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Efficacy of home-based non-pharmacological interventions for treating depression: a systematic review and network meta-analysis of randomized-controlled trials

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Abstract:

Objectives: To systematically review and compare the efficacy of all available home-based non-pharmacological treatments of depression.

Design: Systematic review and network meta-analysis of randomized controlled trials.

Data sources: Medline, Scopus, and CINAHL databases were searched since initiations to7th August 2016.

Eligibility criteria: Randomized controlled trials comparing the efficacy of home-based non-pharmacological interventions with usual care of depressed patients were included in the review.

Main outcomes: Depression symptom scores and disease remission rates at the end of treatment.

Results: Seventeen studies were included in the review. Home-based non-pharmacological interventions were categorized as 1) home-based psychological intervention, 2) home-based exercise, 3) combined home-based psychological intervention with exercise, and 4) complimentary or alternative medicine. Complementary and alternative medicine approaches were excluded from the meta-analysis due to heterogeneity.

The standardized mean differences of post-treatment depression symptom scores between usual care groups and home-based psychological intervention, home-based exercise, and combined home-based psychological intervention with exercise were -0.57 (95%CI:-0.84, -0.31), -1.03 (95%CI:-2.89, 0.82), and -0.78 (95% CI:-1.09,-0.47), respectively. These results suggest that only home-based psychological intervention and combined home-based psychological intervention with exercise could significantly decrease depression scores. Compared with usual care groups, the disease remission rate was also significantly higher for home-based psychological intervention (pooled risk ratio = 1.53; 95% CI: 1.19, 1.98) and combined home-based psychological intervention with exercise (pooled risk ratio = 3.47; 95% CI: 2.11, 5.70). Of all the studied interventions, combined home-based psychological intervention with exercise had the highest probability of resulting in disease remission.

Conclusion: Our study confirms the efficacy of home-based psychological intervention and combined home-based psychological intervention with exercise in the treatment of depression. Combined home-based psychological intervention and exercise was the best treatment and should be considered for inclusion in clinical guidelines for managing depression.

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Strengths and limitations of this study

- Our analysis provides the first comprehensive review of the efficacy of home-based non-pharmacological interventions in treating depression.
- A comprehensive search was undertaken to identify as many relevant studies as possible.
- We performed a network meta-analysis to compare the efficacy of home-based interventions in order to identify the best treatment regimen.
- The quality of included studies in the area of allocation concealment was not optimal.
- Participants in our included studies were aware of their own intervention and the outcomes were subjective.

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INTRODUCTION

Recent studies have highlighted the international recognition of depression as one of the leading global burdens of disease (GBD)[1]. Depression is associated not only with greater morbidity and mortality but also with increasing health service use and costs[2]. In addition, untreated depression has been recognized as a strong predictor of poor health outcomes in elderly[3-5] and adult patients with chronic disease[6-8].

Both pharmacological and non-pharmacological interventions, such as psychotherapy or supervised exercise, have been accepted as standard treatments of depression. However, concerns about drug side effects and dependency appear to make patients prefer psychological interventions. One study showed that around 70% of depressed patients were non-compliant with antidepressants because of concerns about their side effects[9]. Even though non-pharmacological interventions were preferred over antidepressants[10 11], only a very small percentage of patients referred for psychotherapy were able to enter and complete this treatment[12]. This inconsistency between patient preference and low rates of initiation and adherence to treatment could be a consequence of barriers to obtaining treatment. Non-pharmacological interventions are usually clinic or hospital-based and require visits on a weekly or monthly basis. In one study, 70% of patients reported structural barriers preventing them from attending psychotherapy sessions regularly and cited time constraints, transportation problems and cost as being significant obstacles[13].

Among older patients, whose prevalent rate of depression is very high, these problems were aggravated by concurrent medical illness, social isolation, functional impairment or being home-bound [14-20]. Overcoming these barriers by providing interventions in patients' own homes may achieve better treatment adherence and thereby greater treatment success than clinic or hospital-based interventions.

Home-based non-pharmacological interventions, such as problem solving therapy[21-25] and home-based exercise[26 27], have developed over several years. Although some studies have suggested that these approaches can improve depressive symptoms and rates of remission when compared with standard usual care[26 28 29], other studies have reported conflicting results[27 30 31]. Until now, no study has systematically reviewed all possible home-based non-pharmacological interventions and summarised the treatment effect of each intervention. Our systematic review and network meta-analysis was, therefore, undertaken with the aim of reviewing all available home-based

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non-pharmacological interventions, pooling the effect sizes of each intervention on symptom improvement and indirectly comparing treatment efficacy between the different interventions. The results of this review should be useful for identifying the most beneficial home-based non-pharmacological interventions and for informing clinical guidelines for treating depression.

METHODS

Search strategy

Relevant studies were identified using Medline, Scopus, and CINAHL databases searched from inceptions to7th August 2016. Reference lists of included studies were also explored. Search terms and search strategies for each database are presented in a Supplementary Appendix.

Selection of studies

Initially studies were selected from titles and abstracts by two independent reviewers (K.S. and T.A.). Full articles were retrieved to aid decision making if decision could not be made based on titles and abstracts. Disagreement between the two reviewers was resolved by discussion. Percentage agreement between the two reviewers was estimated using kappa statistics.

Inclusion criteria

Randomized-controlled trials published in English were eligible for the review if they met all of the following criteria:

1. Study participants were adults aged more than 18 years with a diagnosis of any degree of depressive disorder using the criteria of the Diagnostic and Statistical Manual of Mental Disorders 4th Edition (DSM-IV) or any diagnostic tool used for diagnosis or screening for depression. Participants who were children, adolescents or postpartum women were excluded.
2. Interested interventions were non-pharmacological and provided in the patient's home, such as cognitive behavioral therapy, problem solving therapy, family therapy, or home-based exercise.
3. Treatment comparison was the standard care of depression in outpatient clinics or hospital settings.

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4. Outcomes were measured by the level or severity of depressive symptoms or the incidence of disease remission at the end of the intervention.
5. Studies provided sufficient data for analysis, such as number of participants (n), mean depression score, standard deviation (SD) for each intervention group, and the number of patients per intervention group with or without disease remission.

Data extraction

Two reviewers (KS and TA) independently used a standardized data record form to extract baseline characteristics of included studies and outcomes of interest. Disagreement between the two reviewers was resolved by discussion and corresponding authors of studies were contacted if information was incomplete.

Interested interventions

Home-based non-pharmacological intervention was defined as any care or management of depression provided by health care professionals at a patient's place of residence. Home-based interventions had to have a clear and definite objective. Home visits that provided only health-education, social or emotional support were, therefore, excluded from this study.

Outcomes of interest

The outcomes of interest were depressive symptom scores and disease remission rates at the end of treatment. Disease remission was defined according to the criteria of the original article. Included studies used several tools for measuring the severity of depressive symptoms, namely the Hamilton Depression Rating Scale (HAM-D)[21 22 30 32 33], Patient Health Questionnaire-9 (PHQ-9)[24 34], Geriatric Depression Scale (GDS)[23 26 28], Hopkins Symptom Checklist-20 (HSCL-20)[35 36], Montgomery Asberg Depression Rating Scale (MADRS)[18 25 27], Beck Depression Inventory-Fast Screen (BDI-FS)[37] and Center of Epidemiologic Studies Depression Scale (CES-D)[38]. These tools have different score ranges (HAM-D = 0-53, PHQ-9 = 0-27, GDS = 0-15, HSCL-20 = 0-4, MADRS = 0-60, BDI-FS = 0-21, and CES-D = 0-60) with higher scores in all tools representing increasing severity of depressive symptoms.

Risk of bias assessment

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To assess the quality of included studies, a risk of bias assessment tool [39] was applied by two independent reviewers (K.S., T.A.). Six domains were evaluated as follows: 1) random sequence generation 2) allocation concealment 3) blinding of participants and personnel 4) blinding of outcome assessors 5) incomplete outcome data 6) selective outcome reporting 7) other sources of bias. The quality of the studies was classified as being at high, unclear, or low risk of bias. Disagreement between the two reviewers was settled by discussion.

Statistical analysis

Because depression scores were measured differently among the studies, for direct comparison the mean differences of depressive scores between intervention and control groups were estimated for each study and then were pooled using the standardized mean difference (SMD). Heterogeneity between studies was estimated by Q test and I^2 statistic. Heterogeneity between studies was considered if the P-value from Q test was less than 0.10 or if I^2 was equal to or greater than 25%[40]. If heterogeneity was presented, the SMD was estimated by applying the random effect model. Otherwise the fix effect model was applied.

For dichotomous outcomes, relative risks (RR) of disease remission were calculated for each study. The random effect model was used for pooling RR if there was evidence of heterogeneity between studies. Otherwise the inverse variance method was used. Sources of heterogeneity were explored by considering possible factors one by one in a meta-regression model (e.g. mean age, severity of depression at baseline and types of intervention delivery).

For network meta-analysis, treatment effects for each study were estimated using a two-stage network meta-analysis. Firstly, summary data was expanded into individual patient data using the 'expand' command in STATA program. Binary regression was applied to estimate log (RR) and variance-covariance of each treatment using 'mvmeta' make command. A multivariate random effect meta-analysis was used to calculate the pooled RRs and their 95% confidence intervals (CI). Riley's method was used for considering subject-study correlation. Treatment ranking was made according to the linear predictor of each study. Disagreement between direct and indirect estimations (inconsistency assumption) was examined by measuring the inconsistency factor, i.e. the difference between lnRRs estimated from direct and indirect meta-analyses.

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Publication bias was assessed using Egger test and funnel plot. If the funnel plot showed asymmetry, a contour enhanced funnel plot was performed to explore whether asymmetry was the result of heterogeneity between studies or arisen from publication bias. All analyses were performed using STATA version 14. A two-sided test with P-value less than 0.05 was considered statistically significant, except for the Q test, in which a P-value less than 0.10 was applied.

Patient involvement

Patients were not involved in the design of the study, development of outcome measures, or conduct of the study. We did not ask patients for advice on interpreting or writing up results. There are no plans to disseminate the results of the research to study participants.

RESULTS

We identified 385, 534, 255, and 2 articles from Medline, Scopus, CINAHL databases and reference lists respectively. After deleting duplications, the titles and abstracts of 768 studies were reviewed. Finally, 17 studies met our inclusion criteria and were eligible in the review (Figure 1). Agreement of study selection between the two reviewers was high at 86.7% (Kappa = 0.50).

Study participants

The baseline characteristics of included studies are presented in Table 1. The type and severity of depression of participants differed between studies. Four studies[25 28 32 33] included patients with major depressive disorder, four[22 23 36 38] included patients with minor depression and nine[18 21 24 26 27 30 34 35 37] included patients with mixed severities of depression. Ten studies included elderly patients[18 21-26 28 36 38] while seven studies included adults with ages greater than 18 years[27 30 32-35 37]. Ten studies included depressed patients with other co-morbidities (i.e. epilepsy[35], heart diseases[22 30 34], disability[18], and mild to moderate cognitive impairment[25]). Twelve studies[21 23 24 26-28 32 33 36-38] included patients without co-morbidity. Use of anti-depressants at baseline varied widely between studies, ranging from 0% to 95%.

Home-based interventions

The composition of home-based non-pharmacological interventions differed among the included studies. The effect of interventions on depressive symptoms was, therefore, analyzed using

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four general categories: 1) home-based psychological intervention 2) home-based exercise 3) combined home-based psychological intervention with home-based exercise 4) complementary or alternative medicine. Eight, 3 and 3 studies compared home-based psychological intervention with usual care, home-based psychological intervention with usual care, and combined home-based psychological intervention with home-based exercise with usual care, respectively. One study compared the efficacy between home-based psychological intervention, home-based exercise, combined home-based psychological intervention with home-based exercise, and usual care. Since interventions in the category of complementary or alternative medicine were heterogeneous, they were not included in the meta-analysis but were subjected to qualitative analysis. Details of each home-based intervention are summarised below:

Home-based psychological intervention

Home-based psychological intervention was classified as home-based problem-solving treatment or home-based cognitive behavioral therapy.

1. *Home-based problem-solving treatment* (6 studies[21 22 24 25 28 29])

Home-based problem-solving treatment (PST) is a skill-enhancing behavioral treatment of depression usually delivered by social workers and psychologists. This approach assumes that depressive symptoms are caused and maintained by problems of daily life and that these can be reduced by identifying and addressing them systematically. Each PST session comprises 1) defining and formulating the nature of the depressive problem 2) generating a range of alternative solutions to the problem 3) systematically evaluating the possible consequences of each solution then selecting the most appropriate one 4) monitoring and evaluating the actual outcome. In addition, PST identifies patients' pleasurable activities and encourages them to participate in these activities.

2. *Home-based cognitive behavioral therapy* (CBT) (3 studies[30 37 38])

The aim of CBT is to modify the dysfunctional emotions, behaviours, and thoughts of depressed patients. This type of intervention was identified in 3 studies, of which 2 studies were CBT-based bibliotherapy. In this approach, participants received self-help books or leaflets that included instruction on cognitive behavioral self-help, mood management skills, and tasks to practice. During the intervention period, participants were visited by home care nurses or contacted by telephone by

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study investigators to assess their symptoms and encourage them to follow the course at their own pace.

Home-based exercise

Home-based exercise was employed in 4 studies. Exercise included both progressive resistance training, aerobic exercise [26 27] and aerobic exercise only[30 33]. Participants were required to perform the exercises for at least 30 minutes three times a week.

Combined home-based psychological intervention with exercise

Home-based psychological intervention combined with exercise was the interested intervention in 4 studies. Each of these applied aerobic exercise as a home-based exercise but psychological therapies differed among them (PST in two studies[35 36], cognitive behavioral therapy in one study[30] and family therapy with bereavement counselling and social interventions in one study[18]).

Complementary or alternative medicine

This intervention refers to a broad set of health care practices or activities that are not integrated into the dominant health care system. This type of intervention was used in 2 studies. One involved home-based deep-breathing exercise[34] aimed at stimulating a relaxation response, (i.e. to decrease arousal, heart rate and blood pressure, and to reduce responsiveness of the sympathetic nervous system). Deep-breathing exercises can also help patients to disregard negative and distracting thoughts. Patients were trained by experienced nurses to breathe at a rate of six breaths per minute. During the treatment period, this was undertaken in a quiet environment for a period of ten minutes, three times each day.

The other intervention employed a spirituality teaching programme[41] aiming to promote contemplation of the inter-relation between meaning and purpose, connectedness with others, nature or the divine, and values such as compassion, love, justice, and forgiveness. The programme comprised eight sessions involving explanation of the divine aspect of the self, teaching breathing and visualization practice, helping patients to connect with the divine through prayer or meditation, letting go of regret and fostering gratitude, practicing self-awareness relating to the five senses, and building upon connectedness with others. Participants were also advised to avoid forming expectations and to

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refrain from judging outcomes. Initially patients participated in a workshop run by psychiatrists and were then required to practice by themselves with the help of audio CDs.

Treatment comparison

Usual care, defined as the standard care of depression managed in a clinic or hospital setting, was applied as a treatment comparator for all studies. In addition to usual care, three studies[25 26 29] included home visits and two[21 34] included telephone support. However, these interventions provided education about depression together with general social or emotional support but did not offer specific psychological help or exercise. With the exception of one study[41], almost all used anti-depressant medication as a co-intervention but the decision to initiate or maintain this was dependent on the judgement of patients and their physicians.

Risk of bias assessment

Results of risk of bias assessment are presented in Supplementary Table 1. Most of the studies (14 studies) reported low risk of bias in the domain of random sequence generation, while 3 studies[21 22 30] reported unclear risk. For allocation concealment, 11 studies[18 21 22 25-30 37 38] had unclear risk of bias, while 6 studies[24 33-36 41] had low risk of bias. All studies reported high risk of bias in the domain of blinding of participants and personnel and low risk of bias in other domains. Ten studies[18 22 25-27 29 30 33 35 41] had low risk of bias for blinding of outcome assessors, whereas 7 studies[21 24 28 34 36-38] had unclear risk. For the domain of incomplete outcome data, 13 studies[18 22 24-27 29 30 33 35 36 38 41] reported low risk of bias and 4 studies[21 28 34 37] reported high risk. Almost all studies (16 studies) had low risk of bias for selective outcome reporting, while only one study[35] had high risk of bias.

Pooled mean difference of depression score

Home-based psychological intervention vs usual care

Nine studies were analyzed[21 22 24 25 28-30 37 38] comparing home-based psychological intervention with usual care (N = 739). Depression scores were assessed at the end of treatment, which ranged from 6 to 48 weeks. The mean differences and 95% CIs of depression scores for each study are presented in Table 2. SMD of home-based psychological intervention versus usual care was -0.57 (95% CI: -0.84, -0.31), suggesting that home-based psychological intervention can significantly decrease depression scores when compared with usual care.

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Moderate heterogeneity was found between studies, with I^2 of 63.5%. Sources of heterogeneity were explored but none of the factors decreased I^2. Subgroup analyses were performed according to the severity of depression (i.e. major depressive disorder (MDD), minor depression and mixed severity of depression). These showed that SMDs in patients with MDD, minor depression, and mixed severity of depression were -0.95 (95% CI: -1.35, -0.55; I^2 = 16.5%), -0.61 (95% CI: -1.28, 0.06; I^2 = 82.1%), and -0.41, (95% CI: -0.62, -0.19; I^2 = 0%) respectively (see Supplementary Figure 1). These suggest that home-based psychological intervention reduces depression scores significantly in the groups of MDD and mixed severity of depression. In addition, the efficacy of this intervention in patients with MDD was better than the efficacy in patients with minor depression.

Home-based exercise vs usual care

Three studies[26 30 33] (N = 321) were pooled to compare the effect of home-based exercise with usual care. The SMD was -1.03 (95% CI: -2.89, 0.82; I^2 = 97.9%) (Table 2 and Supplementary Figure 2A). The mean depression score in the home-based exercise group was therefore 0.03 units lower than the mean depression score in the usual care group. However, this effect did not reach statistical significance.

Combined home-based psychological intervention with exercise vs usual care

Only two studies[30 36] (N = 169) had sufficient data for pooling the effect on the depression score of combined home-based psychological intervention with exercise. Mean depression scores were measured at the ends of the treatments, namely at 12 weeks[30] and 24 weeks[36]. Table 2 shows the mean depression scores and 95% CIs for each study. SMD was -0.78 (95% CI: -1.09, -0.47; I^2 = 0.0%) (Supplementary Figure 2B). This indicates that patients receiving combined home-based psychological intervention and exercise had significantly lower mean depression scores (by 0.78 units) than patients receiving usual care.

Pooled risk ratio of disease remission

Home-based psychological intervention vs usual care

Four studies (N = 459) comparing the effectiveness of home-based psychological intervention with usual care had remission rates as their outcome of interest. Remission from depression was defined as HAMD score ≤ 7 in one studies[25], PHQ-9 ≤ 4 in one study[24], BDI < 4 in one study[37] and

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CES-D < 16 in one study[38] (Table 3). The pooled RR was 1.53 (95% CI: 1.19, 1.98) (Supplementary Figure 3), suggesting that patients receiving home-based psychological intervention were approximately 1.7 times more likely to have remission from depression than patients receiving usual care. The results among studies were homogeneous with I^2 of 0%.

Home-based exercise vs usual care

Two studies (N = 248) reported their outcome as disease remission and had sufficient data for pooling. Disease remission was defined as HAMD score ≤ 7[33] or symptoms no longer meeting the criteria for major and minor depression according to DSM-IV criteria[27] (Table 3). The pooled RR was 0.99 (95% CI: 0.79, 1.24; I^2 = 0.0%) (Supplementary Figure 4A), indicating that there was no significant difference between home-based exercise and usual care in the likelihood of having remission from depression.

Combined home-based psychological intervention and exercise vs usual care

Three studies (N =279) were pooled to compare remission rates between combined psychological intervention and usual care. Disease remission was defined as HSCL-20 score < 0.5 for two studies[35 36] but in Banerjee's study[18] the outcome was not clearly defined (Table 3). Pooled RR was 3.47 (95% CI: 2.11, 5.70; I^2 = 19.7%) suggesting that the combination of home-based psychological intervention and exercise significantly increased the likelihood of remission from depression when compared with usual care (Supplementary Figure 4B).

Network meta-analysis

Disease remission rate

Nine studies (N = 987) were included in the network meta-analysis. Supplementary Figure 5 shows the network plot of home-based psychological intervention, home-based exercise, combined home-based psychological intervention with exercise, and usual care. Size of node and edge reflect the number of studies and patients respectively. From the plot, usual care was the common comparator and had the largest sample size of the four treatment regimes. Home-based psychological intervention versus usual care had the largest number of studies.

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Pooled RRs for each treatment comparison are presented in Figure 2. Compared with usual care, only combined home-based psychological intervention with exercise and home-based psychological intervention alone significantly increased the likelihood of disease remission, with pooled RRs of 3.12 (95% CI: 1.71, 5.70) and 1.50 (95% CI: 1.17, 1.93) respectively. In addition, the incidence of disease remission in home-based psychological intervention and combined home-based psychological intervention with exercise groups was significantly higher than in the home-based exercise group, having pooled RRs of 1.49 (95% CI: 1.07, 2.10) and 3.10 (95% CI: 1.63, 5.90), respectively. When compared with home-based psychological intervention alone, combined home-based psychological intervention with exercise also significantly improved the rate of disease remission (pooled RR = 2.08; 95% CI: 1.08, 3.99).

Treatment ranking was assessed by estimating the probability of each treatment being the best. This yielded probabilities of 99.5%, 0.5%, and 0% for combined home-based psychological intervention with exercise, home-based psychological intervention alone, and home-based exercise respectively. Combined home-based psychological intervention with exercise therefore emerged as the best intervention for achieving remission from depression.

Applying inconsistency assumptions to the treatments, inconsistency factors were calculated as 0.020 (Z=0.183, P-value=0.912) for home-based psychological intervention, -0.018 (Z=0.110, P-value=0.913) for home-based exercise, and 0.106 (Z=0.107, P-value=0.915) for combined home-based psychological intervention with exercise. These figures find no significant difference between the direct and indirect comparison of estimated treatment effects.

Efficacy of complementary or alternative medicine

Results from a study comparing the efficacy of home-based deep-breathing exercises with usual care showed that patients receiving this intervention had significantly lower depression scores than patients receiving usual care, with a mean difference of -1.34 (95% CI: -1.17, -0.17). Another study compared the efficacy of home-based spiritual therapy with usual care. Findings from this study suggested that home-based spiritual therapy could significantly decrease depression scores when compared with usual care, with a mean difference of -1.11 (95% CI: -1.57, -0.65), In addition, this study found that patients receiving home-based spiritual therapy were more likely to have disease

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remission than patients receiving usual care. The risk ratio of disease remission (defined as HAMD score ≤ 7) from this study was 13.85 (95% CI: 1.88, 101.74)

Publication bias

Egger tests and Funnel plots did not suggest any publication bias for pooling the effect of home-based psychological intervention (coefficient = -0.05, P-value = 0.882) and home-based exercise (coefficient = 6.94, P-value = 0.818) (see Supplementary Figure 6A and 6B). For combined home-based psychological intervention and exercise, the Egger test did not suggest publication bias but a funnel plot showed asymmetry (Supplementary Figure 7A). The cause of this asymmetry was explored by performing a contour enhanced funnel plot which showed that most of the studies fell inside the significant area. The asymmetrical plot may, therefore, result from a small study effect rather than heterogeneity between studies (see Supplementary Figure 7B).

DISCUSSION

Our study found that a combination of home-based psychological intervention with exercise and home-based psychological intervention alone both significantly decreased depressive symptoms and increased the likelihood of disease remission when compared with usual care. However, we could not demonstrate any benefit of home-based exercise alone when compared with usual care. In addition, combined home-based psychological intervention with exercise had the highest probability of remission from depression compared both with home-based psychological intervention and home-based exercise.

The effectiveness of clinic-based psychological intervention for treating depression has been confirmed by previous studies[42-44]. The results of our study also support the efficacy of this intervention when performed in the patient's home. In our review, the majority of participants in the included studies were depressed patients with comorbidities such as epilepsy[35] or heart disease[22 30 34], or were elderly patients with disabilities[18] or cognitive impairment[25]. These groups have a high prevalence of depression and should therefore be expected to receive a significant share of mental health provision. However, their ability to access conventional clinic-based mental health services is restricted by mobility problems and low motivation to seek help. With its ability to overcome these barriers, home-based psychological intervention is particularly appropriate in these situations.

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In addition to demonstrating the efficacy of home-based psychological intervention overall, subgroup analysis within our study raises an interesting point**.** Home-based psychological intervention decreased symptoms of depression for all types of depression but the effect was statistically significant only in patients with MDD and mixed severity depression, not for those with minor depression. This inconsistent finding may result from the so called “ceiling” effect. The level of depressive symptoms in minor depression is relatively low at baseline when compared with major depression, which could limit the potential for symptom improvement[45]. This ceiling effect was also found in the studies reviewing the use of antidepressant medication for minor depressive symptoms.

The rationale for home-based exercise rests on the theory that increasing physical activity can improve depressive symptoms through psychological and physiological routes. Exercise serves as a distraction from worries and depressive thoughts, increases self-efficacy, and gives a sense of mastery. Possible physiological mechanisms include an increase in body temperature, leading to a feeling of relaxation and reduced muscle tension, an increase in levels of endorphins related to positive mood and a sense of well-being, and increases in the availability of the central neurotransmitters dopamine, norepinephrine and serotonin[43,46 47]. Although the advantages of clinic-based or supervised exercise to treat depression have been confirmed by previous literature[48], our study found no benefit from home-based exercise in ameliorating depressive symptoms. The difference in these findings may be explained by poorer treatment compliance in the home-based exercise group, as to achieve significant benefit patients have to practice the exercise programme at a prescribed intensity and frequency. Lack of motivation and inattention are common symptoms in depression and may account for unsupervised patients failing to achieve the prescribed levels of activity when compared with those given encouragement through supervision. This assumption corresponds with findings from the home-based exercise studies[26 27] that the physical health of patients in this group (i.e. cardio-respiratory capacity, BMI, and lower limb strength), the surrogate endpoints of exercise intervention, did not change significantly from baseline.

Although our study did not find any advantages of home-based exercise over usual care, when combined with psychological intervention the combined approach had a significantly greater benefit than either of these interventions alone. The combination may have a synergistic effect, with

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psychological intervention improving motivation to initiate and maintain an exercise programme while the latter in turn enhances the benefits of psychological intervention.

Looking at complimentary or alternative medicine approaches, results from Chung et al and Rickhi et al showed that home-based deep-breathing training and spiritual teaching programmes could significantly reduce depressive symptoms when compared with usual care. However, these two studies had small sample sizes and included specific populations, namely coronary heart disease patients for Chung's study and middle-aged females for Rickhi's study. Their findings may not, therefore, be generalizable to other populations.

Strengths and limitations

Our study has several strengths. Given the potential of home-based interventions to treat depression and the increasing use of these interventions, our analysis provides the first comprehensive review of the efficacy of home-based interventions in treating depression. A comprehensive search was undertaken to identify as many relevant studies as possible and two reviewers selected the studies independently with a high level of agreement. Selection bias was, therefore, unlikely. In addition, we performed a network meta-analysis to compare the efficacy of all available home-based interventions in order to identify the best treatment regime.

We are aware that our study may have some limitations. Firstly, the quality of included studies in the area of allocation concealment was not optimal. The results from our study might, therefore, be affected by selection bias and should be interpreted with caution. Secondly, participants in our included studies were aware both of their own intervention and their subjective outcome, including the self-reported depression score. However, in most of the included studies this bias from non-blinded intervention was minimized by blinding the outcome assessors. Thirdly, some of the included studies considered home visits as a treatment comparator. This may have resulted in an underestimated treatment effect for the home-based interventions.

Clinical implication and further study

Depression is a common disorder, particularly among the elderly and in those with a chronic disease. Many of these patients have difficulty accessing mental health services due to physical disabilities and transportation problems. Home-based interventions to treat depression have the

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potential to overcome these barriers and have been shown by our study to be effective. This information should prove helpful when designing clinical guidelines. However, there are obvious logistical differences between home-based treatments for depression and conventional clinic-based care. Our study has not investigated these aspects of treatment design and, in particular, has not considered manpower implications or transport costs. An economic evaluation study is needed before general implementation of a home-based care model can be recommended unequivocally.

Although a randomized-controlled trial is considered to be the gold standard for therapeutic research, in a real world setting this design may not be ideal for examining patient preferences and adherence to treatment. To maximize treatment efficacy, studies should determine the effects of patient preferences for different treatment approaches and modes of delivery as well as examine the factors that influence these preferences.

CONCLUSION

Our study has confirmed the efficacy both of home-based psychological intervention and combined home-based psychological intervention with exercise in decreasing symptoms of depression and improving rates of remission. In addition, the combination of home-based psychological intervention and exercise has the highest probability of being the best treatment out of all available home-based interventions. This approach should, therefore, be considered when formulating clinical guidelines for treating depression.

Contributors: KS, PI, and TA were involved in the conception and design of the review. KS and TA developed the search strategy, performed study selection, extracted data from included studies and analyzed the data. KS, ML, PI, AD, AT and TA were involved in the interpretation and discussion of results. KS and TA drafted the manuscript. PI, AD, AT and TA revised it critically for important intellectual content. All authors approved the final version of the article. All authors had access to all of the data in the study and can take responsibility for the integrity of the data and the accuracy of the data analysis. TA is guarantor.

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Competing interests: All authors have completed the ICMJE uniform disclosure form at www.icmje.org/coi_disclosure.pdf and declare: no support from any organisation for the submitted work; no financial relationships with any organisations that might have an interest in the submitted work in the previous three years; no other relationships or activities that could appear to have influenced the submitted work.

Ethical approval: Not required.

Data sharing: No additional data available.

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Table 1. Characteristics of included studies

Author	Setting	Type of depression	Participants							Study's intervention		
			N	Age (mean)	Female (%)	Living alone (%)	Married (%)	Baseline depression score (mean)	Anti-depressants use (%)	Type of intervention	Duration (weeks)	Comparison
Kiosses[25]	U.S.	Major depressive disorder	74	80.91	74.3	NA	NA	21.25[a]	63.51	PST-HC	12 weeks	Usual care with home visit
Choi[21]	U.S.	Mixed depression	121	65.21	77.7	63.6	NA	24.55[b]	NA	PST-HC	12 weeks	Usual care with telephone support call
Gitlin[24]	New Zealand	Mixed depression	208	69.57	78.4	56.8	12.0	13.01[c]	19.3	PST-HC	16 weeks	Usual care
Klug[28]	Australia	Major depressive disorder	60	74.9	90.0	78.3	NA	8.91[e]	95	PST-HC	52 weeks	Usual care
Gellis[22]	U.S.	Minor depression	36	75.9	91.6	88.9	8.3	18.05[b]	0	PST-HC	6 weeks	Usual care
Gellis[29]	U.S.	Minor depression	62	77.67	87.5	80.0	20.0	20.52[a]	NA	PST-HC	6 weeks	Usual care with home visit

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Author	Setting	Type of depression	Participants							Study's intervention		
			N	Age (mean)	Female (%)	Living alone (%)	Married (%)	Baseline depression score (mean)	Anti-depressants use (%)	Type of intervention	Duration (weeks)	Comparison
Naylor[37]	U.S.	Mixed depression	38	51.45	84.2	NA	NA	7.9[f]	NA	Home-based CBT	6 weeks	Usual care
Joling[38]	Netherland	Minor depression	170	81.45	73.5	NA	29.4	21.6	NA	Home-based CBT	12 weeks	Usual care
Pfaff[27]	U.S.	Mixed depression	200	60.97	63.0	21.6	53.0	NA	54.5	Home-based exercise	12 weeks	Usual care
Kerse[26]	Austria	Mixed depression	193	81.1	58.5	51.8	NA	3.7[e]	26.4	Home-based exercise	24 weeks	Usual care with home visit
Blumenthal[33]	U.S.	Major depressive disorder	102	52.52	74.5	NA	NA	16.52[b]	0	Home-based exercise	16 weeks	Usual care
Ciechanowski[35]	U.S.	Mixed depression	80	43.9	52.5	NA	68.8	2.00[d]	40%	Combined PST-HC with home-based exercise	19 weeks	Usual care
Ciechanowski[36]	U.S.	Minor depression	138	73	79	72.0	11.0	1.3[d]	51	Combined PST-HC with home-based exercise	19 weeks	Usual care
Banerjee[18]	Taiwan	Mixed depression	69	80.71	82.9	78.3	15.9	26.25[a]	11.39	Combined family therapy, bereavement counselling, social interventions with	24 weeks	Usual care

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Author	Setting	Type of depression	Participants							Study's intervention		
			N	Age (mean)	Female (%)	Living alone (%)	Married (%)	Baseline depression score (mean)	Anti-depressants use (%)	Type of intervention	Duration (weeks)	Comparison
										home-based exercise		
Gary[30]	U.S.	Mixed depression	74	65.8	57.1	NA	39.2	20.7[f]	29.7	Home-based CBT, home-based exercise, combined home-based CBT with home-based exercise	12 weeks	Usual care
Rickhi[41]	U.K.	Major depressive disorder	84	44.05	77.4	NA	58.3	20.35[b]	0	Spiritual teaching program	8 weeks	Usual care
Chung[34]	U.S.	Mixed depression	62	71.50	30.6	NA	NA	7.53[c]	1.61	Home-based deep breathing exercise	4 weeks	Usual care with telephone support call

[a]MADRS; [b]HAMD; [c]PHQ-9; [d]HSCL-20; [e]GDS; [f]BDI

PST-HC, problem solving therapy-home care; CBT, cognitive behavioural therapy

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Table 2. Mean difference of depression score after treatment between intervention and control groups

Author	Year	Follow up time	Intervention			Control			Mean difference (95% CI)
			N	Mean	SD	N	Mean	SD	
Home-based Psychological intervention									
Kiosses [25]	2015	12 weeks	37	10.6	6.08	37	15.6	6.81	-0.77 (0.30, -1.25)
Choi [21]	2014	12 weeks	35	14.44	7.04	31	19.16	7.02	-0.67 (-1.17, -0.17)
Gitlin [24]	2013	16 weeks	106	6.4	6.18	102	8.9	6.06	-0.41 (-0.13, -0.68)
Joling [38]	2011	12 weeks	86	16.60	6.41	84	17.27	6.53	-0.10 (-0.40, 0.20)
Gary [30]	2010	12weeks	17	8.2	6.3	15	9.3	4.9	0.19 (0.50, -0.89)
Gellis [22]	2010	6 weeks	18	11.4	8.3	18	17.3	8.1	0.72 (-0.04, -1.39)
Klug [28]	2010	48 weeks	29	6.11	3.00	29	10.43	4.2	-1.18 (-0.62, -1.74)
Naylor [37]	2010	6 weeks	15	4.40	5.30	18	4.90	5.30	-0.09 (-0.78, 0.59)
Gellis [29]	2007	6 weeks	30	8.11	4.3	32	13.64	5.6	1.10 (-0.57, -1.64)
SMD (95% CI)									**-0.57 (-0.84, -0.31)**
Home-based Exercise									
Kerse [26]	2010	24 weeks	94	2.4	0.2	92	3.1	0.3	-2.75 (-2.35, -3.15)
Gary [30]	2010	12 weeks	18	8.4	5.6	15	9.3	4.9	-0.17 (0.52, -0.86)
Blumenthal [33]	2007	16 weeks	53	9.5	7.43	49	10.5	5.36	-0.15 (0.24, -0.54)
SMD (95% CI)									**-1.03 (-2.89, 0.82)**
Combine psychological intervention and exercise									
Gary [30]	2010	12 weeks	16	6.5	3.7	15	9.3	4.9	-0.65 (0.08, -1.37)
Ciechanowski [36]	2004	24 weeks	72	0.71	0.6	66	1.17	0.53	-0.81 (-0.46, -1.16)
SMD (95% CI)									**-0.78 (-1.09, -0.47)**

CI, confidence interval; SD, standard deviation; SMD, standardized mean difference

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Table 3. Risk ratios of incidence of remission between intervention and control groups

Author	Year	Follow up time	Intervention		Control		RR (95% CI)
			Remission	No Remission	Remission	No Remission	
Home-based psychotherapy							
Kiosses [25]	2015	12 weeks	14	23	5	32	2.80 (1.12, 6.98)
Gitlin [24]	2013	16 weeks	39	50	25	68	1.63 (1.08, 2.46)
Joling [38]	2011	12 weeks	31	55	25	59	1.47 (0.84, 2.55)
Naylor [37]	2010	6 weeks	11	4	9	9	1.21 (0.79, 1.87)
Pooled RR (95% CI)							**1.53 (1.19, 1.98)**
Home-based Exercise							
Ptaff [27]	2014	12 weeks	49	29	40	28	1.07 (0.82-1.39)
Blumenthal [33]	2007	16 weeks	21	32	23	26	0.84 (0.54-1.32)
Pooled RR (95% CI)							**0.99 (0.79, 1.24)**
Combine psychotherapy and exercise							
Ciechanowski [35]	2010	19 weeks	4	36	0	40	9.00 (0.50-161.86)
Ciechanowski [36]	2004	19 weeks	30	42	6	60	4.58 (2.04-10.31)
Banerjee [18]	1996	24 weeks	19	10	9	23	2.33 (1.26-4.30)
Pooled RR (95% CI)							**3.47 (2.11, 5.70)**

CI, confidence interval; RR, risk ratio

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Figure legends

Figure 1. Flow chart of study selection

Figure 2. Network meta-analysis of disease remission among home-based interventions

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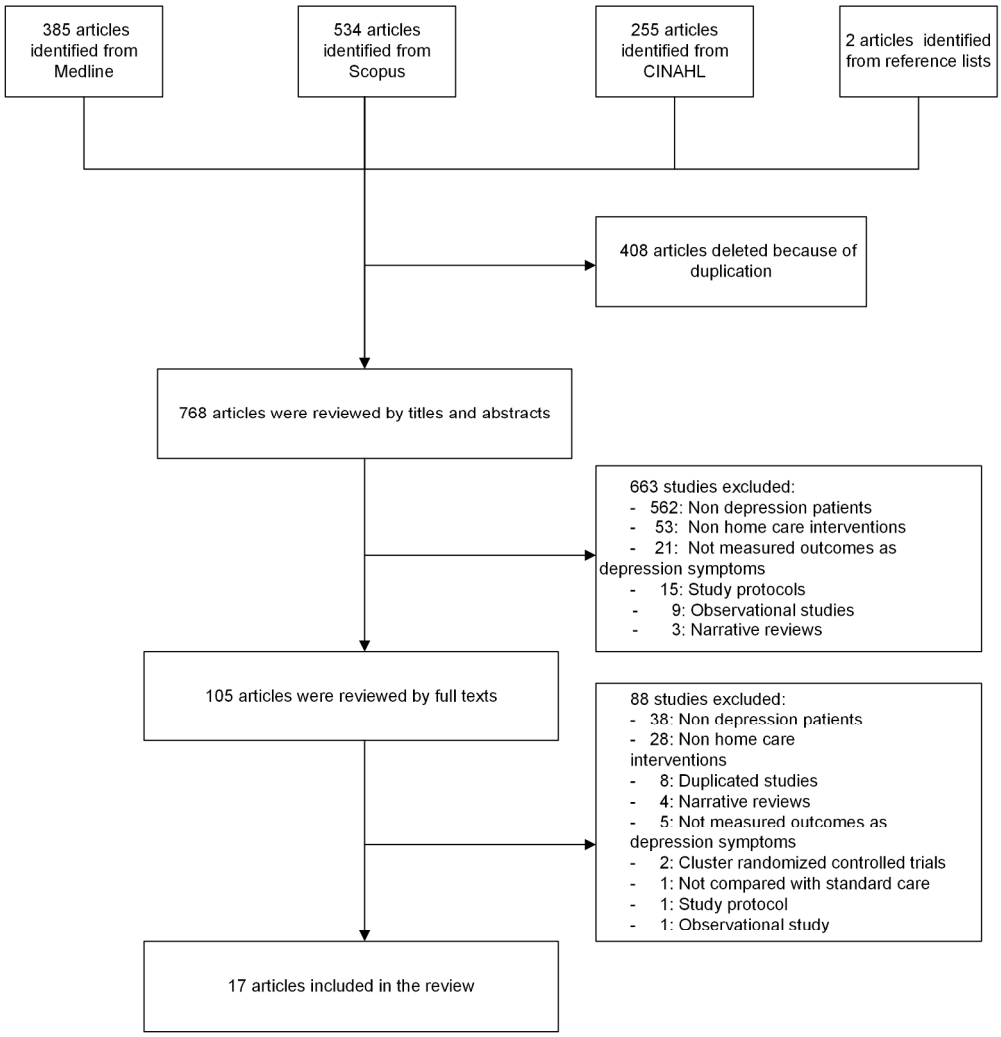

Figure 1. Flow chart of study selection

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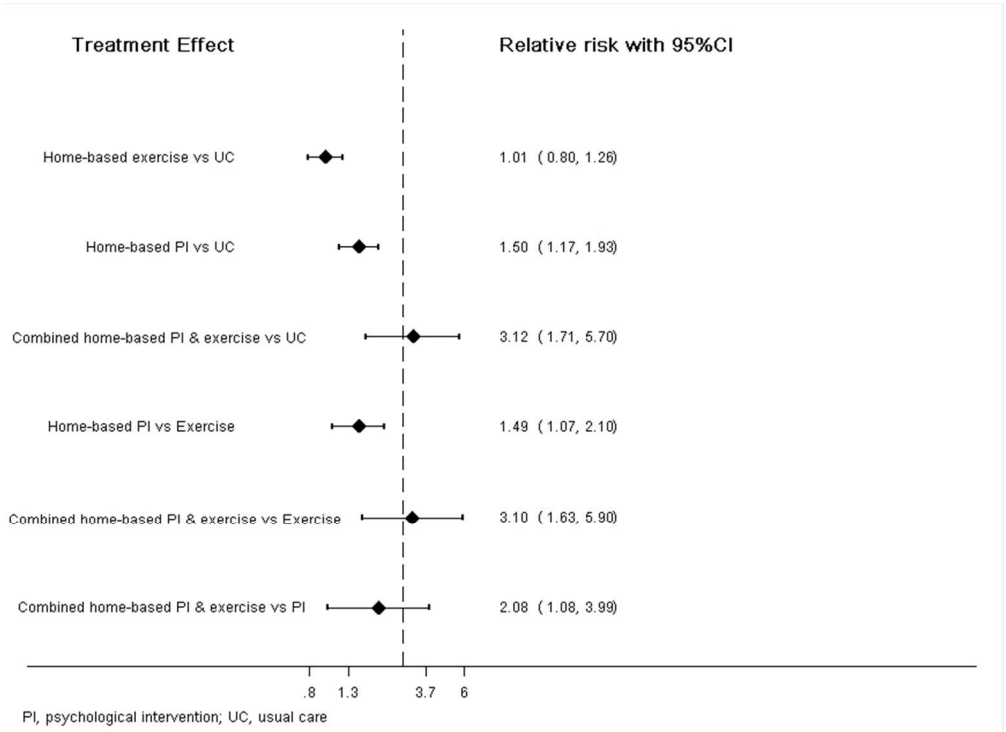

Figure 2. Network meta-analysis of disease remission among home-based interventions

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Supplementary Table 1. Risk of bias assessment

Author (Year)	Year	Random sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessors	Incomplete outcome data	Selective outcome reporting	Other bias
Rickhi	2011	Low	Low	High	Low	Low	Low	Low
Banerjee	1996	Low	Unclear	High	Low	Low	Low	Low
Blumenthal	2007	Low	Low	High	Low	Low	Low	Low
Choi	2014	Unclear	Unclear	High	Unclear	High	Low	Low
Chung	2010	Low	Low	High	unclear	High	Low	Low
Ciechanowski	2010	Low	Low	High	Low	Low	High	Low
Ciechanowski	2004	Low	Low	High	Unclear	Low	Low	Low
Gary	2010	Unclear	Unclear	High	Low	Low	Low	Low
Gellis	2010	Unclear	Unclear	High	Low	Low	Low	Low
Gellis	2008	Low	Unclear	High	Low	Low	Low	Low
Gitlin	2013	Low	Low	High	Unclear	Low	Low	Low
Kerse	2010	Low	Unclear	High	Low	Low	Low	Low
Kiosses	2015	Low	Unclear	High	Low	Low	Low	Low
Klug	2010	Low	Unclear	High	Unclear	High	Low	Low
Pfaff	2014	Low	Unclear	High	Low	Low	Low	Low
Joling	2011	Low	Unclear	High	Unclear	Low	Low	Low
Naylor	2010	Low	Unclear	High	Unclear	High	Low	Low

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Supplementary Figure legends

Supplementary Figure 1. Pooled standardized mean difference between home-based psychological intervention and usual care according to severities of depression

Supplementary Figure 2. Pooled standardized mean difference between home-based exercise, combined psychological intervention with exercise and usual care

Supplementary Figure 3. Pooled risk ratio of disease remission between home-based psychological intervention and usual care

Supplementary Figure 4. Pooled risk ratio of disease remission between home-based exercise, combined psychological intervention with exercise and usual care

Supplementary Figure 5. Network plot of all available home-based interventions

Supplementary Figure 6. Funnel plots of home-based psychological intervention and home-based exercise

Supplementary Figure 7. Funnel and contour enhanced funnel plot of combined psychological intervention with exercise

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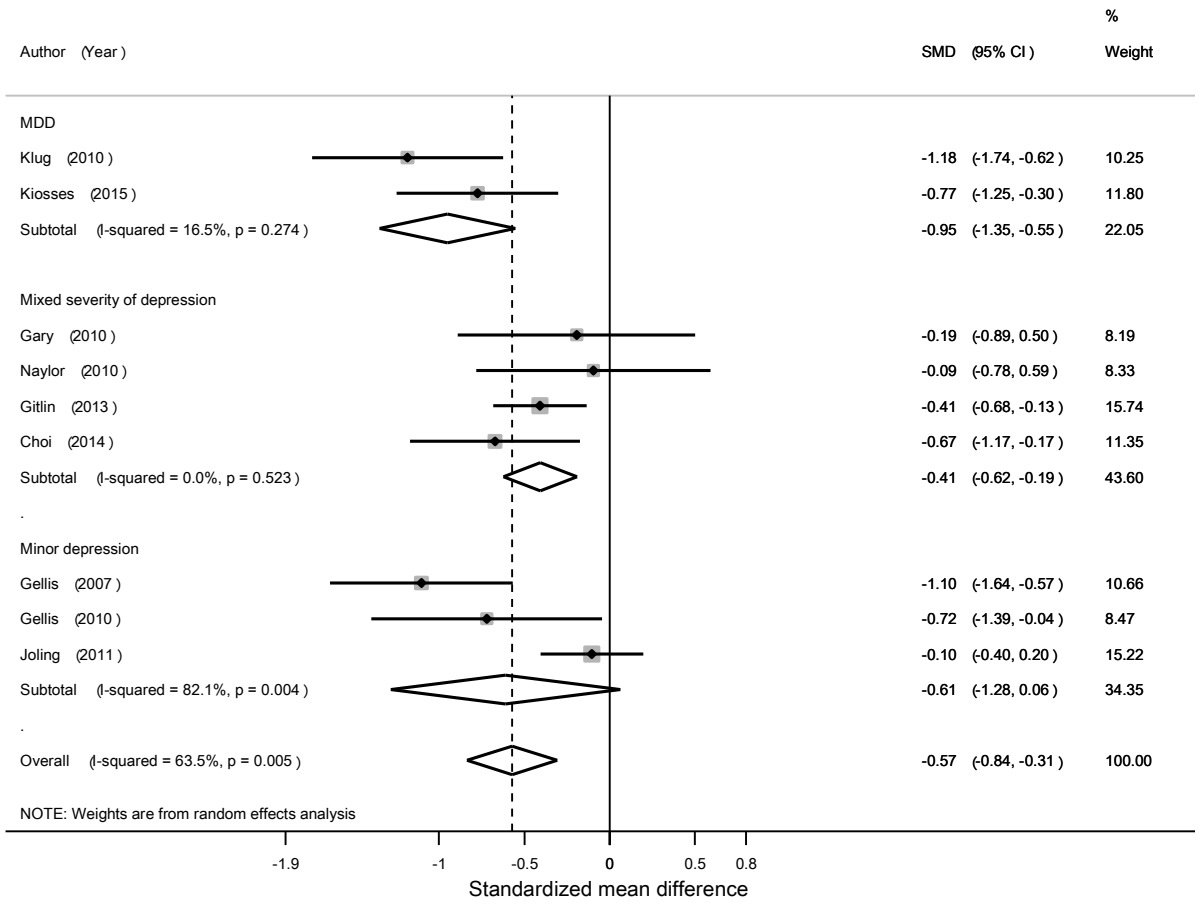
Supplementary Figure 1



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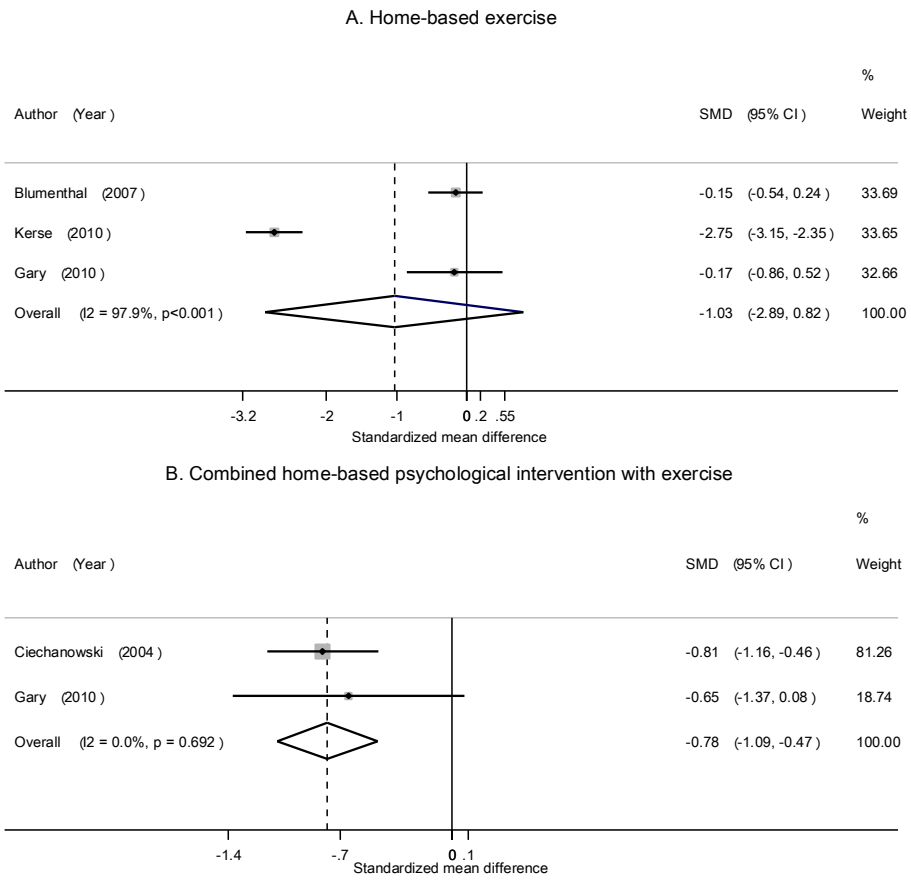
Supplementary Figure 2



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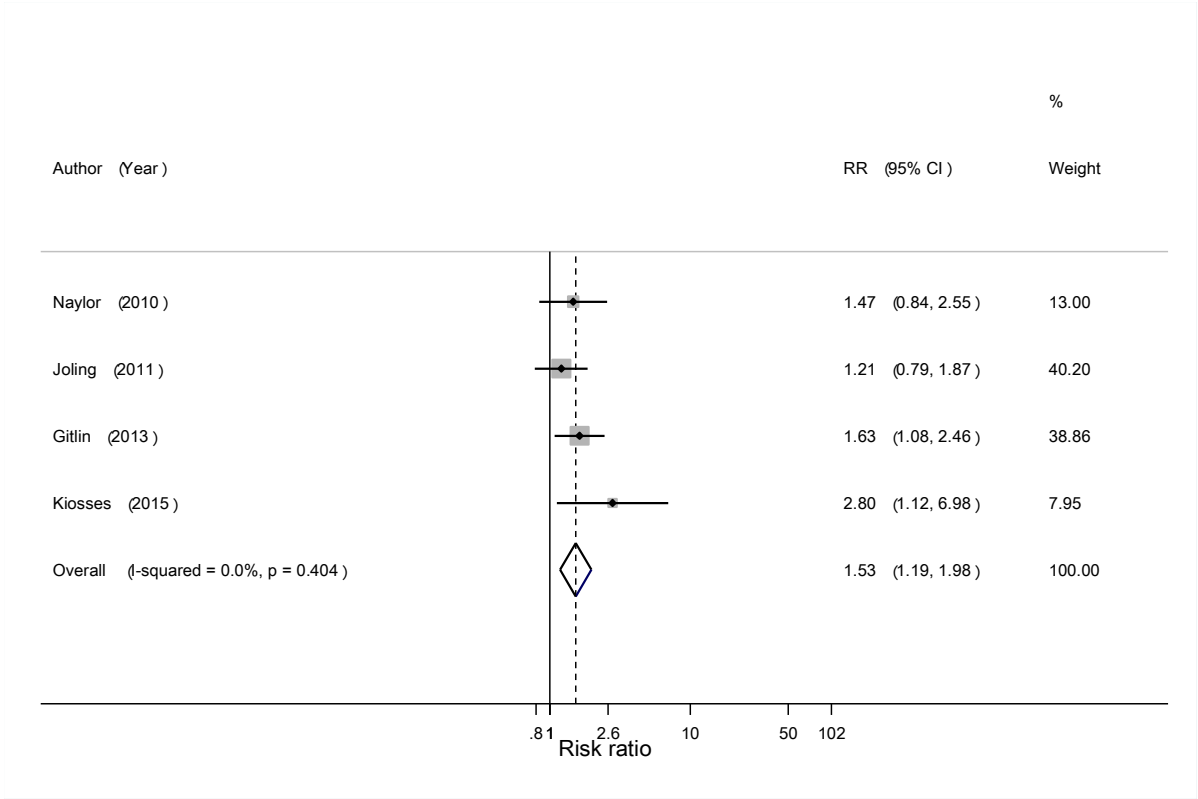
Supplementary Figure 3



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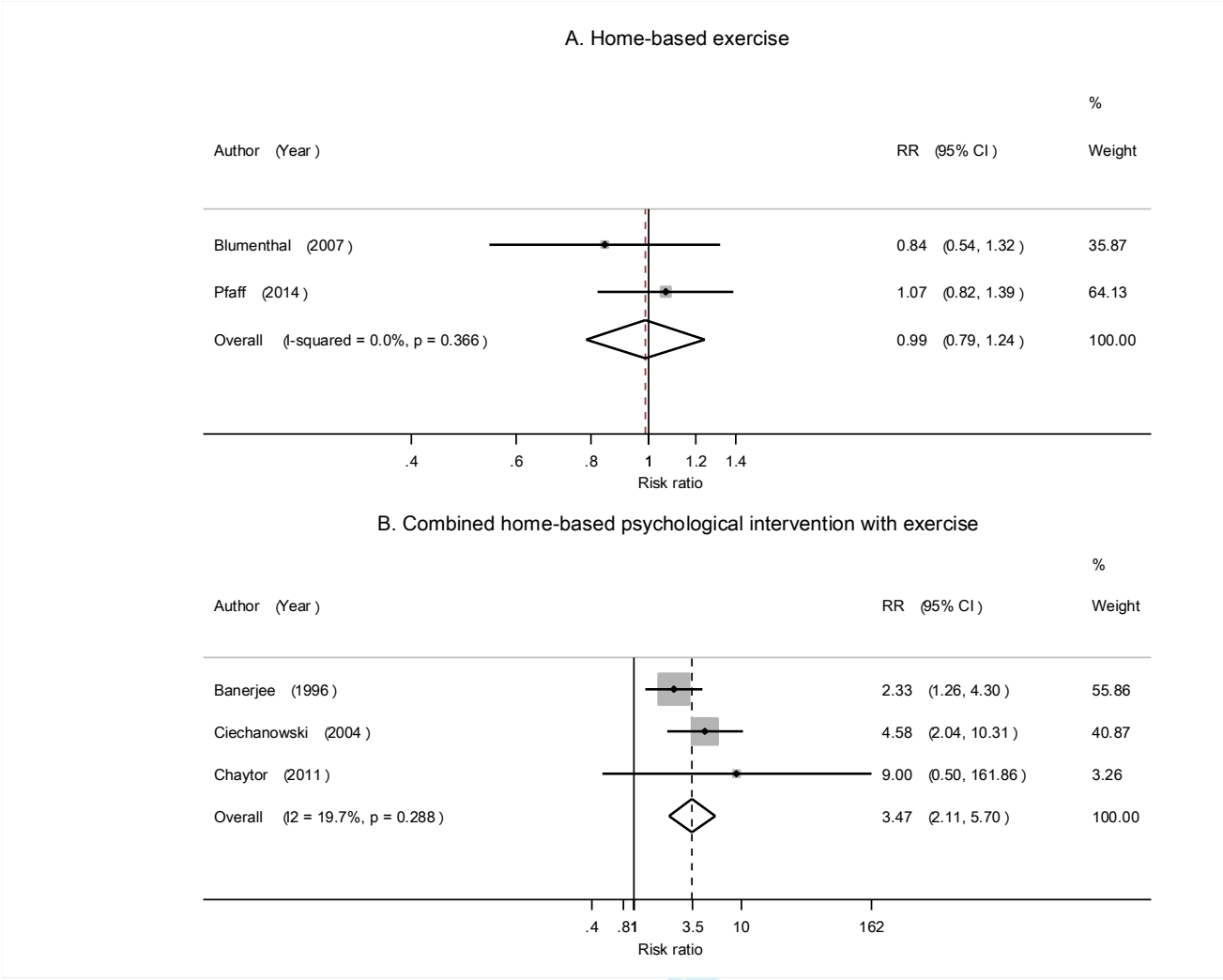
Supplementary Figure 4



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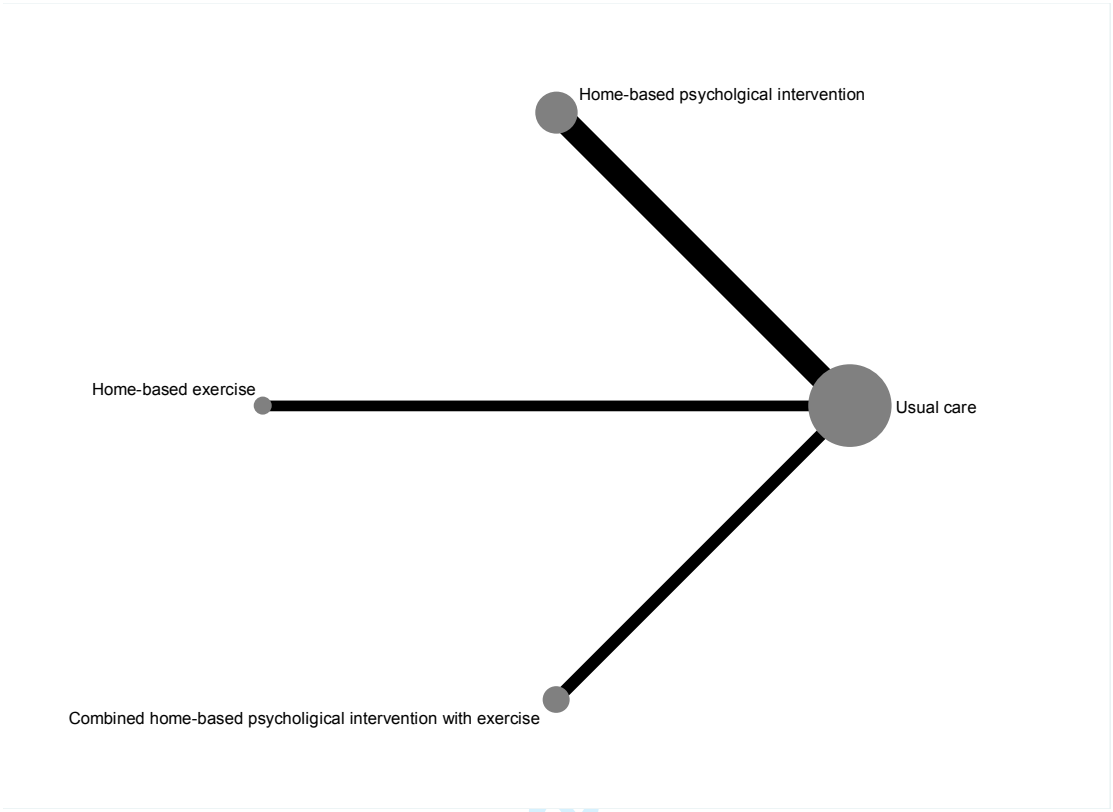
Supplementary Figure 5



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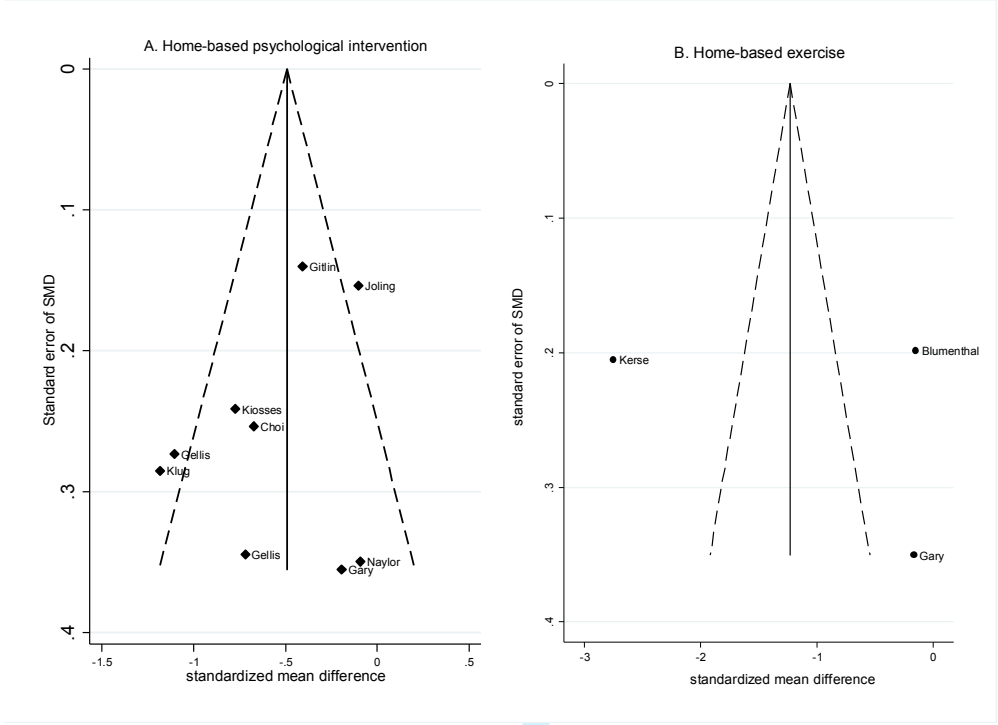
Supplementary Figure 6



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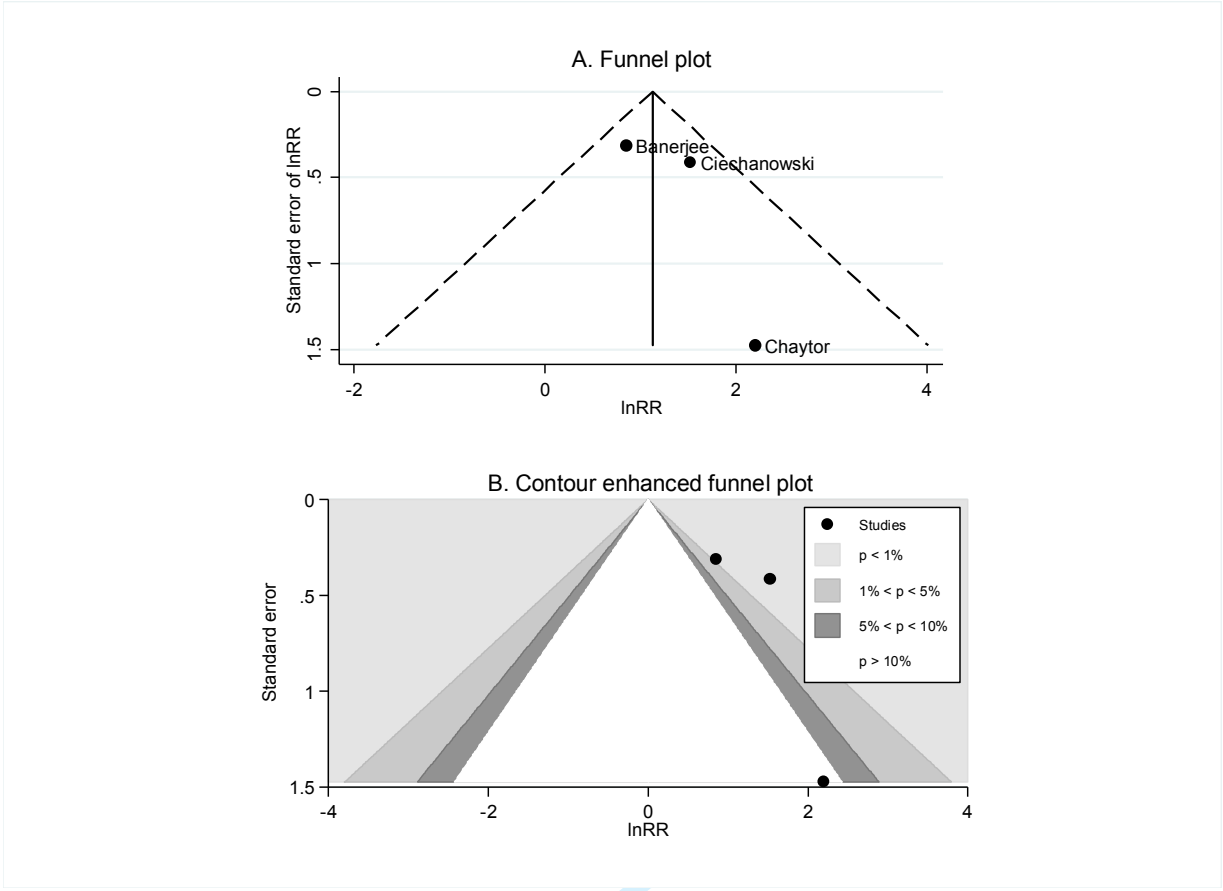
Supplementary Figure 7



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Supplementary Appendix

Search strategy for Medline

(Depressive OR depression OR depressed) AND ("Home Care Services"[MeSH] OR "Home Care Agencies"[MeSH] OR "Home Nursing"[MeSH] OR "House Calls"[MeSH] OR "Community Health Planning"[MeSH] OR "Health Systems Agencies"[MeSH] OR "Community Health Nursing"[MeSH] OR "Social Support"[MeSH]) OR ("Home Based" OR "home support" OR (“home treatment” OR “home treatments”) OR “home care” OR ("home visits" OR "Home visit") OR ("Health visits" OR "Health visit") OR (“home service” OR “home services”)) Filters: Randomized Controlled Trial

Search strategy for Scopus

(Depressive OR depression OR depressed) AND ("Home Based" OR "home support" OR (“home treatment” OR “home treatments”) OR “home care” OR ("home visits" OR "Home visit") OR ("Health visits" OR "Health visit") OR (“home service” OR “home services”) OR “home health care”)

CINAHL

Search strategy for CINAHL

(depressive OR depression OR depressed) AND ("Home Based" OR "home support" OR (“home treatment” OR “home treatments”) OR “home care” OR ("home visits" OR "Home visit") OR ("Health visits" OR "Health visit") OR (“home service” OR “home services”) OR “home health care”) AND (randomized OR randomized)

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PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	3
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	5
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	5, 6
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	-
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	6, 7
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	6
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	Supplementary Appendix
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	6
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	7
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	7
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	8
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	8
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	8

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PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	9
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	8
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	9, Figure 1
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	9, 10, 11, 12 & Table 1
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	12 & Supplementary Table 1
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	Tables 2 & 3 Figure 2 Supplementary Figure1, 2, 3, 4
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	12-16
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	16
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	12-16
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	16-19
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	18
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	19
FUNDING			

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PRISMA 2009 Checklist

Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	19

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BMJ Open

Efficacy of home-based non-pharmacological interventions for treating depression: a systematic review and network meta-analysis of randomized-controlled trials

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Efficacy of home-based non-pharmacological interventions for treating depression: a systematic review and network meta-analysis of randomized-controlled trials

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Key words: depression; treatment; home-based intervention; systematic review; network meta-analysis

Word count: 5,551 words

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Abstract:

Objectives: To systematically review and compare the efficacy of all available home-based non-pharmacological treatments of depression.

Design: Systematic review and network meta-analysis of randomized controlled trials.

Data sources: Medline, Scopus, and CINAHL databases were searched since inceptions to7th August 2016.

Eligibility criteria: Randomized controlled trials comparing the efficacy of home-based non-pharmacological interventions with usual care of depressed patients were included in the review.

Main outcomes: Depression symptom scores and disease remission rates at the end of treatment.

Results: Seventeen studies were included in the review. Home-based non-pharmacological interventions were categorized as 1) home-based psychological intervention, 2) home-based exercise intervention, 3) combined home-based psychological intervention with exercise intervention, and 4) complimentary or alternative medicine. Complementary and alternative medicine approaches were excluded from the meta-analysis due to heterogeneity. The standardized mean differences of post-treatment depression symptom scores between usual care groups and home-based psychological intervention, home-based exercise intervention, and combined home-based psychological intervention with exercise intervention were -0.57 (95%CI:-0.84, -0.31), -1.03 (95%CI:-2.89, 0.82), and -0.78 (95% CI:-1.09,-0.47), respectively. These results suggest that only home-based psychological intervention and combined home-based psychological intervention with exercise intervention could significantly decrease depression scores. Compared with usual care groups, the disease remission rate was also significantly higher for home-based psychological intervention (pooled risk ratio = 1.53; 95% CI: 1.19, 1.98) and combined home-based psychological intervention with exercise intervention (pooled risk ratio = 3.47; 95% CI: 2.11, 5.70). Of all the studied interventions, combined home-based psychological intervention with exercise intervention had the highest probability of resulting in disease remission.

Conclusion: Our study confirms the efficacy of home-based psychological intervention and combined home-based psychological intervention with exercise intervention in the treatment of depression.

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Combined home-based psychological intervention and exercise intervention was the best treatment and should be considered for inclusion in clinical guidelines for managing depression.

Strengths and limitations of this study

- Our analysis provides the first comprehensive review of the efficacy of home-based non-pharmacological interventions in treating depression.
- A comprehensive search was undertaken to identify as many relevant studies as possible.
- We performed a network meta-analysis to compare the efficacy of home-based interventions in order to identify the best treatment regimen.
- The quality of included studies in the area of allocation concealment was not optimal.
- Participants in our included studies were aware of their own interventions and the outcomes were subjective.

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INTRODUCTION

Recent studies have highlighted the international recognition of depression as one of the leading global burdens of disease (GBD)[1]. Depression is associated not only with greater morbidity and mortality but also with increasing health service use and costs[2]. In addition, untreated depression has been recognized as a strong predictor of poor health outcomes in elderly[3-5] and adult patients with chronic disease[6-8].

Both pharmacological and non-pharmacological interventions, such as psychotherapy or supervised exercise intervention, have been accepted as standard treatments of depression. However, concerns about drug side effects and dependency appear to make patients prefer psychological interventions. One study showed that around 70% of depressed patients were non-compliant with antidepressants because of concerns about their side effects[9]. Even though non-pharmacological interventions were preferred over antidepressants[10 11], only a very small percentage of patients referred for psychotherapy were able to enter and complete this treatment[12]. This inconsistency between patient preference and low rates of initiation and adherence to treatment could be a consequence of barriers to obtaining treatment. Non-pharmacological interventions are usually clinic or hospital-based and require visits on a weekly or monthly basis. In one study, 70% of patients reported structural barriers preventing them from attending psychotherapy sessions regularly and cited time constraints, transportation problems and cost as being significant obstacles[13].

Among older patients, whose prevalent rate of depression is very high, these problems were aggravated by concurrent medical illness, social isolation, functional impairment or being home-bound [14-20]. Overcoming these barriers by providing interventions in patients' own homes may achieve better treatment adherence and thereby greater treatment success than clinic or hospital-based interventions.

Home-based non-pharmacological interventions, such as problem solving therapy[21-25] and home-based exercise intervention [26 27], have developed over several years. Although some studies have suggested that these approaches can improve depressive symptoms and rates of remission when compared with standard usual care[26 28 29], other studies have reported conflicting results[27 30 31]. In recent years new home-based interventions have been introduced to treat depression, such as spirituality teaching programme[32] and combined home-based psychotherapy with exercise intervention but their efficacy is still controversial. Therefore, our systematic review and network meta-

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analysis was undertaken with the aim of reviewing all available home-based non-pharmacological interventions, pooling the effect sizes of each intervention on symptom improvement and indirectly comparing treatment efficacy between the different interventions. The results of this review should be useful for identifying the most beneficial home-based non-pharmacological interventions and for informing clinical guidelines for treating depression.

METHODS

Search strategy

Relevant studies were identified using Medline, Scopus, and CINAHL databases searched from inceptions to7th August 2016. Reference lists of included studies were also explored. Search terms and search strategies for each database are presented in a Supplementary Appendix.

Selection of studies

Initially studies were selected from titles and abstracts by two independent reviewers (K.S. and T.A.). Full articles were retrieved to aid decision making if decision could not be made based on titles and abstracts. Disagreement between the two reviewers was resolved by discussion. Percentage agreement between the two reviewers was estimated using kappa statistics.

Inclusion criteria

Randomized-controlled trials published in English were eligible for the review if they met all of the following criteria:

1. Study participants were adults aged more than 18 years with a diagnosis of any degree of depressive disorder using the criteria of the Diagnostic and Statistical Manual of Mental Disorders 4th Edition (DSM-IV) or any diagnostic tool used for diagnosis or screening for depression. Participants who were children, adolescents or postpartum women were excluded.
2. Interventions of interest were non-pharmacological and provided in the patient's home, such as cognitive behavioral therapy, problem solving therapy, family therapy, or home-based exercise intervention.
3. Treatment comparison was the standard care of depression in outpatient clinics or hospital settings.

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4. Outcomes were measured by the level or severity of depressive symptoms or the incidence of disease remission at the end of the intervention.
5. Studies provided sufficient data for analysis, such as number of participants (n), mean depression score, standard deviation (SD) for each intervention group, and the number of patients per intervention group with or without disease remission.

Data extraction

Two reviewers (KS and TA) independently used a standardized data record form to extract baseline characteristics of included studies and outcomes of interest. Disagreement between the two reviewers was resolved by discussion and corresponding authors of studies were contacted if information was incomplete.

Interventions of interest

Home-based non-pharmacological intervention was defined as any care or management of depression provided by health care professionals at a patient's place of residence. Home-based interventions had to have a clear and definite objective. Home visits that provided only health-education, social or emotional support were, therefore, excluded from this study.

Outcomes of interest

The outcomes of interest were depressive symptom scores and disease remission rates at the end of treatment. Disease remission was defined according to the criteria of the original article. Included studies used several tools for measuring the severity of depressive symptoms, namely the Hamilton Depression Rating Scale (HAM-D)[21 22 30 33 34], Patient Health Questionnaire-9 (PHQ-9)[24 35], Geriatric Depression Scale (GDS)[23 26 28], Hopkins Symptom Checklist-20 (HSCL-20)[36 37], Montgomery Asberg Depression Rating Scale (MADRS)[18 25 27], Beck Depression Inventory-Fast Screen (BDI-FS)[38] and Center of Epidemiologic Studies Depression Scale (CES-D)[39]. These tools have different score ranges (HAM-D = 0-53, PHQ-9 = 0-27, GDS = 0-15, HSCL-20 = 0-4, MADRS = 0-60, BDI-FS = 0-21, and CES-D = 0-60) with higher scores in all tools representing increasing severity of depressive symptoms.

Risk of bias assessment

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To assess the quality of included studies, a risk of bias assessment tool [40] was applied by two independent reviewers (K.S., T.A.). Seven domains were evaluated as follows: 1) random sequence generation 2) allocation concealment 3) blinding of participants and personnel 4) blinding of outcome assessors 5) incomplete outcome data 6) selective outcome reporting 7) other sources of bias. The quality of the studies was classified as being at high, unclear, or low risk of bias. We added the domain of power to determine the likelihood of any studies making a true difference to outcome, classifying any study as being at high risk of bias if it reported a power less than 80%. Disagreement between the two reviewers was settled by discussion.

Statistical analysis

Because depression scores were measured differently among the studies, for direct comparison the standardized mean differences (SMD) of depressive scores between intervention and control groups were estimated for individual studies and then were pooled across studies. Heterogeneity between studies was estimated by Q test and I^2 statistic. Heterogeneity between studies was considered if the P-value from Q test was less than 0.10 or if I^2 was equal to or greater than 25%[41]. If heterogeneity was presented, the SMD was estimated by applying the random effect model. Otherwise the fixed effect model was applied.

For dichotomous outcomes, relative risks (RR) of disease remission were calculated for each study. The random effect model was used for pooling RR if there was evidence of heterogeneity between studies. Otherwise the inverse variance method was used. Sources of heterogeneity were explored by considering possible factors one by one in a meta-regression model (e.g. mean age, severity of depression at baseline and types of intervention delivery).

A network meta-analysis was applied to indirectly assess intervention effects for all home-based interventions, i.e., home-based psychological intervention, home-based exercise intervention, combined home-based psychological intervention and exercise intervention, and usual care. This method allows us to perform indirect comparison using common comparator. For instance, some studies compared home-based psychological intervention with usual care, some others compared home-based exercise intervention with usual care, non or few studies compared home-based psychological intervention with home-based exercise intervention. Using common comparator as usual care would allow to indirectly compare home-based psychological intervention with home-based

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exercise intervention[42]. Treatment effects for each study were estimated using a two-stage network meta-analysis. Firstly, summary data was expanded into individual patient data using the 'expand' command in STATA program. Binary regression was applied to estimate log (RR) and variance-covariance of each treatment using 'mvmeta' make command. A multivariate random effect meta-analysis was used to calculate the pooled RRs and their 95% confidence intervals (CI). Riley's method was used for considering subject-study correlation. Treatment ranking was made according to the linear predictor of each study. In addition, a consistency assumption (i.e., discrepancy of intervention effects between direct and indirect meta-analyses) was assessed using the standardized normal test (Z).

Publication bias was assessed using Egger test and funnel plot. If the funnel plot showed asymmetry, a contour enhanced funnel plot was performed to explore whether asymmetry was the result of heterogeneity between studies or arisen from publication bias. All analyses were performed using STATA version 14. A two-sided test with P-value less than 0.05 was considered statistically significant, except for the Q test, in which a P-value less than 0.10 was applied.

Patient involvement

Patients were not involved in the design of the study, development of outcome measures, or conduct of the study. We did not ask patients for advice on interpreting or writing up results. There are no plans to disseminate the results of the research to study participants.

RESULTS

We identified 385, 534, 255, and 2 articles from Medline, Scopus, CINAHL databases and reference lists respectively. After deleting duplications, the titles and abstracts of 768 studies were reviewed. Finally, 17 studies met our inclusion criteria and were eligible in the review (Figure 1). Agreement of study selection between the two reviewers was high at 86.7% (Kappa = 0.50). All but one[18] of the included studies reported protocol approval by an ethics committee.

Study participants

The baseline characteristics of included studies are presented in Table 1. The type and severity of depression of participants differed between studies. Four studies[25 28 33 34] included patients with major depressive disorder, four[22 23 37 39] included patients with minor depression and nine[18 21 24 26

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[27 30 35 36 38] included patients with mixed severities of depression. Ten studies included elderly patients[18 21-26 28 37 39] while seven studies included adults with ages greater than 18 years[27 30 33-36 38]. Ten studies included depressed patients with other co-morbidities (i.e. epilepsy[36], heart diseases[22 30 35], disability[18], and mild to moderate cognitive impairment[25]). Twelve studies[21 23 24 26-28 33 34 37-39] included patients without co-morbidity. Use of anti-depressants at baseline varied widely between studies, ranging from 0% to 95%.

Home-based interventions

The composition of home-based non-pharmacological interventions differed among the included studies but could be categorized into 4 groups: 1) home-based psychological intervention 2) home-based exercise intervention 3) combined home-based psychological intervention with home-based exercise intervention 4) complementary or alternative medicine. Eight, 3 and 3 studies compared home-based psychological intervention with usual care, home-based exercise intervention with usual care, and combined home-based psychological intervention with home-based exercise intervention with usual care, respectively. One study compared the efficacy between home-based psychological intervention, home-based exercise intervention, combined home-based psychological intervention with home-based exercise intervention, and usual care. Since interventions in the category of complementary or alternative medicine were heterogeneous, they were not included in the meta-analysis but were subjected to qualitative analysis. Details of each home-based intervention are summarised below:

Home-based psychological intervention

Home-based psychological intervention was classified as home-based problem-solving treatment or home-based cognitive behavioral therapy.

1. *Home-based problem-solving treatment* (6 studies[21 22 24 25 28 29])

Home-based problem-solving treatment (PST) is a skill-enhancing behavioral treatment of depression usually delivered by social workers and psychologists. This approach assumes that depressive symptoms are caused and maintained by problems of daily life and that these can be reduced by identifying and addressing them systematically. Each PST session comprises 1) defining and formulating the nature of the depressive problem 2) generating a range of alternative solutions to

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the problem 3) systematically evaluating the possible consequences of each solution then selecting the most appropriate one 4) monitoring and evaluating the actual outcome. In addition, PST identifies patients' pleasurable activities and encourages them to participate in these activities.

2. *Home-based cognitive behavioral therapy* (CBT) (3 studies[30 38 39])

The aim of CBT is to modify the dysfunctional emotions, behaviours, and thoughts of depressed patients. This type of intervention was identified in 3 studies, of which 2 studies were CBT-based bibliotherapy. In this approach, participants received self-help books or leaflets that included instruction on cognitive behavioral self-help, mood management skills, and tasks to practice. During the intervention period, participants were visited by home care nurses or contacted by telephone by study investigators to assess their symptoms and encourage them to follow the course at their own pace.

Home-based exercise intervention

Home-based exercise intervention was employed in 4 studies. Exercise included both progressive resistance training, aerobic exercise [26 27] and aerobic exercise only[30 34]. Participants were required to perform the exercises for at least 30 minutes three times a week.

Combined home-based psychological intervention with exercise intervention

Home-based psychological intervention combined with exercise intervention was the interested intervention in 4 studies. Each of these applied aerobic exercise as a home-based exercise intervention but psychological therapies differed among them (PST in two studies[36 37], cognitive behavioral therapy in one study[30] and family therapy with bereavement counselling and social interventions in one study[18]).

Complementary or alternative medicine

This intervention refers to a broad set of health care practices or activities that are not integrated into the dominant health care system. This type of intervention was used in 2 studies. One involved home-based deep-breathing exercise[35] aimed at stimulating a relaxation response, (i.e. to decrease arousal, heart rate and blood pressure, and to reduce responsiveness of the sympathetic nervous system). Deep-breathing exercises can also help patients to disregard negative and

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distracting thoughts. Patients were trained by experienced nurses to breathe at a rate of six breaths per minute. During the treatment period, this was undertaken in a quiet environment for a period of ten minutes, three times each day.

The other intervention employed a spirituality teaching programme[32] aiming to promote contemplation of the inter-relation between meaning and purpose, connectedness with others, nature or the divine, and values such as compassion, love, justice, and forgiveness. The programme comprised eight sessions involving explanation of the divine aspect of the self, teaching breathing and visualization practice, helping patients to connect with the divine through prayer or meditation, letting go of regret and fostering gratitude, practicing self-awareness relating to the five senses, and building upon connectedness with others. Participants were also advised to avoid forming expectations and to refrain from judging outcomes. Initially patients participated in a workshop run by psychiatrists and were then required to practice by themselves with the help of audio CDs.

Treatment comparison

Usual care, defined as the standard care of depression managed in a clinic or hospital setting, was applied as a treatment comparator for all studies. In addition to usual care, three studies[25 26 29] included home visits and two[21 35] included telephone support. However, these interventions provided education about depression together with general social or emotional support but did not offer specific psychological help or exercise intervention. With the exception of one study[32], almost all used anti-depressant medication as a co-intervention but the decision to initiate or maintain this was dependent on the judgement of patients and their physicians.

Risk of bias assessment

Results of risk of bias assessment are presented in Supplementary Table 1. Most of the studies (14 studies) reported low risk of bias in the domain of random sequence generation, while 3 studies[21 22 30] reported unclear risk. For allocation concealment, 11 studies[18 21 22 25-30 38 39] had unclear risk of bias, while 6 studies[24 32 34-37] had low risk of bias. All studies reported high risk of bias in the domain of blinding of participants and personnel and low risk of bias in other domains. Ten studies[18 22 25-27 29 30 32 34 36] had low risk of bias for blinding of outcome assessors, whereas 7 studies[21 24 28 35 37-39] had unclear risk. For the domain of incomplete outcome data, 13 studies[18 22 24-27 29 30 32 34 36 37 39]

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reported low risk of bias and 4 studies[21 28 35 38] reported high risk. Almost all studies (16 studies) had low risk of bias for selective outcome reporting, while only one study[36] had high risk of bias. In the domain of power, 10 studies had unclear risk of bias, 6 reported low risk and 1 had high risk of bias.

Pooled mean difference of depression score

Home-based psychological intervention vs usual care

Nine studies were analyzed[21 22 24 25 28-30 38 39] comparing home-based psychological intervention with usual care (N = 739). Depression scores were assessed at the end of treatment, which ranged from 6 to 48 weeks. The mean differences and 95% CIs of depression scores for each study are presented in Table 2. SMD of home-based psychological intervention versus usual care was -0.57 (95% CI: -0.84, -0.31), suggesting that home-based psychological intervention can significantly decrease depression scores when compared with usual care.

Moderate heterogeneity was found between studies, with I^2 of 63.5%. Sources of heterogeneity were explored but none of the factors decreased I^2. Subgroup analyses were performed according to the severity of depression (i.e. major depressive disorder (MDD), minor depression and mixed severity of depression). These showed that SMDs in patients with MDD, minor depression, and mixed severity of depression were -0.95 (95% CI: -1.35, -0.55; I^2 = 16.5%), -0.61 (95% CI: -1.28, 0.06; I^2 = 82.1%), and -0.41, (95% CI: -0.62, -0.19; I^2 = 0%) respectively (see Supplementary Figure 1). These suggest that home-based psychological intervention reduces depression scores significantly in the groups of MDD and mixed severity of depression. In addition, the efficacy of this intervention in patients with MDD was better than the efficacy in patients with minor depression.

Home-based exercise intervention vs usual care

Three studies[26 30 34] (N = 321) were pooled to compare the effect of home-based exercise intervention with usual care. The SMD was -1.03 (95% CI: -2.89, 0.82; I^2 = 97.9%) (Table 2 and Supplementary Figure 2A). The mean depression score in the home-based exercise intervention group was therefore 1.03 units lower than the mean depression score in the usual care group. However, this effect did not reach statistical significance.

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Combined home-based psychological intervention with exercise intervention vs usual care

Only two studies[30 37] (N = 169) had sufficient data for pooling the effect on the depression score of combined home-based psychological intervention with exercise intervention. Mean depression scores were measured at the ends of the treatments, namely at 12 weeks[30] and 24 weeks[37]. Table 2 shows the mean depression scores and 95% CIs for each study. SMD was -0.78 (95% CI: -1.09, -0.47; I^2 = 0.0%) (Supplementary Figure 2B). This indicates that patients receiving combined home-based psychological intervention and exercise intervention had significantly lower mean depression scores (by 0.78 units) than patients receiving usual care.

Pooled risk ratio of disease remission

Home-based psychological intervention vs usual care

Four studies (N = 459) comparing the effectiveness of home-based psychological intervention with usual care had remission rates as their outcome of interest. Remission from depression was defined as HAMD score ≤ 7 in one studies[25], PHQ-9 ≤ 4 in one study[24], BDI < 4 in one study[38] and CES-D < 16 in one study[39] (Table 3). The pooled RR was 1.53 (95% CI: 1.19, 1.98) (Supplementary Figure 3), suggesting that patients receiving home-based psychological intervention were approximately 1.7 times more likely to have remission from depression than patients receiving usual care. The results among studies were homogeneous with I^2 of 0%.

Home-based exercise intervention vs usual care

Two studies (N = 248) reported their outcome as disease remission and had sufficient data for pooling. Disease remission was defined as HAMD score ≤ 7[34] or symptoms no longer meeting the criteria for major and minor depression according to DSM-IV criteria[27] (Table 3). The pooled RR was 0.99 (95% CI: 0.79, 1.24; I^2 = 0.0%) (Supplementary Figure 4A), indicating that there was no significant difference between home-based exercise intervention and usual care in the likelihood of having remission from depression.

Combined home-based psychological intervention and exercise intervention vs usual care

Three studies (N =279) were pooled to compare remission rates between combined psychological intervention and usual care. Disease remission was defined as HSCL-20 score < 0.5 for

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two studies[36 37] but in Banerjee's study[18] the outcome was not clearly defined (Table 3). Pooled RR was 3.47 (95% CI: 2.11, 5.70; I^2 = 19.7%) suggesting that the combination of home-based psychological intervention and exercise intervention significantly increased the likelihood of remission from depression when compared with usual care (Supplementary Figure 4B).

Network meta-analysis

Disease remission rate

Nine studies (N = 987) were included in the network meta-analysis. Supplementary Figure 5 shows the network plot of home-based psychological intervention, home-based exercise intervention, combined home-based psychological intervention with exercise intervention, and usual care. Size of node and edge reflect the number of studies and patients respectively. From the plot, usual care was the common comparator and had the largest sample size of the four treatment regimes. Home-based psychological intervention versus usual care had the largest number of studies.

Pooled RRs for each treatment comparison are presented in Figure 2. Compared with usual care, only combined home-based psychological intervention with exercise intervention and home-based psychological intervention alone significantly increased the likelihood of disease remission, with pooled RRs of 3.12 (95% CI: 1.71, 5.70) and 1.50 (95% CI: 1.17, 1.93) respectively. In addition, the incidence of disease remission in home-based psychological intervention and combined home-based psychological intervention with exercise intervention groups was significantly higher than in the home-based exercise intervention group, having pooled RRs of 1.49 (95% CI: 1.07, 2.10) and 3.10 (95% CI: 1.63, 5.90), respectively. When compared with home-based psychological intervention alone, combined home-based psychological intervention with exercise intervention also significantly improved the rate of disease remission (pooled RR = 2.08; 95% CI: 1.08, 3.99).

Treatment ranking was assessed by estimating the probability of each treatment being the best. This yielded probabilities of 99.5%, 0.5%, and 0% for combined home-based psychological intervention with exercise intervention, home-based psychological intervention alone, and home-based exercise intervention respectively. Combined home-based psychological intervention with exercise intervention therefore emerged as the best intervention for achieving remission from depression.

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Applying inconsistency assumptions to the treatments, inconsistency factors were calculated as 0.020 (Z=0.183, P-value=0.912) for home-based psychological intervention vs usual care, -0.018 (Z=0.110, P-value=0.913) for home-based exercise intervention vs usual care, and 0.106 (Z=0.107, P-value=0.915) for combined home-based psychological intervention with exercise intervention versus usual care. These figures find no significant difference between the direct and indirect comparison of estimated treatment effects.

Efficacy of complementary or alternative medicine

Results from a study comparing the efficacy of home-based deep-breathing exercises with usual care showed that patients receiving this intervention had significantly lower depression scores than patients receiving usual care, with a mean difference of -1.34 (95% CI: -1.17, -0.17). Another study compared the efficacy of home-based spiritual therapy with usual care. Findings from this study suggested that home-based spiritual therapy could significantly decrease depression scores when compared with usual care, with a mean difference of -1.11 (95% CI: -1.57, -0.65), In addition, this study found that patients receiving home-based spiritual therapy were more likely to have disease remission than patients receiving usual care. The risk ratio of disease remission (defined as HAMD score ≤ 7) from this study was 13.85 (95% CI: 1.88, 101.74)

Publication bias

Egger tests and Funnel plots did not suggest any publication bias for pooling the effect of home-based psychological intervention (coefficient = -0.05, P-value = 0.882) and home-based exercise intervention (coefficient = 6.94, P-value = 0.818) (see Supplementary Figure 6A and 6B). For combined home-based psychological intervention and exercise intervention, the Egger test did not suggest publication bias but a funnel plot showed asymmetry (Supplementary Figure 7A). This inconsistency might be due to Egger's test having insufficient power to detect a difference when only 3 studies were considered in the analysis.

The cause of this asymmetry was further explored by performing a contour enhanced funnel plot which showed that most of the studies fell inside the significant area. The asymmetrical plot may, therefore, result from a small study effect rather than heterogeneity between studies (see Supplementary Figure 7B).

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DISCUSSION

Our study found that a combination of home-based psychological intervention with exercise intervention and home-based psychological intervention alone both significantly decreased depressive symptoms and increased the likelihood of disease remission when compared with usual care. The SMD of home-based psychological intervention vs usual care was -0.57, which reflects the moderate magnitude of treatment effect, while SMD of combined home-based psychological intervention with exercise intervention vs usual care was -0.78 revealing the high magnitude[43]. Treatment effect of these two interventions were comparable with selective serotonin reuptake inhibitor, which had SMD of 0.05, for treatment of depression[44]. However, we could not demonstrate any benefit of home-based exercise intervention alone when compared with usual care. In addition, combined home-based psychological intervention with exercise intervention had the highest probability of remission from depression compared both with home-based psychological intervention and home-based exercise intervention.

The effectiveness of clinic-based psychological intervention for treating depression has been confirmed by previous studies[39 45 46]. The results of our study also support the efficacy of this intervention when performed in the patient's home. In our review, the majority of participants in the included studies were depressed patients with comorbidities such as epilepsy[36] or heart disease[22 30 35], or were elderly patients with disabilities[18] or cognitive impairment[25]. These groups have a high prevalence of depression and should therefore be expected to receive a significant share of mental health provision. However, their ability to access conventional clinic-based mental health services is restricted by mobility problems and low motivation to seek help. With its ability to overcome these barriers, home-based psychological intervention is particularly appropriate in these situations.

In addition to demonstrating the efficacy of home-based psychological intervention overall, subgroup analysis within our study raises an interesting point**.** Home-based psychological intervention decreased symptoms of depression for all types of depression but the effect was statistically significant only in patients with MDD and mixed severity depression, not for those with minor depression. This inconsistent finding may result from the so called "ceiling" effect. The level of depressive symptoms in minor depression is relatively low at baseline when compared with major

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depression, which could limit the potential for symptom improvement[47]. This ceiling effect was also found in the studies reviewing the use of antidepressant medication for minor depressive symptoms.

The rationale for home-based exercise intervention rests on the theory that increasing physical activity can improve depressive symptoms through psychological and physiological routes. Exercise serves as a distraction from worries and depressive thoughts, increases self-efficacy, and gives a sense of mastery. Possible physiological mechanisms include an increase in body temperature, leading to a feeling of relaxation and reduced muscle tension, an increase in levels of endorphins related to positive mood and a sense of well-being, and increases in the availability of the central neurotransmitters dopamine, norepinephrine and serotonin[43,39 48]. Although the advantages of clinic-based or supervised exercise to treat depression have been confirmed by previous literature[1], our study found no benefit from home-based exercise intervention in ameliorating depressive symptoms. The differences in these findings may be explained by poorer treatment compliance in the home-based exercise intervention group, as to achieve significant benefit patients have to practice the exercise programme at a prescribed intensity and frequency. Lack of motivation and inattention are common symptoms in depression and may account for unsupervised patients failing to achieve the prescribed levels of activity when compared with those given encouragement through supervision. This assumption corresponds with findings from the home-based exercise studies[26 27] that the physical health of patients in this group (i.e. cardio-respiratory capacity, BMI, and lower limb strength), the surrogate endpoints of exercise intervention, did not change significantly from baseline.

Although our study did not find any advantages of home-based exercise intervention over usual care, when combined with psychological intervention the combined approach had a significantly greater benefit than either of these interventions alone. The combination may have a synergistic effect, with psychological intervention improving motivation to initiate and maintain an exercise programme while the latter in turn enhances the benefits of psychological intervention.

Reviewing complimentary or alternative medicine approaches, results from Chung et al[35] and Rickhi et al[32] showed that home-based deep-breathing training and spiritual teaching programmes could significantly reduce depressive symptoms when compared with usual care. However, these two studies had small sample sizes and included specific populations, namely coronary heart disease

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patients for Chung's study and middle-aged females for Rickhi's study. Their findings may not, therefore, be generalizable to other populations.

Strengths and limitations

Our study has several strengths. Given the potential of home-based interventions to treat depression and the increasing use of these interventions, our analysis provides the first comprehensive review of the efficacy of home-based interventions in treating depression. A comprehensive search was undertaken to identify as many relevant studies as possible and two reviewers selected the studies independently with a high level of agreement. Selection bias was, therefore less likely. In addition, we performed a network meta-analysis to compare the efficacy of all available home-based interventions in order to identify the best treatment regime.

We are aware that our study may have some limitations. Firstly, the quality of included studies in the area of allocation concealment was not optimal. The results from our study might, therefore, be affected by selection bias and should be interpreted with caution. Secondly, participants in our included studies were aware both of their own interventions and their subjective outcomes, including the self-reported depression scores. However, in most of the included studies this bias from non-blinded intervention was minimized by blinding the outcome assessors. Thirdly, some of the included studies considered home visits as a treatment comparator. This may have resulted in an underestimated treatment effect for the home-based interventions.

A network meta-analysis is a useful technique and has been increasingly applied because it allows indirectly compare efficacy of all possible interventions given that there are some common comparators. However, this technique is required two important assumptions, i.e., transitivity and consistency[49]. The transitivity requires that characteristics of patients and studies of those directs comparisons that performed indirect comparisons should be similar. For instance, characteristics of patients of home-based psychological intervention versus usual care and home-based exercise intervention versus usual care should be similar to perform indirect comparison of home-based psychological intervention versus home-based exercise intervention. This assumption cannot be directly assessed and tested but consistency testing is a manifestation of transitivity. Therefore, we assessed consistency assumption by comparing intervention effects between direct and indirect estimates. However, numbers of included studies might play a role in this assessment, i.e., false

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negative result might be present when direct and indirect estimates were not statistically different. For our study, the inconsistency factors ranged from -0.018 to 0.106, which should be less likely to face with false negative result.

We could not check consistency assumption in 3 indirect comparisons because of lack of direct comparisons. We therefore explored characteristics of patients (i.e. mean age, types of depression, percentage of anti-depressants use) and duration of intervention and found that they mostly varied between studies and comparisons (see Supplementary Table 2). This heterogeneity within and between interventions across included studies may affect the transitivity and consistency assumptions of our network met-analysis. Therefore, the results from indirect comparison, e.g. the efficacy of home-based psychological intervention and combined home-based psychological intervention with exercise intervention over home-based exercise alone, should therefore be interpreted with caution and be confirmed by undertaking further randomized-controlled trials directly comparing these two interventions with home-based exercise intervention.

Clinical implication and further study

Depression is a common disorder, particularly among the elderly and in those with a chronic disease. Many of these patients have difficulty accessing mental health services due to physical disabilities and transportation problems. Home-based interventions to treat depression have the potential to overcome these barriers and have been shown by our study to be effective. This information should prove helpful when designing clinical guidelines. However, there are obvious logistical differences between home-based treatments for depression and conventional clinic-based care. Our study has not investigated these aspects of treatment design and, in particular, has not considered manpower implications or transport costs. An economic evaluation study is needed before general implementation of a home-based care model can be recommended unequivocally.

Although a randomized-controlled trial is considered to be the gold standard for therapeutic research, in a real world setting this design may not be ideal for examining patient preferences and adherence to treatment. In this review, most of the studies (n=10) did not report the degree of adherence with the prescribed intervention. Seven studies demonstrated the effect of adherence on outcomes but used different definitions to assess adherence. To maximize treatment efficacy, further studies should determine the effects of patient preferences and adherence to treatment for different

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approaches and modes of delivery as well as examine the factors that influence preferences and adherence.

CONCLUSION

Our study has confirmed the efficacy both of home-based psychological intervention and combined home-based psychological intervention with exercise intervention in decreasing symptoms of depression and improving rates of remission. In addition, the combination of home-based psychological intervention and exercise intervention has the highest probability of being the best treatment out of all available home-based interventions. This approach should, therefore, be considered when formulating clinical guidelines for treating depression.

Contributors: KS, PI, and TA were involved in the conception and design of the review. KS and TA developed the search strategy, performed study selection, extracted data from included studies and analyzed the data. KS, ML, PI, AD, AT and TA were involved in the interpretation and discussion of results. KS and TA drafted the manuscript. PI, AD, AT and TA revised it critically for important intellectual content. All authors approved the final version of the article. All authors had access to all of the data in the study and can take responsibility for the integrity of the data and the accuracy of the data analysis. TA is guarantor.

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Table 1. Characteristics of included studies

Author	Setting	Type of depression	Participants							Study's intervention		
			N	Age (mean)	Female (%)	Living alone (%)	Married (%)	Baseline depression score (mean)	Anti-depressants use (%)	Type of intervention	Duration (weeks)	Comparison
Kiosses[25]	U.S.	Major depressive disorder	74	80.91	74.3	NA	NA	21.25[a]	63.51	PST-HC	12 weeks	Usual care with home visit
Choi[21]	U.S.	Mixed depression	121	65.21	77.7	63.6	NA	24.55[b]	NA	PST-HC	12 weeks	Usual care with telephone support call
Gitlin[24]	New Zealand	Mixed depression	208	69.57	78.4	56.8	12.0	13.01[c]	19.3	PST-HC	16 weeks	Usual care
Klug[28]	Australia	Major depressive disorder	60	74.9	90.0	78.3	NA	8.91[e]	95	PST-HC	52 weeks	Usual care
Gellis[22]	U.S.	Minor depression	36	75.9	91.6	88.9	8.3	18.05[b]	0	PST-HC	6 weeks	Usual care
Gellis[29]	U.S.	Minor depression	62	77.67	87.5	80.0	20.0	20.52[a]	NA	PST-HC	6 weeks	Usual care with home visit

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Author	Setting	Type of depression	Participants							Study's intervention		
			N	Age (mean)	Female (%)	Living alone (%)	Married (%)	Baseline depression score (mean)	Anti-depressants use (%)	Type of intervention	Duration (weeks)	Comparison
Naylor[38]	U.S.	Mixed depression	38	51.45	84.2	NA	NA	7.9[f]	NA	Home-based CBT	6 weeks	Usual care
Joling[39]	Netherland	Minor depression	170	81.45	73.5	NA	29.4	21.6	NA	Home-based CBT	12 weeks	Usual care
Pfaff[27]	U.S.	Mixed depression	200	60.97	63.0	21.6	53.0	NA	54.5	Home-based exercise	12 weeks	Usual care
Kerse[26]	Austria	Mixed depression	193	81.1	58.5	51.8	NA	3.7[e]	26.4	Home-based exercise	24 weeks	Usual care with home visit
Blumenthal[34]	U.S.	Major depressive disorder	102	52.52	74.5	NA	NA	16.52[b]	0	Home-based exercise	16 weeks	Usual care
Ciechanowski[36]	U.S.	Mixed depression	80	43.9	52.5	NA	68.8	2.00[d]	40%	Combined PST-HC with home-based exercise	19 weeks	Usual care
Ciechanowski[37]	U.S.	Minor depression	138	73	79	72.0	11.0	1.3[d]	51	Combined PST-HC with home-based exercise	19 weeks	Usual care
Banerjee[18]	Taiwan	Mixed depression	69	80.71	82.9	78.3	15.9	26.25[a]	11.39	Combined family therapy, bereavement counselling, social interventions with	24 weeks	Usual care

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Author	Setting	Type of depression	Participants							Study's intervention		
			N	Age (mean)	Female (%)	Living alone (%)	Married (%)	Baseline depression score (mean)	Anti-depressants use (%)	Type of intervention	Duration (weeks)	Comparison
										home-based exercise		
Gary[30]	U.S.	Mixed depression	74	65.8	57.1	NA	39.2	20.7[f]	29.7	Home-based CBT, home-based exercise, combined home-based CBT with home-based exercise	12 weeks	Usual care
Rickhi[32]	U.K.	Major depressive disorder	84	44.05	77.4	NA	58.3	20.35[b]	0	Spiritual teaching program	8 weeks	Usual care
Chung[35]	U.S.	Mixed depression	62	71.50	30.6	NA	NA	7.53[c]	1.61	Home-based deep breathing exercise	4 weeks	Usual care with telephone support call

[a]MADRS; [b]HAMD; [c]PHQ-9; [d]HSCL-20; [e]GDS; [f]BDI

PST-HC, problem solving therapy-home care; CBT, cognitive behavioural therapy

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Table 2. Mean difference of depression score after treatment between intervention and control groups

Author	Year	Follow up time	Intervention			Control			Mean difference (95% CI)
			N	Mean	SD	N	Mean	SD	
Home-based Psychological intervention									
Kiosses [25]	2015	12 weeks	37	10.6	6.08	37	15.6	6.81	-0.77 (0.30, -1.25)
Choi [21]	2014	12 weeks	35	14.44	7.04	31	19.16	7.02	-0.67 (-1.17, -0.17)
Gitlin [24]	2013	16 weeks	106	6.4	6.18	102	8.9	6.06	-0.41 (-0.13, -0.68)
Joling [39]	2011	12 weeks	86	16.60	6.41	84	17.27	6.53	-0.10 (-0.40, 0.20)
Gary [30]	2010	12weeks	17	8.2	6.3	15	9.3	4.9	0.19 (0.50, -0.89)
Gellis [22]	2010	6 weeks	18	11.4	8.3	18	17.3	8.1	0.72 (-0.04, -1.39)
Klug [28]	2010	48 weeks	29	6.11	3.00	29	10.43	4.2	-1.18 (-0.62, -1.74)
Naylor [38]	2010	6 weeks	15	4.40	5.30	18	4.90	5.30	-0.09 (-0.78, 0.59)
Gellis [29]	2007	6 weeks	30	8.11	4.3	32	13.64	5.6	1.10 (-0.57, -1.64)
SMD (95% CI)									**-0.57 (-0.84, -0.31)**
Home-based Exercise									
Kerse [26]	2010	24 weeks	94	2.4	0.2	92	3.1	0.3	-2.75 (-2.35, -3.15)
Gary [30]	2010	12 weeks	18	8.4	5.6	15	9.3	4.9	-0.17 (0.52, -0.86)
Blumenthal [34]	2007	16 weeks	53	9.5	7.43	49	10.5	5.36	-0.15 (0.24, -0.54)
SMD (95% CI)									**-1.03 (-2.89, 0.82)**
Combine psychological intervention and exercise									
Gary [30]	2010	12 weeks	16	6.5	3.7	15	9.3	4.9	-0.65 (0.08, -1.37)
Ciechanowski [37]	2004	24 weeks	72	0.71	0.6	66	1.17	0.53	-0.81 (-0.46, -1.16)
SMD (95% CI)									**-0.78 (-1.09, -0.47)**

CI, confidence interval; SD, standard deviation; SMD, standardized mean difference

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Table 3. Risk ratios of incidence of remission between intervention and control groups

Author	Year	Follow up time	Intervention		Control		RR (95% CI)
			Remission	No Remission	Remission	No Remission	
Home-based psychotherapy							
Kiosses [25]	2015	12 weeks	14	23	5	32	2.80 (1.12, 6.98)
Gitlin [24]	2013	16 weeks	39	50	25	68	1.63 (1.08, 2.46)
Joling [39]	2011	12 weeks	31	55	25	59	1.47 (0.84, 2.55)
Naylor [38]	2010	6 weeks	11	4	9	9	1.21 (0.79, 1.87)
Pooled RR (95% CI)							**1.53 (1.19, 1.98)**
Home-based Exercise							
Ptaff [27]	2014	12 weeks	49	29	40	28	1.07 (0.82-1.39)
Blumenthal [34]	2007	16 weeks	21	32	23	26	0.84 (0.54-1.32)
Pooled RR (95% CI)							**0.99 (0.79, 1.24)**
Combine psychotherapy and exercise							
Ciechanowski [36]	2010	19 weeks	4	36	0	40	9.00 (0.50-161.86)
Ciechanowski [37]	2004	19 weeks	30	42	6	60	4.58 (2.04-10.31)
Banerjee [18]	1996	24 weeks	19	10	9	23	2.33 (1.26-4.30)
Pooled RR (95% CI)							**3.47 (2.11, 5.70)**

CI, confidence interval; RR, risk ratio

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Figure legends

Figure 1. Flow chart of study selection

Figure 2. Network meta-analysis of disease remission among home-based interventions

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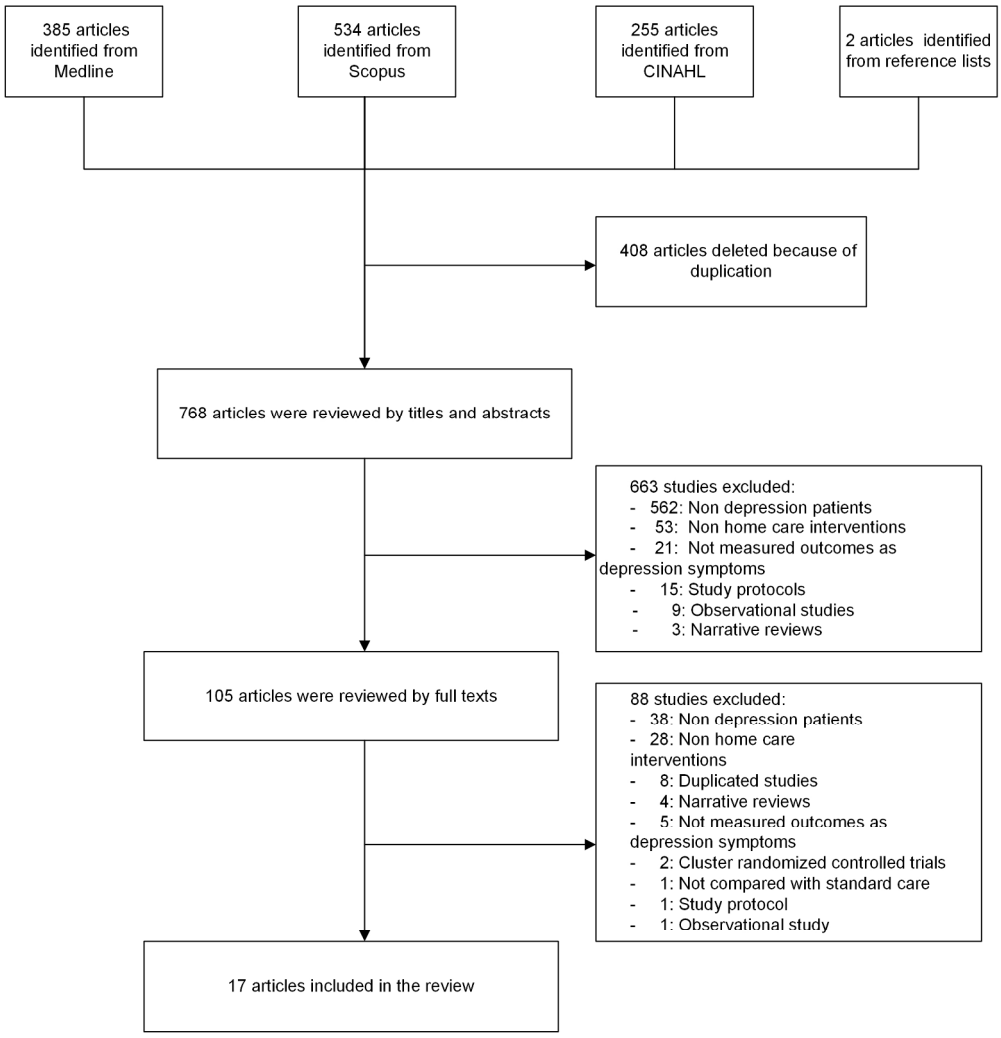

Figure 1. Flow chart of study selection

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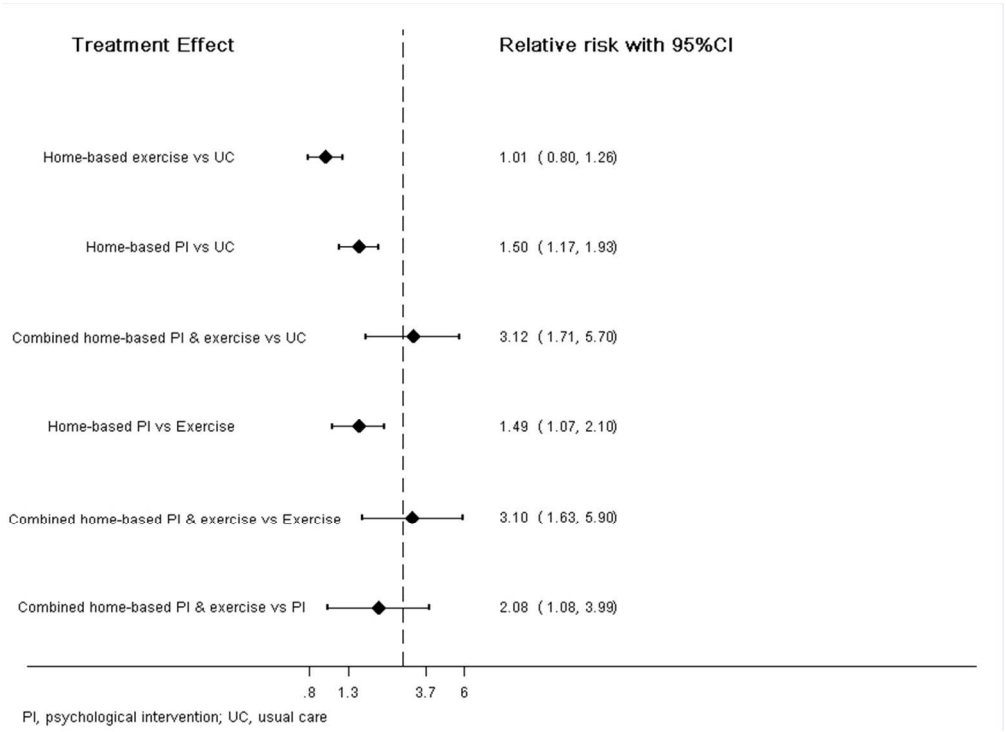

Figure 2. Network meta-analysis of disease remission among home-based interventions

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Supplementary Figure legends

Supplementary Figure 1. Pooled standardized mean difference between home-based psychological intervention and usual care according to severities of depression

Supplementary Figure 2. Pooled standardized mean difference between home-based exercise, combined psychological intervention with exercise and usual care

Supplementary Figure 3. Pooled risk ratio of disease remission between home-based psychological intervention and usual care

Supplementary Figure 4. Pooled risk ratio of disease remission between home-based exercise, combined psychological intervention with exercise and usual care

Supplementary Figure 5. Network plot of all available home-based interventions

Supplementary Figure 6. Funnel plots of home-based psychological intervention and home-based exercise

Supplementary Figure 7. Funnel and contour enhanced funnel plot of combined psychological intervention with exercise

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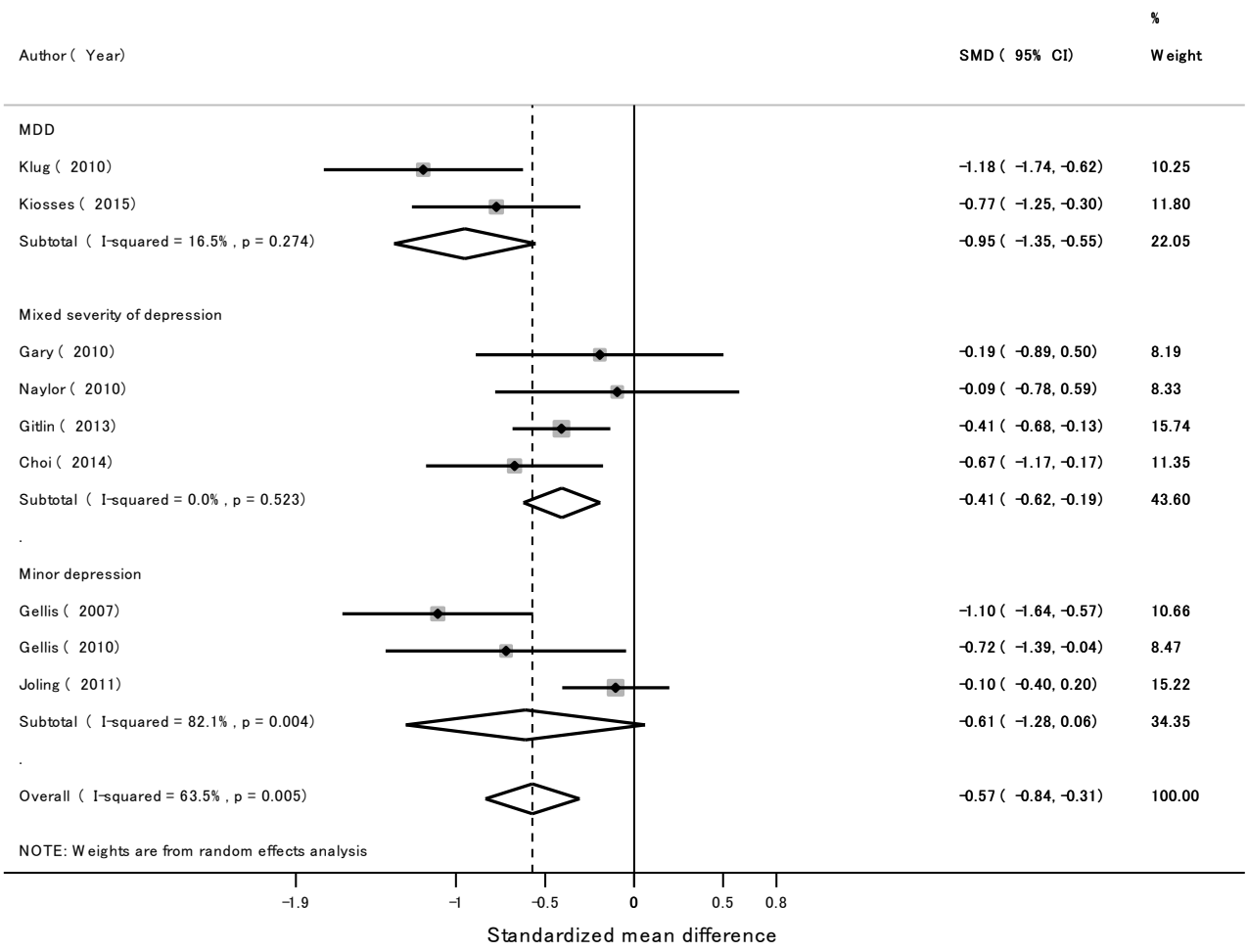
Supplementary Figure 1



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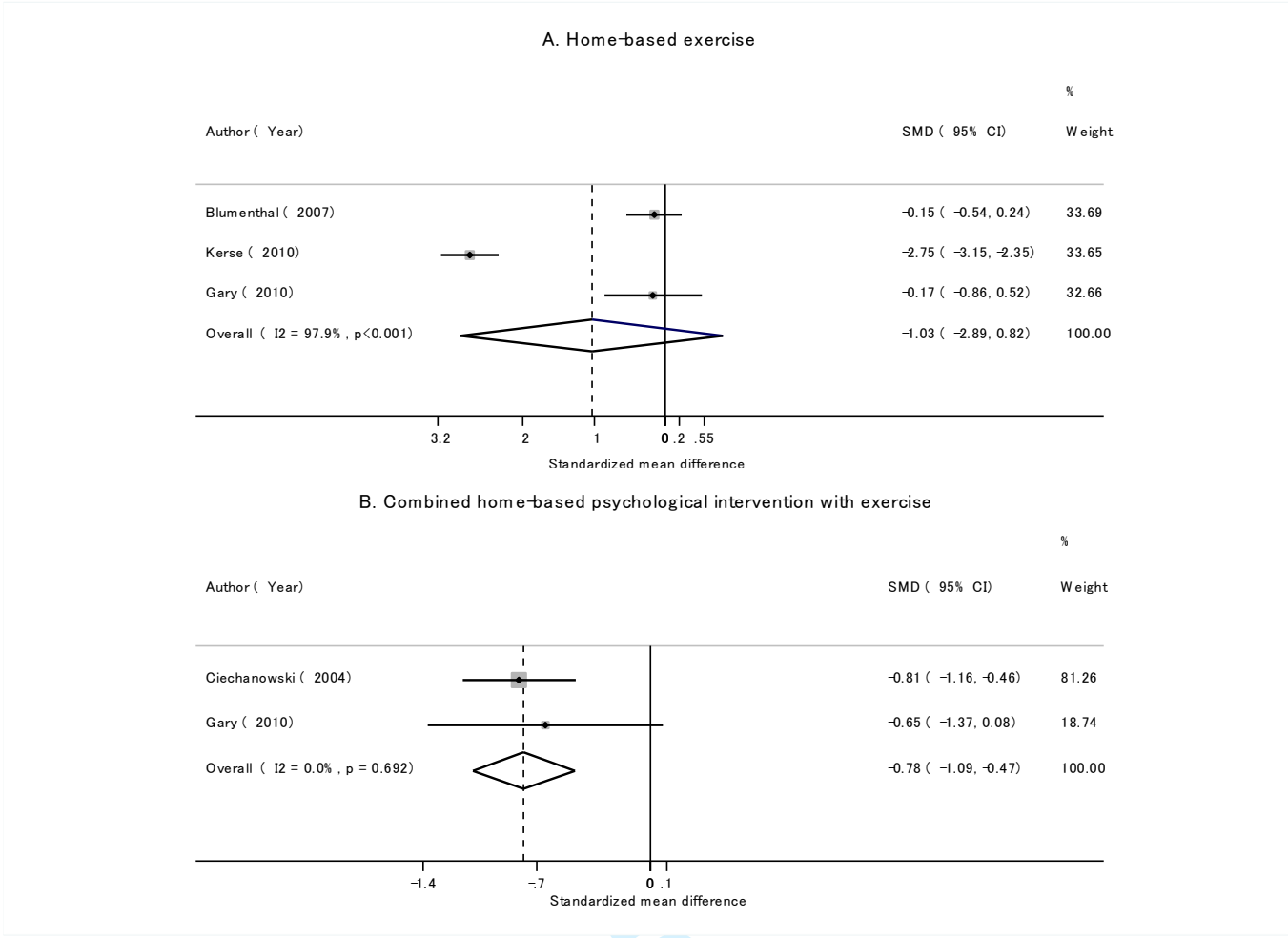
Supplementary Figure 2



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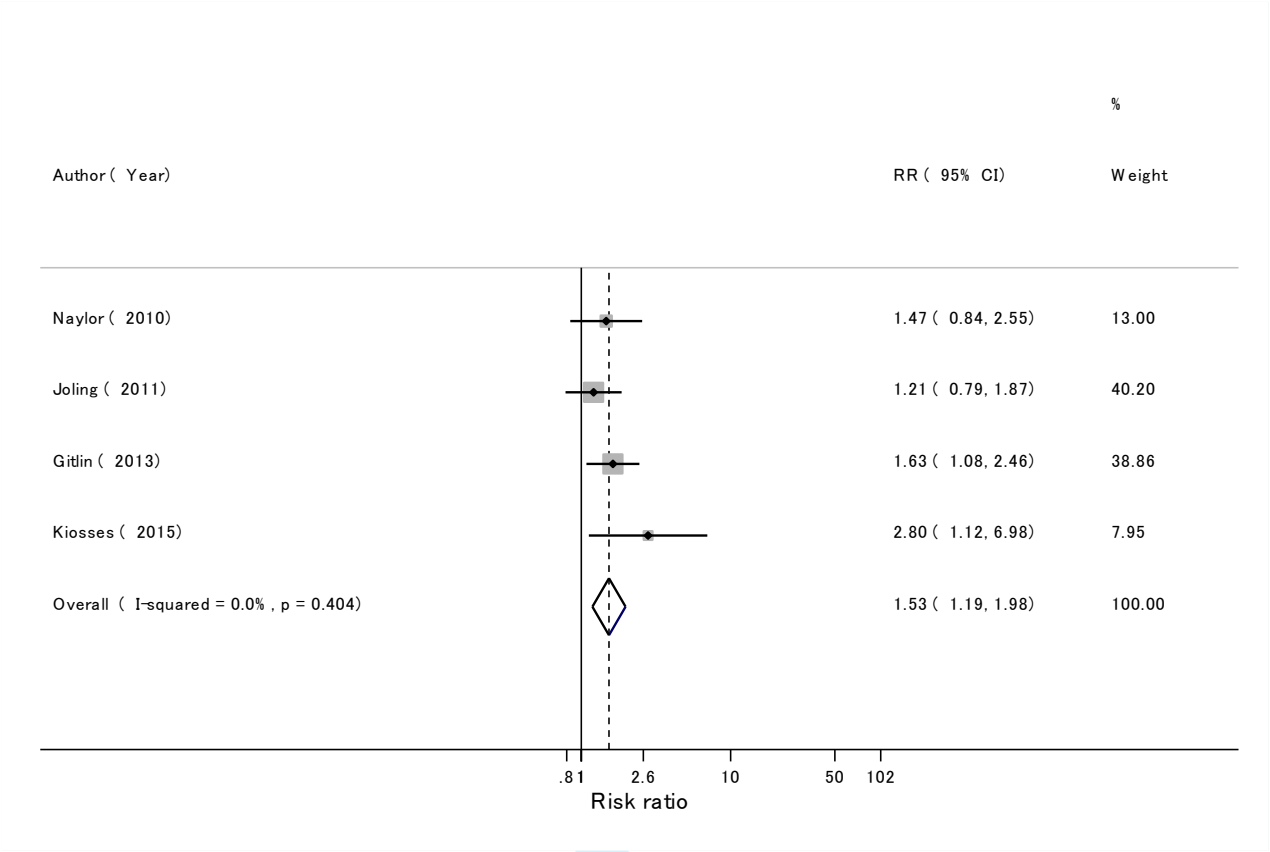
Supplementary Figure 3



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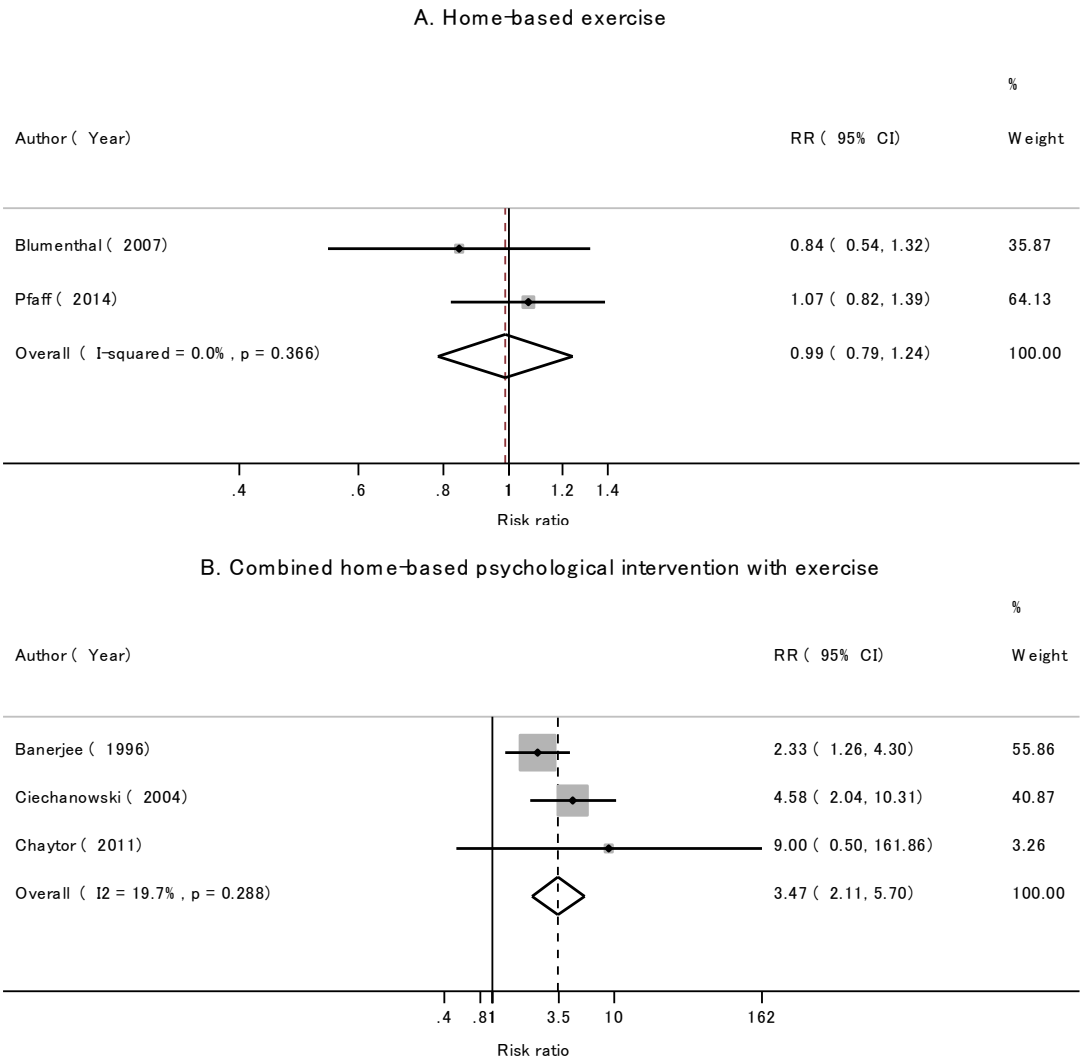
Supplementary Figure 4



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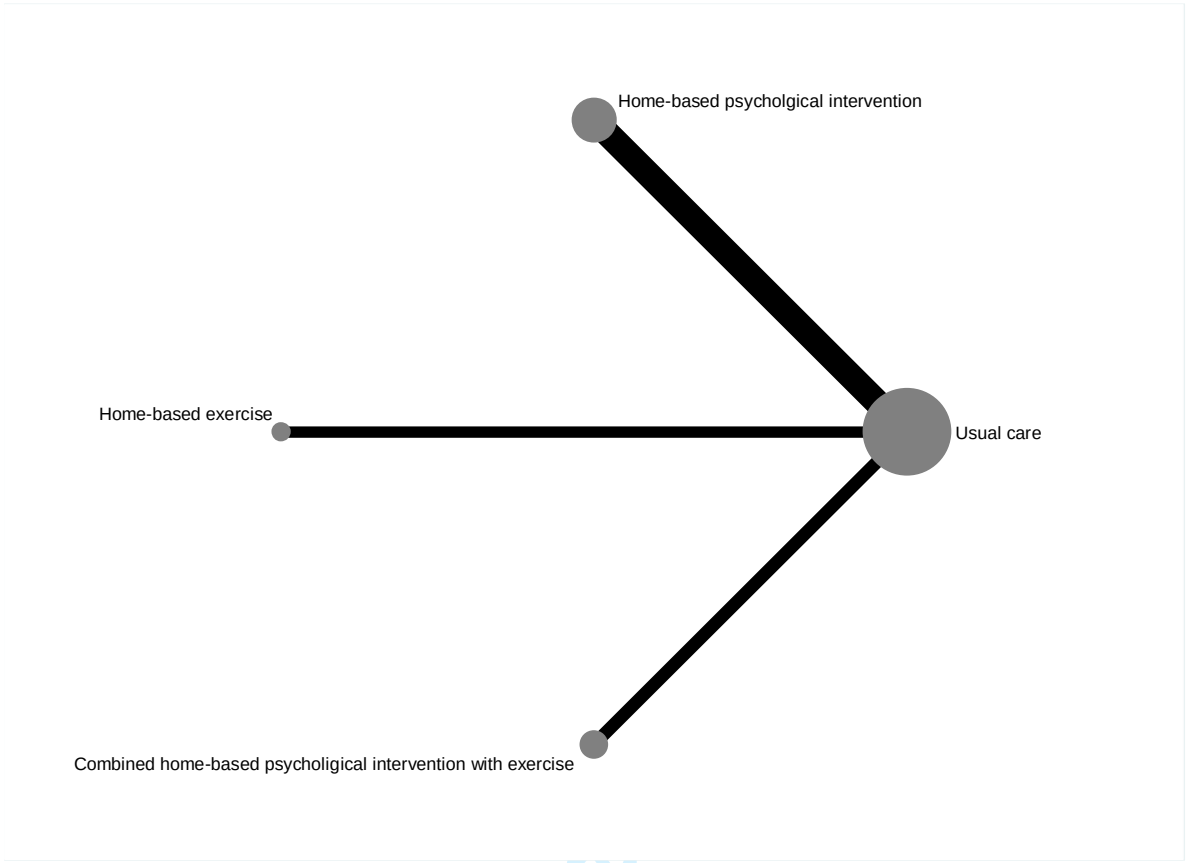
Supplementary Figure 5



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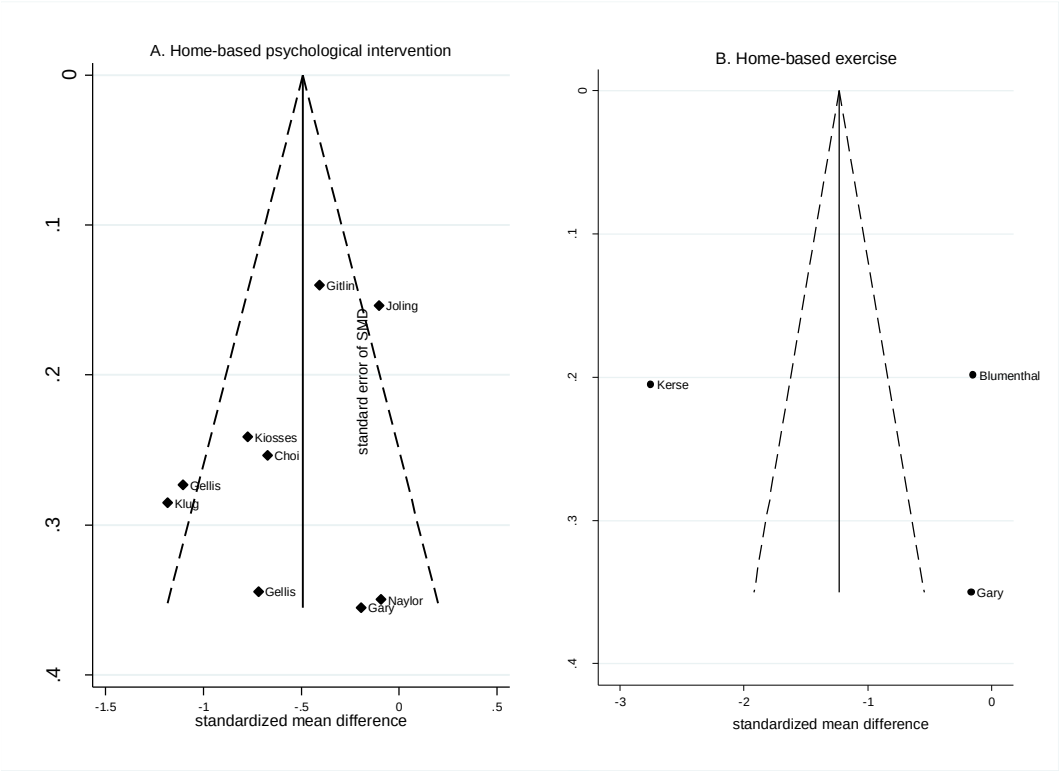
Supplementary Figure 6



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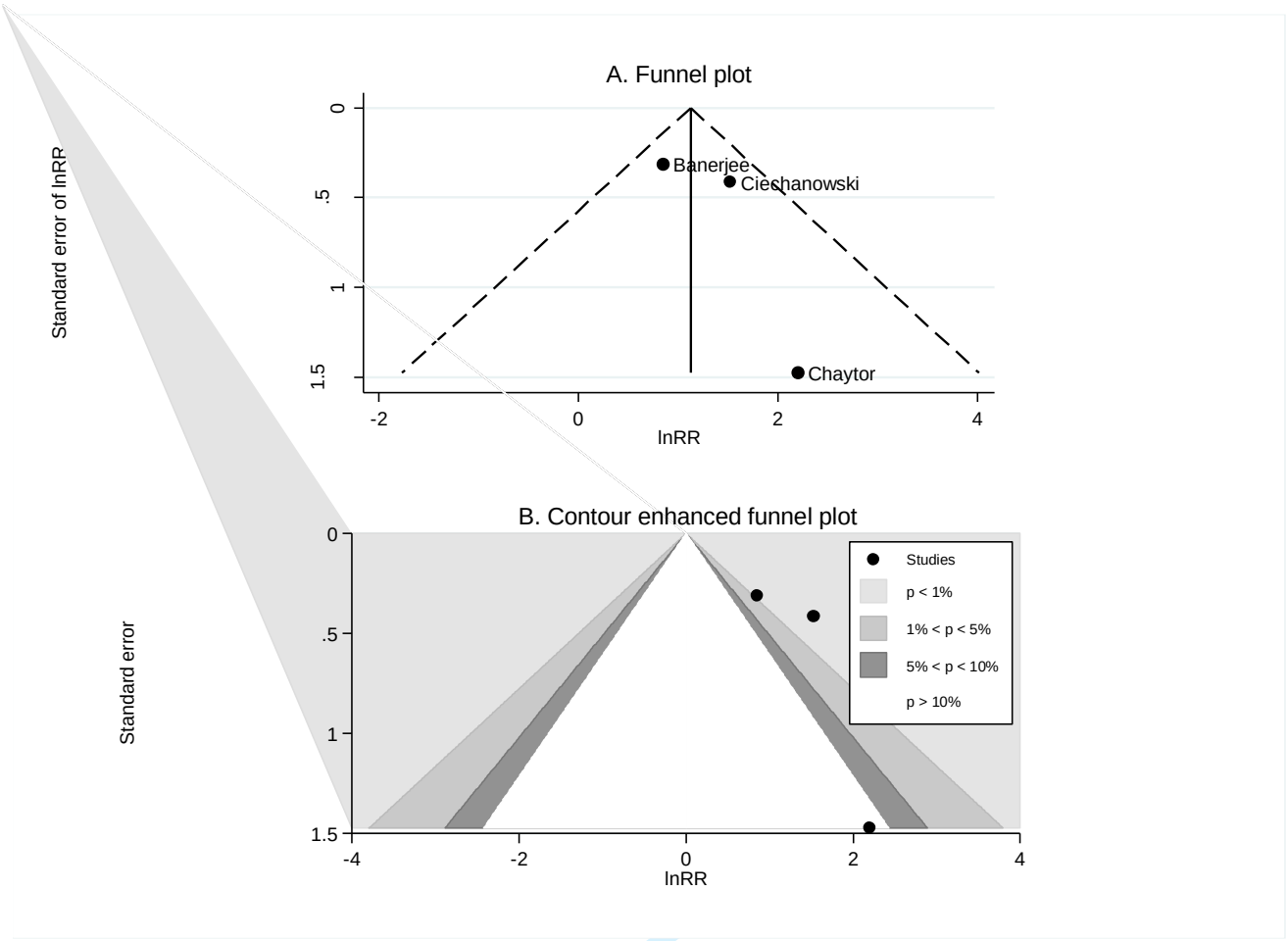
Supplementary Figure 7



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Supplementary Table 1. Risk of bias assessment

Author (Year)	Year	Random sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessors	Incomplete outcome data	Selective outcome reporting	Other bias	Power of study
Rickhi	2011	Low	Low	High	Low	Low	Low	Low	Low
Banerjee	1996	Low	Unclear	High	Low	Low	Low	Low	Unclear
Blumenthal	2007	Low	Low	High	Low	Low	Low	Low	Low
Choi	2014	Unclear	Unclear	High	Unclear	High	Low	Low	Unclear
Chung	2010	Low	Low	High	unclear	High	Low	Low	Unclear
Ciechanowski	2010	Low	Low	High	Low	Low	High	Low	Unclear
Ciechanowski	2004	Low	Low	High	Unclear	Low	Low	Low	Unclear
Gary	2010	Unclear	Unclear	High	Low	Low	Low	Low	Unclear
Gellis	2010	Unclear	Unclear	High	Low	Low	Low	Low	Unclear
Gellis	2008	Low	Unclear	High	Low	Low	Low	Low	Unclear
Gitlin	2013	Low	Low	High	Unclear	Low	Low	Low	Low
Kerse	2010	Low	Unclear	High	Low	Low	Low	Low	Low
Kiosses	2015	Low	Unclear	High	Low	Low	Low	Low	Low
Klug	2010	Low	Unclear	High	Unclear	High	Low	Low	Low
Pfaff	2014	Low	Unclear	High	Low	Low	Low	Low	High
Joling	2011	Low	Unclear	High	Unclear	Low	Low	Low	Unclear
Naylor	2010	Low	Unclear	High	Unclear	High	Low	Low	Unclear

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Supplementary Table 2. Characteristics of studies included in network meta-analysis

Author		Type of depression	Participants							Study's intervention	
			N	Age (mean)	Female (%)	Living alone (%)	Married (%)	Baseline depression score (mean)	Anti-depressants use (%)	Duration (weeks)	Comparator
Home-based Psychological intervention											
Kiosses	Intervention	Major depressive disorder	37	80.78	70.27	NA	NA	21.08[a]	64.86	12 weeks	Usual care with home visit
	Control		37	81.03	78.38	NA	NA	21.41[a]	62.16		
Gitlin	Intervention	Mixed depression	106	68.9	79.3	47.32	15.1	13.65[c]	22.6	16 weeks	Usual care
	Control		102	70.3	77.5	66.7	8.8	12.9[c]	15.8		
Naylor	Intervention	Mixed depression	19	48.6	94.7	NA	NA	8.3[f]	NA	6 weeks	Usual care
	Control		19	54.3	73.7	NA	NA	7.5[f]	NA		
Joling	Intervention	Minor depression	86	81.8	69.8	NA	30.2	21.17[g]	NA	12 weeks	Usual care
	Control		84	81.1	77.4	NA	28.6	22.05g	NA		
Home-based Exercise											
Pfaff	Intervention	Mixed depression	108	61.2	62	22.4	48.1	NA	60.2	12 weeks	Usual care
	Control		92	60.7	64.1	20.7	58.7	NA	47.8		
Blumenthal	Intervention	Major depressive disorder	53	53	74	NA	NA	17+/-5[b]	0	16 weeks	Usual care
	Control		49	52	75	NA	NA	16+/-4[b]	0		

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Author		Type of depression	Participants							Study's intervention	
			N	Age (mean)	Female (%)	Living alone (%)	Married (%)	Baseline depression score (mean)	Anti-depressants use (%)	Duration (weeks)	Comparator
Combined home-based psychological intervention with exercise											
Ciechanowski	Intervention	Mixed depression	40	43.4	47.5	NA	65	2.1[d]	37.5	19 weeks	Usual care
	Control		40	44.1	57.5	NA	72.5	1.9[d]	42.5		
Ciechanowski	Intervention	Minor depression	72	72.6	82	78	11.0	1.3[d]	40	19 weeks	Usual care
	Control		66	73.5	76	65	11.0	1.2 [d]	30		
Banerjee	Intervention	Mixed depression	33	80.4	85	82	18	27.5[a]	11	24 weeks	Usual care
	Control		36	81	81	75	14	25.1 [a]	12		

[a]MADRS; [b]HAMD; [c]PHQ-9; [d]HSCL-20; [e]GDS; [f]BDI

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Supplementary Appendix

Search strategy for Medline

(Depressive OR depression OR depressed) AND ("Home Care Services"[MeSH] OR "Home Care Agencies"[MeSH] OR "Home Nursing"[MeSH] OR "House Calls"[MeSH] OR "Community Health Planning"[MeSH] OR "Health Systems Agencies"[MeSH] OR "Community Health Nursing"[MeSH] OR "Social Support"[MeSH]) OR ("Home Based" OR "home support" OR (“home treatment” OR “home treatments”) OR “home care” OR ("home visits" OR "Home visit") OR ("Health visits" OR "Health visit") OR (“home service” OR “home services”)) Filters: Randomized Controlled Trial

Search strategy for Scopus

(Depressive OR depression OR depressed) AND ("Home Based" OR "home support" OR (“home treatment” OR “home treatments”) OR “home care” OR ("home visits" OR "Home visit") OR ("Health visits" OR "Health visit") OR (“home service” OR “home services”) OR “home health care”)

CINAHL

Search strategy for CINAHL

(depressive OR depression OR depressed) AND ("Home Based" OR "home support" OR (“home treatment” OR “home treatments”) OR “home care” OR ("home visits" OR "Home visit") OR ("Health visits" OR "Health visit") OR (“home service” OR “home services”) OR “home health care”) AND (randomized OR randomized)

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PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	3
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	5
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	5, 6
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	-
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	6, 7
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	6
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	Supplementary Appendix
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	6
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	7
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	7
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	8
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	8
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	8

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PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	9
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	8
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	9, Figure 1
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	9, 10, 11, 12 & Table 1
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	12 & Supplementary Table 1
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	Tables 2 & 3 Figure 2 Supplementary Figure1, 2, 3, 4
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	12-16
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	16
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	12-16
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	16-19
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	18
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	19
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	19

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PRISMA 2009 Checklist

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(6): e1000097. doi:10.1371/journal.pmed1000097

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Efficacy of home-based non-pharmacological interventions for treating depression: a systematic review and network meta-analysis of randomized-controlled trials

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Primary Subject Heading:	Mental health
Secondary Subject Heading:	Evidence based practice, General practice / Family practice
Keywords:	depression, treatment, home-based intervention, systematic review, network meta-analysis

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Efficacy of home-based non-pharmacological interventions for treating depression: a systematic review and network meta-analysis of randomized-controlled trials

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Key words: depression; treatment; home-based intervention; systematic review; network meta-analysis

Word count: 5,694 words

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Abstract:

Objectives: To systematically review and compare the efficacy of all available home-based non-pharmacological treatments of depression.

Design: Systematic review and network meta-analysis of randomized controlled trials.

Data sources: Medline, Scopus, and CINAHL databases were searched since inceptions to7th August 2016.

Eligibility criteria: Randomized controlled trials comparing the efficacy of home-based non-pharmacological interventions with usual care of depressed patients were included in the review.

Main outcomes: Depression symptom scores and disease remission rates at the end of treatment.

Results: Seventeen studies were included in the review. Home-based non-pharmacological interventions were categorized as 1) home-based psychological intervention, 2) home-based exercise intervention, 3) combined home-based psychological intervention with exercise intervention, and 4) complimentary or alternative medicine. Complementary and alternative medicine approaches were excluded from the meta-analysis due to heterogeneity. The standardized mean differences of post-treatment depression symptom scores between usual care groups and home-based psychological intervention, home-based exercise intervention, and combined home-based psychological intervention with exercise intervention were -0.57 (95%CI:-0.84, -0.31), -1.03 (95%CI:-2.89, 0.82), and -0.78 (95% CI:-1.09,-0.47), respectively. These results suggest that only home-based psychological intervention and combined home-based psychological intervention with exercise intervention could significantly decrease depression scores. Compared with usual care groups, the disease remission rate was also significantly higher for home-based psychological intervention (pooled risk ratio = 1.53; 95% CI: 1.19, 1.98) and combined home-based psychological intervention with exercise intervention (pooled risk ratio = 3.47; 95% CI: 2.11, 5.70). Of all the studied interventions, combined home-based psychological intervention with exercise intervention had the highest probability of resulting in disease remission.

Conclusion: Our study confirms the efficacy of home-based psychological intervention and combined home-based psychological intervention with exercise intervention in the treatment of depression.

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Combined home-based psychological intervention and exercise intervention was the best treatment and should be considered for inclusion in clinical guidelines for managing depression.

Strengths and limitations of this study

- Our analysis provides the first comprehensive review of the efficacy of home-based non-pharmacological interventions in treating depression.
- A comprehensive search was undertaken to identify as many relevant studies as possible.
- We performed a network meta-analysis to compare the efficacy of home-based interventions in order to identify the best treatment regimen.
- The quality of included studies in the area of allocation concealment was not optimal.
- Participants in our included studies were aware of their own interventions and the outcomes were subjective.

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INTRODUCTION

Recent studies have highlighted the international recognition of depression as one of the leading global burdens of disease (GBD)[1]. Depression is associated not only with greater morbidity and mortality but also with increasing health service use and costs[2]. In addition, untreated depression has been recognized as a strong predictor of poor health outcomes in elderly[3-5] and adult patients with chronic disease[6-8].

Both pharmacological and non-pharmacological interventions, such as psychotherapy or supervised exercise intervention, have been accepted as standard treatments of depression. However, concerns about drug side effects and dependency appear to make patients prefer psychological interventions. One study showed that around 70% of depressed patients were non-compliant with antidepressants because of concerns about their side effects[9]. Even though non-pharmacological interventions were preferred over antidepressants[10 11], only a very small percentage of patients referred for psychotherapy were able to enter and complete this treatment[12]. This inconsistency between patient preference and low rates of initiation and adherence to treatment could be a consequence of barriers to obtaining treatment. Non-pharmacological interventions are usually clinic or hospital-based and require visits on a weekly or monthly basis. In one study, 70% of patients reported structural barriers preventing them from attending psychotherapy sessions regularly and cited time constraints, transportation problems and cost as being significant obstacles[13].

Among older patients, whose prevalent rate of depression is very high, these problems were aggravated by concurrent medical illness, social isolation, functional impairment or being home-bound [14-20]. Overcoming these barriers by providing interventions in patients' own homes may achieve better treatment adherence and thereby greater treatment success than clinic or hospital-based interventions.

Home-based non-pharmacological interventions, such as problem solving therapy[21-25] and home-based exercise intervention [26 27], have developed over several years. Although some studies have suggested that these approaches can improve depressive symptoms and rates of remission when compared with standard usual care[26 28 29], other studies have reported conflicting results[27 30 31]. In recent years new home-based interventions have been introduced to treat depression, such as spirituality teaching programme[32] and combined home-based psychotherapy with exercise intervention but their efficacy is still controversial. Therefore, our systematic review and network meta-

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analysis was undertaken with the aim of reviewing all available home-based non-pharmacological interventions, pooling the effect sizes of each intervention on symptom improvement and indirectly comparing treatment efficacy between the different interventions. The results of this review should be useful for identifying the most beneficial home-based non-pharmacological interventions and for informing clinical guidelines for treating depression.

METHODS

Search strategy

Relevant studies were identified using Medline, Scopus, and CINAHL databases searched from inceptions to7th August 2016. Reference lists of included studies were also explored. Search terms and search strategies for each database are presented in a Supplementary Appendix.

Selection of studies

Initially studies were selected from titles and abstracts by two independent reviewers (K.S. and T.A.). Full articles were retrieved to aid decision making if decision could not be made based on titles and abstracts. Disagreement between the two reviewers was resolved by discussion. Percentage agreement between the two reviewers was estimated using kappa statistics.

Inclusion criteria

Randomized-controlled trials published in English were eligible for the review if they met all of the following criteria:

1. Study participants were adults aged more than 18 years with a diagnosis of any degree of depressive disorder using the criteria of the Diagnostic and Statistical Manual of Mental Disorders 4th Edition (DSM-IV) or any diagnostic tool used for diagnosis or screening for depression. Participants who were children, adolescents or postpartum women were excluded.
2. Interventions of interest were non-pharmacological and provided in the patient's home, such as cognitive behavioral therapy, problem solving therapy, family therapy, or home-based exercise intervention.
3. Treatment comparison was the care of depression in outpatient clinics or hospital settings.

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4. Outcomes were measured by the level or severity of depressive symptoms or the incidence of disease remission at the end of the intervention.
5. Studies provided sufficient data for analysis, such as number of participants (n), mean depression score, standard deviation (SD) for each intervention group, and the number of patients per intervention group with or without disease remission.

Data extraction

Two reviewers (KS and TA) independently used a standardized data record form to extract baseline characteristics of included studies and outcomes of interest. Disagreement between the two reviewers was resolved by discussion and corresponding authors of studies were contacted if information was incomplete.

Interventions of interest

Home-based non-pharmacological intervention was defined as any care or management of depression provided by health care professionals at a patient's place of residence. Home-based interventions had to have a clear and definite objective. Home visits that provided only health-education, social or emotional support were, therefore, excluded from this study.

Web or internet-based interventions were excluded from this review due to their variability in terms of content, accessibility, usability, methods of delivery and supplementary tools[33].

Outcomes of interest

The outcomes of interest were depressive symptom scores and disease remission rates at the end of treatment. Disease remission was defined according to the criteria of the original article. Included studies used several tools for measuring the severity of depressive symptoms, namely the Hamilton Depression Rating Scale (HAM-D)[21 22 30 34 35], Patient Health Questionnaire-9 (PHQ-9)[24 36], Geriatric Depression Scale (GDS)[23 26 28], Hopkins Symptom Checklist-20 (HSCL-20)[37 38], Montgomery Asberg Depression Rating Scale (MADRS)[18 25 27], Beck Depression Inventory-Fast Screen (BDI-FS)[39] and Center of Epidemiologic Studies Depression Scale (CES-D)[40]. These tools have different score ranges (HAM-D = 0-53, PHQ-9 = 0-27, GDS = 0-15, HSCL-20 = 0-4, MADRS = 0-60, BDI-FS = 0-21, and CES-D = 0-60) with higher scores in all tools representing increasing severity of depressive symptoms.

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Risk of bias assessment

To assess the quality of included studies, a risk of bias assessment tool [41] was applied by two independent reviewers (K.S., T.A.). Seven domains were evaluated as follows: 1) random sequence generation 2) allocation concealment 3) blinding of participants and personnel 4) blinding of outcome assessors 5) incomplete outcome data 6) selective outcome reporting 7) other sources of bias. The quality of the studies was classified as being at high, unclear, or low risk of bias. We added the domain of power to determine the likelihood of any studies making a true difference to outcome, classifying any study as being at high risk of bias if it reported a power less than 80%. Disagreement between the two reviewers was settled by discussion.

Statistical analysis

Because depression scores were measured differently among the studies, for direct comparison the standardized mean differences (SMD) of depressive scores between intervention and control groups were estimated for individual studies and then were pooled across studies. Heterogeneity between studies was estimated by Q test and I^2 statistic. Heterogeneity between studies was considered if the P-value from Q test was less than 0.10 or if I^2 was equal to or greater than 25%[42]. If heterogeneity was presented, the SMD was estimated by applying the random effect model. Otherwise the fixed effect model was applied.

For dichotomous outcomes, relative risks (RR) of disease remission were calculated for each study. The random effect model was used for pooling RR if there was evidence of heterogeneity between studies. Otherwise the inverse variance method was used. Sources of heterogeneity were explored by considering possible factors one by one in a meta-regression model (e.g. mean age, severity of depression at baseline and types of intervention delivery).

A network meta-analysis was applied to indirectly assess intervention effects for all home-based interventions, i.e., home-based psychological intervention, home-based exercise intervention, combined home-based psychological intervention and exercise intervention, and usual care. This method allows us to perform indirect comparison using common comparator. For instance, some studies compared home-based psychological intervention with usual care, some others compared home-based exercise intervention with usual care, non or few studies compared home-based

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psychological intervention with home-based exercise intervention. Using common comparator as usual care would allow to indirectly compare home-based psychological intervention with home-based exercise intervention[43]. Treatment effects for each study were estimated using a two-stage network meta-analysis. Firstly, summary data was expanded into individual patient data using the 'expand' command in STATA program. Binary regression was applied to estimate log (RR) and variance-covariance of each treatment using 'mvmeta' make command. A multivariate random effect meta-analysis was used to calculate the pooled RRs and their 95% confidence intervals (CI). Riley's method was used for considering subject-study correlation. Treatment ranking was made according to the linear predictor of each study. In addition, a consistency assumption (i.e., discrepancy of intervention effects between direct and indirect meta-analyses) was assessed using the standardized normal test (Z).

Publication bias was assessed using Egger test and funnel plot. If the funnel plot showed asymmetry, a contour enhanced funnel plot was performed to explore whether asymmetry was the result of heterogeneity between studies or arisen from publication bias. All analyses were performed using STATA version 14. A two-sided test with P-value less than 0.05 was considered statistically significant, except for the Q test, in which a P-value less than 0.10 was applied.

Patient involvement

Patients were not involved in the design of the study, development of outcome measures, or conduct of the study. We did not ask patients for advice on interpreting or writing up results. There are no plans to disseminate the results of the research to study participants.

RESULTS

We identified 385, 534, 255, and 2 articles from Medline, Scopus, CINAHL databases and reference lists respectively. After deleting duplications, the titles and abstracts of 768 studies were reviewed. Finally, 17 studies met our inclusion criteria and were eligible in the review (Figure 1). Agreement of study selection between the two reviewers was high at 86.7% (Kappa = 0.50). All but one[18] of the included studies reported protocol approval by an ethics committee.

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Study participants

The baseline characteristics of included studies are presented in Table 1. The type and severity of depression of participants differed between studies. Four studies[25 28 34 35] included patients with major depressive disorder, four[22 23 38 40] included patients with minor depression and nine[18 21 24 26 27 30 36 37 39] included patients with mixed severities of depression. Ten studies included elderly patients[18 21-26 28 38 40] while seven studies included adults with ages greater than 18 years[27 30 34-37 39]. Ten studies included depressed patients with other co-morbidities (i.e. epilepsy[37], heart diseases[22 30 36], disability[18], and mild to moderate cognitive impairment[25]). Twelve studies[21 23 24 26-28 34 35 38-40] included patients without co-morbidity. Use of anti-depressants at baseline varied widely between studies, ranging from 0% to 95%.

Home-based interventions

The composition of home-based non-pharmacological interventions differed among the included studies but could be categorized into 4 groups: 1) home-based psychological intervention 2) home-based exercise intervention 3) combined home-based psychological intervention with home-based exercise intervention 4) complementary or alternative medicine. Eight, 3 and 3 studies compared home-based psychological intervention with usual care, home-based exercise intervention with usual care, and combined home-based psychological intervention with home-based exercise intervention with usual care, respectively. One study compared the efficacy between home-based psychological intervention, home-based exercise intervention, combined home-based psychological intervention with home-based exercise intervention, and usual care. Since interventions in the category of complementary or alternative medicine were heterogeneous, they were not included in the meta-analysis but were subjected to qualitative analysis. Details of each home-based intervention are summarized below:

Home-based psychological intervention

Home-based psychological intervention was classified as home-based problem-solving treatment or home-based cognitive behavioral therapy.

1. *Home-based problem-solving treatment* (6 studies[21 22 24 25 28 29])

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Home-based problem-solving treatment (PST) is a skill-enhancing behavioral treatment of depression usually delivered by social workers and psychologists. This approach assumes that depressive symptoms are caused and maintained by problems of daily life and that these can be reduced by identifying and addressing them systematically. Each PST session comprises 1) defining and formulating the nature of the depressive problem 2) generating a range of alternative solutions to the problem 3) systematically evaluating the possible consequences of each solution then selecting the most appropriate one 4) monitoring and evaluating the actual outcome. In addition, PST identifies patients' pleasurable activities and encourages them to participate in these activities.

2. *Home-based cognitive behavioral therapy* (CBT) (3 studies[30 39 40])

The aim of CBT is to modify the dysfunctional emotions, behaviours, and thoughts of depressed patients. This type of intervention was identified in 3 studies, of which 2 studies were CBT-based bibliotherapy. In this approach, participants received self-help books or leaflets that included instruction on cognitive behavioral self-help, mood management skills, and tasks to practice. During the intervention period, participants were visited by home care nurses or contacted by telephone by study investigators to assess their symptoms and encourage them to follow the course at their own pace.

Home-based exercise intervention

Home-based exercise intervention was employed in 4 studies. Exercise included both progressive resistance training, aerobic exercise [26 27] and aerobic exercise only[30 35]. Participants were required to perform exercises of moderate-intensity for at least 30 minutes three times a week.

Combined home-based psychological intervention with exercise intervention

Home-based psychological intervention combined with exercise intervention was the interested intervention in 4 studies. Each of these applied aerobic exercise as a home-based exercise intervention but psychological therapies differed among them (PST in two studies[37 38], cognitive behavioral therapy in one study[30] and family therapy with bereavement counselling and social interventions in one study[18]).

Complementary or alternative medicine

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This intervention refers to a broad set of health care practices or activities that are not integrated into the dominant health care system. This type of intervention was used in 2 studies. One involved home-based deep-breathing exercise[36] aimed at stimulating a relaxation response, (i.e. to decrease arousal, heart rate and blood pressure, and to reduce responsiveness of the sympathetic nervous system). Deep-breathing exercises can also help patients to disregard negative and distracting thoughts. Patients were trained by experienced nurses to breathe at a rate of six breaths per minute. During the treatment period, this was undertaken in a quiet environment for a period of ten minutes, three times each day.

The other intervention employed a spirituality teaching programme[32] aiming to promote contemplation of the inter-relation between meaning and purpose, connectedness with others, nature or the divine, and values such as compassion, love, justice, and forgiveness. The programme comprised eight sessions involving explanation of the divine aspect of the self, teaching breathing and visualization practice, helping patients to connect with the divine through prayer or meditation, letting go of regret and fostering gratitude, practicing self-awareness relating to the five senses, and building upon connectedness with others. Participants were also advised to avoid forming expectations and to refrain from judging outcomes. Initially patients participated in a workshop run by psychiatrists and were then required to practice by themselves with the help of audio CDs.

Treatment comparison

Usual care was defined as the care of depression managed by health care providers (i.e. general practitioners, psychiatrists, nurses or social workers) and could include onward referral to appropriate treatment services if specified in the study protocol. In addition to usual care, three studies[25 26 29] included home visits and two[21 36] included telephone support. However, these interventions provided education about depression together with general social or emotional support but did not offer specific psychological help or exercise intervention. With the exception of one study[32], almost all used anti-depressant medication as a co-intervention but the decision to initiate or maintain this was dependent on the judgments of patients and their physicians.

Risk of bias assessment

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Results of risk of bias assessment are presented in Supplementary Table 1. Most of the studies (14 studies) reported low risk of bias in the domain of random sequence generation, while 3 studies[21 22 30] reported unclear risk. For allocation concealment, 11 studies[18 21 22 25-30 39 40] had unclear risk of bias, while 6 studies[24 32 35-38] had low risk of bias. All studies reported high risk of bias in the domain of blinding of participants and personnel and low risk of bias in other domains. Ten studies[18 22 25-27 29 30 32 35 37] had low risk of bias for blinding of outcome assessors, whereas 7 studies[21 24 28 36 38-40] had unclear risk. For the domain of incomplete outcome data, 13 studies[18 22 24-27 29 30 32 35 37 38 40] reported low risk of bias and 4 studies[21 28 36 39] reported high risk. Almost all studies (16 studies) had low risk of bias for selective outcome reporting, while only one study[37] had high risk of bias. In the domain of power, 10 studies had unclear risk of bias, 6 reported low risk and 1 had high risk of bias.

Pooled mean difference of depression score

Home-based psychological intervention vs usual care

Nine studies were analyzed[21 22 24 25 28-30 39 40] comparing home-based psychological intervention with usual care (N = 739). Depression scores were assessed at the end of treatment, which ranged from 6 to 48 weeks. The mean differences and 95% CIs of depression scores for each study are presented in Table 2. SMD of home-based psychological intervention versus usual care was -0.57 (95% CI: -0.84, -0.31), suggesting that home-based psychological intervention can significantly decrease depression scores when compared with usual care.

Moderate heterogeneity was found between studies, with I^2 of 63.5%. Sources of heterogeneity were explored but none of the factors decreased I^2. Subgroup analyses were performed according to the severity of depression (i.e. major depressive disorder (MDD), minor depression and mixed severity of depression). These showed that SMDs in patients with MDD, minor depression, and mixed severity of depression were -0.95 (95% CI: -1.35, -0.55; I^2 = 16.5%), -0.61 (95% CI: -1.28, 0.06; I^2 = 82.1%), and -0.41, (95% CI: -0.62, -0.19; I^2 = 0%) respectively (see Supplementary Figure 1). These suggest that home-based psychological intervention reduces depression scores significantly in the groups of MDD and mixed severity of depression. In addition, the efficacy of this intervention in patients with MDD was better than the efficacy in patients with minor depression.

Home-based exercise intervention vs usual care

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Three studies[26 30 35] (N = 321) were pooled to compare the effect of home-based exercise intervention with usual care. The SMD was -1.03 (95% CI: -2.89, 0.82; I^2 = 97.9%) (Table 2 and Supplementary Figure 2A). The mean depression score in the home-based exercise intervention group was therefore 1.03 units lower than the mean depression score in the usual care group. However, this effect did not reach statistical significance.

Combined home-based psychological intervention with exercise intervention vs usual care

Only two studies[30 38] (N = 169) had sufficient data for pooling the effect on the depression score of combined home-based psychological intervention with exercise intervention. Mean depression scores were measured at the ends of the treatments, namely at 12 weeks[30] and 24 weeks[38]. Table 2 shows the mean depression scores and 95% CIs for each study. SMD was -0.78 (95% CI: -1.09, -0.47; I^2 = 0.0%) (Supplementary Figure 2B). This indicates that patients receiving combined home-based psychological intervention and exercise intervention had significantly lower mean depression scores (by 0.78 units) than patients receiving usual care.

Pooled risk ratio of disease remission

Home-based psychological intervention vs usual care

Four studies (N = 459) comparing the effectiveness of home-based psychological intervention with usual care had remission rates as their outcome of interest. Remission from depression was defined as HAMD score ≤ 7 in one studies[25], PHQ-9 ≤ 4 in one study[24], BDI < 4 in one study[39] and CES-D < 16 in one study[40] (Table 3). The pooled RR was 1.53 (95% CI: 1.19, 1.98) (Supplementary Figure 3), suggesting that patients receiving home-based psychological intervention were approximately 1.7 times more likely to have remission from depression than patients receiving usual care. The results among studies were homogeneous with I^2 of 0%.

Home-based exercise intervention vs usual care

Two studies (N = 248) reported their outcome as disease remission and had sufficient data for pooling. Disease remission was defined as HAMD score ≤ 7[35] or symptoms no longer meeting the criteria for major and minor depression according to DSM-IV criteria[27] (Table 3). The pooled RR was 0.99 (95% CI: 0.79, 1.24; I^2 = 0.0%) (Supplementary Figure 4A), indicating that there was no

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significant difference between home-based exercise intervention and usual care in the likelihood of having remission from depression.

Combined home-based psychological intervention and exercise intervention vs usual care

Three studies (N =279) were pooled to compare remission rates between combined psychological intervention and usual care. Disease remission was defined as HSCL-20 score < 0.5 for two studies[37 38] but in Banerjee's study[18] the outcome was not clearly defined (Table 3). Pooled RR was 3.47 (95% CI: 2.11, 5.70; I^2 = 19.7%) suggesting that the combination of home-based psychological intervention and exercise intervention significantly increased the likelihood of remission from depression when compared with usual care (Supplementary Figure 4B).

Network meta-analysis

Disease remission rate

Nine studies (N = 987) were included in the network meta-analysis. Supplementary Figure 5 shows the network plot of home-based psychological intervention, home-based exercise intervention, combined home-based psychological intervention with exercise intervention, and usual care. Size of node and edge reflect the number of studies and patients respectively. From the plot, usual care was the common comparator and had the largest sample size of the four treatment regimes. Home-based psychological intervention versus usual care had the largest number of studies.

Pooled RRs for each treatment comparison are presented in Figure 2. Compared with usual care, only combined home-based psychological intervention with exercise intervention and home-based psychological intervention alone significantly increased the likelihood of disease remission, with pooled RRs of 3.12 (95% CI: 1.71, 5.70) and 1.50 (95% CI: 1.17, 1.93) respectively. In addition, the incidence of disease remission in home-based psychological intervention and combined home-based psychological intervention with exercise intervention groups was significantly higher than in the home-based exercise intervention group, having pooled RRs of 1.49 (95% CI: 1.07, 2.10) and 3.10 (95% CI: 1.63, 5.90), respectively. When compared with home-based psychological intervention alone, combined home-based psychological intervention with exercise intervention also significantly improved the rate of disease remission (pooled RR = 2.08; 95% CI: 1.08, 3.99).

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Treatment ranking was assessed by estimating the probability of each treatment being the best. This yielded probabilities of 99.5%, 0.5%, and 0% for combined home-based psychological intervention with exercise intervention, home-based psychological intervention alone, and home-based exercise intervention respectively. Combined home-based psychological intervention with exercise intervention therefore emerged as the best intervention for achieving remission from depression.

Applying inconsistency assumptions to the treatments, inconsistency factors were calculated as 0.020 (Z=0.183, P-value=0.912) for home-based psychological intervention vs usual care, -0.018 (Z=0.110, P-value=0.913) for home-based exercise intervention vs usual care, and 0.106 (Z=0.107, P-value=0.915) for combined home-based psychological intervention with exercise intervention versus usual care. These figures find no significant difference between the direct and indirect comparison of estimated treatment effects.

Efficacy of complementary or alternative medicine

Results from a study comparing the efficacy of home-based deep-breathing exercises with usual care showed that patients receiving this intervention had significantly lower depression scores than patients receiving usual care, with a mean difference of -1.34 (95% CI: -1.17, -0.17). Another study compared the efficacy of home-based spiritual therapy with usual care. Findings from this study suggested that home-based spiritual therapy could significantly decrease depression scores when compared with usual care, with a mean difference of -1.11 (95% CI: -1.57, -0.65), In addition, this study found that patients receiving home-based spiritual therapy were more likely to have disease remission than patients receiving usual care. The risk ratio of disease remission (defined as HAMD score ≤ 7) from this study was 13.85 (95% CI: 1.88, 101.74)

Publication bias

Egger tests and Funnel plots did not suggest any publication bias for pooling the effect of home-based psychological intervention (coefficient = -0.05, P-value = 0.882) and home-based exercise intervention (coefficient = 6.94, P-value = 0.818) (see Supplementary Figure 6A and 6B). For combined home-based psychological intervention and exercise intervention, the Egger test did not suggest publication bias but a funnel plot showed asymmetry (Supplementary Figure 7A). This

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inconsistency might be due to Egger's test having insufficient power to detect a difference when only 3 studies were considered in the analysis.

The cause of this asymmetry was further explored by performing a contour enhanced funnel plot which showed that most of the studies fell inside the significant area. The asymmetrical plot may, therefore, result from a small study effect rather than heterogeneity between studies (see Supplementary Figure 7B).

DISCUSSION

Our study found that a combination of home-based psychological intervention with exercise intervention and home-based psychological intervention alone both significantly decreased depressive symptoms and increased the likelihood of disease remission when compared with usual care. The SMD of home-based psychological intervention vs usual care was -0.57, which reflects the moderate magnitude of treatment effect, while SMD of combined home-based psychological intervention with exercise intervention vs usual care was -0.78 revealing the high magnitude[44]. Treatment effect of these two interventions were comparable with selective serotonin reuptake inhibitor, which had SMD of 0.05, for treatment of depression[45]. However, we could not demonstrate any benefit of home-based exercise intervention alone when compared with usual care. In addition, combined home-based psychological intervention with exercise intervention had the highest probability of remission from depression compared both with home-based psychological intervention and home-based exercise intervention.

The effectiveness of clinic-based psychological intervention for treating depression has been confirmed by previous studies[40 46]. The results of our study also support the efficacy of this intervention when performed in the patient's home. In our review, the majority of participants in the included studies were depressed patients with comorbidities such as epilepsy[37] or heart disease[22 30 36], or were elderly patients with disabilities[18] or cognitive impairment[25]. These groups have a high prevalence of depression and should therefore be expected to receive a significant share of mental health provision. However, their ability to access conventional clinic-based mental health services is restricted by mobility problems and low motivation to seek help. With its ability to overcome these barriers, home-based psychological intervention is particularly appropriate in these situations.

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In addition to demonstrating the efficacy of home-based psychological intervention overall, subgroup analysis within our study raises an interesting point**.** Home-based psychological intervention decreased symptoms of depression for all types of depression but the effect was statistically significant only in patients with MDD and mixed severity depression, not for those with minor depression. This inconsistent finding may result from the so called “ceiling” effect. The level of depressive symptoms in minor depression is relatively low at baseline when compared with major depression, which could limit the potential for symptom improvement[47]. This ceiling effect was also found in the studies reviewing the use of antidepressant medication for minor depressive symptoms.

The rationale for home-based exercise intervention rests on the theory that increasing physical activity can improve depressive symptoms through psychological and physiological routes. Exercise serves as a distraction from worries and depressive thoughts, increases self-efficacy, and gives a sense of mastery. Possible physiological mechanisms include an increase in body temperature leading to a feeling of relaxation and reduced muscle tension, an increase in levels of endorphins related to positive mood and a sense of well-being, increases in the availability of the central neurotransmitters dopamine, norepinephrine and serotonin, and changes in neurobiological response[48-50]. Although previous literature has demonstrated the benefit of supervised exercise in treating depression[51 52], our study found no benefit from home-based exercise intervention in ameliorating depressive symptoms. The differences in these findings may be explained by poorer treatment compliance in the home-based exercise intervention group, as to achieve significant benefit patients have to practice the exercise programme at a prescribed intensity and frequency. Lack of motivation and inattention are common symptoms in depression and may account for unsupervised patients failing to achieve the prescribed levels of activity when compared with those given encouragement through supervision. This assumption corresponds with findings from the home-based exercise studies[26 27] that the physical health of patients in this group (i.e. cardio-respiratory capacity, BMI, and lower limb strength), the surrogate endpoints of exercise intervention, did not change significantly from baseline.

Although our study did not find any advantages of home-based exercise intervention over usual care, when combined with psychological intervention the combined approach had a significantly greater benefit than either of these interventions alone. The combination may have a synergistic

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effect, with psychological intervention improving motivation to initiate and maintain an exercise programme while the latter in turn enhances the benefits of psychological intervention[53].

Reviewing complimentary or alternative medicine approaches, results from Chung et al[36] and Rickhi et al[32] showed that home-based deep-breathing training and spiritual teaching programmes could significantly reduce depressive symptoms when compared with usual care. However, these two studies had small sample sizes and included specific populations, namely coronary heart disease patients for Chung's study and middle-aged females for Rickhi's study. Their findings may not, therefore, be generalizable to other populations.

Strengths and limitations

Our study has several strengths. Given the potential of home-based interventions to treat depression and the increasing use of these interventions, our analysis provides the first comprehensive review of the efficacy of home-based interventions in treating depression. A comprehensive search was undertaken to identify as many relevant studies as possible and two reviewers selected the studies independently with a high level of agreement. Selection bias was, therefore less likely. In addition, we performed a network meta-analysis to compare the efficacy of all available home-based interventions in order to identify the best treatment regime.

We are aware that our study may have some limitations. Firstly, the quality of included studies in the area of allocation concealment was not optimal. The results from our study might, therefore, be affected by selection bias and should be interpreted with caution. Secondly, participants in our included studies were aware both of their own interventions and their subjective outcomes, including the self-reported depression scores. However, in most of the included studies this bias from non-blinded intervention was minimized by blinding the outcome assessors. Thirdly, although all studies used usual care as a treatment comparator, descriptions of usual care differed among the included studies (see Supplementary Table 2). For instance, usual care in Blumenthal's study consisted of each participant in the control group being prescribed antidepressant medication while home-based exercise participants received none. This may be responsible for a high remission rate in the control group, resulting in an underestimated treatment effect for home-based exercise.

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Network meta-analysis allows indirect comparison of the efficacy of all possible interventions, given the presence of some common comparators. However, this technique requires two important assumptions, namely transitivity and consistency[54]. Transitivity requires that the characteristics of patients and studies subjected to direct and indirect comparisons should be similar. For instance, the characteristics of patients in a study comparing home-based psychological intervention with usual care and of patients in a study of home-based exercise versus usual care should be similar in order to perform an indirect comparison of home-based psychological intervention versus home-based exercise. This assumption cannot be directly assessed or tested. However, consistency testing is a manifestation of transitivity. We therefore made a consistency assumption by comparing intervention effects between direct and indirect estimates. The number of included studies may play a role in this assessment, i.e. a false negative result might be present when direct and indirect estimates are not statistically different. For our study, inconsistency factors ranged from -0.018 to 0.106, at which levels a false negative result is unlikely.

We were unable to check consistency assumption in three of the indirect comparisons due to a lack of direct comparisons. For each of these studies, we therefore explored patient characteristics (mean age and types of depression), the duration of the intervention, the percentage of antidepressant use in the intervention and control groups, and the description of usual care (see Supplementary Table 2) and found variations between studies and comparisons. For example, the definitions of usual care in the studies of combined home-based psychological intervention with exercise were not clearly defined, while the common definition of usual care in the studies into home-based psychological intervention was the standard treatment of depression by psychiatrists. This heterogeneity within and between interventions across included studies may impact both on the results and on the transitivity and consistency assumptions of our network met-analysis. Results from indirect comparison, e.g. the efficacy of home-based psychological intervention and combined home-based psychological intervention with exercise versus home-based exercise alone should therefore be interpreted with caution. Ideally, confirmation should be sought by undertaking further randomized-controlled trials directly comparing these two interventions with home-based exercise.

Clinical implication and further study

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Depression is a common disorder, particularly among the elderly and in those with a chronic disease. Many of these patients have difficulty accessing mental health services due to physical disabilities and transportation problems. Home-based interventions to treat depression have the potential to overcome these barriers and have been shown by our study to be effective. This information should prove helpful when designing clinical guidelines. However, there are obvious logistical differences between home-based treatments for depression and conventional clinic-based care. Our study has not investigated these aspects of treatment design and, in particular, has not considered manpower implications or transport costs. An economic evaluation study is needed before general implementation of a home-based care model can be recommended unequivocally.

Although a randomized-controlled trial is considered to be the gold standard for therapeutic research, in a real world setting this design may not be ideal for examining patient preferences and adherence to treatment. In this review, most of the studies (n=10) did not report the degree of adherence with the prescribed intervention. Seven studies demonstrated the effect of adherence on outcomes but used different definitions to assess adherence. To maximize treatment efficacy, further studies should determine the effects of patient preferences and adherence to treatment for different approaches and modes of delivery as well as examine the factors that influence preferences and adherence.

CONCLUSION

Our study has confirmed the efficacy both of home-based psychological intervention and combined home-based psychological intervention with exercise intervention in decreasing symptoms of depression and improving rates of remission. In addition, the combination of home-based psychological intervention and exercise intervention has the highest probability of being the best treatment out of all available home-based interventions. This approach should, therefore, be considered when formulating clinical guidelines for treating depression.

Contributors: KS, PI, and TA were involved in the conception and design of the review. KS and TA developed the search strategy, performed study selection, extracted data from included studies and analyzed the data. KS, ML, PI, AD, AT and TA were involved in the interpretation and discussion of results. KS and TA drafted the manuscript. PI, AD, AT and TA revised it critically for important intellectual content. All authors approved the final version of the article. All authors had access to all

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of the data in the study and can take responsibility for the integrity of the data and the accuracy of the data analysis. TA is guarantor.

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Table 1. Characteristics of included studies

Author	Setting	Type of depression	Participants							Study's intervention		
			N	Age (mean)	Female (%)	Living alone (%)	Married (%)	Baseline depression score (mean)	Anti-depressants use (%)	Type of intervention	Duration (weeks)	Comparison
Kiosses[25]	U.S.	Major depressive disorder	74	80.91	74.3	NA	NA	21.25[a]	63.51	PST-HC	12 weeks	Usual care with home visit
Choi[21]	U.S.	Mixed depression	121	65.21	77.7	63.6	NA	24.55[b]	NA	PST-HC	12 weeks	Usual care with telephone support call
Gitlin[24]	New Zealand	Mixed depression	208	69.57	78.4	56.8	12.0	13.01[c]	19.3	PST-HC	16 weeks	Usual care
Klug[28]	Australia	Major depressive disorder	60	74.9	90.0	78.3	NA	8.91[e]	95	PST-HC	52 weeks	Usual care
Gellis[22]	U.S.	Minor depression	36	75.9	91.6	88.9	8.3	18.05[b]	0	PST-HC	6 weeks	Usual care
Gellis[29]	U.S.	Minor depression	62	77.67	87.5	80.0	20.0	20.52[a]	NA	PST-HC	6 weeks	Usual care with home visit

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Author	Setting	Type of depression	Participants							Study's intervention		
			N	Age (mean)	Female (%)	Living alone (%)	Married (%)	Baseline depression score (mean)	Anti-depressants use (%)	Type of intervention	Duration (weeks)	Comparison
Naylor[39]	U.S.	Mixed depression	38	51.45	84.2	NA	NA	7.9[f]	NA	Home-based CBT	6 weeks	Usual care
Joling[40]	Netherland	Minor depression	170	81.45	73.5	NA	29.4	21.6	NA	Home-based CBT	12 weeks	Usual care
Pfaff[27]	U.S.	Mixed depression	200	60.97	63.0	21.6	53.0	NA	54.5	Home-based exercise	12 weeks	Usual care
Kerse[26]	Austria	Mixed depression	193	81.1	58.5	51.8	NA	3.7[e]	26.4	Home-based exercise	24 weeks	Usual care with home visit
Blumenthal[35]	U.S.	Major depressive disorder	102	52.52	74.5	NA	NA	16.52[b]	0	Home-based exercise	16 weeks	Usual care
Ciechanowski[37]	U.S.	Mixed depression	80	43.9	52.5	NA	68.8	2.00[d]	40%	Combined PST-HC with home-based exercise	19 weeks	Usual care
Ciechanowski[38]	U.S.	Minor depression	138	73	79	72.0	11.0	1.3[d]	51	Combined PST-HC with home-based exercise	19 weeks	Usual care
Banerjee[18]	Taiwan	Mixed depression	69	80.71	82.9	78.3	15.9	26.25[a]	11.39	Combined family therapy, bereavement counselling, social interventions with	24 weeks	Usual care

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Author	Setting	Type of depression	Participants							Study's intervention		
			N	Age (mean)	Female (%)	Living alone (%)	Married (%)	Baseline depression score (mean)	Anti-depressants use (%)	Type of intervention	Duration (weeks)	Comparison
										home-based exercise		
Gary[30]	U.S.	Mixed depression	74	65.8	57.1	NA	39.2	20.7[f]	29.7	Home-based CBT, home-based exercise, combined home-based CBT with home-based exercise	12 weeks	Usual care
Rickhi[32]	U.K.	Major depressive disorder	84	44.05	77.4	NA	58.3	20.35[b]	0	Spiritual teaching program	8 weeks	Usual care
Chung[36]	U.S.	Mixed depression	62	71.50	30.6	NA	NA	7.53[c]	1.61	Home-based deep breathing exercise	4 weeks	Usual care with telephone support call

[a]MADRS; [b]HAMD; [c]PHQ-9; [d]HSCL-20; [e]GDS; [f]BDI

PST-HC, problem solving therapy-home care; CBT, cognitive behavioural therapy

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Table 2. Mean difference of depression score after treatment between intervention and control groups

Author	Year	Follow up time	Treatment Adherence (%)	Intervention			Control			Mean difference (95% CI)
				N	Mean	SD	N	Mean	SD	
Home-based Psychological intervention										
Kiosses [25]	2015	12 weeks	Not reported	37	10.6	6.08	37	15.6	6.81	-0.77 (0.30, -1.25)
Choi[21]	2014	12 weeks	Not reported	35	14.44	7.04	31	19.16	7.02	-0.67 (-1.17, -0.17)
Gitlin [24]	2013	16 weeks	93.3%	106	6.4	6.18	102	8.9	6.06	-0.41 (-0.13, -0.68)
Joling [40]	2011	12 weeks	41%	86	16.60	6.41	84	17.27	6.53	-0.10 (-0.40, 0.20)
Gary [30]	2010	12weeks	72%	17	8.2	6.3	15	9.3	4.9	0.19 (0.50, -0.89)
Gellis [22]	2010	6 weeks	Not reported	18	11.4	8.3	18	17.3	8.1	0.72 (-0.04, -1.39)
Klug [28]	2010	48 weeks	Not reported	29	6.11	3.00	29	10.43	4.2	-1.18 (-0.62, -1.74)
Naylor [39]	2010	6 weeks	50.9%	15	4.40	5.30	18	4.90	5.30	-0.09 (-0.78, 0.59)
Gellis [29]	2007	6 weeks	Not reported	30	8.11	4.3	32	13.64	5.6	1.10 (-0.57, -1.64)
Home-based exercise										
SMD (95% CI)										**-0.57 (-0.84, -0.31)**
Kerse [26]	2010	24 weeks	33%	94	2.4	0.2	92	3.1	0.3	-2.75 (-2.35, -3.15)
Gary [30]	2010	12 weeks	82 %	18	8.4	5.6	15	9.3	4.9	-0.17 (0.52, -0.86)
Blumenthal [35]	2007	16 weeks	68%	53	9.5	7.43	49	10.5	5.36	-0.15 (0.24, -0.54)
SMD (95% CI)										**-1.03 (-2.89, 0.82)**
Combined home-based psychological intervention with exercise										
Gary [30]	2010	12 weeks	85%	16	6.5	3.7	15	9.3	4.9	-0.65 (0.08, -1.37)
Ciechanowski [38]	2004	24 weeks	Not reported	72	0.71	0.6	66	1.17	0.53	-0.81 (-0.46, -1.16)
SMD (95% CI)										**-0.78 (-1.09, -0.47)**

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Table 3. Risk ratios of incidence of remission between intervention and control groups

Author	Year	Follow up time	Treatment Adherence	Intervention		Control		RR (95% CI)
				Remission	No Remission	Remission	No Remission	
Home-based Psychological intervention								
Kiosses [25]	2015	12 weeks	Not reported	14	23	5	32	2.80 (1.12, 6.98)
Gitlin [24]	2013	16 weeks	93.3%	39	50	25	68	1.63 (1.08, 2.46)
Joling [40]	2011	12 weeks	41%	31	55	25	59	1.47 (0.84, 2.55)
Naylor [39]	2010	6 weeks	50.9%	11	4	9	9	1.21 (0.79, 1.87)
Pooled RR (95% CI)								**1.53 (1.19, 1.98)**
Home-based exercise								
Ptaff [27]	2014	12 weeks	Not reported	49	29	40	28	1.07 (0.82-1.39)
Blumenthal [35]	2007	16 weeks	68%	21	32	23	26	0.84 (0.54-1.32)
Pooled RR (95% CI)								**0.99 (0.79, 1.24)**
Combined home-based psychological intervention with exercise								
Ciechanowski [37]	2010	19 weeks	Not reported	4	36	0	40	9.00 (0.50-161.86)
Ciechanowski [38]	2004	19 weeks	Not reported	30	42	6	60	4.58 (2.04-10.31)
Banerjee [18]	1996	24 weeks	Not reported	19	10	9	23	2.33 (1.26-4.30)
Pooled RR (95% CI)								**3.47 (2.11, 5.70)**

CI, confidence interval; RR, risk ratio

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Figure legends

Figure 1. Flow chart of study selection

Figure 2. Network meta-analysis of disease remission among home-based interventions

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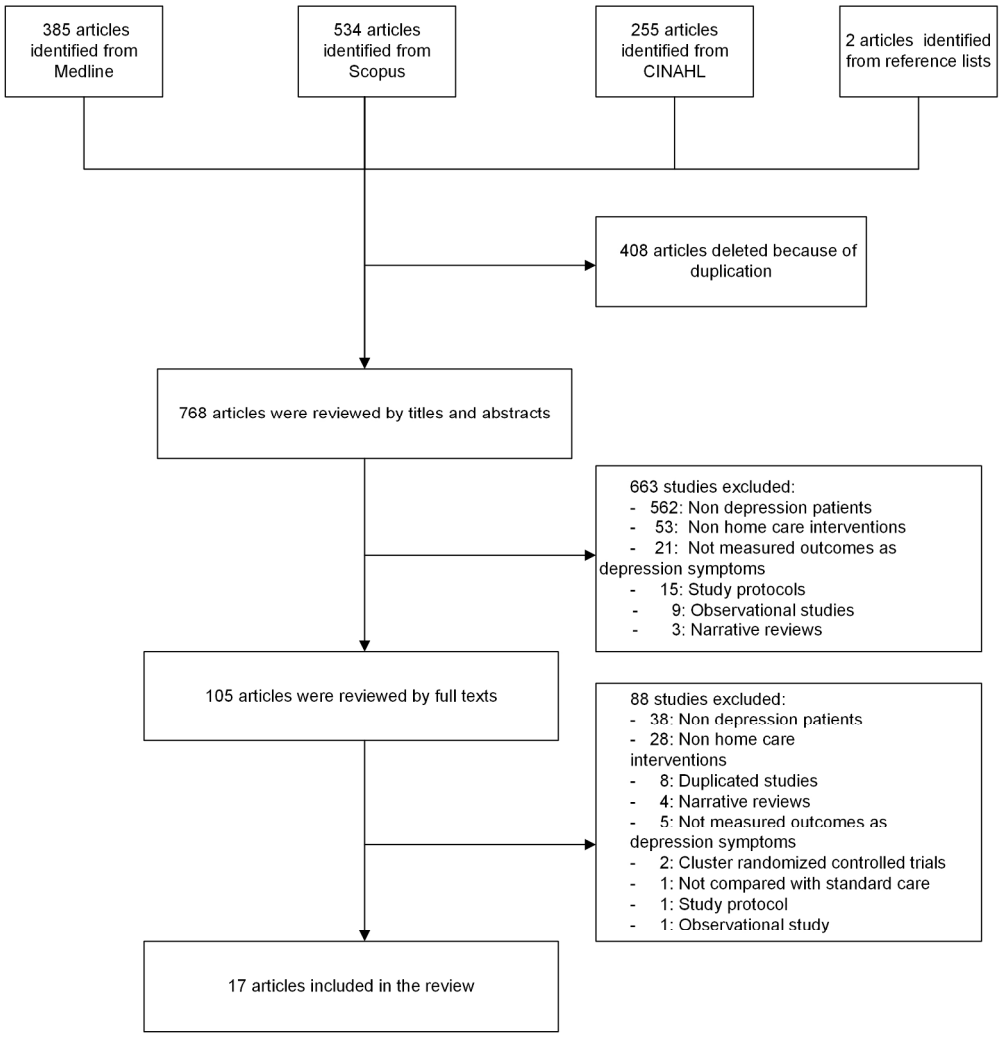

Figure 1. Flow chart of study selection

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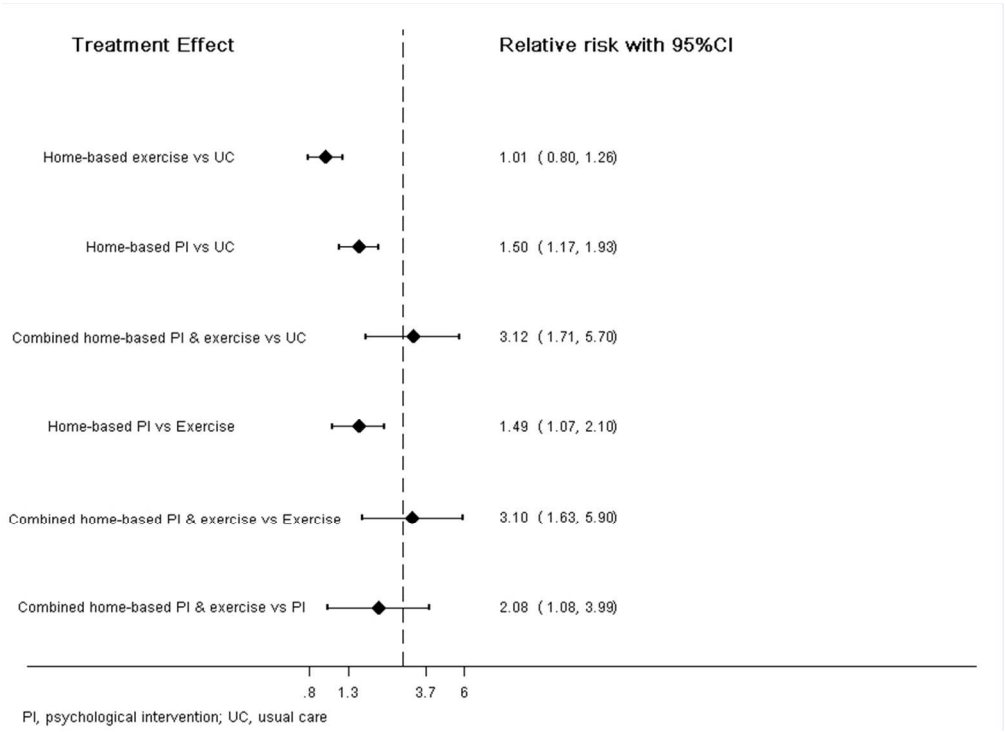

Figure 2. Network meta-analysis of disease remission among home-based interventions

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Supplementary Appendix

Search strategy for Medline

(Depressive OR depression OR depressed) AND ("Home Care Services"[MeSH] OR "Home Care Agencies"[MeSH] OR "Home Nursing"[MeSH] OR "House Calls"[MeSH] OR "Community Health Planning"[MeSH] OR "Health Systems Agencies"[MeSH] OR "Community Health Nursing"[MeSH] OR "Social Support"[MeSH]) OR ("Home Based" OR "home support" OR (“home treatment” OR “home treatments”) OR “home care” OR ("home visits" OR "Home visit") OR ("Health visits" OR "Health visit") OR (“home service” OR “home services”)) Filters: Randomized Controlled Trial

Search strategy for Scopus

(Depressive OR depression OR depressed) AND ("Home Based" OR "home support" OR (“home treatment” OR “home treatments”) OR “home care” OR ("home visits" OR "Home visit") OR ("Health visits" OR "Health visit") OR (“home service” OR “home services”) OR “home health care”)

CINAHL

Search strategy for CINAHL

(depressive OR depression OR depressed) AND ("Home Based" OR "home support" OR (“home treatment” OR “home treatments”) OR “home care” OR ("home visits" OR "Home visit") OR ("Health visits" OR "Health visit") OR (“home service” OR “home services”) OR “home health care”) AND (randomized OR randomized)

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Supplementary Table 1. Risk of bias assessment

Author (Year)	Year	Random sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessors	Incomplete outcome data	Selective outcome reporting	Other bias	Power of study
Rickhi	2011	Low	Low	High	Low	Low	Low	Low	Low
Banerjee	1996	Low	Unclear	High	Low	Low	Low	Low	Unclear
Blumenthal	2007	Low	Low	High	Low	Low	Low	Low	Low
Choi	2014	Unclear	Unclear	High	Unclear	High	Low	Low	Unclear
Chung	2010	Low	Low	High	unclear	High	Low	Low	Unclear
Ciechanowski	2010	Low	Low	High	Low	Low	High	Low	Unclear
Ciechanowski	2004	Low	Low	High	Unclear	Low	Low	Low	Unclear
Gary	2010	Unclear	Unclear	High	Low	Low	Low	Low	Unclear
Gellis	2010	Unclear	Unclear	High	Low	Low	Low	Low	Unclear
Gellis	2008	Low	Unclear	High	Low	Low	Low	Low	Unclear
Gitlin	2013	Low	Low	High	Unclear	Low	Low	Low	Low
Kerse	2010	Low	Unclear	High	Low	Low	Low	Low	Low
Kiosses	2015	Low	Unclear	High	Low	Low	Low	Low	Low
Klug	2010	Low	Unclear	High	Unclear	High	Low	Low	Low
Pfaff	2014	Low	Unclear	High	Low	Low	Low	Low	High
Joling	2011	Low	Unclear	High	Unclear	Low	Low	Low	Unclear
Naylor	2010	Low	Unclear	High	Unclear	High	Low	Low	Unclear

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Supplementary Table 2. Characteristics of studies included in network meta-analysis

Author		Type of depression	Participants							Study's intervention	
			N	Age (mean)	Female (%)	Living alone (%)	Married (%)	Baseline depression score (mean)	Anti-depressants use (%)	Duration (weeks)	Definition of usual care
Home-based Psychological intervention											
Kiosses	Intervention	Major depressive disorder	37	80.78	70.27	NA	NA	21.08[a]	64.86	12 weeks	Care includes antidepressant medication and home visiting.
	Control		37	81.03	78.38	NA	NA	21.41[a]	62.16		
Gitlin	Intervention	Mixed depression	106	68.9	79.3	47.32	15.1	13.65[c]	22.6	16 weeks	Not clearly defined.
	Control		102	70.3	77.5	66.7	8.8	12.9[c]	15.8		
Naylor	Intervention	Mixed depression	19	48.6	94.7	NA	NA	8.3[f]	NA	6 weeks	Care includes antidepressant medication and referral to psychotherapy if needed.
	Control		19	54.3	73.7	NA	NA	7.5[f]	NA		
Joling	Intervention	Minor depression	86	81.8	69.8	NA	30.2	21.17[g]	NA	12 weeks	Care includes antidepressant medication.
	Control		84	81.1	77.4	NA	28.6	22.05g	NA		
Home-based Exercise											
Pfaff	Intervention	Mixed depression	108	61.2	62	22.4	48.1	NA	60.2	12 weeks	Not clearly defined.
	Control		92	60.7	64.1	20.7	58.7	NA	47.8		

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Author		Type of depression	Participants							Study's intervention	
			N	Age (mean)	Female (%)	Living alone (%)	Married (%)	Baseline depression score (mean)	Anti-depressants use (%)	Duration (weeks)	Definition of usual care
Blumenthal	Intervention	Major depressive disorder	53	53	74	NA	NA	17+/-5[b]	0	16 weeks	Antidepressant medication only.
	Control		49	52	75	NA	NA	16+/-4[b]	100		
Combined home-based psychological intervention with exercise											
Ciechanowski	Intervention	Mixed depression	40	43.4	47.5	NA	65	2.1[d]	37.5	19 weeks	Not clearly defined.
	Control		40	44.1	57.5	NA	72.5	1.9[d]	42.5		
Ciechanowski	Intervention	Minor depression	72	72.6	82	78	11.0	1.3[d]	40	19 weeks	Not clearly defined
	Control		66	73.5	76	65	11.0	1.2 [d]	30		
Banerjee	Intervention	Mixed depression	33	80.4	85	82	18	27.5[a]	11	24 weeks	Care by general practitioners, with psychiatric referral if needed.
	Control		36	81	81	75	14	25.1 [a]	12		

[a]MADRS; [b]HAMD; [c]PHQ-9; [d]HSCL-20; [e]GDS; [f]BDI

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Supplementary Figure legends

Supplementary Figure 1. Pooled standardized mean difference between home-based psychological intervention and usual care according to severities of depression

Supplementary Figure 2. Pooled standardized mean difference between home-based exercise, combined psychological intervention with exercise and usual care

Supplementary Figure 3. Pooled risk ratio of disease remission between home-based psychological intervention and usual care

Supplementary Figure 4. Pooled risk ratio of disease remission between home-based exercise, combined psychological intervention with exercise and usual care

Supplementary Figure 5. Network plot of all available home-based interventions

Supplementary Figure 6. Funnel plots of home-based psychological intervention and home-based exercise

Supplementary Figure 7. Funnel and contour enhanced funnel plot of combined psychological intervention with exercise

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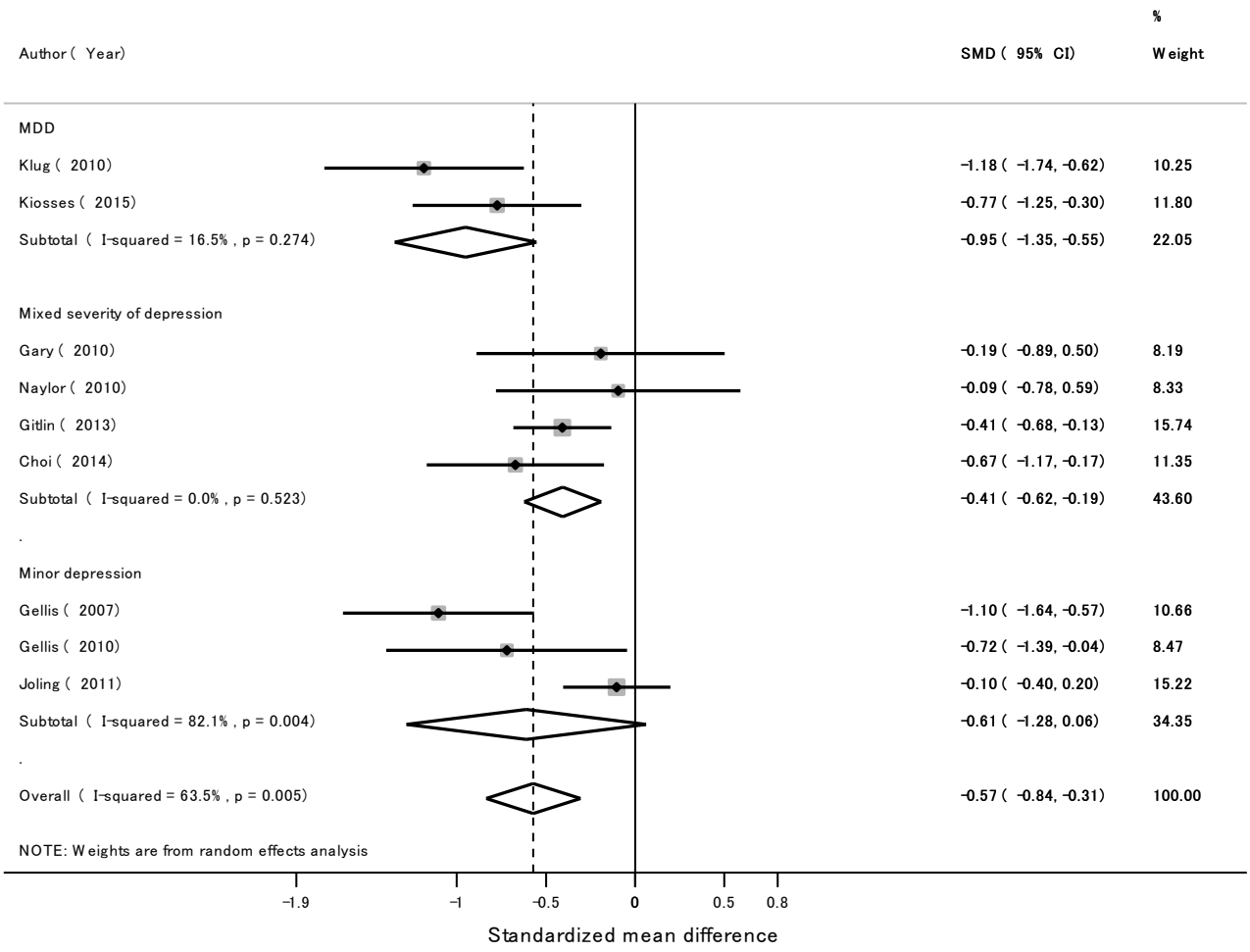
Supplementary Figure 1



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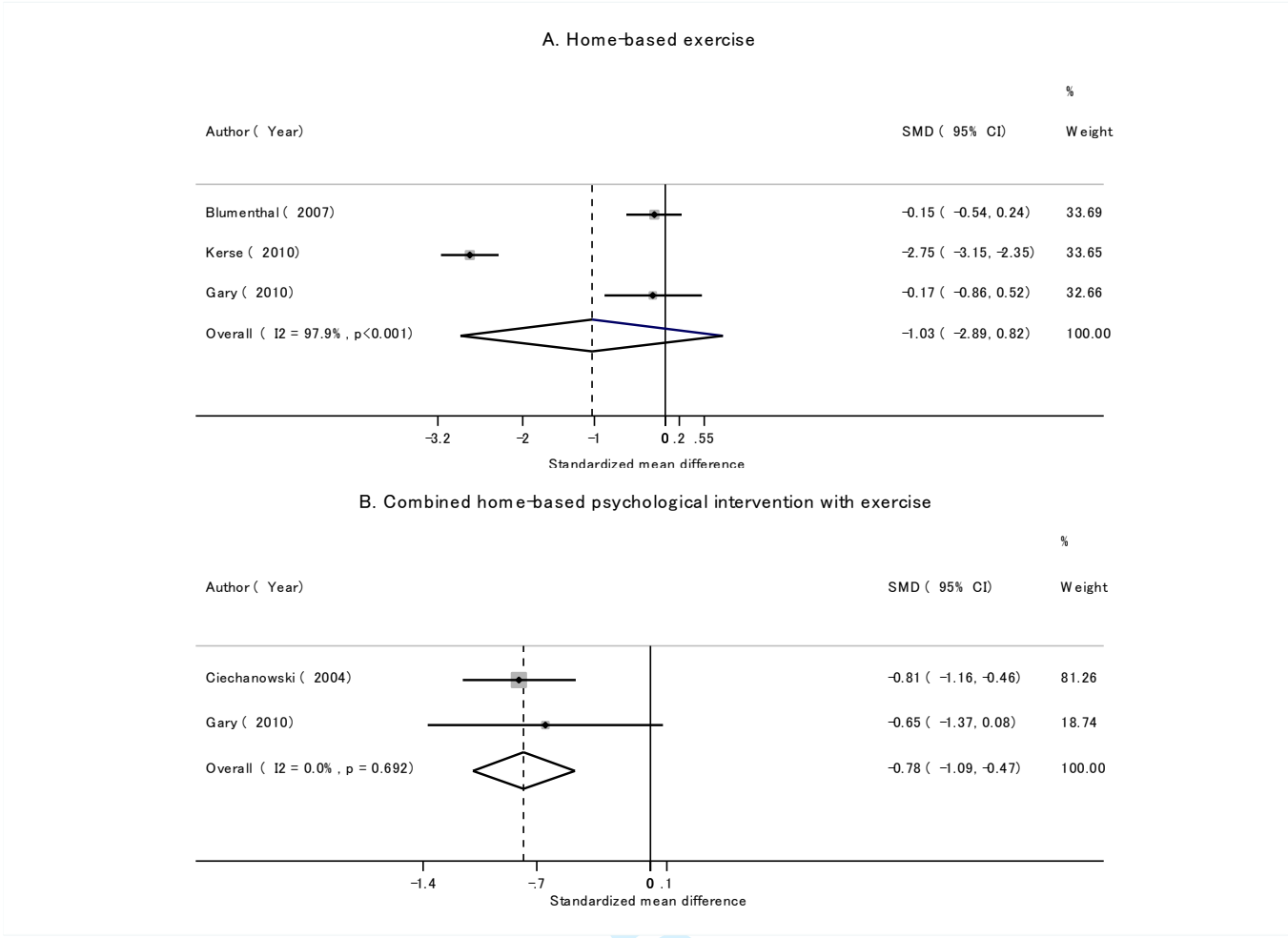
Supplementary Figure 2



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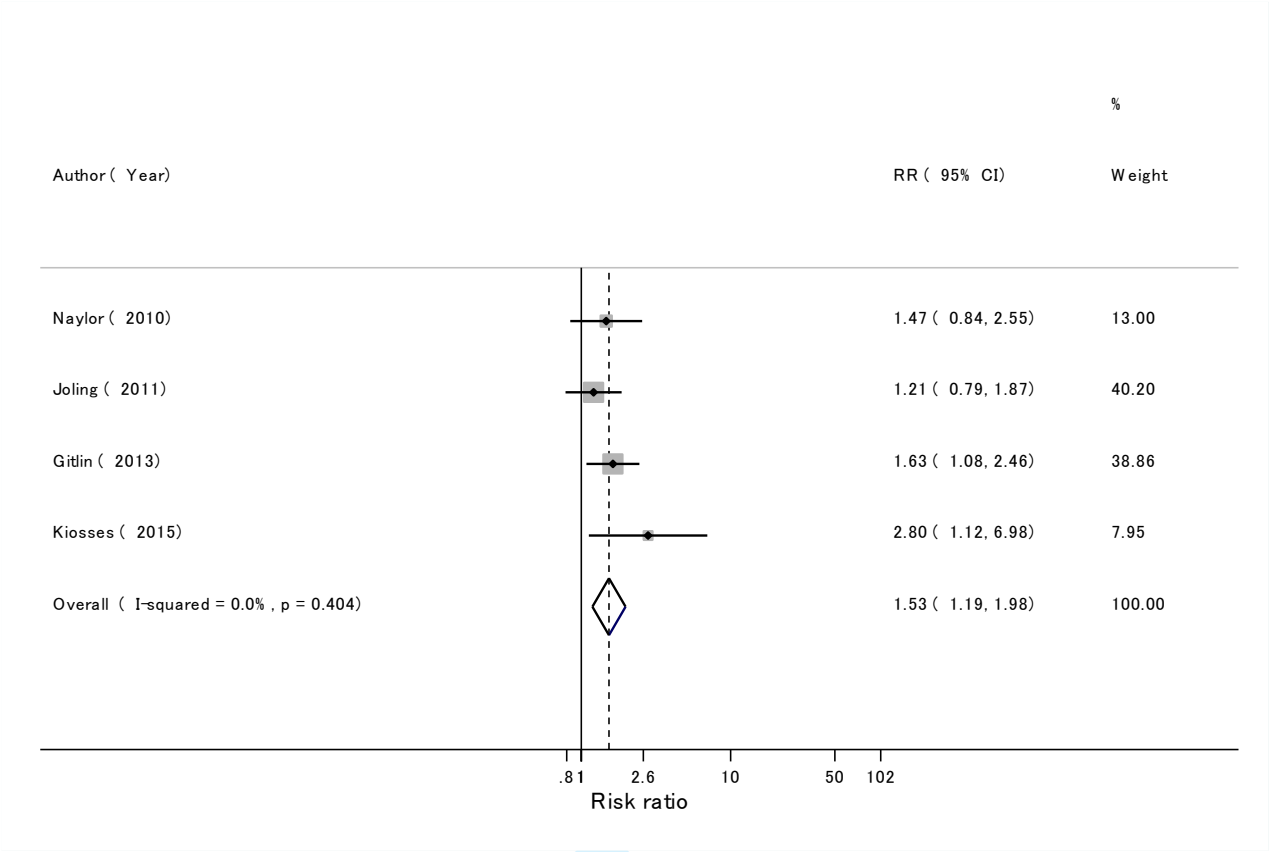
Supplementary Figure 3



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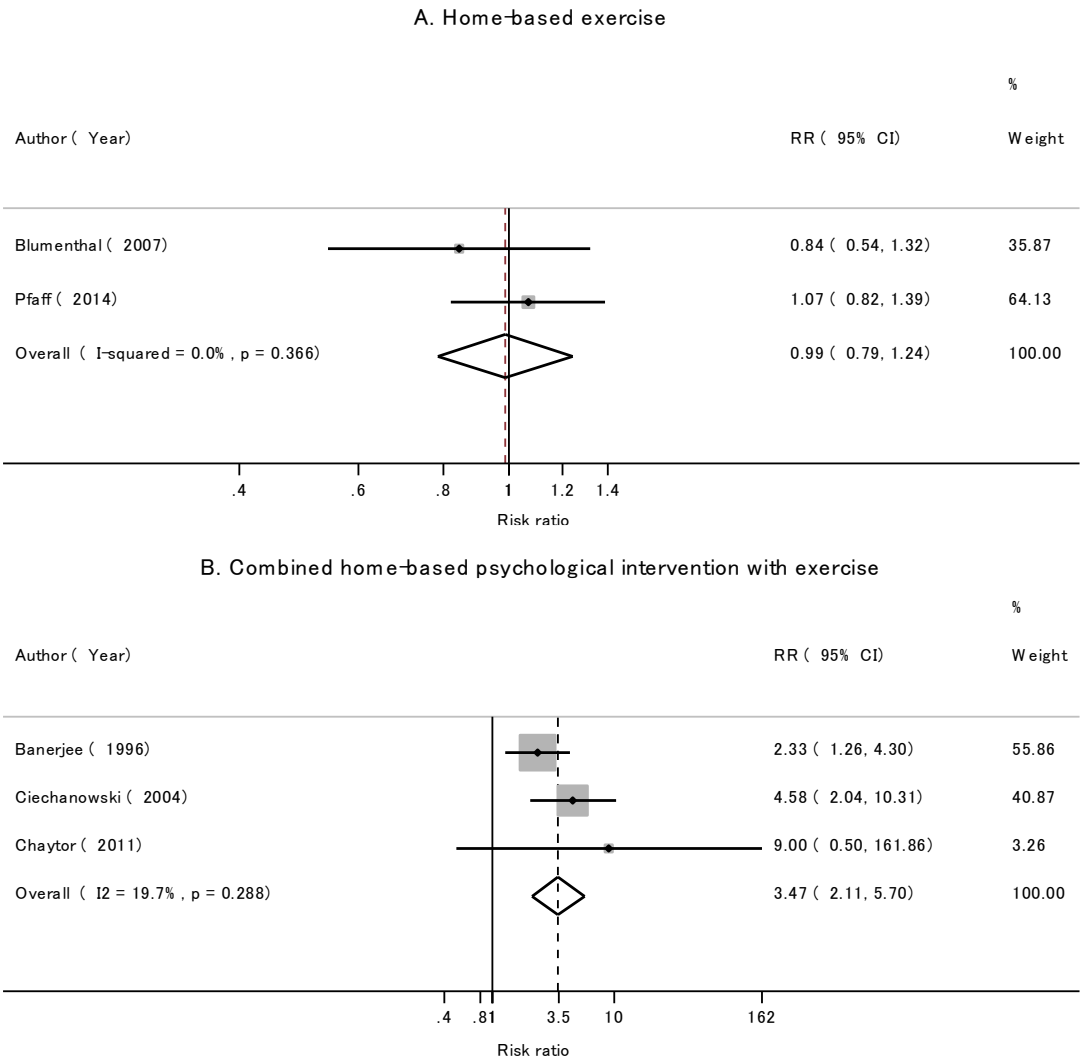
Supplementary Figure 4



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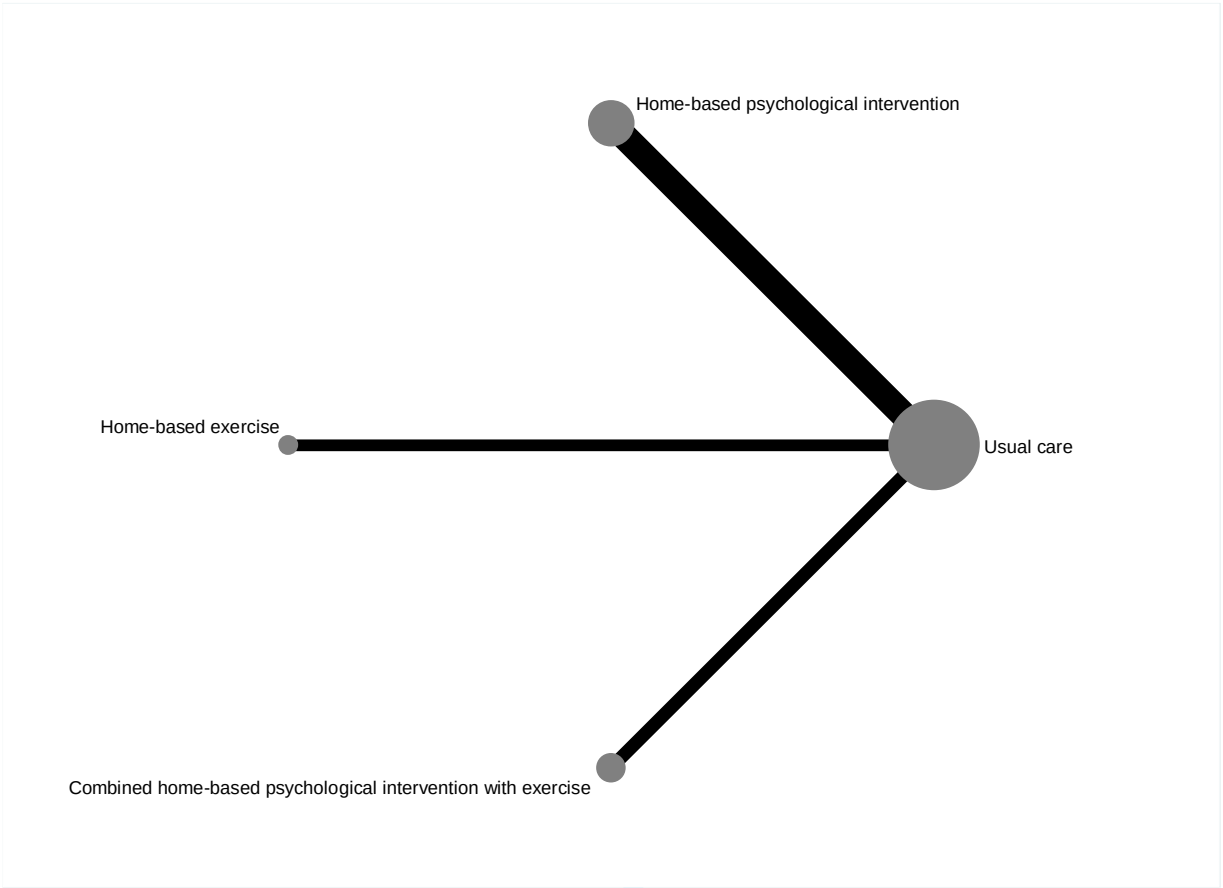
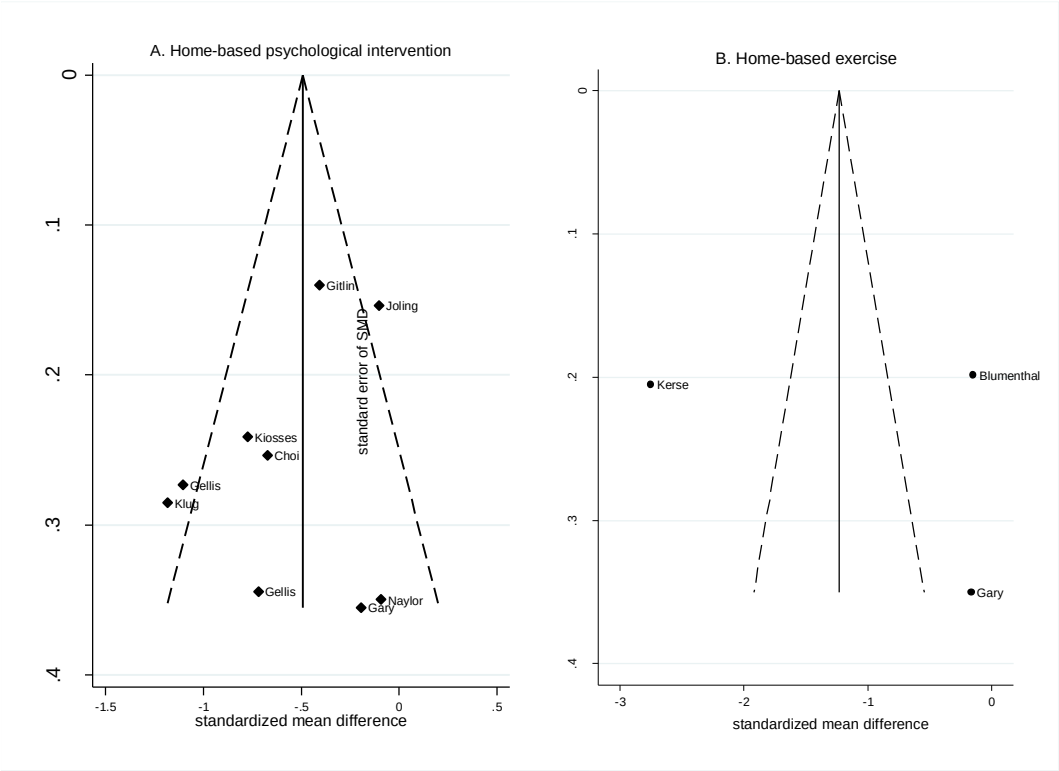
Supplementary Figure 5



view only

Supplementary Figure 6



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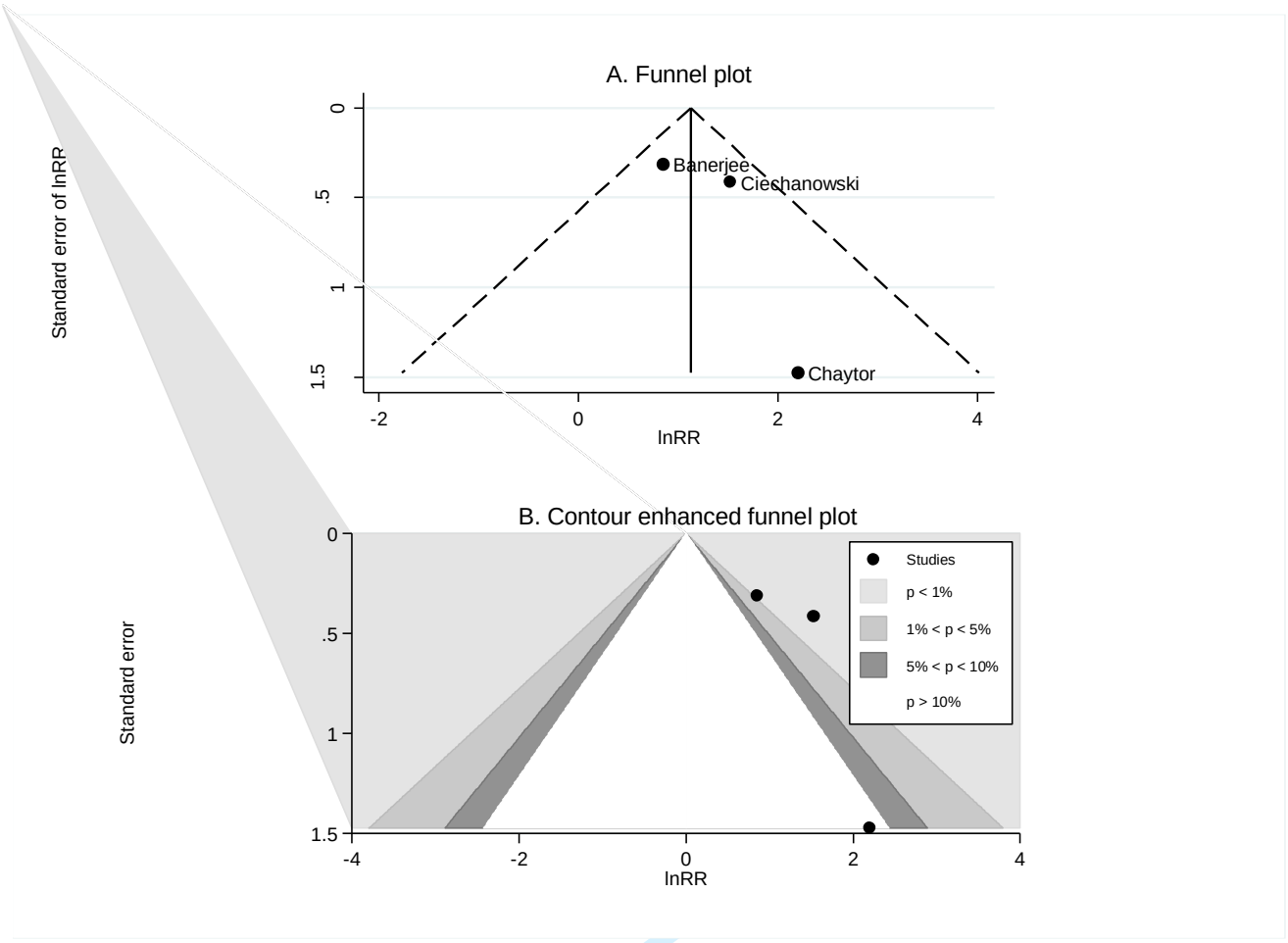
Supplementary Figure 7



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Supplementary Table 1. Risk of bias assessment

Author (Year)	Year	Random sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessors	Incomplete outcome data	Selective outcome reporting	Other bias	Power of study
Rickhi	2011	Low	Low	High	Low	Low	Low	Low	Low
Banerjee	1996	Low	Unclear	High	Low	Low	Low	Low	Unclear
Blumenthal	2007	Low	Low	High	Low	Low	Low	Low	Low
Choi	2014	Unclear	Unclear	High	Unclear	High	Low	Low	Unclear
Chung	2010	Low	Low	High	unclear	High	Low	Low	Unclear
Ciechanowski	2010	Low	Low	High	Low	Low	High	Low	Unclear
Ciechanowski	2004	Low	Low	High	Unclear	Low	Low	Low	Unclear
Gary	2010	Unclear	Unclear	High	Low	Low	Low	Low	Unclear
Gellis	2010	Unclear	Unclear	High	Low	Low	Low	Low	Unclear
Gellis	2008	Low	Unclear	High	Low	Low	Low	Low	Unclear
Gitlin	2013	Low	Low	High	Unclear	Low	Low	Low	Low
Kerse	2010	Low	Unclear	High	Low	Low	Low	Low	Low
Kiosses	2015	Low	Unclear	High	Low	Low	Low	Low	Low
Klug	2010	Low	Unclear	High	Unclear	High	Low	Low	Low
Pfaff	2014	Low	Unclear	High	Low	Low	Low	Low	High
Joling	2011	Low	Unclear	High	Unclear	Low	Low	Low	Unclear
Naylor	2010	Low	Unclear	High	Unclear	High	Low	Low	Unclear

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Supplementary Table 2. Characteristics of studies included in network meta-analysis

Author		Type of depression	Participants							Study's intervention	
			N	Age (mean)	Female (%)	Living alone (%)	Married (%)	Baseline depression score (mean)	Anti-depressants use (%)	Duration (weeks)	Definition of usual care
Home-based Psychological intervention											
Kiosses	Intervention	Major depressive disorder	37	80.78	70.27	NA	NA	21.08[a]	64.86	12 weeks	Care includes antidepressant medication and home visiting.
	Control		37	81.03	78.38	NA	NA	21.41[a]	62.16		
Gitlin	Intervention	Mixed depression	106	68.9	79.3	47.32	15.1	13.65[c]	22.6	16 weeks	Not clearly defined.
	Control		102	70.3	77.5	66.7	8.8	12.9[c]	15.8		
Naylor	Intervention	Mixed depression	19	48.6	94.7	NA	NA	8.3[f]	NA	6 weeks	Care includes antidepressant medication and referral to psychotherapy if needed.
	Control		19	54.3	73.7	NA	NA	7.5[f]	NA		
Joling	Intervention	Minor depression	86	81.8	69.8	NA	30.2	21.17[g]	NA	12 weeks	Care includes antidepressant medication.
	Control		84	81.1	77.4	NA	28.6	22.05g	NA		
Home-based Exercise											
Pfaff	Intervention	Mixed depression	108	61.2	62	22.4	48.1	NA	60.2	12 weeks	Not clearly defined.
	Control		92	60.7	64.1	20.7	58.7	NA	47.8		

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Author		Type of depression	Participants							Study's intervention	
			N	Age (mean)	Female (%)	Living alone (%)	Married (%)	Baseline depression score (mean)	Anti-depressants use (%)	Duration (weeks)	Definition of usual care
Blumenthal	Intervention	Major depressive disorder	53	53	74	NA	NA	17+/-5[b]	0	16 weeks	Antidepressant medication only.
	Control		49	52	75	NA	NA	16+/-4[b]	100		
Combined home-based psychological intervention with exercise											
Ciechanowski	Intervention	Mixed depression	40	43.4	47.5	NA	65	2.1[d]	37.5	19 weeks	Not clearly defined.
	Control		40	44.1	57.5	NA	72.5	1.9[d]	42.5		
Ciechanowski	Intervention	Minor depression	72	72.6	82	78	11.0	1.3[d]	40	19 weeks	Not clearly defined
	Control		66	73.5	76	65	11.0	1.2 [d]	30		
Banerjee	Intervention	Mixed depression	33	80.4	85	82	18	27.5[a]	11	24 weeks	Care by general practitioners, with psychiatric referral if needed.
	Control		36	81	81	75	14	25.1 [a]	12		

[a]MADRS; [b]HAMD; [c]PHQ-9; [d]HSCL-20; [e]GDS; [f]BDI

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Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	3
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	5
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	5, 6
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	-
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	6, 7
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	6
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	Supplementary Appendix
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	6
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	7
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	7
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	8
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	8
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	8

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PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	9
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	8
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	9, Figure 1
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	9, 10, 11, 12 & Table 1
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	12 & Supplementary Table 1
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	Tables 2 & 3 Figure 2 Supplementary Figure1, 2, 3, 4
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	12-16
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	16
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	12-16
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	16-19
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	18
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	19
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	19

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From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(6): e1000097. doi:10.1371/journal.pmed1000097

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