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Review Article

Effects of medication adherence interventions for older adults with chronic illnesses: a systematic review and meta-analysis

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ABSTRACT

This systematic review and meta-analysis aimed to understand the characteristics of medication adherence interventions for older adults with chronic illnesses, and to investigate the average effect size by combining the individual effects of these interventions. Data from studies meeting the inclusion criteria were systematically collected in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analysis guidelines. The results showed that the average effect size (Hedges' *g*) of the finally selected medication adherence interventions for older adults with chronic illnesses calculated using a random-effects model was 0.500 (95% confidence interval [CI], 0.342–0.659). Of the medication adherence interventions, an implementation intention intervention (using face-to-face meetings and telephone monitoring with personalized behavioral strategies) and a health belief model–based educational program were found to be highly effective. Face-to-face counseling was a significantly effective method of implementing medication adherence interventions for older adults with chronic illnesses (Hedges' $g = 0.531$, 95% CI, 0.186–0.877), while medication adherence interventions through education and telehealth counseling were not effective. This study verified the effectiveness of personalized behavioral change strategies and cognitive behavioral therapy based on the health belief model, as well as face-to-face meetings, as medication adherence interventions for older adults with chronic illnesses.

Keywords: Aged; Chronic disease; Medication adherence; Meta-analysis; Review

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Introduction

Corrective and effective medications are the best way to manage chronic illnesses. Approximately 50% of older adults in South Korea have at least 3 chronic diseases, increasing the risk of polypharmacy in terms of non-adherence to medications [1,2]. Around 37% of Korean older adults with chronic illnesses take 5 or more medications [2]; among Organisation for Economic

Co-operation and Development members, South Korea was reported to have the highest consumption of digestive and metabolic medicines and an antibiotic prescription rate 1.7 times higher than average [3].

The estimated rate of adherence to long-term medication regimens is approximately 50.0% in older adults, and this rate is lower in older adults due to numerous comorbidities and consequent polypharmacy [1]. Non-adherence reduces the efficacy of chronic illness treatment [4], and patients with chronic illnesses and low socioeconomic status have shown high rates of medication non-adherence [5]. Older adults reportedly stop taking medications due to complicated drug delivery regimens and high prices [1]. According to a previous study, 74.1% of older adults who take 4 or more medications daily stated that medication regimen complexity was the main barrier to medication adherence. Furthermore, 68.3% of patients over the age of 60 did not know the name of the medications they were taking and were unable to correctly take medications due to lack of knowledge about the disease (63.3%), inadequate knowledge regarding therapy (60.0%), taking many pills at the same time (51.7%), forgetfulness (50.8%), difficulty remembering to take all their pills (48.3%), and difficulty in refilling prescriptions on time (20.0%) [6]. Various factors, such as the patients themselves, medications, health care providers, health care systems, and socioeconomic factors, have been shown to influence medication adherence in older adults. Nonetheless, medication adherence is important for ensuring that therapeutic benefits are delivered to patients [7].

Older adults with chronic diseases living in the community have to take long-term medications, and it can be difficult for the elderly to take their own medications and manage side effects. For this, nursing interventions are needed to help them take medicines correctly. Regarding interventions for promoting medication adherence among patients with chronic illnesses, reminder calls based on medication event monitoring systems are more effective than motivational interviewing, and are also cost-effective [4]. Applying home-based nurse-driven follow-up care for outpatients with hypertension improved the physical component of health-related quality of life, and significantly improved medication adherence and symptom counts [8]. Educational short message services, reminder short message services for medications, and structured telephone support have also been shown to improve self-care behavior, including medication compliance, for patients with chronic illnesses [9]. Text messaging and an interactive voice response intervention to promote adherence among this high-risk group were found to be efficacious [5]. Psychological interventions, such as cognitive behavioral therapy (CBT), including motivational interviewing, also help improve adherence to medication [10].

It is necessary to systematically analyze the characteristics, methods, and effects on outcome variables of various medication adherence programs applied to older adults with chronic diseases, and use these outcomes as a basis for developing effective medication adherence interventions for this population. However, many studies have either not addressed interventions focused on older adults, making it difficult to expect the same effect when applied to this group [4,11,12], or approached medication adherence as part of overall chronic illness management instead of the sole focus [13–15]. Thus, it has been difficult to find strategies to improve medication adherence, which is essential for the management of chronic illnesses, considering the cognitive and physical characteristics of older adults. Therefore, this study aimed to identify the effects of various medication adherence intervention programs for older adults with chronic illnesses to develop effective interventions for evidence-based nursing practice, improve the medication adherence of older adults, and provide directions for future research.

The purpose of this study was to conduct a meta-analysis of the effects of intervention programs related to medication adherence in older patients with chronic illnesses. First, this study aimed to identify the characteristics of intervention programs, assess the methodological quality of medication adherence intervention program studies that were randomized controlled trials (RCTs), analyze the effect size of the medication adherence intervention programs, and evaluate publication bias.

Materials and Methods

Literature Selection Criteria

This study was conducted according to the Cochrane Collaboration's systematic literature review handbook on mediation methods [16], and the guidelines for reporting on systematic literature reviews suggested by the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) group for the intervention method of the Cochrane Collaboration [17]. However, this review study was not registered. The following selection criteria were utilized within the participants, intervention, comparisons, outcomes, timing, setting, and study design (PICOTS-SD) framework.

Selection criteria

Participants

The participants of the studies were older men and women aged 60 years and above who had been diagnosed with 1 or more chronic diseases by a doctor and were taking medications regularly.

Interventions

The types of interventions related to medication adherence included education or information, counseling or psychotherapy, behavioral therapy, social support, or interventions that combined these methods.

Comparisons

The participants were compared with older patients with chronic illnesses who did not receive the medication adherence interventions and were receiving usual care from the hospital or community health centers.

Outcomes

The major outcomes of the intervention were medication adherence and physical and psychological variables related to medication adherence.

Timing

Only results measured immediately after major interventions were included.

Setting

Only interventions conducted on an outpatient basis at a health center, hospital, public hospital's outpatient clinic, general practice, or primary health care unit were included. Interventions conducted while patients were admitted to the hospital were excluded.

Study design

Since the study design has an important effect on the reliability and generalizability of the results of intervention studies, only RCTs were included.

Literature Search and Selection Process

Literature search strategy

The literature search and selection were conducted using electronic databases, targeting papers published in English over the last 10 years until August 11, 2020. We searched Medline and PubMed as electronic databases indexing research in the medical field, as well as the Cumulative Index to Nursing and Allied Health Literature (CINAHL).

Search terms

The following search terms were selected, including Medical Subject Headings (MeSH) for the literature search: "aged" (MeSH) OR "elderly" AND "chronic disease" (MeSH) OR "chronic illness" OR "hypertension" OR "diabetes mellitus" OR "arthritis" for participants, and "medication adherence" (MeSH) OR "medication compliance" (MeSH) for interventions. Searching only for the term "chronic diseases" could have excluded studies on specific chronic diseases, such as hypertension, diabetes, and arthritis; therefore, the search formula was expanded to include the names of major chronic diseases. Search modifiers included full text, RCTs over the last 10 years, English, and humans.

Data selection

All 3 researchers independently participated in the search and data selection process, selected studies based on the selection and exclusion criteria, focusing on the core questions, and conducted discussions to resolve any disagreements. The researchers reached a consensus in all cases.

The final number of studies found based on the search strategy for each database was 706: 56 in Medline, 615 in PubMed, and 35 in CINAHL. Of these, 188 papers were extracted after reviewing the titles and abstracts to exclude duplicate studies, studies on interventions unrelated to the topic, simple drug therapy studies, and studies not including interventions. The core questions were re-examined based on the full text of the extracted studies. As a result, 7 studies were selected, excluding 108 that did not meet the criteria for selecting participants, 9 in which the intervention content did not center on medication adherence, and 64 that did not measure medication adherence as an outcome variable. All 7 studies were included in the meta-analysis after quality assessment (Figure 1).

Ethical Considerations

This study was exempted from review by the Institutional Review Board of Cheongju University, the institution of the lead researcher, to ensure ethical and scientific validity for the overall research (approval number: 1041107-201904-HR-017-01).

Quality Assessment of the Included Studies

To enhance the validity of the research results, a methodological quality assessment was conducted on the 7 studies ultimately selected. Since all 7 studies were RCTs, we used Cochrane's Risk of Bias tool [16], which consists of 7 items, including sequence generation, allocation concealment, blinding of participants, personnel and outcome assessors, incomplete outcome data, selective outcome reporting, and other sources of bias. Each

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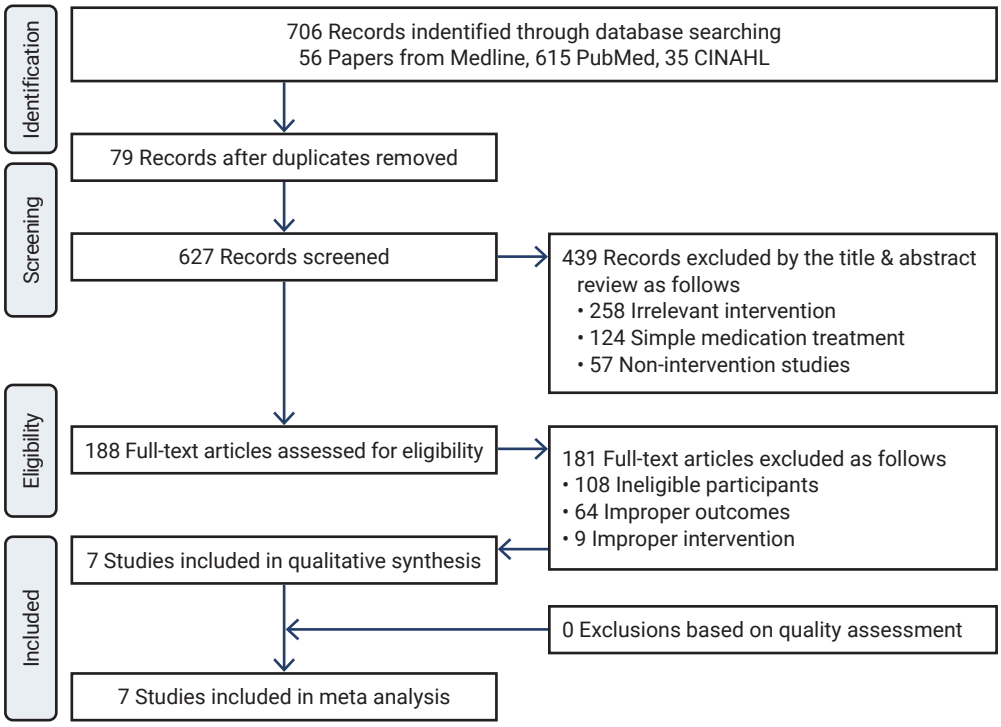

Figure 1. Flow diagram depicting the process of study selection for the meta-analysis.

item is assessed as "yes," "no," or "unclear." Independent quality assessments were conducted by the 3 researchers, whose main fields of study were related to the topics of this study and who were professors of nursing and experienced with systematic literature reviews and meta-analyses. If there was any disagreement regarding an item, the results were determined by sufficient discussion and rigorous re-examination.

Data Analysis

The 7 selected studies were analyzed using the Comprehensive Meta-Analysis 3.0 program (Biostat Inc., Englewood, NJ, USA). After testing for homogeneity between studies through the Q-test, the average effect size was calculated by combining the effect sizes of the individual studies. If the studies were not homogeneous, the average effect size was calculated using a random-effects model that reset the weights considering the variation among participants included in individual studies and the heterogeneity of each study [18]. In the present study, the standardized mean difference, Cohen's *d*, as a measure of effect size, was converted into Hedges' *g*, as Cohen's *d* tends to overestimate the effect size in small samples [19]. A Hedges' *g* value in the range from 0.2 to less than 0.5 indicates a small effect, a value from 0.5 to less than 0.8 indicates a medium effect, and a value of 0.8 or greater indicates a large effect [20]. A visual analysis was performed to test for publication bias using a funnel plot, which was a scatter plot drawn with the treatment effect measured in each study on the x-axis and a scale indicating the precision of the study (number of samples or standard error) on the y-axis. The statistical analysis of asymmetry was performed using Egger regression analysis.

Results

Descriptive Summary of the Included Studies

Table 1 summarizes the characteristics of the 7 studies selected for analysis [21–27]. The following types of medication adherence interventional programs for older adults with chronic illnesses were ultimately selected: an educational program based on the health belief model [21], a remote medication monitoring program [22], a structured pharmacist-led intervention [23], a pharmacist-led care program [24], a complex intervention on prioritizing multiple medications [25], a motivational interviewing program [26], and an implementation intention intervention [27]. All the selected studies except 1 [23] included both male and female participants. Five studies selectively applied interventions to patients with certain chronic illnesses (hypertension, chronic heart failure, chronic obstructive pulmonary disease [COPD], and diabetes), and 2 studies selected participants with "chronic diseases." In all 7 studies, the average age of

Table 1. Descriptive summary of studies included in the meta-analysis

No.	Study	Year of publication	Study design	Participants		Interventions				Interventions for control group	Follow-up	Measured outcomes
				Gender/ chronic diseases	Sample size/mean age (y)	Major type	Program context	Application	Session/ duration			
1	Yazdanpanah et al. [21]	2019	RCT	Both/ hypertension	IG:30/69.1 CG:30/63.9	Educational program	Eight educational sessions based on the health belief model (susceptibility, perceived severity and susceptibility, teaching perceived severity and susceptibility, patient's familiarity with perceived benefits and barriers, promoted self-efficacy, stimulus of cue to action)	Lectures, questions and answers, group discussions, use of desirable role behavior model using supplementary tools and guide sheets	8 sessions /60 min/ for a month	Typical routine services	None	- Medication adherence (MMAS-8)
2	Hale et al. [22]	2016	RCT	Both/Chronic heart failure	IG:13/68.4 CG:16/74.4	Telehealth & counseling (remote medication monitoring system)	The MedSentry medication monitoring system: a remotely monitored electronic device that alerts participants when it is time to take their medications. A monitoring center with advisors who contact participants and caregivers when medications are not taken. The device is installed in the participant's home and data are transmitted to the monitoring center via the internet.	The MedSentry medication monitoring system (device) used several methods to ensure participants take their medications as prescribed (visual cue, audio alarm, etc.)	90 d	Usual medication reminder method	None	- Medication adherence (MOS) - Health status - Depression (PHQ-8) - HRQoL (MLHFQ) - Unplanned hospitalizations - Emergency department visits
3	Abdulsalim et al. [23]	2018	RCT	Male (≥ 94%)/ chronic obstructive pulmonary disease	IG:130/60.6 CG:130/61.1	Structured pharmacist-led counseling intervention	Pharmacist intervention placed emphasis on (1) compliance, (2) smoking cessation, (3) exercise, (4) inhaler use and (5) need for timely follow-up. The counseling sessions (15–20 min) and patient information leaflets emphasized (1) the importance of medication compliance, (2) dose and frequency of medications, (3) need for smoking cessation, (4) simple exercise, (5) proper use of inhaler devices and (6) need for timely monitoring	Pharmacist counseling	6 mo	Standard hospital care	Every 6 mo for 2 y	- Medication adherence (MAQ)

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Table 1. Continued

No.	Study	Year of publication	Study design	Participants		Interventions				Interventions for control group	Follow-up	Measured outcomes
				Gender/ chronic diseases	Sample size/mean age (y)	Major type	Program context	Application	Session/ duration			
4	Korcegez et al. [24]	2017	RCT	Both/type 2 diabetes mellitus	IG:79/61.8 CG:80/62.2	Pharmacist-led educational program	Five face-to-face educational programs with a pharmacist who reviewed medication and treatment plans. Explanation to each patient of the importance of self-monitoring blood glucose, a healthy diet, physical exercise, and smoking cessation and also provision of a different pamphlet during each visit. The pamphlets contained information about type 2 diabetes, complications, medications, treatment goals, and self-care.	Clinical pharmacist's face-to-face education, discussion, recommendations for medication regimens	5 sessions /12 mo	Usual care	None	- Medication adherence (Morisky-Green test) - Hemoglobin A1c, BP, lipid profile, BMI, WC - Self-care activities
5	Muth et al. [25]	2016	RCT	Both/ ≥ 3 chronic conditions	IG:50/75.8 CG:50/75.2	Counseling intervention (complex intervention on prioritizing multiple medications)	Checklist-based interviews with patients on medication-related problems and reconciliation of their medications. Assisted by a computerized decision-support system, discussions of medication intake with patients and adjustments of their medication regimens.	Checklist-based pre-consultation interview, brown bag review, computerized decision support system, physician-patient consultation	5 wk	Usual care	After 6 and 12 wk	- Medication adherence (Morisky-Green test, MAI, MARS) - HRQoL (EQ-5D) - Depression (GDS) - Beliefs in medicine Questionnaire
6	Moral et al. [26]	2015	RCT	Both/chronic diseases	IG:70/75.6 CG:84/76.1	Counseling intervention (motivational interviewing)	MI is a counseling method that involves enhancing a patient's motivation to change behavior. Experimental group providers followed these steps: (1) assessment of ambivalence; (2) exploration of patients' ideas and concerns about their lack of adherence; (3) application of specific interviewing skills for reframing and promoting self-efficacy (using empathy, developing discrepancies, avoiding arguments, confronting barriers and problems, supporting the patient, and others).	Face-to-face motivational interview, counseling	15 min/ 6 mo	Informative personal advice	None	- Medication adherence (Morisky-Green test)

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Table 1. Continued

No.	Study	Year of publication	Study design	Participants		Interventions				Interventions for control group	Follow-up	Measured outcomes
				Gender/chronic diseases	Sample size/mean age (y)	Major type	Program context	Application	Session/duration			
7	Trevisan et al. [27]	2020	RCT	Both/type 2 diabetes	IG:45/61.1 CG:45/61.8	Telehealth & counseling (implementation intention intervention)	The intervention was tailored based on the elaboration of action and coping plans, with their respective overcoming strategies. A form specified 3 action plans covering when, where, and how they intended to take their oral anti-diabetic medication over the next 2 months.	Face-to-face meetings, telephone monitoring, in-person behavioral strategies	4 times 15 wk (105 days)	Standard care	None	- Medication adherence (IAGAM) - Hemoglobin A1c

RCT, randomized controlled trial; IG, intervention group; CG, control group; MMAS-8, Morisky Medication Adherence Scale-8; MOS, Medical Outcomes Study; PHQ-8, the 8-Item Patient Health Questionnaire; HRQoL, health-related quality of life; MLHFQ, Minnesota Living with Heart Failure Questionnaire; MAQ, Medication Adherence Questionnaire; BP, blood pressure; BMI, body mass index; WC, waist circumference; MAI, Medication Appropriateness Index; MARS, Medication Adherence Rating Scale; EQ-5D, EuroQol Five Dimension Scale; GDS, Geriatric Depression Scale; IAGAM, Global Evaluation of Medication Adherence.

the participants was 60 years or older, and the number of participants varied from 13 to 130; except for 1 study [22], the number of participants was 30 or more.

All studies were RCTs. There were 3 studies on pharmacist- and physician-led counseling and consultation [23,25,26], 2 on educational programs including lecture lectures [21] and face-to-face education [24], 2 on interventions using group discussion [21,23], and 2 that used medication monitoring systems and telephone monitoring [22,27]. The durations of the programs varied from 1 to 12 months. In most studies, the usual or standard hospital care was applied to the control group, and 2 studies evaluated the results through follow-up. Three studies only measured medication adherence, and 4 studies also evaluated depression, quality of life, and body composition. The Morisky-Green test was the most common tool used to measure medication adherence, as it was used in 3 studies, and other tools included the Morisky Medication Adherence Scale-8 (MMAS-8), Medication Adherence Questionnaire (MAQ), MAI, Medication Appropriateness Index (MAI); Medication Adherence Rating Scale (MARS), Medication Outcomes Study (MOS), Global Evaluation of Medication Adherence (IAGAM).

Quality Assessment of the Included Studies

All 7 studies were RCTs. The qua lity assessment performed using the Cochrane Risk of Bias tool showed that there were 4 studies with sequence generation; 2 studies with allocation concealment; 3 studies with blinding of participants, personnel, and outcome assessors; 7 studies with incomplete outcome data; and 7 studies with selective outcome reporting. The risk of bias was low in all 7 studies. No studies were excluded from the meta-analysis after quality assessment, as there were no cases of a high risk of bias for any item. Three studies were evaluated as "unclear" for sequence generation, 5 for allocation concealment, and 4 for blinding (Figure 2).

Effectiveness of the Medication Adherence Interventions

Effect size of medication adherence by intervention program

In this study, the results of calculating the corrected standardized mean difference (Hedges' g) for 7 studies that applied medication adherence interventions for older adults with chronic illnesses are presented as forest plots in Figures 3 and 4. The heterogeneity of all studies—that is, the ratio of the variance between studies to the total variance—was represented by $I^2 = 63.17\%$ ($Q = 16.29$, $p = 0.012$), and the average effect size calculated using a random-effects model, Hedges' g, was 0.500 (95% confidence interval

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[CI], 0.342–0.659), indicating a significant effect size. Of the medication adherence interventions, a study [27] that utilized an implementation intention intervention (face-to-face meetings and telephone monitoring with personalized behavioral strategies) had the largest effect size, with a Hedges' *g* of 1.222 (95% CI, 0.619–1.826), and an educational program based on the health belief model [21] was also highly effective, with a Hedges' *g* of 0.883 (95% CI, 0.359–1.407).

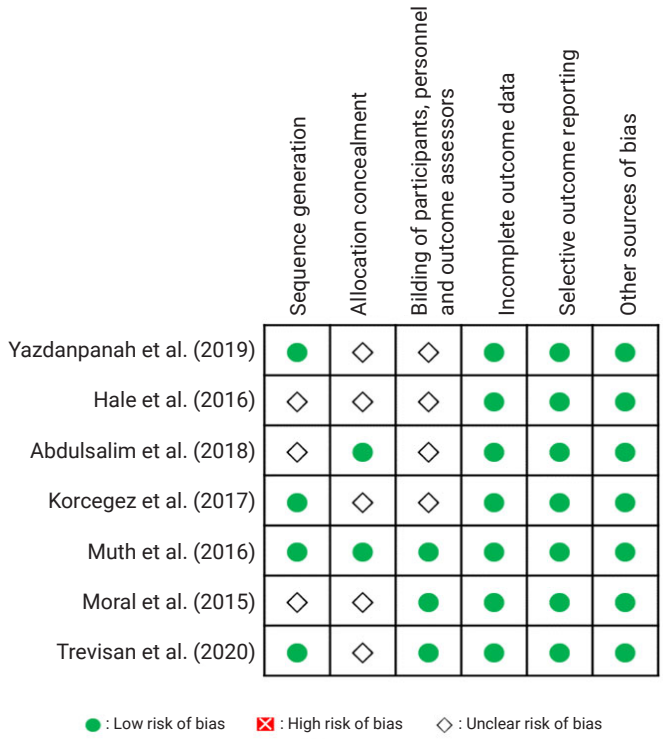

Figure 2. Risk of bias in the included studies.

Effect size according to intervention method

Of the 7 studies, 5 implemented counseling and 2 used education as the major intervention method. Two studies implemented personalized counseling through monitoring with the use of telehealth. Remote intervention methods during a pandemic of an infectious disease such as coronavirus disease 2019 can be highly valuable; therefore, the effects of such interventions were also analyzed in this study.

The average effect sizes of the studies were calculated using a random-effects model. The studies with counseling as a major intervention method had a significant average effect size, with a Hedges' *g* of 0.531 (95% CI, 0.186–0.877; I^2=65.17%; Q=11.48; p=0.022). The studies with education as a major intervention method had a significant average effect size, with a Hedges' *g* of 0.513 (95% CI, −0.157 to 1.184; I^2=77.47%; Q=4.44; p=0.035). The studies with personalized counseling through monitoring with the use of telehealth had a large average effect size, with a Hedges' *g* of 0.717, but this was not statistically significant (95% CI, −0.386 to 1.820; I^2=74.48%; Q=3.92; p=0.048).

Analysis of publication bias

A visual analysis of publication bias was performed using a funnel plot, and Egger regression analysis was performed to objectively interpret the asymmetry of the funnel plot. Egger regression analysis describes the relationship between the effect size and standard error of each study using a regression equation. For the total effect size of the medication adherence intervention programs analyzed in this study, clear asymmetry was not found in the funnel plot. The intercept was 0.65 (t=0.65, p=0.784), indicating that the effect size was not asymmetric.

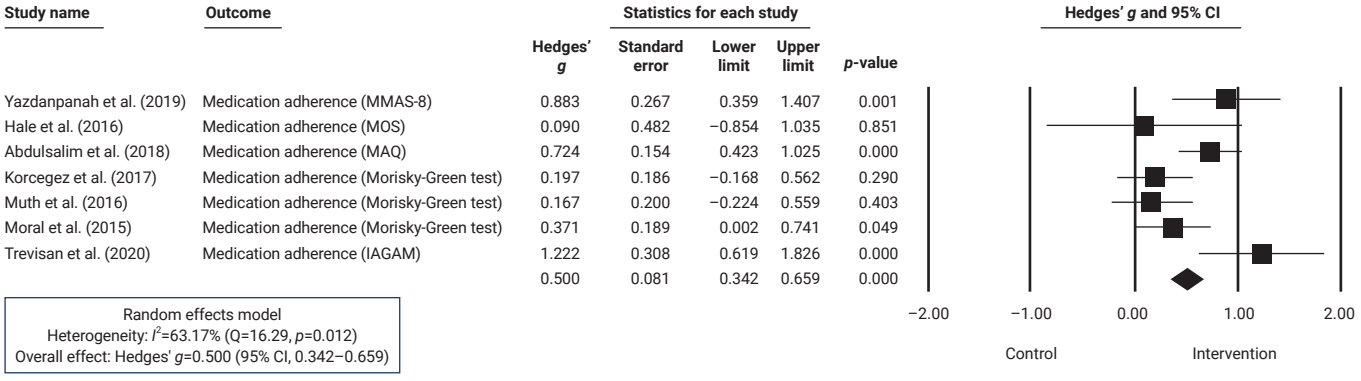

Figure 3. Forest plots of the effects of medication adherence interventions on medication adherence for older adults with chronic illnesses (random-effects model).
CI, confidence interval; MMAS-8, Morisky Medication Adherence Scale-8; MOS, Medical Outcomes Study; MAQ, Medication Adherence Questionnaire; IAGAM, Global Evaluation of Medication Adherence.

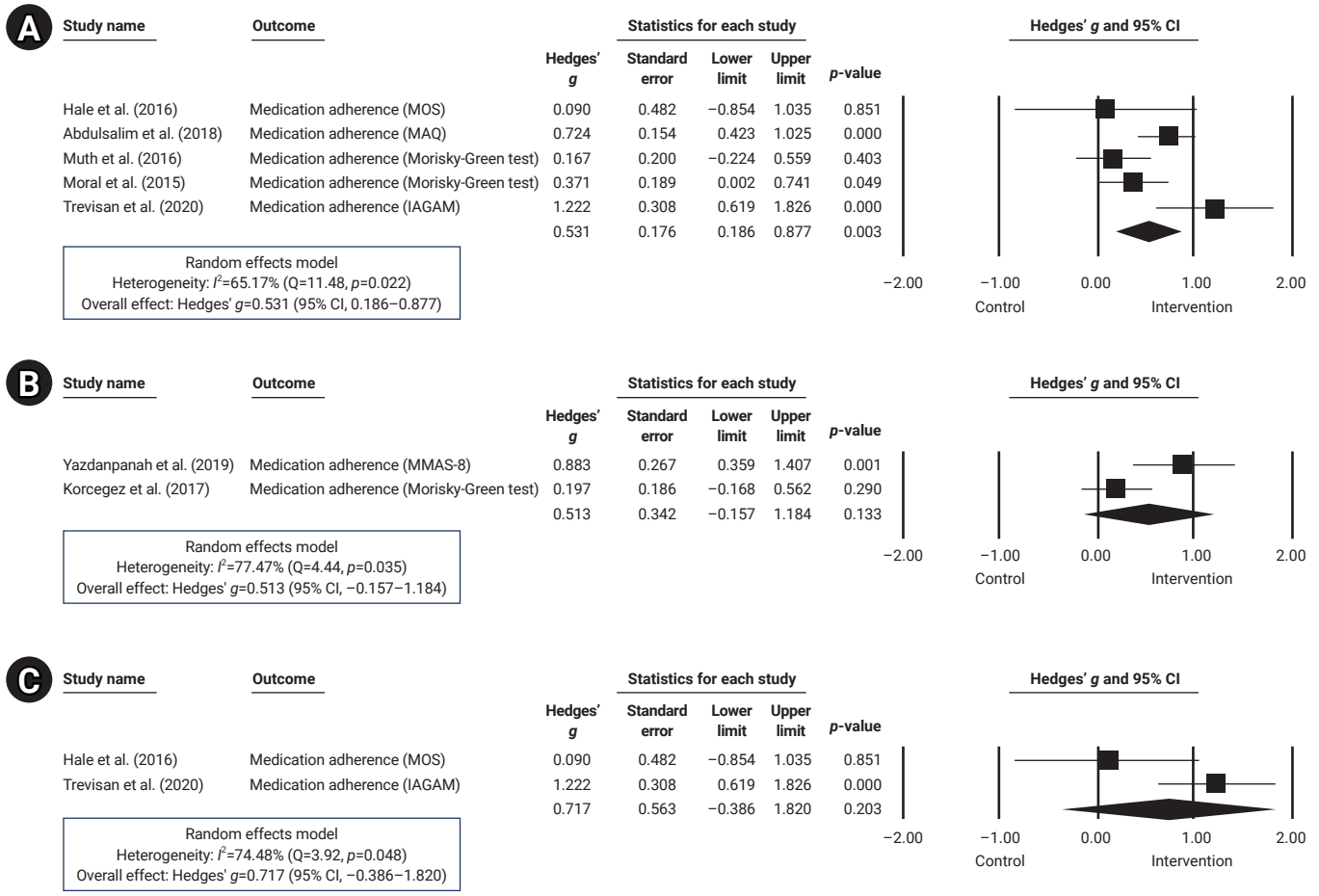

Figure 4. Forest plots of the effects of medication adherence programs according to intervention methods (random-effects model). (A) The effects of medication adherence programs consisting of counseling. (B) The effects of medication adherence programs consisting of education. (C) The effects of medication adherence programs consisting of telehealth and counseling.
CI, confidence interval; MOS, Medical Outcomes Study; MAQ, Medication Adherence Questionnaire; IAGAM, Global Evaluation of Medication Adherence; MMAS-8, Morisky Medication Adherence Scale-8.

Discussion

This study conducted a systematic review and meta-analysis to integrate and analyze the results of RCTs that investigated the effectiveness of medication adherence-related intervention programs for older patients with chronic illnesses. Quality assessments with the Cochrane's Risk of Bias tool were performed for the 7 selected studies, and all showed a low risk of bias. However, 3 studies were assessed as unclear for sequence generation, 5 as unclear for allocation concealment, and 4 as unclear for blinding of participants, personnel, and outcome assessors. The types of medication adherence interventions for older adults with chronic illnesses applied in the 7 selected studies included an educational program based on the health belief model [21], a remote medication monitoring program [22], a structured pharmacist-led intervention [23], a pharmacist-led care program [24], a complex intervention on prioritizing multiple medications [25], a motivational interviewing program [26], and an implementation intention intervention [27].

Yazdanpanah et al. [21] used the health belief model for older adult patients, based on the assumption that their belief in the effectiveness of prescribed medications would determine their medication adherence and use of appropriate medications. The program aimed to raise awareness about the possibility and severity of the corresponding diseases, induce behavioral triggers, and inspire confidence in behaviors, considering the perceived benefits and disadvantages of behavioral changes. Changes in the beliefs of older adults in the low-rate medication adherence stage resulted in a significant improvement in medication adherence post-intervention [21]. The remote medication monitoring program implemented by Hale et al. [22] applied telemonitoring and telehealth

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medication adherence technologies, and was reported to be a helpful intervention to improve patient self-management and quality of patient care; furthermore, it reduced health care utilization and expenditures for patients with chronic diseases requiring complex medication regimens.

Medication adherence telehealth interventions have been reported to act as patient education systems to enhance health literacy, pharmacist consultations, phone-based adherence assessments and positive behavior encouragement, and electronic reminders, thereby improving medication adherence [28]. It is necessary to monitor the health status of older adults with chronic illnesses in real time for regular administration of medications and health management, as well as to provide customized health management information accordingly. Therefore, telephone-based intervention methods can replace some face-to-face meetings between patients and medical staff in the context of chronic disease management and help maintain the quality and quantity of care.

Abdulsalim et al. [23] reported that enhancing patient self-efficacy as part of self-management education was important to promote long-term adherence. Self-efficacy is a key factor that influences human motivation and behavior, and the most important factor in determining the relationship between knowledge and behavior [29]. Furthermore, self-efficacy can play an important role in changing medication adherence habits into desirable behaviors and sustaining them. Older adults could experience physical and cognitive difficulties with the daily intake of specialized and complex medications, resulting in low self-efficacy and confidence in relation to proper medication adherence. Participation from pharmacists, who are experts on medication, in shared decision-making during the initial and regular follow-up visits helped improve patient self-efficacy associated with taking medications and augmented the partnership between patients and physicians, thereby facilitating adherence, improving patient outcomes, and diminishing economic and social burdens [23]. The pharmacist-led care program educated patients regarding correct medication use, reinforced treatment adherence, and developed their knowledge on drug therapy and health conditions [24].

According to Moral et al. [26], a face-to-face motivational approach in primary care could help older patients with chronic diseases receiving polypharmacy treatment improve treatment adherence to a greater degree than usual care for providing information and advice. Motivational interviewing is a counseling method that involves enhancing a patient's motivation to change behavior [30]. Moral et al. [26] used (1) assessment of ambivalence, (2) exploration of patients' ideas and concerns about their lack of adherence, and (3) application of specific interviewing skills to reframe and promote self-efficacy (e.g., empathy, developing discrepancies, avoiding arguments, confronting barriers and problems, and supporting the patient) through motivational interviewing as an experimental intervention, and obtained significant results. The strategies reported by Trevisan et al. [27] strategies for coping planning encouraged patients to anticipate barriers to taking their medication and formulate strategies to overcome them. Cognitive-behavioral coaching to improve patients' coping ability is an integrated approach that combines cognitive, behavioral, and imaginary problem-solving techniques and strategies within a cognitive-behavioral model to achieve realistic goals set by the patient [31]. This is expected to be helpful in promoting medication adherence in older adults, as it can help them overcome real problems and address the emotional, psychological, and behavioral difficulties that hinder their performance and goal achievement.

Of the 7 studies, 5 selectively applied interventions to patients with certain chronic illnesses (hypertension, chronic heart failure, COPD, and diabetes), and 2 selected participants with "chronic diseases." There were 3 studies on pharmacist- and physician-led counseling and consultation [23,25,26], 2 on educational programs including lectures [21] and face-to-face education [24], 2 on interventions that used group discussions [21,23], and 2 that used medication monitoring systems and telephone monitoring [22,27]. Individual counseling and consultation methods were generally tailored to the characteristics and severity of chronic diseases, with varying precautions for administration. Routine monitoring of daily drug administration was required, and educational methods involving lectures by experts and group discussions with individuals with chronic diseases were effective, given older adults' general level of knowledge about medications and the need to provide accurate information on new medications. In most of the selected studies, usual or standard hospital care was provided to the control group, and 2 studies evaluated the results through follow-up.

Considering the total effect of the applied medication adherence intervention programs, taking medications is important for older adults with chronic illnesses, and interventions beyond usual or standard hospital care are required. It is important to evaluate long-term effects in chronic disease management; therefore, follow-up to assess program effectiveness needs to be considered as an important component in program development. The Morisky-Green test, which was used in 3 studies, was the most commonly used tool to measure medication adherence; other tools included

the MMAS-8, MAQ, and IAGAM. The Morisky-Green test evaluates whether patients forget to take medication, are careless about taking medication, or stop taking medication when their health status improves or worsens [32]. According to Roy et al. [6], levels of medication adherence may differ according to the measurement tool used to assess older adults taking multiple medications. Thus, when selecting high-risk groups for medication adherence, careful selection of assessment tools is necessary.

For the 7 studies included in the systematic review, the total effect size was medium (Hedges' $g = 0.500$), which was statistically significant when calculated using a random-effects model in consideration of heterogeneity. Of the medication adherence programs, the implementation intention intervention applying face-to-face meetings and telephone monitoring with individualized behavioral strategies [27] and the educational program based on the health belief model [21] were highly effective, with Hedges' g values of 0.8 or higher. The most effective interventions related to medication adherence reported in previous studies were tailored to the client and included aspects of counseling (e.g., education, motivational interviewing, CBT) [33]. The implementation intention intervention [27] was tailored with an elaboration of action and coping plans and their respective strategies. Kim [34] reported that older adults with chronic illnesses who took many medications, but did not know their exact administration methods or purpose of medication use, misused medications by re-using them after the expiration date, sharing them with others, or arbitrarily changing the timing of administration. However, compliance with medication adherence can be improved only if interventions are applied in a way that depends on physical, psychological, and functional factors for each older patient [35]. This should be followed by the use of other adherence-targeting interventions tailored to patients' individual needs. It is also necessary to identify older adults' health beliefs regarding taking medications, understand the obstacles in changing those beliefs, and devise strategies to adjust them.

Based on the results of the effect size analysis according to intervention method, face-to-face meetings had a significant effect, whereas education and meetings via telehealth did not. In particular, neither interventions focused on face-to-face education [24] nor monitoring via telehealth [22] had significant effects. However, both education based on the health belief model [21] and telehealth with utilization of CBT were found to be effective interventions for older adults with chronic illnesses [27]. Thus, intervention programs for older adults with chronic illnesses should mainly utilize face-to-face meetings, while education based on the health belief model and CBT can enhance interventions' effects. However, since only a small number of studies were ultimately selected for review, it is difficult to generalize the results of this meta-analysis. As another limitation of this study, it was conducted according to the PRISMA guidelines for reporting systematic literature reviews, but this review was not registered.

Conclusion

This study conducted a meta-analysis based on a systematic literature review of RCTs for medication adherence programs applied to older patients with chronic illnesses conducted in the last 10 years. Of the 7 medication adherence programs, an implementation intention intervention based on face-to-face meetings and telephone monitoring with individualized behavioral strategies and an educational program based on the health belief model were highly effective. Meeting face-to-face was found to be a more effective method than education and meeting via telehealth for implementing medication adherence intervention programs for older adults with chronic illnesses. Future studies should devise intervention strategies with impacts on physical and psychological health related to medication adherence in older adults for integrated health management.

In this study, we determined the characteristics and application methods of interventions that are helpful in improving medication adherence in older patients with chronic illnesses. We confirmed that interventions including individualized behavior modification strategies and cognitive behavioral coaching strategies based on health beliefs could be helpful in improving medication adherence among older adults.

Notes

Ethics Approval

This study was exempted from a review by the Institutional Review Board of Cheongju University, the institution of the lead researcher, to ensure ethical and scientific validity for the overall research (approval number: 1041107-201904-HR-017-01).

Conflicts of Interest

The authors have no conflicts of interest to declare.

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Availability of Data

The datasets are not publicly available but are available from the corresponding author upon reasonable request.

Authors' Contributions

Conceptualization: HOJ; Methodology: HOJ; Data curation: HOJ, MOC,

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AK; Formal analysis: HOJ, MOC, AK; Supervision: HOJ; Software: HOJ; Validation: HOJ; Investigation: HOJ; Funding acquisition: HOJ; Project administration: HOJ; Resources: HOJ; Visualization: HOJ; Writing original draft: HOJ; Writing-Review & Editing: HOJ, MOC, AK.

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References

1. Midao L, Giardini A, Menditto E, et al. Adherence to medication in older adults as a way to improve health outcomes and reduce healthcare system spending. In: D'Onofrio G, Greco A, Sancarlo D, editors. Gerontology. London: IntechOpen; 2017. p. 38–45.
2. Ministry of Health and Welfare, Korea Institute for Health and Social Affairs (KIHASA). 2017 national survey of older Koreans [Internet]. Sejong: KIHASA; 2018 [cited 2019 Sep 9]. Available from: https://meta.narastat.kr/metasvc/index.do?confmNo=117071. Korean.
3. Organisation for Economic Co-operation and Development (OCED). OECD health statistics 2019 [Internet]. Paris: OCED; 2019 [cited 2020 Mar 31]. Available from https://stats.oecd.org/Index.aspx?ThemeTreeId=9.
4. Cook PF, Schmiege SJ, Mansberger SL, et al. Motivational interviewing or reminders for glaucoma medication adherence: Results of a multi-site randomised controlled trial. Psychol Health 2017;32:145–65.
5. Nelson LA, Mulvaney SA, Gebretsadik T, et al. The MEssaging for Diabetes (MED) intervention improves short-term medication adherence among low-income adults with type 2 diabetes. J Behav Med 2016;39:995–1000.
6. Roy NT, Sajith M, Bansode MP. Assessment of factors associated with low adherence to pharmacotherapy in elderly patients. J Young Pharm 2017;9:272–6.
7. Yap AF, Thirumoorthy T, Kwan YH. Medication adherence in the elderly. J Clin Gerontol Geriatr 2016;7:64–7.
8. Bolarinwa OA, Juni MH, Nor Afiah MZ, et al. Mid-term impact of home-based follow-up care on health-related quality of life of hypertensive patients at a teaching hospital in Ilorin, Nigeria. Niger J Clin Pract 2019;22:69–78.
9. Chen C, Li X, Sun L, et al. Post-discharge short message service improves short-term clinical outcome and self-care behaviour in chronic heart failure. ESC Heart Fail 2019;6:164–73.
10. Ferguson A, Ibrahim FA, Thomas V, et al. Improving medication adherence in rheumatoid arthritis (RA): a pilot study. Psychol Health Med 2015;20:781–9.
11. Inauen J, Bierbauer W, Luscher J, et al. Assessing adherence to multiple medications and in daily life among patients with multimorbidity. Psychol Health 2017;32:1233–48.
12. Farmer A, Hardeman W, Hughes D, et al. An explanatory randomised controlled trial of a nurse-led, consultation-based intervention to support patients with adherence to taking glucose lowering medication for type 2 diabetes. BMC Fam Pract 2012;13:30.
13. Kim JY, Wineinger NE, Steinhubl SR. The influence of wireless self-monitoring program on the relationship between patient activation and health behaviors, medication adherence, and blood pressure levels in hypertensive patients: a substudy of a randomized controlled trial. J Med Internet Res 2016;18:e116.
14. Farazian F, Emami Moghadam Z, Heshmati Nabavi F, et al. Effect of self-care education designed based on Bandura's self-efficacy model on patients with hypertension: a randomized clinical trial. Evid Based Care J 2019;9:44–52.
15. Plant N, Mallitt KA, Kelly PJ, et al. Implementation and effectiveness of 'care navigation', coordinated management for people with complex chronic illness: rationale and methods of a randomised controlled trial. BMC Health Serv Res 2013;13:164.
16. Higgins JP, Green S. Cochrane handbook for systematic reviews of interventions version 5.1.0 [Internet]. London: The Cochrane Collaboration; 2011 [updated Mar 2011; cited 2014 Jun 9]. Available from: https://handbook-5-1.cochrane.org/.
17. Moher D, Liberati A, Tetzlaff J, et al. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. Ann Intern Med 2009;151:264–9.
18. Hwang SD. Meta-analysis. Seoul: Hakjisa Corporation; 2014. Korean.
19. Borenstein M, Hedges LV, Higgins JPT, et al. Introduction to meta-analysis. West Sussex: Wiley & Sons; 2009.
20. Hedges LV, Olkin I. Statistical methods for meta-analysis. Orlando: Academic Press Inc.; 1985.
21. Yazdanpanah Y, Saleh Moghadam AR, Mazlom SR, et al. Effect of an educational program based on health belief model on medication adherence in elderly patients with hypertension. Evid Based Care J 2019;9:52–62.
22. Hale TM, Jethwani K, Kandola MS, et al. A remote medication monitoring system for chronic heart failure patients to reduce readmissions: a two-arm randomized pilot study. J Med Internet Res 2016;18:e91.
23. Abdulsalim S, Unnikrishnan MK, Manu MK, et al. Structured pharmacist-led intervention programme to improve medication adherence in COPD patients: a randomized controlled study. Res Social Adm Pharm 2018;14:909–14.
24. Korcegez EI, Sancar M, Demirkan K. Effect of a pharmacist-led program on improving outcomes in patients with type 2 diabetes mellitus from Northern Cyprus: a randomized controlled trial. J Manag Care Spec Pharm 2017;23:573–82.
25. Muth C, Harder S, Uhlmann L, et al. Pilot study to test the feasibility of a trial design and complex intervention on PRIoritising MUltimedication in Multimorbidity in general practices (PRIMUMpilot). BMJ Open 2016;6:e011613.
26. Moral RR, Torres LA, Ortega LP, et al. Effectiveness of motivational interviewing to improve therapeutic adherence in patients over 65 years old with chronic diseases: a cluster randomized clinical trial in primary care. Patient Educ Couns 2015;98:977–83.
27. Trevisan DD, Sao-Joao T, Cornelio M, et al. Effect of an 'implementation

intention' intervention on adherence to oral anti-diabetic medication in Brazilians with type 2 diabetes. Patient Educ Couns 2020;103:582–8.
28. Kvedar J, Coye MJ, Everett W. Connected health: a review of technologies and strategies to improve patient care with telemedicine and telehealth. Health Aff (Millwood) 2014;33:194–9.
29. Bandura A. Self-efficacy: the exercise of control. New York: W. H. Freeman and Company; 1997.
30. Rollnick S, Miller WR, Butler CC. Motivational interviewing in health care: helping patients change behavior. New York: Gilford Press; 2008.
31. Palmer S, Szymanska, K. Cognitive behavioral coaching: an integrative approach. In: Palmer S, Whybrow A, editors. Handbook of coaching psychology: a guide for practitioners. London: Routledge; 2007. p. 86–117.
32. Morisky DE, Green LW, Levine DM. Concurrent and predictive validity of a self-reported measure of medication adherence. Med Care 1986;24:67–74.
33. Nieuwlaat R, Wilczynski N, Navarro T, et al. Interventions for enhancing medication adherence. Cochrane Database Syst Rev 2014; 2014:CD000011.
34. Kim JS. Experiences of medication misuse and abuse behaviors in elderly people with chronic disease in community. J Korea Contents Assoc 2016;16:791–805.
35. Jeon HO. Correlation of physical, psychological, and functional factors with independent medication adherence in Korean older adults with chronic illness: using the 2017 national survey of older Koreans. Arch Gerontol Geriatr 2020;90:104130.

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