Old age is defined as an age higher than 65 and 60 in developed and developing countries, respectively (1). The aging population is progressively growing worldwide. According to the 2011 national census in Iran, there were more than six million people with an age of more than sixty in Iran, comprising 8.2% of the total population of the country (2).

Because of age-related physiological changes, older adults are at the risk of various health problems including cardiovascular diseases (3). On the other hand, one out of two older adults suffers from cardiovascular problems. Currently, around half of people over 60 suffer from severe coronary artery stenosis and more than 50% of them show no symptoms (4). Cardiovascular disease is associated with high disability and mortality rates, low quality of life, massive costs, and a medley of social problems (5, 6). The obtained data from eighteen provinces of Iran indicate that cardiovascular disease is responsible for 46% of all deaths (7).

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The Effect of Pillbox Use on Medication Adherence Among Elderly Patients: A Randomized Controlled Trial

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Abstract

Background: Poor medication adherence may cause unfortunate consequences such as disease progression and even death, particularly in older adults. This study aimed to evaluate the effect of pillbox use on medication adherence among older adults with cardiovascular diseases.

Materials and Methods: This study was conducted as a two-group randomized controlled trial in a clinic in Kerman, Iran in 2017. Participants included seventy patients who were randomly allocated to either a control or an intervention group. The patients in the intervention group were verbally educated to manage their medications using a pillbox for four consecutive weeks while their counterparts received their medications without the use of any drug reminders.

Results: The mean score of all participants’ medication adherence was 4.02 ± 2.19 at the beginning of the study. Medication adherence significantly improved in the intervention group during the study (P < 0.001) while it remained poor in the control group (P > 0.99). Finally, medication adherence was significantly better in the intervention group compared to the control group at the end of the study (P = 0.001).

Conclusion: In general, pillbox use can promote medication adherence in older adults with cardiovascular diseases thus it is recommended for improving medication adherence and minimizing the consequences of non-adherence.

Keywords: Cardiovascular disease, Medication adherence, Elderly, Pillbox

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of an individual's behavior with health care providers' recommendations (12). According to estimates, the rate of medication adherence among older adults is 27.8%-75%. This rate grows with an increase in the duration of treatment and the number of medications (13, 14). Forgetfulness is another factor behind older adults' medication adherence (15). A study on 24000 adult patients demonstrated that 62% of them forgot to take their medications (16). Poor medication adherence is associated with different problems and complications, mainly frequent re-hospitalizations, disease progression, symptom aggravation, and even death (13, 14). Around 33%-66% of all re-hospitalizations are attributed to poor medication adherence (17).

The use of simple drug reminders (18) such as pillboxes is considered as a potentially useful and cost-effective method for overcoming older adults' forgetfulness and promoting their medication adherence (19). Pillboxes, also known as pill organizers, can increase medication adherence by 53%-68% (20), help older adults to have an independent life, and facilitate achieving the treatment outcomes (20, 21). A systematic review of thirty studies on the effects of drug reminders has endorsed their positive impact on medication adherence (22). Contrarily, several studies found that pillbox use can be ineffective in promoting medication adherence (23, 24).

Despite the importance of medication adherence for patient outcomes, few interventional studies have focused on this issue in Iran. Moreover, to the best of our knowledge, no research is available regarding the effects of pillboxes on medication adherence in Iran. Therefore, the present study sought to evaluate the impact of pillbox use on medication adherence among older adults with cardiovascular diseases.

**Material and Methods**

**Sampling Procedures**

This randomized controlled trial was conducted in the Social Security Clinic of Kerman, in the southeast of Iran. Participants included seventy older adults with cardiovascular diseases. The sample size was estimated to be 35 per group according to earlier interventional study results (25), with a power of 0.90 and a confidence level of 0.95 ($\mu_1 = 52.13$, $S_1 = 3.5$; $\mu_2 = 56.53$, and $S_2 = 4.45$). All included participants completed the study.

The eligible participants were selected by using the convenience sampling method. In addition, the inclusion criteria were an age of 60 years ol or higher, a history of at least one cardiovascular disorder (i.e., acute coronary syndrome, hypertension, congestive heart failure, myocardial infarction, or atrial fibrillation) as determined by a cardiologist, the consumption of at least four medications daily, access to the telephone for follow-up assessments, no history of cognitive problems such as different types of dementia, and physical ability to fill the pillbox. On the other hand, participants were excluded if they experienced any changes in their treatment regimen, were hospitalized, or changed their place of residence during the study.

The selected participants were randomly allocated to either a control or an intervention group using the drawing lots method. Accordingly, 35 cards labeled 1 (the intervention) and 35 cards marked 2 (control) were prepared, and each newly recruited participant was asked to select a random card. Based on the label on the selected card, the patient was assigned to either of the groups and random assignment was performed after baseline data collection.

**Measurements**

A socio-demographic and clinical characteristics questionnaire and Morisky Medication Adherence Scale-8 were used to collect the data. The items of the first tool were age, gender, marital and employment status, educational level, the duration of suffering from the cardiovascular disease, the type of cardiovascular disease, the number of medications taken daily, and blood pressure. The eight-item Morisky Medication Adherence Scale included seven Yes/No questions and one item scored on a five-point Likert-type scale as “Never/rare”, “Once in a while”, “Sometimes”, “Often”, “Usually and all the time”. The possible total score of the scale could range from 0 to 8 and scores less than 6, 6-8, and equal to 8 were considered as poor, moderate, and very high medication adherence, respectively (26). A former study in Iran reported a Cronbach's alpha of 0.72 for the scale (27).

**Data Collection**

Participants of the intervention group, together with one of their family members received verbal education about filling the pillbox, and each of them was provided with one. Then, they were allowed to fill their pillboxes under the first author’s supervision and guidance. Afterward, they were asked to use their pillboxes for organizing their medication for four weeks and then refer to the study setting at the end of the four-week course of the intervention. However, those in the control group were provided with neither pillbox nor pillbox-related education. All participants were asked to complete the medication adherence scale at the beginning of the study and four weeks afterward.

The applied pillbox in this study was a seven-day four times a day pillbox (Fanavar Teb Spadana Company, Yazd, Iran). The box had seven columns for a whole week labeled by weekday names and four cells for each day marked Morning, Noon, Evening, and Night (28 cells in total). The door of the cells was made out of transparent plastic. Further, the pillbox had a low price and an adequate place for several medications and could be bought from pharmacies and medical supply stores in Kerman province, Iran.
Data Analysis
The data were analyzed using SPSS, version 18.0. Given the normal distribution of all study variables, within- and between-group comparisons respecting medication adherence were performed via the paired- and independent-sample t tests, respectively. Eventually, between-group comparisons regarding participants' baseline characteristics were made through the chi-square and the independent-sample t tests. The level of significance in all statistical tests was set at less than 0.05.

Results
The mean age of the participants was 71.21 ± 7.9 and most of them (52.9%) were males, had primary education (51.4%), were married (78.6%), and were diagnosed with myocardial infarction (41.4%). The duration of cardiovascular disease among 62.8% of participants was more than three years. Furthermore, the mean number of taken daily medications was 7.8 ± 3.28. Moreover, participants’ demographic and clinical characteristics were not different between the two groups (P > 0.05), the details of which are provided in Table 1.

Additionally, the total mean score of medication adherence among all study participants was 4.02 ± 2.19 at the beginning of the study, showing poor medication adherence. The mean score of medication adherence significantly increased from 4.28 ± 1.84 in the pretest to 6.74 ± 2.17 in the posttest in the intervention group (P < 0.001). However, the results (Table 2) indicated that medication adherence did not change dramatically in the control group (P > 0.99). In addition, the pretest mean scores of medication adherence were not different between the study groups (P = 0.16). On the other hand, the mean score of medication adherence was significantly higher after the intervention, in the intervention group compared to the control group (P = 0.001), related data are presented in Table 2. More precisely, medication adherence improved in the intervention group compared to the control group.

Further, 57.14% (n = 20) of the participants of the intervention group had poor medication adherence at the beginning of the study while only 11.4% (n = 4) of them had poor medication adherence at the end of the study. In the control group, 65.7% (n = 23) of participants had poor medication adherence at the beginning of the study while 60% (n = 21) of them had poor medication adherence at the end of the survey (Table 3).

Discussion
The findings revealed that participants suffered from polypharmacy and poor medication adherence while pillbox use significantly improved medication adherence. Our participants took more than seven pills a day, denoting that they suffered from polypharmacy. Similarly, previous studies reported that older adults took 4-8 different types

Table 1. Participants’ Baseline Demographic and Clinical Characteristics

| Variable            | Group                        | Statistical Test | P Value |
|---------------------|------------------------------|------------------|---------|
|                     | Intervention (n = 35)        | Control (n = 35) |         |
| Age (y), mean ± SD  | 71.25 ± 8.05                 | 71.17 ± 7.87     | t = 0.045 | 0.964 |
| Total prescribed medications (Daily), mean ± SD | 7.94 ± 2.31 | 6.08 ± 1.75 | t = 3.784 | 0.060 |
| Sex, No. (%)        | Male                        | Female           | χ² = 0.057 | 0.811 |
|                     | 18 (51.4)                   | 17 (48.6)        |         |
|                     | Female                      | 19 (54.2)        |         |
|                     | 16 (45.7)                   |                 |         |
| Education, No. (%)  | Primary                     | High school      | χ² = 0.262 | 0.882 |
|                     | 19 (54.3)                   | 12 (34.3)        |         |
|                     | Primary                     | Academic         |         |
|                     | 17 (48.6)                   | 4 (5.7)          |         |
|                     | High school                 | 13 (37.1)        |         |
| Type of disease, No. (%) | HTN                     | CHF              |         |
|                     | 2 (5.7)                     | 6 (17.1)         |         |
|                     | MI                          | 14 (30)          | χ² = 1.826 | 0.870 |
|                     | ACS                         | 10 (28.6)        |         |
|                     | AF                          | 3 (8.6)          |         |
| Duration of disease, No. (%) | Six months to 1 year | 1-3 years(s) | >3 years |         |
|                     | 2 (5.7)                     | 3 (28.6)         | 23 (65.7) |         |
|                     | 1 (2.9)                     | 13 (37.1)        | 21 (60)  |         |
|                     | 1 (2.9)                     |                 |         |

Note: SD: Standard deviation; HTN: Hypertension; CHF: Chronic heart failure; MI: Myocardial infarction; ACS: Acute coronary syndrome; AF: Atrial fibrillation.
of medication daily (9-11, 28). Such a high number of drugs taken daily in our research is attributable to the over-the-counter use of medications among Iranians, the easy accessibility of most medications in Iran, and the physicians’ prescription of new medications without obtaining a complete drug history (29, 30).

Another finding of the present study was the participants’ poor medication adherence at the beginning of the study. Previous research reported that the rate of medication adherence among older adults ranged from 27.8% to 75% (15), which is in line with the finding of the current study. Another study demonstrated that more than half of older adults with hypertension discontinued their medications during the first year of treatment and those who continued their medications had poor adherence (26). Forgetfulness due to memory impairments is one of the most common reasons behind poor medication adherence (17, 28). Studies are needed to provide more detailed information about factors contributing to older adults’ poor medication adherence.

Our findings indicated the effectiveness of one-month pillbox use in promoting medication adherence among older adults. Similarly, a former study reported that pillbox use improved medication adherence by 53%-68% (20). Moreover, 85% of patients in another study represented that pillbox use helped them to effectively manage their medications (31). Based on the findings of another study, a significant positive correlation was found between pillbox use and medication adherence so that the medication adherence rate was 28% higher among patients who regularly used a pillbox compared to others and patients were satisfied with using it (28). The results of a systematic review of thirty studies also showed the effectiveness of drug reminders such as pillboxes in promoting medication adherence (23). The positive effects of pillbox use on medication adherence are attributable to its reminder effects. Considering that forgetfulness is a significant factor behind poor medication adherence (16, 31), coming across the pillbox during other daily activities can instantly remind patients of their medications and may compel them to check whether they have taken their drugs or not. Moreover, pillboxes are small and light devices, and patients can easily carry them in their bags when they are on a trip, at work, or parties. Besides, their use is straightforward, and hence, patients can independently use them to manage their medications.

Contrary to our findings, one study reported the ineffectiveness of pillbox use in promoting medication adherence among patients with hypertension (23). Another study on patients with chronic conditions showed that simple, inexpensive drug reminders such as pillboxes are not effective in promoting medication adherence (24). Such discrepancies among studies are attributed to the type of pillbox and the type of tools that were used in the studies for medication adherence assessment. The present study used the self-report Morisky Medication Adherence Scale although medication adherence in the above-mentioned studies was assessed using the medication possession ratio. This ratio is calculated through dividing the doses of medications taken by the total prescribed doses and medication possession ratios of 80 or more are considered as good medication adherence. On the other hand, this study evaluated drug adherence to all medications of the patient while the results of a survey revealed that drug adherence varies according to

| Table 2. Participants’ Medication Adherence Before and After the Study |
|---------------------------------|-----------------|-----------------|----------------|-----------------|-----------------|
| Group                          | Time            | Paired T Test   | P Value        | After-Before Difference (Mean ± SD) |
| Intervention                   | Before (Mean ± SD) | After (Mean ± SD) |                |                  |
|                                 | 4.28 ± 1.84     | 6.74 ± 1.17     | 5.44           | < 0.001          | 2.46 ± 2.7      |
| Control                        | 3.91 ± 2.17     | 4 ± 1.91        | 0.001          | > 0.99           | 0.09 ± 1.89     |
| Independent t-test             | 1.59            | 3.62            |                |                  | 2.37            |
| P value                        | 0.16            | 0.001           |                |                  | < 0.001         |

Note: SD: Standard deviation.

| Table 3. The Frequency of Good and Poor Medication Adherence Before and After the Study in Both Groups |
|---------------------------------|-----------------|-----------------|----------------|-----------------|-----------------|
| Group                          | Time            | Medication Adherence Before Intervention | Medication Adherence After Intervention |
|                                |                 | No. (%) | No. (%)          |                  |
| Intervention                   | Moderate        | 15 (42.86) | 31 (88.6)        |                  |
|                                | Poor            | 20 (57.14) | 4 (11.4)         |                  |
| Control                        | Moderate        | 12 (34.3)  | 14 (40)          |                  |
|                                | Poor            | 23 (65.7)  | 21 (60)          |                  |
| χ²                             | 2.837           | 7.47     |                  |                  |
| P value                        | 0.15            | 0.01     |                  |                  |
the drug class, and therefore, it was suggested to measure drug adherence to each drug category separately (29). The differences can be explained in relation to the influence of factors such as the patient's perception of the disease, the patient's perspective on drug use, and the burden of the disease on drug adherence (30).

The present study had some limitations. All participants were provided with the same type of pillbox irrespective of their underlying cardiovascular disease and the number of medications taken daily. Thus, future studies are recommended to use pillboxes based on the patients' needs, daily medications, and manual dexterity. Although none of our participants reported problems such as the accidental opening of cell doors in using the pillbox, some of them were dissatisfied with the small space in its cells. Accordingly, it is recommended that these patients use pillboxes with larger cells.

In our study, older adults with cardiovascular diseases suffered from polypharmacy, and poor medication adherence and pillbox use significantly promoted their medication adherence. Given the significant consequences of poor medication adherence, the use of pillbox is recommended to encourage medication adherence and to improve treatment outcomes among older adults with chronic conditions, particularly cardiovascular diseases.

Conflict of Interest Disclosure
The authors have no conflict of interests.

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Ethical Statement
The protocol of this study was approved by the Ethics Committee of Rafsanjan University of Medical Sciences (code: IR.RUMS.REC.1396.97) and registered in the Iranian Registry of Clinical Trials (identifier: IRCT20160503027736N5). In addition, participants were provided with explanations regarding the aims of the study and were ensured of data confidentiality and the lack of the effect of their responses on provided healthcare services. Finally, data collection tools were anonymous and included no identification symbols or numbers.

Author's Contribution
In this article, the first, second, third, and fourth authors were responsible for collecting data, contributing to the writing of the article, analyzing the data, editing the article and supervising the entire research process, and writing the article, respectively.

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Informed Consent
All participants signed written informed consent.

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