A network meta-analysis of 12,116 individuals from randomized controlled trials in the treatment of depression after acute coronary syndrome

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Abstract

Background
Post-acute coronary syndrome (ACS) depression is a common but not well understood complication experienced by ACS patients. Research on the effectiveness of various therapies remains limited. Hence, we sought to conduct a network meta-analysis to assess the efficacy of different interventions for post-ACS depression in improving patient outcomes.

Methods and findings
Three electronic databases were searched for randomised controlled trials describing different depression treatment modalities in post-ACS patients. Each article was screened based on inclusion criteria and relevant data were extracted. A bivariate analysis and a network meta-analysis was performed using risk ratios (RR) and standardized mean differences (SMD) for binary and continuous outcomes, respectively.

A total of 30 articles were included in our analysis. Compared to standard care, psycho-social therapy was associated with the greatest reduction in depression scores (SMD=-1.21, 95% CI: -1.81 to -0.61, p<0.001), followed by cognitive behavioural therapy (CBT) (SMD: -0.75, 95% CI: -0.99 to -0.52, p<0.001), antidepressants (SMD: -0.73, 95% CI: -1.14 to -0.31, p<0.001), and lastly, combination therapy (SMD: -0.15, 95% CI: -0.28 to -0.03, p = 0.016). No treatment modalities was found to be more effective in reducing depression scores when compared to one another. Additional analysis showed that these treatment...
modalities did not have significant impact on the overall mortality, cardiac mortality and recurrent myocardial infarction.

**Conclusion**
This network meta-analysis found that the treatment effect of the various psychological modalities on depression severity were similar. Future trials on psychological interventions assessing clinical outcomes and improvement in adherence to ACS-specific interventions are needed.

**Introduction**
Acute coronary syndrome (ACS) remains one of the leading causes of mortality and morbidity in the world [1]. While there has been significant progress in the optimization of medical treatment after ACS, the psychological wellbeing of patients are often forgotten with an estimated 46.7% of the patients affected by depression after an ACS event [2–4]. While the exact mechanisms linking depression and ACS complications are not well understood [5], studies consistently show that the development of depression after ACS can be detrimental to patients both physically and psychologically [6,7]. It is estimated that ACS patients with depression are subjected to a two-fold increase in mortality risk and 1.6-fold increase in risk of adverse cardiovascular events, along with higher rate of hospitalization [6,8,9]. Furthermore, post-ACS depression are associated with medical noncompliance and a sedentary lifestyle, both of which are risk factors for recurrent cardiac events [10,11].

Currently, guidelines from the American Heart Association (AHA) and American Academy of Family Physicians (AAFP) recommend the use of antidepressants and cognitive behavior therapy (CBT) for the treatment of post-ACS depression [12,13]. Meta-analyses by Ha et al and Fernandes et al found that selective serotonin reuptake inhibitors (SSRIs) improve depression scores and can reduce the risk of some cardiac complications associated with post-ACS depression [14,15]. CBT, a form of psychotherapy involving dedicated counselling sessions aimed at assessing and addressing the cognitive and behavioral aspects of the patient, thereby enabling patients to recognize and challenge their maladaptive thought processes, was found to be an efficacious treatment option for depression after ACS [12,16]. Psychosocial therapy constituted of various methods including group counselling, education and lifestyle change programmes which generally provide flexibility in the management of the patient where the care can be tailored according to patient’s changing needs [17]. In addition, there exists a multitude of other interventions for post-ACS depression all with varying effectiveness. Examples include supplements such as omega-3 fatty acids, n-3 polyunsaturated fatty acids, and probiotics [18–20], and teleinterventions [21]. However, while these therapies have been shown to be effective measures for post-ACS depression, their comparative effectiveness is less well-understood due to a lack of direct head-to-head comparison studies [12]. Additionally, there is limited research on the relationship between therapy for post-ACS depression and hard clinical endpoints. Hence, this network meta-analysis sought to assess the efficacy of the interventions for post-ACS depression in improving depression scores, as well as mortality and cardiovascular outcomes.

**Materials and methods**

**Search strategy**
In accordance to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [22], three major electronic databases (Medline, Embase and PsycINFO)
were searched for randomised controlled trials relating to treatments for depression in post-ACS patients on 26 July 2021. A copy of the search strategy can be found in S1 Table. To ensure a comprehensive search of literature, references of related reviews and included articles were screened for relevant articles. Following the initial search, duplicates were removed using Endnote X9 prior to screening and article selection.

**Selection criteria and data extraction**

Four authors (GEHL, AT, YHC and ASM) independently screened all articles and did the full text review according to the selection criteria, with a fifth independent author (NWSC) resolving any discrepancies through a consensus. Only original research articles were included, with study protocols, reviews, letters, and conference abstracts being excluded. All included studies were randomized controlled trials (RCTs), and retrospective and prospective cohorts were excluded. To generalize the findings, intervention groups were classified with clinical consultation from a psychiatrist (RH). There were 7 groups of interventions included, namely: (1) standard care; (2) psychosocial therapy; (3) antidepressants; (4) supplements; (5) CBT; (6) tele-intervention; (7) combination therapy, a combination of antidepressants with CBT. Standard care was defined as patients in the control arm of studies without intervention, while ACS as conditions resulting in reduced blood flow to the heart, inclusive of unstable angina and myocardial infarction (MI) [23]. Psychosocial therapy was defined as therapy designed to assist patients’ re-integration into society through counselling, education, or a change in lifestyle [24]. CBT was focused on correcting the maladaptive thought processes affecting the patient’s behaviour and functionality [25,26]. Antidepressants were inclusive of any pharmacological drugs administered to treat depression [27]. Supplements consisted of non-pharmacological agents that complemented the diet of patients including omega-3 fatty acids, n-3 polyunsaturated fatty acids, and probiotics [18–20]. Tele-intervention entails the use of telephone-based care aimed at improving patients’ mental state through health coaching and cognitive restructuring [21]. The four authors working in pairs extracted data that included but not limited to author, year, country, treatment duration, sample size, patients’ age, gender and mean depression scores and the depression scale used. When mean and standard deviation was not provided, an estimation was calculated using a formula provided by Wan et al. [28] The primary outcome of interest was reduction in depression scores. The secondary outcomes included overall mortality, cardiac mortality, and myocardial infarction (MI).

**Risk of bias assessment**

Quality assessment was conducted using Cochrane Risk-of-Bias 2.0 (RoB2) for RCTs. RoB2 analyses the risk of bias by grading the quality of evidence through 5 bias domains including randomization process, deviation from intended outcomes, missing outcome data, outcome measurement and reported result selection [29].

**Statistical analysis**

The primary outcome measure was standard mean difference (SMD) that accounts for variability in the type of instrument measures used to objectify depression. Binary outcomes were analysed in risk ratio (RR). Firstly, a standard bivariate analysis was conducted in RStudio (Version 1.4.1717) using the meta package. The inverse variance method and Hedges’ g were utilized to pool the results and obtain a weighted mean effect. Mantel-Haenszel RR estimates with corresponding 95% confidence intervals (CI) were pooled using the DerSimonian and Laird model [30]. Heterogeneity measures were quantified from within-design Q statistic (of which p<0.10 indicates significant heterogeneity) and the heterogeneity statistic I². The I²
measures the degree of heterogeneity within our analysis, with an I² value of 25%, 50% and 75% equating to small, moderate and large amounts of heterogeneity respectively [31]. Next, a network meta-analysis was then performed in STATA 16.1 with reference to White et al to draw indirect comparisons between the treatment groups [32]. A network diagram was plotted, and the thickness of each line represents the number of studies included in the analysis [33]. Binary outcomes were first log-transformed prior to pooling and exponentiated to obtain the RR. To analyse the validity of the indirect comparisons, consistency was measured using local nodes splitting and Wald testing [34,35]. Publication bias was addressed through a visual inspection of the funnel plot (S1 Appendix). Quality and certainty of the individual outcomes of the meta-analysis were assessed using the Grading of Recommendations, Assessment, Development and Evaluations (GRADE) framework [36].

Results

Summary of included articles

A total of 2,050 articles were identified in the initial search strategy. After removal of duplicates, 1,606 articles were screened, of which 129 articles were included for full text review. In total, 30 articles were included in this meta-analysis (Fig 1). Ten articles originated from USA [25,37–45], 3 from Australia [24,46,47], Iran [48–50] and Netherlands [51–53], 2 from Canada [27,54] and Italy [55,56], and 1 each from China [57], India [58], Poland [59], Portugal [60], Singapore [20], South Korea [61], and Sweden [62]. All 30 articles were RCTs with low to moderate risk of bias (S2 Table). In total, there were 12,116 patients included in the analysis, with the mean age ranging from 49.9 to 68.8 and proportion of female from 0.050 to 0.679. Of all patients, 3,118 received supplements [25,49,59], 1,619 received CBT [27,37–39,47,48,55,62], 1,123 patients received psychosocial therapy [20,43–45,50,52,54,56,57,60] 597 received antidepressants [40,41,51,53,58,61], and 202 received tele-intervention [24,46]. Combination therapy, a combination of antidepressants with CBT, was used in a study of 499 patients by Kronish et al. [42] The mean duration of follow-up was 10.6 months (Standard Deviation: 9.6). The summary of included articles can be found in S3 Table, and a summary of the direct to indirect comparisons for each network meta-analysis can be seen in S2 Appendix.

Reduction in depression scores

The network diagram depicts the comparison of the standard care to the different treatment modalities for the reduction in depression scores (Fig 2). Compared to standard care, the reduction of depression scores in all treatment modalities was statistical significance except for supplements, with moderate to high certainty of results following the GRADE score (Table 1, Fig 3). The largest reduction was observed with psychosocial therapy when compared to standard care (SMD: -1.21, 95% CI: -1.81 to -0.61, p<0.001) followed by CBT (SMD: -0.75, 95% CI: -0.99 to -0.52, p<0.001), antidepressants (SMD: -0.73, 95% CI: -1.14 to -0.31, p<0.001), and lastly combination therapy (SMD: -0.15, 95% CI: -0.28 to -0.03, p = 0.016). When comparing between the treatment modalities, there were no significant differences between the six treatment modalities in reducing depression, and there was high levels of heterogeneity noted (I² = 97.4%) between the comparisons (Table 2). Compared to psychosocial therapy, the reduction in depression scores with antidepressants (SMD: 0.47, 95% CI: -0.67 to 1.61, p = 0.422) and CBT (SMD: 0.36, 95% CI: -0.68 to 1.41, p = 0.497) did not differ significantly. Moreover, the reduction in depression scores with antidepressants and CBT (SMD: 0.10, 95% CI: -1.08 to 1.29, p = 0.863) was also similar.
All treatment modalities did not affect the overall mortality as compared to standard care with moderate to high certainty of results following the GRADE score (Table 1). When compared to standard care, antidepressants (RR: 0.54, 95% CI: 0.13 to 2.29, p = 0.406), CBT (RR: 0.98, 95% CI: 0.80 to 1.19, p = 0.847), combination therapy (RR: 1.28, 95% CI: 0.70 to 2.34, p = 0.423) and psychosocial therapy (RR: 1.34, 95% CI: 0.83 to 2.16, p = 0.227) did not significantly affect the overall mortality risk. When comparing between the treatment modalities, there were no significant differences between all six treatment modalities in affecting the overall mortality (Table 3), and the heterogeneity within the comparisons were noted to be high ($I^2 = 89.4\%$). Psychosocial therapy did not decrease overall mortality when compared to antidepressants (RR: 2.27, 95% CI: 0.54 to 9.39, p = 0.263) or CBT (RR: 1.35, 95% CI: 0.81 to 2.23, p = 0.253). Treatment with antidepressants also did not reduce the overall mortality when compared to CBT (RR: 0.59, 95% CI: 0.15 to 2.32, p = 0.455).
Cardiac mortality

Compared to standard care, none of the treatment modalities was found to significantly reduce the cardiac mortality with moderate certainty of results following the GRADE score (Table 1). Further, each of these treatment modalities did not significantly differ from one another in their effects on cardiac mortality (S4 Table), and the heterogeneity within the comparisons was low ($I^2 = 0.0\%$). The cardiac mortality among patients who received psychosocial therapy was similar to those who received CBT (RR: 1.65, 95\% CI: 0.93 to 2.92, p = 0.085), or antidepressants (RR: 1.48, 95\% CI: 0.03 to 75.19, p = 0.846). Treatment with antidepressants or CBT was also associated with similar cardiac mortality (RR: 1.12, 95\% CI: 0.02 to 55.70, p = 0.956).

Myocardial infarction

MI was reported in studies that used psychosocial therapy, antidepressant, and CBT only. These 3 treatment modalities did not significantly affect the incidence of MI as compared to standard care, with moderate certainty of results following the GRADE (Table 1). Their effects on the incidence of MI also did not differ significantly from one another (S5 Table), and the heterogeneity within the comparisons was low ($I^2 = 0.0\%$). Patients who received psychosocial therapy experienced similar risk of subsequent MI in comparison to antidepressants (RR: 1.19, 95\% CI: 0.44 to 3.19, p = 0.728), or CBT (RR: 1.01, 95\% CI: 0.61 to 1.67, p = 0.978). Treatment with antidepressants or CBT was also found to have no difference in the risk of subsequent MI (RR: 0.84, 95\% CI: 0.35 to 2.08, p = 0.713).
Discussion

This network meta-analysis is the first to examine the effects of various psychological interventions in the treatment of depression after ACS (Fig 4). Statements from the American Heart Association (AHA) and the European Society of Cardiology (ESC) both identified post ACS depression to be a significant risk factor for cardiac morbidity and mortality \[63,64\], with recent consensus describing the importance of regular screening for depression in patients suffering from coronary artery disease with consideration of CBT and SSRIs for the treatment of their depression \[65\]. While previous meta-analysis has examined the effects of CBT \[66\] and the use of SSRIs \[67,68\] in treating depression after ACS, no study has done a ranking assessment between all the possible treatments for post-ACS depression. Thus, we add to these findings by (1) conducting a network meta-analysis between treatments (2) pooling the effects of intervention on clinical outcomes. The main findings of the present study include the identification of a large reduction in depression scores upon initiation of any psychological interventions aside from the use of non-pharmacological supplements. However, there was no significant association in psychological interventions with prognostic outcomes such as overall mortality, cardiac death, or MI. Interestingly, there were no statistically significant differences between different interventions in the reduction of depression scores.

The largest reduction in depression scores was observed with psychosocial therapy (SMD: -1.21), CBT (SMD: -0.75), and antidepressant use (SMD: -0.73). Though psychosocial therapy and CBT is shown to be more effective in the reduction of depression scores compared to usual care with antidepressants, its effectiveness is dependent on many factors, such as the qualification of the healthcare professional in charge and the receptivity of the patient to treatment, which can also limit its scalability \[69\]. Additionally, both are also restricted by the fact that the execution of these specialized treatment may be limited from a lack of sufficiently

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Table 1. Summary of bivariate analysis.

| Intervention vs Standard of care | Studies | Total | I² | SMD/RR (95% CI) | P-value | GRADE score |
|---------------------------------|---------|-------|----|----------------|---------|-------------|
| **Depression scores**           |         |       |    |                |         |             |
| Psychosocial therapy            | 10      | 2193  | 96.20% | -1.21 (-1.81 to -0.61) | <0.001  | High        |
| Antidepressants                 | 6       | 1042  | 86.20% | -0.73 (-1.14 to -0.31) | <0.001  | Moderate    |
| Supplements                     | 3       | 4212  | 82.80% | -0.39 (-0.98 to 0.20) | 0.195   | High        |
| CBT                             | 8       | 3252  | 75.90% | -0.75 (-0.99 to -0.52) | <0.001  | High        |
| Tele-intervention               | 2       | 418   | 0.00% | -0.21 (-0.40 to -0.02) | 0.033   | Moderate    |
| Combination therapy             | 1       | 999   | -    | -0.15 (-0.28 to -0.03) | 0.016   | Moderate    |
| **Overall Mortality**           |         |       |    |                |         |             |
| Psychosocial therapy            | 5       | 1729  | 0.00% | 1.34 (0.83 to 2.16) | 0.227   | High        |
| Antidepressants                 | 3       | 477   | 0.00% | 0.54 (0.13 to 2.29) | 0.406   | Moderate    |
| CBT                             | 1       | 2481  | -    | 0.98 (0.80 to 1.19) | 0.847   | Moderate    |
| Combination therapy             | 1       | 999   | -    | 1.28 (0.70 to 2.34) | 0.423   | Moderate    |
| **Cardiac Death**               |         |       |    |                |         |             |
| Psychosocial therapy            | 4       | 1665  | -   | 1.42 (0.84 to 2.39) | 0.189   | Moderate    |
| CBT                             | 2       | 2581  | 0.00% | 0.84 (0.65 to 1.09) | 0.184   | Moderate    |
| **Myocardial Infarction**       |         |       |    |                |         |             |
| Psychosocial therapy            | 2       | 1440  | 0.00% | 1.00 (0.63 to 1.58) | 0.998   | Moderate    |
| Antidepressants                 | 2       | 386   | 0.00% | 0.84 (0.35 to 2.01) | 0.693   | Moderate    |
| CBT                             | 1       | 2481  | -    | 0.99 (0.81 to 1.21) | 0.939   | Moderate    |

P-value <0.05 is significant; * - Values given in SMD (95%CI); CBT, cognitive based therapy; SMD, standard mean difference; RR, Risk Ratio.

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trained mental health professionals to meet the growing demands [70,71]. In contrast, though antidepressants has been noted to be less effective than CBT and psychosocial therapy, they offer a cost effective and scalable alternative for areas without sufficiently trained mental health professionals. However, there exists limitations to the use of antidepressants. Antidepressants

![Forest plot of bivariate analysis for depression scores.](https://doi.org/10.1371/journal.pone.0278326.g003)

Table 2. Summary of network analysis for depression scores.

| Study                        | Estimate [95% CI] |
|------------------------------|-------------------|
| Psychosocial therapy vs Standard Care | -1.21 [-1.81, -0.61] |
| Antidepressants vs Standard Care | -0.73 [-1.14, -0.31] |
| Supplements vs Standard Care | -0.39 [-0.98, 0.20] |
| CBT vs Standard Care | -0.75 [-0.99, -0.52] |
| Tele-intervention vs Standard Care | -0.21 [-0.40, -0.02] |
| Combination therapy vs Standard Care | -0.15 [-0.28, -0.03] |

Values given in SMD (95%CI); CBT, cognitive based therapy; SMD, standardised mean difference.

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Table 3. Summary of network analysis for overall mortality.

|                     | Psychosocial therapy | Antidepressants | Supplements | CBT           | Tele-intervention | Combination therapy |
|---------------------|----------------------|-----------------|-------------|---------------|-------------------|---------------------|
| **Psychosocial**    | -                    | 2.27 (0.54 to 9.39, p = 0.263) | 1.32 (0.03 to 65.37, p = 0.890) | 1.35 (0.81 to 2.23, p = 0.253) | 1.20 (0.02 to 60.95, p = 0.930) | 1.03 (0.48 to 2.20, p = 0.941) |
| **Antidepressants** | 0.44 (0.11 to 1.84, p = 0.263) | -               | 0.58 (0.01 to 35.52, p = 0.797) | 0.59 (0.15 to 2.32, p = 0.455) | 0.53 (0.01 to 33.12, p = 0.762) | 0.45 (0.10 to 1.99, p = 0.297) |
| **Supplements**     | 0.76 (0.02 to 38.09, p = 0.890) | 1.72 (0.03 to 104.58, p = 0.797) | -           | 1.02 (0.02 to 49.90, p = 0.992) | 0.90 (0.00 to 223.63, p = 0.972) | 0.78 (0.02 to 39.65, p = 0.902) |
| **CBT**             | 0.74 (0.45 to 1.23, p = 0.253) | 1.68 (0.43 to 6.55, p = 0.455) | 0.98 (0.02 to 47.94, p = 0.992) | -               | 0.89 (0.02 to 44.70, p = 0.952) | 0.76 (0.41 to 1.45, p = 0.411) |
| **Tele-intervention** | 0.84 (0.02 to 43.38, p = 0.930) | 1.90 (0.03 to 119.10, p = 0.762) | 1.11 (0.00 to 273.14, p = 0.971) | 1.13 (0.02 to 56.83, p = 0.952) | -               | 0.86 (0.02 to 45.15, p = 0.942) |
| **Combination**     | 0.97 (0.45 to 2.08, p = 0.941) | 2.20 (0.50 to 9.58, p = 0.297) | 1.28 (0.03 to 64.72, p = 0.902) | 1.31 (0.69 to 2.46, p = 0.411) | 1.16 (0.02 to 60.34, p = 0.942) | -               |

Values given in RR (95%CI); CBT, cognitive based therapy; RR, Risk Ratio.

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Fig 4. Effectiveness of interventions based on cost-effectiveness, reduction in depression and scalability.

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provide symptomatic relief but do not address the root cause of post-ACS depression. They also require prolonged usage to prevent relapse, which is not without its adverse effects [72]. Moreover, most anti-depressants are associated with prolonged QT, which can predispose patients to arrhythmic events, which can worsen their outcomes post-ACS. This may place additional burden on the healthcare system with closer surveillance of its associated adverse effects, that may lead to further investigations and treatment. Although SSRIs are the first line treatment for depression [73], they are cytochrome P450 inhibitors which can potentially alter the pharmacokinetics of statins commonly prescribed after ACS [74]. Additionally, up to 60% of ACS patients are elderly who are commonly subjected to polypharmacy due to the presence of multiple comorbidities [75,76].

In this network analysis, reduction in depression score and prognostic outcomes associated with tele-intervention was not statistically different from those of antidepressants, CBT or psychosocial therapy. Tele-intervention has been widely used in the management of chronic conditions other than post-ACS depression with promising results and these include stroke [77], chronic obstructive pulmonary disease [78]. The role of tele-intervention encompasses monitoring for symptoms and quality of life, as well as providing timely treatment remotely in patients afflicted with coronary artery disease [79]. Tele-intervention has, in recent times, been widely implemented during the present SARS-CoV-2 pandemic that limits accessibility to consultation and treatment with encouraging outcomes for both patients with mental health conditions [80] or ACS [81–83]. Additionally, tele-intervention provide a wider outreach to rural societies that can often be neglected by healthcare systems [84]. Alternative treatments such as electroconvulsive therapy is a rapidly evolving treatment modality for depression which has proven to be highly effective [85]. However, more studies have to be conducted on its safety and efficacy in post-ACS patients [86].

Despite reduction in depression scores, current analysis did not find any interventions that significantly reduce overall mortality, cardiac death, or MI. In a meta-analysis of 6367 patients, van Melle et al found that suffering from depression after ACS is associated with 2 to 2.5 times increased risk of death and MI [9]. However, beyond the effects on clinical outcomes, treating depression can result in an improvement in quality of life. Improving the dignity of patients has since been a key metric of the healthcare system performance. Additionally, while the treatment of depression may not directly affect clinical outcomes, patients with depression are often less adherent to treatment which, in turn, can affect the adherence of medications used after ACS treatment, leading to an indirect adverse impact on clinical outcomes [10,11,87].

**Limitations**

The present analysis represents the largest network analysis of randomized controlled trials for the treatment of depression after ACS. However, there are a few limitations. The studies included in current analysis were predominantly conducted in the West with approximately 10% of the studies conducted in the East, and it remains to be seen if the results are transferable. Moreover, the analysis of clinical outcomes was not adjusted for established other cardiac prognostic factors (such as left ventricular ejection fraction, kidney impairment etc) as the data were not available. Furthermore, we were unable to control for the varied scales used to measure depression scores, due to insufficient included articles examining each outcome, which greatly affected the impression of the severity of depression of the patients examined and the accuracy of the change in their scores. To help reduce the effect of the latter on our analysis, we opted to use SMD, which helps reduce the variability in the measurement different scores. However, some caution should be done in interpreting our results on the improvement of depression scores as it would not completely remove all differences and biases between the
various depression scales used in the included papers. Additionally, all of our analyses derived from the network meta-analyses were indirect comparisons, and there was a lack of direct head-to-head comparisons between the six different forms of treatment. All of the included studies compared their intervention to usual care, which may have added additional biases and imprecision to our study. Future head-to-head studies comparing the different interventions should be considered, which can improve future research and aid future treatment decisions. Next, there was large variations in the duration of follow-up times between each study, and thus some long-term outcomes, such as cardiac mortality and MI, may not be truly reflective of the clinical outcome. Additionally, we were unable to incorporate a cost-effective analysis of various treatment modalities used in the studies included in this analysis.

Conclusions

This network meta-analysis found that psychological interventions, including psychosocial therapy, antidepressants, CBT, tele-intervention and/or combination therapy, have an important role in alleviating symptoms of depression in patients who have suffered from ACS. No significant difference in treatment effect of the various psychological treatment modalities on depression. Future longer duration studies on psychological interventions, and head-to-head studies assessing the clinical outcomes and adherence to ACS-specific interventions will be needed, which can help to improve the precision of the future analyses on this important topic.

Supporting information

S1 Table. Full search strategy.
(DOCX)

S2 Table. Cochrane risk-of-bias 2 tool for included articles.
(DOCX)

S3 Table. Summary of included articles.
(DOCX)

S4 Table. Summary of network analysis for cardiac mortality.
(DOCX)

S5 Table. Summary of network analysis for myocardial infarction.
(DOCX)

S6 Table. PRISMA checklist of items to include when reporting a systematic review involving a network meta-analysis.
(DOCX)

S1 Appendix. Funnel plots.
(DOCX)

S2 Appendix. Summary of direct and indirect evidence for the various network meta-analysis outcomes.
(DOCX)

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References

1. Singh A, Museedi AS, Grossman SA. Acute Coronary Syndrome. StatPearls. 2021.
2. Dessotte CA, Silva FS, Boelea F, Rossi LA, Dantas RA. Presence of depressive symptoms in patients with a first episode of acute coronary syndrome. Rev Lat Am Enfermagem. 2013; 21(1):325–31. Epub 2013/04/03. https://doi.org/10.1590/s0104-11692013000100006 PMID: 23546315.
3. Perez GH, Nicoleau JC, Romano BW, Laranjeira R. Depression and Acute Coronary Syndromes: gender-related differences. Arq Bras Cardiol. 2005; 85(5):319–26. Epub 2005/12/17. https://doi.org/10.1590/s0066-782x2005001800004 PMID: 16358147.
4. Go AS, Mozaffarian D, Roger VL, Benjamin EJ, Berry JD, Blaha MJ, et al. Heart disease and stroke statistics—2014 update: a report from the American Heart Association. Circulation. 2014; 129(3):e28–e292. Epub 2013/12/20. https://doi.org/10.1161/01.cir.0000441139.02102.80 PMID: 24352519; PubMed Central PMCID: PMC408159.
5. Penninx BW. Depression and cardiovascular disease: Epidemiological evidence on their linking mechanisms. Neurosci Biobehav Rev. 2017; 74(Pt B):277–86. Epub 2016/07/28. https://doi.org/10.1016/j.neubiorev.2016.07.003 PMID: 27461915.
6. Vaccarino V, Badimon L, Bremner JD, Cenko E, Cubedo J, Dorobantu M, et al. Depression and coronary heart disease: 2018 position paper of the ESC working group on coronary pathophysiology and microcirculation. European heart journal. 2020; 41(17):1687–96. https://doi.org/10.1093/eurheartj/ehy913 PMID: 30698764.
7. Nicholson A, Kuper H, Hemingway H. Depression as an aetiologic and prognostic factor in coronary heart disease: a meta-analysis of 6362 events among 146 538 participants in 54 observational studies. Eur Heart J. 2006; 27(23):2763–74. Epub 2006/11/04. https://doi.org/10.1093/eurheartj/ehl338 PMID: 17082208.
8. Smolderen KG, Buchanan DM, Gosch K, Whooley M, Chan PS, Vaccarino V, et al. Depression Treatment and 1-Year Mortality After Acute Myocardial Infarction. Circulation. 2017; 135(18):1681–9. https://doi.org/10.1161/CIRCULATIONAHA.116.025140 PMID: 28209727.
9. van Melle JP, de Jonge P, Spijkerman TA, Tijsse n JGP, Ormel J, van Veldhuisen DJ, et al. Prognostic Association of Depression Following Myocardial Infarction With Mortality and Cardiovascular Events: A Meta-analysis. Psychosomatic Medicine. 2004; 66(6). https://doi.org/10.1097/01.psy.0000146294.82810.9c PMID: 15564344

10. Carney RM, Freedland KE. Depression and coronary heart disease. Nature Reviews Cardiology. 2017; 14(3):145–55. https://doi.org/10.1038/nrcardio.2016.181 PMID: 27853162

11. Myers V, Gerber Y, Benyamini Y, Goldbour t U, Drory Y. Post-myocardial infarction depression: increased hospital admissions and reduced adoption of secondary prevention measures—a longitudinal study. J Psychosom Res. 2012; 72(1):5–10. Epub 2011/12/28. https://doi.org/10.1016/j.jpsychores.2011.09.009 PMID: 22200515.

12. Frost JL, Rich RL Jr., Robbins CW, Stevermer JJ, Chow RT, Leon KK, et al. Depression Following Acute Coronary Syndrome Events: Screening and Treatment Guidelines from the AAFP. Am Fam Physician. 2019; 99(12):Online. Epub 2019/06/14. PMID: 31194478.

13. Lichtman JH, Bigger JT, Blumenthal JA, Frasure-Smith N, Kaufman n PG, Lespé rance F, et al. Depres sion and Coronary Heart Disease: A Science Advisory From the American Heart Association Prevention Committee of the Council on Cardiovascular Nursing, Council on Clinical Cardiology, Council on Epide miology and Prevention, and Interdisciplinary Council on Quality of Care and Outcomes Research. Circulation. 2008; 118:1768–75.

14. Dowlati Y, Herrmann N, Swardfager WL, Reim EK, Lancto ˆ t KL. Efficacy and Tolerability of Antidepressants for Treatment of Depression in Coronary Artery Disease: A Meta-Analysis. The Canadian Journal of Psychiatry. 2010; 55(2):91–9. https://doi.org/10.1177/070674371005500205 PMID: 20181304

15. Fernandes N, Prada L, Rosa MM, Ferreira JJ, Costa J, Pinto FJ, et al. The impact of SSRI s on mortality and cardiovascular events in patients with coronary artery disease and depression: systematic review and meta-analysis. Clinical Research in Cardiology. 2021; 110(2):183–93. https://doi.org/10.1007/s00392-020-01697-8 PMID: 32617669

16. Roest AM, Carney RM, Freedland KE, Martens EJ, Denollet J, de Jonge P. Changes in cognitive versus somatic symptoms of depression and event-free survival following acute myocardial infarction in the Enhancing Recovery In Coronary Heart Disease (ENRICHD ) study. J Affect Disord. 2013; 149(1– 3):335–41. Epub 2013/03/16. https://doi.org/10.1016/j.jad.2013.02.008 PMID: 23489396; PubMed Central PMCID: PMC3672326.

17. Renn BN, Areán PA. Psychosocial Treatment Options for Major Depressive Disorder in Older Adults. Curr Treat Options Psychiatry. 2017; 4(1):1–12. Epub 2017/09/22. https://doi.org/10.1007/s40501-017-0100-6 PMID: 28932652; PubMed Central PMCID: PMC5602587.

18. Bloch MH, Hanestad J. Omega-3 fatty acids for the treatment of depression: systematic review and meta-analysis. Molecular Psychiatry. 2012; 17(12):1272–82. https://doi.org/10.1038/mp.2011.100 PMID: 21931319

19. Grosso G, Micek A, Marventano S, Castellano S, Mistretta A, Pajak A, et al. Dietary n-3 PUFA, fish consumption and depression: A systematic review and meta-analysis of observational studies. Journal of Affective Disorders. 2016; 205:269–81. https://doi.org/10.1016/j.jad.2016.08.011 PMID: 27544316

20. Huang R, Wang K, Hu J. Effect of Probiotics on Depression: A Systematic Review and Meta-Analysis of Randomized Controlled Trials. Nutrients. 2016; 8(8). https://doi.org/10.3390/nu8080483 PMID: 27509521

21. O’Neil A, Taylor B, Hare DL, Sanderson K, Cyril S, Venugopal K, et al. Long-term efficacy of a tele-health intervention for acute coronary syndrome patients with depression: 12-month results of the MoodCare randomized controlled trial. Eur J Prev Cardiol. 2015; 22(9):1111–20. Epub 2014/08/28. https://doi.org/10.1177/2047487314547655 PMID: 25159700.

22. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Melpolder DJ, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ. 2021; 372:n71. https://doi.org/10.1136/bmj.n71 PMID: 33782057

23. Acute Coronary Syndromes: American College of Cardiology; [cited 2021 23 September]. Available from: https://www.acc.org/Education-and-Meetings/Products-and-Resources/Guideline-Education/Acute-Coronary-Syndromes.

24. O’Neil A, Taylor B, Hare DL, Sanderson K, Cyril S, Venugopal K, et al. Long-term efficacy of a tele-health intervention for acute coronary syndrome patients with depression: 12-month results of the MoodCare randomized controlled trial. European journal of preventive cardiology. 2015; 22(9):1111– 20. https://doi.org/10.1177/2047487314547655 PMID: 25159700

25. Giltay EJ, Geleijnsje JM, Kromhout D. Effects of n-3 fatty acids on depressive symptoms and dispositional optimism after myocardial infarction. American Journal of Clinical Nutrition. 2011; 94(6):1442–50. https://doi.org/10.3945/ajcn.111.018259 PMID: 22030221
44. Stern MJ, Gorman PA, Kaslow L. The group counseling v exercise therapy study. A controlled intervention with subjects following myocardial infarction. Archives of internal medicine. 1983; 143(9):1719–25. PMID: 6615094

45. Warber SL, Ingerman S, Moura VL, Wunder J, Northrop A, Gillespie BW, et al. Healing the heart: A randomized pilot study of a spiritual retreat for depression in acute coronary syndrome patients. Explore: The Journal of Science and Healing. 2011; 7(4):222–33. https://doi.org/10.1016/j.explore.2011.04.002 PMID: 21724155

46. O’Neil A, Hawkes AL, Atherton JJ, Patrao TA, Sanderson K, Wolfe R, et al. Telephone-delivered health coaching improves anxiety outcomes after myocardial infarction: The ‘ProActive Heart’ trial. European Journal of Preventive Cardiology. 2014; 21(1):30–8. https://doi.org/10.1177/2047487312460515 PMID: 22956633

47. Turner A, Murphy BM, Higgins RO, Elliott PC, Le Grande MR, Goble AJ, et al. An integrated secondary prevention group programme reduces depression in cardiac patients. European Journal of Preventive Cardiology. 2014; 21(2):153–62. https://doi.org/10.1177/2047487312467747 PMID: 23147275

48. Ghiasi F, Jalali R, Paveh B, Hashemian AH, Eyi S. Investigating the impact of cognitive-behavioral therapy on the mental health status of patients suffering from myocardial infarction. Annals of Tropical Medicine and Public Health. 2018;3(Special Issue):S15.

49. Moludi J, Alizadeh M, Mohammadzad MHS, Davari M. The Effect of Probiotic Supplementation on Depressive Symptoms and Quality of Life in Patients after Myocardial Infarction: Results of a Preliminary Double-Blind Clinical Trial. Psychosomatic Medicine. 2019; 81(9):770–7. https://doi.org/10.1097/PSY.0000000000000748 PMID: 31592939

50. Bagherian Sararoudi R, Motmaen M, Maracy MR, Pishghadam E, Kheirabadi GR. Efficacy of illness perception focused intervention on quality of life, anxiety, and depression in patients with myocardial infarction. Journal of Research in Medical Sciences. 2016; 21(9).

51. Honig A, Kuyper AMG, Schene AH, Van Malle JP, De Jonge P, Tulner DM, et al. Treatment of post-myocardial infarction depressive disorder: A randomized, placebo-controlled trial with mirtazapine. Psychosomatic Medicine. 2007; 69(7):606–13. https://doi.org/10.1097/PSY.0b013e31814b260d PMID: 17846258

52. Jarstad HT, Minneboo M, Helmes HJM, Fagel ND, Scholte op Reimer WJ, Tijssen JGP, et al. Effects of a nurse-coordinated prevention programme on health-related quality of life and depression in patients with an acute coronary syndrome: Results from the RESPONSE randomised controlled trial. BMC Cardiovascular Disorders. 2016; 16(1). https://doi.org/10.1186/s12872-016-0321-4 PMID: 27391321

53. Strik JJMH, Honig A, Lousberg R, Lousberg AHP, Cheriex EC, Tuynman-Qua HG, et al. Efficacy and safety of fluoxetine in the treatment of patients with major depression after first myocardial infarction: Findings from a double-blind, placebo-controlled trial. Psychosomatic Medicine. 2000; 62(6):783–9. https://doi.org/10.1097/00006842-200011000-00007 PMID: 11138997

54. Frasure-Smith N, Lespérance F, Prince RH, Verrier P, Garber RA, Juneau M, et al. Randomised trial of home-based psychosocial nursing intervention for patients recovering from myocardial infarction. Lancet. 1997; 350(9076):473–9. https://doi.org/10.1016/S0140-6736(97)02142-9 PMID: 9274583

55. Raffanelli C, Gostoli S, Buzzichelli S, Guidi J, Sirri L, Gallo P, et al. Sequential Combination of Cognitive-Behavioral Treatment and Well-Being Therapy in Depressed Patients with Acute Coronary Syndromes: A Randomized Controlled Trial (TREATED-ACS Study). Psychotherapy and Psychosomatics. 2020; 89 (6):345–56. https://doi.org/10.1159/000501006 PMID: 32791501

56. Roncella A, Pristipino C, Cianfranca C, Scorza S, Pasceri V, Pelliccia F, et al. One-year results of the randomized, controlled, short-term psychotherapy in acute myocardial infarction (STEP-IN-AMI) trial. International Journal of Cardiology. 2013; 170(2):132–9. https://doi.org/10.1016/j.ijcard.2013.08.094 PMID: 24239154

57. Liang H, Liu L, Hu H. The effects of mindfulness-based stress reduction on the mental states, sleep quality, and medication compliance of patients with acute myocardial infarction after percutaneous coronary intervention. International Journal of Clinical and Experimental Medicine. 2019; 12(12):13514–23.

58. Mohapatra PK, Kar N, Kar GC, Behera M. Effectiveness of sertraline in treatment of depression in a consecutive sample of patients with acute myocardial infarction: Six month prospective study on outcome. Clinical Practice and Epidemiology in Mental Health. 2005;1. https://doi.org/10.1186/1745-0179-1-26 PMID: 16336682

59. Haberka M, Mizia-Stec K, Mizia M, Giesczczyk K, Chmiel A, Slitnik-Warchulska K, et al. Effects of n-3 polyunsaturated fatty acids on depressive symptoms, anxiety and emotional state in patients with acute myocardial infarction. Pharmacological Reports. 2013; 65(1):59–68. https://doi.org/10.1016/s1734-1140(13)70964-2 PubMed Central PMCID: PMCSolvay(Germany). PMID: 23563024
60. Fernandes AC, McIntyre T, Coelho R, Prata J, Maciel MJ. Brief psychological intervention in phase I of cardiac rehabilitation after acute coronary syndrome. Revista Portuguesa de Cardiologia. 2017; 36(9):641–9. https://doi.org/10.1016/j.repc.2017.01.005 PMID: 28882655

61. Kim SW, Bae KY, Kim JM, Shin IS, Hong YJ, Ahn Y, et al. The use of statins for the treatment of depression in patients with acute coronary syndrome. Translational Psychiatry. 2015; 5(8). https://doi.org/10.1038/tp.2015.116 PMID: 26285130

62. Humphries SM, Waltjer J, Norlund F, Wallin E, Burell G, Von Essen L, et al. Internet-based cognitive behavioral therapy for patients reporting symptoms of anxiety and depression after myocardial infarction: U-CARE heart randomized controlled trial twelve-month follow-up. Journal of Medical Internet Research. 2021; 23(5). https://doi.org/10.2196/25465 PMID: 34028358

63. Lichtman JH, Froelicher ES, Blumenthal JA, Carney RM, Doering LV, Frasure-Smith N, et al. Depression as a risk factor for poor prognosis among patients with acute coronary syndrome: systematic review and recommendations: a scientific statement from the American Heart Association. Circulation. 2014; 129(12):1350–69. Epub 2014/02/26. https://doi.org/10.1161/CIR.000000000000019 PMID: 24566200.

64. Vaccarino V, Badimon L, Bremner JD, Cenko E, Cubedo J, Dorobantu M, et al. Depression and coronary heart disease: 2018 position paper of the ESC working group on coronary pathophysiology and microcirculation. European Heart Journal. 2020; 41(17):1687–96. https://doi.org/10.1093/eurheartj/ehy913 PMID: 30698764.

65. Depression and CAD: American College of Cardiology; 2018 [cited 2021 20 September]. Available from: https://www.acc.org/latest-in-cardiology/articles/2018/09/28/08/depression-and-cad.

66. Yu H, Ma Y, Lei R, Xu D. A meta-analysis of clinical efficacy and quality of life of cognitive-behavioral therapy in acute coronary syndrome patients with anxiety and depression. Ann Palliat Med. 2020; 9(4):1886–95. Epub 2020/06/25. https://doi.org/10.21037/apm-20-974 PMID: 32576008.

67. Fernandes N, Prada L, Rosa MM, Ferreira JJ, Costa J, Pinto FJ, et al. The impact of SSRI s on mortality and cardiovascular events in patients with coronary artery disease and depression: systematic review and meta-analysis. Clin Res Cardiol. 2021; 110(2):183–93. Epub 2020/07/04. https://doi.org/10.1007/s00392-020-01697-8 PMID: 32617669.

68. Mazza M, Lotrionte M, Blondi-Zoccai G, Abbate A, Sheikh I, Romagnoli E. Selective serotonin reuptake inhibitors provide significant lower re-hospitalization rates in patients recovering from acute coronary syndromes: evidence from a meta-analysis. J Psychopharmacol. 2010; 24(12):1785–92. Epub 2009/12/08. https://doi.org/10.1177/0269881109348176 PMID: 19965939.

69. Dickerson JF, Lynch FL, Leo MC, DeBar LL, Pearson J, Clarke GN. Cost-effectiveness of Cognitive Behavioral Therapy for Depressed Youth Declining Antidepressants. Pediatrics. 2018; 141(2): e20171969. https://doi.org/10.1542/peds.2017-1969 PMID: 29351965.

70. Patel V, Flisher AJ, Hetrick S, McGorry P. Mental health of young people: a global public-health challenge. Lancet. 2007; 369(9569):1302–13. Epub 2007/09/07. https://doi.org/10.1016/S0140-6736(07)60368-7 PMID: 17434406.

71. Acharya B, Hirachan S, Mandel JS, van Dyke C. The Mental Health Education Gap among Primary Care Providers in Rural Nepal. Acad Psychiatry. 2016; 40(4):667–71. Epub 2016/06/05. https://doi.org/10.1007/s40596-016-0572-5 PMID: 27259491; PubMed Central PMCID: PMC4938769.

72. Batelaan NM, Bosman RC, Muntingh A, Scholten WD, Huijbregts KM, van Balkom A. Risk of relapse after antidepressant discontinuation in anxiety disorders, obsessive-compulsive disorder, and post-traumatic stress disorder: systematic review and meta-analysis of relapse prevention trials. Br J Psychiatry. 2017; 358: j3927. Epub 2017/09/15. https://doi.org/10.1136/bmj.j3927 PMID: 28903922; PubMed Central PMCID: PMC5596392 www.icmje.org/coi_disclosur e.pdf (available on request from the corresponding author) 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; no other relationships or activities that could appear to have influenced the submitted work.

73. Nieuwsma JA, Williams JW Jr, Namdari N, Washam JB, Raizt G, Blumenthal JA, et al. Diagnostic Accuracy of Screening Tests and Treatment for Post–Acute Coronary Syndrome Depression. Annals of Internal Medicine. 2017; 167(10):725–35. https://doi.org/10.7326/M17-1811 PMID: 29132152

74. Andrade C. Selective serotonin reuptake inhibitor drug interactions in patients receiving statins. J Clin Psychiatry. 2014; 75(2):e95–9. Epub 2014/03/08. https://doi.org/10.4088/JCP.1308941 PMID: 24602259.

75. Dai X, Busby-Whitehead J, Alexander KP. Acute coronary syndrome in the older adults. J Geriatr Cardiol. 2016; 13(2):101–8. Epub 2016/05/12. https://doi.org/10.11909/j.issn.1671-5411.2016.02.012 PMID: 27168733; PubMed Central PMCID: PMC4854946.
76. Disdier Moulder MPA, Hendricks AK, Ou NN. Towards appropriate polypharmacy in older cardiovascular patients: How many medications do I have to take? Clin Cardiol. 2020; 43(2):137–44. Epub 2019/12/12. https://doi.org/10.1002/clc.23304 PMID: 31825133; PubMed Central PMCID: PMC7021656.

77. Sarfo FS, Ulasavets U, Opare-Sem OK, Ovbiagele B. Tele-Rehabilitation after Stroke: An Updated Systematic Review of the Literature. J Stroke Cerebrovasc Dis. 2018; 27(9):2306–18. Epub 2018/06/09. https://doi.org/10.1016/j.jstrokecerebrovasdis.2018.05.013 PMID: 29880211; PubMed Central PMCID: PMC6087671.

78. Hong Y, Lee SH. Effectiveness of tele-monitoring by patient severity and intervention type in chronic obstructive pulmonary disease patients: A systematic review and meta-analysis. Int J Nurs Stud. 2019; 92:1–15. Epub 2019/01/29. https://doi.org/10.1016/j.ijnurstu.2018.12.006 PMID: 30690162.

79. Oksman E, Linna M, Höhrhammer I, Lamminrakenen J, Talja M. Cost-effectiveness analysis for a tele-based health coaching program for chronic disease in primary care. BMC Health Serv Res. 2017; 17(1):138. Epub 2017/02/21. https://doi.org/10.1186/s12913-017-2088-4 PMID: 28202032; PubMed Central PMCID: PMC5312514.

80. Yue JL, Yan W, Sun YK, Yuan K, Su SZ, Han Y, et al. Mental health services for infectious disease outbreaks including COVID-19: a rapid systematic review. Psychol Med. 2020; 50(15):2498–513. Epub 2020/11/06. https://doi.org/10.1017/S0033291720003888 PMID: 33148347; PubMed Central PMCID: PMC7642960.

81. Chew NWS, Ow ZGW, Teo VXY, Heng RRY, Han Ng C, Lee CH, et al. The Global Effect of the COVID-19 Pandemic on STEMI Care: A Systematic Review and Meta-analysis. Can J Cardiol. 2021; 37(9):1450–9. Epub 2021/04/14. https://doi.org/10.1016/j.cjca.2021.04.003 PMID: 33848599; PubMed Central PMCID: PMC8056787.

82. Chew NW, Sia CH, Wee HL, Benedict LJ, Rastogi S, Kojojiyo P, et al. Impact of the COVID-19 Pandemic on Door-to-Balloon Time for Primary Percutaneous Coronary Intervention- Results From the Singapore Western STEMI Network. Circ J. 2021; 85(2):139–49. Epub 2020/11/10. https://doi.org/10.1253/circj.CJ-20-0800 PMID: 33162491.

83. Phua K, Chew NWS, Sim V, Zhang AA, Rastogi S, Kojojiyo P, et al. One-year outcomes of patients with ST-segment elevation myocardial infarction during the COVID-19 pandemic. J Thromb Thrombolysis. 2021;1–11. Epub 2021/08/28. https://doi.org/10.1007/s11239-021-02557-6 PMID: 34448103; PubMed Central PMCID: PMC8390088.

84. Weightman M. Digital psychotherapy as an effective and timely treatment option for depression and anxiety disorders: Implications for rural and remote practice. J Int Med Res. 2020; 48(6):30060520928668. Epub 2020/06/13. https://doi.org/10.1177/0300060520928668 PMID: 32527170; PubMed Central PMCID: PMC7294488.

85. Herrima AP, Glass OM, Shafi H, McDonald WM. Electroconvulsive Therapy in Depression: Current Practice and Future Direction. The Psychiatric clinics of North America. 2018; 41(3):341–53. https://doi.org/10.1016/j.psc.2018.04.001 PMID: 30098649

86. Pourafkari N, Pourafkari L, Nader ND. Electroconvulsive therapy for depression following acute coronary syndromes: a concern for the anesthesiologist. J Clin Anesth. 2016; 31:223–8. Epub 2016/05/18. https://doi.org/10.1016/j.jclinane.2016.01.045 PMID: 27185716.

87. Grenard JL, Munjas BA, Adams JL, Suttrop M, Maglione M, McGlynn EA, et al. Depression and medication adherence in the treatment of chronic diseases in the United States: a meta-analysis. J Gen Intern Med. 2011; 26(10):1175–82. Epub 2011/05/03. https://doi.org/10.1007/s11606-011-1704-y PMID: 21533823; PubMed Central PMCID: PMC3181287.