

A PILOT INTERVENTION TO IMPROVE MEDICATION ADHERENCE IN
NONADHERENT INFLAMMATORY BOWEL DISEASE PATIENTS

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NONADHERENT INFLAMMATORY BOWEL DISEASE PATIENTS

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And hereby certify that in their opinion it is worthy of acceptance.

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DEDICATION

I dedicate this dissertation to my family, friends, co-workers, and patients. First of all, my family has been my biggest supporter. My parents, Greg and Cindy, have prayed daily for the necessary physical and emotional strength to maintain my health, my well being, and my focus. *I can do all things through Christ who strengthens me (Philippians 4:13)*. My parents have beamed with pride at my accomplishments and supported me in my darkest hours. My daughters, Katherine and Emma, have watched me juggle home, work, school, ball, piano/violin schedules, and my weight over the last five years. To my daughters, I strive to be role model for a strong, independent, educated, and faithful woman. My strength to complete this process came from my daughters, to show them anything can be accomplished with hard work, perseverance and faith in God. Paul, who chose to move to Columbia to provide a better education for his daughters, gave the same opportunity to me, for which I am grateful.

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A PILOT INTERVENTION TO IMPROVE MEDICATION ADHERENCE IN
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Abstract

Background: Medication nonadherence in inflammatory bowel disease (IBD) can lead to suboptimal control of the disease, decreased quality of life, and poorer outcomes. This pilot study evaluated the feasibility, intervention mechanism, and potential effectiveness of a three-month continuous self-improvement (CSI) intervention to enhance medication adherence in adult nonadherent IBD patients.

Methods: Adult IBD patients taking a daily or twice-daily dosed maintenance medication were screened for two months to determine baseline medication adherence levels. Adherence was monitored electronically. Nonadherent IBD participants were randomized to receive either the CSI intervention or the attention control intervention and then monitored for three-months. The CSI intervention consisted of a data evaluation and system refinement process in which personal system changes were identified and implemented. The attention control group was given only educational information regarding IBD disease process, extra-intestinal manifestations of IBD, and medical therapy actions and side effects. Demographic statistics, change scores for within and between-group differences, and effect size estimates were calculated.

Results: Nine nonadherent participants (medication adherence score $<.85$) were eligible for randomization. The intervention was found to be feasible and acceptable. System

thinking scores trended in the anticipated direction. Although no statistically significant improvement in medication adherence was found ($p=0.14$), medication adherence improved in 3 of 4 of the CSI group and only 1 of 2 in the attention control group. The effect size calculation of 1.9 will determine the sample size for future study.

Conclusions: The results of this pilot study showed the intervention was feasible and had a positive effect on the medication adherence change score and on adherence levels. A larger fully powered study is needed to test of the effectiveness of this innovative intervention.

Key Words: adherence, IBD, intervention

CHAPTER ONE: INTRODUCTION

The proposed pilot project is a randomized controlled trial testing the feasibility and potential effectiveness of a continuous self-improvement intervention (CSI) on medication adherence in adult patients with inflammatory bowel disease (IBD) assessed electronically by the Medication Event Monitoring System (MEMS) (AARDEX, 2011). The dissertation's four chapters include two manuscript chapters. Chapter one introduces the problem of nonadherence to IBD maintenance medications and the studies performed to date dealing with the problem. Chapter two is a manuscript that systematically appraises the CSI literature. Chapter three addresses the methods used in this dissertation research. Chapter four is a manuscript detailing the results, discussion, and conclusions of this research.

In the United States, 1.4 million people have been diagnosed with IBD (Loftus, 2004), a chronic disease including Crohn's disease (CD), ulcerative colitis (UC), and indeterminate colitis. The disease course involves frequent relapses and remissions. Lifelong medication therapy is necessary (Hanauer, 2006). Although IBD's etiology is not well understood, genetics, infection, and environment have contributed to susceptibility to the disease. Crohn's disease involves transmural inflammation throughout the gastrointestinal tract; whereas inflammation from UC affects the colon alone. The goal for IBD patients is to induce and maintain remission, and to minimize the frequency, severity, and duration of relapses (Hanauer, 2006). Relapses have been described as increased stool frequency and abdominal cramping, rectal bleeding, fecal urgency with decreasing stool form. IBD maintenance medication therapy utilizes a combination of immunosuppressants, antibiotics, aminosalicylates, steroids, and

biologics administered by various routes (oral, rectal, and intravenous). IBD's medication regimen is complex and lifelong, and nonadherence ranges from 7-72% in adult patients (Selinger, Robinson, & Leong, 2011; Jackson, Clatworthy, Robinson & Horne, 2010; Kane, 2003; Bernal, Domenech, Garcia-Planella, Marin, Manosa, Navarro, ... & Gassull, 2006; Bokemeyer, Teml, Roggel, Hartmann, Fischer, Schaeffeler, & Schwab, 2007; Cervený, Bortlik, Kubena, Viecek, Lakatos, & Lukas, 2007; D'Inca, Bertomoro, Mazzocco, Vettorato, Rumiati, & Sturniolo, 2008). Increased complexity of medication regimens has been shown to increase medication nonadherence rates (Cervený, et al., 2007; Fine, R. N., Becker, Y., De Geest, S., Eisen, H., Ettenger, R., Evans, R.... & Dobbels, F. 2009; Hawthorne, Rubin, & Ghosh, 2008; McDonald, Garg, & Haynes, 2002). Medication nonadherence in UC decreases quality of life and productivity while increasing resource utilization, morbidity, and mortality (Kane, 2003; Kane, 2007; Kane, 2008; Bassi, Dodd, Williamson, & Bodger, 2004; Higgins, Rubin, Kaulback, Schoenfield, & Kane, 2009).

The purpose of this pilot randomized control trial is to assess the feasibility and potential effectiveness of a three-month continuous self improvement intervention on maintenance therapy medication adherence as assessed by electronic monitoring in adult IBD patients. The study's specific aims are:

Aim 1. To pilot test a three-month CSI intervention on maintenance therapy medication adherence in adult IBD patients and solicit feedback from participants on the protocol.

Aim 2. To evaluate the feasibility of testing the CSI intervention to improve medication adherence through refining the protocol, and evaluating intervention effect (if possible).

Medication nonadherence across chronic diseases

Medication nonadherence is a critical barrier to successful treatment and remains a challenge to healthcare professionals across all acute and chronic diseases (Simpson, Eurich, Majumdar, Padwal, Tsuyuki, Varney, & Johnson, 2006). The Nonadherence Consensus Conference Summary Report (2009) found nonadherence to be more prevalent than providers realize, and difficult to measure accurately (Fine et al., 2009). Nonadherence has many potential confounding variables, confers poorer outcomes, and lacks effective interventions (Fine et al, 2009). Treatment factors affecting nonadherence in chronic disease relate to complexity of the medication regimen, patients (side effects of the medications), disease characteristics, socioeconomic status, providers and healthcare setting (Cervený et al., 2007; Fine et al., 2009; Hawthorne, Rubin, & Ghosh, 2008; McDonald, Garg, & Haynes, 2002). Medication nonadherence rates across chronic diseases average 50%; no acceptable level of medication nonadherence exists (Haynes, et al., 2005; Kripalani, Yao, & Haynes, 2007; McDonald, et al., 2002; Roter, Hall, Merisca, Nordstrom, Cretin, & Svarstad, 1998). Medication nonadherence in chronic disease results in decreased quality of life and productivity, and increased medical costs due to hospitalization, morbidity and mortality (Takemoto, Pinsky, Schnitzler, Lentine, Willoughby, Burroughs, & Bunnapradist, 2007; Dew, DiMartini, Dabbs, Myaskovsky, Steel, Unruh, ... & Greenhouse, 2007; Schafer-Keller, Lyon, Van-Gelder, & De Geest, 2006).

Medication nonadherence rates in IBD

Self-reported and direct measurement of medication nonadherence in CD and UC ranges from 7-72% of adult IBD patients in the United States (Jackson, Clatworthy, Robinson, Horne, 2010; Bernal, et al, 2006, Bokemeyer et al., 2007; Cervený, et al., 2007; D’Inca, et al, 2008; Ediger, Walker, Graff, Lix, Clara, Rawsthorne, ... & Bernstein, 2007; Horne, Parham, Driscoll, & Robinson, 2009; Kane, 2006). In chronic disease, the average nonadherence rate is approximately 50% (Sabate, 2003). Robinson’s (2004) study using international data found that IBD patients’ self-reported nonadherence rates for taking aminosalyslate medications range from 13% in France to 46% in Germany.

Outcomes of medication nonadherence for IBD patients

Medication nonadherence in IBD can increase relapse rates, absenteeism, resource utilization, personal strife, morbidity, and mortality (Hawthorne, et al., 2008; Lakatos, 2009; Richardson, Sculpher, Kennedy, Nelson, Reeves, Roberts, . . . & Thompson, 2006; Robinson, Thompson, Wilkin, & Roberts, 2001). Nonadherence increased the risk five-fold of clinical relapse among patients with quiescent UC (Kane, Huo, Aikens, & Hanauer, 2003). Bassi (2004) found compared to quiescent IBD, increasing relapse rates were associated with a two- to three-fold increase in outpatient care costs and a 20-fold increase in inpatient care (Bassi, Dodd, Williamson, & Bodger, 2004). Nonadherent patients utilize more in-patient and out-patient services and incur 12.5% higher medical costs (Higgins et al., 2009; Kane, Huo, Aikens, & Hanauer, 2003; Kane, 2008; Richardson et al., 2006).

For individuals, medication nonadherence can negatively affect daily quality of life. Psychosocial factors including mood disorders, poor body image, decreased levels of

intimacy, and sexual function due to fecal incontinence and bad odors affect personal relationships which can further decrease quality of life. (Hawthorne et al., 2008; Larson, Davies, Dozois, Cima, Piotrowicz, Anderson, . . . & Pemberton, 2008; Palm, Bernklev, Moum, & Gran, 2005; Robinson, Thompson, Wilkin, & Roberts, 2001; Timmer, Kemptner, Bauer, Taksas, Ott, & Furst, 2008).

As patients' relapse rates increase, so also may their resource use, personal strife and risk of concomitant illness. In UC, medication nonadherence leads to increased morbidity and possibly mortality due to the increased risk of colorectal cancer (Hawthorne et al., 2008).

Medication nonadherence predictors in IBD

Intervention research targets predictors or factors that increase nonadherence. However, predictors of IBD medication nonadherence have been inconsistent. A recent systematic review revealed that nonadherence was not consistently linked with any demographic, clinical, or treatment variables (Jackson, Clatworth, Robinson, & Horne, 2010). However, the reviewers found nonadherence was associated with psychological distress (depression, chronic stress or mood disorders), doctor-patient discordance (relationship between the patient and the physician), and patients' beliefs about medications (Jackson, Clatworth, Robinson, & Horne, 2010; Horne, et al, 2009).

Adherence intervention research in chronic diseases

Adherence-enhancing interventions reported in the chronic illness literature have been directed toward patients through cognitive, behavioral, and affective strategies. Cognitive interventions involve imparting knowledge; behavioral interventions target, shape, and/or reinforce behavior; and affective interventions seek to change values and

beliefs (Peterson, et al, 2003; Roter, et al., 1998; Schafer-Keller, Lyon, Van-Gelder, & De Geest, 2006).

Interventions focusing on individuals' intention and motivation have had little effect in enhancing medication adherence (Roter et al. 1998; McDonald et al. 2002; Kripalani et al. 2007; De Bleser, Matteson, Dobbels, Russell, & De Geest, 2009; Matteson & Russell, 2010; Peterson et al., 2003; Conn, Hafdahl, Cooper, Ruppap, Mehr, & Russell, 2009). For example, education regarding medications or disease (cognitive interventions) presented in the traditional multi-page brochure format had no significant impact on medication adherence (ES=0.48) (Conn et al., 2009). Affective interventions focusing on social support, beliefs, intentions, and motivation have not been effective (Conn, Valentine, & Cooper, 2002). However, in a recent meta-analysis, Conn (2009) found that behavioral interventions produced more consistent increases in medication adherence in chronic diseases (ES=0.67).

Adherence interventional research in IBD

The adherence intervention research in IBD consists of just five studies (Table 1.1, Intervention Studies in IBD). Interventions included: IBD education alone (cognitive) (Waters, Jensen, & Fedorak, 2005); education combined with cognitive behavioral therapy (Keefer, Doerfler, & Artz, 2011); tailored education with a motivational program (Moshkovska, Stone, Smith, Bankart, Baker, & Mayberry, 2011) or with motivational interviewing (Cook, Emiliozzi, El-Hajj, & McCabe, 2010); and education combined with options for practical changes in reminders or dosing, such as decreased dosing when possible, and multiple types of electronic reminders (Moss, Chaudhary, Tukey, Junior, Cury, Falchuk & Cheifetz, 2010).

Study years ranged from 2005 to 2011 with research designs including four RCT's, and one pre-experimental (post-test only). Two studies were performed outside of the U.S. (Moshkovska et al, 2011; Waters et al, 2005). Sample sizes ranged from 28- 278 (Keefer et al, 2011; Cook et al, 2010). Adherence measures included a medication adherence diary (Waters et al, 2005), Medication Adherence Scale (MAS) (Keefer, 2011), Urinary 5-ASA and N-acetyl-5-ASA concentrations (Moshkovska, et al., 2011), structured interview (Cook, et al., 2010), and refill rates (Moss, 2010). Urinary 5-ASA and N-acetyl-5-ASA are urinary metabolite tests which can be expensive and time consuming and reflect only recent aminosalicylate adherence (Moshkovska, et al., 2011).

The intervention dose, when reported, ranged from 13.5 minutes (Cook, 2010) to three hours (Waters, et al., 2005), duration ranged from 4 weeks (Waters, et al., 2005) to 48 weeks (Moshkovska, et al., 2011). Interventionists were nurses (Moss, 2010; Cook, 2010), a physician (Moshkovska, et al., 2011), a team consisting of a nurse practitioner, dietician, and physician (Waters, et al., 2005), and a health psychologist (Keefer, et al., 2011). Theory was the basis for the interventions in two studies, with one intervention deriving from a combination of social learning theory and health behavior change theory (Keefer, et al., 2011), and the other utilizing Leventhal's Theory (Cook, et al., 2010).

The studies' operational definitions of nonadherence were diverse and inconsistent. Moss (2009) defined adherence as >80% refill rate, whereas Cook (2010) specified $\geq 80\%$ on a self-report interview. Keefer (2011) utilized a MAS score of 0, indicating 100% adherence; Moshkoska (2011) utilized urine 5-ASA concentration of $\geq 30\mu\text{g/ml}$ or N-Acetyl-5-ASA level $\geq 90\mu\text{g/ml}$ as the definition of adherence. Finally,

Waters (2005) used three self-report measures, but did not operationally define adherence.

The reviewed studies have several limitations. Sample sizes were generally small, and power analysis was performed in only two studies (Keefer, 2011; Moss, 2010). Four of the five studies employed self-report adherence measures. Self-report is convenient but often overestimates adherence (Polit & Beck, 2012). Electronic monitoring has been proposed as the standard for monitoring medication adherence because it is accurate, reliable, and reflects timing of medication taking (Russell et al., 2007).

The interventions themselves had weaknesses. They were short in dose and duration with no long-term follow-up or impact on outcomes noted. None of the reviewed studies focused on nonadherent participants. Homogeneous samples allow smaller sample sizes by reducing the variation of a sample, focusing on the trait to be analyzed (Polit & Beck, 2012). Administering a medication adherence intervention to the adherers constrains the potential effectiveness of the intervention by limiting the achievable change or creating a ‘ceiling’ effect.

IBD education was included in four of the studies. Education alone has not been sufficient to increase adherence (Conn et al, 2009; Roter et al., 1998; Petersen et al., 2003). Finally, a theoretical basis was noted in only two studies. Horne (2005) suggests a theoretical framework guiding the intervention. Strengths of the reviewed studies include the powerful RCT study design.

Conceptual/Theoretical Framework

Researchers have used many psychological and nursing theories to examine medication adherence. These theories have been the theoretical basis for cognitive,

behavioral or affective interventions, which have relied on intention and motivation of the individual to change behavior. Investigators have long used systems-based interventions based on continuous quality improvement (CQI) principles that Deming initiated in the 1950's in the manufacturing sector (Deming, 1986). CQI is a data- and system-based intervention designed to optimize productivity and decrease system error. CQI has been successful in optimizing the manufacturing industry and in the 1980's began to revolutionize the health care industry. Applying CQI principles in hospital has decreased system-based errors and improved patient care (Edmonds & Zagami, 1992; Oetker & Cole, 1996; Ramirez & Lawhon, 1994).

Given CQI's success in organizational system change in manufacturing and health care, Alemi, Pawloski, and Fallon (2003) postulated that its principles could improve exercise and eating behaviors at the level of personal systems. Alemi established that personal habits are a function of environment, not motivation, and published a guide to help people change their personal systems to improve health behaviors (Alemi & Neuhauser, 2006). Personal system thinking is conceptually defined as the process of understanding how people and circumstances are linked (Alemi et al., 2000). Alemi and colleagues call this approach continuous self improvement (CSI).

CSI has been successful in managing life style changes to enhance exercise, weight loss, and medication adherence in chronic diseases including asthma and renal disease (Matteson & Russell, 2011). A recent CSI intervention study in adult renal transplant patients found a statistically significant improvement in medication adherence scores in the CSI group over the attention-control group ($p=.03$) with an effect size of 1.4 (Russell et al., 2010).

Alemi borrows concepts from existing theories of change (Alemi et al., 2000, p. 81) and proposes four new mechanisms: —the system is the cause of change; habits involve linked decisions; process owners need to join in supporting change; system change is based on data” (p. 81).

The first assumption of continuous self-improvement is that the system is the cause of change (Alemi et al., 2000). Since individual behavior occurs within a system, any change in that system results in a change in behavior. Berwick (1996) wrote, —Every system is perfectly designed to achieve the results it achieves” (p. 619). Systems can be altered purposefully in a manner to achieve desired changes. Alemi et al. (2000) states —discipline and will power are not a personality trait, but a function of the environment in which the individual functions... motivation itself is manipulated, engineered, or influenced by the system with which the person has surrounded himself or herself” (p. 81). This framework removes blame from patient but not their responsibility for participating in care or their accountability for selecting environments that produce certain behaviors (Alemi et al., 2000). This personal system approach is consistent with a recent World Health Organization’s report on suggesting that shifting blame from the patients to the environments in which they function may enhance adherence (Sabaté, 2003).

The second assumption is that habits involve linked decisions (Alemi et al., 2000). A habit is a behavior pattern that is repeated, predictable and ingrained; at times the person is unaware the behavior was performed (Merriam-Webster Dictionary, 2011). Deming states that improvement is not a single effort (Walton, 1986). A decision influences the decision before it and the decision that follows it; repeating these series of

linked decisions forms habits. Examining personal systems highlights not only habits but also possibilities for changing these linked decisions. Systems change is meant to be a coil of continuous motion. Within the dynamic health care system, improvement must be a continuous process, always striving for better system outcomes (Deming, 1994).

The third assumption of CSI is that process owners need to join in supporting change. ~~Knowledge~~ Knowledge of the dynamic relationships of the system and the people that work in it are necessary to manage the system effectively” (Walton, 1986, p. 97). When others are involved in the personal system, their ~~touch~~ involvement is essential to affect change (Alemi et al., 2000). Their impact on the system must be analyzed systematically. This pre-requisite knowledge enhances the system assessment, leading to better interventions, and ultimately to improved behavior.

The fourth assumption is that system change is based on data. Systems are improved by collecting and analyzing objective data. Data measuring the targeted behavior should be systematically gathered, organized, and reviewed by those involved in the system change. The CSI framework is based on data collected by patients and their healthcare teams and not on assumptions, emotions, or experience who uses data to assess the system, monitor success, and evaluate the interventions (Vokurka, 2001; Walton, 1986). No change can be achieved without data derived from the system. ~~In~~ God we trust, all others must use data,” (Walton, 1986, p. 96).

In summary, health behavior change interventions show inconsistent results when directed toward patient characteristics, motivation, and intention. Shifting the focus of health behavior change research to CSI, a personal systems-based intervention may yield effective health behavior change.

Conclusion

Based on this project's integration of adherence intervention literature in chronic disease and the five IBD intervention studies, an IBD medication adherence intervention study should include a theory-based individualized behavior change intervention, a randomized control trial (RCT) study design, and a reliable measure of medication adherence.

Therefore, moving the field forward requires performing a randomized controlled trial utilizing a personal system focused intervention directed toward nonadherent IBD patients as measured by electronic monitoring. The strengths of this proposed study are establishing the feasibility of the innovative CSI intervention, including a nonadherent sample, using a randomized controlled design, and measuring adherence using electronic monitoring. The primary investigator has experience with the population, intervention, and electronic monitoring. This pilot study is significant in that it will establish the feasibility and potential effectiveness of the intervention for a future, fully powered study.

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Author (Year) Purpose	Sample/Setting	Intervention	Theory	Measures	Results	Strengths/Weakness
Waters, Jensen & Fedorak (2005) Purpose: Evaluate the effects of a formalized educational intervention in IBD patients	N=89 Age: (18-74) Male: 51/89 Education: High school 35/89 Setting: IBD Specialty clinic in Canada	Classification: Cognitive Interventionist: Nurse Practitioner, dietician, physician Dose: weekly for four weeks Duration: Three hours weekly Content: First two weeks of education was provided by the NP and included: anatomy/physiology; symptomatology; therapy; purpose of medications; side effects of medications and their management. Dietician education included: nutrition management and common complications and individual dietary counseling. Surgeon provided information regarding surgical options and benefits of surgery. Small group discussion was moderated by facilitators discussing IBD, sexuality, childbearing, symptom management, stress reduction, cancer risks and surveillance and medication management.	NONE	Medication adherence diary; CCKNOW (educational tool); KQ (educational tool), CDAI/AI (Crohn's disease activity Index/UC Activity Index; IBDQ and RFIPC (QOL instruments); Visual analog scale for perceived IBD knowledge and health status; Healthcare use; patient satisfaction Data Collection: baseline, immediate post-intervention, and 8 weeks later	No statistically significant results in nonadherence, but rate of nonadherence trended lower Statistically significant increase in healthcare use in poor adhering patients (p=0.01); statistically significant increases in education scores (p=0.000), perceived knowledge rating (p=0.01), and patient satisfaction (p=0.001).	Strengths: RCT Weaknesses: -No randomization procedures discussed -Short duration of intervention and f/u (four weeks intervention, eight week f/u) -list wise deletion (Increase type II error by decreasing sample size) -measure of medication adherence a self-report diary -Limited generalizability secondary to homogenous sample, specialty clinic and high % male sample -no power analysis performed

Author (Year) Purpose	Sample/Setting	Intervention	Theory	Measures	Results	Strengths/Weakness
Keefer, Doerfler, & Artz (2011) Purpose: determine feasibility, acceptability, and the effect of project management (PM) program on medication adherence in Crohns' patients	N=28 Crohns patients without apparent psychological distress Age range: 18-70 Male 8/18 92% Caucasian Setting: Northwestern University, Illinois/USA Exploratory RCT	Classification: Behavioral Interventionist: Health psychologist, PhD (PI) Dose: weekly session for 60 minutes with health psychologist (cognitive behavioral therapy) Duration: six weeks Content: CBT training program to assist in self-management	Cognitive behavioral principles based on health behavior change and social learning theories	Repeated measures of: Inflammatory bowel disease self efficacy scale (IBDSES) Medication Adherence Scale (MAS) Perceived stress questionnaire (PSQ) Inflammatory bowel disease questionnaire (IBDQ)	Statistically significant change in the IBD SES (p=.003; d=0.17); PSQ (p=.01; d=0.13); and IBDQ (p=.001). No statistically significant difference in medication adherence score (p=ns). IBDQ(total): p=.001; d=0.45 IBDQ (bowel): p=.02; d=.45 IBDQ (systemic): P=.007; d=0.37 IBDQ (emotional): p=ns IBDQ (social): P=ns	Strengths: RCT Theory based 85% powered for IBDQ -Limitations: no attention control; just usual care -pilot study - measurement of medication adherence was self report -short duration of study; unsure of long-term outcomes.

Author (Year) Purpose	Sample/Setting	Intervention	Theory	Measures	Results	Strengths/Weakness
<p>Moshkovska, Stone, Smith, Bankart, Baker, & Mayberry (2011)</p> <p>Purpose: determine effect of a tailored education and motivational program on mesalamine medication adherence in UC patients</p>	<p>N=71 UC patients on a 5-ASA</p> <p>Setting: UK</p> <p>RCT</p>	<p>Classification: cognitive/behavioral</p> <p>Interventionist: Physician</p> <p>Dose: 20-30 minutes</p> <p>Duration: 48 weeks</p> <p>Content: tailored education and motivational components with options including simplified dosing regimens and reminders (pill dispensers). 1:1 educational/motivational session to identify barriers and assist to motivate, convince and educate patient regarding medication adherence. F/u phone call at 4 weeks; and 10 minute reinforcement session at 24 weeks. Participants offered free choice up to 3 practical interventions ranging from simpler dosing, medication reminders or charts, daily electronic pillbox with alarms, weekly electronic pillbox, weekly non-electric pillbox, and mobile telephone alarm set-up.</p> <p>Control group had 0-24-48 week urine testing and questionnaires</p>	None	<p>Urinary 5-ASA and N-acetyl-5-ASA concentrations</p> <p>Beliefs about Medications Questionnaire (BMQ)</p> <p>Satisfaction with Information about Medicines Scale (SIMS)</p>	<p>Baseline adherence (0 weeks) was 71% for control group; 81% for intervention group (p=.3); 17/71 non-adherent at baseline; 14/71 non adherent at end of study; 18/54 adherent at baseline and became nonadherent at end of study Control group (p=001) and non-adherence at baseline (p=.002) were predictors of nonadherence</p>	<p>Strengths- -urine 5-asa levels as measure of adherence utilized</p> <p>Limitations: -not fully powered -10 subjects lost to f/u</p>

Author (Year) Purpose	Sample/Setting	Intervention	Theory	Measures	Results	Strengths/Weakness
<p>Moss, Chaudhary, Tukey, Junior, Cury, Falchuk, & Cheifetz (2010)</p> <p>Purpose: determine whether a patient-support program (PSP) over 23 weeks would improve mesalamine adherence at 3 and six months in patients with ulcerative colitis</p>	<p>N=81 UC patients on mesalamine (21 in PSP; 60 in standard care group)</p> <p>Setting: Massachusetts, USA</p> <p>Prospective cohort trial with well matched cohorts</p> <p>Age average of PSP group=44; control=47</p>	<p>Classification: Cognitive/behavioral</p> <p>Interventionist: nurse</p> <p>Dose: phone calls at 24 hours, 3 weeks, 7 weeks, 15 weeks, and 23 weeks (5 phone calls)</p> <p>Duration: 23 weeks</p> <p>Content: Script assist, independent treatment program, providing disease specific education and promotion of medication adherence</p> <p>Assess risk for on-compliance with intervene with psychological techniques to improve medication persistence</p> <p>Log of conversation sent to physician</p> <p>Nurse blinded to study involvement</p>	None	<p>Medication adherence determined by refill rates based on Steiner's formula->80% defined adherent</p> <p>At 3 and 6 months</p> <p>SIBDQ</p> <p>QOL</p> <p>SCAI</p>	<p>No statistically significant change in medication adherence or quality of life at 3 or 6 months.</p> <p>No statistically significant change in QOL</p> <p>Medication adherence at 3 months: 71% in PSP vs. standard care 74% (p=.7)</p> <p>At six months: 73% adherence in standard care group vs. 84% in PSP group (p=.4)</p>	<p>Strengths:</p> <p>Power analysis performed</p> <p>Limitations:</p> <p>Randomization was changed in study (sponsor cancelled PSP program)</p>

Author (Year) Purpose	Sample/Setting	Intervention	Theory	Measures	Results	Strengths/Weakness
Cook, Emiliozzi, El-Hajj, & McCabe (2010) Purpose: To test telephone nurse counseling and motivational interviewing for six months to increase medication adherence in by targeting cognitive and emotional barriers to nonadherence.	N=276 participants Setting: Colorado, USA No control group, no randomization, all participants received intervention; post-test only design	Interventionist: RN Dose: 13.5 minutes average Duration: six months Content: IBD patients on average received a median of 2.1 calls from a registered nurse who used cognitive-behavioral and motivational interviewing techniques to increase medication adherence to mesalamine.	Leventhal	Adherence was measured by a structured interview after the intervention and was compared to the expected population adherence rate.	Cook (2010) found that adherence following the telephone intervention was improved (binomial $z=7.22$, $p<.001$, $\Phi=0.5$) over population baseline. Demographic and clinical variables did not predict adherence but self-efficacy ($p=.016$) and increased reported adverse drug events ($p<.001$) did.	The weaknesses of the Cook (2010) study was the self-report measurement of adherence, high attrition rates (51% over six months), and self-selection of possibly higher motivated patients.

Systematic Review of Continuous Self Improvement Interventions

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Abstract

Although health care providers advise healthy and chronically ill adults to adopt positive health behaviors, traditional interventions focused on motivation and intention have been largely ineffective. Researchers have tested the ability of continuous self-improvement (CSI), an innovative personal system-based intervention, to affect health behavior change at the individual level. This paper systematically reviews CSI interventions focused on improving health behaviors. A search of Cumulative Index of Nursing and Allied Health Literature (CINAHL) (1982- May 2010), MEDLINE (1950- May 2010), PsycINFO (1806-May 2010), Google Scholar, Scopus, and all Evidence-Based Medicine (EBM) Reviews (Cochran DSR, ACP Journal Club, DARE, CCTR) identified studies testing the CSI intervention in healthy or chronically ill adults. Eight studies met inclusion criteria. CSI shows promise as an effective intervention across a broad age range for a variety of difficult-to-change behaviors. Future research should address methodologic weaknesses.

Keywords: continuous self-improvement, systematic review, interventions, health behavior change.

Systematic Review of Continuous Self-Improvement Interventions

Health care providers routinely advise healthy and chronically ill adults to adopt positive health behaviors to improve the quality and longevity of life. However, chronically ill adults do not follow nearly half of such recommendations (Kripalani, Yao, & Haynes, 2007; McDonald, Garg, & Haynes, 2002; Roter et al., 1998). Although intervention research has attempted to enhance these health-promoting behaviors through motivation and intention, changing health behaviors has proven to be a difficult and complex task (Conn, 2010). The costs of failure in this endeavor are high. For example, if medication nonadherence rates increase, subsequent increases in morbidity and mortality may occur. Medication nonadherence results in decreased quality of life and productivity, increased medical costs due to hospitalization, and increased morbidity and mortality (Takemoto et al., 2007; Dew et al., 2007; Schafer-Keller, Lyon, Van-Gelder, & De Geest, 2006).

Health behavior change interventions have focused primarily at the patient level by enhancing motivation and intention through cognitive, affective, and associated behavioral strategies. Cognitive interventions impart knowledge, whereas affective interventions attempt to change attitudes, values and beliefs (Peterson, Takiya, & Finley, 2003; Roter et al., 1998). Behavioral interventions shape and/or reinforce behavior (Peterson et al., 2003).

Health behavior change interventions directed toward individuals have had little effect in enhancing medication adherence (Roter et al. 1998; McDonald et al. 2002; Kripalani et al. 2007; DeBleser et al., 2009; Matteson & Russell, 2010; Peterson et al., 2003; Conn et al., 2009). For example, medication or disease education (cognitive

interventions) had no significant impact on medication adherence when presented in the traditional brochure-type format (Conn et al., 2009; Roter et al., 1998; Peterson et al., 2003). Affective interventions focusing on social support, beliefs, intentions, and motivation have not been effective (Conn, Valentine, & Cooper, 2002). These results, when combined with methodologic problems such as small sample sizes, short intervention doses, poor adherence measures, and lack of long-term follow up, leave a gap in the intervention literature.

In summary, health behavior change interventions based on motivation or intention directed at individuals have shown inconsistent results. Health behavior change research must make a paradigm shift toward interventions focused on the personal systems operating within that environment. This review addresses a knowledge gap by systematically appraising the CSI intervention literature. This systematic evaluation will guide clinicians and researchers regarding the degree of effectiveness of systems-based interventions, an approach that departs from traditional behavior-change interventions.

Systems-based interventions have been used with continuous quality improvement (CQI) principles Deming initiated in the 1950's in the manufacturing sector (Deming, 1986). CQI is a data-driven, system-based intervention for optimizing productivity and decreasing system error. In the 1980s, CQI began to revolutionize the health care industry. Applying CQI principles in hospitals has decreased system-based errors and improved patient care (Edmonds & Zagami, 1992; Oetker & Cole, 1996; Ramirez & Lawhon, 1994)

Another organizational system improvement framework is the Langley et al., (2009) Model of Improvement, which focuses on change. The model's three key

questions define the system –endpoint:” “What are we trying to accomplish?”, “How will we know if change is improvement?”, and “What changes can we make that will result in improvement?” (Langley et al., 2009, p. 5). This model systematically optimizes the intervention through modification by utilizing Plan-Do-Check-Act process (PDCA), flow charts, fishbone diagrams, Pareto charts, histograms, and/or run charts when system insight is needed.

The Model for Improvement concepts are based on change: developing, testing, implementing, and spreading change (Langley, et al., 2009). *Developing change* requires creativity and may occur by redesigning the current system or designing a new one. Often, searching for the perfect change may inhibit real change. *Testing a change* refers to cycles of learning. Testing on a small scale minimizes risks and allows for learning from the change. *Implementing a change* must be integrated into the system and must be sustainable by the people within the system. *Spreading the change* within an organization relies on five principles: strong leadership, presentation of tested and successful interventions, a spread plan (communication, measurement and work plan), communication system (create awareness and provide technical support), and monitoring of the change spread (Langley et al., 2009).

Based on the successes in organizational system change in the manufacturing and health care industries, Alemi, Pawloski, and Fallon (2003) postulated that CQI principles could improve exercise and eating behaviors at the personal systems level. Alemi established that personal habits are a function not of motivation but rather of environment, and published a guide to assist people in personal system-based changes to improve health behaviors (Alemi & Neuhauser, 2006). Personal system thinking is

conceptually defined as the process of understanding how people and circumstances are linked (Alemi et al., 2000). Alemi and colleagues called this approach Continuous Self-improvement (CSI). CSI is a personal system-focused intervention to change behavior by influencing the personal environmental system in which the patient functions (his or her personal system). This approach does not blame patients for lack of behavior change and/or maintenance but rather focuses on improving the system that creates and maintains the behavior (Alemi & Neuhauser, 2006; Gustafson, Cats-Baril, & Alemi, 1992; Russell, 2010). Through the data evaluation and system refinement process called PDCA, personal system changes are identified and implemented; health behaviors become ritualistic and habitual, with less effort, motivation, and intention required to maintain the desired health behavior change.

Alemi proposes four mechanisms in the framework: —the system is the cause of change; habits involve linked decisions; process owners need to join in supporting change; system change is based on data” (Alemi et al., 2000, p. 81).

The first assumption of continuous self-improvement is that the system is the cause of change (Alemi et al., 2000). Since individual behavior occurs within a system, any change in that system results in a change in behavior; Berwick (1996) wrote, —Every system is perfectly designed to achieve the results it achieves” (p. 619). These systems can be purposefully altered to achieve the desired changed. Alemi et al. (2000) state —discipline and will power are not a personality trait, but a function of the environment in which the individual functions ... motivation itself is manipulated, engineered, or influenced by the system with which the persona has surrounded himself or herself” (p. 81). Although this framework removes blame from patients, they remain responsible for

participating in care or accountable for selecting the environment that produces the behavior (Alemi et al., 2000). This personal system approach is consistent with a recent World Health Organization's report on adherence, which suggests that shifting blame from the patient to their environment may enhance adherence (Sabaté, 2003).

The second assumption is that habits involve linked decisions (Alemi et al., 2000). A habit is a repeated pattern of behavior that is predictable and ingrained; at times the person is unaware the behavior was performed (Merriam-Webster Dictionary, 2011). According to Deming, improvement is not a single effort (Walton, 1986). Rather, a decision influences the decision before it and the decision that follows it. Repeating this series of linked decisions forms habits. Examining the personal system allows one to see existing habits and to identify possible changes in these linked decisions. Systems change is meant to be a coil of continuous motion. Within the dynamic health care system, improvement must be a continuous process, always striving for better system outcomes (Deming, 1994).

The third assumption of CSI is that process owners need to join in supporting change. ~~K~~nowledge of the dynamic relationships of the system and the people that work in it are necessary to manage the system effectively" (Walton, 1986, p. 97). When others are involved in the personal system, their ~~touch~~" or involvement is essential to affect change (Alemi et al., 2000). Their impact on the system must be analyzed systematically. This prerequisite knowledge enhances the system assessment, leading to better interventions, and ultimately improves behavior.

The fourth assumption is that system change is based on data. Systems are improved by collecting and carefully analyzing objective data. These data, which should

measure the targeted behavior, should be systematically gathered, organized, and reviewed by those involved in the system change. “In God we trust, all others must use data,” (Walton, 1986, p. 96). The CSI framework is based on data collected by the patient and the healthcare team. The data are not based on assumptions, emotions, or experience (Vokurka, 2001; Walton, 1986). Data are used to assess the system, monitor success, and evaluate the interventions. No change can be achieved without data derived from the system; change without data is opinion.

In summary, health behavior change interventions have shown inconsistent results when directed towards individuals. Shifting the focus of health behavior change research to CSI, a personal systems-based intervention, may yield effective health behavior change. The purpose of this review is to analyze the CSI literature to date, and address the lack of information on this innovative health behavior change intervention.

Methods

A search of Cumulative Index of Nursing and Allied Health Literature (CINAHL) (1982- May 2010), MEDLINE (1950- May 2010), PsycINFO (1806-May 2010), Google Scholar, Scopus, and all Evidence-Based Medicine (EBM) Reviews (Cochran DSR, ACP Journal Club, DARE, CCTR) was conducted to identify studies testing the CSI intervention in healthy or chronically ill adults. The search term ‘continuous self-improvement’ was used. The literature published by key CSI expert authors was searched, with no limits set on search terms. Retrieved abstracts were reviewed for inclusion. The sentinel articles of key authors were then subjected to the “cited by” function on all search engines. This maneuver identified studies that referenced these sentinel studies. Inclusion criteria were studies utilizing CSI as an intervention across any

age in healthy or chronically ill samples. Eight studies met inclusion criteria (Figure 1. Study flow diagram). Data from the eight studies were extracted, including: author and year, sample/setting, study design, intervention description (dose, duration), theoretical constructs, measures/outcomes, results, methodological strengths and weaknesses, and STROBE/CONSORT scoring. Although STROBE and CONSORT criteria were designed to be used as guidelines to improve the reporting of research in manuscripts, De Bleser and colleagues used these criteria as quality indicators of the methodological rigor of studies (De Bleser et al., 2009; Schulz, Altman, & Moher, 2010; von Elm et al., 2007).

Results

Descriptions of studies

Sample: Eight studies were eligible for inclusion. The published studies ranged in date from 1993 to 2010 (Russell et al., 2010; Scott, 1993), with all but one published after the year 2000. Sample sizes ranged from 1 to 82 participants, whose ages ranged from 19 to 70 (Alemi et al., 2000; Alemi et al., 2003; Lundeen, Fisher-Pai, & Neuhauser, 2001; Scott, 1993). Seven studies were performed in the United States and one in Norway (Kyrkjebo & Hanestad, 2003). Three of the eight studies were performed in academic settings with the aim of teaching quality improvement principles of CQI to students (Alemi et al., 2000; Bacon & Stewart, 2001; Kyrkjebo & Hanestad, 2003). Six studies focused on healthy adults attempting to enhance personal lifestyle improvements such as studying, eating, exercise, work habits, and stress (Alemi et al., 2000; Alemi et al., 2003; Bacon & Stewart, 2001; Kyrkjebo & Hanestad, 2003; Lundeen et al., 2001; Scott, 1993). In the remaining two studies focusing on chronically ill adults, CSI was utilized to augment renal transplantation immunosuppression medication adherence (Russell et al.,

2010) and to decrease cardiac risk factors through weight loss (Moore, 2003). Data from included studies are reported in Table 1 (CSI Systematic Review of Included Studies).

Design

Three studies used a case study design, three a post-test design, one a post-test non-equivalent control group design, and one a randomized controlled trial (RCT) design (Russell et al., 2010). STROBE criteria are utilized for non-experimental studies (von Elm et al., 2007); CONSORT scoring criteria are used for judging randomized controlled trial (RCT) quality (Schulz et al., 2010). Data for STROBE and CONSORT scoring were gathered from the studies by one reviewer (MM) and verified for accuracy by a second reviewer (CR); discrepancies were discussed and mutually agreed upon. Scoring of the STROBE and CONSORT criteria consisted of 0 (not documented), 0.5 (partially documented), or 1.0 (documented); lower scores indicate less documentation or methodological rigor (De Bleser et al., 2009). Studies with scores from 0 to 7 are classified as weak, 8 to 16 as moderately strong studies, and 17 to 22 as strong (De Bleser et al., 2009). STROBE scoring details are found in Table 3 and CONSORT scoring details in Table 2. Reporting of the seven non-experimental studies ranged from weak to moderate (7.0-16.0 out of 22) (Alemi et al., 2003; Kyrkjebo & Hanestad, 2003). The study detail reporting was weak or less precise, implying weak methodological rigor. CONSORT scoring was performed on one RCT meeting our study inclusion criteria, and the reporting was found to be strong (19.5 out of 22), indicating stronger methodological rigor (Russell et al., 2010).

Intervention characteristics

The CSI intervention characteristics are based on CQI. PDCA is one tool employed by the CSI framework to assist in testing of the intervention. Other important tools include those to assess the system (fishbone, process diagrams, and Pareto charts) and those that measure variation (run charts and control charts). System tools are used prior to initiating PDCA. CSI is a comprehensive personal quality improvement approach to system change, in which the person functions by utilizing system tools and PDCA. Data derived from the PDCA cycles optimize the quality of the system (Deming, 1986; McLaughlin & Kaluzny, 2006). The individual PDCA concepts are defined by Deming as follows: *Plan* involves identifying and analyzing the individual's environmental system leading to desired change. *Do* is the implementation of identified systems changes. *Check* determines the effectiveness of the system change by monitoring the desired change. *Act* evaluates the effectiveness of the system change based on the individual's desired change. At this juncture, the individual can adopt the solution, abandon it, or reprocess the solution through the PDCA cycle again. The cycles continue until the system is optimized and the desired health behavior change is achieved and maintained.

Intervention concepts

Use of the PDCA concepts within the 8 studies varied slightly. Although seven studies used PDCA, three studies identified this process as PDSA (Plan-Do-Study-Act) (Kyrkjebo & Hanestad, 2003; Lundeen et al., 2001; Moore, 2003). The authors used *Check* interchangeably with *Study*. Bacon and Stewart (2001) used a six-step process for system change (set quality improvement goals, take actions to achieve goals, collect information using data, identify defects, analyze data, act to eliminate defects). Despite small differences, all aspects of the cycle were present in all of the studies.

Plan involves identifying and analyzing the individual's environmental system (Deming, 1986; Russell et al., 2010). All eight studies included this step, though one author used a slightly different description. Bacon and Stewart (2001) described the *Plan* step as setting personal improvement goals to be accomplished in the projected time period followed by development of a tracking form to follow progress.

The second step, *Do*, is the implementation of identified systems changes (Deming, 1986; Russell et al., 2010). Only seven studies clearly specified the *Do* step; but all eight studies utilized such a step. Bacon and Stewart (2001) describe the *Do* step as taking actions to achieve goals set in the *Plan* step. Taking action is similar to 'doing,' performing or working on a task. *Check* is the next step in the cycle and is examining and determining the state of the system.

All eight studies used the *Check* step, which was where most of the subtle differences existed. The name of the step varied, With *Check* specified by four investigations (Alemi et al., 2000; Alemi et al., 2003; Russell et al., 2010; Scott, 1993); and 'Study' by three (Kyrkjebo & Hanestad, 2003; Lundeen et al., 2001; Moore, 2003). Kyrkjebo and Hanestad described *Study* as data analysis, comparing data to predictions, and summarizing what is learned, which is very similar to Deming's 'Check,' which is examining and determining the state of the system (Deming, 1986; Russell et al., 2010). Bacon and Stewart (2001) defined this step as identifying defects, analyzing data, and identifying patterns of defects; similarly, Bacon and Stewart (2001) defined this step as examining the personal system data by checking or studying the system.

The final stage, *Act*, involves evaluating the effectiveness of the system change, determining whether to adopt the solution, abandon it, or reprocess the solution through the cycle again (Deming, 1986; Russell et al., 2010). All eight studies specified *Act* as the cycle's final part; Bacon and Stewart (2001) described *Act* as understanding and eliminating defects and realizing goals. The remaining seven studies defined *Act* as evaluating the change and determining effectiveness (Deming, 1986; Russell et al., 2010).

Methods guiding personal improvement

Authors used various data collection tools within the *Check* step of the PDCA cycle, including flow charts, fishbone diagrams, Pareto charts, histograms, and/or run charts. These varied tools facilitated visualization and analysis of data. A flow chart is a diagram of the system processes that shows how one event leads to another (Alemi et al., 2006; Walton, 1986). A fishbone diagram is a fishbone-shaped cause-and-effect diagram used in brainstorming sessions to identify system factors influencing a behavior (Walton, 1986). A Pareto chart is a common graphic tool that uses bars in descending order to represent individual values and a line in ascending order to represent the cumulative total value. Histograms use bars representing values over a discrete time period to identify behavior frequency; and a run chart displays data in sequence over time using dots and lines (Walton, 1986). For example, Alemi and colleagues (2003) used the Pareto chart to examine a person's poor eating behavior. Within the participant's personal system, the Pareto chart prioritized leaving late from work as the major influence on junk food intake. With data from the Pareto chart, the participant changed his system changes by

changing driving behavior. He participated in a carpool that left work daily at the same time. This personal system change was key to improving eating behaviors.

Three studies utilized Alemi and Neuhauser's 2006 CSI workbook, which marks the origin of the CSI movement (Alemi et al., 2000; Kyrkjebo & Hanestad, 2003; Lundeen et al., 2001). The workbook guides personal system change problem solving to help the general public manage body weight. The workbook's step-by-step personal system approach helps improve diet and exercise behaviors by training readers to study their personal systems using data collection tools such as routine analysis, flow charts, and PDCA cycles. Lundeen et al. (2001) utilized the workbook in addition to statistical modeling with regression to identify her personal system processes to change her behavior and improve her symptoms.

Intervention dose

Five studies did not document the CSI intervention doses. Documented dose frequencies ranged from daily (Lundeen et al., 2001) to twice weekly (Moore, 2003) to monthly (Russell et al., 2010). The duration of interventions ranged from four weeks (Moore, 2003) to six months (Russell et al., 2010). None of the eight studies documented long-term follow up or long-term outcomes.

Measurement

Seven studies measured the targeted behavior using self-report. One study utilized electronic monitoring of medication-taking behavior (Medication Event Monitoring System [MEMS]) as the adherence outcome measure (Russell et al., 2010). The MEMS uses a cap for medication bottles whose electronic chip measures the date and time of cap removal (MEMS, 2011). The cap has good reliability and has been used

in over 500 studies (Riekert & Rand, 2002). The electronic monitoring is shown to have a failure rate below 0.5% and less than a 2% malfunction rate (Denhaerynck et al., 2008; Russell et al., 2007).

The seven studies utilizing self report did not report reliability or validity data on those measures. Behaviors were measured using relapse documentation (Alemi et al., 2003), the Roberts personal checklist (Bacon & Stewart, 2001), and 24-hour calorie counts and weekly weights (Moore, 2003). The Roberts personal checklist was utilized by Bacon and Stewart to focus on “a goal-directed behavior,” which motivational theorists say can lead to behavior change (p. 72). The checklist assists in goal setting, identifying defects and specific variables to monitor defects (Bacon & Stewart, 2001).

Results

All eight CSI intervention studies demonstrated improved behavioral outcomes in their targeted samples. Improved outcomes included lifestyle changes, stress, weight loss, work habits, and medication adherence.

Of the six studies dealing with lifestyle changes in healthy adults, three were performed with college students. Alemi et al. (2000) found that 83% of students reported a “measured or significant improvement” in their individual lifestyle projects (p. 84). Bacon and Stewart (2001) found a 50% improvement in students’ lifestyle behaviors, whereas Kyrkjebo and Hanestad (2003) found that 45% of nursing students showed an improvement in their lifestyle behaviors. Nursing and Medical schools across the country have utilized CQI to improve students’ performance through practice-based learning, which applies these skills to practice settings.

The remaining three of the six studies in healthy adults dealt with stress, weight loss, and work habits. Lundeen et al. (2001) utilized PDCA to identify stress as the underlying problem with her symptoms of indigestion, food intolerance, back and abdominal pain, pounding heart, and inability to sleep. Alemi et al. (2003) found participating in a carpool led to decrease the amount of junk food ingested, which contributed to weight loss. Scott (1993) enhanced his productivity as a Quality Improvement (QI) manager by identifying situations in which his QI expertise was not needed. He decreased work group facilitation by 58% and communication by 50% and so was able to concentrate his QI expertise where it was most useful.

The two remaining studies were performed with chronically ill adults. Moore's (2003) CSI intervention focused on individuals meeting a five-pound weight loss goal. All six participants met their goal and appreciated the feedback from the process improvement team. Russell et al.'s (2010) CSI intervention for adult kidney transplant adults showed a statistically significant improvement in immunosuppressant medication adherence between the CSI treatment and attention-control ($p=0.03$) groups at six months; a large effect size (Cohen's $d=1.38$) was also found.

Discussion

The purpose of this systematic review of literature was to investigate CSI intervention research across reports from healthy and chronically ill adults and to determine the potential for CSI as a health behavior change intervention. Our review of the eight studies from the last 17 years indicates that CSI shows promise as an intervention for changing health behavior outcomes across a wide age range. These

findings should be considered preliminary due to the studies' methodological weaknesses.

Interventionists could employ CSI to address numerous health behaviors needing change in the clinical setting. Numerous qualified interventionists are available because most healthcare providers have participated in quality improvement (QI) projects in medical or nursing education or training (Wong, Etchells, Kuper, Levinson, & Shojanian, 2010; Kyrkjebo, Hanssen, Haugland, 2001; Huntington et al., 2009). Patient safety and QI are core concepts for practice and for involvement in institutional improvement plans (Wong et al., 2010; Kyrkjebo et al., 2001; Huntington et al., 2009). Whether addressing weight loss, smoking cessation or medication adherence, all of these health behaviors would be amenable to personal system changes through CSI.

This familiarity with continuous quality improvement tools such as PDCA across multiple disciplines and patients will help translate CSI from the organizational to the personal level. Several opportunities exist for learning about and using CSI. Alemi and Neuhauser (2006) published *A Thinking Person's Weight Loss and Exercise Program* to help lay persons apply CSI principles to their lives. University courses are available to students in the area of process improvement (George Washington University, 2009). Healthcare professionals familiar with CSI are testing its use to improve health behaviors. Early indications are that patients become engaged in CSI and are capable of learning its techniques when taught by healthcare professionals (Russell, Ruppert, & Matteson, 2011). Although participants' age was absent in several reviewed articles, older adults who self-administer medications may benefit from CSI. For example, an older adult who self-administers medications may enhance medication taking behaviors through CSI;

however, residents in assisted living facilities may have multiple people touching their system, potentially having less impact on the desired medication taking behaviors.

The strength of this review is that it addresses a gap in the intervention literature. Although CQI has been an effective process improvement tool for more than 60 years in business and healthcare (Deming, 1986), it appears that enhancing health behavior change may require a paradigm shift in order to apply CQI to personal system improvement. Data supporting the effectiveness of CSI are preliminary, but this approach appears to be a promising health behavior change intervention.

Limitations of the reviewed studies include weak designs, small sample sizes, single center studies, limited dose and duration of the intervention, use of instruments with questionable reliability and validity, and lack of long-term outcomes. Methodologic quality was poor for most studies. Case study design, one of the weakest study designs, was used in three of the reports (Polit & Beck, 2004). The STROBE scores of these studies were weak to moderate, indicating lower methodological and reporting rigor; whereas the CONSORT scoring of the RCT was strong, reflecting the study's methodological and reporting strengths.

The second limitation of the reviewed studies is lack of statistical power. Since sample size affects studies' statistical power, the effect of intervention studies that are not fully powered may not be adequately tested or realized (Polit & Beck, 2004). Though the study by Russell et al. (2010) was not powered to detect a difference between groups, the study did find a statistically significant difference between the groups, which supports the large effect size of the personal improvement intervention.

Third, the dose and duration of the interventions were brief, which may limit their effectiveness. Despite these limitations, CSI showed promise as a behavior change intervention with behavior changes trending in the desired direction. Russell et al. (2010) found the CSI intervention was effective immediately, which indicates that providers may be able to deliver it brief patient encounters.

Fourth, no long-term outcomes were documented in the eight reviewed studies. The longest follow-up time period was six months. The extent of human and financial resources needed to maintain the behavior is also unknown.

Finally, seven of the studies employed self-report instruments. Self-report depends on patients' honesty and recall. If self-report data are gathered during interviews, then the interviewer's skill also is a variable that can influence data validity and reliability.

Overall, the results of this systematic review of the CSI intervention research thus far have been positive and show promise. Most nurses have been involved in CQI projects during education or practice. Nurses' familiarity with organizational system change can be easily adapted and applied to patients' personal systems. In inpatient or outpatient settings that include nursing practice, nurses could easily implemented CSI to affect health behavior change regarding medication adherence, weight management, and smoking cessation. With further experience and research, confidence in CSI as an intervention should continue to expand and strengthen.

Conclusion

In conclusion, CQI has long been used successfully at the organizational level. During the past few years, researchers have investigated CSI as a health behavior change

intervention for individuals. Although this review found that CSI shows great promise as a behavior change intervention, the methodological quality of the reviewed studies is weak. Fully powered randomized controlled trials with diverse populations and long term follow-up are needed to further study the effectiveness of the CSI intervention.

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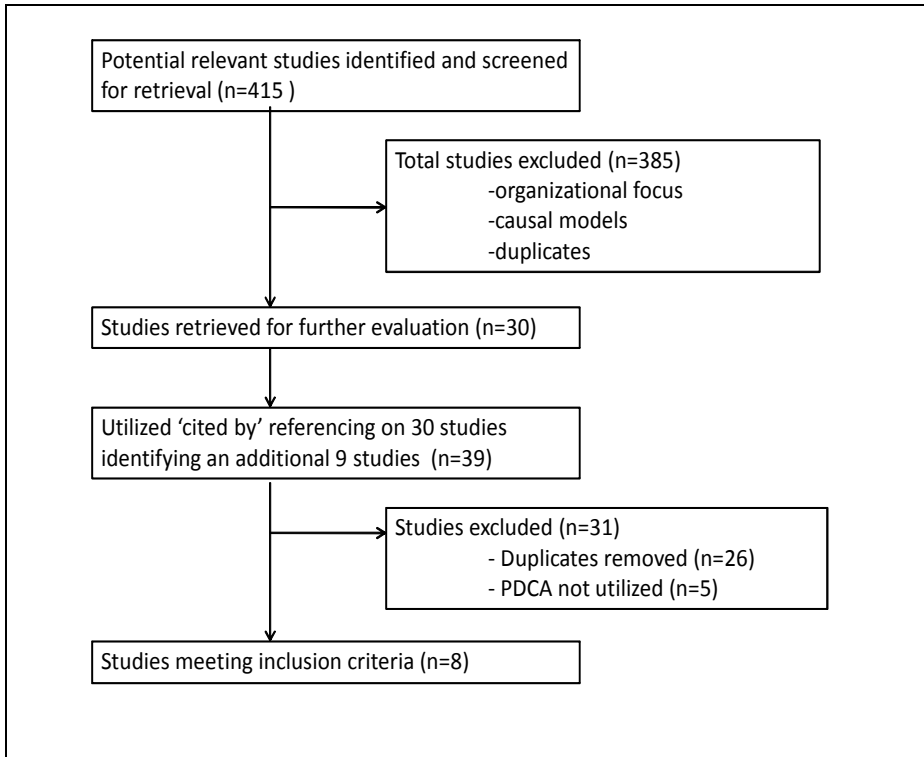


Figure 1. Study Inclusion Flow Chart.

Table 2.2

CONSORT scoring (0=not documented; 0.5 partially documented; 1=documented)

			Russell 2010
1	Title & abstract	How participants were allocated to interventions (e.g. random allocation, randomized or randomly assigned)	1
	Introduction		
2	Background	Scientific background and explanation of rationale	1
	Methods		
3	Participants	Eligibility criteria for participants and the settings and locations where the data were collected	1
4	Interventions	Precise details of the interventions intended for each group and how and when they were actually administered	1
5	Objectives	Specific objectives and hypotheses	0.5
6	Outcomes	Clearly defined primary and secondary outcome measures and, when applicable, any methods used to enhance the quality of measurements (e.g. Multiple observations, training of assessors)	1
7	Sample Size	How sample size was determined and, when applicable, explanation of any interim analyses and stopping rules	1
	<i>Randomization</i>		
8	Sequence generation	Method used to generate the random allocation sequence, including details of any restriction (e.g. blocking, stratification)	1
9	Allocation concealment	Method used to implement the random allocation sequence (e.g. Numbered containers or central telephone), clarifying whether the sequence was concealed until interventions were assigned	0
10	Implementation	Who generated the allocation sequence, who enrolled participants, and who assigned participants to their groups	0.5
11	Blinding (masking)	Whether or not participants, those administering the interventions, and those assessing the outcomes were blinded to group assignment. If done, how the success of blinding was evaluated	1
12	Statistical methods	Statistical methods used to compare groups for primary outcome(s); methods for additional analyses, such as subgroup analyses and adjusted analyses.	1
	Results		
13	Participant flow	Flow of participants through each stage (a diagram is strongly recommended). Specifically, for each group report the numbers of participants randomly assigned, receiving intended treatment, completing the study protocol, and analyzed for the primary outcome. Describe protocol deviations from study as planned, together with reasons.	1
14	Recruitment	Dates defining the periods of recruitment and follow-up.	1
15	Baseline data	Baseline demographic and clinical characteristics of each group.	1
16	Numbers analyzed	Number of participants (denominator) in each group included in each analysis and whether the analysis was by intention to treat. State the results in absolute numbers when feasible (e.g. 10/20, not 50%)	1
17	Outcomes and estimation	For each primary and secondary outcome, a summary of results for each group, and the estimated effect size and its precision (e.g. 95% confidence interval)	1
18	Ancillary analyses	Address multiplicity by reporting any other analyses performed, including subgroup analyses and adjusted analyses, indicating those pre-specified and those exploratory.	1
19	Adverse events	All important adverse events of side effects in each intervention group	0.5
	Discussion		
20	Interpretation	Interpretation of the results, taking into account study hypotheses, sources of potential bias or imprecision and the dangers associated with multiplicity of analyses and outcomes	1
21	Generalizability	Generalizability (external validity) of the trial findings	1
22	Overall evidence	General interpretation of the results in the context of current evidence	1
	Total score		19.5

Table 2.3

STROBE scoring (0=not documented; 0.5= partially documented; 1=documented)

	Item No	Recommendation	Alemi et al. (2000)	Lundeen et al. (2001)	Alemi et al. (2003)	Bacon & Stewart (2001)	Scott (1993)	Kyrkjebo & Hanasted (2003)	Moore (2003)
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	0	0.5	0	0	0.5	0	0
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	0	0.5	0	0	0	1	0
Introduction Background	2	Explain the scientific background and rationale for the investigation being reported	1	1	1	1	1	1	1
Objectives	3	State specific objectives, including any pre-specified hypotheses	1	1	0	0	1	1	0.5
Study design	4	Present key elements of study design early in the paper	0	0.5	0.5	0.5	0	0	0.5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	0	1	0.5	0	1	1	0.5
Participants	6	<i>Case-control study</i> —Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls	0	0.5	0.5	0.5	0	0	0.5
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	0.5	1	0.5	0.5	1	1	0.5
Data sources/ measurement	8	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	0.5	1	1	0.5	0	1	0.5
Bias	9	Describe any efforts to address potential sources of bias	0.5	0.5	0.5	0.5	0	0.5	0.5
Study size	10	Explain how the study size was arrived at	0	0	0	0.5	0.5	1	1
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	0	1	0	0.5	0.5	1	0.5
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	0	1	0	0.5	0.5	1	0.5
		(b) Describe any methods used to examine subgroups and interactions	0	0	0	0	0	0	0
		(c) Explain how missing data were addressed	0	0	0	0	0	0	0
		(d) <i>Case-control study</i> —If applicable, explain how matching of cases and controls was addressed	0	0	0	0	0	0	0
		(e) Describe any sensitivity analyses	0	0	0	0	0	0	0
RESULTS Participants	13	(a) Report numbers of individuals at each stage of study—e.g. numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analyzed	0	0	0	0	0	0	0
		(b) Give reasons for non-participation at each stage	0	0	0	0	0	0	0
		(c) Consider use of a flow diagram	0	0	0	0	0	0	0
Descriptive data	14	(a) Give characteristics of study participants (e.g. demographic, clinical, social) and information on exposures and potential confounders	0	0	0	0	0	1	0
		(b) Indicate number of participants with missing data for each variable of interest	0	0	0	0	0	0	0

			Alemi et al. (2000)	Lundeen et al. (2001)	Alemi et al. (2003)	Bacon & Stewart (2001)	Scott (1993)	Kyrkjebo & Hammsted (2003)	Moore (2003)
Outcome data	15	<i>Case-control study</i> —Report numbers in each exposure category, or summary measures of exposure	0.5	0.5	0	0.5	0	0.5	0
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (e.g., 95% confidence interval). Make clear which confounders were adjusted for and why they were included	0	0	0	0	0	0	0
		(b) Report category boundaries when continuous variables were categorized	0	0	0	0	0	1	0
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	0	0	0	0	0	0	0
Other analyses	17	Report other analyses done—e.g. analyses of subgroups and interactions, and sensitivity analyses	0	0	0	0	0	0	0
Key results	18	Summarizes key results with reference to study objectives	1	1	0.5	0.5	0.5	1	0.5
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	1	1	0.5	0	0.5	1	0.5
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	1	1	0.5	0.5	0.5	1	0.5
Generalizability	21	Discuss the generalizability (external validity) of the study results	1	1	1	1	0.5	1	0.5
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	0	0	0	0	0	0	0
Totals	22		8	14	7	7.5	10.5	16	8.5

Table 2.1

CSI Systematic Review of Included Studies

Author (Year)	Theory/concepts	Sample/setting	Design	Intervention	Measure/outcome	Results	Strengths/limitations
Alemi, Neuhauser, Ardito, Headrick, Moore, Hekelman & Norman (2000)	<p>CSI 8 step theory of behavior change:</p> <ul style="list-style-type: none"> -training in CSI -include others if they influence the process -clearly define the problem -understand the process that leads to the desired outcome -suggest and select solutions -carry out a series of small change cycles -monitor progress and reasons for variations in outcomes -publicly disclose intentions <p>Four concepts:</p> <ul style="list-style-type: none"> -system and not will power is the cause of change <p>Habits involve linked decisions (change system and change the habit)</p> <ul style="list-style-type: none"> -process owner should be organized to support change -change is data driven 	<p>Behavior: Lifestyle management</p> <p>N=82</p> <p>Medical, nursing and administrative students at CaseWestern Reserve University and Vanderbilt University (1996-1998).</p>	<p>Post-test only, non-equivalent control group design</p>	<p>CSI Workbook (n=65); no workbook (n=17)</p> <p>Dose: unknown</p> <p>Duration: 15 weeks</p>	<p>Multiple single, individual self-report on various outcomes/goals (lifestyle)</p>	<p>83% of students using the workbook reported a measured or significant improvement</p> <p>30% of the no workbook group had a measured improvement</p> <p>Examples: Decreased time in the bathroom for an obsessive compulsive female from >100 minutes to a low of <40 minutes</p> <p>Weight lifting increase strength from 42.5 pounds to 93pounds</p> <p>Reducing fatigue at work by monitoring a fatigue score</p> <p>Improving personal work habits</p>	<p>3 professional student groups from 2 institutions</p> <p>Self-reports of improvement</p> <p>Short duration of intervention</p> <p>No long-term outcomes</p>

Author (Year)	Theory/concepts	Sample/setting	Design	Intervention	Measure/outcome	Results	Strengths/limitations
Lundeen, Fisher-Pai, & Neuhauser (2001)	PDSA with statistical modeling with regression modeling; no changes in environment to change the system-system monitoring only	Behavior: Stress N=1 (student) New York	Case study	Personal Improvement workbook Dose: unknown Duration: 3-10 weeks	Correlations, process diagrams over time Statistical modeling Self report on 16 stress variables everyday	Observation Personal stress model developed	Single case Self report data No long-term follow-up
Alemi, Pawloski, Fallon (2003)	System thinking: -look to environment -identify life routines -describe causes and effects -select system solutions -incorporate change into routines -implement greater than one solution -examine data	Behavior: Eating N=1 Male physician US	Case study	CSI Dose: unknown Duration: 3 months	Relapse documentation (number of days of failure since last success) identifying patterns across events	Diet change with carpooling, decrease in junk food	Single case Self-report data No long-term data or outcomes
Russell, Conn, Ashbaugh, Madsen, Wakefield, Webb, Coffey, Peace (2010)	PDCA	Behavior: Transplant medication adherence N=15 Avg age=51 Female=8 80% Caucasian Midwestern US transplant facility	RCT	CSI Dose: monthly with electronic monitoring reports Duration=6 mo	Electronic monitoring of immunosuppressant medication adherence	Statistically significant difference between the intervention and attention-control at six months (p=0.0396); Effect size (Cohen's d=1.38)	Pilot RCT No long-term outcomes Electronic monitoring measure with good reliability and validity

Author (Year)	Theory/concepts	Sample/setting	Design	Intervention	Measure/outcome	Results	Strengths/limitations
Bacon & Stewart (2001)	Six steps: set QI goals, take actions to achieve goals, collect information (data), identify defects, analyze data, and act to eliminate defects. Roberts Personal exercise check list utilized along with PDCA tools	Behavior: Lifestyle changes in students (personal development, increase efficiency, improving punctuality) N=51 (2 sections of students N=18; N=33) Colorado	Post-test Design	Six steps of QI Dose: unknown Duration: one semester	Variety of quality tools (run chart, Pareto chart, histogram)	50% of the class reported substantial improvement in behavior	Self-report data No statistical data No long-term outcomes
Scott (1993)	PDCA with Pareto charts, role mapping and run charts	Behavior: Office efficiency N=1 US	Case study	CSI Dose: unknown Duration: 9/10-10/14/92; and 11/5-12/1/92	Learning, facilitation, communication, one on one, any improvement work, informational meetings, PDCA, administration	Facilitation decreased by 58% (34 hours to 14.5 hours) Communication decreased by 50% (20 hours to 7.5 hours) QI improvement increased from 15 hours to 27 hours	Single case Dose of PDCA unknown Short duration of study No long-term outcomes
Kyrkjebo & Hanestad (2003)	PDSA cycles	Lifestyle changes among nursing students N=44 Norwegian nursing students 39 female 5 male Age average=22; range 19-32	Post-test Design	PDSA workbook and questionnaire Dose: unknown Duration: 8 weeks	Personal improvement projects in nursing student-generally in lifestyle or study habits (13 students-study habits; 12 sleep; 6 physical exercise; 5 eating/drinking habits; 2 smoking; 2 money management; 1 asthma; 1 housekeeping; 1 TV viewing; 1 short term memory improvement)	45% of nursing students had an improvement in their study habits or lifestyle 89% reported project helped them learn CQI 75% reported they saw a benefit for clinical practice	First year nursing students with limited knowledge of CQI Short duration of intervention No long-term follow-up

Author (Year)	Theory/concepts	Sample/setting	Design	Intervention	Measure/outcome	Results	Strengths/limitations
Moore (2003)	CSI with diary keeping, benefits/barriers assessment, assessment for readiness to change.	Decrease cardiac risk factors (weight reduction 5pounds) N=6 age range 60-70 years US	Post-test Design	Information included decreasing daily calories, transition from calorie counting to portion control, eating techniques during special occasions, encouragement to exercise, education on low fat and low calorie foods. Dose: CSI with nurse feedback on data 2-3 times per week Duration: one month	Eating patterns (24 hour calorie count twice a week for one month) Exercise amount Weekly weights Client satisfaction with the diet regimen and with the improvement team processes used	All participants lost 5 pounds Patients liked the feedback by the improvement team.	Small sample size No control group No statistics utilized

19 *Abbreviations: Continuous Self Improvement (CSI); Continuous Quality Improvement (CQI), Plan-Do-Check-Act (PDCA), Randomized Controlled Trial (RCT), Quality Improvement (QI), Plan-Do-Study-Act (PDSA)*

CHAPTER THREE

DESIGN

A pilot randomized controlled trial was conducted to determine the feasibility and potential effectiveness of a three-month CSI intervention on medication adherence rates in adult inflammatory bowel disease patients. Four phases of the study are as follows in Figure 3.1(Research Design).

Sample

The University of Missouri IBD team follows more than 100 IBD patients. Based on literature documenting medication nonadherence rates of 7-72% in IBD patients, an estimated 50% of these IBD patients may be nonadherent (Jackson, Clatworthy, Robinson, & Horne, 2010). A sample of 40 adult IBD patients was screened by electronic monitoring for two months to determine their level of medication adherence. Initially, it was proposed 20 nonadherent would enter the intervention group, 10 participants in the CSI intervention group and 10 participants in the attention control group. However, 19 participants completed the screening period with nine non-adherent participants identified.

Instruments

Mini-Mental Status Examination. Mini-Mental Status Examination (Appendix B) measures cognition as a screening tool for dementia. An MMSE score of less than 24 is considered cognitively impaired. The MMSE has a specificity of 82% and a sensitivity of 87% for detecting dementia and delirium in hospitalized patients (Anthony, 1982; Folstein, 1975).

Demographics. At the initial visit, demographic information was collected: name; gender; date of birth; age at diagnosis with IBD; maintenance therapy medication name, dose and timing of medication; ethnicity; race; educational level; marital status; employment status; body mass index (BMI); smoking status; IBD diagnosis (UC-pan vs. Left vs. Right vs. rectal; Crohns-small intestine only, large intestine only, small/large intestinal disease, fistulizing disease); last dose of oral/rectal steroids; number of all medications; and use of medication planner/pillbox (Appendix B).

Systems Thinking Survey. The Systems Thinking Survey was administered at the initial visit and at the end of the intervention period for the intervention group (Appendix B). The survey consists of 17 system statements ranked on a 5-point Likert scale (1-not important; 5-very important) that document the intervention's effectiveness in order to increase its internal validity. No psychometric data are available at this time (Moore, 2011).

End of Study Interview Form (Feasibility Survey). End of Study Interview Form (Feasibility survey) was administered at the close of the intervention phase to both groups (Appendix B). The 15-question survey solicits participants' opinions regarding their time burden, visits, telephone calls, and overall impression of the study. Other feasibility data collected were the length of time to recruit the subjects, rates of adherence among the screened group, the patterns of attrition of the nonadherent intervention groups, and the time required to perform the intervention and collect data.

Variables

Independent Variable: CSI. CSI is a systems-focused approach to changing behavior. This intervention uses the Plan-Do-Check-Act process to target participants'

personal systems. The PI and the participant used electronic monitoring as an objective measure of adherence as the basis to collaboratively discuss medication taking patterns (dosing and timing). The PI and participant sought system solutions to improve medication taking, which the PI then monitored for effectiveness.

Dependent Variable: Medication adherence. Medication adherence was measured by the MEMS electronic monitoring device (Medication Event Management System®, MEMS Track Cap™). The device reports whether the medication container was opened within ± 1.5 hours of the prescribed medication administration time. The PI can correct deviations from this window or accidental openings recorded by the participant in the MEMS diary (Appendix B). The corrected report then represents ingestion of a dose of medication. From this report, a medication adherence score was calculated using SPSS/SAS. The MEMS records the dynamic nature of medication-taking by documenting dates and times of container openings without adding to the patients' burden and device failure is infrequent (Reikert, 2002). Advantages of electronic monitoring include the ability to measure patterns of drug use. Limitations include cost, electronic malfunction, interference with established adherence routines, reactivity (knowledge of being monitored), and inability to confirm ingestion with each bottle opening (Reikert, 2002). However, utilizing the MEMS diary will increase the validity of the MEMS monitoring by documenting openings that were not ingestions. No psychometric data are available on the MEMS caps at this time, but it does appear to have good reliability; validity remains to be established (Denhaerynck, et al., 2008). Battery life is 18 months and its failure rate is below 0.5%.

Recruitment

The recruitment phase lasted from November 2010 to April 2011. The PI, who works in the gastroenterology clinic at the University of Missouri, briefed gastroenterology physicians on the study and gave them information for potential participants that included the PI's name and phone number to contact if interested. The PI also recruited potential participants from the clinic through flyers in the waiting room and examination rooms. Flyers included information regarding the study with the PI's name and phone number to contact if interested in participating in the study. A research assistant (RA) also assisted with patient enrollment by being present during the IBD clinic times.

Once the PI/RA received a call from a potential participant, an appointment with the PI/RA was arranged at the gastroenterology clinic or in the participant's home. At that time, consent issues were thoroughly discussed, including the study's risks and benefits. The PI/RA asked participants questions and allowing them to verbalize their understanding. After all questions regarding study participation were answered by the PI/RA, a signed consent was obtained from the participant by the PI/RA. The participant was then screened via the inclusion/exclusion criteria and administered the MMSE by the PI/RA (Appendix B). Participants whose MMSE scores were below 24 were thanked for their interest in the study and excluded by the PI. Participants who met inclusion criteria and did not meet exclusion criteria supplied demographic information to the PI.

Inclusion criteria and *Exclusion criteria* are noted in Figure 3.2 and Figure 3.3.

Demographic data were: name; gender; date of birth; age at diagnosis with IBD; maintenance therapy medication name, dose and timing of medication; ethnicity; race; educational level; marital status; employment status; Body Mass Index (BMI); smoking

status; IBD diagnosis (UC-pan vs. Left vs. Right vs. rectal; Crohns-small intestine only, large intestine only, small/large intestinal disease, fistulizing disease); last dose of oral/rectal steroids; number of all medications; and use of medication planner/pillbox (Appendix B).

Training Participants on MEMS and MEMS Diary Use

The PI/RA trained all participants in the use of the MEMS caps and MEMS diary. The PI/RA demonstrated the MEMS caps, and participants demonstrated their understanding by using the caps as PI/RA watched. A minimum three-second interval between bottle opening and closing is required to accurately record the medication taking behavior. To promote accuracy of the instrument, the PI/RA reinforced the importance of the three-second interval. One week after the training, the PI/RA phoned participants to ensure their proper use of the MEMS and answer any questions. A MEMS diary was given to each participant to document late/missed doses, such as hospitalizations, doctor's appointments, or activities altering medication taking (Appendix B).

Screening Phase

This two month screening phase identified participants who were nonadherent to their maintenance therapy medications by monitoring timing and dosing of medications. For this study, medication nonadherence is operationally defined as a medication adherence score less than 0.85; this definition has been utilized in previous studies (Russell, et al., 2007). The score is discussed further in the Instruments section. The PI/RA thanked adherent participants (medication adherence score $>.85$) for their participation, praised them for their adherence, gave them a \$10 Wal-Mart gift card, and exited them from the study. The PI randomized nonadherent participants into the trial by

computer-generated random numbers in sequence of admission through sealed numbered envelopes. MEMS caps were utilized on IBD patients' physician-prescribed maintenance therapy medications. Although IBD patients usually are prescribed multiple IBD medications, only one medication was monitored. In the case of participants taking two maintenance therapy medications, the oral medication taken twice a day was monitored. For participants with medication planners, the PI/RA placed a candy reminder in the planner as a reminder to take maintenance therapy in the MEMS bottle. To decrease attrition, subjects were paid with a \$10 gift card to Wal-Mart after the screening phase. There was a two-week period after the screening phase, during which the PI/RA downloaded MEMS data, corrected it using the MEMS diary, returned the MEMS by mail or in person, and scheduled a follow-up visit.

Intervention Phase

CSI Intervention-Months 1-3

After randomization, the three-month intervention phase began. Nonadherent participants randomized to the CSI intervention group received the system-focused intervention to increase maintenance therapy medication adherence. The PI visited each participant, identified key individuals to assist participants' with the intervention, and used the Important People Form to survey them regarding their level of involvement in participants' lives (Form 1: Important People Form (adapted from Alemi, 2003, Appendix B). The Important People Form is based on the results of the interview with the participant and is documented by the PI. It was not necessary to have "Important People" to participate in the CSI intervention. The next intervention tool was the Life Routines Form (Adapted from Alemi, 2003) (Form 2, Appendix B) and Cycles Form (Adapted

from Alemi, 2003) (Form 3, Appendix B), which identifies the routines in participants' environments, or "cycles of activities where a routine leads to another set of routines that eventually lead back to the starting routine" (p.19) (Alemi, 2005). Identifying these cycles or routines can lead to modification of the medication-taking routines. The PI analyzed MEMS data and participants' cycles for patterns or areas of nonadherence that could improve through system changes. These modifications were trialed and changes made simultaneously (Form 4: Possible Solutions Form (Adapted from Alemi, 2003, Appendix B). Participants were asked to work at specific system changes for three months.

During the initial visit of approximately 60 minutes, the PI explained CSI and systems theory to participants and administered a Systems Thinking Survey to document baseline systems thinking. Two weeks after the visit, the PI phoned participants to determine if they had made changes to their personal systems, check for MEMS use, and answer any follow-up questions. The MEMS monitoring continued for three months post intervention. In addition to the CSI intervention, the intervention group continued to receive usual care by the IBD team.

Attention Control-Months 1-3

Those in the attention control group had an initial visit by the PI/RA discussing education provided by the Crohn's and Colitis Foundation. During the 60-minute visit, the PI used a Power Point presentation to instruct the participant on the IBD disease process, predictors and prevalence of IBD, and extra-intestinal manifestations of IBD. All handouts were mailed or given to the participant by the PI at the initial visit. Attention control participants were told that their MEMS score were below 0.85 and no discussion

of the pattern of nonadherence were performed. In addition to the attention control intervention, the participants continue to receive usual care given by the IBD clinic and staff.

Completion Phase

At the completion of the intervention phase, the CSI intervention group returned the MEMS and MEMS diary at a scheduled visit or by mail. The Feasibility survey and a post- intervention Systems Thinking survey was provided to the participant by the PI (Appendix B). The participant also received a \$10 Wal-Mart gift card for their participation during the intervention phase of the study. MEMS data were then uploaded for comparison to the CSI intervention group.

Procedure

After obtaining informed consent, the PI will collect MMSE and demographic data from participants. The PI will instruct the participant on the use of the MEMS. One week before the end of the two-month screening phase, the PI phoned participants to remind them to return the MEMS for evaluation by mail or in the clinic. MEMS data were downloaded and the MEMS report manually corrected using the MEMS diary. Participants whose medication adherence score was above .85 exited the study after the PI thanked them for participating and gave them a \$10 Wal-Mart gift card. Participants whose medication adherence score was less than .85 were randomized to the CSI intervention group or the attention-control group.

The PI contacted participants randomized to the CSI intervention, and arranged to meet. At this visit, the PI discussed the Important People Form, Life Routines form, Cycles Form and possible solutions for systems improvements, and administered the

Systems Thinking survey. At the end of the three-month intervention, the PI retrieved the MEMS and MEMS diary (either in person or by mail), administered the Feasibility and Systems Thinking survey to participants and gave them a \$10 Wal-Mart gift card.

During a 60-minute visit, participants randomized to the attention-control group received IBD education and continued to use the MEMS device for three months. The PI instructed participants during a Power Point presentation regarding IBD's disease process as well as its predictors, prevalence, and extra-intestinal manifestations. The PI gave the participants the IBD presentation handouts after the education session. MEMS results were not discussed with the attention control group, but were analyzed at the end of the study period. After retrieving the MEMS from the participant at the end of three months, the data from the MEMS were uploaded for comparison to the CSI intervention group. The participants in both groups continued to receive usual care given by the IBD clinic and staff.

Data analysis

Aim 1. To determine the feasibility of the CSI intervention in adult IBD patients.

Feasibility was determined by participant input based on results of the Feasibility survey and on the PI's time burden to administer the intervention. The time burden was measured through participant recruitment time, intervention delivery time, and time to collect the data.

Aim 2. To determine the potential effect of the CSI intervention in adult IBD patients in this pilot study.

Descriptive statistics, such as means or standard deviations of MEM scores at baseline, at 3 months, were computed. Changes between two time points, as well as 95%

confidence intervals for differences within and between two groups, were computed. Change scores (3-month MEMS score minus the baseline MEMS score) within a groups and between two groups were compared using the paired t-test or a two sample t-test, respectively. In keeping with the intention of a pilot study, we were interested in obtaining estimates for the effect size. The level of significance of 0.05 was used for all t-tests and descriptive statistics; 95% confidence intervals for differences within and between groups were computed. The estimate of the mean group difference as well as estimates of the standard deviation of the group differences in MEMS scores will be useful in determining appropriate sample size for a future large-scale study.

Limitations/Strengths

Limitations of the proposed study are the lack of power, the MEMS and the CSI intervention. The study is not intended to have adequate power to perform hypothesis testing; however, if the pilot study finds a trend towards statistical significance, a fully powered RCT will follow. Electronic monitoring (MEMS) is not a direct measure of adherence. It is assumed when the bottle records an opening, the medication is ingested. Also, the MEMS may have a Hawthorne effect; however, by excluding the first month's data during the screening period, this effect should be minimized. Finally, the CSI intervention has not been utilized in the IBD population and is dependent on the experience of the person leading the intervention and the self-management/insight skills of the participant. The PI has taken instruction in the method, and the co-investigator has performed it successfully in renal transplant patients.

Strengths of the study are its design, the innovation of the intervention, the homogeneity of the sample, measurement of change in systems thinking, and the

measurement of medication adherence. Although MEMS is not a direct measure of adherence, it is considered the strongest indirect measure. A randomized control trial is the strongest study design and this pilot study will be contributing to the sparse IBD adherence intervention literature (Polit & Beck, 2012). The innovative application of the CSI systems focused intervention to change behavior has been successful in other lifestyle modifications and disease processes. Testing the CSI intervention in IBD can further validate the intervention.

Electronic monitoring (MEMS) is considered the strongest indirect measurement of medication adherence. The PI has two years of experience working with the MEMS technology, and the co-investigator has seven years of experience with it. Combining a strong study design in a homogeneous nonadherent population increases the power of the study (Polit & Beck, 2012). Applying an intervention to an adherent population may not yield statistically significant results; whereas directing the intervention to those who need it the most may yield statistically significant results.

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Figure 3.1: Research Design.

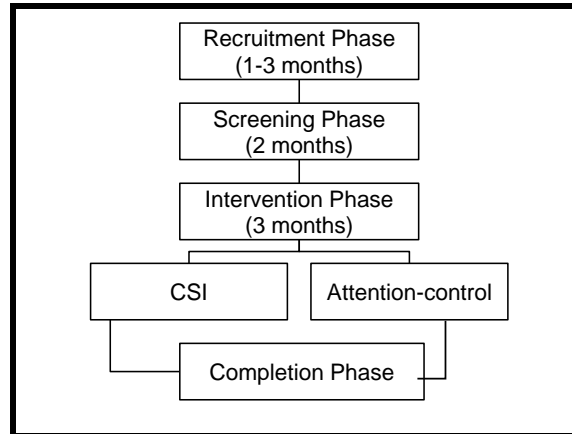


Figure 3.2: Inclusion criteria

- Inclusion criteria:**
- 18 years of age or older
 - Diagnosed with IBD (ulcerative colitis or Crohns disease)
 - Currently prescribed oral maintenance therapy (azothiopurine, aminosalicylate, mercaptoprine, or methotrexate) once or twice a day
 - Ability to speak, hear, and understand English
 - Able to open MEMS caps
 - MMSE ≥ 24

Figure 3.3: Exclusion criteria

- Exclusion criteria:**
- Metastatic cancer or illness that will cause death in less than one year as determined by medical records or primary care provider
 - Take maintenance medication more than twice a day
 - History of bowel surgery
 - Regular long-term follow up appointments by an IBD clinic other than the University of Missouri
 - MMSE ≤ 23

Figure 3.4: Research timeline

Research Activity	Month 1-3	Month 3-6	Month 6-8	Month 8-11
Recruitment: -ID potential participants -contact potential participants -obtain written consent -inclusion/exclusion criteria -MMSE -Demographic information -train on MEMS caps				
Randomization of nonadherent participants only				
Intervention: CSI intervention with MEMS data/diary review monthly x 3 months; attention control intervention to control group				
MEMS Data analysis				
Analyze/Interpret/summarize findings				
Prepare manuscript				

Running Head: CONTINUOUS SELF IMPROVEMENT

A Pilot Study to Improve Maintenance Medication Adherence in Adult Inflammatory
Bowel Disease Patients

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Abstract

Background: Medication nonadherence in inflammatory bowel disease (IBD) can lead to suboptimal control of the disease, decreased quality of life, and poorer outcomes. This pilot study evaluated the feasibility, intervention mechanism, and potential effectiveness of a three-month continuous self-improvement (CSI) intervention to enhance medication adherence in adult nonadherent IBD patients.

Methods: Adult IBD patients taking a daily or twice-daily dosed maintenance medication were screened for two months to determine baseline medication adherence levels. Adherence was monitored electronically. Nonadherent IBD participants were randomized to receive either the CSI intervention or the attention control intervention and then monitored for three-months. The CSI intervention consisted of a data evaluation and system refinement process in which personal system changes were identified and implemented. The attention control group was given only educational information regarding IBD disease process, extra-intestinal manifestations of IBD, and medical therapy actions and side effects. Demographic statistics, change scores for within and between-group differences, and effect size estimates were calculated.

Results: Nine nonadherent participants (medication adherence score $<.85$) were eligible for randomization. The intervention was found to be feasible and acceptable. System thinking scores trended in the anticipated direction. Although no statistically significant improvement in medication adherence was found ($p=0.14$), medication adherence improved in 3 of 4 of the CSI group and only 1 of 2 in the attention control group. The effect size calculation of 1.9 will determine the sample size for future study.

Conclusions: The results of this pilot study showed the intervention was feasible and had a positive effect on the medication adherence change score and on adherence levels. A larger fully powered study is needed to test of the effectiveness of this innovative intervention.

Key Words: adherence, IBD, intervention

A Pilot Study to Improve Maintenance Medication Adherence in Adult Inflammatory Bowel Disease Patients

Introduction

Adherence is defined as “the extent to which a person’s behaviour – taking medication, following a diet, and/or executing lifestyle changes, corresponds with agreed recommendations from a health care provider” (Sabate, 2003, p.3). Medication adherence in chronic diseases averages 50% in developed countries (Sabate, 2003). Poor adherence in chronic disease results in increased health care costs and poor outcomes (Sabate, 2003). Medication adherence interventions have had inconsistent results across chronic illnesses, and no patient-level intervention has consistently enhanced adherence (Roter, Hall, Merisca, et al., 1998; Peterson, Takiya, & Finley, 2003; McDonald, Garg, & Haynes, 2002; Kripalani, Yao, & Haynes, 2007).

Inflammatory bowel disease (IBD), which includes Crohn’s disease (CD), ulcerative colitis (UC), and indeterminate colitis, is characterized by periods of relapse and remission. In the United States, IBD is a chronic disease affecting approximately 1.4 million people, with Crohn’s disease affecting approximately 26.0-198.5 individuals per 100,000 and UC affecting approximately 11 per 100,000 (Loftus, 2004; Lichtenstein, 2010). The medication regimen for IBD is complex and lifelong which increases medication nonadherence rates (Hanauer, 2006). Current medication nonadherence rates in IBD range from 7-72% (Jackson, Clatworthy, Robinson & Horne, 2010). IBD medication nonadherence can lead to suboptimal control of the disease, decreased quality of life, and increased morbidity (Hawthorne, Rubin, & Ghosh, 2008).

Continuous self-improvement (CSI), an innovative intervention for affecting health behavior change, is based on systems theory. A recent systematic review of CSI intervention literature found that it helped change health behaviors, specifically life-style management (exercise and weight loss) and chronic diseases (asthma and kidney transplantation) (Matteson & Russell, 2011). CSI is a unique, systems-focused intervention that seeks to change behavior that focuses on patients' personal systems rather than on their motivation or intention (Russell, 2010; Gustofson, 1992). This study's purpose is to evaluate the feasibility, intervention mechanism, and potential effectiveness of the CSI intervention in adult nonadherent participants in a mid-western IBD clinic.

Materials and Methods

Design

A pilot randomized controlled trial tested the feasibility, intervention mechanism, and possible effectiveness of a three-month CSI intervention to improve medication adherence in adult nonadherent IBD patients.

Sample and Setting

Participants were recruited from a mid-western out-patient IBD clinic by the primary investigator (PI) and/or the research assistant (RA). Initial inclusion criteria were: age 18 years or older; diagnosis of ulcerative colitis or Crohn's disease; currently on IBD maintenance medication therapy (immunosuppressant or 5-aminosalicylic acid); ability to speak, hear, and understand English; able to open Medication Event Monitoring System (MEMS) caps; and Mini-Mental Status Examination (MMSE) score greater than or equal to 24. Of the 41 adult IBD patients who were approached to enter the study, 38

participants consented and enrolled, and three refused to participate (Figure 1. Patient Flow Diagram).

Intervention

Independent variable: Continuous self-improvement intervention. Personal system thinking is conceptually defined as the process of understanding how people and circumstances are linked (Alemi et al., 2000). This approach attempts to improve patients' systems by creating and maintaining a behavior, such as taking medication (Alemi & Neuhauser, 2006; Gustafson, Cats-Baril, & Alemi, 1992; Russell, 2010). Through the data evaluation and system refinement process called Plan, Do, Check, Act (PDCA), patients' personal systems are identified and changes implemented. Further CSI theoretical detail is described elsewhere (Matteson & Russell, 2011) (Figure 2: PDCA).

The CSI process fosters ritualistic and habitual health behaviors and requires less effort, motivation, and intention to maintain the changes. For each participant, the PI performed a one-time face-to-face CSI intervention assessing the screening MEMS data after a brief personal system theory power-point presentation in the IBD clinic. The PI and participant analyzed electronic monitoring data for patterns of nonadherence, identifying potential personal system changes. System changes suggested by participants were performed to the best of their ability throughout the three-month study.

Attention control intervention. A one-time face-to-face educational session performed by the PI included a power-point presentation with a hand-out based on information from the Crohn's and Colitis Foundation of America (www.ccfa.org). IBD education topics

included IBD medical therapy actions and side effects, extra-intestinal manifestations of IBD, and surgical modalities utilized in IBD.

Dependant variables: Feasibility was determined using a 15-question, open-ended, written survey completed by the participants. The survey was used in a previous pilot study (Russell, 2010).

The intervention mechanism was evaluated by the Systems Thinking Survey. This survey was designed to measure change in personal systems thinking, which is a foundational concept of the CSI intervention. This survey, which was originally developed to evaluate physical exercise systems thinking, was adapted for medication taking by two experts in the field (CR and MM). This 17-question survey employed a 5-point Likert scale (1=not important, 5=very important). Scores range from 17 to 85 with higher scores indicating higher levels of systems thinking. No psychometric data are available for the survey (Russell, 2010; Moore, 2010).

Medication nonadherence. The medication nonadherence outcome was measured by the Medication Event Monitoring System ([MEMS], MEMS Track Cap, Apres Corp., Union City, CA, USA) electronic bottle cap. The MEMS cap's effectiveness and reliability are well documented (Russell, Conn, Ashbaugh, et al., 2007; Denhaerynck, Schaefer-Keller, Young, et al., 2008; De Geest & Vanhaecke, 1999; Reikert, 2006; Kruse & Weber, 1990). The MEMS score utilizes binary data (1=yes; 0=no) for evaluating dosing of medications. However, binary data cannot evaluate the timing of medication taking. In order to assess dosing and timing, a medication adherence score was determined to be superior for capturing the dynamics of medication taking (Russell et al., 2006).

A window of time was used to determine medication adherence which then allowed calculation of a medication adherence score. The *_on-time_* window for twice daily dosing was calculated as $\pm 25\%$ of the prescribed medication dosing interval; the *_early_* or *_late_* window was $\pm 50\%$, and the *_missed_* window was a dose not taken within $\pm 50\%$ of the prescribed time. This calculation approach, which captures the variability of adherence in timing and dosing, had been successfully used on twice-daily dosed medications (Russell et al., 2006). However, this approach did not allow calculation of adherence scores for medications dosed three or four times a day, because the dosing windows overlap. Consequently, 15 consented participants who took maintenance medication three or four times a day were withdrawn from the study (Figure 1. Patient Flow Diagram). The Institutional Review Board was contacted and inclusion criteria were changed to reflect the new inclusion criteria of daily or twice-daily dosed maintenance medication therapy.

Participants received MEMS diaries to record accidental openings or purposeful opens when medications were not taken (such as removing a pill to be taken later or refilling the medication bottle). These data are used to correct the MEMS data prior to analysis which increases the internal validity of the MEMS instrument.

Procedure:

The study was approved by the Institutional Review Board at the University of Missouri. Informed consent was obtained from all study participants, and no study participants were harmed during the study.

Screening Phase: A two-month screening phase identified participants who were nonadherent to their maintenance therapy medications. MEMS caps were utilized on

participants' physician-prescribed maintenance therapy medication; when more than one medication was eligible for monitoring, the twice daily medication was monitored. For participants with medication planners, a candy reminder was placed in the planner to remind them to take maintenance therapy from the MEMS bottle. Nonadherence was operationally defined as a medication adherence score less than 0.85 based on a sixty day screening period, a value that was empirically developed and utilized in previous studies (Russell, et al., 2007). The first 30 days of the screening period were removed to account for possible weak intervention effect of the MEMS cap (DeGeest et al., 2006). At the completion of the screening phase, adherent participants (medication adherence score $>.85$) were thanked for their participation by the PI, praised for their adherence, given a \$10 gift card, and exited from the study. Those who were nonadherent were randomized. *Randomization.* The PI used sealed numbered envelopes to block randomize nonadherent participants in sequence of admission into the trial's CSI intervention or attention control group. Participants were blinded to group assignment.

Study completion: For the participants' convenience, after 3 months, a self-addressed stamped envelope was mailed to the participant to facilitate the return of the MEMS cap, MEMS diary, feasibility survey, and System Thinking survey. After participants returned the MEMS cap, forms, and diary, and they were given a \$10 gift card for participating in the study.

Analysis

Data were cleaned and SAS v9.1 (SAS Institute, Inc., Cary, NC) was used by the project biostatistician to conduct all data analyses. Descriptive statistics were performed to characterize the sample. Feasibility was evaluated by frequency of responses. Personal

systems thinking was evaluated by systems survey mean and standard deviations of the change scores. Medication adherence change scores (changes between the two time points) as well as 95% confidence intervals for differences within and between the two groups were computed. Change scores within a group and between two groups were compared using the paired t-test. In keeping with the intention of a pilot study, we were interested in obtaining estimates for the effect size. From the means and standard deviations, the effect size was calculated. The estimate of the mean group difference as well as estimates of the standard deviation of the group differences in MEMS scores will be useful in determining appropriate sample size for a future large-scale study and for comparison to other studies.

Results

Participants were recruited from November 2010 to April 2011. Baseline demographic categorical data of the 19 participants is located in Table 1 (IBD Categorical Demographic Data), including: male 57.9% (11/19), Caucasian 94.7% (18/19), non-smokers 94.7% (18/19), Crohn's disease 52.6% (10/19), and "did not use a pillbox" 73.7% (14/19). IBD continuous demographic data are noted in Table 2 (IBD Continuous Demographic Data). Participants' average age was 44.8 years (SD=13.0 years), with a range of 21-68 years. The age of IBD onset averaged 32.8 years (SD=12.7 years), with a range of 18-63 years. The number of medications taken by participants averaged 5.2 (SD=4.9), with a range of 1 to 16.

Of the 19 participants completing the screening period, nine (47.4%) were found to be nonadherent. Screening MEMS scores across the 19 participants averaged 0.813 (SD=0.153), with a range of 0.475 to 0.987. Three nonadherent participants (3/9) did not

complete the study, as one was taken off her immunosuppressant and two were lost to follow-up despite multiple attempts by the PI to contact them via telephone and mail. Six of the nine participants were randomized, four participants to the CSI group and two to attention control. The duration of the one-time face-to-face intervention ranged from 20-45 minutes in the CSI group and 39-40 minutes in the attention control group. Within the CSI group, the four habits or routines chosen by the participants to link their medication taking to included: administration of dog's insulin twice a day; driving kids to school; drinking morning coffee prior to work; and drinking power shake after his morning workout. Five of the six randomized participants completed the study. One participant died of causes unrelated to IBD. Demographic differences between the CSI and attention control groups were not calculated due to the samples' low statistical power.

What is the feasibility of the CSI intervention in nonadherent adult IBD patients?

All participants reported “very little” (2/5 participants) to “just right” (3/5 participants) for the amount of time required for participation, and they had positive comments regarding their experience. Participants wrote they had “no significant inconvenience” or “no disruption” with their participation or medication taking. One participant wrote, “It took no more time than usual” to take medications. A male participant wrote he liked the “establishing a good medication taking routine”. A female participant wrote, “It helped me link my medication taking with another BID task that is easier to remember”.

What is the change in the intervention mechanism of personal systems thinking?

Of the four CSI participants, two completed pre/post the Systems Thinking Survey; one participant failed to turn in the initial survey and one participant did not turn

in the final survey due to death unrelated to the study. The Systems Thinking Survey mean change in score was -0.50 (SD: 6.36), which provided mixed results. One participant's pre-intervention Systems Thinking score was 48 and decreased to 44 at the end of the study, with the other participant score initially was 47 and improved to 52 at the end of the study.

What is the potential effectiveness of the CSI intervention in nonadherent adult IBD patients?

MEMS change scores for the CSI group did increase, though were not statistically significant (MEMS difference mean= -0.07; SD 0.03). The MEMS change scores for the attention control group decreased slightly and were not statistically significant (MEMS difference mean=0.01, SD=0.06).

Between the two groups, the change scores were not statistically significant ($p=0.14$; CI: -0.19-0.045). Based on the mean change score for the two groups and their corresponding standard deviations, effect size was found to be 1.9. The effect size will assist in estimating the sample size for future study.

Discussion

The purpose of this pilot study was to assess the feasibility, change in personal systems thinking, and potential effectiveness of a three month CSI intervention in nonadherent adult inflammatory bowel disease patients. Our nonadherence rate of 47.4% is consistent with the previous IBD literature nonadherence rate of 7-72% (Jackson et al., 2011) and with the chronic disease literature medication nonadherence rate of 50% (Roter, Hall, Merisca, et al., 1998; Peterson, Takiya, & Finley, 2003; McDonald, Garg, & Haynes, 2002).

Feasibility

One purpose of this pilot study was to determine the feasibility of the three month CSI intervention in adult nonadherent IBD patients. Feasibility of the CSI intervention was found to be positive and without significant participant burden, which was also found in a similar renal transplant sample (Russell, 2010). The single dose of the intervention was adequate to show a trend towards improved adherence without inconveniencing the participants. The goal of any intervention study is to minimize the participant burden while maximizing the dose of the intervention. With a single dose of the CSI intervention in a small sample, trends were noted towards adherence. The participants were active in identifying existing habits and suggesting ways to make their medication taking better.

Personal systems thinking

The Systems Thinking survey change scores were mixed. This indicates that the participants receiving the CSI intervention may or may not have shifted their thinking and consequently their behavior towards using personal systems to improve and support medication adherence. However, caution should be used when interpreting these data due to the small sample and lack of psychometric data of the instrument. A larger more diverse sample is needed before conclusions can be made as to the intervention mechanism and whether personal systems thinking improved with the CSI intervention.

Medication adherence

The change in the medication adherence score for the CSI group was not statistically significant ($p=0.14$) though the trends were in the anticipated direction. No statistically significant findings were noted between the CSI and attention control groups,

which is similar to other IBD medication adherence intervention studies thus far (Waters, Jensen & Fedorak, 2005; Moss, Chaudhary, Tukey, 2010; Cook, Emiliozzi, El-Hajj, & McCabe, 2010; Moshkovska, Stone, Smith, 2011; Keefer, Doerfler, & Artz, 2011). Our attention control group showed a weak intervention effect of the IBD education only intervention (ES=0.17), consistent with the education alone intervention findings across chronic disease (ES=0.29-0.61) (Conn, et al., 2009).

Our effect size (ES=1.9) is larger than the ES calculated across chronic diseases in general (ES: 0.67-1.18) (Conn et al., 2009). Attempts were made to calculate effect sizes for the previously reviewed IBD studies, however, not enough data was published to calculate their scores. Our findings are also consistent with a recent systematic review of CSI intervention literature showing improvement in lifestyle and chronic diseases (Matteson & Russell, 2011). A similar study in kidney transplant patients found an equally strong effect size (ES: 1.4) (Russell, 2010). However, our effect size was calculated to estimate sample size for future study and should be considered a crude estimate based on our small sample size.

Strengths

This IBD medication adherence pilot study is the first to focus on nonadherent participants, utilize electronic monitoring of adherence, and test the innovative CSI intervention in IBD patients. Utilizing a nonadherent, or homogenous, population can increase the study's power, also avoiding the ceiling effect that can be seen in adherent participants (Polit & Beck, 2012).

In the five IBD studies reviewed, this is the first IBD study to utilize electronic monitoring as the adherence measure. Electronic monitoring may be a more expensive monitoring than self-report, but the information gleaned from the data is vital to the CSI intervention (Figure 3. MEMS report before CSI; Figure 4.4. MEMS report after CSI). Electronic monitoring is considered one of the most valid and reliable measures of medication adherence (Russell et al., 2007; Denhaerynck, Schaefer-Keller, Young, et al., 2008; De Geest & Vanhaecke, 1999; Reikert, 2006; De Geest, Schafer-Keller, Denhaerynck et al., 2006).

The innovative CSI intervention identifies patients' daily habits that can be linked with medication-taking and help foster change in their personal systems to enhance adherence. One-time delivery of the intervention shows promise, as evidenced by these preliminary data and prior work (Russell et al., 2010). Routine analysis was helpful to assist the participant in identifying potential habits to target for medication taking. With the MEMS feedback, the participant easily identified the change in the system for the days of nonadherence and made inferences for behavior change.

Consistent with prior CSI intervention studies, participants easily accepted the intervention (Russell et al, 2010). The ability to deliver the intervention in the clinical setting by the PI with patient acceptance indicates that the intervention may more broadly translate into the clinical setting.

The change in personal systems thinking was mixed, but the sample size was small and the instrument lacks psychometric data. Personal system thinking is the concept CSI is designed to change; with no psychometric data to validate the instrument, the tool may not measure what it is intended to measure which threatens the internal

validity of the study. Further testing of the instrument should strengthen the accuracy of the tool.

The World Health Organization (WHO) recommends that patients need to be supported and not blamed for their nonadherence. The WHO also suggests that integrating medication taking with a daily habit may improve adherence (Sabate, 2003). Russell, Ruppert, and Matteson (2011) recommend shifting attention to personal systems change interventions, shaping routines through the PDCA process, and self-monitoring as a means of enhancing medication adherence behaviors. A systematic review found behavioral interventions with self-monitoring and feedback were effective (Kripilani et al., 2007). This pilot study contributes further evidence that behavioral system based personal level interventions have potential to shape patient's behaviors.

Limitations

Limitations of the study include the small sample size, a non-equivalent control group, short dose and duration of the CSI intervention, attrition bias due to the loss of three nonadherent participants, possible testing bias as the system survey was repeated, and the survey possesses no psychometric data. In addition, generalizability of the findings is limited to those taking once and twice daily dosed medications. These limitations are fewer than the previous IBD adherence studies as these studies were not fully powered, had small sample sizes, utilized self-report instruments, lacked specific operational definitions of medication adherence, possessed short duration and dose of intervention, and lacked a theory-based intervention (in three of the five studies).

Generalizability of the study findings is limited due to the small sample size and the homogenous sample.

Conclusion

This pilot study examined the feasibility, intervention mechanism, and potential effectiveness of CSI to enhance maintenance medication adherence in nonadherent adults IBD patients. Within the context of the current evidence, this study contributes to the growing medication adherence literature within IBD. In contrast to the existing IBD studies using cognitive-based interventions, this pilot study with a small nonadherent sample, used an innovative intervention based on personal systems theory using electronic monitoring. A fully powered study should further examine the effectiveness of the CSI intervention in IBD patients.

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Table 1. IBD categorical demographic data.

Variable	Total Sample (n= 19)
Male	11 (57.9%)
Non-Hispanic	19 (100%)
Caucasian	18 (94.7%)
Married	11 (57.9%)
Work Full-time	12 (63.2%)
Non-smoker	18 (94.7%)
Some college	9 (47.4%)
Steroid free	14 (73.7%)
Pillbox NOT used	14 (73.7%)
IBD Diagnosis:	
Crohns	10 (52.6%)
Ulcerative colitis	9 (47.4%)

Table 2. IBD continuous demographic data.

Variable	Mean	Standard Deviation	Range
Age (years)	44.8	13.0	21.7-67.9
Age of IBD onset (years)	32.8	12.7	18-63
Number of medications	5.2	4.9	1-16

Figure 1. Patient flow diagram.

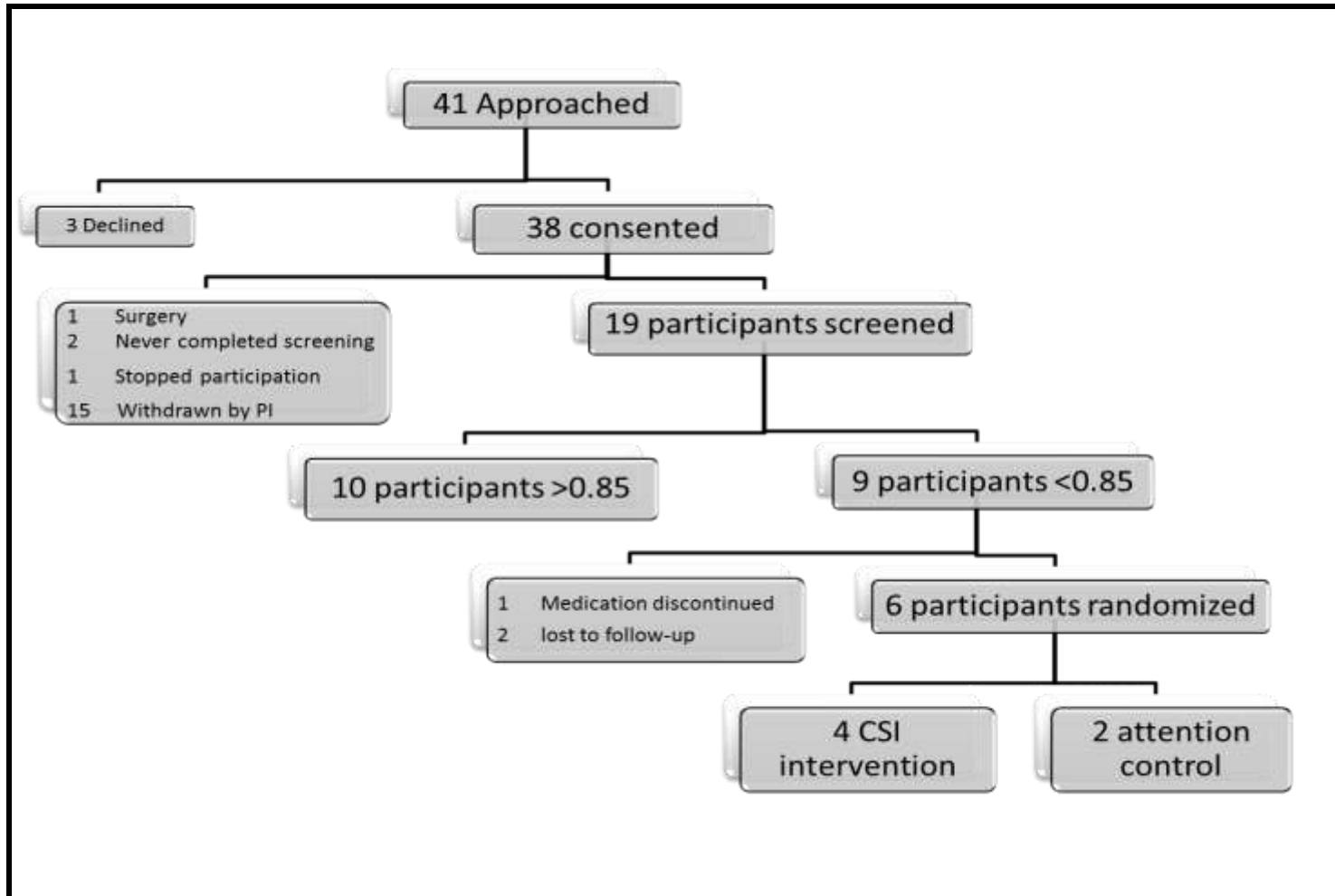


Figure 2. PDCA cycle.

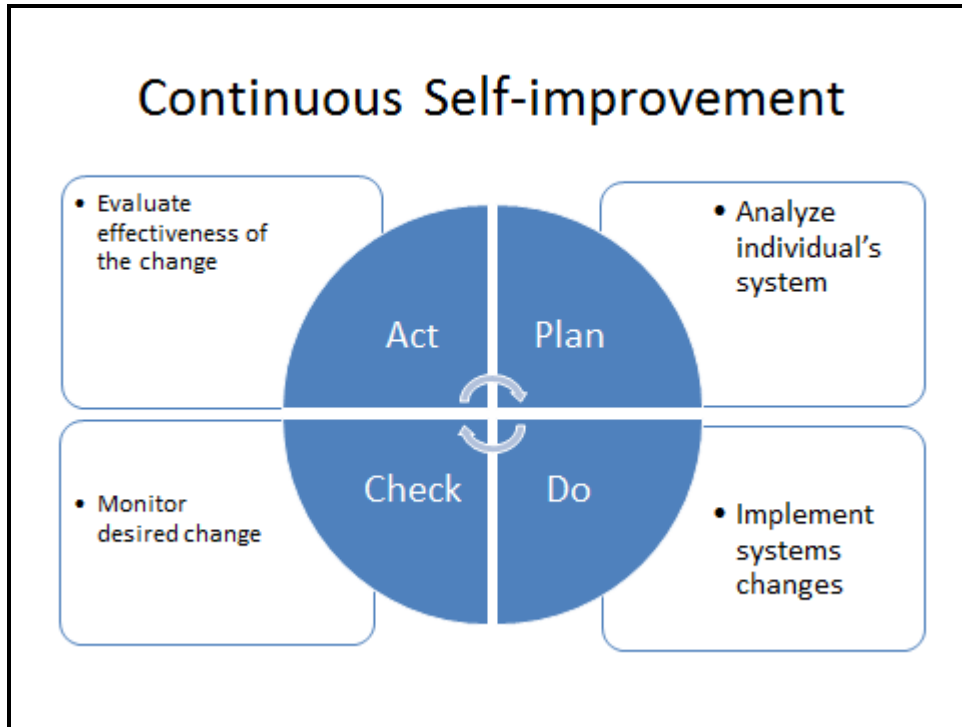
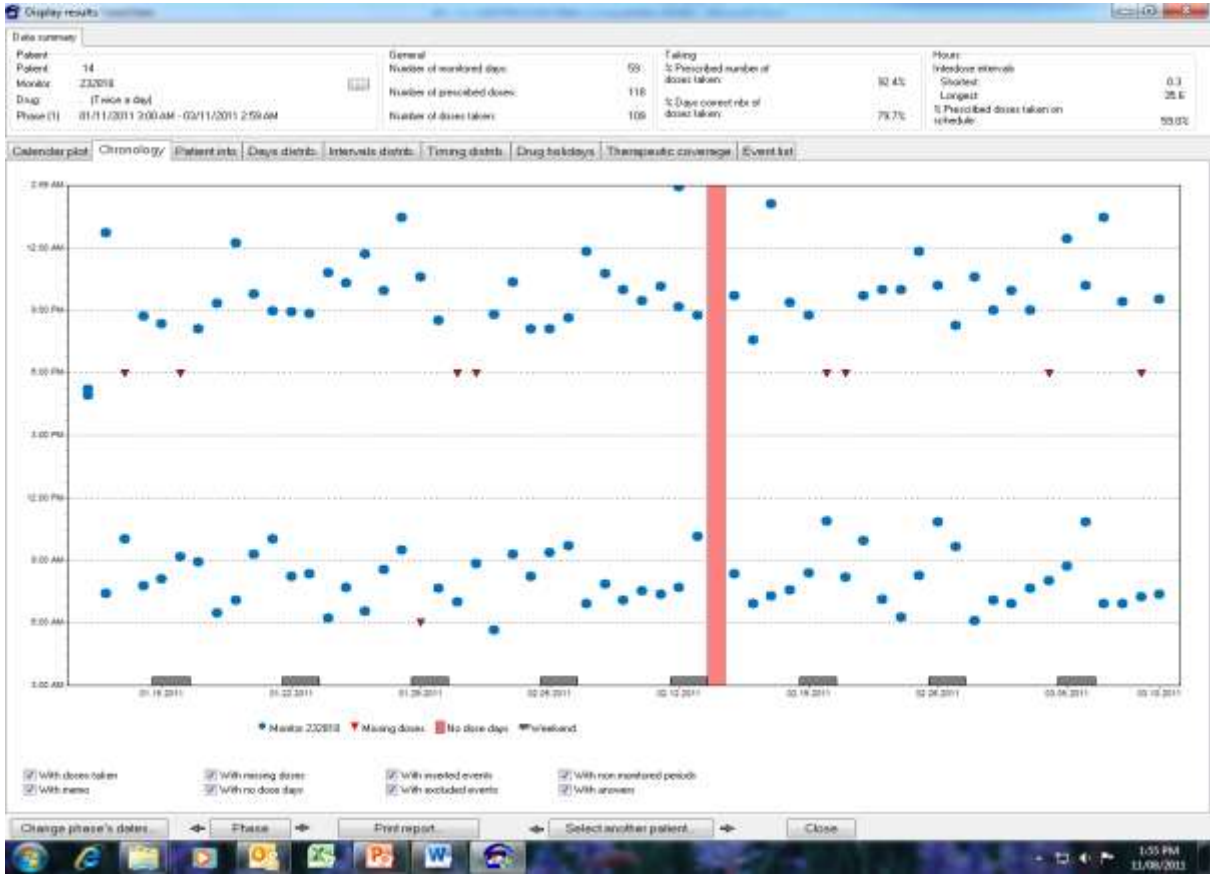
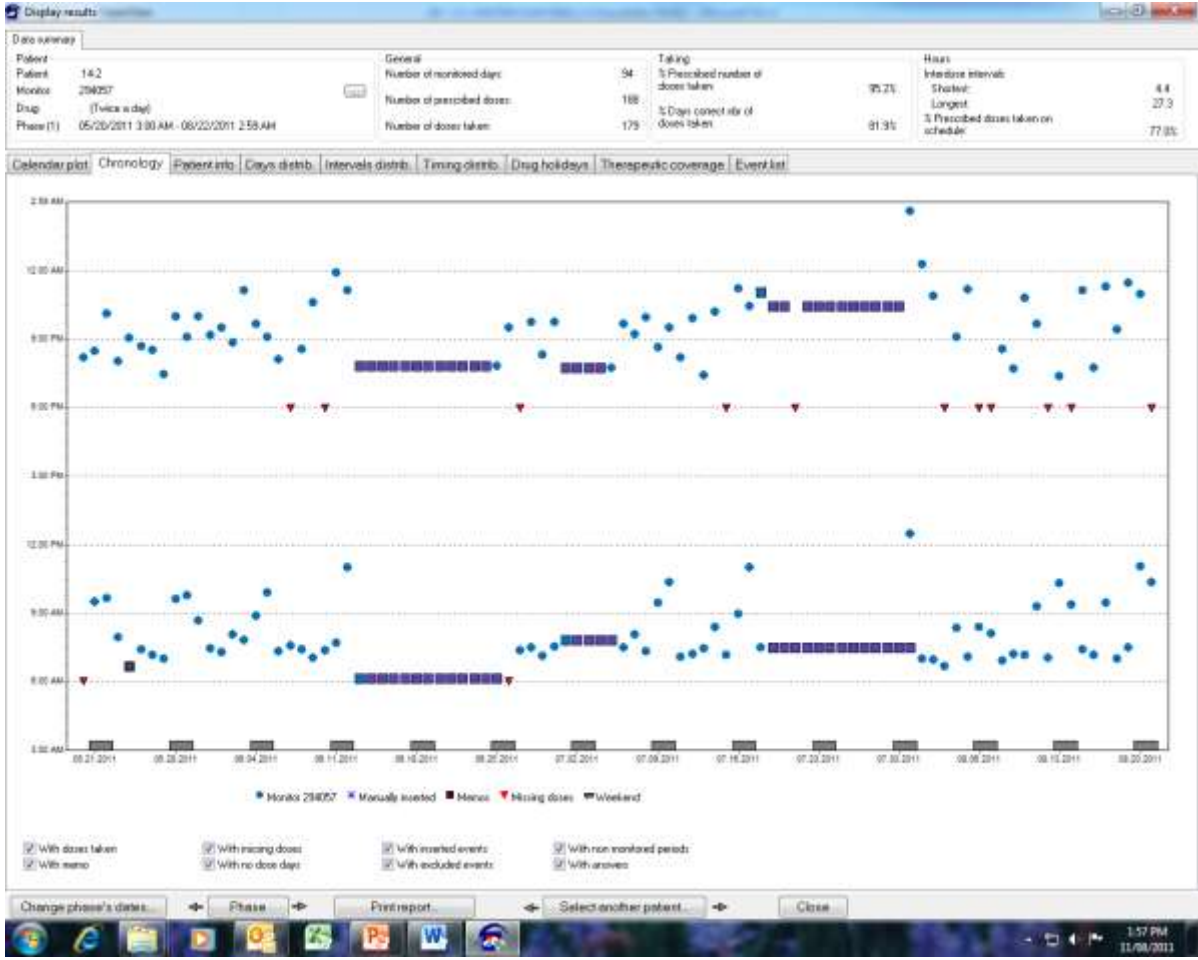


Figure 3. MEMS report before CSI.



100

Figure 4. MEMS report after CSI



Appendix A

A. IRB

- a. IRB approval
- b. Informed Consent
- c. Informed Consent for Declining Participation
- d. HIPAA Authorization Form



**Institutional Review Board
Health Sciences Section**

University of Missouri-Columbia

190 Galena Hall/ Dc074.00

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Columbia, MO 65212

PHONE (573) 882-3181

FAX (573) 884-4401

E-MAIL: irb@missouri.edu

WEB: www.research.missouri.edu/irb

November 23, 2009

Michelle Matteson
Medicine-Gastroenterology
Dc043.00
One Hospital Drive
Columbia, MO 65212

Dear Ms. Matteson,

Regarding your application for approval of the research project, *A pilot intervention to improve immunosuppressant medication adherence in inflammatory bowel disease patients*, the Health Sciences Institutional Review Board (HS IRB) took the following action:

- a. The principal investigator on this study is responsible for all aspects and conduct of this study.
- b. Approved your study through expedited review [as codified under 45 CFR 46.110 (f) (6, & 7)] on November 17, 2009.
- c. Found this protocol, November 5, 2009 to impose minimal risk to the research participant.
- d. Requires that the principal investigator obtain the informed written consent of each research participant.
- e. Reviewed and approved the final version of both consent forms on November 20, 2009. Please use the approved consent displaying the signed IRB approval box when consenting patients.
- f. Reviewed and approved any questionnaires or surveys that were submitted with your application.
- g. Reviewed and approved the HIPAA Authorization on November 20, 2009.
- h. The HS IRB has determined that the degree of risk is such that the approval for this protocol will expire on November 17, 2010. A Continuing Review Report must be submitted a minimum of one month prior to this date.
- i. Upon completion of the study a Completion Form must be submitted to the HS IRB office. If the closure is not documented on the Completion Form, you may close the study at the time of the annual review.

Please reference **IRB Project # 1150958** in all future communications regarding this project.

Pursuant to the HS IRB conflict of interest policy, investigators who are HS IRB members do not vote on protocols in which they are involved.

Deaths occurring in a study at this site must be reported to the HS IRB office within 24 hours of occurrence, whether or not the death is related to the study. All on-site serious adverse events meeting criteria must be reported to the HS IRB office within five (5) days of occurrence.

No change may be made in an approved protocol or recruitment materials unless the change is submitted to and approved by the HS IRB.

Do not depend on the HS IRB for your record keeping.

Sincerely,

Niels Beck, PhD
Chair

Enclosure

Consent Form to Participate in a Research Study

INVESTIGATOR'S NAME: MICHELLE MATTESON

PROJECT # 1150958

DATE OF PROJECT APPROVAL: NOVEMBER 17, 2009

<i>FOR HS IRB USE ONLY</i>	
<i>APPROVED</i>	
_____	_____
HS IRB Authorized Representative	Date
EXPIRATION DATE: _____	

STUDY TITLE: A PILOT INTERVENTION TO IMPROVE MAINTENANCE THERAPY MEDICATION ADHERENCE IN INFLAMMATORY BOWEL DISEASE PATIENTS

INTRODUCTION

This consent may contain words that you do not understand. Please ask the investigator or the study staff to explain any words or information that you do not clearly understand.

This is a research study. Research studies include only people who choose to participate. As a study participant you have the right to know about the procedures that will be used in this research study so that you can make the decision whether or not to participate. The information presented here is simply an effort to make you better informed so that you may give or withhold your consent to participate in this research study.

Please take your time to make your decision and discuss it with your family and friends.

You are being asked to take part in this study because you have INFLAMMATORY BOWEL DISEASE (CROHNS DISEASE OR ULCERATIVE COLITIS) and on a maintenance therapy like azathioprine.

In order to participate in this study, it will be necessary to give your written consent.

We do not have a study sponsor at this time.

WHY IS THIS STUDY BEING DONE?

The purpose of this study is to determine if connecting your medication taking with an existing habit or routine will increase your medication taking. The intervention is called Continuous Self Improvement (CSI). This research is being done because we would like to study the effective of the Continuous Self Improvement intervention on your maintenance therapy medication taking

HOW MANY PEOPLE WILL TAKE PART IN THE STUDY?

About 20 people will take part in this study at the University of Missouri.

WHAT IS INVOLVED IN THE STUDY?

If you chose to participate in the study, we will monitor how you take your maintenance therapy such as azathioprine. You will be given a special pill bottle to keep your medication in that records the time and date every time you open the bottle to take your medication. Initially, your medication taking will be monitored for two months to see if you will continue with the study. If you take your medication less than 85% of the time, we will ask you to continue the study and will give you a \$10 Wal-Mart gift card. If you take your medication greater than 85% of the time, we will thank you for your participation, give you a \$10 Wal-Mart gift card, and you will be finished with the study.

You will be ~~ra~~randomized into one of the study groups described below. Randomization means that you are put into a group by chance. It is like flipping a coin. Neither you nor the researcher will choose what group you will be in. You will have an equal chance of being placed in either group. The two groups both involve the MEMS (Medication Event Monitoring System) device and monthly visits (by phone or in person) lasting approximately 15 minutes.

If you are asked to continue with the study, we will arrange a time to come to your home to set up the Homelink device and discuss your daily routines around the times you normally take your medication.

I will work with you to help link your medication taking to your existing routines. The Homelink is a device that will connect to your telephone line, allowing the data from the cap to be transmitted over the phone lines to Aardex (the company that makes MEMS and the Homelink) which I can access with my computer. There will be no additional charges for using Homelink. For a total of three months, I will call monthly to remind you to send me your MEMS data through the Homelink. I will send you a copy of your monthly MEMS report and discuss with you potential areas of improvement using your

habits and daily routines. You will be asked to keep a MEMS diary of missed doses and why the doses were missed, or record when you opened the bottle but did not take the medication (example: refilling the bottle). The diary will be compared to the MEMS report and can help us determine breaks in your routine or explanations of why you may have missed or were late with a dose of medication.

At the end of the three months, I will make an appointment to come to your home to disconnect the Homelink, and retrieve the MEMS and MEMS diary, give you a survey, and give you a \$10 Wal-Mart gift card. At the end of the study, a survey will ask how to improve the intervention and how feasible the study was for you (ease of participation). For the duration of the study, you will continue to keep your scheduled clinic appointments at the Digestive Health Center or with the University of Missouri. As we are only monitoring an existing medication, you will be responsible for all medication costs and any costs of medical care for your acute or chronic diseases. If you were not in the study, you would be responsible for your medications and medical care.

If you take part in this study, you will not have any additional testing or procedures.

HOW LONG WILL I BE IN THE STUDY?

We think you will be in the study for five months.

The investigator and/or your doctor may decide to take you off this study if your maintenance therapy medication is stopped.

You can stop participating at any time. Your decision to withdraw from the study will not affect in any way your medical care and/or benefits.

WHAT ARE THE RISKS OF THE STUDY?

While on the study, you are at risk for the side effects described below. You should discuss these with the investigator and/or your doctor.

The MEMS caps are not child-proof. Please take the appropriate safeguards to keep the medication out of the reach of children.

You may feel uncomfortable or uneasy about your medication taking being monitored. The MEMS cap has a number assigned to you that is transmitted through the Homelink, so your name will not be on the report, just your number. I am the only person who will know which number is yours.

For the reasons stated above the investigator will observe you closely while giving the treatment described and, if you have any worrisome symptoms or symptoms that the investigator or her associates have described to you, notify the investigator immediately. Investigator's telephone number is 573-882-7776.

ARE THERE BENEFITS TO TAKING PART IN THE STUDY?

If you agree to take part in this study, there may or may not be direct medical benefit to you. You may expect to benefit from taking part in this research to the extent that you are contributing to medical knowledge. We hope the information learned from this study will benefit other patients with _Inflammatory Bowel Disease (Crohn's disease or ulcerative colitis) in the future who have difficulty taking their medications.

Other benefits include that your medication taking may improve as a result of the study. It is very unlikely that your medication taking will worsen as a result of the study.

There is no guarantee that taking part in this research will result in any improvement in your condition.

WHAT OTHER OPTIONS ARE THERE?

An alternative is to not participate in this research study.

Please discuss these and other options with the investigator and your doctor.

WHAT ABOUT CONFIDENTIALITY?

Medical information produced by this study will be stored in the investigators file and identified by only a number. The code key connecting your name with the number will be kept in a separate, secure location. Only persons on the study staff will be viewing your data, and will not be released in a form that could identify you without your written consent, except as required by law. If the investigator conducting this study is not your primary, or regular doctor, the investigator must obtain your permission before contacting

your regular doctor for information about your past medical history or to inform them that you are in this trial.

It is possible that your medical and/or research record, including sensitive information and/or identifying information, may be inspected and/or copied by the study sponsor (and/or its agent), the Food and Drug Administration (FDA), federal or state government agencies, or hospital accrediting agencies, in the course of carrying out their duties. If your record is inspected or copied by the study sponsor (and/or its agents), or by any of these agencies, the institution will use reasonable efforts to protect your privacy and the confidentiality of your medical information.

The results of this study may be published in a medical book or journal or used for teaching purposes. However, your name or other identifying information will not be used in any publication or teaching materials without your specific permission.

In addition, if photographs, audiotapes or videotapes were taken during the study that could identify you, then you must give special written permission for their use. In that case, you will be given the opportunity to view or listen, as applicable, to the photographs, audiotapes or videotapes before you give your permission for their use if you so request.

WHAT ARE THE COSTS?

There is no cost to you for the MEMS caps or the Homelink. We are monitoring an existing medication that has been prescribed to you by a physician. Therefore, you will pay for the cost of your medications and any acute or chronic disease care that may be incurred during the study period. If you were not involved in a study and became ill, you would be responsible for those cost of care.

You or your insurance company will, however, be charged for any other portion of your care that is considered standard care. You or your insurance company will be charged for continuing medical care and/or hospitalization.

WILL I BE PAID FOR PARTICIPATING IN THE STUDY?

You will be paid \$10 Wal-Mart gift card at the end of the screening period and at the completion of the study if you participate in the MEMS portion of the study. You will be paid \$10 Wal-Mart gift card if you only complete the first two months of medication adherence screening.

WHAT ARE MY RIGHTS AS A PARTICIPANT?

Participation in this study is voluntary. You do not have to participate in this study. Your present or future care will not be affected should you choose not to participate. If you decide to participate, you can change your mind and drop out of the study at any time without affecting your present or future care in the Digestive Health Center or the University of Missouri Hospitals and Clinics. Leaving the study will not result in any penalty or loss of benefits to which you are entitled. In addition, the investigator of this study may decide to end your participation in this study at any time after she has explained the reasons for doing so and has helped arrange for your continued care by your own doctor, if needed.

You will be informed of any significant new findings discovered during the course of this study that might influence your health, welfare, or willingness to continue participation in this study.

WHOM DO I CALL IF I HAVE QUESTIONS OR PROBLEMS?

If you have any questions regarding your rights as a participant in this research and/or concerns about the study, or if you feel under any pressure to enroll or to continue to participate in this study, you may contact the University of Missouri Health Sciences Institutional Review Board (which is a group of people who review the research studies to protect participants' rights) at (573) 882-3181.

You may ask more questions about the study at any time. For questions about the study or a research-related injury, contact Michelle Matteson at 573-882-7776.

A copy of this consent form will be given to you to keep.

SIGNATURE

I confirm that the purpose of the research, the study procedures, the possible risks and discomforts as well as potential benefits that I may experience have been explained to me. Alternatives to my participation in the study also have been discussed. I have read this consent form and my questions have been answered. My signature below indicates my willingness to participate in this study.

Subject/Patient* _____
Date

_____	_____
Legal Guardian/Advocate/Witness (if required)**	Date
_____	_____
Additional Signature (if required) (identify relationship to subject)***	Date

*A minor’s signature on this line indicates his/her assent to participate in this study. A minor’s signature is not required if he/she is under 7 years old. Use the “Legal Guardian/Advocate/Witness” line for the parent’s signature, and you may use the "Additional Signature" line for the second parent’s signature, if required.

**The presence and signature of an impartial witness is required during the entire informed consent discussion if the patient or patient’s legally authorized representative is unable to read.

***The "Additional Signature" line may be used for the second parent’s signature, if required. This line may also be used for any other signature which is required as per federal, state, local, sponsor and/or any other entity requirements.

—If required” means that the signature line is signed only if it is required as per federal, state, local, sponsor and/or any other entity requirements.

SIGNATURE OF STUDY REPRESENTATIVE

I have explained the purpose of the research, the study procedures, identifying those that are investigational, the possible risks and discomforts as well as potential benefits and have answered questions regarding the study to the best of my ability.

_____	_____
Study Representative****	Date

****Study Representative is a person authorized to obtain consent. Per the policies of the University of Missouri Health Care, for any 'significant risk/treatment' study, the Study Representative must be a physician who is either the Principal or Co-Investigator. If the study is deemed either 'significant risk/non-treatment' or 'minimal risk,' the Study Representative may be a non-physician study investigator.

CONSENT FORM TO PARTICIPATE IN A RESEARCH STUDY

INVESTIGATOR'S NAME: MICHELLE MATTESON

PROJECT # 1150958

DATE OF PROJECT APPROVAL: NOVEMBER 17, 2009

<i>FOR HS IRB USE ONLY</i>	
<i>APPROVED</i>	
_____	_____
HS IRB Authorized Representative	Date
EXPIRATION DATE: _____	

STUDY TITLE: A PILOT INTERVENTION TO IMPROVE MAINTENANCE THERAPY MEDICATION ADHERENCE IN INFLAMMATORY BOWEL DISEASE PATIENTS

INTRODUCTION

This consent may contain words that you do not understand. Please ask the investigator or the study staff to explain any words or information that you do not clearly understand.

This is a research study. Research studies include only people who choose to participate. As a study participant you have the right to know about the procedures that will be used in this research study so that you can make the decision whether or not to participate. The information presented here is simply an effort to make you better informed so that you may give or withhold your consent to participate in this research study.

Please take your time to make your decision and discuss it with your family and friends.

You are being asked to take part in this study because you have INFLAMMATORY BOWEL DISEASE (CROHNS DISEASE OR ULCERATIVE COLITIS).

We do not have a study sponsor at this time.

In order to participate in this study, it will be necessary to give your written consent.

WHY IS THIS STUDY BEING DONE?

The purpose of this pilot randomized control trial is to assess the effect of a three month Continuous Self-Improvement (CSI) intervention on maintenance therapy medication adherence scores as assessed by Medication Event Monitoring System (MEMS) in nonadherent adult inflammatory bowel disease (IBD) patients.

HOW MANY PEOPLE WILL TAKE PART IN THE STUDY?

About 20 people will take part in this study at the University of Missouri.

WHAT IS INVOLVED IN THE STUDY?

You are electing to not participate in this study. By signing this consent, you authorize me to collect the following information from you: Date of birth, gender, ethnicity, educational level, marital status and employment status. This data will be used to compare to the participants who enrolled in the study.

HOW LONG WILL I BE IN THE STUDY?

You will not be involved in the study other than your data above.

You can stop participating at any time. Your decision to withdraw from the study will not affect in any way your medical care and/or benefits.

WHAT ARE THE RISKS OF THE STUDY?

The only risk to participating in this study is potential loss of confidentiality. This risk is small as your data will be kept separate from this signed consent form, linked only by a number. For more information about risks, ask Michelle Matteson at 573-882-7776.

ARE THERE BENEFITS TO TAKING PART IN THE STUDY?

Since you are declining participation in the study, but allowing the investigator to obtain demographic data, there is no direct benefit to you; however, by taking part in this research you are contributing to medical knowledge. We hope the information learned from this study will benefit other patients with Inflammatory Bowel Disease in the future.

WHAT OTHER OPTIONS ARE THERE?

An alternative is to not participate in this research study.

WHAT ABOUT CONFIDENTIALITY?

Information will be stored in the investigator's file and identified by a code number only. The code key connecting your name to specific information about you will be kept in a separate, secure location. Information contained in your records may not be given to anyone unaffiliated with the University of Missouri in a form that could identify you without your written consent, except as required by law. If the investigator conducting this study is not your primary, or regular doctor, the investigator must obtain your permission before contacting your regular doctor for information about your past medical history or to inform them that you are in this trial.

The results of this study may be published in a medical book or journal or used for teaching purposes. However, your name or other identifying information will not be used in any publication or teaching materials without your specific permission.

WHAT ARE THE COSTS?

There is no cost to you.

WILL I BE PAID FOR PARTICIPATING IN THE STUDY?

You will receive no payment for taking part in this study.

WHAT ARE MY RIGHTS AS A PARTICIPANT?

Participation in this study is voluntary. You do not have to participate in this study. Your present or future care will not be affected should you choose not to participate. If you decide to participate, you can change your mind and drop out of the study at any time without affecting your present or future care in the institution. Leaving the study will not result in any penalty or loss of benefits to which you are entitled.

WHOM DO I CALL IF I HAVE QUESTIONS OR PROBLEMS?

If you have any questions regarding your rights as a participant in this research and/or concerns about the study, or if you feel under any pressure to enroll or to continue to participate in this study, you may contact the University of Missouri Health Sciences

Institutional Review Board (which is a group of people who review the research studies to protect participants' rights) at (573) 882-3181

You may ask more questions about the study at any time. For questions about the study or a research-related injury, contact Michelle Matteson at 573-882-7776.

A copy of this consent form will be given to you to keep.

SIGNATURE

I confirm that the purpose of the research, the study procedures, the possible risks and discomforts as well as potential benefits that I may experience have been explained to me. Alternatives to my participation in the study also have been discussed. I have read this consent form and my questions have been answered. My signature below indicates my willingness to participate in this study.

_____	_____
Subject/Patient*	Date
_____	_____
Legal Guardian/Advocate/Witness (if required)**	Date
_____	_____
Additional Signature (if required) (identify relationship to subject)***	Date

*A minor's signature on this line indicates his/her assent to participate in this study. A minor's signature is not required if he/she is under 7 years old. Use the "Legal Guardian/Advocate/Witness" line for the parent's signature, and you may use the "Additional Signature" line for the second parent's signature, if required.

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SIGNATURE OF STUDY REPRESENTATIVE

I have explained the purpose of the research, the study procedures, identifying those that are investigational, the possible risks and discomforts as well as potential benefits and have answered questions regarding the study to the best of my ability.

Study Representative****

Date

****Study Representative is a person authorized to obtain consent. Per the policies of the University of Missouri Health Care, for any 'significant risk/treatment' study, the Study Representative must be a physician who is either the Principal or Co-Investigator. If the study is deemed either 'significant risk/non-treatment' or 'minimal risk,' the Study Representative may be a non-physician study investigator.

Appendix B

A. Copies of instruments with instructions

- a. Demographics Form
- b. Demographics Form for Participants who decline
- c. MEMS Diary
- d. Important People Form (Adapted from Alemi, 2003)
- e. Life Routines Form (Adapted from Alemi, 2003)
- f. Cycles Form (Adapted from Alemi, 2003)
- g. Solutions Form (Adapted from Alemi, 2003)
- h. Systems Thinking Survey
- i. End of Study Interview Form
- j. Mini-Mental Status Examination
- k. MEMS

DEMOGRAPHICS FORM

NAME: _____ DATE: _____

GENDER: MALE (1) FEMALE (2)

DOB: _____

AGE DIAGNOSED WITH IBD: _____

MAINTENANCE THERAPY (MT): _____

MT DOSE: _____

TIMES OF MT: _____

ETHNICITY: _____
(CAUCASIAN=0; AFRICAN AMERICAN=1; ASIAN=3; OTHER=4)

RACE: _____
(HISPANIC=1; NON-HISPANIC=2)

EDUCATIONAL LEVEL: _____
(HIGHSCHOOL=1; GED=2; SOME COLLEGE=3; COLLEGE DEGREE=4; GRADUATE SCHOOL=5)

MARITAL STATUS: _____
(MARRIED=1; DIVORCED=2; SEPARATED=3; WIDOWED=4; SINGLE=5)

EMPLOYMENT STATUS: _____
(FULL-TIME=1; PART-TIME=2; NONE=3; DISABLED=4)

BMI: _____
SMOKER: YES (1) NO (2)

IBD DIAGNOSIS:
UC: PANCOLITIS LEFT RIGHT RECTAL
CHRON'S: SMALL INTESTINE LARGE INTESTINE
SMALL/LARGE FISTULIZING

LAST DOSE OF STEROIDS (ORAL/IV): _____

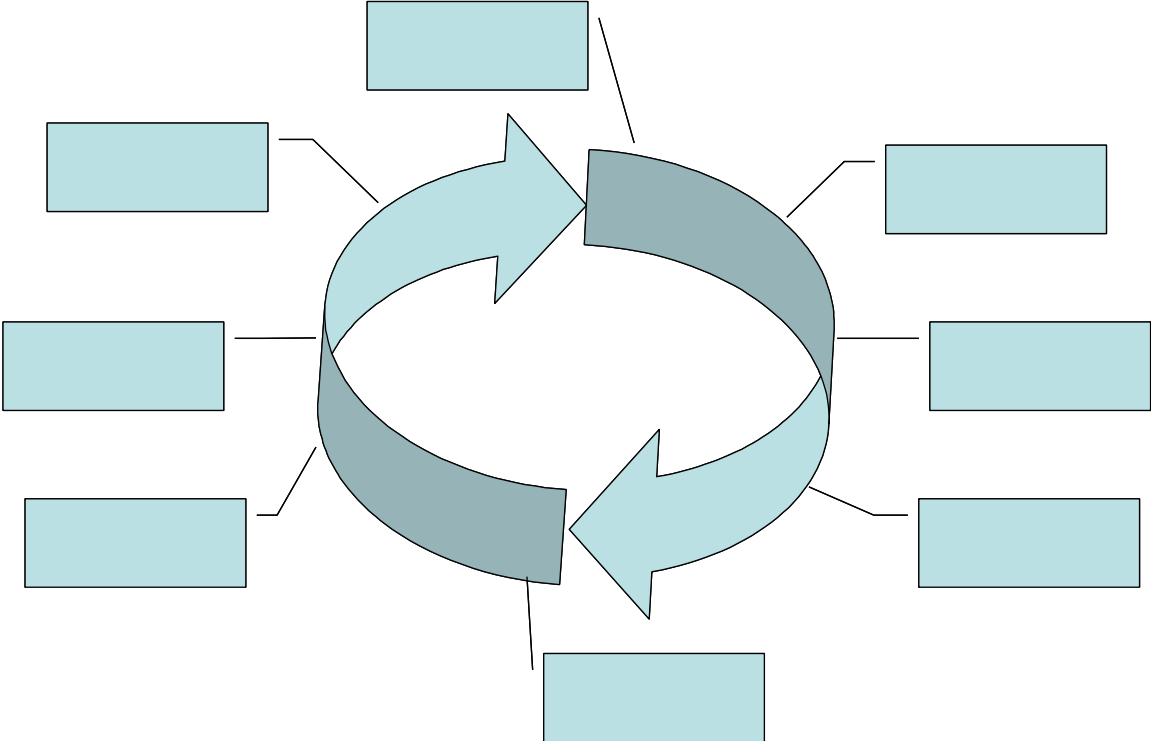
NUMBER OF CURRENT MEDICATIONS: _____

PILLBOX OR MEDICATION PLANNER: YES (1) NO (2)

**Form 1
Important People Form
Adapted from Alemi, 2003¹⁸**

<i>Important People Form</i>		
Name of person:	Yes	No
1. Does this person keep house with you?	<input type="checkbox"/>	<input type="checkbox"/>
2. Do you need to consider this person's schedule when you are deciding the best time to take your medications?	<input type="checkbox"/>	<input type="checkbox"/>
3. Does this person help you in carrying out daily living activities (bathing, eating, cleaning, washing clothes, commuting, etc.)?	<input type="checkbox"/>	<input type="checkbox"/>
4. Can this person's decisions affect time, medication availability, or other resources needed for taking your medications?	<input type="checkbox"/>	<input type="checkbox"/>
5. Does this person's decision affect whether your medications are available for you to take?	<input type="checkbox"/>	<input type="checkbox"/>
6. Do you see each other on a daily basis?	<input type="checkbox"/>	<input type="checkbox"/>
7. Does this person affect how and when you socialize with others?	<input type="checkbox"/>	<input type="checkbox"/>
_____	Total number of yes responses:	<input type="text"/>

Form 3
Cycles Form
Adapted from Alemi, 2003¹⁸



Form 4
Possible Solutions Form
 Adapted from Alemi, 2003¹⁸

<p>Step 1: List ideas for changing the environment to improve medication taking.</p> <p>1.</p> <p>2.</p> <p>3.</p> <p>4.</p> <p>5.</p>
<p>Step 2: Ask these questions of each idea that you have listed above. Give that idea one point for each of these questions that you answer “yes” to.</p>
1. Focuses on events that happen before taking my medications on time.
2. Does not rely on my motivation or commitment.
3. Changes my environment.
4. Once done, stays done. No need to make the change again.
5. If it fails to improve medication taking, it is no one’s fault.
6. If it fails to medication taking plans, no point in trying to do it again and harder.
7. It will increase the time between medication taking failures.
8. It does not rely on my memory to take medications.
9. Indirectly improves medication taking and timing.
10. It is a change in a recurring life routine.
11. Requires more than one person to bring it about.
12. If done today, it will improve medication taking in the future, not today.
13. Leads to timely medication taking as part of another task.
14. Involves a physical change.
15. Provides resources (time, equipment) for timely medication taking.
16. Changes who I spend time with.
17. Affects others who live with me.
18. Changes what I do for fun and social gatherings.
19. Leaves no choice but to take medications on time.
20. Changes a group activity.
21. If it fails to work, it gives me new insights about what to do next.
22. Rearranges the sequence of my daily living activities.
<p>Step 3: Select the idea with highest number of points to prioritize for action.</p>

System Thinking Survey: On the list below, indicate the importance of each item to describe the best way to maintain your medication taking.

How important is it that the best way to make a change your medication taking includes:	Not Important 1	Of little Importance 2	Moderately Important 3	Important 4	Very Important 5
1. Activities that are fun.					
2. Only relying on routines to cue me to take medications.					
3. Medication taking happens without remembering to do it.					
4. A new medication taking plan every day.					
5. Taking medications only when I feel like it.					
6. Not blaming anyone (including myself) if I don't take my medications.					
7. Combining medication taking with another task I normally do.					
8. Not having to remember to take my medications every day.					
9. Taking my medications without me thinking about it.					
10. Plans that affect only what I do today, but not what I do tomorrow or next month.					
11. Keeping me motivated.					
12. Group activities.					
13. Taking my medications without me planning it daily.					
14. Good intentions to take my medications every day, even if I don't always do it.					
15. Blaming myself when I don't take my medications.					
16. Taking my medications only with encouragement from others.					
17. Trying harder tomorrow if I don't take my medications correctly today?					

End of Study Interview Form

A goal of this study is to see if it is feasible for people to be in the study in terms of time and effort. We want your opinion about how much time and effort it took to participate in this pilot study so we can improve future studies.

1. What is your opinion about the amount of time overall that was required to be in this study?
2. Did your involvement in the study take very little time, the right amount of time, or a little too much time?
3. What is your opinion about our home visit(s)?
4. Did the home visit(s) take very little time, about the right amount of time or a little too much time?
5. What is your opinion about our monthly telephone calls?
6. Did the monthly telephone calls take very little time, about the right amount of time or a little too much time?
7. What is your opinion about downloading the MEMS data using the Homelink on your telephone?
8. Did the downloading the MEMS data take very little time, about the right amount of time, or a little too much time?
9. If there was one thing that you really liked about this study, what is it?
10. Tell me about the intervention or nursing assistance that you received in this study.
11. Do you think it was helpful to you?
12. Did you change anything based on this nursing assistance?
13. For this study we had two groups of participants. One group received a treatment to try to improve medication taking. The other group received general inflammatory bowel disease information. Can you tell me which group you think you were assigned to?
14. If there was one think that you could change about this study, what would it be?
15. Is there anything else that you'd like to tell me that I haven't asked?

Subject: _____

Mini-Mental Status Exam

Orientation Score Points

- | | |
|----------------------------|-------|
| 1. What is the year? _____ | ___ 1 |
| What is the season? _____ | ___ 1 |
| What is the date _____ | ___ 1 |
| What is the day? _____ | ___ 1 |
| What is the month? _____ | ___ 1 |
| 2. Where are we? | |
| State _____ | ___ 1 |
| County _____ | ___ 1 |
| Town/city _____ | ___ 1 |
| Hospital _____ | ___ 1 |
| Floor _____ | ___ 1 |

Registration

3. Name 3 objects, taking one second to say each. Then ask the patient all three after you have said them. Give one point for each correct answer. Repeat the answers until the patient learns all three.

- 1: _____ 2: _____ 3: _____ ___ 3

Attention and Calculation:

4. Serial 7s. Give one point for each correct answer. Stop after 5 answers.
 _____ ___ 5
 Alternate: Spell WORLD backwards: _____

Recall

5. Ask for the names of the three objects learned in Question 3. Give 1 point for each correct answer.

- 1: _____ 2: _____ 3: _____ ___ 3

Language

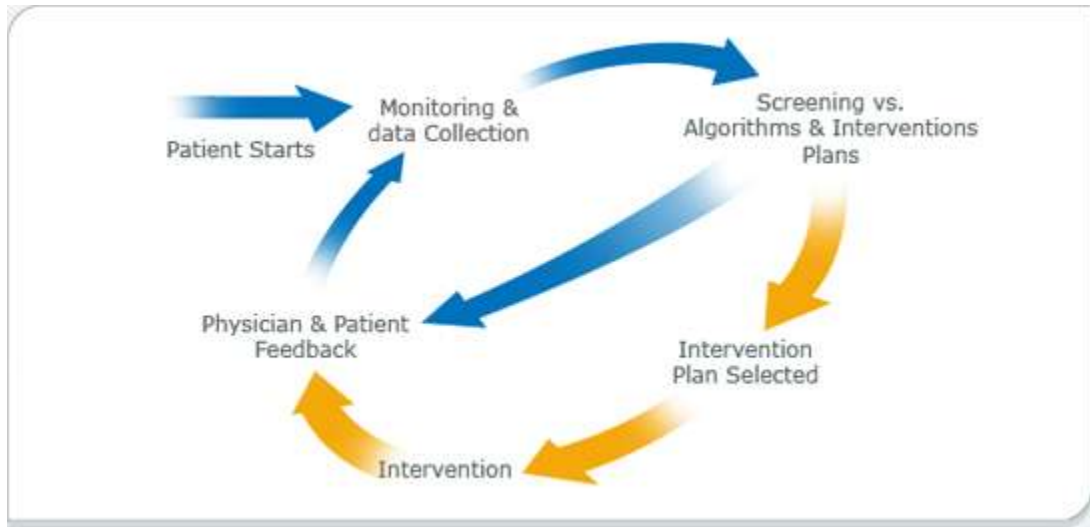
- | | |
|---|-------|
| 6. Point to a pencil and a watch. Have the patient name them as you point. | ___ 2 |
| 7. Have the patient repeat, —N ifs, ands, or buts.” | ___ 1 |
| 8. Have the patient follow a 3-stage command: —Take the paper in your right hand. Fold the paper in half. Put the paper on the floor.” | ___ 3 |
| 9. Have the patient read and obey the following (you write it in large letters): —Close your eyes.” | ___ 1 |
| 10. Have the patient write a sentence of his or her own choosing. (The sentence should contain a subject and an object and should make sense. Ignore spelling errors when scoring.) | ___ 1 |
| 11. Copy the design. | ___ 1 |

___/30

Folstein, Folstein, & McHugh (1975).

MEMS System
(From AARDEX website, [www. Aardexgroup.com](http://www.Aardexgroup.com))

MEMS Smartcap



From AARDEX website, [www. Aardexgroup.com](http://www.Aardexgroup.com)

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VITA

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For seven years she worked as an internal medicine/geriatrics nurse practitioner, before returning to the University of Missouri for her doctorate degree. Working full-time at the Digestive Health Center as a nurse practitioner, she attended the University of Missouri PhD in Nursing program. Michelle Leigh Matteson currently lives in Columbia with her two daughters, Katherine and Emma, and continues her work at the Digestive Health Center.