daugherty, M., & Radi, C. (2006). A randomized trial of motivational interviewing and feedback with heavy drinking college students. *Journal of Drug Education*, *36*(3), 233-246.

Kazak, A. E., Alderfer, M., Rourke, M. T., Simms, S., Streisand, R., & Grossman, J. R. (2004). Posttraumatic stress disorder (PTSD) and posttraumatic stress symptoms (PTSS) in families of adolescent childhood cancer survivors. *Journal of pediatric psychology*, *29*(3), 211-219.

Kenna, L. A., Labbé, L., Barrett, J. S., & Pfister, M. (2005). Modeling and simulation of adherence: approaches and applications in therapeutics. *The AAPS journal*, *7*(2), E390-E407.

Kennard, B. D., Stewart, S. M., Olvera, R., Bawdon, R. E., Lewis, C. P., & Winick, N. J. (2004). Nonadherence in adolescent oncology patients: preliminary data on psychological risk factors and relationships to outcome. *Journal of Clinical Psychology in Medical Settings*, *11*(1), 31-39.

Kersey, J. H. (1997). Fifty years of studies of the biology and therapy of childhood leukemia. *Blood*, *90*(11), 4243-4251.

Kolmodin-MacDonnel, K., Naar, S., Gibson-Scipio, W., Lam, P., & Secord, E. (2016). The Detroit Young Adult Asthma Project: Pilot of a technology-based medication adherence intervention for African-American emerging adults. *Journal of Adolescent Health*, e-publication ahead of print.

Kreman, R., Yates, B. C., Agrawal, S., Fiandt, K., Briner, W., & Shurmur, S. (2006). The effects of motivational interviewing on physiological outcomes. Applied Nursing Research, 19, 167-170.

Kristjanson, L. J., & Ashcroft, T. (1994). The family's cancer journey: A literature review. *Cancer Nursing*, *17*(1), 1-17.

Kyngäs, H., Duffy, M. E., & Kroll, T. (2000). Conceptual analysis of compliance. *Journal of clinical nursing*, *9*(1), 5-12.

Kyngäs, H. A., Kroll, T., & Duffy, M. E. (2000). Compliance in adolescents with chronic diseases: a review1. *Journal of Adolescent Health*, *26*(6), 379-388.

La Greca, A. M., & Schuman, W. B. (1995). Adherence to prescribed medical regimens. In M. C. Roberts (Ed.), *Handbook of pediatric psychology* (pp. 55-83). New York: Guilford Press.

Lancaster, D., Lennard, L., & Lilleyman, J. S. (1997). Profile of non-compliance in lymphoblastic leukaemia. *Archives of disease in childhood*, *76*(4), 365-366.

Landier, W., Chen, Y., Hageman, L., Kim, H., Bostrom, B. C., Casillas, J. N., ... & Ritchey, A. K. (2017). Comparison of self-report and electronic monitoring of 6MP intake in childhood ALL: a Children's Oncology Group study. *Blood*, *129*(14), 1919-1926.

Lansky, S. B., Smith, S. D., Cairns, N. U., & Cairns Jr, G. F. (1983). Psychological correlates of compliance. *Journal of Pediatric Hematology/Oncology*, *5*(1), 87-92.

Lee, C. S., López, S. R., Cobly, S. M., Tejada, M., García-Coll, C., & Smith, M. (2006). Social processes underlying acculturation: a study of drinking behavior among immigrant Latinos in the Northeast United States. *Contemporary drug problems*, *33*, 585.

Lee, C. S., López, S. R., Hernández, L., Colby, S. M., Caetano, R., Borrelli, B., & Rohsenow, D. (2011). A cultural adaptation of motivational interviewing to address heavy drinking among Hispanics. *Cultural diversity and ethnic minority psychology*, *17*(3), 317.

Lee, C. S., López, S. R., Colby, S. M., Rohsenow, D., Hernández, L., Borrelli, B., & Caetano, R. (2013). Culturally adapted motivational interviewing for Latino heavy drinkers: Results from a randomized clinical trial. *Journal of ethnicity in substance abuse*, *12*(4), 356-373.

Lee, C. S., Tavares, T., Popat-Jain, A., & Naab, P. (2015). Assessing treatment fidelity in a cultural adaptation of motivational interviewing. *Journal of ethnicity in substance abuse*, *14*(2), 208-219.

Lee, C. S., Colby, S. M., Magill, M., Almeida, J., Tavares, T., & Rohsenow, D. J. (2016). A randomized controlled trial of culturally adapted motivational interviewing for Hispanic heavy drinkers: Theory of adaptation and study protocol. *Contemporary clinical trials*, *50*, 193-200.

Lee, C. S., Longabaugh, R., Baird, J., Streszak, V., Nirenberg, T., & Mello, M. (2015). Participant report of therapist-delivered active ingredients in a telephone-delivered brief motivational intervention predicts taking steps towards change. *Addiction research & theory*, *23*(5), 421-428.

Lennard, L., Welch, J., & Lilleyman, J. S. (1995). Intracellular metabolites of mercaptopurine in children with lymphoblastic leukaemia: a possible indicator of non-compliance?. *British Journal of Cancer*, *72*(4), 1004.

Li, L., Zhu, S., Tsw, N., Tse, S., & Wong, P. (2016). Effectiveness of motivational interviewing to reduce illicit drug use in adolescents: A systematic review and meta-analysis. *Addiction,* 111(5), 795-805.

Lii, E. F., & Sallan, S. E. (1978). Acute lymphoblastic leukemia: treatment. *Cancer*, *42*(S2), 828-838.

Lilleyman, J. S., & Lennard, L. (1994). Mercaptopurine metabolism and risk of relapse in childhood lymphoblastic leukemia. The Lancet, 343, 1188–1190.

Lim, J. Y. S., Bhatia, S., Robison, L. L., & Yang, J. J. (2014). Genomics of racial and ethnic disparities in childhood acute lymphoblastic leukemia. *Cancer*, *120*(7), 955-962.

Linabery, A. M., & Ross, J. A. (2008). Trends in childhood cancer incidence in the US (1992–2004). *Cancer*, *112*(2), 416-432.

Linet, M. S., Ries, L. A., Smith, M. A., Tarone, R. E., & Devesa, S. S. (1999). Cancer surveillance series: recent trends in childhood cancer incidence and mortality in the United States. *Journal of the National Cancer Institute*, *91*(12), 1051-1058.

Locatelli, F., Moretta, F., & Rutella, S. (2013). Management of relapsed acute lymphoblastic leukemia in childhood with conventional and innovative approaches. *Current opinion in oncology*, *25*(6), 707-715.

Longabaugh, R., Zweben, A., LoCastro, J. S., & Miller, W. R. (2005). Origins, issues and options in the development of the combined behavioral intervention. *Journal of Studies on Alcohol Supplement, 15*, 179-187.

Lundahl, B. W., Kunz, C., Brownell, C., Tollefson, D., & Burke, B. L. (2010). A meta-analysis of motivational interviewing: Twenty-five years of empirical studies. *Research on Social Work Practice*, *20*(2), 137-160.

Maltby, N., & Tolin, D. F. (2005). A brief motivational intervention for treatment-refusing OCD patients. Cognitive Behavioral Therapy, 34, 176-184.

Marlow, D., & Crowne, D. P. (1961). Social desirability and response to perceived situational demands. *Journal of consulting psychology*, *25*(2), 109.

Martins, R. K., & McNeil, D. W. (2009). Review of motivational interviewing in promoting health behaviors. *Clinical psychology review*, *29*(4), 283-293.

McGrady, M. E., Ryan, J. L., Gutiérrez‐Colina, A. M., Fredericks, E. M., Towner, E. K., & Pai, A. L. (2015). The impact of effective paediatric adherence promotion interventions: Systematic review and meta‐analysis. *Child: care, health and development*, *41*(6), 789-802.

Microsoft Corporation. (2010). Microsoft® Word for Mac 2011. Version 14.5.5.

Michie, S. (2005). Changing behavior: theoretical development needs protocol adherence.

Michie, S., Van Stralen, M. M., & West, R. (2011). The behaviour change wheel: a new method for characterising and designing behaviour change interventions. *Implementation science*, *6*(1), 42.

Miller, W. R. (1983). Motivational interviewing with problem drinkers. *Behavioural and Cognitive Psychotherapy*, *11*(2), 147-172.

Miller, W. R. (Ed.) (2004). *Combined Behavioral Intervention manual: A clinical research guide for therapists treatment people with alcohol abuse and dependence* (Vol. 1). Bethesda, MD: National Institute on Alcohol Abuse and Alcoholism.

Miller, W. R., & Rollnick, S. (2012). *Motivational interviewing: Helping people change*. Guilford press.

Miller, W. R., & Rollnick, S. (2014). The effectiveness and ineffectiveness of complex behavioral interventions: impact of treatment fidelity. *Contemporary clinical trials*, *37*(2), 234-241.

Miller, W. R., & Rose, G. S. (2010). Motivational interviewing in relational context. *American Psychologist, 65*(4), 298-299. http://dx.doi.org/10.1037/a0019487

Modi, A. C., Pai, A. L., Hommel, K. A., Hood, K. K., Cortina, S., Hilliard, M. E., ... & Drotar, D. (2012). Pediatric self-management: a framework for research, practice, and policy. *Pediatrics*, *129*(2), e473-e485.

Mohammadi, T. M., Hajizamani, A., & Bozorgmehr, E. (2015). Improving oral Health statys of preschool children using motivational interviewing method. *Journal of Dental Research, 12*(5), 476-481.

Moore, T. (2008). *Rethinking universal and targeted services*. Parkville, VIC, Australia: Centre for Community Child Health.

Morgenstern, J., Kuerbis, A., Amrhein, P., Hail, L., Lynch, K., & McKay, J. R. (2012). Motivational interviewing: a pilot test of active ingredients and mechanisms of change. *Psychology of Addictive Behaviors*, *26*(4), 859.

Morrison, W. B. (2010). Cancer chemotherapy: an annotated history. *Journal of veterinary internal medicine*, *24*(6), 1249-1262.

Moyers, T. B., Manuel, J. K., Ernst, D. (2014). Motivational interviewing treatment integrity coding manual 4.1. Unpublished manual.

Naar-King, S., Wright, K., Parsons, J. T., Frey, M., Templin, T., Lam, P., et al. (2006). Healthy choices: Motivational enhancement therapy for health risk behaviors in HIV-positive youth. AIDS Edu- cation and Prevention, 18, 1-11.

Nyberg, G., Norman, A., Sundblom, E., Zeebari, A., & Elinder, L. S. (2016). Effectiveness of a universal parental support programme to promote health behaviours and prevent overweight and obesity in 6-year-old children in disadvantaged areas, the Healthy School Start Study II, a cluster randomized controlled trial. *International Journal of Behavioral Nutrition and Physical Activity, 21*(13): 4.

Ogedegbe, G., Chaplin, W., Schoenthaler, A., Statman, D., Berger, D., Richardson, T., ... & Allegrante, J. P. (2008). A practice-based trial of motivational interviewing and adherence in hypertensive African Americans. *American journal of hypertension*, *21*(10), 1137-1143.

Osborne, J. W., & Costello, A. B. (2004). Sample size and subject to item ratio in principal components analysis. *Practical assessment, research & evaluation*, *9*(11), 8.

Osterberg, L., & Blaschke, T. (2005). Adherence to medication. *New England journal of medicine*, *353*(5), 487-497.

Pai, A. L., Drotar, D., & Kodish, E. (2008). Correspondence between objective and subjective reports of adherence among adolescents with acute lymphoblastic leukemia. *Children's Health Care*, *37*(3), 225-235.

Patenaude, A. F., & Kupst, M. J. (2005). Psychosocial functioning in pediatric cancer. *Journal of pediatric psychology*, *30*(1), 9-27.

Peugh, J. L., & Enders, C. K. (2004). Missing data in educational research: A review of reporting practices and suggestions for improvement. *Review of educational research*, *74*(4), 525-556.

Prestwich, A., Webb, T. L., & Conner, M. (2015). Using theory to develop and test interventions to promote changes in health behaviour: evidence, issues, and recommendations. *Current Opinion in Psychology*, *5*, 1-5.

Prilleltensky, I., & Nelson, G. (2000). Promoting child and family wellness: Priorities for psychological and social interventions. *Journal of Community & Applied Social Psychology*, *10*(2), 85-105.

Prochaska, J. O., & Velicer, W. F. (1997). The transtheoretical model of health behavior change. *American journal of health promotion*, *12*(1), 38-48.

Relling, M. V., Hancock, M. L., Boyett, J. M., Pui, C. H., & Evans, W. E. (1999). Prognostic importance of 6-mercaptopurine dose intensity in acute lymphoblastic leukemia. *Blood*, *93*(9), 2817-2823.

Resnicow, K., Harris, D., Wasserman, R., Schwartz, R. P., Perez-Rosas, V., Mihalcea, R., & Snetselaar, L. (2016). Advances in motivational interviewing for pediatric obesity:

Results of the brief motivational interviewing to reduce body mass index trial and future directions. *Pediatric Clinics in North America, 63*(3), 539-562.

Riekert, K. A., & Rand, C. S. (2002). Electronic monitoring of medication adherence: when is high-tech best?. *Journal of Clinical Psychology in Medical Settings*, *9*(1), 25-34.

Riekert, K. A., Borrelli, B., Bilderback, A., & Rand, C. S. (2011). The development of a motivational interviewing intervention to promote medication adherence among inner-city, African-American adolescents with asthma. *Patient education and counseling*, *82*(1), 117-122.

Rifas-Shiman, S. L., Taveras, E. M., Gortmaker, S. L., et al. (2016). Two-year follow-up of a primary care-based intervention to prevent and manage childhood obesity: The High Five for Kids study. *Pediatric Obesity,* e-publication ahead of print.

Roberts, M. C., & Steele, R. G. (Eds.). (2010). *Handbook of pediatric psychology*. Guilford Press.

Rogers, C. R. (1995). What understanding and acceptance mean to me. *Journal of Humanistic Psychology*, *35*(4), 7-22.

Rohan, J. M., Fukuda, T., Alderfer, M. A., Wetherington Donewar, C., Ewing, L., Katz, E. R., ... & Drotar, D. (2016). Measuring Medication Adherence in Pediatric Cancer: An Approach to Validation. *Journal of pediatric psychology*, *42*(2), 232-244.

Rollnick, S., Heather, N., & Bell, A. (1992). Negotiating behaviour change in medical settings: the development of brief motivational interviewing. *Journal of Mental Health*, *1*(1), 25-37.

Safeer, R. S., & Keenan, J. (2005). Health literacy: the gap between physicians and patients. *Am Fam Physician*, *72*(3), 463-468.Sample, P. (1986). Compliance of pediatric and adolescent cancer patients. *Cancer*, *58*, 1179-1184.

Sanci, L., Chondros, P., Sawyer, S., et al. (2015). Responding to Young people's Health risks in primnary care: A cluster randomised trial of training clinicians in screening and motivational interviewing. *PLoS One, 10*(9):e0137581.

Sayal, K. (2006). Annotation: Pathways to care for children with mental health problems. *Journal of Child Psychology and Psychiatry*, *47*(7), 649-659.

Schafer, J. L., & Olsen, M. K. (1998). Multiple imputation for multivariate missing-data problems: A data analyst's perspective. *Multivariate behavioral research*, *33*(4), 545-571.

Schmiegelow, K., Nielsen, S. N., Frandsen, T. L., & Nersting, J. (2014). Mercaptopurine/methotrexate maintenance therapy of childhood acute lymphoblastic

leukemia: clinical facts and fiction. *Journal of pediatric hematology/oncology*, *36*(7), 503.

Schmiegelow, K., Schrøder, H., Gustafsson, G., Kristinsson, J., Glomstein, A., Salmi, T., & Wranne, L. (1995). Risk of relapse in childhood acute lymphoblastic leukemia is related to RBC methotrexate and mercaptopurine metabolites during maintenance chemotherapy. Nordic Society for Pediatric Hematology and Oncology. *Journal of Clinical Oncology*, *13*(2), 345-351.

Schlomer, G. L., Bauman, S., & Card, N. A. (2010). Best practices for missing data management in counseling psychology. *Journal of Counseling psychology*, *57*(1), 1.

Seibel, N. L. (2008). Treatment of acute lymphoblastic leukemia in children and adolescents: peaks and pitfalls. *ASH Education Program Book*, *2008*(1), 374-380.

Seibel, N. L. (2008). Acute lymphoblastic leukemia: an historical perspective. *ASH Education Program Book*, *2008*(1), 365-365.

Sellman, J. D., Sullivan, P. F., Dore, G. M., Adamson, S. J., & MacEwan, I. (2001). A randomized controlled trial of motivational enhancement therapy (MET) for mild to moderate alcohol depen- dence. Journal of Studies on Alcohol, 62, 389-396.

Siegel, D. A., Henley, S. J., Li, J., Pollack, L. A., Van Dyne, E. A., & White, A. (2017). Rates and trends of pediatric acute lymphoblastic leukemia—United States, 2001–2014. *MMWR. Morbidity and mortality weekly report*, *66*(36), 950.

Simons, L. E., & Blount, R. L. (2007). Identifying barriers to medication adherence in adolescent transplant recipients. *Journal of Pediatric Psychology*, *32*(7), 831-844.

Sims, J., Smith, F., Duffy, A., & Hilton, S. (1999). The vagaries of self-reports of physical activity: a problem revisited and addressed in a study of exercise promotion in the over 65s in general practice. *Family Practice*, *16*(2), 152-157.

Smith, F. O., & O'brien, M. M. (2015). Thiopurines for the treatment of acute lymphoblastic leukemia in children: What's old is new. *JAMA oncology*, *1*(3), 281-282.

Smith, S. D., Rosen, D., Trueworthy, R. C., & Lowman, J. T. (1979). A reliable method for evaluating drug compliance in children with cancer. *Cancer*, *43*(1), 169-173.

Smith, M. A., Seibel, N. L., Altekruse, S. F., Ries, L. A., Melbert, D. L., O'Leary, M., ... & Reaman, G. H. (2010). Outcomes for children and adolescents with cancer: challenges for the twenty-first century. *Journal of clinical oncology*, *28*(15), 2625-2634.

Soria, R., Legido, A., Escolano, C., et al. (2006). A randomised controlled trial of motivational interviewing for smoking cessation. *British Journal of General Practice, 56*(531), 768-774.

Stanton M. Motivational Interviewing and the Social Context (2010). *American Psychologist*, 65(4):297–298.

Steinberg, M. L., Ziedonis, D. M., Krejci, J. A., & Brandon, T. H. (2004). Motivational interviewing with personalized feedback: A brief intervention for motivating smokers with schizophrenia to seek treatment for tobacco dependence. Journal of Consulting and Clinical Psychology, 72, 723-728.

Stotts, A. L., DeLaune, K. A., Schmitz, J. M., & Grabowski, J. (2004). Impact of a motivational intervention on mechanisms of change in low-income pregnant smokers. Addictive Behaviors, 29, 1649-1657.

Stotts, A. L., Schmitz, J. M., Rhoades, H. M., & Grabowski, J. (2001). Motivational interviewing with cocaine with cocaine- dependent patients: A pilot study. Journal of Consulting and Clin- ical Psychology, 69, 858-862.

Suarez, M., & Mullins, S. (2008). Motivational interviewing and pediatric health behavior interventions. *Journal of Developmental and Behavioral Pediatrics, 29,* 417–428. doi:10.1097/DBP.0b013e31818888b4

Tabachnick & Fidell (2012). *Using Multivariate Statistics* (6th ed.). Upper Saddle River, NJ: Pearson.

Tamowski, K. J., & Simonian, S. J. (1992). Assessing treatment acceptance: The Abbreviated Acceptability Rating Profile. *Journal of Behavioral Therapy and Experimental Psychiatry*, *23*, 101-106.Tebbi, C. K. (1993). Treatment compliance in childhood and adolescence. *Cancer*, *71*(S10), 3441-3449.

Tebbi, C. K. (1993). Treatment compliance in childhood and adolescence. *Cancer*, *71*(S10), 3441-3449.

Tevyaw, T. O. L., & Monti, P. M. (2004). Motivational enhancement and other brief interventions for adolescent substance abuse: foundations, applications and evaluations. *Addiction*, *99*, 63-75.

Thevos, A. K., Quick, R. E., & Yanduli, V. (2000). Motivational Interviewing enhances the adoption of water disinfection practices in Zambia. *Health Promotion International*, *15*(3), 207-214.

Tolan, P. H., & Dodge, K. A. (2005). Children's mental health as a primary care and concern: a system for comprehensive support and service. *American Psychologist*, *60*(6), 601.

Traore, F., O'riordan, M. A., Myers, C., Groth, K., Hoff, A., Angiolillo, A., ... & Kodish, E. (2006). How low is too low? Use of cluster analysis to define low levels of mercaptopurine metabolites. *Pediatric blood & cancer*, *46*(2), 187-192.

Victor, E. C., El-Behadli, A. F., McDonald, W. C., Pratt, C. D., & Faith, M. A. (2018). Motivational Interviewing Training Outcomes Among Providers in a Children's Hospital. *Journal of clinical psychology in medical settings*, 1-8.

Wachtel, T., & Staniford, M. (2010). The effectiveness of brief interventions in the clinical setting in reducing alcohol misuse and binge drinking in adolescents: a critical review of the literature. *Journal of clinical nursing*, *19*(5-6), 605-620.

Wang, Y. C., Stewart, S. M., Mackenzie, M., Nakonezny, P. A., Edwards, D., & White, P. C. (2010). A randomized controlled trial comparing motivational interviewing in education to structured diabetes education in teens with type 1 diabetes. *Diabetes care*, *33*(8), 1741-1743.

Weinstein, N. D. (1993). Testing four competing theories of health-protective behavior. *Health psychology*, *12*(4), 324.

Weinstein, P., Harrison, R., & Benton, T. (2004). Motivating caregivers to prevent caries in their young children: One year findings. Jour- nal of the American Dental Association, 135, 731-738.

Wierdsma, J., van Zuilen, A., & van der Bijl, J. (2011). Self-efficacy and long-term medication use in patients with chronic kidney disease. *Journal of Renal Care*, *37*(3), 158-166.

Wilhelm, S. L., Stephans, M. B. F., Hertzog, M, Rodehorst, T. K. C., & Gardener, P. (2006). Motivational interviewing to promote sustained breastfeeding. Journal of Obstetric, Gynecologic, & Neonatal Nursing, 35, 340-348.