

*Review Article***Effect of early palliative care on caregivers of adult patients with chronic diseases: A systematic review and meta-analysis of randomized controlled trials**Amir Mohammad Kabirirad ^a | Vahid Gholamkar ^b | Samira Kor ^b | Akram Bahranifard ^a  | Amir Hossein Hazrati ^{a*}

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Abstract

The aim of this research was to examine the effects of early palliative care on individuals who provide care for adult patients with chronic diseases. From the earliest date until November 1, 2022, the databases of Scopus, PubMed, Web of Science, Iranmedex, and Scientific Information Database were thoroughly searched using purpose-related keywords. To rate the caliber of randomized control trials and quasi-experimental research, the Joanna Briggs Institute (JBI) critical evaluation checklist was utilized. A total of 800 patients with chronic disease were included in five studies. This study demonstrated that early palliative care treatments had a similar impact on caregivers' quality of life (QoL) as routine care and delayed palliative care interventions (ES: -0.01, 95%CI: -0.20 to 0.17, Z=0.15, I²:0.0%, P=0.88). As compared to the normal care group, the early care group's caregivers' depression was modestly reduced by the intervention, but this difference was not statistically significant (ES: -0.06, 95%CI: -0.36 to 0.23, Z=0.43, I²:0.0%, P=0.67). Early palliative care reduced caregiver anxiety, however, the difference between the intervention group and the group receiving standard care was not statistically significant (ES: -0.25, 95%CI: -0.64 to 0.15, Z=1.23, I²:0.0%, P=0.22). Caregivers' burdens were reported based on three dimensions demand, stress, and objective. Results found the intervention caused a non-significant decrease in the demand dimension (WMD: -0.48, 95% CI: -1.13 to 0.17, Z=1.44, I²:0.0%, P=0.15) and a significant decrease in the stress dimension (WMD: -0.65, 95% CI: -1.26 to -0.04, Z=2.09, I²:0.0%, P=0.04), in the intervention group compared to the routine care. In contrast, the intervention did not affect the objective dimension (WMD: 0.30, 95%CI: -0.48 to 1.08, Z=0.76, I²:0.0%, P=0.45) in the intervention group than in routine care. Therefore, it is suggested that more interventional studies be conducted in this area in the future.

Keywords: Palliative Care, Chronic Disease, Caregivers, Caregiver Burden, Meta-analysis.**1 | Introduction**

Patients who are in the final stages of the disease require special care from family and friends (caregivers) [1]. On the other hand, caring for this group of patients necessitates great levels of strength and endurance and frequently puts a major strain on the caregivers' quality of life (QoL) and mental health [2]. Since most of the necessary care for patients in the end stages of the disease is the responsibility of the caregivers, therefore it is vital to pay attention to the psychological needs of the caregivers to provide high-quality care to the patients [3].

Although palliative care is provided for patients at the end of life, its early initiation at the beginning of the final stage of the disease

and its combination with common care in patients reduces a wide range of complications [4, 5]. To lessen caregiver anxiety and ultimately help caregivers manage their patients effectively, palliative care professionals view supporting patients' caregivers as a crucial component of their work [6]. Clinicians and nurses may reduce the discomfort and problems of caregivers by promoting and strengthening coping abilities and providing effective self-care methods [7]. The perspective of early palliative care is aimed at improving patients' symptoms and assessing and managing the psychological and social needs of patients and their caregivers [8, 9]. Early palliative care has been linked to higher levels of care

satisfaction in caregivers of patients with advanced cancer, according to a Canadian study [10]. A study from the United States also revealed that early palliative care for patients with lung and gastrointestinal cancers lowers caregivers' feelings of worry and depression [11].

To our knowledge, no published studies have reviewed and summarized findings about the effects of early palliative care on patient caregivers. Prior research has evaluated how early palliative care affects patients' caregivers. In light of the importance of the subject and the conflicting results addressing the effect of early palliative care on patients, this research was performed to investigate the impact of early palliative care on caregivers of adult patients with chronic conditions.

2 | Methods

2.1 | Study registration and reporting

The procedures utilized to carry out this systematic review were according to the checklist of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) [12]. Additionally, there is no record of this systematic review in the international prospective register of systematic reviews (PROSPERO) database.

2.2 | Search strategy

With the help of keywords taken from Medical Subject Headings, such as "Palliative care", "Chronic disease", "Caregivers", and "Caregivers burden", a thorough systematic search was carried out in several international electronic databases, such as PubMed, ISI, Scopus, and Persian electronic databases, including Iranmedex. The search strategy was in PubMed including ("Palliative care") OR ("Palliative therapy") OR ("Early palliative care") OR ("Early palliative therapy") AND ("Chronic disease" OR ("Chronic illness")) AND ("Caregivers") OR ("Patient caregivers") OR ("Caregivers burden"). Boolean operators "AND" and "OR" were employed to combine terms. The Persian equivalent of the aforementioned keywords was used to search Persian electronic databases. Two researchers independently carried out the systematic search process. This review study excludes gray literature, which includes expert comments, conference presentations, dissertations, research and committee reports, and ongoing research. Gray literature refers to articles that have been published electronically but have not been reviewed by a for-profit publisher [13].

2.3 | Inclusion and exclusion criteria

Interventional studies that focused on the effect of early palliative care on adult patients with chronic disease caregivers were included in this meta-analysis. This study did not include letters to the editor, case studies, conference papers, cross-sectional studies, research using qualitative designs, or reviews.

2.4 | Study selection

The systematic review's data management tool of choice was EndNote 8X. According to the inclusion and exclusion criteria, the two researchers selected the studies for the present research, independently. The title, abstract, and full text of the articles were evaluated and duplicate papers were removed. References of the selected papers were evaluated to avoid missing articles.

2.5 | Data extraction and quality assessment

Publications included in this systematic review were analyzed for data on the first author, year of publication, location, sample size, age, control group, male/female ratio, tool characteristics, and key findings. To rate the caliber of randomized control trials (RCTs) and quasi-experimental research, the Joanna Briggs Institute (JBI) critical evaluation checklist was utilized [14]. This instrument evaluates 13 and 9 items from RCT and quasi-experimental trials, respectively, for internal validity, participant similarity between compared groups, measurement accuracy, and suitability of statistical analysis. Two researchers independently assessed each study's quality in the systematic review using a three-point scoring methodology that included "yes" (score 1), "no" (score 0), and "not applicable / not clear" (score 0) [15]. The JBI checklists' quality assessment ratings for the studies are good (≥ 8), fair (6-7), and poor (≤ 5) [14].

2.6 | Statistical analysis

The meta-analysis was performed with STATA version 14 software. To determine the effect size of caregivers' QoL; sample size, mean change, and standard deviation (SD) change in both intervention and routine care groups were extracted from the articles. Due to the use of a different questionnaire to measure this outcome, Standard Mean Difference (SMD) was determined to report the effect size (ES). For the outcome of anxiety, one study reported the data in the form of mean and standard deviation, and another study reported the effect size, mean, and confidence interval (CI) of the changes in the two groups of intervention and routine care. Finally, the effect size and confidence interval of each study were calculated and the overall effect size was re-

ported based on ES and CI. Two studies also reported the outcome of caregivers' burden which had three dimensions (objective, demand, and stress). the overall effect size of each of them was reported separately using the mean and standard deviation of the changes. Weighted Mean Difference (WMD) was used to report the effect size of this outcome, considering that the same questionnaire was used in the two studies. The level of significance was assessed using a 95% confidence range. With I^2 , heterogeneity was examined. A low level of heterogeneity is defined as an I^2 value of 25%, a moderate level of 50%, and a high level of 75%. A fixed effect model was employed to report the results because each outcome's heterogeneity was less than 25%. The publishing of bias was not mentioned because there was so little research. Additionally, sensitivity analysis was carried out to assess how each study would affect the total effect size on the outcome of QoL.

3 | Results

3.1 | Study selection

A thorough search of electronic databases yielded a total of 2,238 studies. The elimination of 581 and 1,637 papers, respectively, came as a result of the further stages of examining duplicate research and scrutinizing the article's title and abstract. The full texts

of 14 articles were then evaluated in the subsequent stage; three articles were discarded for lacking the essential data, while six studies were eliminated due to issues with the design and undesirable results. Finally, five studies [10, 11, 16-18] were considered in the present research. A meta-analysis of four research [10, 11, 17, 18] was also carried out (Figure 1).

3.2 | Study characteristics

Five studies [10, 11, 16-18] comprised a total of 800 participants with chronic illnesses. The mean age of the participants was 56.90 (SD=12.32) years. 72.40% of the participants were female and 51.25% of them were in the intervention group. All papers [10, 11, 16-18] had an RCT design. The studies lasted an average of 38.40 months. Additionally, four studies [10, 16-18] reported on the length of the intervention. Three studies [16-18] had a follow-up with a mean of 28 weeks. All included studies [10, 11, 16-18] had a control group. Three studies on depression [11, 17, 18], and two studies each reported the consequences of anxiety [11, 18] and caregiver's burden [17, 18]. To report the overall effect, size the timeline of 16, 24, 16, and 12 weeks were selected for studies of Dionne-Odom (2020), El-Jawahri (2017), McDonald (2017), and Dionne-Odom (2015), respectively ([Supplementary Tables 1 & 2](#)).

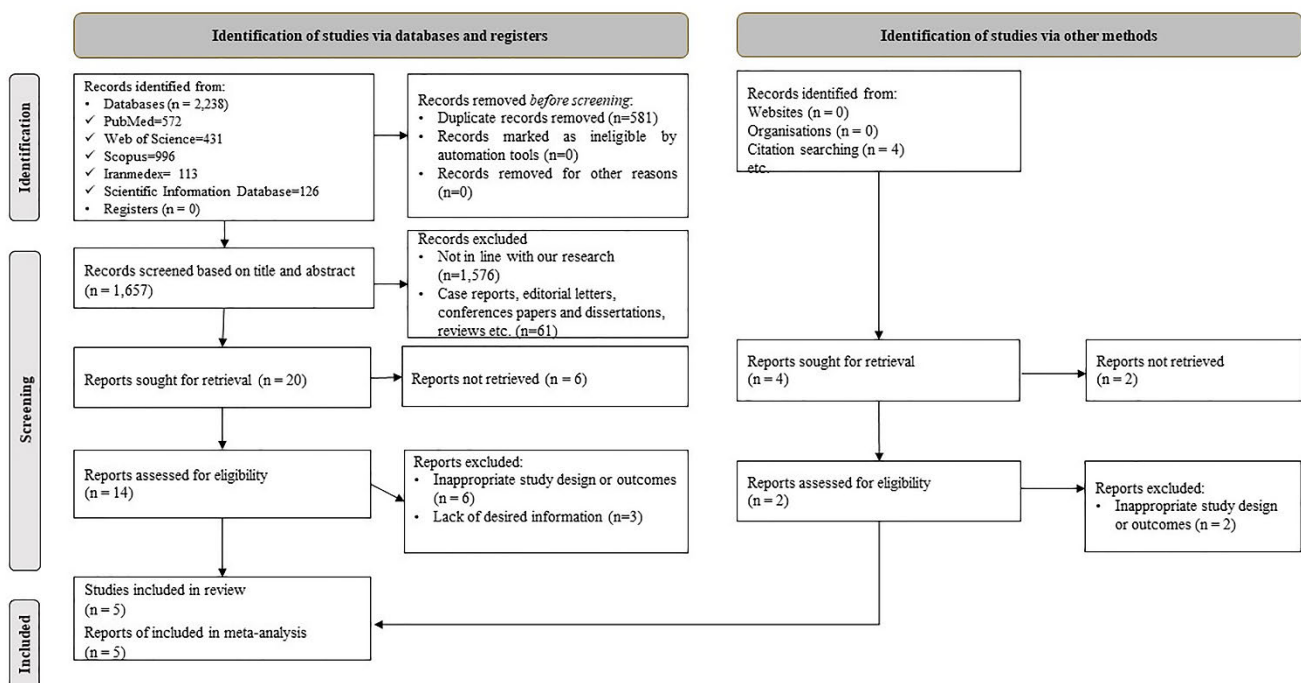


Figure 1. Flow diagram of the study selection process.

3.3 | Methodological evaluation of relevant studies

All studies [10, 11, 16-18] had good quality (Figure 2).

3.4 | A meta-analysis of the effects of early palliative care on the QoL of adult patients with chronic diseases' caregivers

The findings of this study demonstrated that early palliative care treatments had a similar impact on caregivers' QoL as routine care and delayed palliative care interventions (ES: -0.01, 95%CI: -0.20 to 0.17, Z=0.15, I²:0.0%, P=0.88). Additionally, the sensitivity analysis demonstrated that none of the papers included in the final analysis had an impact on the overall effect size (95%CI: -0.28 to 0.22) (Figure 3).

3.5 | A meta-analysis of the effects of early palliative care on depression of adult patients with chronic diseases caregivers

As compared to the normal care group, the early care group's caregivers' depression was modestly reduced by the intervention, but this difference was not statistically significant (ES: -0.06, 95%CI: -0.36 to 0.23, Z=0.43, I²:0.0%, P=0.67) (Figure 4).

3.6 | A meta-analysis of the effects of early palliative care on the anxiety of adult patients with chronic diseases' caregivers

Early palliative care reduced caregiver anxiety, however, the difference between the intervention group and the group receiving standard care was not statistically significant (ES: -0.25, 95%CI: -0.64 to 0.15, Z=1.23, I²:0.0%, P=0.22) (Figure 5).

3.7 | A meta-analysis of the effects of early palliative care on the burden of adult patients with chronic diseases caregivers

Caregivers' burdens were reported based on three dimensions demand, stress, and objective. Results found the intervention caused a non-significant decrease in the demand dimension (WMD: -0.48, 95% CI: -1.13 to 0.17, Z=1.44, I²:0.0%, P=0.15) (Figure 6) and a significant decrease in the stress dimension (WMD: -0.65, 95% CI: -1.26 to -0.04, Z=2.09, I²:0.0%, P=0.04) (Figure 7), in the intervention group compared to the routine care. In contrast, the intervention did not affect the objective dimension (WMD: 0.30, 95%CI: -0.48 to 1.08, Z=0.76, I²:0.0%, P=0.45) (Figure 8) in the intervention group than in routine care.

One study reported the results related to the QoL of caregivers three months before and six months after the death of care recipients. The QoL was not statistically significantly different in the two time periods in the intervention and routine groups, but the level of anxiety and depression (each was not reported separately) showed a significant decrease. Of course, the sample size related to the mentioned period has not been specified in the study [11]. In another study, depression and caregivers' burden in the stress dimension of caregivers less than six months from the patient's death showed a significant decrease in the early palliative care group compared to the routine care, but the QoL and the objective and demand did not show a significant decrease. The sample size related to this period was small (between 8 and 11 caregivers) [18].

	J Nicholas D'onne-Odom <i>et al.</i> , 2015	E-Jawahri <i>et al.</i> , 2017	McDonald <i>et al.</i> , 2017	J Nicholas D'onne-Odom <i>et al.</i> , 2020	J Nicholas D'onne-Odom <i>et al.</i> , 2022
Was true randomization used for assignment of participants to treatment groups?	Y	Y	Y	Y	Y
Was allocation to treatment groups concealed?	Y	Y	Y	Y	Y
Were treatment groups similar at the baseline?	Y	Y	Y	Y	Y
Were participants blind to treatment assignment?	U	U	U	Y	U
Were those delivering treatment blind to treatment assignment?	U	U	U	U	U
Were outcomes assessors blind to treatment assignment?	U	U	U	U	U
Were treatment groups treated identically other than the intervention of interest?	Y	Y	Y	Y	Y
Was follow up complete and if not, were differences between groups in terms of their follow up adequately described and analyzed?	Y	N	N	Y	Y
Were participants analyzed in the groups to which they were randomized?	Y	Y	Y	Y	Y
Were outcomes measured in the same way for treatment groups?	Y	Y	Y	Y	Y
Were outcomes measured in a reliable way?	Y	Y	Y	Y	Y
Was appropriate statistical analysis used?	Y	Y	Y	Y	Y
Was the trial design appropriate, and any deviations from the standard RCT design (individual randomization, parallel groups) accounted for in the conduct and analysis of the trial?	Y	Y	Y	Y	Y

Figure 2. Methodological quality assessment of included studies.

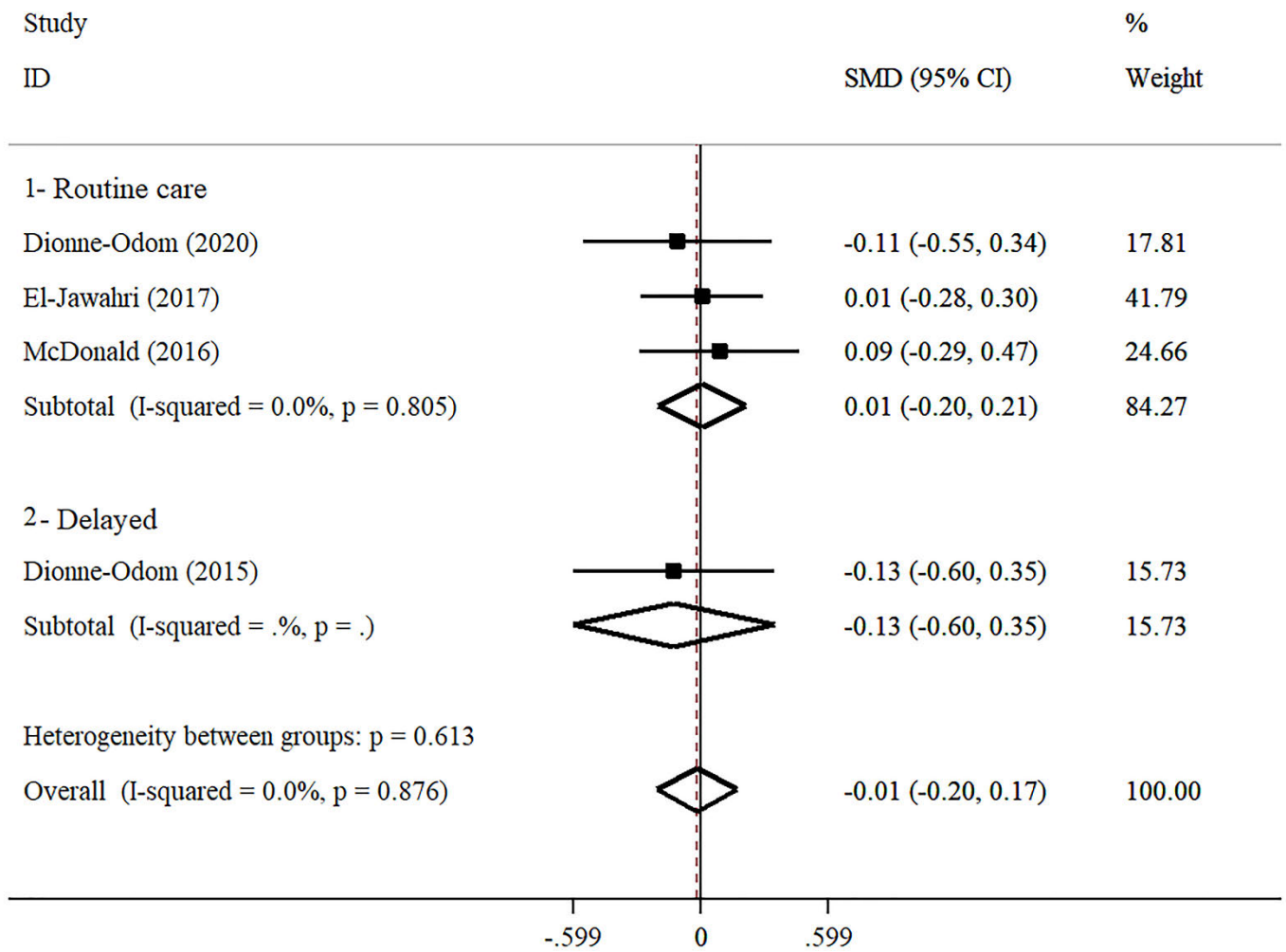


Figure 3. QoL.

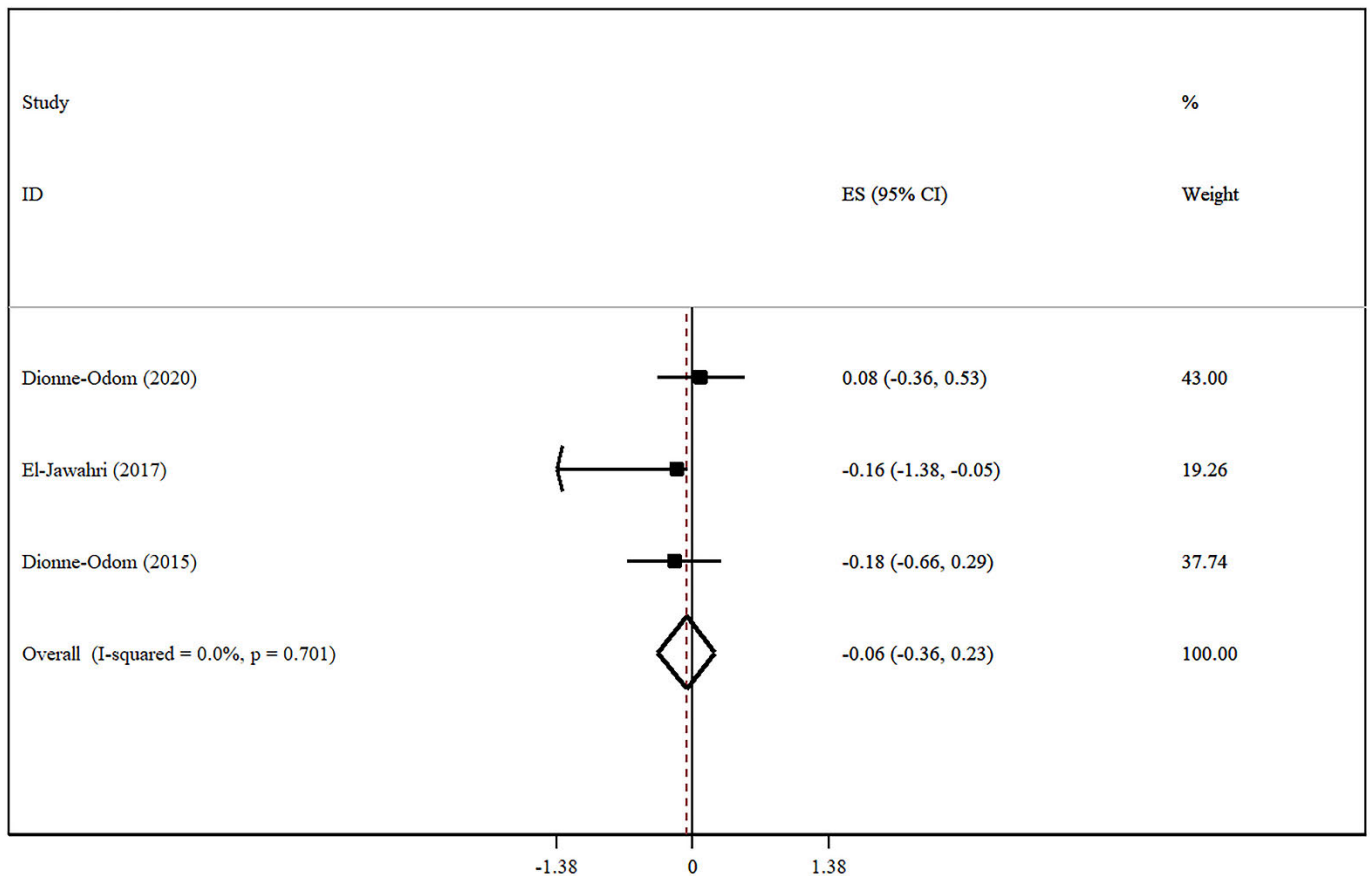


Figure 4. Depression.

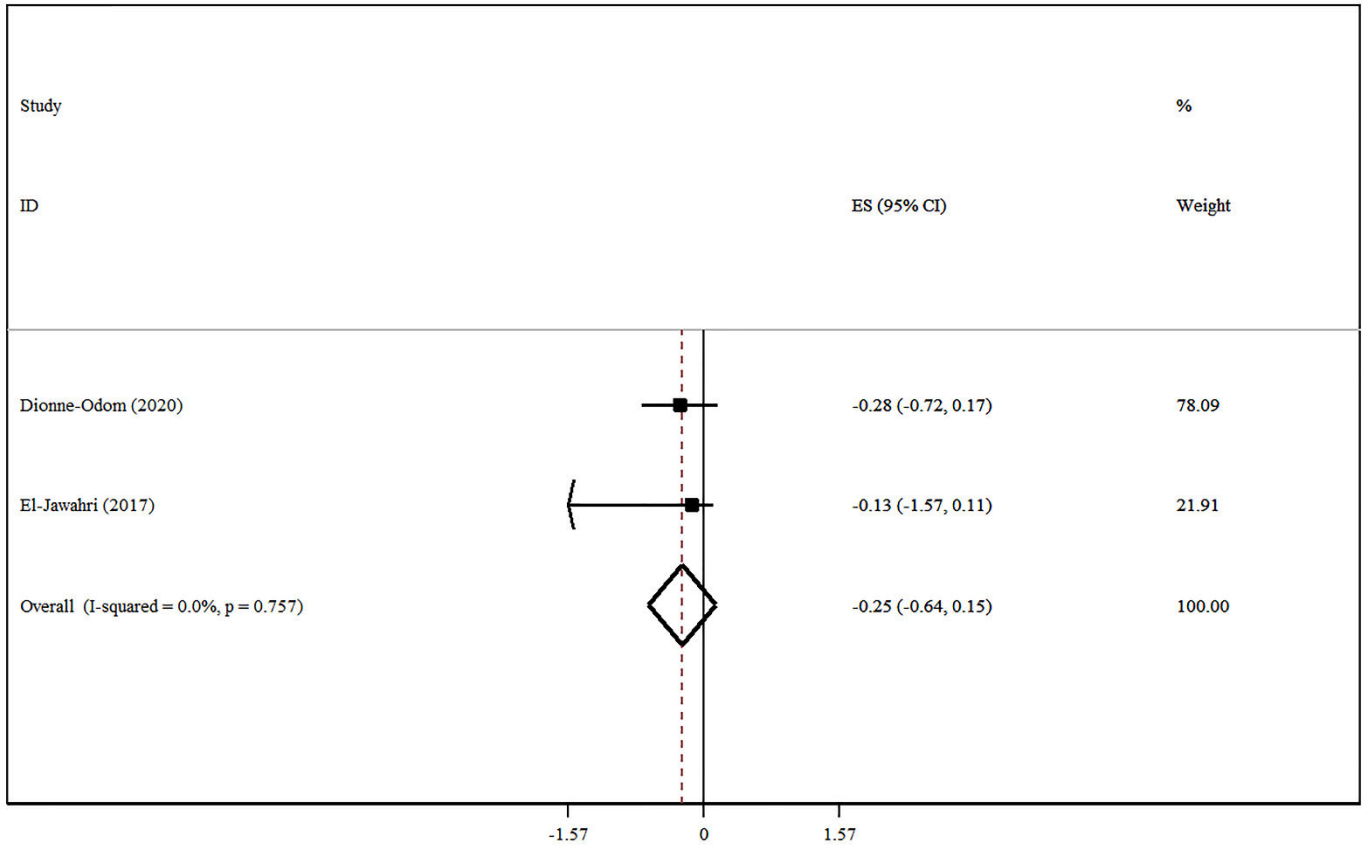


Figure 5. Anxiety.

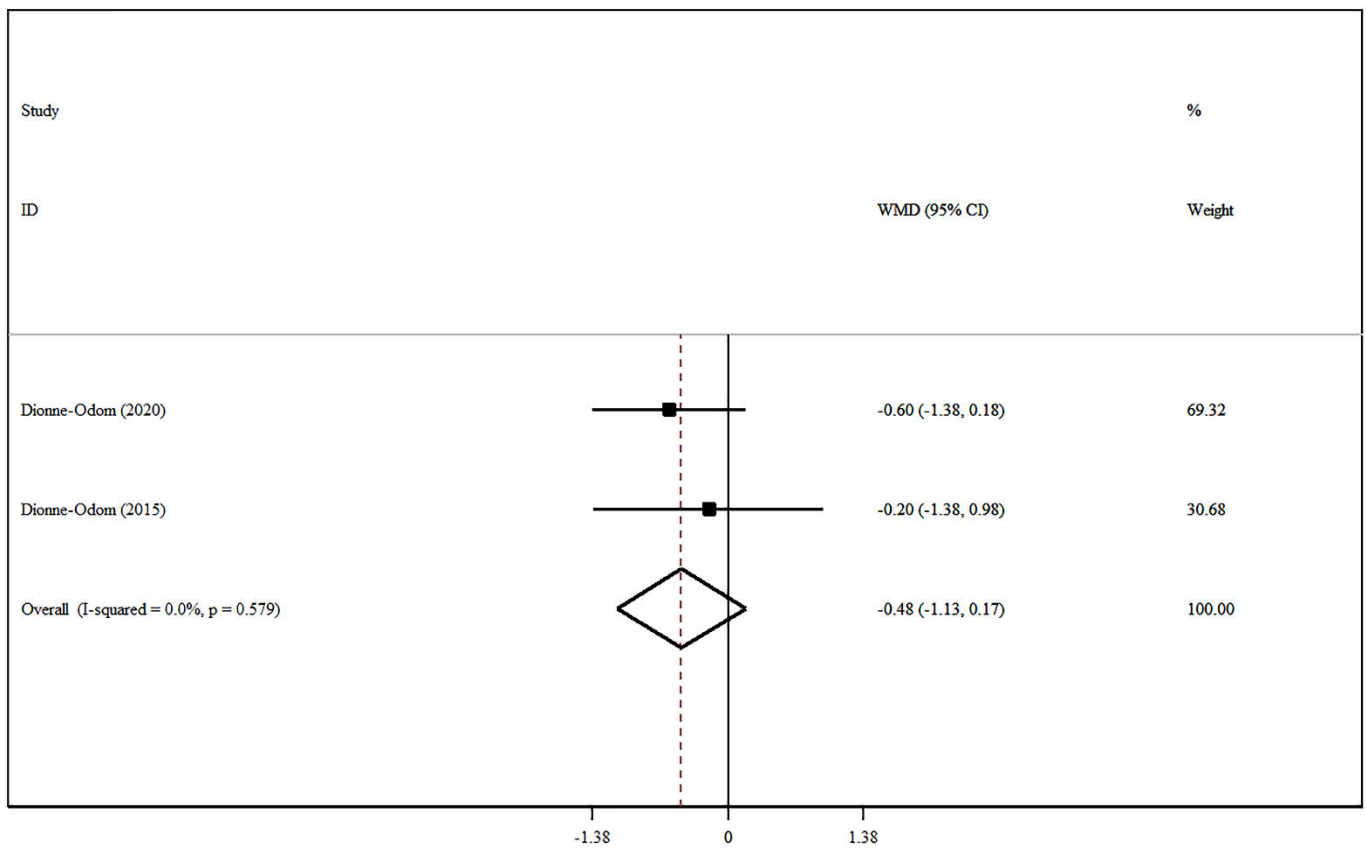


Figure 6. Burden (demand).

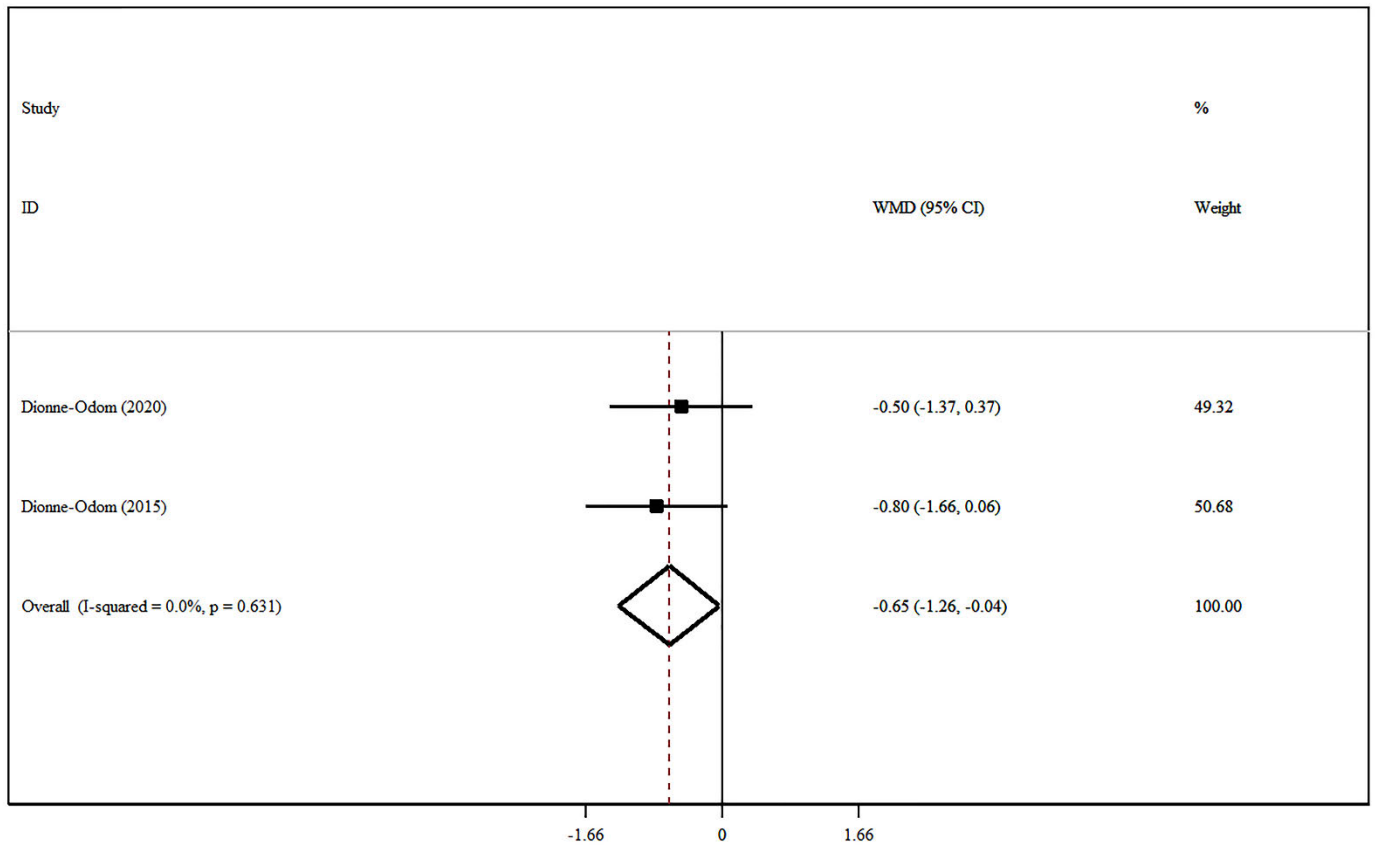


Figure 7. Burden (stress).

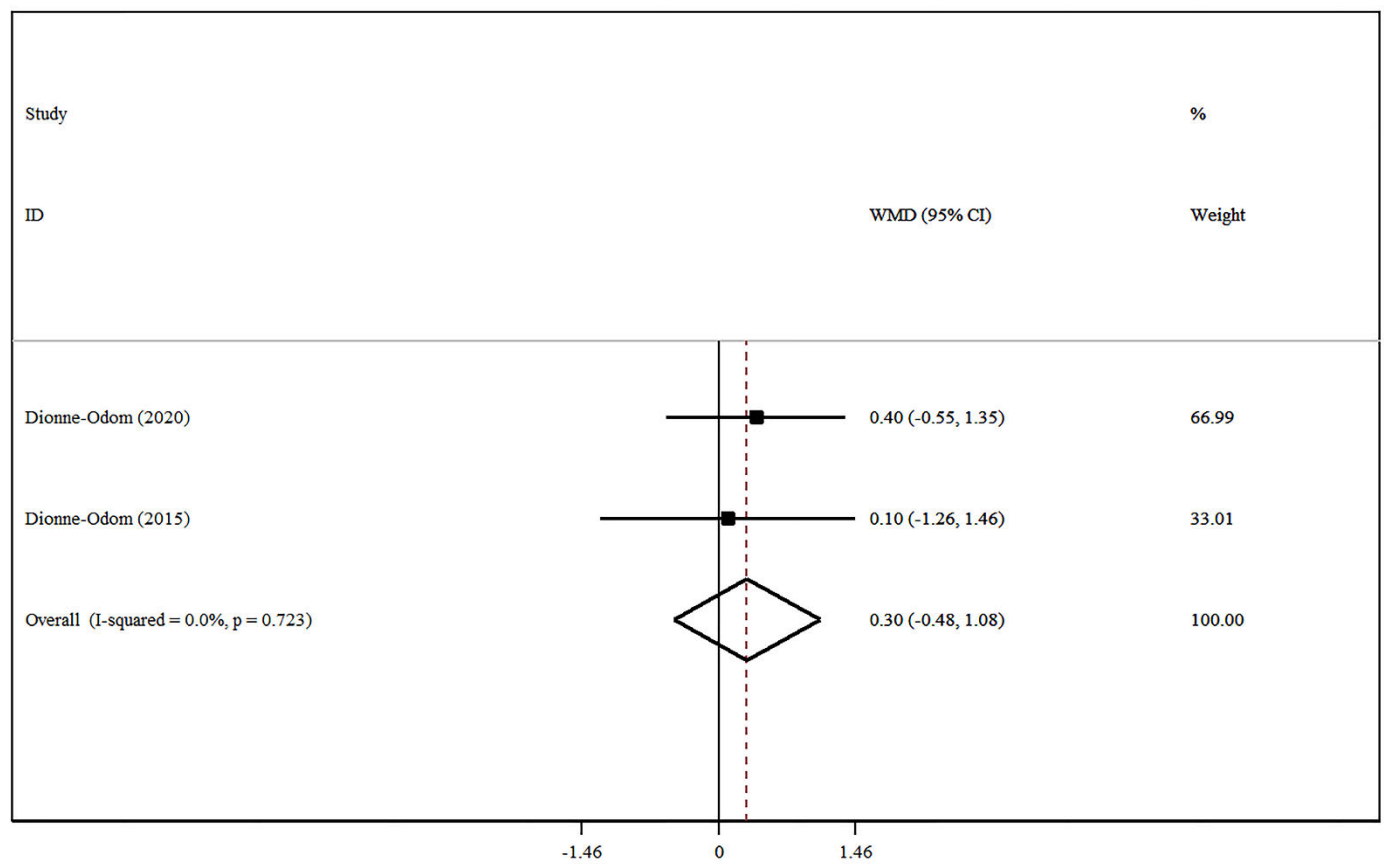


Figure 8. Burden (objective).

4 | Discussion

The current study demonstrated that the QoL for caregivers was not significantly impacted by early palliative care intervention. The reasons for the insignificant effect of the intervention can be investigated separately in each study. In a study [18], caregivers who entered the study did not suffer from distress or low quality of life. Additionally, African Americans made up more than half of the study's participants, who have a higher standard of living and less suffering than white communities. Additionally, 60% of the caregivers had completed all four sessions of telephone intervention for early initiation of palliative care. Education was also provided to the caregivers by telephone, which can be considered another factor that can diminish the effectiveness of the intervention. In a study, it was shown that depression and anxiety decreased significantly at the end of the 12th week, while in the 24th week, this difference was not significant. This could be attributed to the dropout of samples by 33.5% [11]. One of the drawbacks of palliative care studies is dropping samples [17]. In this study, caregivers' QoL was marginally greater than that of the general population, and the intervention had no appreciable impact in raising it [11]. The small sample size in McDonald's study is another reason why the intervention had little effect on people's QoL [10].

In the period around the death of the patient, due to the small sample size and the lack of sufficient data, quantitative analysis was not done. Every study that met the criteria found that the intervention group's anxiety and depression levels following the patients' deaths were significantly lower than those in the control group. Also, the result of the present meta-analysis showed that the intervention reduced these two outcomes in predetermined periods of 12 to 24 weeks but it was not statistically significant. This difference can be due to the use of terminal decline Analyses, which also considered the missing data for analyses related to the patient's death [11]. Early interventions by providing information and improving problem-solving can reduce distress in caregivers. Also, education by the experienced treatment staff increased the skills and knowledge and better overcome the various issues of the caregivers [18].

The results showed that the use of the intervention caused a non-significant decrease in demand and a significant decrease in stress, while the objective dimension of burden in caregivers increased non-significantly in the intervention group compared to routine care. It should be kept in mind that as the duration of the disease increases, the severity of the disease increases in patients, and therefore the need for more care is felt by the caregivers, and

the burden can increase. Although in the present study, early palliative care in two dimensions was able to reduce the burden [18].

4.1 | Limitations

There are some significant limitations to this study. Despite being based on the PRISMA criteria, the current systematic review and meta-analysis are not included in PROSPERO. It's conceivable that not all the studies on this topic were found, even though two researchers investigated online databases. There is a perceived need for further research in this area because of the small number of final papers included in the meta-analysis, which restricts the ability to rely on the findings of the subgroup analysis. Although we made an effort to take non-RCT study data into account while analyzing the qualitative outcomes. It was not possible to differentiate between the different types of massages due to a lack of data, but future research will be able to do so and compare the outcomes of each form of massage independently to help with decision-making. Finally, because only English and Persian studies have been included, studies in other languages may not have been taken into consideration.

4.2 | Implications for nursing managers and policy-makers

In most cases, patients with chronic diseases do not need a caregiver. Caring for these patients can affect the mental and emotional state of the caregivers. Studies have shown that early palliative care can have a positive effect on QoL, anxiety, depression, and burden in caregivers. It is advised that nursing managers and policymakers pay more attention to the caregivers of patients with chronic diseases to provide early palliative care for patients and their caregivers.

4.3 | Recommendations for future research

Given the lack of studies on the impact of early palliative care on caregivers of adult patients with chronic diseases, additional interventional research in this area is advised to be conducted in the future.

5 | Conclusions

The present study's findings generally indicated that early palliative care, when compared to routine treatment and delayed palliative care, had a similar impact on caregivers of adult patients with chronic conditions in terms of QoL. Although the intervention reduced anxiety and depression and the two dimensions of stress and demand from burden outcome, it seems that the design of early interventions based on needs assessment and better prioritization can show its effectiveness.

Supplementary files
[Supplementary Tables 1 & 2.](#)

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Authors' contributions

Substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work: AK, VG, SK, AB, AH; Drafting the work or revising it critically for important intellectual content: AK, VG, SK, AB, AH; Final approval of the version to be published: AK, VG, SK, AB, AH; Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved: AK, VG, SK, AB, AH.

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Ethics approval and consent to participate

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Competing interests

We do not have potential conflicts of interest with respect to the research, authorship, and publication of this article.

Availability of data and materials

The datasets used during the current study are available from the corresponding author on request.

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