Effect of periodontal therapy on the systemic inflammation and metabolic markers in patients undergoing hemodialysis or/and peritoneal dialysis: a systematic review and meta-analysis

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Abstract

Background: This systematic review aimed to investigate whether periodontal treatment can reduce the systemic inflammatory levels and improve the metabolic levels in patients undergoing hemodialysis (HD) or/and peritoneal dialysis (PD). Methods: Electronic databases (PubMed, EMBASE, CENTRAL, NCKI, and WFPD) were searched up to July 2019. The risk of bias within studies was assessed through the Cochrane Collaboration' s risk assessment tool. The systemic inflammatory and metabolic measures were the highly sensitive C-reactive protein (hs-CRP), interleukin 6 (IL-6), tumor necrosis factor-α (TNF-a), the albumin (Alb), and lipid metabolic levels. Meta-analyses (MAs) were performed to calculate the overall effect size where appropriate. Results: Five studies were eligible for this systematic review. The result of four studies revealed a significant difference in the CRP level after periodontal treatment in patients receiving HD or/and PD. Two studies reported the IL-6 and the Alb level after periodontal treatment but revealed no significant difference. No MAs could be performed on the TNF- a level and the lipid metabolic markers. Conclusions: Periodontal treatment may moderately reduce the serum of CRP levels in HD or/and PD patients. For the TNF-a, IL-6, Alb levels and lipid metabolic markers, no sufficient evidence supports the difference after periodontal treatment. Therefore, larger scales and high-quality randomized-controlled trials (RCTs) are required to assess the effect of periodontal treatment on systemic inflammatory and metabolic parameters in HD or/and PD patients.

Background

End-stage renal disease (ESRD) is a disease in which the glomerular filtration rate continues to decline, leading to kidney failure [1-3]. ESRD is an important public health problem in the world with high morbidity and mortality [4]. The life-saving treatment for ESRD includes dialysis treatment and kidney transplantation, and the dialysis treatment including hemodialysis (HD) and peritoneal dialysis (PD) is the most common treatment [4, 5]. Because of the dysfunction of metabolism and immune system, patients undergoing dialysis are more susceptible to suffer from advanced level of highly sensitive C-reactive protein (hs-CRP), interleukin 6 (IL-6) and low level of serum albumin, which are contributed to an increased risk of cardiovascular disease (CVD), atherosclerosis, malnutrition and chronic periodontitis (CP) [6-8]. Accordingly, ESRD has been suggested as one of the inflammatory risk factors of periodontal disease.

CP is a chronic infective disease mainly caused by dental plaque biofilm, characterized by the destruction of the soft and hard tissues surrounding the teeth, If not treated in time, the teeth will eventually lose [9]. It has also been suggested that the production of local proinflammatory and inflammatory factors caused by pathogenic bacteria in dental plaque is related to the host's systemic inflammatory and immunological response [10]. CP has been considered as a potential source for increased levels of systemic inflammatory burden in dialysis patients [11, 12]. In turn, the elevated risk or severity of periodontal disease in dialysis patients may be associated with high levels of serum inflammatory biomarkers [13-15]. Thus, the control of systemic inflammation in dialysis patients may reduce the CVD rate and the pathological progress periodontal diseases [10, 16].

Periodontal therapy (PT) is a standard therapeutic modality to control infection and inflammation of periodontal diseases. PT is a method of teeth debridement that is feasible and easily been performed by periodontal practitioners, including professional oral hygiene instructions (OHI), full-mouth scaling and root planing to remove supra/subgingival biofilm and calculus (SRP). Recently, many scholars have devoted themselves to investigating and studying the effect of PT on systemic inflammation and metabolic status of dialysis patients, but their conclusions are contradictory. Some investigators have shown that PT can decrease the levels of the systemic inflammatory burden and improve the metabolic status of dialysis patients [17-19]. However, some investigators have noted that PT did not significantly reduce systemic inflammation and improve the nutrition markers in ESRD patients [20]. The inconsistent evidence hinders the clinical promotion of periodontal therapy and is disadvantageous for the control of elevated systemic inflammation in dialysis patients.

Therefore, it is imperative to conduct a systematic review and meta-analysis to evaluate whether PT for the treatment of CP can influence systemic inflammatory and metabolic results in ESRD patients undergoing HD and PD. We perform this study to assess the effects of PT on the systemic inflammatory, nutritional and lipid metabolic markers in ESRD patients receiving HD or/and PD.

Methods

We conducted and reported the results following the Cochrane Handbook and the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement [21]. We did not register it at PROSPERO.

Focused question

Do periodontal treatment influence systemic inflammation and metabolic markers in hemodialysis or/and peritoneal dialysis patients with chronic periodontitis?

Search strategy

A comprehensive electronic search of PubMed, EMBASE, the Cochrane Library (CENTRAL), China National Knowledge Infrastructure (CNKI) and Chinese Medicine Premier's Wanfang database (WFPD) was searched from their inception to June 2019 for eligible articles. We (Hui Yue and Yiting Xiao) used the following search terms: “end-stage renal disease”, “renal insufficiency”, “peritoneal dialysis”, “hemodialysis”, “renal dialysis”, “periodontal treatment”, “periodontal therapy”, “dental debridement” and “periodontal debridement”. We also reviewed the reference lists of identified studies and pertinent reviews for additional citations. Databases were searched to include papers published in English and Chinese. Detailed search process is illustrated in the supplementary file S1 and S2.

Eligibility criteria

Two reviewers (Hui Yue and Xinxin Xu) independently evaluated the eligible studies that met the following criteria: (1) study design: randomized controlled clinical trial (RCT); (2) the end-stage renal

disease (ESRD) patients diagnosed with chronic periodontitis (CP); further inclusion were: the patients undergoing peritoneal dialysis (PD) or/and hemodialysis (HD); without other sources of inflammation such as pulpal infections and active caries; no periodontal treatment in past 6 months; (3) intervention group of periodontal treatment (PT) including professional oral hygiene instructions (OHI), full-mouth scaling and root planning (SRP, including ultrasonic and/or hand supra/subgingival biofilm and calculus removal), SRP plus local or systemic antiseptic therapy without surgical flap procedures; (4) control group of age and gender-matched no periodontal treatment, delayed treatment or only including OHI; (5) outcome of systemic inflammatory, nutritional and lipid metabolic markers measures following PT; and follow-up times ≥ 4weeks.

The exclusion criteria were reviews, studies without a comparison group, case reports, and conference abstracts.

Screening and data extraction

Two reviewers (Hui Yue and Xinxin Xu) independently performed the study screening process. First, we excluded duplicated publications and scrutinized titles and abstracts to select literature that may meet the inclusion criteria. Then, we read carefully the full text to further include eligible studies. We implemented data extraction from included studies, and then another reviewer (Xiaozhi Li) checked the results for accuracy. The following information was extracted: the name of first author, publication year, sample size of participants, study methods (such as study design, follow-up duration), intervention, conclusions, clinical and biochemical measures including serum inflammation markers: hs-CRP, IL-6, TNF-a, nutrition markers (albumin, Alb) and lipid metabolic markers (total cholesterol, TC; triglycerides, TG; high-density lipoprotein cholesterol, HDL-C; and low-density lipoprotein cholesterol, LDL-C). Any inconsistent results regarding the eligibility of studies and extraction of data occurred between the two reviewers was resolved by a conversation with a third reviewer (Xiaozhi Li).

Quality assessment

Two reviewers (Hui Yue, Bo Hu) independently performed the quality assessment of the selected studies via the Cochrane Handbook for Systematic Reviews of Interventions for assessing the risk of bias. The tool included six domains: random sequence generation; allocation concealment; blinding of participants and outcome assessors; incomplete outcome data; selective reporting; other biases. All six included issues were evaluated as low risk, high risk or unclear. Any divergence between the two investigators was resolved by discussion with a third reviewer (Qin Liu).

Data analysis

We (Hui Yue, Qin Liu) performed data analysis and pooled in statistical meta-analyses using Stata 15.0 software. In the meta-analysis, we calculated overall effect size (ES) estimates using the standardized mean difference (SMD) and the upper and lower limits of the 95 % confidence intervals (CI) to assess overall efficacy from all the eligible studies. The heterogeneity was assessed by Q statistic (P< 0.10

indicating significant heterogeneity) and *I* squared (I^2) statistic. An I^2 value of more than 50% represented high heterogeneity, thus the random effect model would be adopted. I^2 less than 50% representing low heterogeneity, fixed-effects models were used. Statistical significance was declared if the *p*-value was <0.05. Publication bias and sensitivity analyses would have been conducted if the included trials were at least 10 according to Higgins and Green [22].

Results

Study selection

In total, 308 articles were searched in the databases. After duplicates were removed, 135 articles were retained for the title and abstract identification. The full texts of 17 articles were read carefully and further assessed in strict accordance with the eligible criteria. Three RCTs of which were excluded because two of which did not receive dialysis treatment [23, 24] and one is still going on [25]. Eventually, five RCTs were included for systematic assessment. Screening of the reference lists did not found additional suitable articles in accordance with the inclusion. The process of study selection is displayed as a flow diagram in Figure 1.

Characteristics of the included studies

Table 1 shows details of the summarized characteristics of included studies. 5 included RCTs [18, 20, 26-28] were of parallel design. Fang [20], Li [28] and Ma [18] included patients undergoing HD, Zhang and colleagues [27] included patients undergoing PD, and Wehmeyer and colleagues [26] included patients undergoing HD and PD treatment. The HD treatment time established by Fang [20], Li [28] and Ma [18] was on average 4 h of HD 3 times a week. In the study by Zhang [27] and Wehmeyer [26], the HD or PD treatment time was not mentioned. Included patients in the study were followed-up for at least 1 month, with 2 studies' patients included both a 3-month and 6-month follow-up. Of the five studies included, four [18, 20, 27, 28] reported the hs-CRP levels, two [20, 26] reported the IL-6 and Alb levels, and one [20] reported serum TNF-*a* levels and lipid metabolic markers. The hs-CRP levels data are available in the 4 studies and were collected for the meta-analysis. Five studies provided data for approximately 353 subjects. However, in the study by Fang and colleagues [20], two patients were lost to 6-month follow-up owing to time conflicts in the intervention group; two patient was lost to 6-week and 3-month follow-up in the control group, respectively.

All studies described similar PT based on OHI and SRP without surgical procedures. One study combined SRP with local minocycline administered to all sites with PD >5 mm [26]. Patients in the studies conducted by Zhang [27], Li [28], Ma [18] and Wehmeyer [26] did not receive prophylaxis within follow up periods, in contrast, subjects in the studies by Fang were observed for supragingival prophylaxis at 3 months [20].

Risk of bias

Table 2 presents the methodological and quality of the trials included in the review. Because most of the included studies did not report random sequence generation, and none of the studies reported blinding of outcome assessment of practitioners. All considered studies were judged to exhibit a moderate-risk bias.

Qualitative synthesis

The descriptive synthesis of the included studies is displayed in Table 1. One of the included studies focused on TNF-a, and lipid metabolic levels [20]. The results of the level of TNF-a and lipid metabolic markers showed no significant difference at most points. The result of the level of HDL-C was significantly decreased at 6 weeks in patients after PT in the HD and/or PD patients.

Quantitative synthesis

Hs-CRP

No statistically significant differences were found between PT or delayed PT for hs-CRP in HD and/or PD patients at baseline. (SMD: -0.54; 95 % CI: -1.36 to 0.30; p = 0.21) (Fig. 2). Four studies [18, 20, 27, 28] reported the data of hs-CRP after non-surgical periodontal treatment for hemodialysis or/and peritoneal dialysis patients with chronic periodontitis. However, the results of this study showed that it was statistically decreased at less than or equal to 2 months, 3 months and 6 months after PT the level of serum hs-CRP in the HD and/or PD patients. (Fig. 3) The heterogeneity observed between the studies was high, so a random-effect model was used.

IL-6 and Alb

Two studies [20, 26] reported the data of the IL-6 and Alb levels after PT for hemodialysis or/and peritoneal dialysis patients with chronic periodontitis. This meta-analysis revealed that after PT of periodontitis the levels of IL-6 and Alb in the hemodialysis or/and peritoneal dialysis patients were not decreased at 3 months and 6 months (Fig. 4 and Fig. 5, respectively). Considering the heterogeneity between the studies was high, we selected a random effect model.

Discussion

There may be a bidirectional relationship between ESRD and chronic periodontitis. In ESRD patients receiving HD and/or PD are easier to suffer from the microvascular disease, atherosclerosis, systemic inflammation, malnutrition, and chronic periodontitis [12]. CP is a chronic immunoinflammatory disease which is caused by main gram-negative bacteria that destroys the supporting tissues of the teeth and, if left untreated, eventually results in tooth loss [29]. Local periodontal infections may lead to the systemic burden of inflammatory mediators and aggravate the existing metabolic, endocrine and immune disorders in patients receiving HD and/or PD. The presence of periodontitis is associated with high levels of hs-CRP and protein consumption [6, 30]. Thus, periodontitis may be a potential risk factor of systemic inflammation and malnutrition in ESRD patients [19]. PT is the basis of periodontal treatment and the feasible and easily accessible method to control infection of periodontal disease. Recently, the control of

systemic inflammation and nutritional status through PT in ESRD patients has aroused the interest of clinicians and researchers. However, current evidence showed that the results of the effects of PT on systemic inflammation and metabolic status in these affected patients were inconsistent. This inconsistency is not conducive to the clinical application of PT, the control of systematic inflammation and improvement of metabolism in patients receiving HD and/or PD. Hence, it is imperative to perform this systematic review to determine whether the effect of PT on reducing serum inflammation levels and improving metabolic status in dialysis patients with CP through published RCT evidence.

Relevant inflammatory and metabolic markers played a crucial role in the pathological process and diagnosis of dialysis patients [13, 31]. This systematic review described 3 serum inflammation markers: hs-CRP, IL-6, and/or TNF-α. Hs-CRP is an acute-phase protein produced only by the liver and is considered diagnostic and prognostic markers of inflammatory diseases. As we all know, hs-CRP has been considered to be independent predictors of death in dialysis patients [32]. Hs-CRP can promote the secretion of IL-6. IL-6 is a peptide medium synthesized by a variety of cell types, including T cells, fibroblasts, epithelial cells, and endothelial cells, which mainly work in the immune and inflammatory response [17]. The levels of IL-6 and hs-CRP in dialysis patients have been demonstrated to be higher than those in systemic healthy patients with periodontitis. Additionally, studies have shown that CP is associated with elevated serum hs-CR and IL-6 [33]. Researchers have focused on exploring whether a decline of serum inflammatory factors levels after PT in dialysis patients. On the bias of the existing evidence, we perform two separate meta-analyses for hs-CRP and IL – 6 through PT in ESRD patients with periodontitis. Besides, the inflammation was qualitatively evaluated by the TNF-*a* level. In our study, the included studies ranged from 4 weeks, 6weeks, 8 weeks, 3 months and 6 months evaluation periods for hs-CRP. The duration of the intervention of 4 studies varied from 4 weeks to 2 months, so we perform subgroup analysis by follow-up period in less than or equal to 2 months, at 3 months and 6 months. A subgroup analysis by follow-up time verified a significant reduction in the level of hS-CRP, suggesting a reduction in systemic inflammation after PT in dialysis patients with periodontitis. The level of IL-6 showed a trend towards a decrease following PT, however, the level of serum IL – 6 in the PT group had no statistically significant reduction than the control group. Although the results of these three markers revealed that the reducing levels of inflammation in dialysis patients, only the hs-CRP level was statistically significant. We think these different results may be due to the small size and a limited number of studies, meaning larger scale and more clinical intervention trials are required in the future.

To assess the metabolic markers more comprehensively in dialysis patients, we also evaluated nutrition (albumin, Alb) and lipid metabolic markers (TC, TG, HDL-C, LDL-C). Fang and colleagues showed that the PT achieved a greater increase in lipid metabolic markers than no treatment while no significant differences were found. Regarding Alb markers, two of the included studies compared the Alb parameter. One of the included studies evaluated Alb after 6 weeks, 3 months and 6 months, whereas the other one' s Alb changes had been reported after a 3-month and 6-month study period. Thus, further studies with longer follow-up are needed to elucidate the effects of the PT on serum Alb maker. So we perform subgroup analyses by follow-up periods while no significant differences were found. Wehmeyer and colleagues showed that the PT achieved a greater increase in Alb markers than no treatment while no

significant differences were found. Fang and colleagues found that the PT achieved a significant reduction in Alb. Previous studies reported that a negative correlation between serum inflammatory and nutrition markers, so the results demonstrated improvement in the nutritional parameter. Since PT can achieve better inflammation markers, more Alb level increase can be gained after PT in patients receiving HD and/or PD.

In the present meta-analysis, we observed substantial heterogeneity for the combined SMD of serum biochemical markers after PD in ESRD patients undergoing dialysis. As we know, heterogeneity in clinical research is inevitable. Biochemical markers are associated with the common risk factors of CP and ESRD, including demographic data for the ESRD subjects with or without diabetes, dialysis types, dialysis time, PT with or without auxiliary use of antibiotics and different follow-up times contributed predominantly to the observed heterogeneity. Considering limited studies, we would have not conducted subgroup analyses by these confounders. Thus, it should be remembered that our conclusions are based on limited studies, and therefore needs to be confirmed by more large and well-designed studies.

This is the first systematic review and meta-analysis to analyze the effect on systemic inflammation and metabolic measures after PT for the treatment of periodontitis in HD or/and PD patients. Four of 5 included RCTs were published within the past four years. Thus, the results of this study are reliable. In this study, we quantitatively assessed the systematic inflammation markers and nutrition markers, and the results found potential advantages of serum inflammation markers and biochemical measures after PT in dialysis patients with CP. Simultaneously, several limitations were identified in our systematic review. First, PT, as a traditional technique for the treatment of periodontitis, lacks sufficient original clinical trials in chronic renal diseases, especially HD and/or PD patients with CP, so only 5 articles were included. Second, the heterogeneity noticed among the selected studies is a possible limitation of this study, which is associated with the presence of confounding factors, such as demographic data for the subjects with or without diabetes, dialysis types, dialysis time and different follow-up times. Third, all of the included articles were evaluated as moderate-risk bias. Finally, we did not perform the evaluation of publication bias and sensitivity analyses for a small number of papers. Additionally, we qualitatively analyzed the TNF-a level and lipid metabolic markers since the included studies provided limited information. Considering the above limitations, the effects on serum clinical and biochemical markers after PT for the treatment of periodontitis remain worthy of investigation.

A few studies have evaluated the effect of non-operative periodontal therapy on inflammatory markers in this population. We need a large number of studies to assess the benefits of periodontal treatment in patients undergoing HD and/or PD. Further well-design of studies is needed to provide robust evidence regarding the systematic effects of PT in ESRD patients undergoing HD and/or PD. A longer evaluation time may produce more comparable results when studying clinical parameters of periodontitis.

Conclusion

Periodontal treatment may have a moderate reduction in systematic inflammation by evaluation of hs-CRP in dialysis patients with CP. However, only a few studies have been conducted regarding the level of IL-6, Alb, and TNF-*a* and no sufficient evidence supports the reduction of these markers after PT in ESRD patients. Therefore, practitioners are supposed to undertake a routine PT for HD and/or PD patients with periodontitis to reduce local and systemic inflammation. Further well-design studies with longer evaluation durations are required to explore the effects of the PT on clinical and biochemical parameters in ESRD patients.

Abbreviations

HD: Hemodialysis; PD: Peritoneal dialysis; ESRD: End-stage renal disease; CVD: Cardiovascular disease; CP: Chronic periodontitis; hs-CRP: Highly sensitive C-reactive protein; IL-6 Interleukin 6; TNF-a: Tumor necrosis factor-α;Alb: Albumin; MAs: Meta-analyses; PRISMA: Transparent Reporting of Systematic Reviews and Meta-analyses; PROSPERO: Prospective Register of Systematic Review; RCT: Randomized controlled trial; SMD: Standardised mean difference; CI: Confidence interval; OHI: Oral hygiene instructions; SRP: Scaling and root planning; TC: Total cholesterol; TG: Triglycerides; HDL-C: High-density lipoprotein cholesterol; LDL-C: Low-density lipoprotein cholesterol

Declarations

Ethics approval and consent to participate

Not applicable

Consent to publish

Not applicable

Availability of data and materials

The data supporting the findings are available in the databases PubMed, CNKI, and WFPD.

Competing interests

The authors declare that they have no competing interests

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Authors' contributions

Hui Yue, Xinxin Xu, and Yiting Xiao searched the literature and selected the studies. Hui Yue, Xinxin Xu, and Xiaozhi Li extracted the data. Hui Yue, Qin Liu, and Bo Hu assessed the quality of the included studies. Hui Yue, Qin Liu and Xinxin analyzed the data and drafted the article. Bo Hu designed the study, interpreted the data, and revised the article. All authors approved the submission.

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Tables

Table 1 Characteristics of Populations and Interventions in the Included trails

Study	No. of patients (no. of lost to follow up)	Periodontal definition	Study Methods	Intervention	Outcome measures	Authors' Conclusion
Fang et al., 2015	97 (4)	CAL ≥ 1 mm, including slight, moderate, and severe periodontitis and at least 16 teeth	RCT, 2 groups with ESRD undergoing hemodialysis (HD), on average 4 h of HD 3 times a week; 6-week, 3- and 6-month follow-up	T: OHI, SRP at baseline, supragingival prophylaxis at 3 months C: OHI a single certified periodontist	After 3, 6 months, the levels of hs-CRP, IL-6 and Alb significantly decreased ($P<0.05$); No significant difference for serum TNF-α, TC, TG, HDL-C, and LDL-C levels;	Non-surgical periodontal therapy can effectively improve periodontal, circulating inflammatory and nutritional status in ESRD patients
Wehmeyer et al., 2014	25(0)	≥2 teeth with ≥ 6 mm clinical attachment loss and at least 1 a site with probing depth > 5 mm	RCT, 2 groups undergoing HD and/or peritoneal dialysis (PD); 3- and 6-month follow-up	T: OHI+SRP adjunctive local minocycline when all sites with PD >5 mm C: OHI one of three trained providers	No significant the difference for serum albumin (Alb) and IL-6 levels in the intervention group at any point period (3 and 6 months)	periodontal therapy did not produce an observable impact on serum markers of inflammation
Li et al., 2019	72(0)	At least two sites with CAL≥3mm and PD≥ 4 mm	RCT, 2 groups undergoing HD, on average 4 h of HD 3 times a week; 8-week follow-up	T: OHI+SRP; C: No treatment No report about who performed the therapy	Hs-CRP levels significantly decreased in the intervention group	Non-surgical periodontal therapy can decrease systemic inflammation through Hs-CRP
Zhang et al., 2017	61(0)	At least 6 sites with CAL≥4mm and at least 14 teeth	RCT, 2 groups undergoing PD; 4-week follow-up	T: OHI+SRP; C: No treatment No report about who performed the therapy	Hs-CRP levels significantly decreased in the intervention group	Non-surgical periodontal therapy can reduce systemic inflammation through Hs-CRP

Ma et al.,2018	98(0)	At least 2 sites with CAL≥3mm and PD≥4mm and at least 20 teeth	RCT, 2 groups undergoing HD, on average 4 h of HD 3 times a week; 6-week follow-up	T: OHI+SRP; C: No treatment No report about who performed the therapy	Hs-CRP levels significantly decreased in intervention group	Non-surgical periodontal therapy can reduce systemic inflammation through Hs-CRP

Abbreviations: PD, probing depth; CAL, clinical attachment loss; RCT, randomized clinical trial; ESRD, end-stage renal disease; hs-CRP, high sensitive c-reactive protein; OHI, oral hygiene instructions; SRP scaling and root planning; IL-6, interleukin 6; Alb, albumin; TNF-α, tumor necrosis factor alpha; TC, total cholesterol; TG, triglycerides; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol.

Table 2 Risk of bias assessment for included RCTs

Study	Random sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome	Incomplete outcome data	Selective reporting	Other biases	Overall risk of bias
Fang et al, 2015	low	low	low	unclear	low	low	low	moderate
Wehmeyer et al., 2014	low	low	low	unclear	low	low	low	moderate
Li et al., 2019	unclear	unclear	unclear	unclear	low	low	low	moderate
Zhang et al., 2017	low	unclear	unclear	unclear	low	low	low	moderate
Ma et al.,2018	unclear	unclear	unclear	unclear	low	low	low	moderate

Low risk of bias: six domains were assessed as “low risk”; Moderate risk of bias: one or more domains were assessed as “unclear”; High risk of bias: one or more domains were assessed as “high risk”

Figures

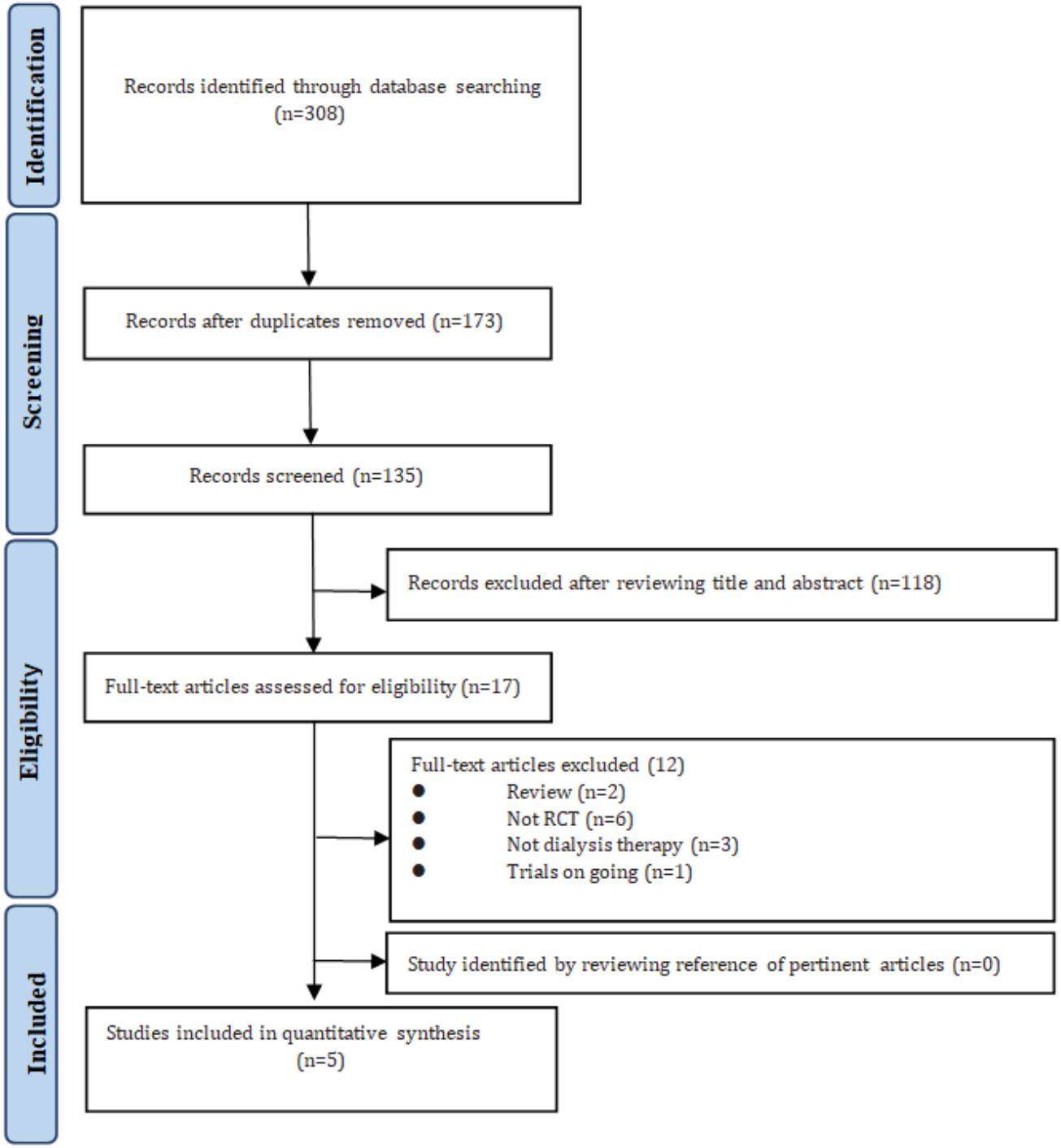

Fig. 1 Flow diagram of the studies identified, included, and excluded.

Figure 1

flow diagram of the studies identified, included and excluded

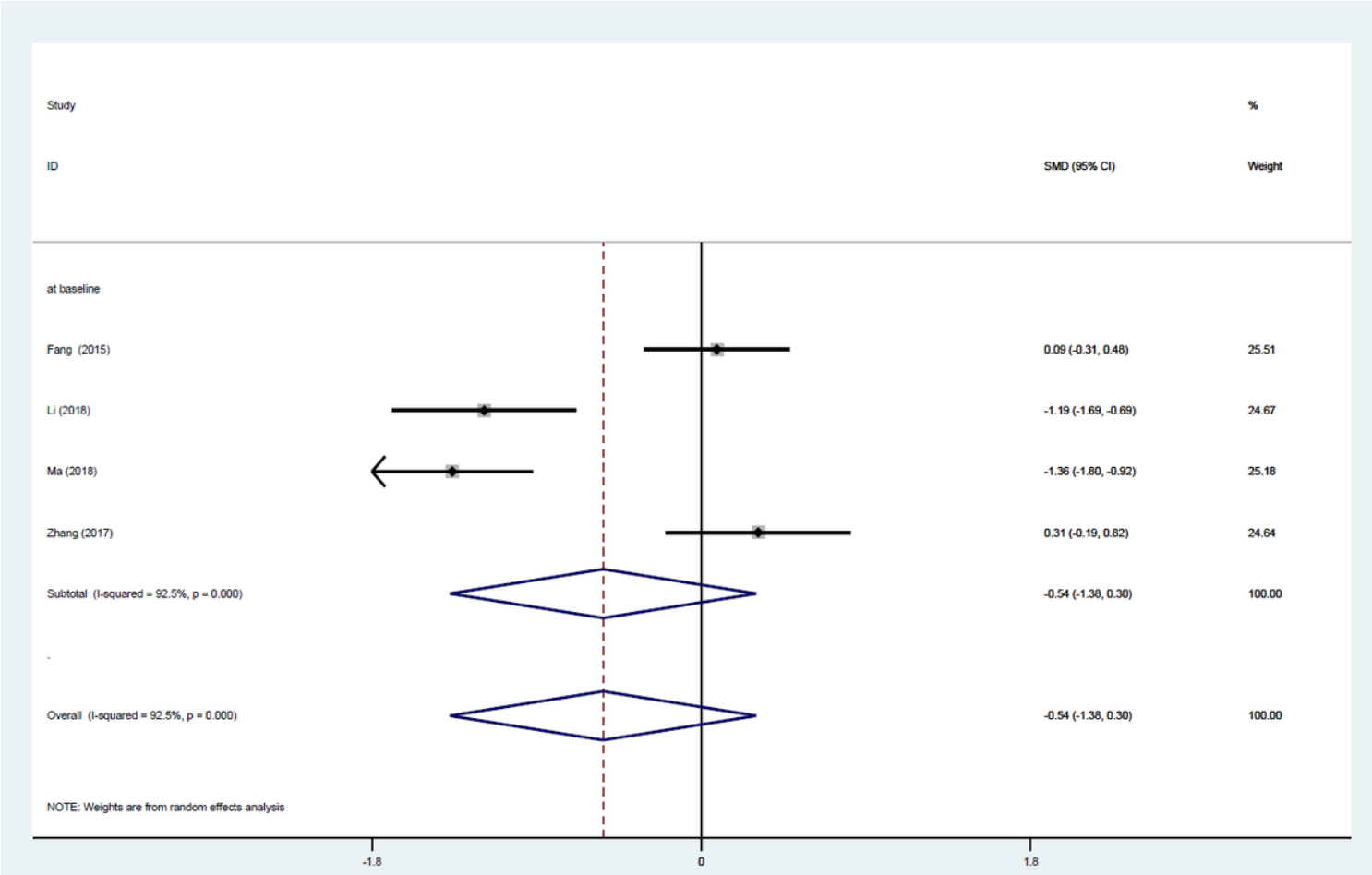

Figure 2

CRP at baseline

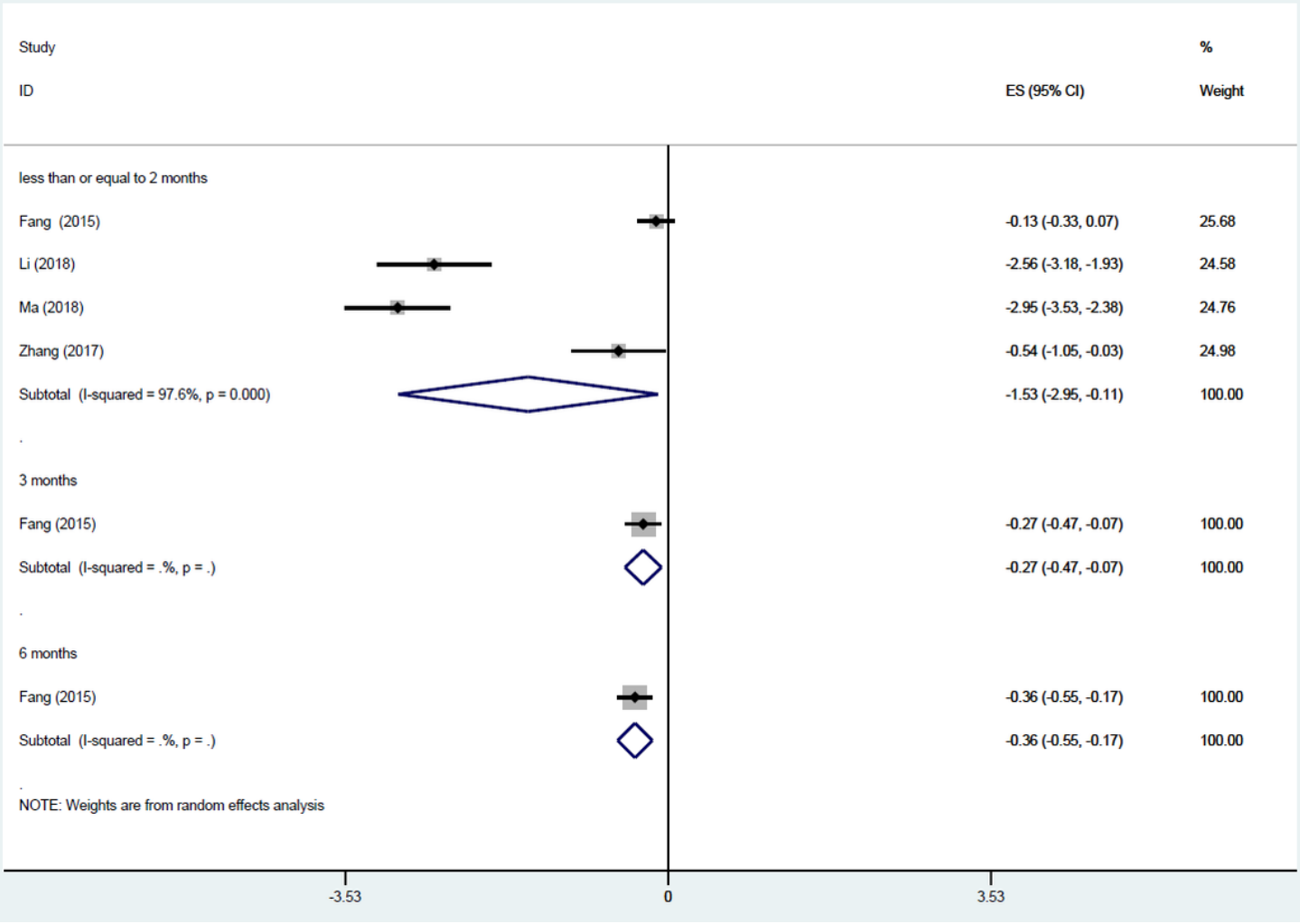
Study
ID
ES (95% CI)
%
Weight
less than or equal to 2 months
Fang (2015)
-0.13 (-0.33, 0.07)
25.68
Li (2018)
-2.56 (-3.18, -1.93)
24.58
Ma (2018)
-2.95 (-3.53, -2.38)
24.76
Zhang (2017)
-0.54 (-1.05, -0.03)
24.98
Subtotal (I-squared = 97.6%, p = 0.000)
-1.53 (-2.95, -0.11)
100.00
3 months
Fang (2015)
-0.27 (-0.47, -0.07)
100.00
Subtotal (I-squared = .%, p = .)
-0.27 (-0.47, -0.07)
100.00
6 months
Fang (2015)
-0.36 (-0.55, -0.17)
100.00
Subtotal (I-squared = .%, p = .)
-0.36 (-0.55, -0.17)
100.00
NOTE: Weights are from random effects analysis
-3.53
0
3.53

Figure 3

CRP

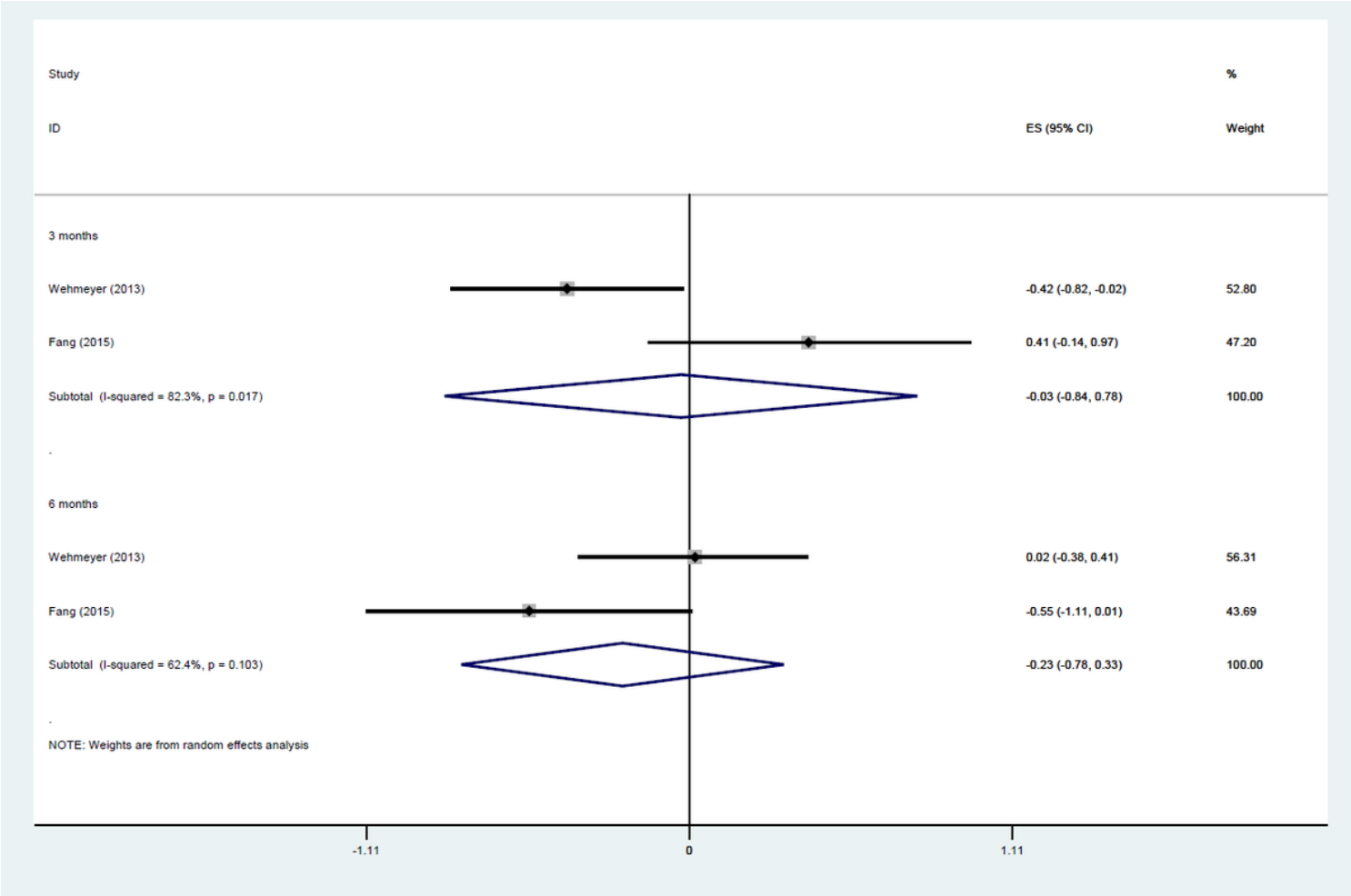
Study
ID
ES (95% CI)
%
Weight
3 months
Wehmeyer (2013)
-0.42 (-0.82, -0.02)
52.80
Fang (2015)
0.41 (-0.14, 0.97)
47.20
Subtotal (I-squared = 82.3%, p = 0.017)
-0.03 (-0.84, 0.78)
100.00
6 months
Wehmeyer (2013)
0.02 (-0.38, 0.41)
56.31
Fang (2015)
-0.55 (-1.11, 0.01)
43.69
Subtotal (I-squared = 62.4%, p = 0.103)
-0.23 (-0.78, 0.33)
100.00
NOTE: Weights are from random effects analysis
-1.11
0
1.11

Figure 4

IL-6

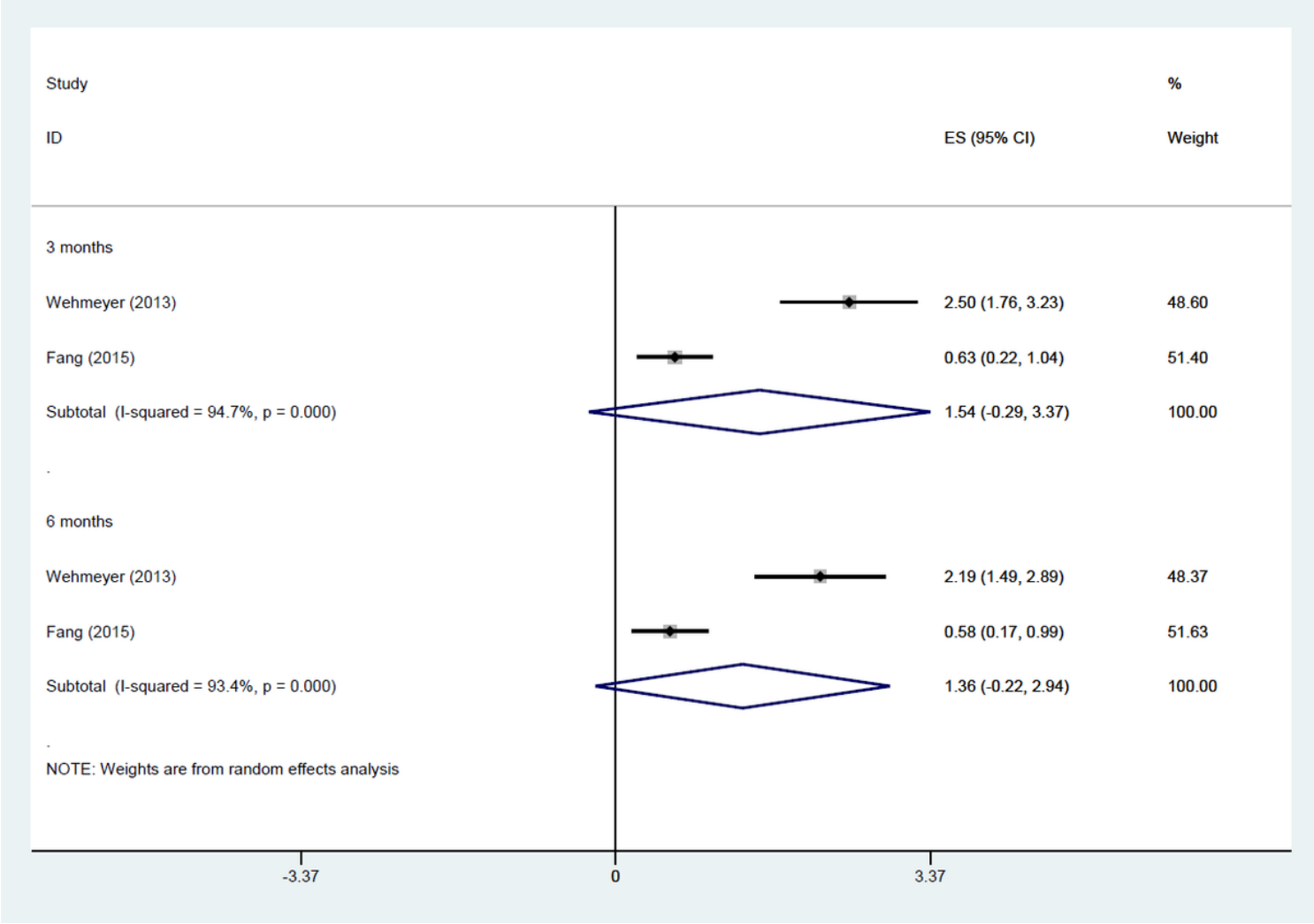

Figure 5

Alb

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- S2.csv
- PRISMAChecklistPTindialysispatients.doc
- Supplementarytable.docx
- S1.docx