Interventions Combining Motivational Interviewing and Cognitive Behavior to Promote Medication Adherence: A Literature Review

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Summary box: "What does this paper contribute to the wider global clinical community?"
- That by combining two proven methods, motivational interviewing and cognitive behavioral therapy, medication adherence may be improved in challenging clinical conditions.
- That a multi-component intervention may be needed to influence medication adherence to a prescription regimen in patients with challenging clinical conditions.

ABSTRACT

Aims and objectives: The World Health Organization has indicated medication adherence is a global problem. Both motivational interviewing (MI) and cognitive behavioral therapy (CBT) interventions alone have been found to be effective at improving medication adherence. This article summarizes research that has combined motivational interviewing and cognitive behavioral therapy to improve medication adherence.

Background: Projections indicate that by 2015, 33% of cancer treatment will be in pill form, shifting responsibility for managing medication adherence to patients. These regimens are often complex, with multiple doses, drugs, or cycling, and patients often experience side effects from symptoms, making adherence difficult. Patients taking cancer treatment in pill form must strictly adhere to their regimen to achieve a therapeutically effective level for cancer treatment.

Design: Literature review.

Methods: Data were obtained from six studies that combined MI and CBT in an intervention to promote medication adherence. Analysis was performed based on an integrative review process.

Results: Five studies on medication adherence rates using combined MI and CBT reported improved medication adherence rates; and one was trending toward improved medication adherence rates.

Conclusions: Combined MI/CBT interventions improved medication adherence in various conditions; and may be effective in challenging clinical conditions, such as when cancer treatment is prescribed in pill form.

Relevance to clinical practice: This review focused on interventions that combined motivational interviewing and cognitive behavioral therapy to promote medication adherence. Findings provide nurses with an overview of interventions that may be used in developing programs to help patients manage adherence to cancer treatment in pill form; as well as in other challenging conditions where medication adherence is crucial. A detailed description of the interventions found to be effective is provided to assist nurses in translating evidence into practice.

INTRODUCTION

The World Health Organization (2003) had identified medication adherence as a global issue, particularly in long-term therapies. For those diagnosed with human immunodeficiency virus (HIV), medication adherence is crucial when prescribed long-term antiretroviral therapy (ART) (Fogarty *et al.* 2002). Medication adherence is also crucial for those diagnosed with cancer treated in pill form. Projections indicate that within the next few years, a third of cancer treatment will be in pill form (Weingart *et al.* 2008). The therapeutic outcome for those treated in pill form depends heavily on the ability to strictly adhere to the prescribed regimen, placing greater responsibility on patients. However, patients with cancer are known to miss as much as one-third of the prescribed dosage required for treatment of their disease (Spoelstra *et al.* 2013, Spoelstra & Given 2011, Weingart *et al.* 2008). Medication adherence is more than likely even worse for those who have comorbid conditions (Koroukian *et al.* 2006, Ogle *et al.* 2000); and the majority of cancer patients are older and take multiple medications. Thus, a critical need exists to promote adherence in cancer patients being treated in pill form. Known barriers to medication adherence in cancer patients include symptoms from side effects of treatment, low self-efficacy, depressive symptoms, beliefs that the medicine will not help, regimen complexity, or lack of motivation (Given *et al.* 2011). Consequently, cancer patients may need a more intensive intervention to address the challenging problem of adherence to cancer treatment in pill.

Combining two proven methods, motivational interviewing (MI) and brief cognitive behavioral therapy (CBT), may be a solution to promoting medication adherence in cancer patients treated in pill form (Viswanathan *et al.* 2012a, Viswanathan *et al.* 2012b). Both MI and CBT alone have improved adherence to medications and treatment regimens (Diiorio *et al.* 2008, Donohoe 2006, Holstad *et al.* 2007, Riekert *et al.* 2011, Tatrow & Montgomery 2006). MI and

CBT have also been combined to improve clinical outcomes in challenging conditions such as human immunodeficiency virus *(*HIV*)*, weight loss in post-surgical bariatric patients, lowering hemoglobin A1c in Type-1 diabetes, and reducing anxiety following traumatic brain injury (Hsieh *et al.* 2012, Ismail *et al.* 2010, Stewart *et al.* 2010). MI and CBT have also been effective at improving difficult behavioral problems such as gambling, or alcohol or drug addiction (Greenwald 2002, Hides *et al.* 2011). In cancer patients prescribed treatment in pill form, CBT alone was not found to be effective in improving medication adherence (Spoelstra *et al.* 2013); and we were unable to find studies using MI, or MI combined with CBT, to improve medication adherence in cancer patients. Thus, this article examines the evidence to promote medication adherence when interventions combine MI and CBT.

Globally, healthcare environments are fast-paced and often burdened by the number of patients seeking care. Consequently, nurses are challenged to focus on medication adherence. Nor have we identified evidence-based practice standards that promote medication adherence. We need to improve the ability of nurses to help patients achieve medication adherence.

BACKGROUND

In general, a review of 50 years of research across diseases found a medication adherence rate of 74.5% (DiMatteo *et al.* 2002). A recent review of studies on those with cancer treatment in pill form found medication adherence rates varied widely, ranging from 16% to 80% (Spoelstra & Given 2011). In our prior study on oral cancer treatment, we found a 67% rate of adherence (Spoelstra *et al.* 2013). In addition, Streeter and colleagues (2011) found 10% of patients newly prescribed oral agents stopped taking their medication in the first month. As a result of poor adherence to cancer treatment in pill form, patients may face treatment failure, hospitalization, and, in some instances, nonadherence may even influence longevity (Given *et al.*

2011, Spoelstra & Given 2011). Medication adherence is a significant clinical problem for those prescribed cancer treatment in pill form, which may compromise the ability of the medication to treat the cancer.

Interventions to Promote Medication Adherence

Research has not conclusively identified interventions that are effective at promoting medication adherence (Conn *et al.* 2009, Ruppar *et al.* 2008). Nonetheless, in a literature review of 64 medication adherence interventions, three types were found to be somewhat effective (Ruppar *et al.* 2008). This included knowledge through patient education (PE); motivation through use of MI; and behavior modification through use of CBT. Contrary to other evidence, a Cochrane review of 19 medication adherence studies ($n = 2159$) in HIV patients suggests that interventions directly targeting practical medication management skills tend to be more effective at improving adherence than those targeting psychological constructs (e.g., self-efficacy, attitudes, motivation) (Rueda *et al.* 2006). However, this review did not evaluate interventions that combined CBT and MI to promote medication adherence.

Cognitive Behavioral Therapy (CBT) for Promoting Medication Adherence

CBT is a short-term, goal-oriented, psychotherapeutic approach that is based on the idea that thoughts cause feelings, and consequently, behaviors (Lambert *et al.* 2004). CBT can be thought of as a combination of psychological and behavioral therapy that includes assessment, reconceptualization, and skill acquisition and application. The psychotherapy component emphasizes the importance of the personal meaning we place on things and how thinking patterns begin in childhood. The behavioral therapy component pays close attention to the relationship between our problems, our behavior, and our thoughts. CBT is based on the theory that the events do not upset a person, but the meanings given to the thoughts about the event,

which can block behaviors such as medication taking (e.g., not believing the pills will help cure the cancer). If thoughts are too negative, it can block taking action, as a patient continues to hold onto the old thoughts and fails to learn new behaviors (e.g., prescription is not refilled and pills are not taken as prescribed).

In a review of 64 medication adherence intervention studies, 48% of the studies using CBT found improvement in medication adherence, with most using face-to-face interactions (Ruppar *et al.* 2008). A meta-analysis of 33 trials on interventions designed to improve medication adherence, found an Effect Size (ES) of .33 for brief CBT (Conn *et al.* 2009). The majority of these CBT interventions were 15-minute face-to-face interactions targeting self-administration which was then supplemented with written instructions. In addition, the meta-analysis found that standardized interventions were more effective than those that were tailored.

Regarding cancer treatment in pill form, there is some evidence of pharmacist- and nurse-led home-based programs to improve medication adherence using CBT. In one pharmacist-led program, initial patient contact was within 24 hours of the prescription being written; and CBT was used to review the regimen schedule, side effects, safe handling, drug-to-drug interactions, how to fill and refill prescription, and a referral was provided for co-pay assistance or free drugs (Khandelwal *et al.* 2011). The program also conducted weekly phone calls to patients during the first cycle of the oral agent to assess adherence and symptoms; and to conduct further CBT. In another pharmacist-led program, an evaluation of the oral agent prescription occurred for appropriateness in terms of dose and indication, labs were checked if appropriate, drug interactions were reviewed, and financial issues resolved (Mancini *et al.* 2011). CBT was provided by the pharmacist, with weekly follow-up of adherence and provision of strategies for symptom management. An oncologist followed-up for treatment efficacy, if needed. In the

nurse-pharmacist–led clinic to promote adherence to capecitabine, they focused on metastatic colorectal cancer patients (MacLeod *et al.* 2007). The primary function of the clinic was to provide CBT for early detection and management of treatment of side effects; and for the clinicians to oversee management of any treatment-related events. Emphasis was placed on the patient's ability to recognize grade 2 toxicities during therapy to reduce the occurrence of serious adverse events. However, none of these 3 programs reported medication adherence rates, making it difficult to determine their effectiveness.

While some experts assert that CBT may be a requisite for medication adherence, it is often not sufficient (Haynes *et al.* 2005). In our prior study on adherence to cancer treatment in pill form, CBT alone did not promote a difference in adherence rates (Spoelstra *et al.* 2013). Further, others have reported that a major barrier to adherence involves motivation (Possidente *et al.* 2005). Adding a motivational approach like MI (Diiorio *et al.* 2008), in addition to CBT, may be needed to promote medication adherence in challenging clinical conditions such as with cancer patients who receive treatment in pill form.

Motivational Interviewing (MI) for Promoting Adherence

Of all approaches to transforming patient reluctance to change, one of the most influential has been the concept of MI. A large body of literature indicates that MI is effective for both cessation of harmful behaviors and for adoption of healthy behaviors (Gance-Cleveland 2007, Rubak *et al.* 2005). There are studies using MI to increase awareness and provide education to promote medication adherence, with an effect size (ES) ranging from .22 to .67. This includes patients with asthma (Riekert *et al.* 2011), HIV (Diiorio *et al.* 2008, Ingersoll *et al.* 2011), osteoporosis (Solomon *et al.* 2012), epilepsy (DiIorio *et al.* 2009), and cardiovascular disease (Johnson *et al.* 2006a, Johnson *et al.* 2006b, Lawrence *et al.* 2008). One HIV study ($n = 45$) that

used semi-structured hour-long face-to-face MI sessions for 6 weeks followed by six biweekly face-to-face MI sessions focused on skill-building (Ingersoll *et al.* 2011). Two large trials (*n* = 404; 1,227) using MI for patients on lipid-lowering drugs and hypertensive drugs reported sustained improvement in medication adherence rates with mailed information (Johnson *et al.* 2006a, Johnson *et al.* 2006b). In contrast, a large trial of 2,087 participants that used MI via the phone to promote adherence to osteoporosis medication did not find improvement. However, this study did not use face-to-face contacts nor did it intervene when the prescription was initiated (Solomon *et al.* 2012). A major gap is that no MI interventions were found promoting medication adherence in cancer patients taking oral agents.

Combining Motivational Interviewing (MI) and Cognitive Behavioral Therapy (CBT)

Several studies combined MI and CBT and are available in the literature. Most focus on behavioral issues (e.g., alcoholism or gambling) and are reported elsewhere. We focused on evidence that combined MI—CBT in clinical conditions.

A randomized control trial in Type-1 diabetes patients examined the affect of a combined MI with CBT intervention on glycemic control in 344 adults (mean age 26 years [range 18 to 65]; 60% female) (Ismail *et al.* 2010). Patients had a starting glycosylated hemoglobin (HbA1c) value between 8.2—15%. The intervention was delivered by Registered Nurses (RNs) in 12 face-to-face sessions over 6-months. Findings indicate the 12-month HbA1c was .45 (Confidence Interval [CI] .15 to .79; *p* = 0.008) lower in the combined MI—CBT group compared to usual care; and .16 (CI .20 to .51; *p* = 0.38) lower for MI alone compared to usual care.

A second randomized control trial on anxiety following moderate to severe traumatic brain injury included 27 patients (age 21 to 73; 78% male) and compared a combined MI—CBT

intervention to reduce anxiety to CBT alone and to usual care (Hsieh *et al.* 2012). The combined MI—CBT intervention was delivered in 12 1-hour individualized face-to-face sessions. Although CBT is the treatment of choice for traumatic brain injury, participants receiving MI showed greater response to CBT in terms of reducing anxiety, stress, and unproductive coping, compared with participants who received CBT alone or usual care ($p < .01$).

A cohort study combined CBT and MI to intervene on weight loss in 14 female bariatric patients (ages 32 to 67; 72% Caucasian and 28% African American) and followed them post-surgically for 18 months (Stewart *et al.* 2010). The intervention included 8-weekly small group sessions, each lasting 90 minutes long delivered by doctoral students supervised by faculty. Each session consisted of a specific topic for education and discussion as well as unstructured time for open discussion. Homework was assigned specific to individual goals. Findings indicated a mean weight loss of 4-pounds (range 0 to 6).

In these three studies (total $n = 385$) combining MI—CBT, there were 12 sessions over 2—6 months with each session lasting 50–120 minutes either individually or in a group. Interventionists were trained psychology doctoral students or RNs. Sessions included emphasizing the interconnected nature of thoughts, feelings, and behaviors; agenda-setting, homework, and feedback focused on diet, exercise, lifestyle behaviors, anxiety, worry, stress management, negative thoughts, impulse control, activities, and assertiveness training; and learning to consolidate gains to future situations. In regard to change, sessions included behavior change, acceptance, and coping flexibility; strategies to enhance readiness for change; level of importance, confidence, and readiness to change; a change plan tailored to individuals' needs and level of motivation; and endorsement of reasons to change. MI combined with CBT significantly improved outcomes of these challenging health conditions.

AIMS

This literature review addresses a gap in the literature by identifying interventions that combine MI and CBT to promote medication adherence, and describing these interventions in detail so that nurses may utilize this information in clinical practice. The ultimate goal was to provide a scientific basis for the development of an intervention to promote adherence in the increasing number of cancer patients being treated in pill form. To date, evidence supports that MI and CBT individually improve medication adherence; and improve health outcomes in some challenging clinical conditions. Therefore, examining the literature on combining MI and CBT to target medication adherence may lead to ways of helping nurses improve medication adherence in cancer patients treated in pill form. The objectives were as follows. (1) To generate a list of combined MI—CBT interventions to promote medication adherence. (2) To determine the effectiveness of the combined MI—CBT intervention on medication adherence rates. (3) To describe the components, mode of delivery, and dose of the intervention that addressed medication adherence.

METHODS

Study design: Integrative review

A integrative review method informed by Whittenmore and Knafl (2005) was adopted for this review. An integrative review is a comprehensive process that involves data collection and extraction of data, which leads to evidence suitable for use in clinical practice. Identifying relevant studies for this article was performed in two steps. First, a search of electronic databases for pertinent articles published over the past 10 years. Second, the reference lists were searched for additional relevant studies.

Inclusion/exclusion criteria

To address the above objectives, research articles reporting on the evaluation of interventions meeting the preset inclusion criteria were selected for this review. The criteria included:

(1) English-language articles published from 2005 to 2014.

(2) An intervention combining MI and CBT to affect a behavioral change to promote medication adherence.

Exclusion criteria included the following:

(1) An intervention not within the scope of nursing practice that could not be implemented without a medical order.

(2) Articles not reporting the influence of the intervention on the rates of adherence.

(3) Studies reporting on non-experimental research studies were excluded; as such designs are limited in generating evidence to determine effective interventions.

Search strategies

Using the integrative review steps, we identified our problem, examined the existing literature on articles that combined MI and CBT in interventions to promote medication adherence, conducted an evaluation of the findings in each article, and summarized the findings for this article. First, a search in Cumulative Index to Nursing and Allied Health Literature (CINAHL) and PubMed for peer reviewed research articles published between 2005 and 2014. Keywords were "motivational interviewing"; "cognitive behavioral therapy"; "intervention", and "medication adherence." Second, the reference lists of those articles were reviewed for other relevant articles.

Data extraction and analysis

Data were extracted on study characteristics, intervention characteristics, and results pertaining to the effects of the MI—CBT intervention on medication adherence rates. Data extraction was performed by four reviewers. The first two independently read the articles, carefully documenting relevant information in a table; the other two reviewed the study reports and confirmed the accuracy of the information. This iterative process continued until consensus was reached on the articles meeting the inclusion criteria included in this review.

Literature search

As shown in the Figure, 2,822 articles were retrieved on "MI" and 48,566 articles were retrieved on "CBT". We narrowed those groups to English language within the past 10 years. The terms "MI and CBT" combined yielded 206 articles. When the term "intervention" was added, 100 articles were found. These 100 articles were examined by four reviewers using the inclusion criteria until consensus was reached on which articles to retain in this review through an iterative process. Six articles were identified as using combined MI—CBT interventions to improve medication adherence, fitting the inclusion criteria.

RESULTS

Study characteristics

As shown in Table 1, the studies included in this review were published between 2005 and 2011. This included a randomized controlled trial (RCT); four cohort studies; and one case study. The setting in which the intervention under investigation was implemented was consistently in patients' homes.

Participant characteristics

Total sample size ranged from one to 402 across studies, with a total of 845 subjects in the six studies. Participant ages varied between 17 and 94, with an overall mean of 47.9 years. The mean percentage of female participants was 75.3% (range 40—100%). Race was not consistently reported. Interventions targeted different types of medications, thus, different populations.

Intervention characteristics

The RCT ($n = 15$; mean age 44; 94% male) was conducted by a therapist with a master's degree in psychology who had training in MI and CBT (Parsons *et al.* 2005). The intervention consisted of individual face-to-face sessions held once-per-week for 1-hour, for 8-weeks; with follow-up by phone for 3-months. Seventy-three percent completed all 8-weekly sessions; with 80% retention over 3-months. The first session was conducted immediately after the baseline interview. Sessions one and two explored ambivalence and building confidence for medication-taking, with feedback to enhance confidence and set goals. The third focused on triggers leading to missing medications. Sessions 4—7 used functional analysis to build content to meet individual needs (see Table 2). The last session focused on acquired skills and future goals. Patients were given self-monitoring cards to track medication adherence. Follow-up calls monitored adherence and attainment of goals.

The next four studies addressed cognitive and emotional reactions as suggested by Leventhal's theory (1999), using MI (Miller & Rollnick 2002) to reduce ambivalence about treatment and CBT (Beck 2000) to address negative beliefs about treatment. Prochaska's (1994) model of readiness to change was to assess ability to adopt medication taking behaviors. Each study conducted an assessment on the first call using an algorithm of factors that included prior

adherence, social support, and treatment complexity, to identify patients at-risk or low-risk for nonadherence (Cook 2006) to determine intervention dose.

The osteoarthritis study ($n = 402$; mean age of 66.9; 94% female) intervened with RNs (4) by phone (Cook *et al.* 2007). Of those in the study, 79% ($n = 317$) were new to treatment; 5% ($n = 30$) were a mean of 13.3 days into treatment; and 15% ($n = 65$) had not started. RNs initiated contact within 14-days of medication start date, and followed patients for a mean of 4.1 (range 0—14) months. On the first call, 64.7% ($n = 260$) were determined to be at-risk for nonadherence and 35.3% ($n = 142$) were low-risk. At-risk received 5-calls (range 3—8); and low-risk received 3-calls (range 2—8). On average, calls lasted 15.3 minutes. RNs asked whether or not patients had started treatment and if currently adherent. If had not started, or stopped but still wanted treatment, calls focused on relationship building and answering questions to build the motivation for treatment. If started treatment but was having difficulty remaining adherent or had questions about the medication, calls focused on problem-solving and support to address patients' concerns. The goal was to resolve barriers to adherence, and increase self-efficacy and motivation for medication adherence. RNs helped patients practice skills to self-manage medication taking behaviors.

The ulcerative colitis study ($n = 278$; mean age 49; 66% female) intervened via RNs by phone, and the intervention was provided by the same RN over the course of the study (Cook *et al.* 2010). RNs had prior work experience in mental health; and attended an eight hour training session, received 3-hours of individual training, and attended weekly team meetings for feedback. Seventy-three percent ($n = 203$) were at-risk for medication nonadherence. RNs initiated contact within 1 day of the medication start date; and followed patients for a mean of 6 months (standard deviation [SD] = 1.35). On average, patients received 4.2 calls (SD = 2.55);

with an average length of call 13.5 minutes (SD = 4.42). Pre-determined scripts were used for the calls. Notably, the intervention was based on patient concerns about readiness to change, addressing both cognitive and emotional reactions rather than simply delivering information. For example, MI questions to reduce ambivalence about treatment and CBT to address negative beliefs about treatment or to cope with adverse events.

The antipsychotic study (*n* = 51; mean age 33; 86% female) intervened with three RNs on the phone, each working with the same patient over time (Cook *et al.* 2008). Participants were members of a managed care plan, new to treatment, and prescribed the medication within the past 30-days. Ninety percent (*n* = 46) of the participants were screened at-risk for nonadherence. At-risk had a mean of 7.2 call attempts; with mean of 3.5 completed over an average of 4.4 months. Average call length was 11 minutes. Total contact time on average per participant was 38.5 minutes. Low-risk for nonadherence received a toll-free number plus 1-call at 6-months. During each call, the RN intervened based on the participant readiness for change and individual barriers to adherence. RNs also mailed follow-up written materials to 45 (88%) participants. A written progress note was sent to the patients' health plan case manager after each call. Participants did not receive incentives. Four participants reported potential serious adverse drug events; and were referred to their primary care provider.

The HIV study (*n* = 98; mean age 44; 67% male) intervened with 10 RNs by phone, with each participant assigned to the same RN (Cook *et al.* 2009). Ninety-two percent (*n* = 90) were new to ART treatment. Those with low-risk for nonadherence only received 1-call at 6 months. Those at-risk for nonadherence received, on average, 3.0 calls (range 1—14). Average call length was 5-minutes (SD 11.7). No standardized script was utilized. The goal was to motivate patient adherence to ART treatment. Emphasis was placed on training RNs to focus on patients

concerns rather than providing information. Information that was provided was not standardized, but in response to the patients requests and needs.

The case study ($n = 1$; age 17; female) was conducted by a trained therapist (Hilliard *et al.* 2011). The intervention included 35-sessions of MI and CBT. The initial assessment was conducted face to face, and an electronic pill bottle to measure adherence was provided. The intervention content is listed in Table 2. Caregivers (parent and sister) were involved throughout the intervention.

Measures of Medication Adherence

Three means of medication adherence were identified (see Table 1). The RCT study measured adherence by self-report. In the cohort studies, adherence was measured by self-report and pharmacy fill records. In the case study, an electronic pill bottle was provided to measure adherence.

Intervention Effect on Medication Adherence

In the RCT, seven participants (46.6%) reported missing at least 1-dose in the prior 2-weeks; five (33%) reported a missed dose in the past 2-days and 2-missed (13.3%) doses within the past 24-hours (Parsons *et al.* 2005). Three-month follow-up found 4-participants (33%) reported missing a dose during the past 2-weeks; one (8.8%) missing a dose over the past 2-days; and none missing a dose within 24-hours. Post-treatment reasons given for missing medication included fear of stigma ($n = 1$) and running out of the medication ($n = 1$). Thus, in the RCT, pretreatment number of missed medication doses in the last 14 days was 5.58 compared to 0.92 post treatment, "trending" toward significance.

In the cohort studies, intervention ES was established. This was done by comparing the study group to national reference data.

In the osteoarthritis study, adherence was higher than the population base rate after 3-months ($X^2 = 7.32$; $p = .007$) and 6-months ($X^2 = 6.75$; $p = .009$) (Cook *et al.* 2007). Average ES of the intervention was 0.19 across time periods (3 and 6 months). A comparison was conducted between the intervention group and those referred but not participating at 6-months with the intervention group at 69% adherence, and referred not participating at 63%, approaching significance ($X^2 = 20.34$; $p = .06$) with a moderate ES of .33.

In the ulcerative colitis study, 4-participants did not start treatment; and three (75%) agreed to start after speaking with the RN (Cook *et al.* 2010). Nineteen (7%) reported stopping at any point in time; and 10 of 19 (53%) agreed to resume. Overall, 6-month adherence was higher than the population norm ($X^2 = 2.22$; $p < .001$). The ES of the intervention was .35. Patient reasons reported for nonadherence included cost of treatment, treatment logistics, forgetting, thinking the medication is not needed, being too sick to take the medication, and having concerns regarding adverse events.

In the anti-psychotic study, pharmacy fill rates for intervention group was 59% ($n = 29$) for 3-consecutive months; and 48% for 6-months, significantly higher than population base ($X^2 = 8.02$; $p = .004$) (Cook *et al.* 2008). For self-report, five (9.8%) did not fill the initial script and18 (38.9%) stopped treatment at some points. Three (of 5; 60%) who did not start and seven (of 18; 38.9%) who stopped agreed to resume treatment after receiving the intervention. Six-month adherence was 50%, higher than the population base ($X^2 = 9.47$; $p = .002$). ES of intervention at 6 months on medication adherence was .22.

In the HIV study, 59% ($n = 29$) received at least three consecutive months of medication, and 48% were adherent for 6-months, a higher rate than the comparison group ($X^2 = 8.01$; $p = .004$) (Cook *et al.* 2009). Self-reported adherence found five (9.8%) participants did not fill an

initial prescription and 18 (35.3%) stopped treatment at some point. Three of five (60%) who did not start and seven of 18 (38.9%) who stopped agreed to resumed treatment after speaking with the RN. Six month adherence was 50%, higher than population base ($X^2 = 9.47$; $p = .002$). Thus, ES of .25 for receipt of script; and .25 for 95% adherence to the medication.

One study used an electronic monitoring device to measure adherence (Hilliard *et al.* 2011). Pretreatment adherence rate in the case study was 25%, compared to post treatment medication adherence of 77% ($p < .01$) on average; and medication adherence 82% ($p < .01$) at the final session in the intervention.

DISCUSSION

Most of the interventions on medication adherence studies that combined MI—CBT included an assessment risk of nonadherence using an algorithm to include prior adherence, social support, and treatment complexity to predict at-risk versus low-risk; and provided intervention dose accordingly. Both intensive face-to-face and brief calls were effective at promoting medication adherence. Interventionists were RNs or a therapist, with MI and CBT training. Initiation of the interventions occurred on days 1, 14, and 60 after the prescription was written, with greater improvement in medication adherence with those timed closer to the date of initiation of treatment (prescription). The content of interventions was consistent, most focusing on readiness for change, reducing ambivalence, problem solving, coping, goal setting, dealing with adverse events, and reviewing acquired medication taking behaviors/skills. The majority tailored to the individual's needs, providing interactions and written materials specific to that person, such as MI questions to reduce ambivalence about treatment and CBT to address negative beliefs about treatment or to cope with adverse events. In addition, one study provided a self-monitoring card to track medication adherence. Five of six studies demonstrated a

significant improvement in medication adherence with ES for face-to-face sessions of .52 and calls ranging from .19 to .35. The sixth study was "trending" toward significance.

Strengths of this review included consistency among intervention approaches; and sample size. Limitations of this review include the strength of the studies, with only one RCT.

CONCLUSION

These findings indicate an intervention with MI—CBT combined may be an effective method for eliciting behavior change and promoting medication adherence. The use of MI, in combination with CBT, may better address patients at their level of readiness to change and places responsibility to change on the person. Combined MI—CBT might be a means of improving medication adherence in challenging clinical conditions, such as in cancer patients prescribed treatment in pill form. With so much at stake for patients prescribed treatment in pill form, medication adherence is critical, and more complex interventions may be needed.

RELEVANCE TO CLINICAL PRACTICE

Multiple strategies are needed to improve medication adherence, especially for cancer patients treated in pill form, to ensure the best possible outcome. MI and CBT are commonly used interventions that can be combined to treat complex clinical issues like medication adherence. Intervening on factors such as motivation, self-efficacy, emotions, and beliefs using a combined MI—CBT approach may improve adherence to oral agents. MI and CBT may be relatively simple to implement, by modifying how nurses talk to patients. Examples of talking points are provided in Table 3. A MI—CBT intervention has the potential to impact other chronic diseases, promoting adherence to treatment regimens.
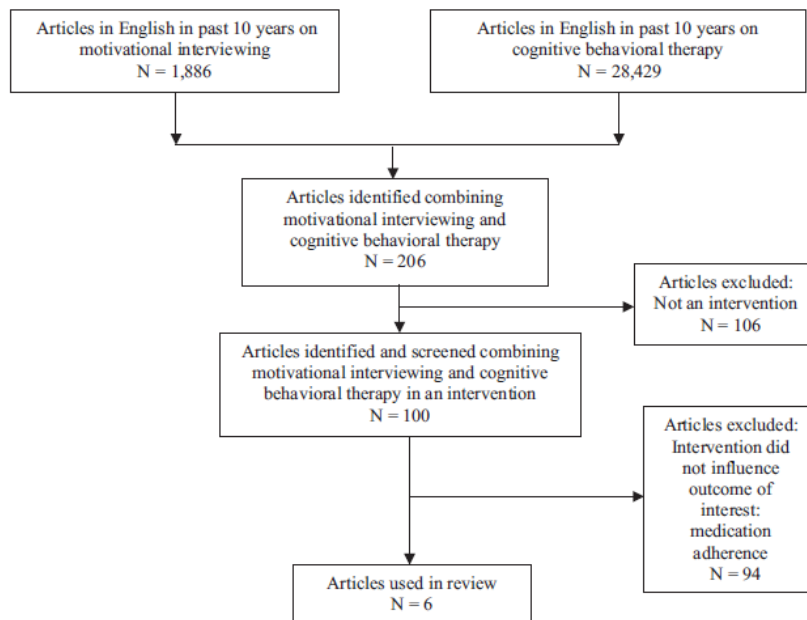
Figure 1 Flow chart of articles found on combined motivational interviewing and cognitive behavioural therapy for this review.

Table 1 Articles in review on motivational interviewing (MI) and cognitive behavioural therapy (CBT) combined on medication adherence: author, year, type of study, mode of delivery, type of intervener, number of contacts, duration of contact, outcome measures and major findings in study

Author (year)	Medication	Sample size (n)	Type of study	Mode of delivery	Type of Intervener	Number of contacts (mean)	Duration of contact (mean)	Duration of intervention (mean)	Outcome Measures	Major findings in study
Cook et al. (2007)	Osteoarthritis	n = 402	Cohort trial	Phone	Registered nurses (RN)	Five calls at-risk; three-calls low-risk	15 minutes	Four months	Pharmacy fill records & self-report	Effect size (ES) of intervention was 0·19 over the 2 time periods (three & six months)
Cook et al. (2008)	Psychiatric	n = 51	Cohort trial	Phone		73·5 calls at-risk; one-call low-risk	11 minutes	4·4 months	Pharmacy fill records & self-report	ES of intervention in six months was 0·22
Cook et al. (2009)	HIV	n = 98	Cohort trial	Phone	RN	Four calls at-risk; one-call low-risk	7·5 minutes	Six months	Pharmacy fill records & self-report	ES 0·25 for receipt of script; and 0·25 for 95% adherence
Cook et al. (2010)	Ulcerative colitis	n = 278	Cohort trial	Phone	RN	4·1 call at-risk; 2·1-calls low-risk	11 minutes	Four months	Pharmacy fill records & self-report	ES of intervention was 0·35
Hilliard et al. (2011)	Fanconi anaemia	n = 1	Case study	Face-to-face	Therapist	35 sessions	One hour	Six months	Electronic monitoring	Adherence: pre-53% post-77%; 82% at final p < 0·01
Parsons et al. (2005)	HIV Antiretroviral therapy	n = 15	Randomised controlled trial pilot	Face-to face and phone	Therapist	Eight sessions face-to-face; phone not reported	One hour	Six months	Self-report adherence	Trend towards better adherence but not statistically significant in small sample size

Table 2 Articles in review on motivational interviewing (MI) and cognitive behavioural therapy (CBT) combined on medication adherence: author, year, components of intervention

Author (year)	Components of interventions
Cook *et al.* (2007)	Assessment of adherence risk factors to determine at-risk or low-risk for nonadherence.
	Follow-up by phone whether or not had started medication and if currently adherent.
	If the medication not started or if it was stopped but patient wanted treatment, focused on relationship building and answering questions to build motivation for adherence.
	If started medication but was having difficulty remaining adherent or had questions about the medication, focused on problem-solving and support to address patients concerns.
	The goal was to resolve barriers to medication adherence by increasing self-efficacy and motivation.
	Practiced medication-taking behaviours and skills on the phone to self-manage
Cook *et al.* (2008)	Assessment of adherence risk factors to determine at-risk or low-risk for nonadherence.
	Each patient worked with the same registered nurses (RN).
	Cued content of phone call on the individual's barriers to adherence and readiness for change.
	Followed-up the phone call by mailing written materials.
	A written progress note was sent to the health plan case manager after each call.
	Adverse events occurrences were reported to primary care providers
Cook *et al.* (2009)	Assessment of adherence risk factors to determine at-risk or low-risk for nonadherence.
	Assessment of concerns and barriers to adherence on each phone call.
	Each patient worked with the same RN.
	The phone call was based on the individual's readiness to change.
	The goal was to motivate patient adherence to antiretroviral therapy medication.
	Emphasis was on patient concerns, to meet their individual needs.
	Educational information was provided in response to the patient requests and needs.
Cook *et al.* (2010)	Assessment of adherence risk factors to determine at-risk or low-risk for nonadherence.
	Assessment of adherence.
	A manual with predetermined phone call scripts was used.
	The content of the phone call was based on patient concerns, and readiness to change.
	Addressed cognitive and emotional reactions during phone calls.
	Questions to reduce ambivalence about treatment were addressed as they occurred.
	Addressed negative beliefs about treatment were addressed as they occurred.
	Addressed coping with adverse events
Hilliard *et al.* (2011)	A treatment plan was devised integrating family involvement in the plan of care.
	Addressed discrepancies between values and behaviours to medication adherence.
	Highlighted barriers and promoters of medication adherence.
	Addressed mood, anxiety and barriers to adherence.
	Goal setting and problem-solving occurred in each interaction
Parsons *et al.* (2005)	Content provided: coping, managing thoughts, reaching out for social support, managing negative moods, communicating with health care providers, making time for oneself, participating in pleasant activities and managing side effects (used as needed).
	A written self-monitoring card to track medication adherence was provided to the patient.
	Phone calls monitored adherence and attainment of goals.
	Focused on acquired skills and future goals in last session

Table 3 Examples of talking point using motivational interviewing (MI) and cognitive behavioural therapy (CBT) to promote medication adherence: topic and example talking point

Topic	Example talking points to promote medication adherence
Introduction	I am going to discuss your care at home regarding your treatment. You and your doctor have decided that taking this medication is the right choice for you. It's important to understand how to go about managing your medication at home. Together, we will decide what things will work best for you and you will decide what your goals are. We will work with the doctor, as a team, to help make managing at home easier
Assessing readiness for change	Taking a new medication is important and requires a change to your usual routine, how ready are you to make these changes?
	It is important for me to get a better understanding how ready you are for change so I am going to ask you a few questions. Is it all right if we proceed?
	How ready are you for change? On a scale of 0–10, with 0 being not ready, 5 being considering change, and 10 being ready for change. How ready are you for change?
	How important is this change to you?
	How confident are you that you can make this change?
	(For those with less than a 10.) Why did you choose a 7 (insert number), not a 10?
	What would have to happen to make it a 10?
Adherence	First, we are going to discuss your medication to identify what you know about your medication; and if you may need additional information.
	Have you ever forgotten to take your pill in the past seven days?
	What would you do if you forgot to take your medication?
	What happens when you take your medication less often than prescribed?
	Would you skip or stop taking your medication because you did not think it was working?
	Would you skip or stop taking your medication because it made you feel bad?
	Have you ever taken more pills that you were prescribed in the past seven days?
	What happens when you take your medication more often than prescribed?
	Did you forget to take your medication and double up a dose?
Goal setting	Next we are going to discuss actions you can take to take your medication properly at home.
	What ideas do you have to help you remember to take your medication?
	Do you take your medication at the same time you usually do something else, like eat breakfast, brush your teeth, or weigh yourself?
	How do you know if you are reaching your health goals?
	What goals to you have for the next week?

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