Efficacy of therapies in the treatment of Guillain-Barre Syndrome: a network meta-analysis

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Abstract

Background

Guillain-Barre syndrome (GBS) is an acute, paralyzing, inflammatory peripheral nerve disease. For treatments of the Guillain-Barre Syndrome, there are many kinds of therapies for this diseases. For comparing all of the therapies, such as immunoglobulin, plasma exchanging, etc. in the treatment of Guillain-Barre Syndrome(GBS) to better inform clinical practice, we use Network meta analysis to get the outcome of the Guillain-Barre Syndrome. The protocol has been submitted to PROSPERO:CRD: 42019119178.

Methods

Web of Science, PubMed, Embase, and the Cochrane library were searched for related articles. We identified citations of these and included 26 trials comprising 2434 patients and control group human beings. Network meta-analysis (NMA) was performed with two kinds of outcomes. We carried on R software with gemtc package and JAGS software to calculate results for different therapies. The consistency of direct and indirect evidence was also assessed by R software.

Results

Concerning for two outcomes, there were no improvement observed in MTP and Pred compared with placebo. PE and IVIg were illustrated to be effective over Placebo. There was no significant difference between different doses and times of PE and IVIg. On consistency examination between direct and indirect evidences, there were no obvious heterogeneity between all of therapies. Funnel plots indicates the possibility of publication bias in this study are small.

Conclusion

PE or IVIg had a significant efficency for GBS patients. The effects of some combination treatments should be further explored. Corticosteroids had no significant effects on GBS.

1. Background

Guillain-Barre Syndrome (GBS) is a demyelinating polyradiculoneuropathy with an acute paralyzing disorder, typically symmetric, ascending and areflexia[1, 2]. Incidence varies between 0.66 and 1.79 cases per 100 000 persons in general population[2, 3]. It is an autoimmune disease caused by an immune reaction against an infectious agent that shares an antigen with nerves[4], This pathological mechanism has led to the use of immune therapies for Guillain-Barre syndrome. The common treatments for Guillain-Barre syndrome includes plasma exchange[5], intravenous immunoglobulin[6] and Corticosteroids[7]. There are many other ways as combination of therapies, non-routine dose and courses of IVIg(intravenous immunoglobulin), and unconventional treatments[8]. Many clinical trials have been conducted to investigate their therapeutic effects on Guillain-Barre Syndrome[9–12]. However, sample sizes of previous studies were relatively limited, and many kinds of therapeutic effects have not been compared with each other, as well as the assessment of Guillain-Barre Syndrome were not in consistence with each other. Thus, a network meta-analysis was needed to help carry out comparative analysis on the efficiency of therapies on Guillian-Barre Syndrome from previous trials with 2 endpoints. Network meta-analysis (NMA) is a statistical technique that allows comparison of multiple treatments in the same meta-analysis simultaneously. NMA can be performed under a frequentist or a Bayesian framework.[13] We carried on R software with gemtc package and JAGS software to calculate the results of different therapies on two outcomes. The protocol has been submitted to PROSPERO:CRD: 42019119178.

2. Methods

2.1. Search strategy

We searched for Web of Science, PubMed, Embase, and the Cochrane library for related articles concerning the therapeutic effects of therapies for Guillian-Barre Syndrome. All therapies were enrolled, including PE, IVIg with different dose and courses, Corticosteroids, CSF filtration, combination of therapies, etc.. Articles published between January 1, 1980 and January 1, 2019 were retrieved in the search. The following Mesh terms and their synonyms and abbreviations were used to find relevant studies: “Guillain-Barre syndrome”, “polyradiculoneuropathy”, “polyneuropathies”, “methylprednisolone”, “prednisolone”, “IVIg or intravenous immunoglubin”, “plasma exchange”, etc.. Two authors independently screened titles and abstracts of retrieved articles to evaluate their qualification according to the inclusion criteria. Reference list of enrolled articles were also reviewed manually to improve the integrity of this study. This analysis was performed in accordance with Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guideline. [14]

2.2. Evaluated outcomes and inclusion criteria

In study, Disability scale grade change after 4 weeks(outcome□) and rates of improvement by ≥ 1 grades of Disability scale after 4 weeks(outcome□)were applied to evaluate the on patients. The Disability scale has some versions, all versions is approximately divided to seven layers: 0. Healthy. 1. Minor symptoms or signs of neuropathy but capable of manual work. 2. Able to walk without support of a stick but incapable of

manual work. 3. Able to walk with a stick, appliance, or support. 4. Confined to bed or chair bound. 5. Requiring assisted ventilation.6. Dead. We included all randomized controlled trials (RCTs) or cohort clinical trials, and included children and adults with GBS of all degrees of severity. We defined GBS according to internationally accepted diagnostic criteria[4] as acute polyradiculoneuropathy causing progressive weakness of two or more limbs, an onset phase not more than four weeks, reduced or absent tendon reflexes, and lacking alternative causes. We included studies that did not conform exactly to these criteria provided that the authors regarded GBS or one of its synonyms, such as acute idiopathic neuropathy or acute inflammatory demyelinating polyradiculoneuropathy, as the preferred diagnosis.

2.3. Data extraction

Two authors extracted relevant data from eligible articles independently. In the current study, information as follows were extracted: last name of first author, year of publication, origin country, type of clinical trial, number of subjects, treatments, outcomes. A 3rd author would resolve discrepancies after discussion. Disability grade change after 4 weeks was considered as the primary outcome in this study.

2.4. Statistical analysis

A network meta-analysis was performed in order to evaluate the efficacy of different treatments on GBS. Consequently, Bayesian network meta-analysis (NMA) was performed with a consistency model using getmc[15] package and JAGS software in R software to compare direct and indirect evidence. Moreover, the forest graph, ranking probability graph, league table heatmap, direct evidence plot, funnel plot and heterogeneity test between direct and indirect evidence would be painted or assessed by R software. Besides getmc package, BUGSnet[16], netmeta[17], and dmetar[18] packages were also be required for making league table heatmap, funnel plot, direct evidence plot and Heterogeneity analysis heatmap. We set the parameters of bayes iterations as n.adapt = 5000, n.iter = 20000 to ensure the convergence.

3. Results

3.1. Study characteristics

A total of 2434 subjects from 26 trials were involved to investigate the efficacy of 14 kinds of therapies for Guillain-Barre Syndrome. Following Figure in Fig. 1 illustrated the process of study selection. Therapies involved in this meta-analysis were Plasmaexchange(PE), Intravenous immunoglobulin(IVIg), methylprednisolone(MTP), prednisolone(Pred), immunoabsorption plasmapheresis(IAPP), IFN-b 1a, BDNF(brain-derived neurotrophic factor), CSF filtration(CSF filter), Tripterygium polyglycoside(TWP), PE followed by IVIg(PE + IVIg), immunoabsorption followed by IVIg(IAPP + IVIg), IVIg (LFB) 0.4 g/kg/day for 3 days(Half dose of IVIg), IVIg 1 g/kg daily(twice dose/day of IVIg), Half-course of treatment of PE.

Table 1

Characteristics of enrolled trials

writer	countary	Research type	treatment	Placebo1	Placebo2	N(T/C)	Outcome
Koningsveld[19] 2004	Netherland,Belgium and Germany	RCT	methylprednisolone	Placebo		112/113	□ □
Steroid[20] 1993	UK	RCT	methylprednisolone	placebo		124/118	□ □
Hughes[21] 1978	UK	RCT	prednisolone	placebo		21/19	□ □
Singh[22] 1996	India	RCT	prednisolone	placebo		24/22	□ □
Shukla[23] 1988	india	RCT	prednisolone	placebo		6/8	□
Bansal[24] 1986	India	RCT	prednisolone	placebo		10/10	□ □
Pritchard[25] 2003	UK	RCT	IFNb-1a	placebo		13/6	□ □
Bensa[26] 2000	UK	RCT	brain-derived neurotrophic factor	placebo		6/4	□ □
Wollinsky[27] 2001	Germany	RCT	CSF filtration	plasma exchange		17/20	□ □
Zhang[28] 2000	China	RCT	Tripterygium polyglycoside	dexamethasone and prednisolone		22/21	□
Bril[29] 1996	Canada	RCT	IVIg 0.5 g/kg daily for 4 days	plasma exchange		26/24	□ □
Diener[30] 2001	Germany	RCT	IVIg 0.4 g/kg daily for 5 days	plasma exchange	immune absorption	20/21/18	□ □
El-Bayoumi[31] 2011	Egypt	RCT	IVIg 0.4 g/kg daily for 5 days	plasma exchange		20/21	□
Haupt[32] 1996	Germany	Non-randomised	Immunoabsorption followed by IVIg	immunoabsorption		21/13	□
Korinthenberg[33] 2005	Germany,Swiss and Austrian	RCT	IVIg 1.0 g/kg daily	placebo	IVIg 0.4 g/kg daily	14/7 and 25/24 *	□
Nomura 2001[34]	Japan	RCT	IVIg 0.4 g/kg daily for 5 days	Plasma exchange		23/24	□ □
PSGBS Group[35] 1997	UK	RCT	IVIg 0.4 g/kg daily for 5 days	Plasma exchange	PE followed by IVIg	130/121/128	□ □
Raphaël[36] 2001	France	RCT	IVIg 0.4 g/kg/day for 3 days	IVIg 0.4 g/kg/day for 6 days		18/21	□
Meché[37] 1992	Netherlands	RCT	IVIg 0.4 g/kg daily for 5 days	Plasma exchange		74/73	□ □
Greenwood[38] 1984	UK	RCT	Plasma exchange	supportive care		14/15	□ □
McKhann[39] 1985	France	RCT	Plasma exchange	supportive care		122/123	□ □
Osterman[40] 1984	Sweden	RCT	Plasma exchange	supportive care		18/20	□
Raphaël[41] 1987	France	RCT	Plasma exchange	supportive care		109/111	□ □
Raphaël[42] 1997	France	RCT	Plasma exchange	supportive care		45/46	□ □
Ashish[43] 2018	India	RCT	IVIg	Plasma exchange		24/16	□
Ye[44] 2015	China	RCT	Plasma exchange	IVIg		30/29	□

Outcomes:□Disability grade change after 4 weeks(SD ± MD)□improvement by ≥ 1 grades after 4 weeks
Some of the data of outcomes can not be found in full-text, we get the data from the Cochrane meta-analysis[9–12], which Included most of the articles in this study.
* In Korinthenberg 2005, there are two stages of trial, and the number of patients is different.

3.2. Quality assessment

25 of 26 trials mentioned randomization, 17 RCTs (68%) used a specific random sequence generation method. Most of these RCTs(14 RCTs) mentioned allocation concealment. Only 8 RCT (30%) referred to the method of blinding. Most trials did not select outcome reporting or have incomplete outcome data, besides more than half(14RCTs) of included RCTs did not provide information about other bias. In addition, all of the included trials described the inclusion criteria or diagnose criteria, but one of these(El-Bayoumi[31] 2011) do not mention exclusion criteria.

3.3 Network meta-analysis results

NMA results

We depicted a network graph of 14 kinds of therapies for GBS. The graph were made by R 3.6.1 software and visNetwork package.

Forest graph

There were 22 studies using Disability grade change after 4 weeks as outcome measure, including 13 treatment options, meanwhile, there were 21 studies using rates of improvement by ≥ 1 grades after 4 weeks as outcome measure, including 9 treatment options. The forest figures on results of network pooled comparisons of the clinical effectiveness of each therapy and their calculated ranking probabilities were shown in Fig. 4 and Fig. 5, the forest figure reference were Placebo, PE and IVIg.

In the assessment on efficiency of treatments for GBS, PE, IVIg, PE followed by IVIg, immunoabsorption followed by IVIg, IVIg 1 g/kg daily for 2 days, Half-course of PE were observed to be significantly effective in treating GBS. (outcome: PE MD=-0.83, 95%CrI[-1.3,-0.38]; IVIg MD=-0.91,95%CrI[-1.5,-0.35]; PE followed by IVIg MD=-1.1, 95%CrI[-1.9,-0.34], immunoabsorption followed by IVIg MD=-1.9, 95%CrI[-3.4,-0.47], IVIg 1 g/kg daily MD=-0.88, 95%CrI[-1.7,-0.068], 2 times of PEs MD=-1.1, 95%CrI[-1.8,-0.35] outcome:PE OR = 2.7,95%CrI[1.7,4.7], IVIg OR = 3.6,95%CrI[1.9,8.0], PE followed by IVIg OR = 3.7,95%CrI[1.5,10.0]). Both PE and IVIg were available for GBS (outcome: PE MD=-0.83, 95%CrI[-1.3,-0.38]; IVIg MD=-0.91,95%CrI[-1.5,-0.35];outcome: PE OR = 2.7,95%CrI[1.7,4.7], IVIg OR = 3.6,95%CrI[1.9,8.0])and all kinds of corticosteroids were be indicated no significant efficiency for GBS (outcome: MTP MD=-0.18, 95%CrI[-0.66,0.30]; Pred MD = 0.81,95%CrI[0.27,1.3];outcome: MTP OR = 1.4,95%CrI[0.72,2.6], Pred OR = 0.61,95%CrI[0.24,1.5]). We transferred the base treatment of forest graph for PE and normal dose of IVIg(Fig. 4-b),c) Fig. 5-b),c)), we could find there were no other therapies being more effective with significant difference. We compared different doses of PE and IVIg (IVIg 0.4–0.5 g/kg daily for 4–5 days, 4–5 times of PE, IVIg 1 g/kg daily, IVIg 0.4 g/kg/day for 3 days, 2 times of PE) and found no significant difference between them. For other kinds of therapies, such as IFNb-1a, brain-derived neurotrophic factor, CSF filtration, Tripterygium Wilfordii Polyglycoside and IVIg 0.4 g/kg/day for 3 days, had no significant difference with placebo.(outcome: IFNb-1a MD = 0.095, 95%CrI[-1.5,1.7]; BDNF MD=-0.83,95%CrI[-2.8,1.1]; CSF filtr MD=-0.86, 95%CrI[-1.8,0.12], IVIg 0.4 g/kg/day for 3 days MD=-0.4, 95%CrI[-1.5,0.71] outcome: IFNb-1a OR = 1.1,95%CrI[0.13,11.0], BDNF OR = 1.1,95%CrI[0.056,19.0], CSF filtr OR = 2.5,95%CrI[0.49,12.0], TWP OR = 4.6,95%CrI[0.6,47.0]). Regarding to the improvement for GBS among PE, IVIg, and Corticosteroid, the three most conventional treatments, IVIg was the most helpful one (compared with PE (MD 0.073[-0.26,0.41],with methylprednisolone 0.72[-0.01,1.5],with prednisolone 1.7[0.96,2.5])), but there was no significant difference between PE and IVIg. The efficacy of the two hormones was lower than that of PE and IVIg. (outcome: MTP VS PE 0.66:[-0.017,1.30] Pred VS PE 1.6 [0.96,2.3] MTP VS IVIg 0.73[-0.011,1.5] Pred VS IVIg 1.7[0.97,2.5] PE VS IVIg 0.078[-0.26,0.41] outcome MTP VS PE 0.51:[0.22,1.1] Pred VS PE 0.22[0.075,0.62] MTP VS IVIg 0.38[0.13,0.92] Pred VS IVIg 0.17[0.048,0.50] PE VS IVIg 0.74[0.44,1.2]).

Ranking probability

A clustered ranking plot was generated and presented NMA results visually. To better understand the results, the ranking graph was calculated to evaluate the ranking probabilities of all medications on the outcomes. Results were presented in Fig. 4d) and Fig. 5d). As suggested by ranking probabilities of outcome, immunoabsorption followed by IVIg had biggest possibility to be a best treatment(P = 0.6), and Half-times of PE, PE followed by IVIg were also likely to be the best treatment. For outcome, TWP had biggest possibility to be a best treatment(p = 0.4), and IVIg 0.4–0.5 g/kg daily for 4–5 days, PE followed by IVIg followed it. For most probability to be worst treatment, in out come was prednisone, followed by IFNb-1a, in out come was prednisone, followed by IFNb-1a and BDNF.

League Table Heatmap

We use nma.league() Function in BUGSnet package to produce League Table Heatmap. The map would show comparison results of each therapy clearly. (Fig. 6 and Fig. 7)

Gelman-Rubin-Brooks plot

As we carried network meta-analysis based on a bayesian hierarchical framework, we should confirm our simulations have resulted in the convergence of the algorithm, which represented the stability of our results. The plot showed well convergence of the algorithm(Fig. 8.).

The order of SUCRA value

If a treatment always ranks first, then SUCRA = 1, and if it always ranks last, it will have SUCRA = 0.[45] We use the SUCRA function in dmetar package to calculate SUCRA Score and ordered it in descending order.(Fig. 9)We found Conventional dose of IVIg, PE followed by IVIg were in the front of therapies queue. The SUCRA score of PE was lower by IVIg in graphs. Corticosteroids on two outcomes were in the bottom. For the outcome, BDNF, CSF filtration, PE, Conventional dose of IVIg, Immunoabsorption, IVIg 1 g/kg daily got a similar SUCRA value, which could from the side indicated that there may be no significant difference in efficacy between these treatments.(Fig. 9)

3.4. Consistency analysis and heterogeneity test

We used I^2 for consistency checks direct results, From the Fig. 10. and Fig. 12, almost all of the I^2 were under 50% which means the heterogeneity of the direct NMA was in a lower rage, the results of direct evidence of the NMA were reliable. We used the fixed effect model for meta-analysis.

The node-splitting method and its Bayesian P value was used to report the inconsistency of our results between direct and indirect results. For the majority of our results, the confidence intervals from direct and indirect evidences were in consistent, with minor differences. In the inconsistency checks, we found that there were some heterogeneity between the four groups in outcome,(G VS B,M VS B,I VS G,M VS I)as there was no obvious heterogeneity in outcome. To further determine the heterogeneity, we used netheat diagrams in the netmeta package for heterogeneity analysis. The results showed that the heterogeneity was within the acceptable range. We further used the direct.evidence.plot function in the dmetar package (from github) to analyze the sources of direct and indirect evidence, and the results showed that the three groups of results (G VS B,I VS G,M VS I) were dominated by direct evidence. The results of M VS B were mostly based on indirect evidence, but the results of network evidence were consistent with its direct evidence, as we thought direct evidence had more credibility. Based on the above results, we believed In outcome, there was no significant heterogeneity in the network meta analysis which may influence the result significantly. In the outcome, we did not find groups with significant heterogeneity. Finally, we could see from the direct.evidence.plot that most of the comparison results in this study are obtained through indirect comparison. Since the indirect results of the meta were calculated based on the bayesian algorithm, they still needed to be verified by a large number of direct comparisons.

3.6 Publication bias.

Funnel plots were used to measure the publication bias. The funnel plot of the improvement in Disability grade change after 4 weeks, and the rates of improvement by ≥ 1 grades after 4 weeks showed potential publication bias of the included RCTs (Fig. 14). It can be seen from the funnel plot that almost all the studies fall within the funnel and the two sides of the funnel were basically symmetrical, so the possibility of publication bias in this study was small.

4. Discussion

On NMA results

PE and IVIg have been widely used in clinical practice to alleviate GBS[10, 12], and recommended by the European guidelines[46, 47] rather there were some evidence indicating corticosteroids had no significant efficiency for GBS [9]. In our studies, PE and IVIg as therapies for GBS are not weaken to every other kinds of therapies. Considering that two therapies are conventional treatments for GBS, our NMA helps to confirm their effectiveness in clinical practice[37–39, 48, 49]. Immunoabsorption followed by IVIg had highest possibility for 1st rank for the improvement Disability grade change after 4 weeks in a small sample, which may infer the better efficiency GBS treatment, However, the number of patients included was 21, .the sample size is insufficient, moreover, the comparison with PE and IVIg is indirect, so its efficacy still needs to be further verified with a large sample. Corticosteroids were not effective as reported before[20, 23]. For Outcome, BDNF, CSF filtration, PE, Conventional dose of IVIg, Immunoabsorption, IVIg 1 g/kg daily got a similar SUCRA value, so, maybe some unconventional therapy should be given more attention on, A larger sample study may yield positive results.

In the aspects of outcome for the GBS, we can find that the results of PE and IVIg were similar to that of outcome, both of which had good therapeutic effects, but there was no significant difference between the two. The rank and SUCRA of IVIg are better than those of PE. Tripterygium Wilfordii Polyglycoside showed its advantage in treatment results. However, with insufficient sample size and unclear adverse reactions, further researches on TWP were needed.

The results of Outcome and outcome are basically the same, which enhanced the reliability of the study. For another hand, However, many of these therapies had only one of the included studies reported the efficacy, and most of the comparison results were obtained through indirect comparison. Therefore, whether the conclusion is accurate or not, more direct comparison and in-depth study are still needed.

In terms of different doses and treatment courses of PE and IVIg, the rank obtained by half course of PE is better than that of PE and IVIg. We can see from the network that the comparison object was placebo, the indirect result with small samples can not be conceived. At the same time, for sufficient IVIg 1 g/kg over 2 days, we can see that the patients of two related trials are different. One was for children, the other was for adults. And the control groups were IVIg and placebo respectively. We calculated that the indirect comparison was superior to the IVIg. because the indirect comparison was easily affected by more other literatures and studies, we believe that direct result—conventional IVIg is better than IVIg 1 g/kg over 2 days. However, there are no significant difference between all of different doses and times of PE and IVIg.

For the immumoabsorption, in two essays[30, 32], we could find it shown equally favorable results in acute GBS. However, on the clinical adverse reaction, treatment-related adverse reactions were, however, fewer in the immunoglobulin group compared to the other groups[30]. immumoabsorption also has been used successfully in myasthenia gravis[50, 51], which is also an autoimmunity disease. So, we thought it is necessary to have further study on immumoabsorption for GBS.

Combination therapy has been somewhat controversial for guillain-barre[46, 47]. PSGBS Group 1997 carried out a result of non-significant trend towards a more favourable outcome on some outcome measures with combined treatment. In our studies, we put its data into the network meta, we would found the higher ranks than IVIg, even if the advantage is slightly. As for Immunoabsorption followed by IVIg, we could find it got highest ranks and SUCRA value in outcome. Haupt [32] showed that immumoabsorption followed by IVIg may lead to a more rapid recovery of patients suffering from GBS when compared to those patients treated with selective immumoabsorption or PE alone. Consequently, we thought the effect of combination therapy, especially for PE followed by IVIg, Immunoabsorption followed by IVIg needs to be further tapped.

On Consistency test and heterogeneity test

In the meta-analysis, we adopted the fixed effect model wholly. Most of I^2 was less than 50%, while only B VS C was 52.1%. However, all the studies showed that B was better than C, so we insisted on adopting the fixed effect model. In terms of the heterogeneity analysis of indirect and direct evidence(Fig. 11.), we can see $P > 0.1$ through the node cracking method, while the yellow and red color of netheat is not very deep, and there is no inverted blue square. In this study, NMA was mainly carried out through bayesian algorithm and gemtc package, but the gemtc package could not draw the heterogeneity heatmap and funnel figure, so we used netmeta package to draw the heterogeneity heatmap and funnel figure. At the same time, previous literature showed that the results from netmeta were very similar with the results from a fixed effect Bayesian analysis[52], so the plot and funnel figure could be transplanted as a reference for heterogeneity analysis and publication bias. We believe that the heterogeneity is under control, so the conclusion obtained through indirect comparison in this paper has certain reference value. In additional, we use BUGSnet package to get League Table Heatmap to show all of NMA analysis results. BUGSnet requires that the user have installed Just Another Gibbs Sampler (JAGS) on their computer, it's result in accordance with getmc package highly[16]. At the same time, for the indirect evidence of well efficiency treatments, such as IVIg followed by PE, tripterygium wilfordii polyglycosides, etc.., we should also carry more clinical trial for compare the efficacy of different treatments.

Previous clinical studies confirmed the efficacy of PE and IVIg, and meta-analysis further confirmed and elucidated the efficacy. We demonstrate the effectiveness of these two approaches from a larger range of treatment options. In the treatment of corticosteroid, the results are opposite, and we demonstrate in a larger context that the efficacy of corticosteroid in treating guillain-barre syndrome is limited. Compared with RCT, our results indicated a more integral conclusion, and the accumulation of evidence from randomized and cohort clinical trials could lead to a more convincible conclusion on the efficacy of therapies on GBS.

Limitation

The primary limitation of this analysis relates to the limited sample size of involved therapies and subjects, especially for some treatments with well feasibility, such as combination treatments of IVIg and PE and immumoabsorption. In addition, there are some different age groups in the included researches. In Korinthenberg[33] 2005, the main patients of GBS were children, in all of other trials were adults. At the same time, since most of the treatment methods of GBS are non-drug treatments, the implement of blind methods will be limited to some extent, so the number of blind methods in the included literatures is relatively small. Besides, the inclusion criteria and disability scale were not identical. Lastly, it has been suggested that a more unified GBS diagnostic criteria and more unified evaluation of curative effect should be established to assess GBS accurately. Larger and well-designed clinical trials on the efficacy of GBS on patients are needed for further investigation.

5. Conclusion

In conclusion, we observed in our meta-analysis that PE or IVIg had a significant efficency for GBS patients. They can help to improve activities of daily living. Different doses of IVIg or PE, combination of PE and IVIg had no significant difference with PE and IVIg alone. The effects of combination therapy, immumoabsorption and Tripterygium Wilfordii Polyglycoside should be further explored. Corticosteroids havd no significant effect on GBS. Larger clinical trials on the efficacy of therapies with GBS are needed for further investigation.

Abbreviations

NMA: network meta analysis, GBS: Guillain-Barre Syndrome, MTP: Methylprednisolone, PbO: Placebo, Pred: Prednisolone, BDNF: Brain-derived neurotrophic factor, CSF filter: Cerebrospinal fluid filtration, PE: Plasma exchange, IVIg: Intravenous immunogloblin 0.4–0.5 g/kg daily for 4–6 days, PE + IVIg: PE followed by IVIg, IAPP + IVIg: Immunoabsorption followed by IVIg, IAPP: Immunoabsorption plasmapheresis, Twice IVIg: 1 g/kg for 2 days, Half IVIg: 0.4 g/kg for 3 days, Half PE: Half course of PE, TWP: Tripterygium Wilfordii Polyglycoside

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Availability of data and material

This study included articles which are available via PubMed. All information analysed in this study was collected in a dataset and this is available from the first author on reasonable request.

Competing interests

On behalf of all authors, the corresponding author states that there is no conflict of interest.

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Authors' contributions

J.Lin and Q.Gao had full accessed to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the meta analysis. J.Lin, K.Xiao and Q.Gao designed the study and determined the content. J.Lin determined the retrieval scheme, collected the data, performed the statistical analysis and drafted the manuscript. Q.Gao supervised the study, doublechecked the statistical analysis. D.Tian and Y.Hu screened articles. Z.Han revised the manuscript. All authors have read and approved the manuscript.

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Figures

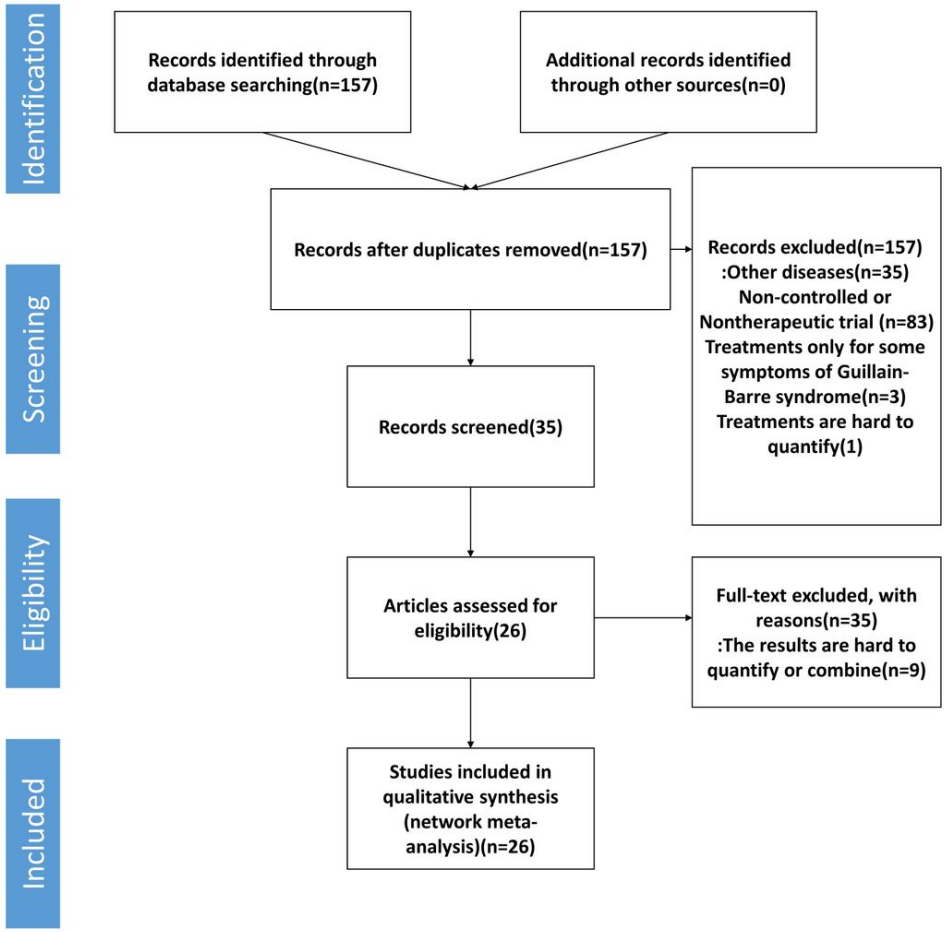

Figure 1

Flow chart of the search for eligible studies

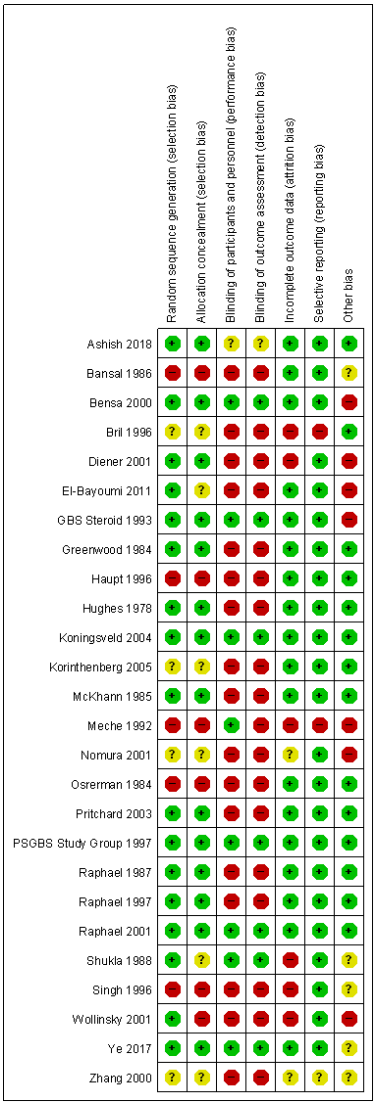

Figure 2

Risk of bias graph

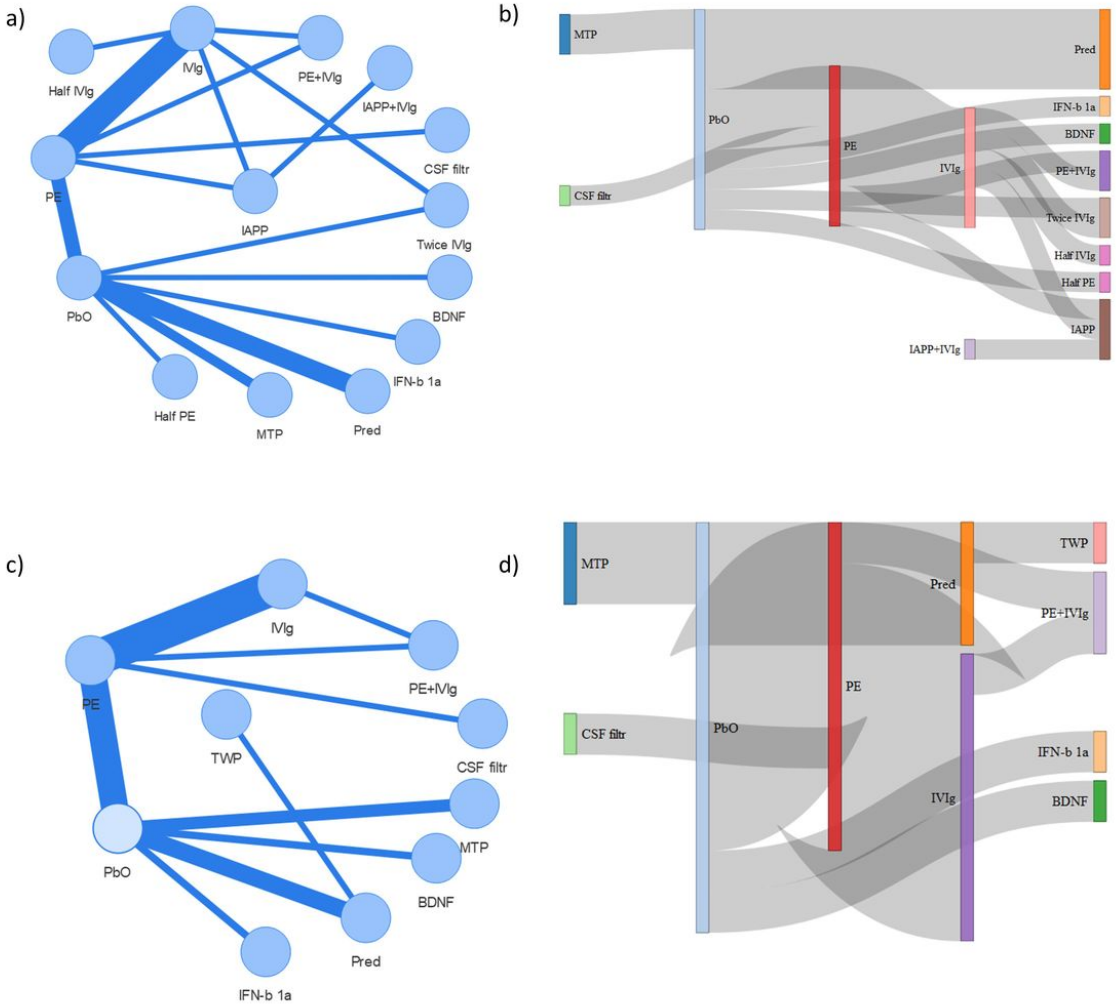

Figure 3

Network graph for therapies of GBS. Note: Line thicknesses correspond to the number of trials used for comparisons. Legends: For b) and d): The width of each therapy represents the number of treatment-related studies MTP: Methylprednisolone, PbO: Placebo, Pred: Prednisolone, BDNF: Brain-derived neurotrophic factor, CSF filter: Cerebrospinal fluid filtration, PE: Plasma ex-change, IVIg: Intravenous immunogloblin 0.4-0.5 g/kg daily for 4-6 days, PE+IVIg: PE followed by IVIg, IAPP+IVIg: Immunoabsorption followed by IVIg, IAPP: Immunoabsorption plasmapheresis, Twice IVIg: 1 g/kg for 2 days, Half IVIg: 0.4 g/kg for 3 days, Half PE: Half course of PE, TWP: Trip-terygium Wilfordii Polyglycoside a) and b):trials with outcome of Disability grade change after 4 weeks. c) and d): trials with outcome of the rates of improvement by≥1 grades after 4 weeks.

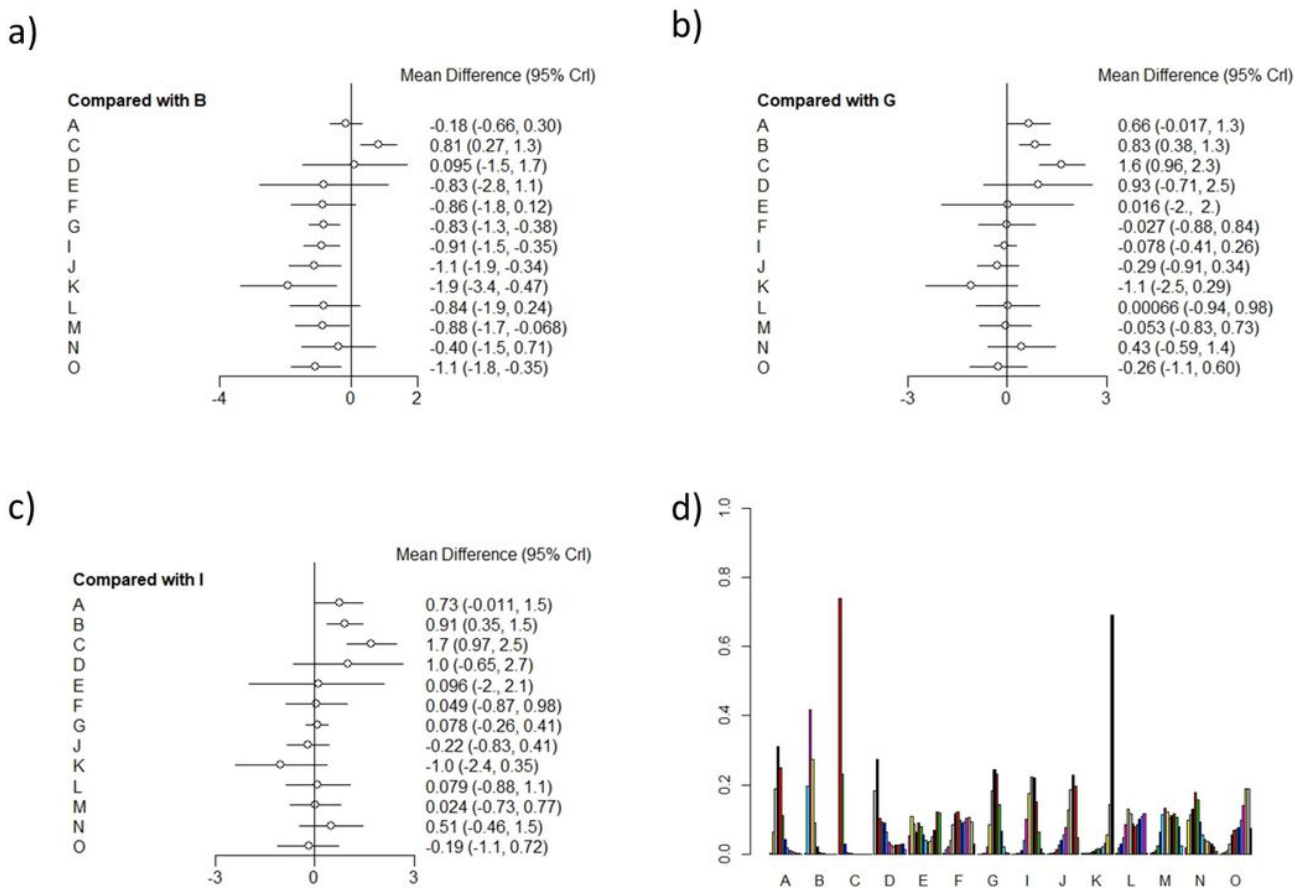

Figure 4

Forest graph and ranking probability graph on outcome Legends: outcome: Disability grade change after 4 weeks. A: methylprednisolone, B: placebo, C: prednisolone , D: IFNb-1a, E: brain-derived neurotrophic factor, F: CSF fil-tration, G: PE, I: IVIg 0.4-0.5 g/kg daily for 4-5 days, J: PE followed by IVIg, K: Immunoabsorption followed by IVIg, L: Immunoabsorption, M: IVIg 1 g/kg daily, N: IVIg 0.4 g/kg/day for 3 days O: Half-times of PE a), b) and c): Rela-tive effect com-paring with placebo group, PE, and IVIg. d): Ranking probability graph.

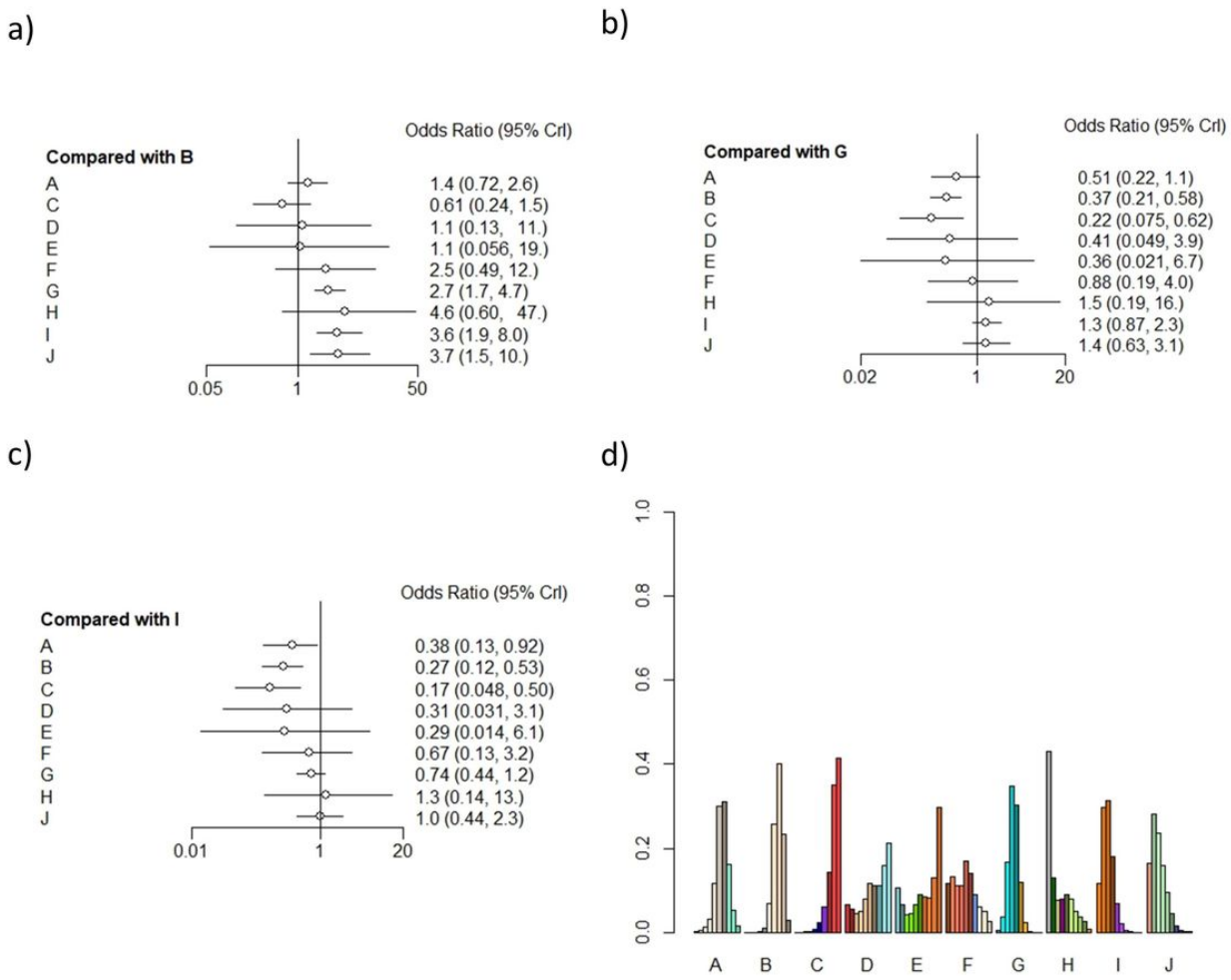

Figure 5

Forest graph and ranking probability graph on outcome Legends: outcome:rates of im-provement by≥1 grades after 4 weeks. A-G, I-J: Same with Fig 4. H: Tripterygium Wilfordii Poly-glycoside a), b) and c): Relative effect comparing with placebo group, PE, and IVIg. d): Ranking probability graph.

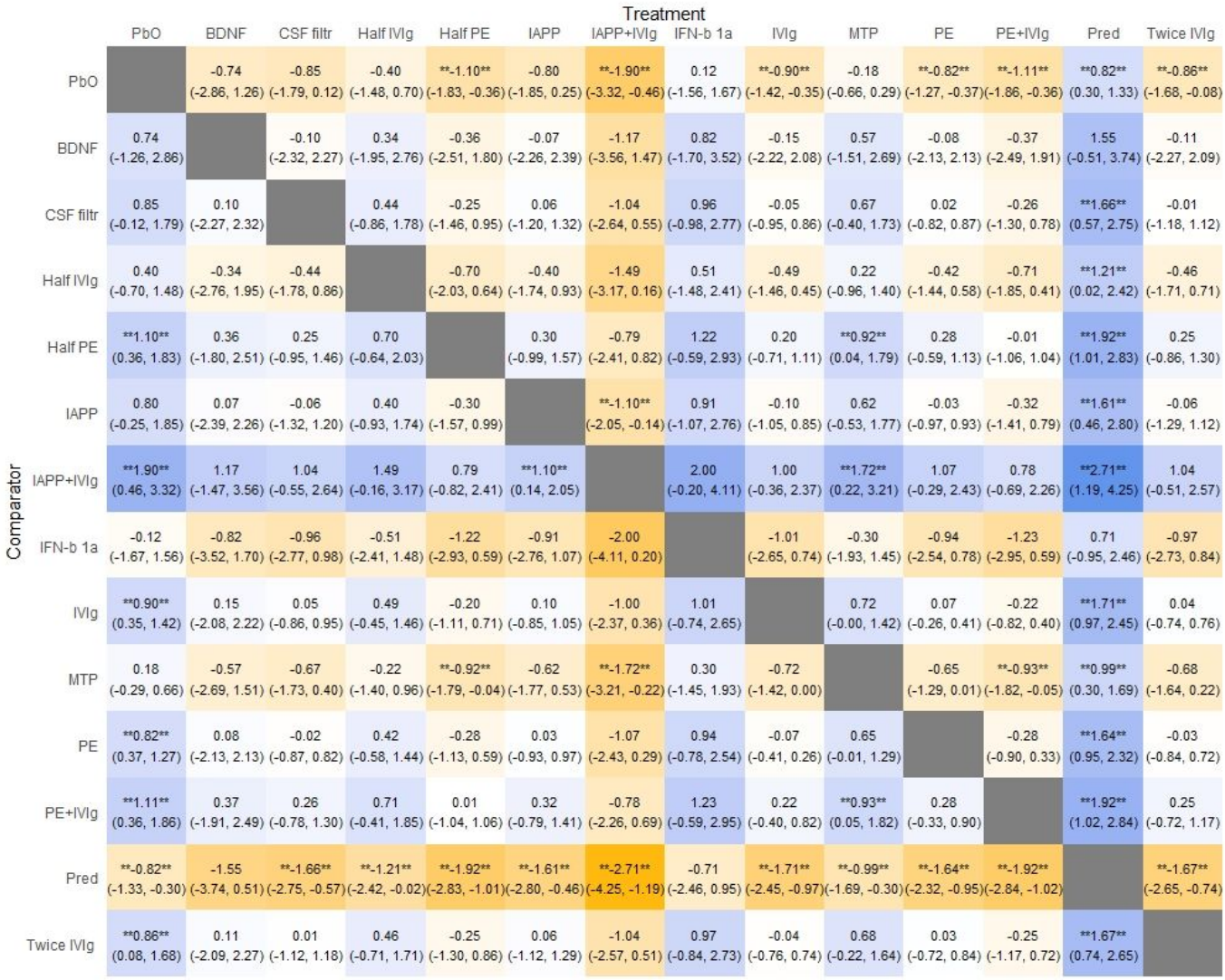

Figure 6

League Table Heatmap Results for outcome Legends: The values in each cell represent the relative treatment effect (and 95% credible intervals) of the treatment on the top, compared to the treatment on the left. A double asterisk indicates statistical significance.

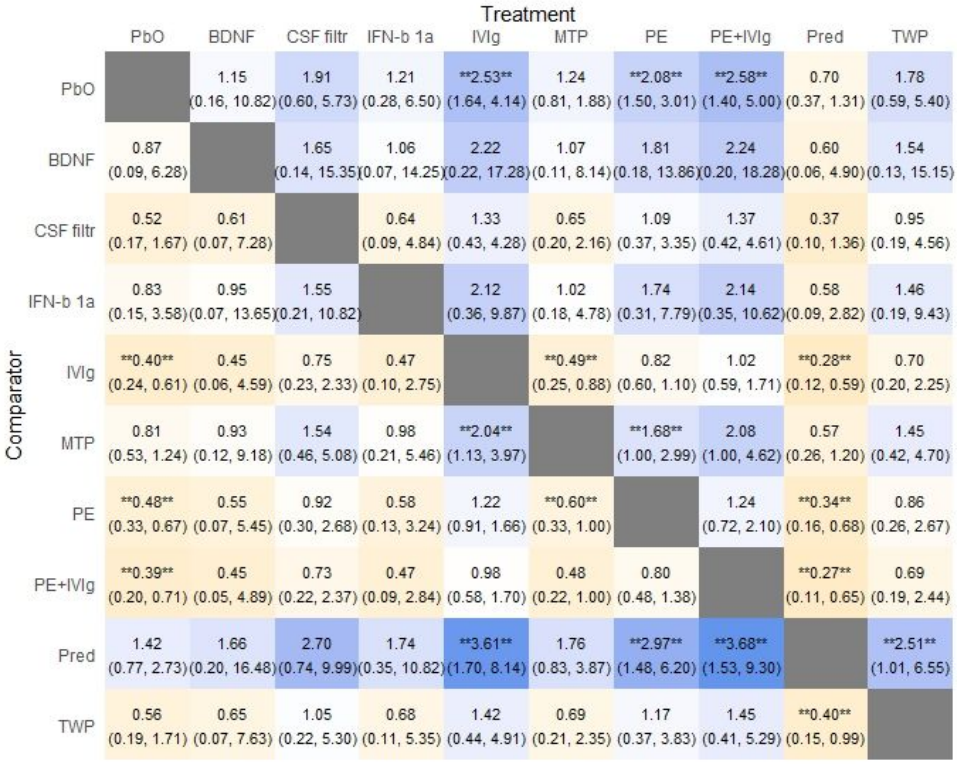

Figure 7

League Table Heatmap Results for outcome Legends are same to Fig 6.

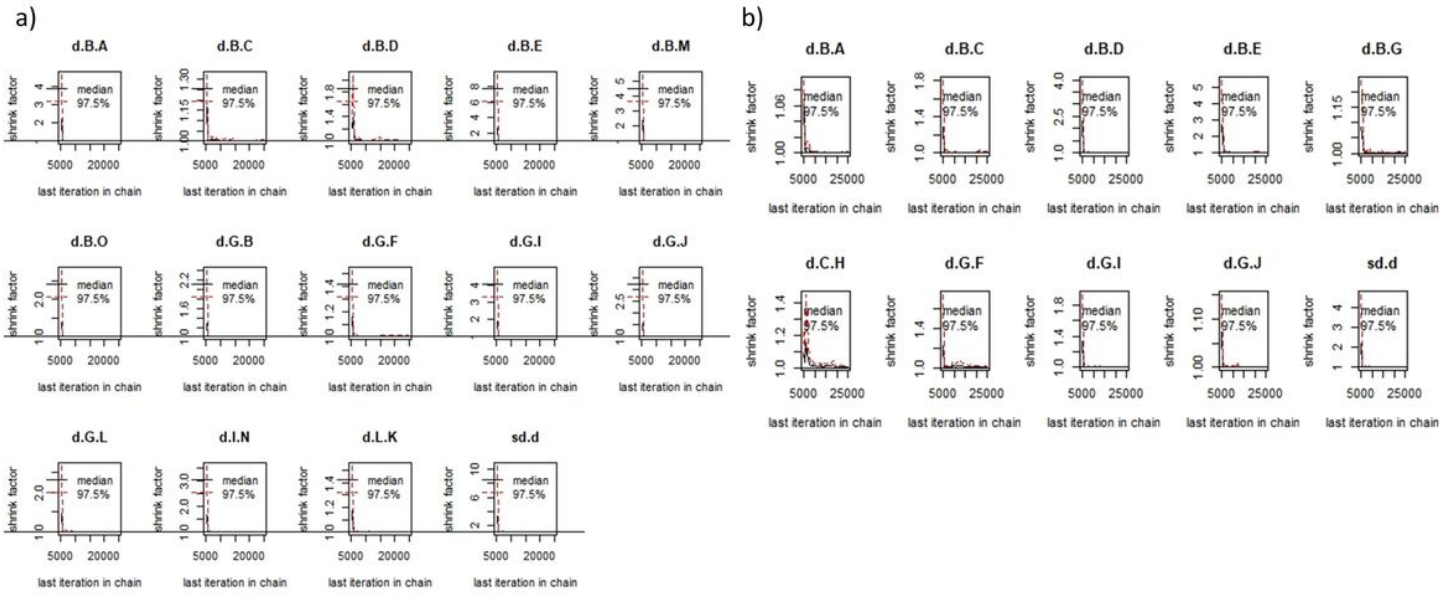

Figure 8

Gelman-Rubin-Brooks plot for NMA. Legends: a)Plot for trials with outcome of Disability grade change after 4 weeks. b): Plot for trials with outcome of the rates of improvement by≥1 grades after 4 weeks.

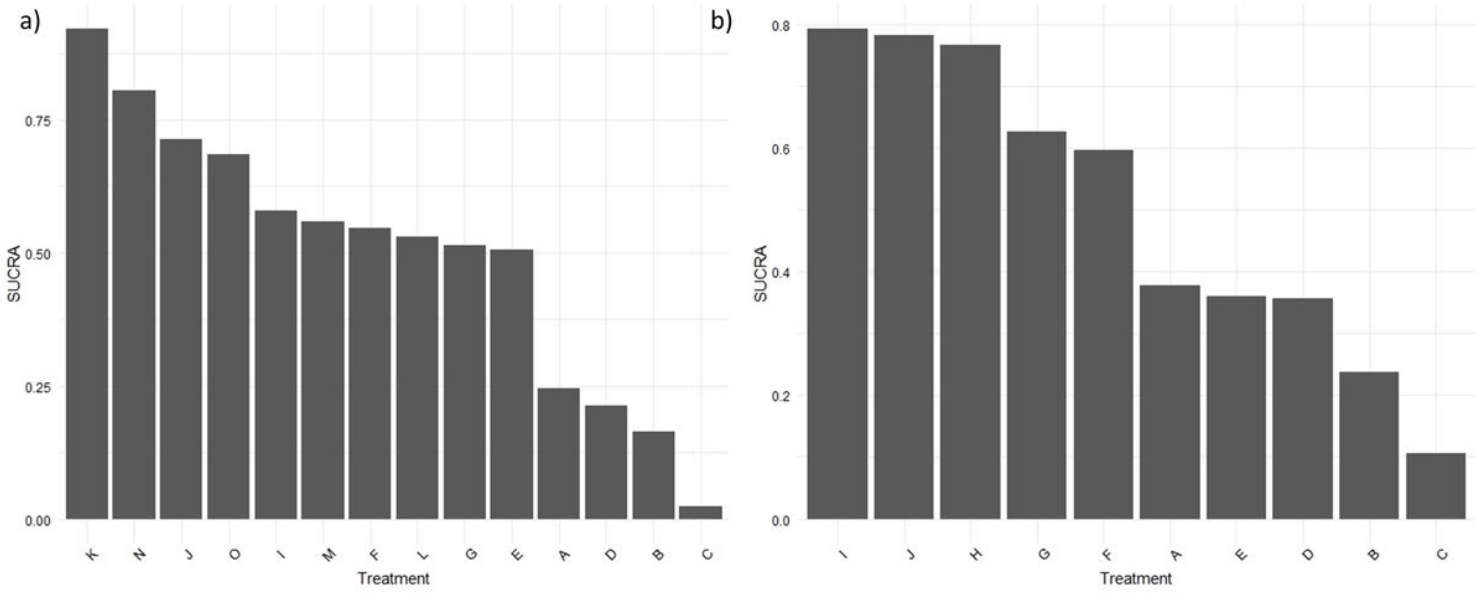

Figure 9

SUCRA value of the treatments(descending order) Legends: a):SUCRA value in outcome A-G, I-J: Same with Fig 4. b): SUCRA value in outcome A-J: Same with Fig 5

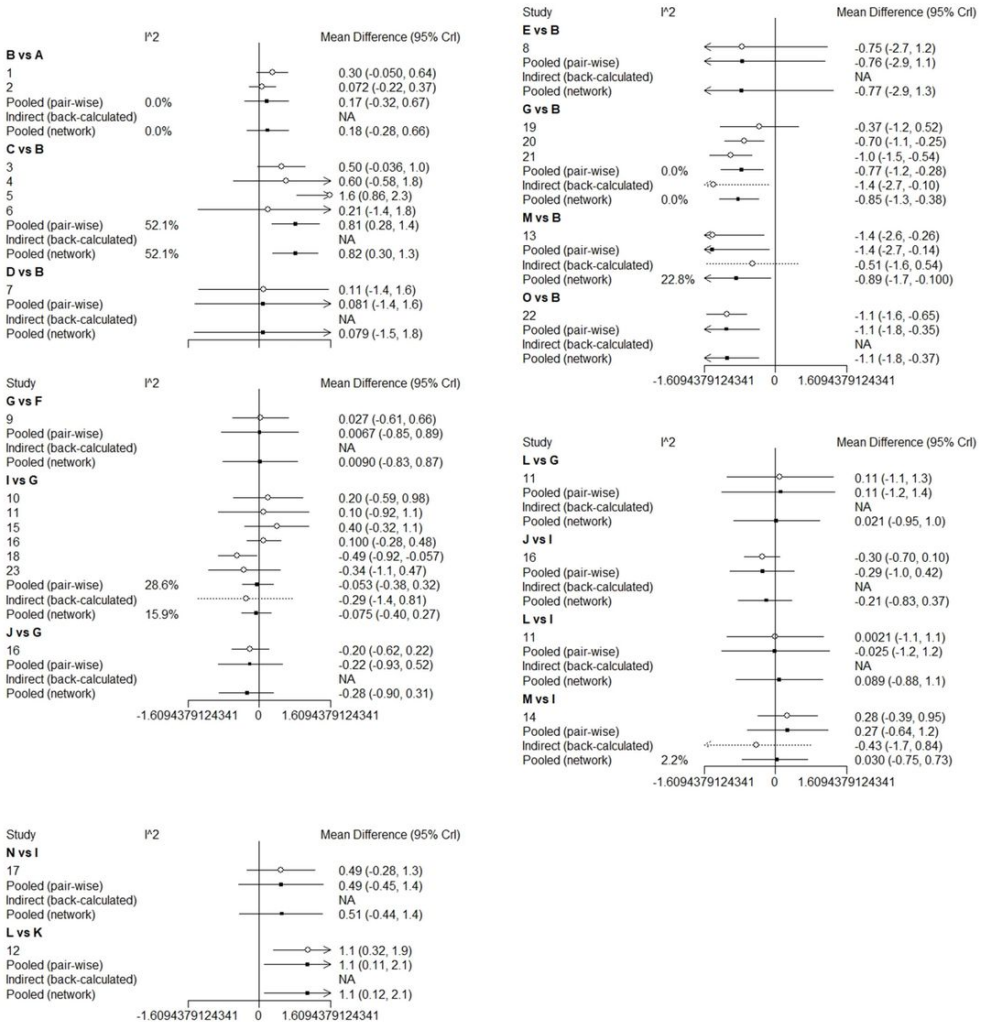

Figure 10

Consistency analysis of outcome Legends: A-G, I-J: Same with Fig 4.

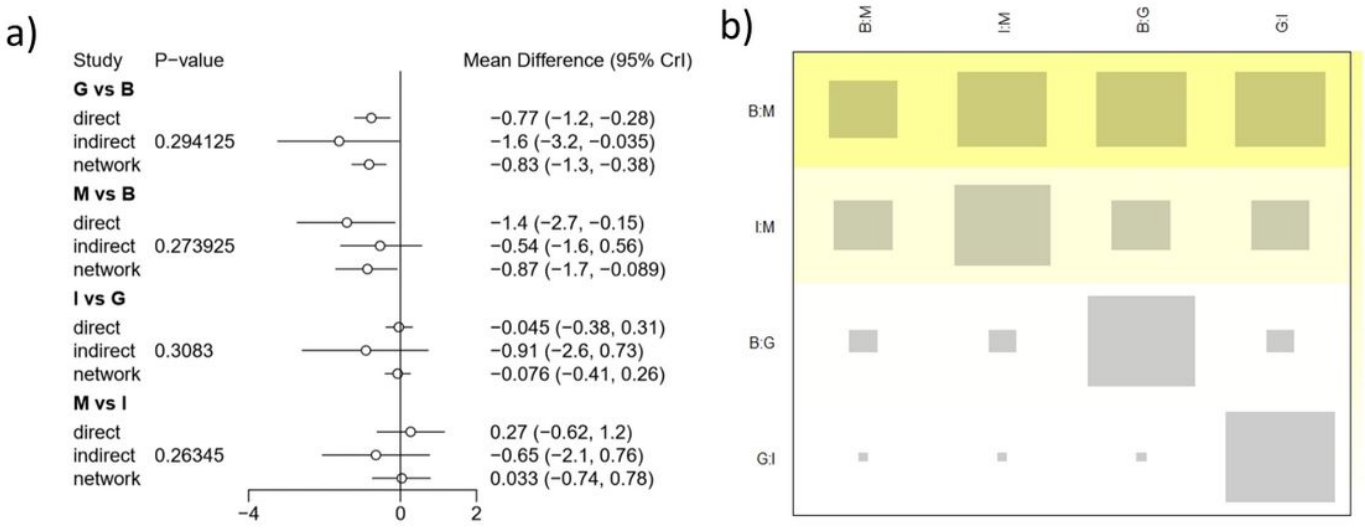

Figure 11

Heterogeneity test of outcome Legends: A-G, I-J: Same with Fig 4.

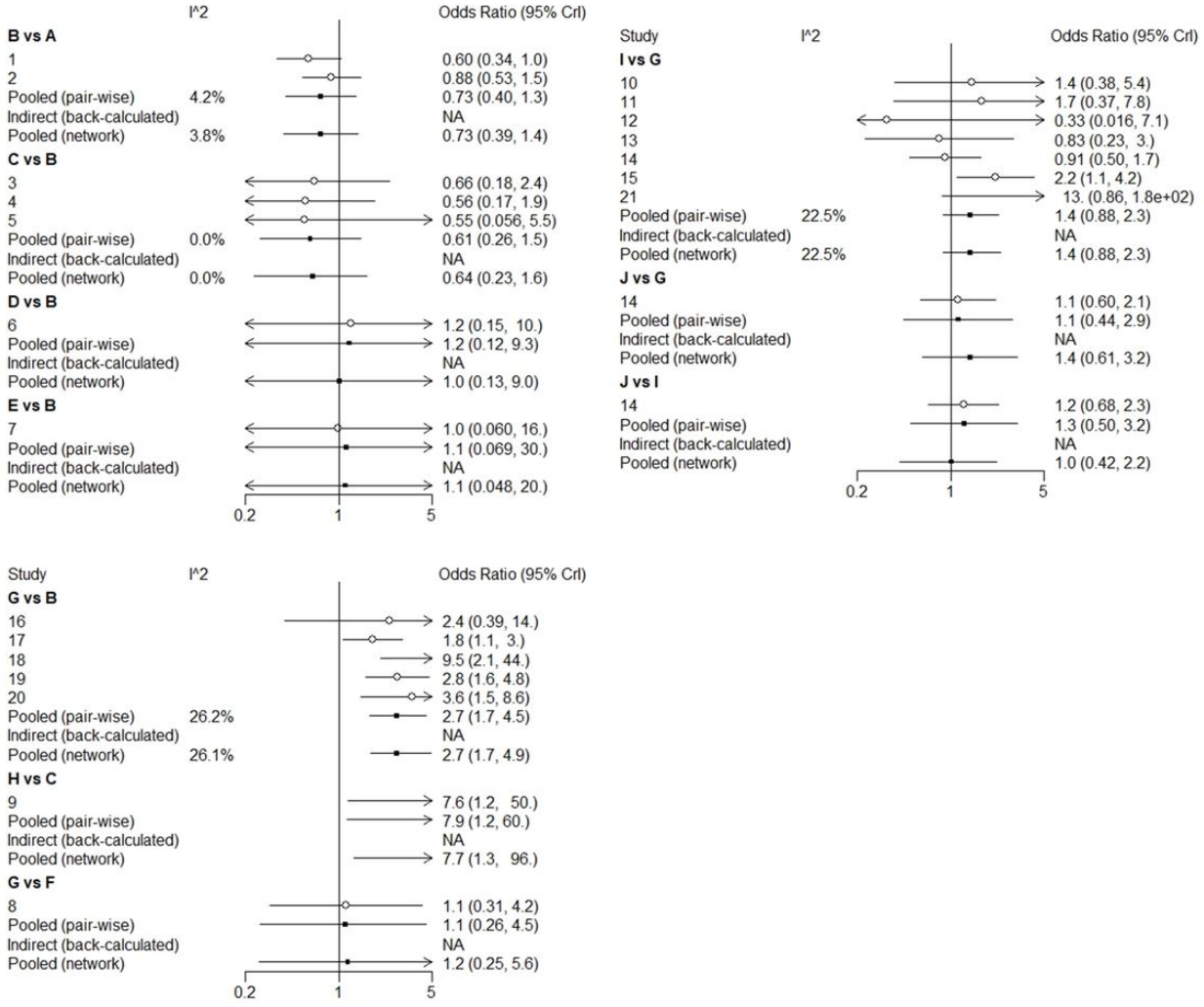

Figure 12

Consistency analysis of outcome Legends: A-J: Same with Fig 4.

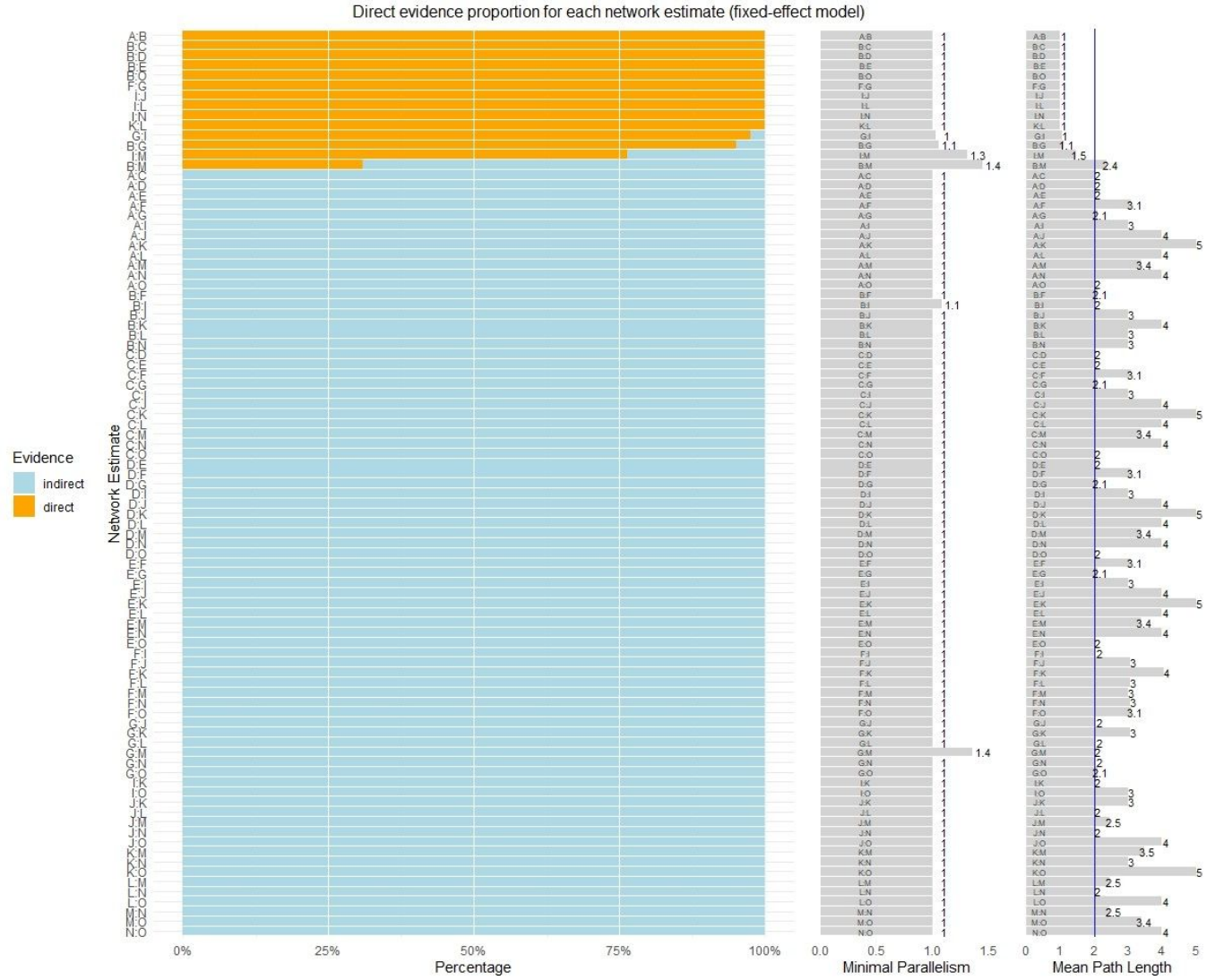

Figure 13

Direct evidence plot for outcome Legends: A-G, I-J: Same with Fig 4.

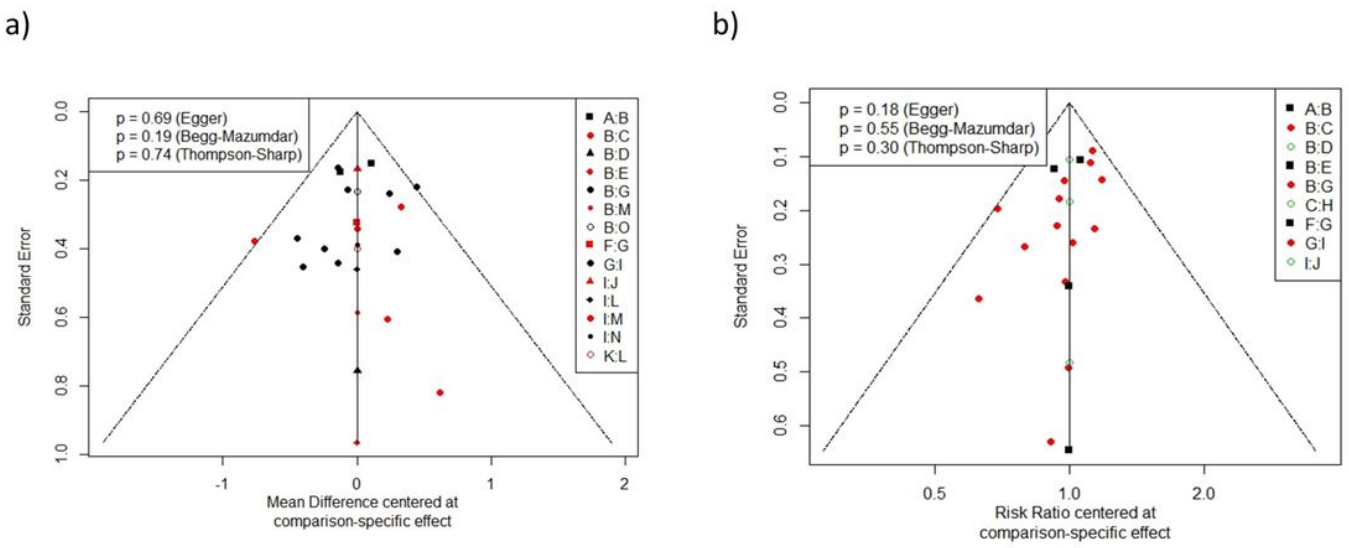

Figure 14

Funnel plots for outcome and outcome

Supplementary Files

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

- Rcodes.txt
- PRISMANMAchecklistNoted.pdf
- test1.csv
- test2.csv