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1 **Can a Multifaceted Intervention Including Motivational Interviewing Improve Medication**  
2 **Adherence, Quality of Life and Mortality Rates in Older Patients Undergoing Coronary**  
3 **Artery Bypass Surgery? A Multicenter Randomized Controlled Trial with 18-month**  
4 **Follow-up**

5 **Short title/running head: Effects of a multifaceted intervention on medication adherence**  
6 **and mortality rates in older CABG patients**

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4 **Compliance with Ethical Standards**

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8 **Conflicts of Interest**

9 Chung-Ying Lin, Mehdi Yaseri, Amir H. Pakpour, Dan Malm, Anders Broström, BengtFridlund,  
10 Andrea Burri and Thomas L. Webb declare that they have no conflicts of interest relevant to the  
11 content of this manuscript.

12

1 **Key points**

- 2 • A multifaceted intervention including psycho-education, motivational interviewing, and short  
3 message services improved medication adherence among patients aged over 65 who were  
4 undergoing coronary artery bypass graft (CABG) surgery.
- 5 • The effects of the multifaceted intervention on medication adherence were maintained  
6 eighteen months following the intervention.
- 7 • Quality of life and survival rates improved as a consequence of increasing medication  
8 adherence.

1 **Abstract**

2 *Background.* Patients undergoing coronary artery bypass graft (CABG) surgery are required to  
3 take a complex regimen of medications for extended periods, and they may have negative  
4 outcomes because they struggle to adhere to this regimen. Designing effective interventions to  
5 promote medication adherence in this patient group is therefore important.

6 *Objective.* The present study aimed to evaluate the long-term effects of a multifaceted  
7 intervention (psycho-education, motivational interviewing, and short message services) on  
8 medication adherence, quality of life (QoL), and mortality rates in older patients undergoing  
9 CABG surgery.

10 *Methods.* Patients aged over 65 years from 12 centers were assigned to the intervention (EXP;  
11  $n=144$ ) or treatment as usual (TAU;  $n=144$ ) groups using cluster randomization at center  
12 level. Medication adherence was evaluated using Medication Adherence Rating Scale (MARS),  
13 pharmacy refill rate, and lipid profile; QoL using Short-Form 36. Data were collected at  
14 baseline; three, six, and eighteen months after intervention. Survival status was followed up at  
15 eighteen months. Multi-level regressions and survival analyses for hazard ratio (HR) were used  
16 for analyses.

17 *Results.* Compared to patients who received TAU, the MARS, pharmacy refill rate, and lipid  
18 profile of patients in the EXP group improved six months after surgery ( $p<0.01$ ) and remained so  
19 eighteen months after surgery ( $p<0.01$ ). QoL also increased among patients in the EXP group as  
20 compared to those who received TAU at eighteen-month post-surgery (physical component  
21 summary score  $p = 0.02$ ; mental component summary score  $p = 0.04$ ). HR in the EXP group  
22 compared to the TAU group was 0.38 ( $p=0.04$ ).

1 *Conclusion.* The findings suggest that a multifaceted intervention can improve medication  
2 adherence in older patients undergoing CABG surgery, with these improvements being  
3 maintained after eighteen months. QoL and survival rates increased as a function of better  
4 medication adherence.  
5 [ClinicalTrials.gov NCT02109523](https://clinicaltrials.gov/ct2/show/study/NCT02109523)

1 **1. Introduction**

2 Coronary artery bypass graft (CABG) surgery is often considered to be the primary  
3 intervention for individuals suffering from severe coronary artery disease and has been shown to  
4 increase quality of life (QoL) and life expectancy [1-3]. The mortality rate during CABG surgery  
5 has declined [4-8], including among older patients, even up to 90 years or above [6,7]. However,  
6 although CABG is a promising surgery for older patients with severe coronary artery disease,  
7 there are some reasons to suspect that older patients may have more negative outcomes after  
8 CABG surgery than younger patients [9,10].

9 Patients undergoing CABG surgery are required to take a complex regimen of  
10 medications over a long period of time [9]. Therefore, one reason why older patients may have  
11 more negative outcomes is that they struggle to adhere to this regimen [10]. Some characteristics  
12 of the geriatric population, including hearing difficulties, impaired cognition, poor manual  
13 dexterity and vision, and low tolerance of the effects of drugs may result in low rates of adherence  
14 [11]. In addition, older patients undergoing CABG surgery share some of the factors that lead to  
15 noncompliance among younger patients, such as poor education about the importance, and  
16 adverse effects of, each medication, polypharmacy (the use of four or more medications), the  
17 need to take multiple doses each day, the cost of medication, and the incorrect use of medication  
18 [12]. Because medication adherence positively influences outcomes (e.g., decreases functional  
19 disability, morbidity, and mortality) [13,14], it is important to design interventions that can  
20 improve medication adherence among older patients undergoing CABG surgery.

21 A meta-analysis of 33 randomized controlled trials of interventions designed to improve  
22 medication adherence among older patients [15] found that the interventions incorporating  
23 psycho-education, behavioral interventions, and interventions based on the theory of planned

1 behavior significantly improved medication adherence (effect size,  $d=0.33$ ) and knowledge about  
2 medications ( $d=0.48$ ) relative to control conditions. However, the meta-analysis defined older  
3 patients in a relatively broad way (i.e., as those older than 60 years). Hence, their results may not  
4 generalize to older populations (i.e., those aged over 65 years); especially as age has been found  
5 to influence medication adherence among people with myocardial infarction [13]. Also, none of  
6 the primary studies focused on promoting medication adherence among older patients undergoing  
7 CABG surgery; therefore, more evidence is needed on interventions that can improve medication  
8 adherence for older patients undergoing CABG surgery.

9 Multifaceted interventions seem to be an appropriate way to promote medication  
10 adherence because many factors can simultaneously influence the behavior [16,17]. For example,  
11 a prospective study found that medication counseling accompanied by planning increased  
12 medication adherence among patients with a mean age of 59 years undergoing CABG surgery  
13 [18]. However, given that older samples (e.g., those aged over 65) may have additional issues that  
14 prevent them from successfully adhering to medications (e.g., further impairments to hearing and  
15 cognition); it is possible that additional intervention components are needed to promote  
16 medication adherence among these patients. Therefore, the present research developed an  
17 intervention that consisted of psycho-education, motivational interviewing (MI) [19-21]  
18 accompanied by planning, and sending reminders via a short message service (SMS)[22] in an  
19 effort to increase medication adherence among patients aged over 65 undergoing CABG surgery.  
20 The intervention also encouraged the patients' family to help because family members may  
21 influence medication adherence among patients undergoing CABG surgery [23], especially in  
22 Eastern cultures where family relationships are particularly valued [24].

1           In addition to identifying effective ways to promote medication adherence, it is also  
2 important to understand how and why interventions are effective – i.e., to identify the underlying  
3 mechanisms. Multifaceted interventions likely change relevant cognitions and self-regulatory  
4 processes that, in turn, lead to changes in the outcomes of interest (namely, medication  
5 adherence). Based on extant research, it seems likely that patients’ intentions, behavioral  
6 automaticity, levels of action and coping planning, perceived behavioral control, self-monitoring,  
7 beliefs about medicines, and illness perceptions could all potentially mediate the effects of the  
8 intervention on outcomes (i.e., medication adherence, QoL, and mortality rate). Intentions reflect  
9 the direction and strength of a person’s motivation to perform the relevant behavior (such as  
10 medication adherence in our study) [18]. Behavioral automaticity reflects whether a patient  
11 engages in a behavior (e.g., taking medication) relatively automatically; that is quickly, easily,  
12 and without the need for conscious thought[25]. Action and coping planning reflect the extent to  
13 which patients have identified obstacles that may prevent them from engaging in a behavior and  
14 made plans specifying how they plan to deal with these; perceived behavioral control reflects  
15 how competent someone feels in their ability to perform a behavior [26]. Self-monitoring  
16 indicates whether someone regularly reflects on and monitors his/her behavior and/or the  
17 outcomes of their behavior [27,28]. Beliefs about medicines refer to a patient’s beliefs about the  
18 necessity and adverse effects of the medication they take [29], and illness perceptions indicate  
19 how a patient understands his/her illness [30]. A number of theoretical frameworks suggest that  
20 these social cognitions and self-regulatory processes affect the likelihood that a person will  
21 engage in a behavior [31-34]. Therefore, we considered that these factors could potentially  
22 mediate the impact of the multifaceted intervention on behavior (i.e., medication adherence).  
23 Moreover, because QoL and mortality rate are further outcomes of medication adherence

1 [13,14], medication adherence should mediate the effect of the intervention on QoL and mortality  
2 rates.

### 3 *1.1 Objectives*

4         The present study aimed to evaluate the long-term effects of a multifaceted intervention  
5 (including psycho-education, motivational interviewing, and a short message service [SMS]) on  
6 medication adherence (primary outcome), and QoL and mortality rates (secondary outcomes) in  
7 older patients undergoing CABG surgery. In addition, we measured a number of relevant social  
8 cognitions (e.g., strength of intentions to take medication) and self-regulatory processes (e.g.,  
9 action and coping planning) as potential mediators of the effects of the intervention on  
10 medication adherence.

## 11 **2. Methods**

12         This trial was registered at ClinicalTrials.gov with the registration number  
13 NCT02109523.

### 14 *2.1 Design and study population*

15         The study adopted an open-label, researcher-blind, randomized controlled design, with  
16 two arms. Specifically, one arm received multifaceted intervention (see *Section 2.3 Intervention*  
17 for more details); another received treatment as usual (see *Section 2.5 Treatment as Usual* for  
18 more details). Patients were recruited from multiple centers across Iran (5 academic centers in  
19 Tehran, 2 in Qazvin and Ahvaz each, 1 in Semnan, Zanjan, and Tabriz each). Inclusion criteria  
20 were that patients: (a) be aged 65 years or above, (b) had undergone CABG surgery, (c) had the  
21 ability to read and write Persian/Farsi, (d) provided informed consent to participate, and (e) had  
22 access to a mobile phone. Exclusion criteria were that patients: (a) had already used Dose boxes  
23 (or similar) to improve medication adherence, (b) were currently enrolled in another clinical trial,

1 (c) suffered from significant dysphasia, severe kidney disease (creatinine clearance < 30 ml/min),  
2 oxygen-dependent chronic obstructive pulmonary disease, active hepatitis, significant hepatic  
3 failure, and/ora prior peptic ulcer (platelet count <  $150 \times 10^9$ ), (d) were having concomitant  
4 surgery,(e) suffered from a severe cognitive impairment (i.e., Mini Mental Status Examination  
5 MMSE score of < 20, (f) had had a myocardial infarction within 48hours of surgery, (g) were  
6 allergic to aspirin, (h) abused alcohol or narcotics, (i) reportedongoing bleeding, (j) had a  
7 terminal condition or were deemed unlikely to survive until six-month follow-up, (k) were not  
8 being responsible for their own medication, and (l) the CABG was conducted as an emergency  
9 surgery. Patients with poor prognosis ( $n=2$ ) and those who had CABG as an emergency surgery  
10 ( $n=3$ ) were excluded to increase the likelihood that we were able to measure relevant outcomes  
11 at eighteen months. Patients requiring emergency or urgent CABG are at higher risk than those  
12 undergoing CABG electively, and emergency CABG is typically carried out if serious  
13 complications develop after a heart attack (e.g., shock, life-threatening abnormalities of the heart  
14 rhythm, or rupture of heart tissues), thus there is an increased risk of mortality among such  
15 patients [9].

16 Five trained general practitioners assessed each participant with respect to  
17 theaforementionedinclusion and exclusion criteria, after which all eligible patientswereinvited to  
18 participate in a group information session in a seminar room in their respective hospitals. In this  
19 session, the principal investigator and a surgeon explained the aims of the study and answered  
20 any questions that the patients had. Interested patients were then asked to sign a consent form  
21 and were assigned a unique study identification (ID) number. Following this, patients  
22 completedbaselinemeasures ( $n=288$ patients completed this assessment). The measures were  
23 repeated at six, twelve, and eighteen months after the intervention.Ethics approval was obtained

1 from the review committees of the different centers and partner institutions who approved the  
2 trial (QUMS.REC.1394.2).The study was conducted in accordance with the Ottawa Statement,  
3 the Helsinki Declaration, and Good Clinical Practice.

#### 4 *2.2 Randomization and blinding*

5 In order to minimize contamination and maximize the efficiency with which the  
6 intervention was delivered, centers were chosen as the units of randomization. Specifically, the  
7 centers were randomly assigned to either the intervention (EXP) or the treatment as usual (TAU)  
8 groups by an independent statistician following a 1:1 scheme using a computer generated list of  
9 random numbers. Six centers were assigned to the EXP group and six centers were assigned to  
10 the TAUgroup. Figure 1 shows the flow of patients through the study.

11 (Insert Figure 1 here)

12 The sample size needed to detect any effects of the intervention was calculated based on  
13 the primary outcome measure (self-reported medication adherence). It was estimated that 144  
14 patients would be needed in each group to detect an effect (*difference*) = 1 score, with 90%  
15 power and a significance level of 5%, assuming a standard deviation of 1.9 in both groups,  
16 design effect of 1.8, and 5% loss at follow up. Exactly 144 patients were therefore allocated to  
17 each group as suggested by the sample size calculation.

18 All researchers responsible for measuring outcomes as well as statisticians were blinded  
19 to the group allocation. However, it was not possible for patients to be blind to group allocation  
20 because of the use of behavioral interventions. Therefore, objective measures of medication  
21 adherence such as total cholesterol, high-density lipoprotein (HDL) and low-density lipoprotein  
22 (LDL) concentrations were also evaluated, alongside self-reported rates of adherence to reduce  
23 the likelihood of demand effects.

1    2.3 *Intervention*

2           Patients in the EXP group received a multifaceted intervention that included: (a) psycho-  
3   education, (b) motivational interviewing (MI), and (c) sending reminders via SMS. The  
4   intervention began the first week after the patients were discharged.

5    2.3.1 *Psycho-education*

6           Patients in the EXP group participated in three weekly sessions accompanied by at least  
7   one family member with whom they had a close relationship (e.g., their father, mother, spouse,  
8   brother or sister). The psycho-education component of the intervention was delivered by  
9   cardiovascular nurses. The contents and topics of psycho-education were discussed and  
10  preselected by cardiovascular nurses as well as cardiologists. The content of the psycho-  
11  education was the same for all patients and delivered orally. Each session lasted for one hour and  
12  the main purpose was to provide information about coronary artery disease and ways of coping  
13  with the disease (e.g., the potential barriers to, and concerns about, coping with the disease). In  
14  addition, patients' experiences during previous visits, a list of previous medications and their  
15  effects and side-effects, the reasons for previous medication non-adherence, as well as the  
16  reactions and communication between the family members about the patients' symptoms were  
17  discussed.

18  2.3.2 *Motivational interviewing (MI)*

19           The patients in the EXP group attended five weekly sessions of MI that each lasted  
20  around 50 minutes. All sessions were held in a quiet, private, and comfortable setting inside the  
21  hospitals. The sessions were delivered by five trained and registered psychologists with  
22  experience (more than 100 hours) in moderating MI sessions. These psychologists used several

1 MI techniques that could potentially help the patients to increase their medication adherence,  
2 including open-ended questions, rolling with resistance, agenda setting, eliciting self-  
3 motivational statements, change talk, and affirmations. Following this, the psychologists  
4 highlighted factors that might interfere with the patients' plans to take their medication (also  
5 called: *action planning*) and asked the patients to anticipate situations in which they might  
6 struggle to take their medication along with possible strategies that they might use to overcome  
7 these barriers (also called: *coping planning*) [18]. At the end of the session, patients were asked to  
8 put the form on which they had written their plan(s) in a place that was easily visible and  
9 accessible for them. Detailed information on the procedure for the MI sessions is provided in  
10 Electronic Supplementary Material Table S1.

### 11 2.3.3 Reminders via SMS

12 Four reminders were sent to patients on a monthly basis via text messages. The content of  
13 the messages differed each month as follows: (1) The only way to improve your health is regular  
14 adherence to your medications; (2) Regular adherence to your medications will greatly help your  
15 recovery process and improve your health; (3) The most important factor for preventing a heart  
16 attack is that you take your medication regularly; and (4) Carefully consider which medication  
17 you take on a daily basis.

### 18 2.4 MI integrity/fidelity

19 In order to assess the quality and integrity of MI, all sessions were audiotaped. To  
20 evaluate integrity, the Motivational Interviewing Treatment Integrity (MITI) scale 3.1.1 was used  
21 [35]. The MITI is a widely used measure of competences in MI. It normally makes use of a 20-  
22 minute segment of each MI session and evaluates this segment based on global scores and

1 behavior counts (two components of the MITI) to capture treatment fidelity. Twenty percent of  
2 the audiotaped sessions were selected randomly for evaluation by an independent/external  
3 coder. The global scores comprise five global ratings including evocation, collaboration,  
4 autonomy/support, direction, and empathy. The behavior counts include providing information,  
5 asking open- and closed-ended questions, providing simple and complex reflections, and making  
6 other statements categorized as MI adherent or not. In addition to the abovementioned  
7 components, five summary scores (i.e., each domain of the global ratings: evocation,  
8 collaboration, autonomy/support, direction, and empathy) were also computed to provide a more  
9 concise measure of competence.

10 Electronic Supplementary Material Table S2 provides the global measures, behavior  
11 counts, and summary scores of the MITI. All of the facilitators who delivered the MI were  
12 competent, according to this measure. Specifically, the means of global measures were between  
13 3.61 and 4.59, and the mean percentage of facilitators who were MI adherent was 93.12. Most  
14 means were slightly below competency, but above beginning proficiency.

## 15 *2.5 Treatment as Usual*

16 Patients allocated to the treatment as usual (TAU) group received the advice commonly  
17 given by surgeons on coronary artery disease and the CABG procedure, along with information on  
18 the importance of healthy diet and nutrition. Patients in the TAU group were further informed  
19 about the importance of medication adherence and encouraged to regularly take their  
20 medications, as well as being reminded of the negative consequences of nonadherence. Providing  
21 this information took approximately 30 minutes and took place in a room in the respective  
22 hospitals before the patients' discharge.

## 1 2.6 Outcomes

2 All outcomes were measured at baseline (before the intervention), and then six, twelve,  
3 and eighteen months post-surgery. Detailed information on each of the measures is described  
4 below. The measures of intentions, action and coping planning, perceived behavioral control, and  
5 self-monitoring were based on similar measures used in previous research [18,25-30], but were  
6 adapted so as to be relevant for Iranian patients undergoing CABG.

### 7 2.6.1 Medication Adherence Rating Scale

8 The Medication Adherence Rating Scale (MARS) is a short self-report scale measuring  
9 medication adherence that consists of 5 items which patients are asked to respond to on a 5-point  
10 Likert scale (from 1: always to 5: never) [36]. Scores range from 5 to 25 with higher  
11 scores indicating better medication adherence [18]. The Persian version of the MARS in the  
12 current study proved internally consistent (Cronbach's  $\alpha=0.89$ ).

### 13 2.6.2 Pharmacy refill rate

14 The pharmacy refill rate was defined as the number of days on which medications were  
15 dispensed to the patient during the study period, divided by the total number of days in the study  
16 period. This figure was then multiplied by 100 to give a percentage. All related information was  
17 collected monthly from 22 pharmacies in 6 cities and included the total number of pills  
18 prescribed along with the dates of each prescription. We assessed the cardiovascular medication  
19 adjusted for inpatient days and medication refills prior to enrollment date as well as information  
20 registered at six and twelve months' follow-up on change in prescriptions.

### 21 2.6.3 Lipid profile

1 Serum lipid profiles were determined for all patients by taking 5ml of venous blood after  
2 overnight fasting. Total cholesterol (TC), triglycerides (TG) and high-density lipoprotein-  
3 cholesterol (HDL-C) concentrations were determined by the enzymatic colorimetric method.  
4 Low-density lipoprotein-cholesterol (LDL-C) concentration, as well as serum TC, TG and HDL-  
5 C concentrations were calculated using the Friedewald formula.

#### 6 2.6.4 Intentions

7 Patients completed a short (5-item) questionnaire designed to measure their intentions to  
8 take medication, with items (e.g., “I intend to regularly take medicine in the future”)  
9 being responded to on a 5-point Likert-type scale (from 1: completely disagree to 5: completely  
10 agree) [18]. The measure of intentions showed satisfactory internal consistency in this study  
11 (Cronbach’s  $\alpha=0.90$ ).

#### 12 2.6.5 Self-report Behavioral Automaticity Index

13 The Self-report Behavioral Automaticity Index (SRBAI) measures the extent to which a  
14 particular behavior (e.g., taking medication) is automatic for an individual [25]. The  
15 SRBAI consists of four statements that begin with “Behavior X is something...”, followed  
16 by different descriptions, such as “I do automatically”; “I do without having to consciously  
17 remember”; “I do without thinking”; “I start doing before I realize I am doing it”. Patients are  
18 asked to rate the extent to which they agree with each of the statements on a 5-point Likert-type  
19 scale (from 1: disagree to 5: agree), and items were summed. The Persian version of the SRBAI  
20 was found to be highly reliable in this study (Cronbach’s  $\alpha = 0.91$ ).

#### 21 2.6.6 Action and coping planning

1 Four items were used to measure action planning: “I have made a detailed plan regarding  
2 when / where / how often /how to take medication. Another four items were used to measure  
3 coping planning. Patients were provided withthe stem: “I have made a detailed plan regarding...”  
4 followed by four different endings: “...what to do if something interferes”; “...what to do if I  
5 forgot it”; “...how to motivate myself if I don’t feel like it”; “...how to prevent being distracted”  
6 [26].All items were rated on a 5-point Likert-type scale (1: completely disagree to 5: completely  
7 agree) and both the measures of action planning (Cronbach’s  $\alpha=0.93$ ) and coping planning  
8 (Cronbach’s  $\alpha=0.91$ ) proved internally consistent.

#### 9 2.6.7 Perceived behavioral control

10 Perceived behavioral control (PBC)was measured with four items, to which patients  
11 responded on5-point Likert-type scales. Items included: “For me to take regular medication in  
12 the future is...” (1: difficult to 5: easy) and “It is up to me to take regular medication...”(1:  
13 strongly disagree to 5: strongly agree) [26].The measure of PBC proved internally consistent in  
14 this study (Cronbach’s  $\alpha=0.93$ ).

#### 15 2.6.8 Self-monitoring

16 Self-monitoring was measured using three items on a scale that ranged from 1 (strongly  
17 disagree) to 5 (strongly agree). Each item consisted of a main sentence: “During the last month, I  
18 have consistently monitored...” with ending variations being: (a) “...when to take  
19 medications”,(b)“...how often to take medications”, and (c)“...how to take medications”  
20 [27].The internal consistency of self-monitoringin the present study was acceptable (Cronbach’s  
21  $\alpha=0.82$ ).

#### 22 2.6.9 Beliefs about medicines

1 Patients' beliefs about medication were measured using the Beliefs about Medicines  
2 Questionnaire (BMQ). Although the BMQ has specific and general sections, only the specific  
3 section, which is thought to be associated with adherence, was used in the present study [26]. The  
4 BMQ-specific reflects beliefs in two domains— necessity and concerns – and patients are asked  
5 to respond to statements reflecting each (e.g., “My health in the future will depend on my  
6 medication” [necessity] and “My medication disrupts my life” [concerns]) on a 5-point Likert-  
7 type scale (from 1: strongly disagree to 5: strongly agree). Scores on each domain can range  
8 from 5 and 25 with higher scores representing more worry about taking medicine. A study with an  
9 Iranian sample with diabetes used the Persian version of BMQ, and showed  
10 satisfactory psychometric properties [29]. The internal consistency of the BMQ-Necessity and  
11 BMQ-Concerns in the present study were Cronbach's  $\alpha = 0.83$  and Cronbach's  $\alpha = 0.85$ ,  
12 respectively.

#### 13 2.6.10 Brief Illness Perception Questionnaire

14 The Brief Illness Perception Questionnaire (BIPQ) consists of 9 items that assess illness  
15 perceptions in the following areas: Identity, consequences, timeline, personal control, treatment  
16 control, concern, understanding, illness comprehensibility, and emotional representations [30].  
17 Each item is rated on an 11-point Likert scale, where a higher score represents a higher level of  
18 illness perception. We used the total score (i.e., summing responses across each of the 9 items),  
19 which represents the degree to which the illness is perceived as threatening or benign [30]. The  
20 internal consistency of the BIPQ in the present study was acceptable (Cronbach's  $\alpha = 0.86$ ).

#### 21 2.6.11 Health related quality of life: Short-Form 36

1           The Health related quality of life: Short-Form 36 (SF-36) includes 36 items, measuring  
2 both physical (PCS; sample item: “In general, would you say your health is...”) and mental  
3 (MCS; sample item: “Have you felt calm and peaceful?”) health. The scores were converted into  
4 a 0-100 scale, with higher scores indicating better QoL [37,38]. The SF-36 has been translated  
5 into Persian and has been validated in a sample of Iranian hemodialysis patients showing  
6 satisfactory psychometric properties [39]. The internal consistencies of SF-36 subscales in the  
7 present study were acceptable and ranged from Cronbach’s  $\alpha = 0.74$  to Cronbach’s  $\alpha = 0.93$ .

## 8 *2.7 Statistical Analysis*

9           Background information, clinical characteristics, and all outcome measures are described  
10 using means and standard deviations (*SD*) for continuous variables and frequency and/or  
11 percentages (%) for categorical variables. Multilevel linear mixed models were used to  
12 investigate the efficacy of the intervention taking into account the hierarchical nature of the data  
13 (i.e., that the patients were clustered in different centers) and repeated measures (i.e., that a  
14 number of outcomes were measured at several time points). Intention to treat (ITT) analysis was  
15 used, such that outcomes among all patients allocated to the groups were analyzed, whether they  
16 completed the intervention or not. We used three levels of analysis (repeated measures as the  
17 first, patients as the second, and centers as the third levels) with a restricted iterative generalized  
18 least square (RIGLS) estimation. This RIGLS computes unbiased estimates of the random  
19 parameters. In addition, we used univariate multilevel analyses to investigate the effects of  
20 potential confounding variables including age, education, family income, and body mass index.  
21 Confounding variables with a *p* value < 0.20 were controlled for in the multivariate models. As  
22 consequence, each model was adjusted for the following potential confounding variables: age,  
23 sex, Charlson comorbidity index, and body mass index.

1 Potential mediators of the relationship between the intervention and medication  
2 adherence and between the intervention and QoL were examined using Sobel tests. Finally,  
3 survival analyses accounting for cluster effects of the hospitals were performed, with the cluster  
4 effects of centers being adjusted. All tests were two-tailed using a significance level of  $<0.05$ .  
5 Benjamini and Hochberg false discovery rate was used to adjust p-values for multiple  
6 comparisons where appropriate. Multilevel linear mixed modeling was conducted using MLwiN  
7 2.27 software. Survival analyses were performed using the survival package in R (R Core Team,  
8 2014).

### 9 **3. Results**

10 After screening a total of 462 patients, 288 patients from 12 centers were eligible to  
11 participate in the study and the centers were randomly assigned to either the TAU or the  
12 EXP groups (Figure 1). Thirty-five patients in the two groups dropped out during treatment. Table  
13 1 summarizes the baseline and clinical characteristics of the two groups. The mean age of  
14 patients in the TAU group was 75.23 ( $SD = 5.82$ ) years and 74.32 ( $SD = 5.26$ ) years for the EXP  
15 group and nearly two thirds of the patients were male (65.3% in TAU and 67.4% in EXP).

16 (Insert Table 1 here)

17 The descriptive statistics for medication adherence (including the MARS, objective  
18 pharmacy refill rate, and serum level of lipid profile), beliefs about medication, and QoL across  
19 the 18 months are reported in Table 2. Overall, patients in the EXP group showed better  
20 medication adherence after six months compared to patients in the TAU group, as indicated by  
21 the MARS (baseline:  $7.68 \pm 2.45$  in EXP and  $7.62 \pm 2.76$  in TAU; six months:  $13.67 \pm 2.80$  in EXP  
22 and  $7.69$  in TAU), pharmacy refill rate (baseline:  $62.30 \pm 16.22\%$  in EXP and  $61.41 \pm 16.30\%$  in

1 TAU; six months: 73.81±18.56% in EXP and 63.14±17.21% in TAU), HDL-C (baseline:  
2 34.54±9.89% in EXP and 34.42±9.74% in TAU; six months: 42.74±10.41% in EXP and  
3 34.18±9.38% in TAU), and LDL-C (baseline: 113.75±33.06 mg/dLin EXP and  
4 115.20±32.76mg/dL in TAU; six months: 99.26±36.75 mg/dLin EXP and 110.01±35.78  
5 mg/dLin TAU). Furthermore, medication adherence did not decrease after eighteen months in the  
6 EXP group and patients in this group reported slightly better QoL, including PCS and MCS, than  
7 patients in the TAU group after six months.

8 (Insert Table 2 here)

9 After considering multicenter and other potential confounding factors and effects, the  
10 three-level multiple linear regression models showed that patients in the EXP group had better  
11 medication adherence after six, twelve, and eighteen months compared to patients in the TAU  
12 group (see Table 3) as indicated by the MARS ( $B = 3.97$  at six months, 3.83 at twelve months,  
13 and 4.24 at eighteen months;  $p < 0.01$ ), pharmacy refill rate ( $B = 9.82\%$  at six months, 10.64% at  
14 twelve months, and 10.40% at eighteen months;  $p < 0.01$ ), total cholesterol ( $B = -7.40$  mg/dL at  
15 six months, -8.77mg/dL at twelve months, and -8.60 mg/dL at eighteen months;  $p < 0.01$ ), LDL-  
16 C ( $B = -12.45$  mg/dL at six months, -13.71 mg/dL at twelve months, and -13.59 mg/dL at  
17 eighteen months;  $p < 0.01$ ), HDL-C ( $B = 8.41$  mg/dL at six months, 8.71mg/dL at twelve  
18 months, and 8.87 mg/dL at eighteen months;  $p < 0.01$ ), and triglycerides ( $B = -16.83$  mg/dL at  
19 six months, -18.86mg/dL at twelve months, and -18.21 mg/dL at eighteen months;  $p < 0.01$ ).

20 (Insert Table 3 here)

21 About 11.1% of the patients in the TAU group and 4.2% of the patients in the EXP group  
22 had died before the end of follow-up (Figure 2). When considering the loss at follow-up and

1 drop-outs, a Gamma frailty survival model on the time of death showed that the crude hazard  
2 ratio (HR) in the EXP compared to the TAU group was 0.36 (95% CI: 0.14 to 0.91,  $p=0.036$ ).  
3 After adjusting for the effects of age, sex, and number of diseased vessels, this hazard  
4 ratio continued to show a lower rate of death in the EXP group compared to the TAU group  
5 (adjusted HR = 0.38, 95% CI: 0.15 to 0.97,  $p=0.044$ ).

6 (Insert Figure 2 here)

7 Electronic Supplementary Material Tables S3 and S4 show the effects of intervention on  
8 intentions, perceived behavioral automaticity, self-monitoring, action and coping planning,  
9 beliefs about medicines, illness perceptions, and QoL. Patients in the EXP group reported better  
10 QoL than did patients in the TAU group after eighteen months ( $B = 1.77$  and  $p = 0.02$  for PCS;  $B$   
11  $= 1.68$  and  $p = 0.04$  for MCS). The interactions between group and time tended to be significant  
12 such that patients in the EXP group (relative to those in the TAU group) tended to have more  
13 positive beliefs about taking medication, reported stronger intentions to take medication, and had  
14 perceptions of increased control over medication use. They were also more likely to have formed  
15 action and coping plans to support medication adherence and self-monitor their medication use;  
16 and reported that taking medication had become relatively automatic for them. Social cognitions  
17 and self-regulatory processes all mediated the effects of the intervention on medication adherence  
18 (See Electronic Supplementary Material Table S5). An additional mediation analysis showed that  
19 medication adherence mediated the effects of the intervention on outcomes such as QoL and  
20 survival rates.

#### 21 **4. Discussion**

1           The present findings suggest that a multifaceted intervention with three components  
2 (psycho-education, motivational interviewing [or MI], and SMS reminders) can improve  
3 medication adherence, QoL, and mortality rates among older patients undergoing CABG surgery.  
4 Specifically, patients who received the multifaceted intervention program (i.e., patients in the  
5 EXP group) showed increased MARS scores and higher pharmacy refill rates six- and eighteen-  
6 months post-surgery. In contrast, MARS scores and pharmacy refill rates did not increase among  
7 patients who received conventional treatment and information (i.e., among patients in the TAU  
8 group). Other measures used to objectively assess medication adherence (including total  
9 cholesterol, HDL-C, TDL-C, and triglycerides) supported these conclusions and showed that  
10 patients in the EXP group were in better physiological health than were patients in the TAU  
11 group in the six to eighteen month after the intervention. In addition to medication adherence,  
12 patients who received the multifaceted intervention also reported better QoL and had a higher life  
13 expectancy compared to patients in the TAU group.

14           Previous studies have also reported beneficial effects of MI on medication adherence,  
15 albeit among different samples than those studied here, such as older people (aged 53-73 years)  
16 [40] and people with epilepsy [26]. Furthermore, previous studies attest to the efficacy of  
17 combining medical counseling with planning for promoting medication adherence among  
18 patients undergoing CABG [18]. However, although a number of studies have shown the  
19 beneficial effects of such interventions, the current study combined the intervention components  
20 and, perhaps as a result, seemed to be even more effective in increasing medication adherence in  
21 older patients ( $d = 2.13$  in the present research;  $d = 0.30$  to  $1.02$  in previous studies [18, 26, 40]).  
22 In short, the present findings support the effects of similar interventions conducted in

1 otherpopulations [21,26,40],such as patients with epilepsy, and show that MI andcounseling can  
2 effectively enhance medication adherence in older individuals [41-44].

3         The present research also builds on previous studies by showing that a multifaceted  
4 intervention not only increases medication adherence but, as a result, can improveQoL and  
5 increaselife expectancy in olderpatients receiving CABG. Interestingly, theeffects on QoLwere  
6 only observed at eighteenmonths post-surgery,compared to the changes in medication  
7 adherence,which were observed at sixmonths after surgery.However, this is to be expected given  
8 that both previous and the present research show that QoL is influenced by medication adherence  
9 and thus takes time to change [45-47]. In terms of the effects of the intervention on survival  
10 rates, previous studies have demonstrated that psycho-education and MI can reduce mortality in  
11 patients with different diseases [48-50],including coronary heart disease patients. Our results  
12 echo suchfindings andfurthersupport the idea that the combination of psycho-education and MI  
13 can improve survival rates through medication adherence.

#### 14 *4.1 Strengths and limitations*

15         There are several strengths to our study. First, an eighteen-month follow-up without  
16 further intervention was used to investigate the long-term effects of the intervention on  
17 medication adherence and a number of health-related outcomes in patients undergoing CABG.  
18 As such, the findingsprovide important insights for clinicians in regards to the long-term effects  
19 of such interventions, not only on medication adherence but also on patients' overall health and  
20 QoL. Second, the present study included a variety of objective outcome measures to assess  
21 medication adherence and did not rely on self-report alone; therefore minimizing social  
22 desirability and reporting biases. Third, robust statistical analyses were conducted that accounted

1 for potential confounding variables. By using multilevel linear mixed models, shared variance  
2 (e.g., accruing from recruiting patients from the same hospital) were minimized [51].

3           However, there are also some limitations that need to be considered when interpreting the  
4 findings. First, the effects of the intervention may not be generalizable to Western countries and  
5 cultures, particularly as the present research incorporated an element of family engagement.  
6 Unlike Western cultures that tend to emphasize individualism [52], family plays a crucial role for  
7 people with a Middle Eastern cultural background [53]. Second, patients with serious and/or  
8 specific health conditions (e.g., suffering from cognitive impairment or from a severe kidney  
9 disease) were excluded from the present research. Therefore, the findings may not generalize to  
10 other patients undergoing CABG who have additional health problems. Further studies are  
11 therefore warranted to investigate the effects of similar interventions in such groups. Third,  
12 because the present research developed and implemented a multifaceted intervention, the  
13 individual effects of each component cannot be separated. In other words, it is unclear which of  
14 the three components (psycho-education, MI, and SMS reminders) were effective in promoting  
15 medication adherence, and could potentially be used as individual components, or whether the  
16 outcomes were dependent on a joint effect. The larger effect size reported in the present research,  
17 relative to other studies that tested the effects of interventions that only incorporated one or some  
18 of these components suggest that the multifaceted intervention was particularly beneficial, but  
19 factorial designs that directly compare interventions with different components are needed  
20 corroborate this assertion. Lastly, the intervention used in the present research was relatively  
21 intensive and required a substantial time commitment from both the patients and those delivering  
22 the intervention. Although the findings were promising, further research could evaluate the cost-

1 effectiveness of the intervention relative to, for example, less complex interventions. Again, a  
2 factorial design would appear to be appropriate for this purpose.

### 3 **5. Conclusion**

4 In conclusion, the findings of the present study suggest that a multifaceted intervention  
5 consisting of psycho-educational, MI, and SMS reminders can promote medication adherence in  
6 older patients undergoing CABG, and that these effects are maintained eighteen months post-  
7 surgery. The increase in medication adherence as a function of the intervention also improved  
8 other health-related outcomes. Clinicians may therefore consider using multifaceted  
9 interventions to improve health and survival rates in older patients undergoing CABG.

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## **Figure Legends**

**Fig. 1:**Flow diagram for random assignment of patients in the study.MMSE = Mini Mental Status Examination; CABG = coronary artery bypass graft

**Fig. 2:** Survival rates for patients in multifaceted intervention group (EXP) and those in treatment as usual group (TAU).

## **Supplementary Materials Legends**

**Electronic Supplementary Material TableS1:**The procedure for Motivational interviewing (MI) sessions.

**Electronic Supplementary Material TableS2:** MITI global measures, behavior counts, and summary scores.

**Electronic Supplementary Material TableS3:** Three-level multiple linear regression models predicting intention, perceived behavioral control, behavioral automaticity, self-monitoring, action planning and coping planning.

**Electronic Supplementary Material TableS4:** Three-level multiple linear regression models predicting beliefs about medicines, illness perceptions, and quality of life (QoL).

**Electronic Supplementary Material TableS5:** Direct and mediated effects of group on medication adherence, quality of life (QoL) and survival rates.

## Tables

**Table 1**

*Comparison of clinical characteristics between the intervention (EXP) and treatment as usual (TAU) groups at baseline*

|  | Treatment as usual<br>(n = 144) | Intervention<br>(n = 144) |
|--|---------------------------------|---------------------------|
| Age, years; median (IQR)                               | 76 (70-80)                      | 75 (69-79)                |
| Years of education; median (IQR)                       | 4 (1-12)                        | 4 (1-12)                  |
| Household income, rials <sup>a</sup> ; median (IQR)    | 848.65 (453.40-1295.44)         | 893.06 (942.88-1286.88)   |
| Body mass index, kg/m <sup>2</sup> ; mean±SD           | 28.84±5.57                      | 28.64±4.03                |
| Marital status; n (%)                                  |                                 |                           |
| Single   | 4 (2.8%)                        | 6 (4.2%)                  |
| Married  | 90 (62.5%)                      | 92 (63.9%)                |
| Divorced/widowed                                       | 50 (34.7%)                      | 46 (31.9%)                |
| Sex; n (%)   |                                 |                           |
| Male   | 94 (65.3%)                      | 97 (67.4%)                |
| Female   | 50 (34.7%)                      | 47 (32.6%)                |
| Ejection fraction; mean±SD                             | 45.23±6.12                      | 44.82±7.02                |
| Cross clamp time, minutes; mean±SD                     | 52.42±25.81                     | 54.21±27.62               |
| Cardiopulmonary bypass duration time, minutes; mean±SD | 96.68±39.42                     | 97.92±40.35               |
| Cardiac risk factors; n (%)                            |                                 |                           |
| Diabetes mellitus                                      | 55 (38.2%)                      | 52 (36.1%)                |
| Hypertension   | 107 (74.3%)                     | 110 (76.4%)               |
| Dyslipidemia   | 61 (42.4%)                      | 52 (36.1%)                |
| Myocardial infarction                                  | 86 (59.7%)                      | 90 (62.5%)                |
| Chronic lung disease                                   | 17 (11.8%)                      | 15 (10.4%)                |
| Prior cardiac surgery; n (%)                           | 12 (8.3%)                       | 9 (6.2%)                  |
| Current smoker; n (%)                                  | 21 (14.6%)                      | 18 (12.5%)                |
| No. of major vessels/branches bypassed; n (%)          |                                 |                           |
| 1 vessel   | 21 (14.6%)                      | 14 (9.7%)                 |
| 2 vessels  | 49 (34.0%)                      | 46 (31.9%)                |

|  |             |             |
|--|-------------|-------------|
| 3 vessels                                | 74 (51.4%)  | 84 (58.3%)  |
| CCSC; n (%)                              |             |             |
| I  | 12 (8.3%)   | 10 (6.9%)   |
| II                                       | 24 (16.7%)  | 15 (10.4%)  |
| III                                      | 48 (33.3%)  | 51 (35.4%)  |
| IV                                       | 60 (41.7%)  | 68 (47.2%)  |
| Charlson comorbidity index; n (%)        |             |             |
| 0  | 40 (27.8%)  | 36 (25.0%)  |
| 1-3                                      | 79 (54.9%)  | 81 (56.2%)  |
| ≥4                                       | 25 (17.4%)  | 27 (18.8%)  |
| Medications; n (%)                       |             |             |
| Aspirin                                  | 135 (93.8%) | 132 (91.7%) |
| Beta blockers                            | 115 (79.9%) | 122 (84.7%) |
| Angiotensin converting enzyme inhibitors | 98 (68.1%)  | 90 (62.5%)  |
| Lipid lowering                           | 105 (72.9%) | 109 (75.7%) |
| Number of centers                        | 6           | 6           |
| Number of patients in each center        | 24          | 24          |

*Note.* IQR = interquartile range, SD = standard deviation, CCSC: Canadian Cardiovascular Society Classification

<sup>a</sup> 3,500 rials = US \$1 (April 2016)

**Table 2**

*Descriptive statistics for all outcome measures across time in the intervention group (EXP) and the treatment as usual (TAU) group*

| Variable (normal range)                         | Group | Mean (SD)      |                |                |                |
|---|-------|----------------|----------------|----------------|----------------|
|   |       | Baseline       | Month 6        | Month 12       | Month 18       |
| BMQ-Necessity (5-25)                            | TAU   | 14.62 (3.22)   | 14.54 (3.30)   | 14.41 (2.42)   | 14.40 (3.07)   |
|   | EXP   | 14.37 (2.24)   | 18.69 (2.49)   | 18.64 (2.48)   | 18.53 (2.57)   |
| BMQ-Concerns (5-25)                             | TAU   | 13.23 (4.05)   | 13.27 (4.0)    | 13.31 (4.27)   | 13.33 (4.12)   |
|   | EXP   | 12.92 (3.29)   | 7.81 (3.22)    | 6.02 (3.09)    | 4.78 (3.01)    |
| Perceived behavioral control (1-5)              | TAU   | 2.50 (0.93)    | 2.43 (0.98)    | 2.41 (0.99)    | 2.40 (0.93)    |
|   | EXP   | 2.49 (0.89)    | 3.00 (1.10)    | 2.98 (1.01)    | 2.99 (1.12)    |
| Intention (1-5)                                 | TAU   | 2.67 (0.65)    | 2.73 (0.69)    | 2.70 (0.70)    | 2.69 (0.69)    |
|   | EXP   | 2.72 (0.74)    | 3.44 (1.03)    | 3.41 (1.01)    | 3.42 (1.13)    |
| Self-monitoring (1-5)                           | TAU   | 1.94 (0.40)    | 1.92 (0.51)    | 1.96 (0.75)    | 1.91 (0.82)    |
|   | EXP   | 2.06 (0.54)    | 2.65 (1.00)    | 2.67 (1.04)    | 2.66 (1.02)    |
| Action planning (1-5)                           | TAU   | 1.93 (0.58)    | 1.190 (0.52)   | 1.88 (0.50)    | 1.86 (0.61)    |
|   | EXP   | 1.88 (0.57)    | 2.73 (1.13)    | 2.71 (1.30)    | 2.74 (1.29)    |
| Coping planning (1-5)                           | TAU   | 1.68 (0.51)    | 1.64 (0.56)    | 1.61 (0.52)    | 1.62 (0.60)    |
|   | EXP   | 1.64 (0.54)    | 2.49 (1.11)    | 2.48 (1.19)    | 2.50 (1.26)    |
| Self-report Behavioral Automaticity Index (1-5) | TAU   | 1.91 (0.80)    | 1.87 (0.82)    | 1.86 (0.99)    | 1.83 (1.01)    |
|   | EXP   | 1.86 (0.87)    | 2.39 (0.94)    | 2.40 (0.98)    | 2.40 (1.14)    |
| MARS (5-25)                                     | TAU   | 7.62 (2.76)    | 7.69 (2.70)    | 7.71 (2.79)    | 7.63 (2.88)    |
|   | EXP   | 7.68 (2.45)    | 13.67 (2.80)   | 13.61 (2.82)   | 13.70 (2.75)   |
| Illness perception (0-90)                       | TAU   | 36.43 (11.67)  | 35.57 (11.66)  | 36.63 (11.54)  | 36.67 (11.47)  |
|   | EXP   | 37.07 (11.78)  | 33.93 (12.53)  | 33.80 (12.72)  | 33.46 (10.17)  |
| Pharmacy refill rate (0-100)                    | TAU   | 61.41 (16.30)  | 63.14 (17.21)  | 62.03 (18.77)  | 62.03 (18.77)  |
|   | EXP   | 62.30 (16.22)  | 73.81 (18.56)  | 73.48 (18.44)  | 73.24 (15.33)  |
| Quality of life: PCS (0-100)                    | TAU   | 46.07 (11.66)  | 48.23 (11.70)  | 47.88 (12.05)  | 47.08 (10.10)  |
|   | EXP   | 46.88 (10.68)  | 50.04 (12.41)  | 50.29 (12.69)  | 49.93 (9.65)   |
| Quality of life: MCS (0-100)                    | TAU   | 43.42 (12.76)  | 46.77 (11.41)  | 46.82 (11.33)  | 46.48 (10.35)  |
|   | EXP   | 44.92 (10.14)  | 49.39 (12.60)  | 49.76 (10.93)  | 49.69 (11.84)  |
| Total cholesterol concentration (mg/dL)         | TAU   | 182.90 (38.69) | 180.76 (33.89) | 180.71 (33.51) | 180.53 (35.81) |
|   | EXP   | 181.85 (39.00) | 172.32 (40.71) | 170.92 (32.12) | 171 (32.00)    |

|                       |     |                |                |                |                |
|-----------------------|-----|----------------|----------------|----------------|----------------|
| HDL-C (mg/dL)         | TAU | 34.42 (9.74)   | 34.18 (9.38)   | 33.88 (10.52)  | 33.52 (8.16)   |
|                       | EXP | 34.54 (9.89)   | 42.74 (10.41)  | 42.63 (11.29)  | 42.41 (9.31)   |
| LDL-C (mg/dL)         | TAU | 115.20 (32.76) | 110.01 (35.78) | 113.32 (35.57) | 114.51 (35.65) |
|                       | EXP | 113.75 (33.06) | 99.26 (36.75)  | 98.26 (27.32)  | 98.69 (27.41)  |
| Triglycerides (mg/dL) | TAU | 166.37 (66.60) | 167.07 (65.99) | 167.52 (55.43) | 165.27 (65.21) |
|                       | EXP | 167.61 (69.38) | 151.55 (66.55) | 150.13 (58.05) | 149.33 (68.90) |

*Note.* BMQ= Beliefs about Medicines Questionnaire; MARS= Medication Adherence Rating Scale; PCS= Physical Component Summary; MCS= Mental Component Summary; HDL-C = high-density lipoprotein cholesterol; LDL-C = low-density lipoprotein cholesterol

**Table 3***Three-level multiple linear regression models predicting medication adherence*

| Variable                         | MARS            |                 | Pharmacy refill rate |                 | Total cholesterol |                 | LDL-C            |                 | HDL-C           |                 | Triglycerides     |                 |
|----------------------------------|-----------------|-----------------|----------------------|-----------------|-------------------|-----------------|------------------|-----------------|-----------------|-----------------|-------------------|-----------------|
|                                  | B (SE)          | <i>p</i> value  | B (SE)               | <i>p</i> value  | B (SE)            | <i>p</i> value  | B (SE)           | <i>p</i> value  | B (SE)          | <i>p</i> value  | B (SE)            | <i>p</i> value  |
| Group (Ref: TAU)                 | 0.30<br>(0.66)  | 0.36            | 2.37<br>(2.62)       | 0.26            | -3.30<br>(7.25)   | 0.36            | -3.01<br>(5.94)  | 0.35            | 15.52<br>(5.64) | <b>0.01</b>     | -4.54<br>(9.73)   | 0.36            |
| Time (Ref: baseline)             |                 |                 |                      |                 |                   |                 |                  |                 |                 |                 |                   |                 |
| 6 months                         | 0.38<br>(0.16)  | <b>0.02</b>     | 1.81<br>(0.66)       | <b>0.01</b>     | -2.21<br>(1.34)   | 0.10            | -2.22<br>(1.29)  | 0.09            | 0.12<br>(0.43)  | 0.38            | -0.61<br>(1.79)   | 0.38            |
| 12 months                        | 0.30<br>(0.14)  | <b>0.045</b>    | 0.66<br>(0.46)       | 0.14            | -2.26<br>(1.60)   | 0.15            | -1.97<br>(1.31)  | 0.13            | 0.54<br>(0.40)  | 0.16            | -1.21<br>(1.94)   | 0.33            |
| 18 months                        | 0.05<br>(0.16)  | 0.38            | 0.91<br>(0.78)       | 0.20            | -2.45<br>(1.60)   | 0.12            | -1.79<br>(1.30)  | 0.16            | 0.92<br>(0.31)  | <b>0.01</b>     | -1.38<br>(1.86)   | 0.30            |
| Group×time                       |                 |                 |                      |                 |                   |                 |                  |                 |                 |                 |                   |                 |
| EXP vs. TAU at 6 months          | 3.97<br>(0.22)  | <b>&lt;0.01</b> | 9.82<br>(0.93)       | <b>&lt;0.01</b> | -7.40<br>(1.88)   | <b>&lt;0.01</b> | -12.45<br>(1.80) | <b>&lt;0.01</b> | 8.41<br>(0.60)  | <b>&lt;0.01</b> | -16.83<br>(2.52)  | <b>&lt;0.01</b> |
| EXP vs. TAU at 12 months         | 3.83<br>(0.23)  | <b>&lt;0.01</b> | 10.64<br>(0.95)      | <b>&lt;0.01</b> | -8.77<br>(1.92)   | <b>&lt;0.01</b> | -13.71<br>(1.93) | <b>&lt;0.01</b> | 8.71<br>(0.73)  | <b>&lt;0.01</b> | -18.86<br>(2.80)  | <b>&lt;0.01</b> |
| EXP vs. TAU at 18 months         | 4.24<br>(0.26)  | <b>&lt;0.01</b> | 10.40<br>(0.98)      | <b>&lt;0.01</b> | -8.60<br>(1.99)   | <b>&lt;0.01</b> | -13.59<br>(1.78) | <b>&lt;0.01</b> | 8.87<br>(0.60)  | <b>&lt;0.01</b> | -18.21<br>(2.70)  | <b>&lt;0.01</b> |
| Age                              | -0.19<br>(0.14) | 0.17            | -0.13<br>(0.13)      | 0.25            | 1.40<br>(1.41)    | 0.24            | 0.61<br>(1.23)   | 0.35            | -0.92<br>(0.35) | <b>0.01</b>     | 0.46<br>(1.91)    | 0.39            |
| Sex (Ref: females)               | 0.33<br>(0.47)  | 0.31            | -8.32<br>(2.58)      | <b>&lt;0.01</b> | 2.52<br>(1.63)    | 0.12            | 5.16<br>(3.68)   | 0.15            | 0.12<br>(0.10)  | 0.20            | 0.62<br>(0.86)    | 0.31            |
| Charlson comorbidity index       | -0.92<br>(0.65) | 0.15            | -1.69<br>(0.75)      | <b>0.03</b>     | 9.59<br>(7.22)    | 0.17            | -11.85<br>(6.91) | 0.09            | -6.64<br>(1.49) | <b>&lt;0.01</b> | 2.28<br>(0.98)    | <b>0.03</b>     |
| Body mass index                  | -0.06<br>(0.04) | 0.16            | -0.31<br>(0.61)      | 0.35            | 3.26<br>(1.26)    | <b>0.01</b>     | 1.76<br>(4.01)   | 0.36            | -0.35<br>(0.19) | 0.07            | 8.37<br>(0.91)    | <b>&lt;0.01</b> |
| Intercept                        | 11.14<br>(2.32) | <b>&lt;0.01</b> | 55.19<br>(8.66)      | <b>&lt;0.01</b> | 164.84<br>(23.06) | <b>&lt;0.01</b> | 11.02<br>(2.26)  | <b>&lt;0.01</b> | 15.21<br>(5.64) | <b>0.01</b>     | 187.83<br>(45.75) | <b>&lt;0.01</b> |
| $\hat{\sigma}_{st}^2$ (patients) | 14.97<br>(0.96) | <b>&lt;0.01</b> | 103.90<br>(13.19)    | <b>&lt;0.01</b> | 46.70<br>(9.18)   | <b>&lt;0.01</b> | 53.59<br>(8.41)  | <b>&lt;0.01</b> | 93.12<br>(5.98) | <b>&lt;0.01</b> | 46.91<br>(15.61)  | <b>&lt;0.01</b> |

|                                 |                |                 |                  |             |                 |                 |                 |                 |                |             |                  |             |
|---------------------------------|----------------|-----------------|------------------|-------------|-----------------|-----------------|-----------------|-----------------|----------------|-------------|------------------|-------------|
| $\hat{\sigma}_{sc}^2$ (centers) | 3.52<br>(0.12) | <b>&lt;0.01</b> | 32.08<br>(11.64) | <b>0.01</b> | 26.23<br>(8.58) | <b>&lt;0.01</b> | 37.21<br>(6.81) | <b>&lt;0.01</b> | 9.49<br>(3.88) | <b>0.02</b> | 24.92<br>(16.10) | <b>0.12</b> |
|---------------------------------|----------------|-----------------|------------------|-------------|-----------------|-----------------|-----------------|-----------------|----------------|-------------|------------------|-------------|

*Note.* Ref. = reference group for comparison; TAU=treatment as usual group; EXP= intervention group; MARS= Medication Adherence Rating Scale; LDL-C= low-density lipoprotein cholesterol; HDL-C= high-density lipoprotein cholesterol;  $\hat{\sigma}_{st}^2$  = the variance at patient level;  $\hat{\sigma}_{sc}^2$  = the variance at center level; SE = standard error.  

*p* values < 0.05 are in **bold**

**Electronic Supplementary Material Table S1. The procedure for motivational interviewing (MI) sessions.**

|                |  |
|----------------|--|
| First session  | The facilitator introduced himself/herself to the patients and assured them that the conversations would be kept private. The facilitators then elicited problems that the patients faced by asking questions such as “How do you describe your problem?”; “What do you think has caused your problem?”; “What do you fear most about your illness?”. Patients had the chance to describe their condition(s) and talk about their concerns with the facilitator. The facilitators further encouraged the patients to discuss any concerns that may interfere with their willingness and/or motivation to adhere to their medication. Facilitators also provided specific information on the medication that patients were asked to take (e.g., dosage and timing, adverse effects, contradictions, and treatment process). |
| Second session | The patients were encouraged to talk about their feelings regarding their condition and medication adherence. Open ended questions, including “How have things gone this week?” and “How have you been feeling?” were used to assess the patient’s feelings during the past week (e.g., feelings about new stressors, changes in condition, etc.). Facilitators also inquired about the patients’ adherence and their reaction to the medication to obtain an overall impression of the emotional experiences of the patients.   |
| Third session  | The third session focused on helping the patients to evaluate the perceived costs and benefits of medication adherence. The goal was to identify the positive and negative consequences of taking medication, (e.g., “What do you see as the positive and negative consequences of taking medication?” and “What are some of the long-term and short-term effects of regularly taking your medication?”). Alternative courses of action were also considered during this session. For example, patients were encouraged to think about what the future would look like if they adhered to their medication. Questions to illicit these thoughts were e.g. “If you are successful in regularly taking medicine, how could things be different in the future?”, or “What will be the impact on your quality of life?”.       |
| Fourth session | The fourth session focused on the patients’ values and goals. The facilitators assisted the patients in recognizing and attaining their values and goals by encouraging them to engage in confidence talk to increase their motivation for medication adherence.   |
| Fifth session  | The facilitators helped the patients to review their progress, reinforce their motivation and recognize their success in adherence. Following this, the patients were advised to keep a daily diary and to note the frequency of the medications that they have to take. The facilitators also encouraged the patients to form specific plans and identify strategies that would help them to take their medication (i.e., action planning). They were then asked to imagine themselves in this specific situation and evaluate how their strategies might help them to remember to take their medication. The patients wrote their plans on a form and were encouraged to sign it and consider it as a contract.  |

**Electronic Supplementary Table S2. MITI global measures, behavior counts and summary scores.**

| Measurers                         | Mean $\pm$ SD<br>( <i>n</i> =140) | Minimum | Maximum | Beginning<br>proficiency | Competency |
|-----------------------------------|-----------------------------------|---------|---------|--------------------------|------------|
| <b>Global measures</b>            |                                   |         |         |                          |            |
| Evocation                         | 4.12 (0.72)                       | 1       | 5       |                          |            |
| Collaboration                     | 3.61 (0.51)                       | 1       | 5       |                          |            |
| Autonomy/support                  | 3.98 (0.58)                       | 1       | 5       |                          |            |
| Direction                         | 4.23 (0.67)                       | 1       | 5       |                          |            |
| Empathy                           | 4.59(0.71)                        | 1       | 5       |                          |            |
| <b>Behavior counts</b>            |                                   |         |         |                          |            |
| Giving information                | 0.65 (0.39)                       | 0       | 6       |                          |            |
| MI-Adherent                       | 7.93 (3.12)                       | 0       | 25      |                          |            |
| MI-Non-adherent                   | 1.02 (0.93)                       | 0       | 5       |                          |            |
| Closed questions                  | 12.39 (8.65)                      | 0       | 38      |                          |            |
| Open questions                    | 18.81 (4.43)                      | 0       | 41      |                          |            |
| Simple reflections                | 16.28 (9.10)                      | 0       | 61      |                          |            |
| Complex reflections               | 12.02 (6.12)                      | 1       | 35      |                          |            |
| <b>Summary scores</b>             |                                   |         |         |                          |            |
| Global spirit rating              | 3.93(0.52)                        | 1.97    | 4.95    | 3.5                      | 4          |
| Percentage of complex reflections | 47.69 (12.88)                     | 10.00   | 100.00  | 40%                      | 50%        |
| Percentage of open questions      | 62.57(16.34)                      | 25.39   | 100.00  | 50%                      | 70%        |
| Reflection-to-question ratio      | 1.05 (2.13)                       | 0.31    | 16.35   | 1                        | 2          |
| Percentage MI-Adherent            | 93.12(8.20)                       | 61.08   | 100.00  | 90%                      | 100%       |

*Note.* MITI= Motivational Interviewing Treatment Integrity; MI=motivational interviewing

**Electronic Supplementary Material Table S3. Three-level multiple linear regression models predicting intention, perceived behavioral control, behavioral automaticity, self-monitoring, action planning and coping planning.**

| Variable                 | INT            |                 | PBC            |                 | SRBAI          |                 | SM             |                 | AP             |                 | CP             |                 |
|--------------------------|----------------|-----------------|----------------|-----------------|----------------|-----------------|----------------|-----------------|----------------|-----------------|----------------|-----------------|
|                          | B (SE)         | p value         | B (SE)         | P value         | B (SE)         | P value         | B (SE)         | P value         | B (SE)         | P value         | B (SE)         | P value         |
| Group (Ref: TAU)         | 0.06<br>(0.12) | 0.35            | 0.12<br>(0.18) | 0.32            | 0.02<br>(0.08) | 0.38            | 0.09<br>(0.15) | 0.34            | 0.14<br>(0.13) | 0.21            | 0.14<br>(0.12) | 0.20            |
| Time (Ref: baseline)     |                |                 |                |                 |                |                 |                |                 |                |                 |                |                 |
| 6 months                 | 0.06<br>(0.04) | 0.13            | 0.06<br>(0.04) | 0.11            | 0.04<br>(0.04) | 0.22            | 0.02<br>(0.02) | 0.24            | 0.01<br>(0.03) | 0.37            | 0.02<br>(0.05) | 0.37            |
| 12 months                | 0.03<br>(0.03) | 0.30            | 0.08<br>(0.02) | <b>&lt;0.01</b> | 0.04<br>(0.03) | 0.15            | 0.06<br>(0.05) | 0.21            | 0.04<br>(0.05) | 0.28            | 0.05<br>(0.04) | 0.21            |
| 18 months                | 0.02<br>(0.03) | 0.34            | 0.10<br>(0.04) | <b>0.01</b>     | 0.09<br>(0.04) | 0.051           | 0.08<br>(0.04) | <b>0.049</b>    | 0.06<br>(0.05) | 0.18            | 0.07<br>(0.08) | 0.28            |
| <b>group × time</b>      |                |                 |                |                 |                |                 |                |                 |                |                 |                |                 |
| EXP vs. TAU at 6 months  | 0.61<br>(0.05) | <b>&lt;0.01</b> | 0.58<br>(0.05) | <b>&lt;0.01</b> | 0.57<br>(0.05) | <b>&lt;0.01</b> | 0.54<br>(0.06) | <b>&lt;0.01</b> | 0.84<br>(0.06) | <b>&lt;0.01</b> | 0.85<br>(0.07) | <b>&lt;0.01</b> |
| EXP vs. TAU at 12 months | 0.61<br>(0.06) | <b>&lt;0.01</b> | 0.57<br>(0.06) | <b>&lt;0.01</b> | 0.47<br>(0.06) | <b>&lt;0.01</b> | 0.54<br>(0.06) | <b>&lt;0.01</b> | 0.87<br>(0.07) | <b>&lt;0.01</b> | 0.87<br>(0.06) | <b>&lt;0.01</b> |
| EXP vs. TAU at 18 months | 0.63<br>(0.05) | <b>&lt;0.01</b> | 0.61<br>(0.06) | <b>&lt;0.01</b> | 0.50<br>(0.06) | <b>&lt;0.01</b> | 0.58<br>(0.06) | <b>&lt;0.01</b> | 0.93<br>(0.07) | <b>&lt;0.01</b> | 0.95<br>(0.08) | <b>&lt;0.01</b> |

|                                  |                 |                 |                  |                 |                 |                 |                 |                 |                 |                 |                 |                 |
|----------------------------------|-----------------|-----------------|------------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|
| Age                              | -0.03<br>(0.02) | <b>&lt;0.01</b> | 0.01<br>(0.03)   | 0.38            | 0.03<br>(0.03)  | 0.25            | -0.04<br>(0.02) | 0.07            | -0.02<br>(0.03) | 0.28            | -0.03<br>(0.03) | 0.27            |
| Sex (Ref: females)               | -0.11<br>(0.09) | 0.17            | 0.21<br>(0.20)   | 0.23            | 0.03<br>(0.02)  | 0.14            | -0.28<br>(0.15) | 0.07            | -0.17<br>(0.10) | 0.09            | -0.16<br>(0.09) | 0.09            |
| Charlson comorbidity index       | -0.35<br>(0.12) | <b>&lt;0.01</b> | -0.30<br>(0.08)  | <b>&lt;0.01</b> | -0.09<br>(0.02) | <b>&lt;0.01</b> | -0.20<br>(0.10) | 0.06            | -0.47<br>(0.13) | <b>&lt;0.01</b> | -0.46<br>(0.14) | <b>&lt;0.01</b> |
| Body mass index                  | 0.05<br>(0.08)  | 0.34            | -0.054<br>(0.10) | 0.59            | -0.03<br>(0.05) | 0.34            | -0.01<br>(0.07) | 0.39            | -0.05<br>(0.09) | 0.33            | -0.05<br>(0.93) | 0.40            |
| Intercept                        | 3.27<br>(0.42)  | <b>&lt;0.01</b> | 2.49<br>(0.52)   | <b>&lt;0.01</b> | 2.20<br>(0.49)  | <b>&lt;0.01</b> | 2.86<br>(0.38)  | <b>&lt;0.01</b> | 2.60<br>(0.47)  | <b>&lt;0.01</b> | 2.37<br>(0.49)  | <b>&lt;0.01</b> |
| $\hat{\sigma}_{st}^2$ (patients) | 0.50<br>(0.03)  | <b>&lt;0.01</b> | 0.67<br>(0.04)   | <b>&lt;0.01</b> | 0.61<br>(0.04)  | <b>&lt;0.01</b> | 0.30<br>(0.02)  | <b>&lt;0.01</b> | 0.58<br>(0.04)  | <b>&lt;0.01</b> | 0.58<br>(0.04)  | <b>&lt;0.01</b> |
| $\hat{\sigma}_{sc}^2$ (centers)  | 0.06<br>(0.02)  | <b>0.02</b>     | 0.22<br>(0.07)   | <b>&lt;0.01</b> | 0.17<br>(0.05)  | <b>&lt;0.01</b> | 0.13<br>(0.04)  | <b>&lt;0.01</b> | 0.09<br>(0.03)  | <b>0.01</b>     | 0.09<br>(0.03)  | <b>0.01</b>     |

Note. Ref. = reference group for comparison; TAU = treatment as usual group; EXP = intervention group; INT = intention. PBC = Perceived behavioral control; SRBAI = Self-report Behavioral Automaticity Index; SM = Self-monitoring; AP = Action planning; CP = Coping planning;  $\hat{\sigma}_{st}^2$  = the variance at patient level;  $\hat{\sigma}_{sc}^2$  = the variance at center level; SE = standard error.

$p$ -values < 0.05 are in **bold**

**Electronic Supplementary Material Table S4. Three-level multiple linear regression models predicting beliefs about medicines, illness perceptions, and quality of life (QoL).**

| Variable                         | BMQ-Necessity |                 | BMQ-Concerns |                 | Illness perceptions |                 | QoL: PCS      |                 | QoL: MCS      |                 |
|----------------------------------|---------------|-----------------|--------------|-----------------|---------------------|-----------------|---------------|-----------------|---------------|-----------------|
|                                  | B (SE)        | p value         | B (SE)       | p value         | B (SE)              | p value         | B (SE)        | p value         | B (SE)        | P value         |
| Group (Ref: TAU)                 | 0.35 (0.70)   | 0.35            | -0.24 (0.66) | 0.37            | -0.17 (1.54)        | 0.40            | 1.11 (1.95)   | 0.34            | 1.55 (1.73)   | 0.27            |
| Time (Ref: baseline)             |               |                 |              |                 |                     |                 |               |                 |               |                 |
| 6 months                         | 0.08 (0.12)   | 0.33            | -0.35 (0.16) | <b>0.03</b>     | -0.14 (0.31)        | 0.36            | 2.27 (0.52)   | <b>&lt;0.01</b> | 3.50 (0.64)   | <b>&lt;0.01</b> |
| 12 months                        | 0.63 (0.12)   | <b>&lt;0.01</b> | -0.21 (0.15) | 0.16            | -0.21 (0.13)        | 0.11            | 2.14 (0.50)   | <b>&lt;0.01</b> | 3.12 (0.80)   | <b>&lt;0.01</b> |
| 18 months                        | 0.66 (0.13)   | <b>&lt;0.01</b> | -0.30 (0.16) | 0.06            | 0.25 (0.35)         | 0.31            | 1.30 (0.50)   | <b>0.01</b>     | 3.15 (0.93)   | <b>&lt;0.01</b> |
| <b>group × time</b>              |               |                 |              |                 |                     |                 |               |                 |               |                 |
| EXP vs. TAU at 6th month         | 4.27 (0.17)   | <b>&lt;0.01</b> | -7.40 (0.22) | <b>&lt;0.01</b> | -3.31 (0.43)        | <b>&lt;0.01</b> | 0.92 (0.70)   | 0.17            | 1.02 (0.90)   | 0.21            |
| EXP vs. TAU at 12th month        | 4.77 (0.17)   | <b>&lt;0.01</b> | -7.88 (0.24) | <b>&lt;0.01</b> | -3.52 (0.47)        | <b>&lt;0.01</b> | 1.23 (0.62)   | 0.055           | 1.40 (0.96)   | 0.14            |
| EXP vs. TAU at 18th month        | 4.82 (0.18)   | <b>&lt;0.01</b> | -7.81 (0.23) | <b>&lt;0.01</b> | -3.91 (0.50)        | <b>&lt;0.01</b> | 1.77 (0.73)   | <b>0.02</b>     | 1.68 (0.80)   | <b>0.04</b>     |
| Age                              | -0.08 (0.70)  | 0.40            | 0.09 (0.11)  | 0.28            | 0.22 (0.31)         | 0.31            | -0.50 (0.69)  | 0.31            | -0.271 (0.61) | 0.66            |
| <b>Sex</b> (Ref: females)        | -0.75 (0.70)  | 0.22            | 1.50 (0.65)  | <b>0.03</b>     | 3.26 (2.54)         | 0.17            | 0.13 (0.21)   | 0.33            | 3.67 (2.72)   | 0.16            |
| Charlson index                   | -0.14 (0.11)  | 0.18            | 0.05 (0.35)  | 0.39            | 0.50 (0.12)         | <b>&lt;0.01</b> | -1.82 (1.39)  | 0.17            | -1.61 (1.78)  | 0.27            |
| Body mass index                  | -0.12 (0.20)  | 0.34            | 0.07 (0.32)  | 0.39            | 0.24 (0.31)         | 0.30            | -1.11 (1.21)  | 0.26            | -0.04 (0.87)  | 0.40            |
| Intercept                        | 16.34 (1.58)  | <b>&lt;0.01</b> | 10.96 (1.79) | <b>&lt;0.01</b> | 41.88 (6.77)        | <b>&lt;0.01</b> | 33.56 (10.62) | <b>&lt;0.01</b> | 46.12 (12.96) | <b>&lt;0.01</b> |
| $\hat{\sigma}_{st}^2$ (patients) | 5.50 (0.36)   | <b>&lt;0.01</b> | 7.66 (0.51)  | <b>&lt;0.01</b> | 117.04 (7.24)       | <b>&lt;0.01</b> | 43.76 (2.70)  | <b>&lt;0.01</b> | 58.14 (1.98)  | <b>&lt;0.01</b> |

|                                 |             |                 |                |                 |                 |                 |                 |                 |                 |                 |
|---------------------------------|-------------|-----------------|----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|
| $\hat{\sigma}_{sc}^2$ (centers) | 2.21 (0.08) | <b>&lt;0.01</b> | 3.54<br>(0.12) | <b>&lt;0.01</b> | 13.70<br>(0.46) | <b>&lt;0.01</b> | 33.43<br>(1.17) | <b>&lt;0.01</b> | 17.96<br>(2.57) | <b>&lt;0.01</b> |
|---------------------------------|-------------|-----------------|----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|

*Note.* Ref. = reference group for comparison; TAU = treatment as usual group; EXP = intervention group; BMQ = Beliefs about Medicines Questionnaire; PCS = Physical Component Summary; MCS = Mental Component Summary;  $\hat{\sigma}_{st}^2$  = the variance at patient level;  $\hat{\sigma}_{sc}^2$  = the variance at center level; SE = standard error.

*p* values < 0.05 are in **bold**

**Electronic Supplementary Material Table S5. Direct and mediated effects of group on medication adherence, quality of life (QoL) and survival rates.**

| Outcome                 | Time<br>(months) | Mediator        | Coefficient (SE)                     |                                       |                                  |                             |               |
|-------------------------|------------------|-----------------|--------------------------------------|---------------------------------------|----------------------------------|-----------------------------|---------------|
|                         |                  |                 | A. Intervention<br>effect on outcome | B. Intervention effect<br>on mediator | C. Mediator effect<br>on outcome | Mediated effect<br>(=B * C) |               |
| Medication<br>adherence | 6                |                 | 3.97 (0.22)**                        |                                       |                                  |                             |               |
|                         |                  | BMQ-Necessity   |                                      | 4.27 (0.17)**                         | 0.32 (0.03)**                    | 1.37 (0.14)**               |               |
|                         |                  | BMQ-Concerns    |                                      | -7.40 (0.22)**                        | -0.27 (0.02)**                   | 2.00 (0.16)**               |               |
|                         |                  | PBC             |                                      | 0.58 (0.05)**                         | 0.66 (0.10)**                    | 0.38 (0.07)**               |               |
|                         |                  | Intention       |                                      | 0.61 (0.05)**                         | 0.85 (0.12)**                    | 0.52 (0.08)**               |               |
|                         |                  | Self monitoring |                                      | 0.54 (0.06)**                         | 1.22 (0.11)**                    | 0.66 (0.09)**               |               |
|                         |                  | Action planning |                                      | 0.84 (0.06)**                         | 0.95 (0.10)**                    | 0.80 (0.10)**               |               |
|                         |                  | Coping planning |                                      | 0.85 (0.07)**                         | 0.95 (0.10)**                    | 0.81 (0.11)**               |               |
|                         |                  | SRBIA           |                                      | 0.57 (0.05)**                         | 0.22 (0.10)*                     | 0.12 (0.06)*                |               |
|                         | 12               |                 |                                      | 3.83 (0.23)**                         |                                  |                             |               |
|                         |                  | BMQ-Necessity   |                                      |                                       | 4.77 (0.17)**                    | 0.25 (0.03)**               | 1.19 (0.15)** |
|                         |                  | BMQ-Concerns    |                                      |                                       | -7.88 (0.24)**                   | -0.29 (0.04)**              | 2.29 (0.33)** |
|                         |                  | PBC             |                                      |                                       | 0.57 (0.06)**                    | 0.61 (0.11)**               | 0.35 (0.07)** |
|                         |                  | Intention       |                                      |                                       | 0.61 (0.06)**                    | 0.88 (0.11)**               | 0.54 (0.08)** |
|                         |                  | Self monitoring |                                      |                                       | 0.54 (0.06)**                    | 1.20 (0.13)**               | 0.65 (0.10)** |
|                         |                  | Action planning |                                      |                                       | 0.87 (0.07)**                    | 0.98 (0.11)**               | 0.85 (0.12)** |
|                         |                  | Coping planning |                                      |                                       | 0.87 (0.06)**                    | 0.96 (0.09)**               | 0.83 (0.10)** |
|                         |                  | SRBIA           |                                      |                                       | 0.47 (0.06)**                    | 0.14 (0.10)                 | 0.06 (0.05)   |
|                         | 18               |                 |                                      | 4.24 (0.26)**                         |                                  |                             |               |
|                         |                  | BMQ-Necessity   |                                      |                                       | 4.82 (0.18)**                    | 0.26 (0.04)**               | 1.25 (0.20)** |
|                         |                  | BMQ-Concerns    |                                      |                                       | -7.81 (0.23)**                   | -0.31 (0.05)**              | 2.24 (0.40)** |
| PBC                     |                  |                 |                                      | 0.61 (0.06)**                         | 0.60 (0.09)**                    | 0.37 (0.06)**               |               |
| Intention               |                  |                 |                                      | 0.63 (0.05)**                         | 0.92 (0.14)**                    | 0.58 (0.10)**               |               |
| Self monitoring         |                  |                 |                                      | 0.58 (0.06)**                         | 1.32 (0.14)**                    | 0.77 (0.11)**               |               |
| Action planning         |                  |                 |                                      | 0.93 (0.07)**                         | 0.96 (0.09)**                    | 0.89 (0.11)**               |               |
| Coping planning         |                  |                 |                                      | 0.95 (0.08)**                         | 0.93 (0.12)**                    | 0.88 (0.14)**               |               |
| SRBIA                   |                  |                 |                                      | 0.50 (0.06)**                         | 0.16 (0.10)                      | 0.10 (0.05)*                |               |

|               |                 |                      |                |                |                |               |
|---------------|-----------------|----------------------|----------------|----------------|----------------|---------------|
| PCS           | 6               |                      | 0.92 (0.70)    |                |                |               |
|               |                 | Medication adherence |                | 3.97 (0.22)**  | 0.18 (0.05)**  | 0.71 (0.20)** |
|               |                 | Pharmacy refill rate |                | 9.82 (0.93)**  | 0.07 (0.02)**  | 0.69 (0.21)** |
|               | 12              |                      | 1.23 (0.062)   |                |                |               |
|               |                 | Medication adherence |                | 3.83 (0.23)**  | 0.160 (0.01)** | 0.61 (0.05)** |
|               |                 | Pharmacy refill      |                | 10.64 (0.95)** | 0.06 (0.02)**  | 0.64 (0.11)** |
| MCS           | 18              |                      | 1.77 (0.73)*   |                |                |               |
|               |                 | Medication adherence |                | 4.24 (0.26)**  | 0.102 (0.04)** | 0.42 (0.17)*  |
|               |                 | Pharmacy refill      |                | 10.40 (0.98)** | 0.09 (0.03)**  | 0.94 (0.32)** |
|               | 6               |                      | 1.02 (0.90)    |                |                |               |
|               |                 | Medication adherence |                | 3.97 (0.22)**  | 0.28 (0.04)**  | 1.11 (0.17)** |
|               |                 | Pharmacy refill      |                | 9.82 (0.93)**  | 0.05 (0.01)**  | 0.49 (0.11)** |
| Survival rate | 12              |                      | 1.40 (0.96)    |                |                |               |
|               |                 | Medication adherence |                | 3.83 (0.23)**  | 0.30 (0.06)**  | 1.15 (0.24)** |
|               |                 | Pharmacy refill      |                | 10.64 (0.95)** | 0.06 (0.02)**  | 0.64 (0.22)** |
|               | 18              |                      | 1.68 (0.80)*   |                |                |               |
|               |                 | Medication adherence |                | 4.24 (0.26)**  | 0.29 (0.05)**  | 1.23 (0.22)** |
|               |                 | Pharmacy refill      |                | 10.40 (0.98)** | 0.04 (0.01)**  | 0.42 (0.11)** |
| Survival rate | 6               |                      | 1.92 (0.67)**  |                |                |               |
|               |                 | Medication adherence |                | 3.97 (0.22)**  | 0.06 (0.02)**  | 0.24 (0.08)** |
|               |                 | Pharmacy refill      |                | 9.82 (0.93)**  | 0.12 (0.04)**  | 1.18 (0.41)** |
|               | 12              |                      | 2.14 (0.38)**  |                |                |               |
|               |                 | Medication adherence |                | 3.83 (0.23)**  | 0.08 (0.03)**  | 0.31 (0.11)** |
|               |                 | Pharmacy refill      |                | 10.64 (0.95)** | 0.19 (0.03)**  | 2.02 (0.34)** |
| Survival rate | 18              |                      | 2.87 (0.47)**  |                |                |               |
|               |                 | Medication adherence |                | 4.24 (0.26)**  | 0.07 (0.01)**  | 0.30 (0.05)** |
|               | Pharmacy refill |                      | 10.40 (0.98)** | 0.31 (0.11)**  | 3.22 (1.18)**  |               |

BMQ= Beliefs about Medicines Questionnaire; PBC= Perceived behavioral control; SRBIA= Self-report Behavioral Automaticity Index; PCS = Physical Component Summary; MCS = Mental Component Summary; SE = standard error.

\* $p < 0.05$ ; \*\* $p < 0.01$ .