INTERNATIONAL JOURNAL OF DRUG DISCOVERY AND HERBAL RESEARCH (IJDDHR)
2(1): January –March: (2012), 308-322
ISSN: 2231-6078

Research Article

Clinical Effects of Panax Ginseng: A Meta-Analysis Approach

Antoine Al-Achi[1], Ijeoma Uwakwe[1], Brenda Jamerson[1,2] and Robert J. Schmid[1]

1, Campbell University College of Pharmacy and Health Sciences, P.O. Box 1090, Buies Creek, North Carolina 27506

2, Veterans Administration Medical Center, GRECC, Durham, North Carolina

Introduction

Much of the clinical activity of P. ginseng can be attributed to its ginsenosides content.[2] Collectively, the ginsenosides have been shown to have a stimulatory effect on the nitric oxide system in vivo with subsequent effect on the immune system components, the vascular system, and erectile tissues.[2] In addition, ginsenosides have a direct effect on the hypothalamus-pituitary-adrenal axis, as demonstrated in its ability to raise adrenocorticotropic hormone and corticosterone in serum.[1] The main uses of P. ginseng by the public revolve around these mechanisms of action of its ginsenosides: to combat stress,[4,5] improve physical and mental performance,[4,5] improve sexual performance,[5] and as a tonic to improve overall health (rejuvenating and restoring vitality).[2] A recent systematic review of adverse effects and drug interactions of P. ginseng in 146 clinical trials concluded that it is well tolerated in most users; with the most frequently experienced adverse effects (e.g, diarrhea, nausea, insomnia) being mild and reversible.[6] The more severe side effects reported in the literature are tachycardia,[4] hypertension,[4,7] and hypoglycemia.[7,8] The potential of drug/herb interactions considering these adverse events is real since theoretically ginseng could act to either potentiate the effect of hypoglycemic medications or decrease the efficacy of antihypertensive medications.

***Corresponding Author**
E-mail: alachi@campbell.edu
Mob. 910.893.1703

The popularity of P. ginseng use in the United States is on the increase. It is estimated that over six million people in the US use P. ginseng products annually.[4] However, despite the popular use and belief of its usefulness, there is still uncertainty as to whether well conducted clinical studies support the purported clinical effects. In this report, we present a meta-analysis method for evaluating relevant published clinical studies documenting specific clinical effects of this herb. Specifically, we examined if randomized controlled clinical trials provided evidence that P. ginseng improves the immune system components, exercise endurance, well-being, or cognitive function.

Investigational Plan

Study Design

The meta-analysis design is a (note, retrospective is the only kind of meta analysis, right?) meta-analysis review of randomized controlled clinical trials using Panax ginseng in exercise, wellbeing, cognitive and immune system functions. The primary end point was the difference in mean effect between P. ginseng and placebo groups.

Study Population

The inclusion criteria for the articles within each of the four areas evaluated were Jadad Score greater than or equal to 3, P. ginseng as a mono-therapy, full articles, English language, and randomized controlled clinical trial. The exclusion criteria were non-human studies, less than two studies being available to evaluate the endpoint, and study duration of less than 14 days.

Study procedure

Study Search Method

A literature search was performed using the following databases: Pubmed, Ovid, Cinahl, and Cochrane review articles. The keyword for the searches was Panax Ginseng with the limits set for clinical trials and human. Studies that were available between X Date and X date were evaluated. Data collection was done during summer 2006.

Study Selection

A total of 36 randomized controlled studies were found using P. ginseng as mono-therapy (Table 1) for the indications previously identified. Five studies were excluded because they were written in foreign language. One study was excluded because only the citation was available. Two studies were excluded for not discussing the study objectives, 11 studies were excluded for having Jadad score of 2 or less (see below).[9] A total of 17 studies were initially selected for inclusion in this meta-analysis.

Six studies were excluded during the meta-analysis for reason specified in the results section of this report. Figure 1 is a schematic diagram of the study selection procedure. Publication bias was examined by plotting a funnel plot of effect size vs. sample size of the studies. The heterogeneity of the studies was determined using the Q-statistics as described by Deeks et al (see Appendix).[10]

Trial quality scoring

The quality of studies used in this meta-analysis was determined by using the Jadad scoring method.[9] The studies were scored based on inclusion of the following; randomizations, clear method of randomization, double blinding, clear method of blinding, intent- to treat or number of drop-outs mentioned. The maximum points possible are 5 and a score of 3 points or more is required for a study to be classified as a high-quality study. Studies with 2 points or less are classified as low-quality studies."[9] Only studies that scored 3 points and above were used in this meta-analysis. The Jadad scoring of the studies that were used in this meta-analysis are shown in Table 2.

Data Analysis

The meta-analysis was performed using the fixed effects method as described by Deeks et al. [21] The calculations were performed using Comprehensive Meta-Analysis (Biostat, Englewood, NJ). The mean from each study was determined for the variable of interest in each group. A 95% Confidence Interval (CI) on the difference between the means was constructed. A p value of 0.05 or less was considered significant.

Results and Discussion

The aim of this meta-analysis was to determine the potential use of Panax ginseng in therapy by evaluating randomized placebo controlled clinical trials using P. Ginseng as mono-therapy. Specifically, the meta-analysis looked at the effects of P. Ginseng in improving exercise ability, cognitive function, immune system and wellbeing. The results indicated that there could be potential use for P. Ginseng in improving the immune system, as well as improving general health.

A total of 11 studies were included in the final meta-analysis. Figure 2 gives a break down of the study selection for the final meta-analysis, describing the studies included and excluded and reasons. The results from the individual end-points are shown below.

1. Improvement in Exercise

A total of four studies were included for the final meta-analysis for the exercise endpoint. Table 3 describes the studies included and the studies excluded from the final analysis. The outcomes looked at for this endpoint include Volume of oxygen consumption (VO_2), Respiratory exchange ratio (RER), Minute ventilation (VE), Heart rate (HR), Peak anaerobic power, Indexes of habitual physical activity (leisure, sport, work and total activity). The duration of the studies were 8 weeks, and the P. ginseng used were G115 at different doses. P. ginseng was found to be not significantly different from placebo in any of the outcomes (Table 4).

2. Improvement in Immune System Functiont

A total of three studies were included for the final analysis for the immune system function endpoint (Table 5).The duration of the studies ranged from 8-12 weeks. The P.ginseng used in the studies, were either G115 or a standardized P. ginseng extract. The outcomes looked at to determine the effectiveness of P. ginseng in enhancing immune system function include; total lymphocytes, total leukocytes, natural killer cells, % neutrophils, % basophils, % monocytes and, % eosinophils. P. ginseng significantly enhanced the amount of natural killer cells ($p < 0.0001$) and the % basophils ($p < 0.0001$) when compared to placebo. P. ginseng was not significantly better than placebo at enhancing the amount of total lymphocyte, total leukocytes, % neutrophils, % monocytes or % eosinophils (Table 6).

3. Improvement in Cognitive Function

A total of 2 studies were included for the final meta-analysis for the cognitive function endpoint while 2 studies were excluded. Table 7 describes the characteristics of these studies. The duration of the studies ranged from 8-12 weeks. The P. ginseng formulas used were either G115 or standardized P. ginseng extract. To determine if P. ginseng enhanced cognitive function, the following parameters were looked at; auditive reaction time, visual reaction time, finger tapping test and, cancellation test. P. ginseng was not significantly better than placebo in enhancing any of the outcomes (Table 8).

4. Improvement in Well Being

Two studies were included for the final meta-analysis of the well-being endpoint while one study was excluded (Table 9). The duration of the studies ranged from 8-16 weeks. The P. ginseng product used for the studies was G115 at a dose of 200mg/day. The only two outcomes that were used to verify the effects of P. ginseng that was common to both studies were health and vitality. P. ginseng was significantly better than placebo at improving health as measured by X ($p = 0.019$) but was not significantly better than placebo at improving vitality as measured by X (Table10).

Publication Bias analysis

The results of the funnel plot of mean effect size vs. sample size were symmetrical indicating that there was no bias in the publication of the studies using P. ginseng as a mono- therapy (Fig 3).

Heterogeneity Test

The Q statistics performed on the studies to determine if the effect sizes were homogenous indicated that all the studies were homogenous apart from the end-points of % basophils and total lymphocytes which were heterogeneous (see appendix for equations).[13] For the heterogeneous outcomes, a random-effects model was used instead of a fixed model.

Strengths and Limitations of the Study

The results from clinical trials using P. Ginseng as mono-therapy has been equivocal, thus giving rise to the need for this present meta-analysis. The strength of this meta-analysis is that only high quality studies meeting the high standards of Jadad scoring were used in the evaluation. Another strength of this meta-analysis is that only studies using P. Ginseng as mono-therapy were included in the analysis which reduced the confounding factor seen when it is combined with other herbal products.

The limitations of the study include the following:

1) The number of studies utilized for the meta- analysis was limited. For the two (2) end-points where P. Ginseng was found to be significantly better than placebo only two studies were used in the meta-analysis in each case.

2) Only published studies were utilized in this meta-analysis and only studies written in English were used. However, the results of the publication bias indicated that there was no bias in the publication of either positive or negative studies.

3) There are variations in the type and dose of P. Ginseng used in the studies that may have affected the conclusion of this analysis as well as the duration of the studies varied.

4) The method used in measuring the outcomes varied from one study to another.

5) Finally, because this is a meta-analysis, we cannot account for any confounding factors in the individual studies. However, since randomized clinical trials were used, a better control for these confounders might be reasonably expected.

Conclusions

The use of Panax ginseng is on the increase in the general population as the awareness for herbal products and alternative medicines grows. Thus, there is a need for more quality studies to be done using P. Ginseng as mono-therapy especially looking at its effect in improving immune system and general health. This meta-analysis suggests that there is a potential use for P. Ginseng in improving the immune system and general health.

References

1. Briskin DP. Medicinal plants and phytomedicines. Linking plant biochemistry and physiology to human health. Plant Physiol 2000; 124:507-514.
2. Bucci LR. Selected herbals and human exercise performance. Am J Clin Nutr 2000; 72(suppl):624S-636S.
3. Harkey MR, Henderson GL, Gershwin ME, Stern JS, and Hackman RM. Variability in commercial ginseng products: An analysis of 25 preparations. Am J Clin Nutr 2001; 73:1101-1106.
4. O'Hara M, Kiefer D, Farrell K, and Kemper K. A review of 12 commonly used medicinal herbs. Arch Fam Med 1998; 7:523-536.
5. Anonymous. Harvard Men's Health Watch. Harvard Health Online. August 2000.
6. Coon JT and Ernst E. Panax ginseng a systemic review of adverse effects and drug interactions. Drug Safety 2002; 25(5):323-344.
7. Wilkinson JM and Simpson MD. Complementary therapy use by nursing, pharmacy and biomedical students. Nursing and Health Sciences 2001; 3:19-27.
8. Meredith MJ. Herbal nutriceuticals: A Primer for dentists and dental hygenists. The Journal of Complementary Dental Practice 2001; 2(2):1-15.
9. Khan KS, Daya S, Jadad AR. The importance of quality of primary studies in producing unbiased systematic reviews. Arch Intern Med 1996; 156:661-666.
10. Deeks JJ, Altman DG, Bradburn MJ. Statistical methods for examining heterogeneity and combining results from several studies in meta-analysis. In Egger M, Davey SG, Altman DG (ED). Systematic Reviews in health care: Meta-analysis in context (2nd Edition). London: BMJ publication Group, 2001.
11. SAS Institute Inc. JMP IN version 4. Found inside Sall J, Lehman A, Creighton L. JMP Start Statistics A Guide to statistics and data analysis. Second Edition. CA, USA. Duxbury publications 2001.
12. Scaglione F, Cattaneo G, Alessandria M, Cogo R. Efficacy and safety of the standardised Ginseng extract G115 for potentiating vaccination against the influenza syndrome and protection against the common cold [corrected]. Drugs Exp Clin Res. 1996;22(2):65-72.
13. Everitt BS. Statistical Inference. In *Statistical Methods For Medical Investigations.* Second Edition; Halsted Press, New York; 1994.

Table 1. Total number of studies located Using P. ginseng as Mono-therapy

1. Cardinal BJ, Engels HJ. Ginseng does not enhance psychological well being in healthy, young adults results of a double blind placebo. Controlled randomized clinical trial . J Am Diet Assoc. 2001;101:655-660.
2. Xia Z, Liu X, Zhan L, He Y, Luo T, Xia Z. Ginsenosides compound (shenfu) attenuated gastro Intestinal injury and inhibits inflammatory response after cardiopulmonary bypass in patients with congenial heart disease. The Journal of Thoracic and Cardiovascular Surgery. 2005; 130:258-264.
3. Engels H J, Kolokouri I, Cieslak II T J, Wirth J C. Effects of ginseng supplementation on supra maximal exercise performance and short term

recovery. Journal of Strength and Conditioning Research, 2001; 15(3): 290-295.
4. Youl Kang H, Hwan Kim S, Jun Lee W, Byrne HK. Effects of ginseng ingestion on growth hormone, testosterone, cortisol, and Insulin like growth factor 1 responses to acute resistance exercise. J Strength Cond Res. 2002 May;16(2):179-83.
5. Caron MF, Hotsko AL, Robertson S, Mandybur L, Kluger J, White CM. Electrocardiographic and Hemodynamic effects of Panax Ginseng. Ann Pharmacother. 2002 May;36(5):758-63.
6. Suh SO, Kroh M, Kim NR, Joh YG, Cho MY. Effects of Red ginseng upon post operative immunity and survival in patients with stage 111 gastric cancer. The American Journal of Chinese Medicine. 2002;30(4):483-495.
7. Wiklund IK, Mattsson LA, Lindgren R, Limoni C. Effects of standardized ginseng extract on quality of life and physiological parameters in symptomatic menopausal women; a double blind, placebo-controlled trial. Int J Clin Pharmacol Res. 1999;19(3):89-99.
8. Sorensen H, Sonne J. A double – masked study of the effects of ginseng on cognitive functions. Current Therapeutic Research. 1996;57(12) :959-968.
9. Allen JD, McLung J, Nelson AG, Welsch M. Ginseng supplementation does not enhance healthy young aduts peak aerobic exercise performance. J Am Coll Nutr. 1998 Oct;17(5):462-6.
10. Ellis JM, Reddy P. Effects of Panax Ginseng on quality of life. Ann Pharmacother. 2002 Mar;36(3):375-9.
11. Sung H, Kang SM, Lee MS, Kim TG, Cho YK. Korean red ginseng slows depletion of CD4 T cells in Human Immunodeficiency virus Type 1 – infected patients. Clin Diagn Lab Immunol. 2005 Apr;12(4):497-501.
12. Hong B, Ji YH, Hong JH, Nam KY, Ahn TY. A double-blind crossover study evaluating the efficacy of Korean red ginseng in patients with erectile dysfunction. A preliminary report. J Urol. 2002 Nov;168(5):2070-3.
13. Engels HJ, Fahlman MM, Wirth JC. Effects of Ginseng on secretory 1gA, performance and Recovery from internval exercise. Med Sci Sports Exerc. 2003 Apr;35(4):690-6.
14. Cho YK, Sung H, Lee HJ, Joo CH, Cho GJ. Long-term intake of Korean ginseng in HIV- 1- infected patients: development of resistance mutation to Zidovudine is delayed. Int Immunopharmacol. 2001 Jul;1(7):1295-1305.
15. Kim SH, Park KS. Effects of Panax Ginseng extract on lipid metabolism in humans. Pharmacol Res. 2003 Nov;48(5):511-3.
16. Engels H, Said JM, Wirth JC. Failure of chronic ginseng supplementation to affect work performance and energy metabolism in healthy adult females. Nutrition Research. 1996;16(8):1295-1305.
17. Engels HJ, Wirth JC. No ergogenic effects of ginseng (Panax Ginseng C.A. Meyer) during graded maximal aerobic exercise. J Am Diet Assoc. 1997 Oct;97(10):1110-5.
18. Ziemba AW, Chmura J, Kaciuba-Uscilko H, Nazar K, Wisnik P, Gawronski W. Ginseng treatment improves psychomotor performance at rest and during graded exercise in young athletes. Int J Sport Nutr. 1999 Dec;9(4):371-7.
19. Kim SH, Park KS, Chang MJ, Sung JH. Effects of ginseng extract on exercise – induced oxidative stress. J Sports Med Phys. Fitness. 2005;45:178-82.
20. Reay JL, Kennedy DO, Scholey AB. Single doses of Panax Ginseng (G115) reduce blood glucose levels and improve cognitive performance during sustained mental activity. J Psychopharmacol. 2005 Jul;19(4):357-65.
21. Gross D, Shenkman Z, Bleiberg B, Dayan M, Gittelson M, Efrat R. Ginseng improves pulmonary functions and exercise capacity in patients with COPD. Monaldi Arch Chest Dis. 2002 Oct-Dec;57(5-6):242-6.
22. Sotaniemi EA, Haapakoski E, Rautio A. Ginseng therapy in non-insulin-dependent diabetic patients. Diabetes Care. 1995 Oct;18(10):1373-5.
23. Choi HK, Seong DH, Rha KH. Clinical efficacy of Korean red ginseng for erectile dysfunction. Int J Impot Res. 1995 Sep;7(3):181-6.
24. Scaglione F, Ferrara F, Dugnani S, Falchi M, Santoro G, Fraschini F. Immunomodulatory effects of two extracts of Panax Ginseng C.A. Meyer. Drugs Exp Clin Res. 1990;16(10):537-42
25. D'Angelo L, Grimaldi R, Caravaggi M et al. A double-blind, placebo-controlled clinical study on the effect of a standardized ginseng extract on psychomotor performance in healthy volunteers. J Ethnopharmacol. 1986 Apr-May;16(1):15-22.
26. Morris AC, Jacobs I, McLellan TM, Klugerman A, Wang LCH, Zamecnik J. No ergogenic effects of ginseng ingestion. International Journal of Sport Nutrition. 1996;6:263-271.
27. Scaglione F, Cattaneo G, Alessandria M, Cogo R. Efficacy and safety of the standardised Ginseng extract G115 for potentiating vaccination against the influenza syndrome and protection against the common cold [corrected]. Drugs Exp Clin Res. 1996;22(2):65-72.
28. Sung J, Han KH, Zo JH, Park HJ, Kim CH, Oh BH. Effects of red ginseng upon vascular endothelial function in patients with essential hypertension. Am J Chin Med. 2000;28(2):205-16.
29. Kennedya DO, Scholeya AB, Wesnes KA. Dose dependent changes in cognitive performance and mood following acute administration of Ginseng to

healthy young volunteers. Nutr Neurosci. 2001;4(4):295-310.
30. Srisurapanon S, Rungroeng K, Apibal S, et al. The effect of standardized ginseng extract on peripheral blood leukocytes and lymphocyte subsets: a preliminary study in young health adults. J Med Assoc Thai. 1997 Sep;80 Suppl 1:S81-5.
31. A placebo controlled, crossover study of Panax Ginseng in augmentation of antipsychotic treatment in 60 partial treatment- responsive patients with schizophrenia. Chiu SS (citation)
32. Thommessen B, Laake K. Ginseng – No identifiable effect in geriatric rehabilitation. Tidsskr nor laegeforen. 1997 Oct 30; 117(26): 3839-41. (article in Norwegian).
33. Xie FY, Zeng Zf, Huang HY. Clinical observation on nasopharyngeal carcinoma treated with combined therapy of radio therapy and ginseng polysaccharide injection. . Zhongguo Zhong Xi YI Jie He Za Zhi. 2001 May: 21 (5) : 332-4. (article in Chinese).
34. Ding DZ, Shen TK, Cui YZ. Effects of red ginseng on the congestive heart failure and its mechanism. . Zhongguo Xi Yi Jie He Za Zhi. 1995 Jun; 15 (6) : 325-327. (Article in Chinese).
35. Zhan Y, Xu XH, Jiang YP..Protective effects of ginsenoside on myocardiac ischemic and reperfusion injuries. Zhonghua Yi Xue Za Zhi. 1994 Oct ; 74 (10) : 626-8,648 (Article in Chinese).
36. Zhao XZ. Antisenility effect of ginseng Rhizome saponin. Zhong Xi Yi Jie He Za Zhi. 1990 Oct; 10 (10) : 586-9,579.(article in Chinese).

Table 2. The Jadad's Scoring of The studies

#	STUDY AUTHOR	RAN-DOM-IZED	METHOD OF RAN-DOM-IZATION	DOUBLE BLINDED	METHOD OF BLIND-ING	INTENT TO TREAT OR NUMBER OF DROP OUTS MENTIONED	TOTAL JADAD'S SCORE
1	Cardinal B J, et al	1	1	1	1	0	4
2	Xia et al.	1	0	1	0	0	2
3	Engels, et al.	1	0	1	1	1	4
4	Kang et al.	1	0	0	0	0	1
5	Caron MF, et al	1	0	1	0	1	3
6	Suh So, Et al.	1	0	0	0	1	2
7	Wiklund IK, et al	1	0	1	1	1	4
8	Sorensen et al.	1	0	1	1	1	4
9	Allen et al.	1	0	1	1	1	4
10	Ellis JM, et al.	1	1	1	1	1	5
11	Sung H, et al.	0	0	0	0	0	0
12	Hong et al.	1	1	1	1	0	4
13	Engels HJ, et al.	1	0	1	1	1	4
14	Cho YK, et al.	0	0	0	0	0	0
15	Kim S.L, et al.	0	0	0	0	0	0
16	Engels HJ, et al.	1	0	1	1	0	3
17	Engels H.J, et al.	1	0	1	1	1	4
18	Ziemba A.W, et al.	0	0	1	1	0	2
19	Kim SH, et al.	0	0	0	0	0	0
20	Reay J.L, et al.	1	1	1	1	0	4
21	Gross D, et al.	1	1	1	1	1	5
22	Sotaniemi EA, et al.	1	0	1	0	0	2
23	Choi HK, et al.	1	0	0	0	0	1
24	Scaglione f ,et al.	1	0	1	1	1	4
25	D'Angelo L, et al.	1	0	1	1	1	4
26	Morris a,et al.	1	0	1	1	1	4
27	Scaglione f, et al.	1	1	1	1	1	5
28	Jidong sung, et al.	1	0	0	0	1	2
29	Kennedya d o ,et al.	1	1	1	1	0	4
30	Srisuraparion s, et al.	1	0	1	1	0	3
31	Chiu SS	0	0	0	0	0	0

Figure 1. Study selection Decision making Process Diagram.

Study Selection Procedure

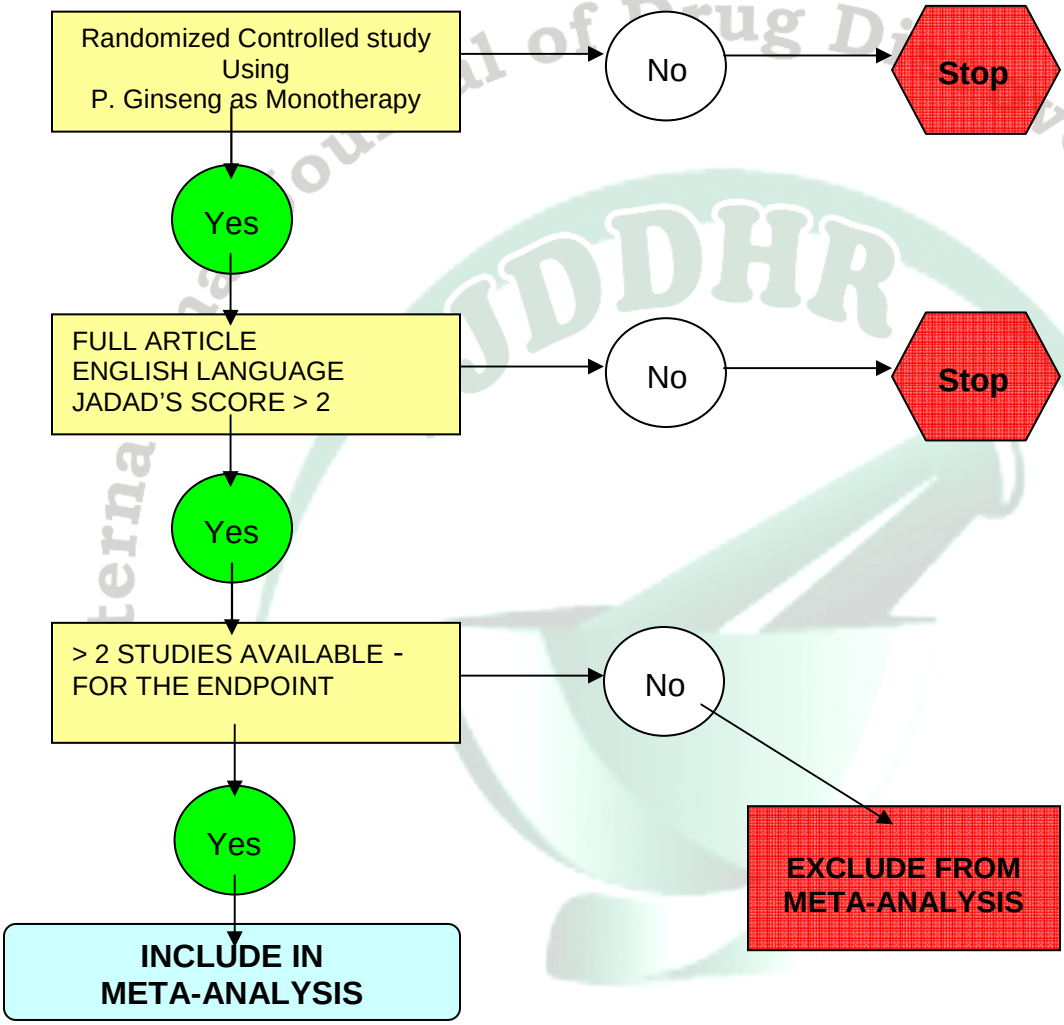


Figure 2. Schematic Diagram of the study selection procedure

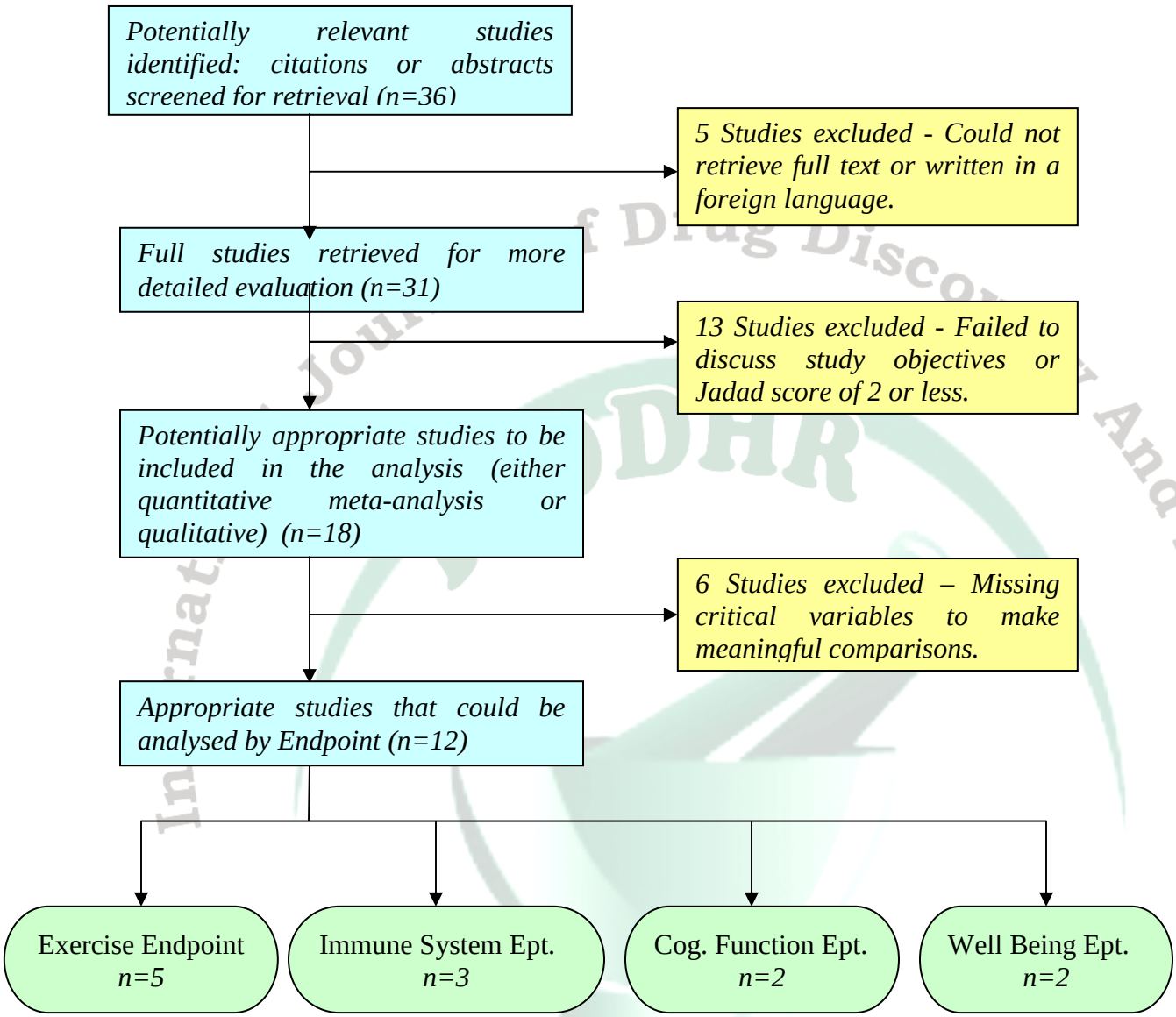


Figure 2 was adapted from Moher et al. "Improving the quality of reports of meta-analyses of randomised controlled trials: the QUORUM statement. Quality of Reporting of Meta-analyses." *The Lancet* 1999 Nov 27; 354(9193): 1896-900.

Table 3. Studies status with regard to their inclusion or exclusion from the analysis.

Studies included for exercise endpoint

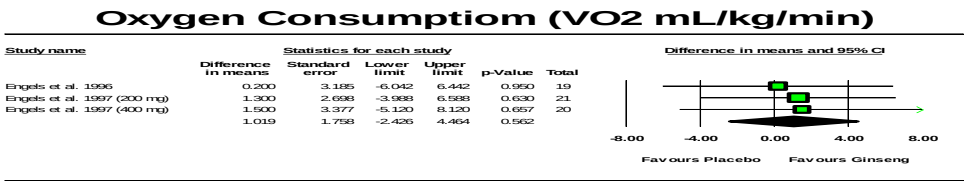
First Author, year (study #)	N	M	F	Mean age	Study Duration	Panax Ginseng Type used/Dose	Jadad's Score
1. Engels et.al 2001 (23)	19	-	-	22.4+-6.0	8 weeks	G115/400mg/day	4
2. Engels et.al 1996 (24)	19	-	-	26.3+-1.4	8 weeks	G115/200mg/day	3
3. Engels et.al 1997 (25)	20	-	-	26.5+-1.2	8 weeks	G115/200mg/day	4
4. Engels et.al 1997 (25)	21	-	-	25.0+-1.2	8 weeks	G115/400mg/day	4
5. Engels et.al 2003 (26)	27	17	10	26.2+-1.8	8 weeks	G115/400mg/day	3

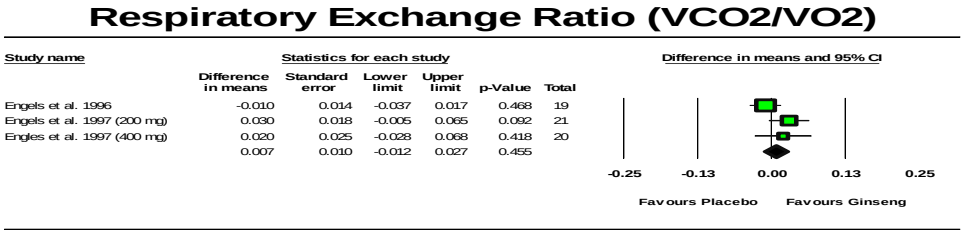
M = male; F= female; N = number of patients.

Studies excluded from final meta-analysis for exercise endpoint.

First Author, year (study #)	Reason for exclusion
Allen et.al. 1998 (27)	Standard deviation not included in results
Morris et.al. 1996 (28)	Duration of study 7 days and Data presentation difficult to extrapolate
Gross et.al. 2002 (29)	Study used COPD patients while the studies included in the analysis used healthy subjects.

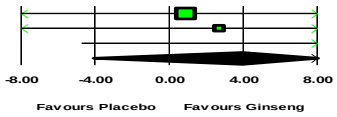
Table 4. Results of the outcome in exercise endpoints.





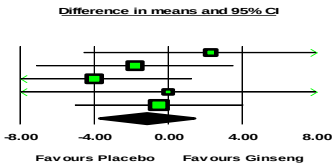
Minute Ventilation (VE) (L/min)

Study name	Difference in means	Standard error	Lower limit	Upper limit	p-Value	Total
Engels et al. 1996	0.900	5.722	-10.314	12.114	0.875	19
Engels et al. 1997 (200 mg)	2.700	10.438	-17.758	23.158	0.796	21
Engels et al. 1997 (400 mg)	9.200	7.113	-4.741	23.141	0.196	20
	3.935	4.100	-4.100	11.971	0.337	



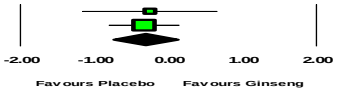
Heart Rate (beats/min)

Study name	Difference in means	Standard error	Lower limit	Upper limit	p-Value	Total
Engels et al. 1996	2.300	3.510	-4.580	9.180	0.512	19
Engels et al. 1997 (200 mg)	-1.800	2.724	-7.139	3.539	0.509	21
Engels et al. 1997 (400 mg)	-4.000	2.696	-9.284	1.284	0.138	20
Engels et al. 2001	0.000	4.199	-8.230	8.230	1.000	19
Engels et al. 2003	-0.500	2.328	-5.062	4.062	0.830	27
	-1.174	1.297	-3.716	1.367	0.365	



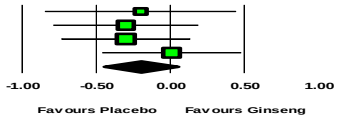
Peak Anaerobic Power (Watts/kg)

Study name	Difference in means	Standard error	Lower limit	Upper limit	p-Value	Total
Engels (2001)	-0.250	0.467	-1.165	0.665	0.592	19
Engels (2003)	-0.330	0.244	-0.809	0.149	0.177	27
	-0.313	0.216	-0.737	0.111	0.148	



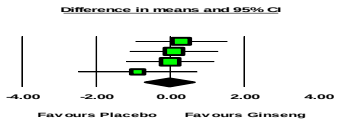
Leisure

Study name	Difference in means	Standard error	Lower limit	Upper limit	p-Value	Total
Engels et al. 1996	-0.200	0.330	-0.847	0.447	0.545	19
Engels et al. 1997 (200 mg)	-0.300	0.251	-0.792	0.192	0.232	21
Engels et al. 1997 (400 mg)	-0.300	0.223	-0.738	0.138	0.179	20
Engels et al. 2001	0.010	0.240	-0.461	0.481	0.967	19
	-0.199	0.127	-0.447	0.049	0.116	



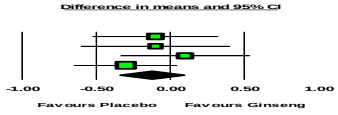
Sport

Study name	Difference in means	Standard error	Lower limit	Upper limit	p-Value	Total
Engels et al. 1996	0.300	0.636	-0.947	1.547	0.637	19
Engels et al. 1997 (200 mg)	0.100	0.613	-1.101	1.301	0.870	21
Engels et al. 1997 (400 mg)	0.000	0.610	-1.195	1.195	1.000	20
Engels et al. 2001	-0.880	0.824	-2.495	0.735	0.285	19
	-0.031	0.328	-0.674	0.612	0.924	



Work

Study name	Difference in means	Standard error	Lower limit	Upper limit	p-Value	Total
Engels et al. 1996	-0.100	0.217	-0.526	0.326	0.645	19
Engels et al. 1997 (200 mg)	-0.100	0.258	-0.605	0.405	0.698	21
Engels et al. 1997 (400 mg)	0.100	0.224	-0.338	0.538	0.655	20
Engels et al. 2001	-0.300	0.179	-0.650	0.050	0.093	19
	-0.126	0.107	-0.336	0.083	0.238	



Total Activity

Study name	Difference in means	Standard error	Lower limit	Upper limit	p-Value	Total
Engels et al. 1996	-0.200	0.882	-1.929	1.529	0.821	19
Engels et al. 1997 (200 mg)	-0.300	0.781	-1.831	1.231	0.701	21
Engels et al. 1997 (400 mg)	-0.100	0.717	-1.506	1.306	0.889	20
Engels et al. 2001	-1.180	0.942	-3.027	0.667	0.211	19
	-0.379	0.408	-1.180	0.422	0.353	

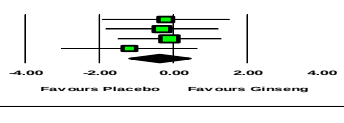
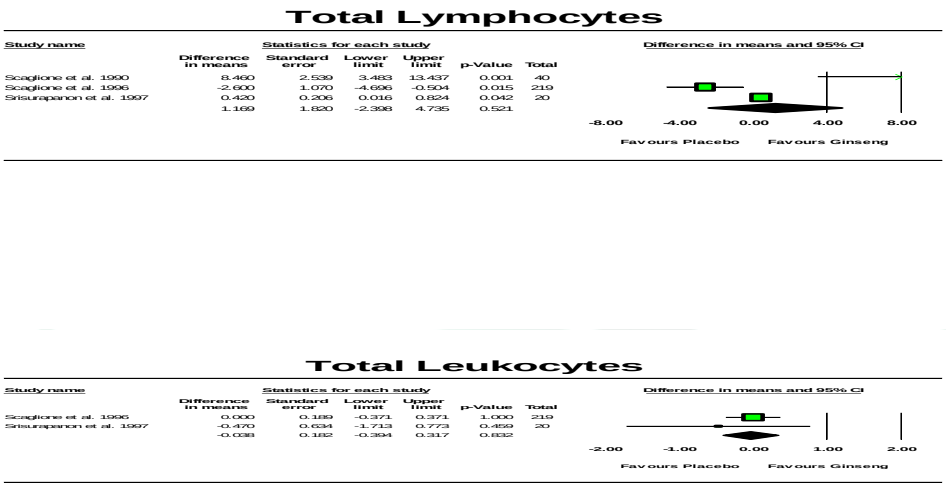


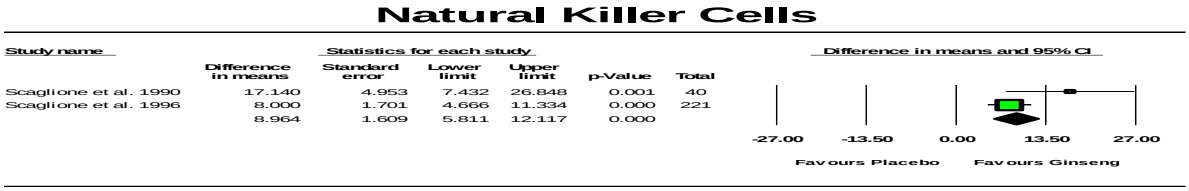
Table 5. Studies Included for Immune System Function Endpoint.

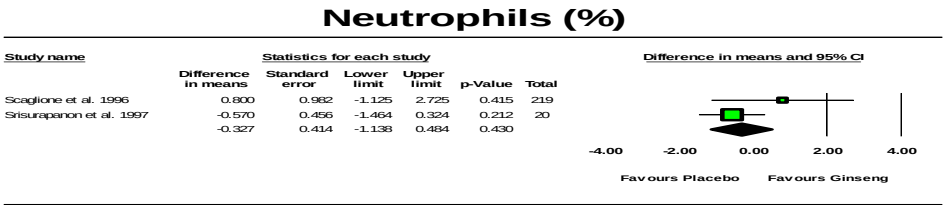
First Author, year (study #)	N	M	F	Mean age	Study Duration	Panax Ginseng Type used/Dose	Jadad's Score
1. Scaglione et.al 1996 (30)	227	66	48	48.5	12 weeks	G115/200mg/day	5
2. Scaglione et.al 1990 (31)	40	-	-	18-50	8 weeks	G115/100mg/day	4
3. Srisura panon et.al 1997 (32)	20	-	-	21-22	8 weeks	Standardized P.ginseng extract/ 300mg/day	3

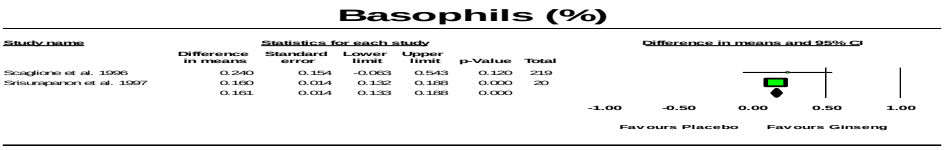
N= number of patients, M= male, F= female.

Table 6. Results from immune system function endpoints.









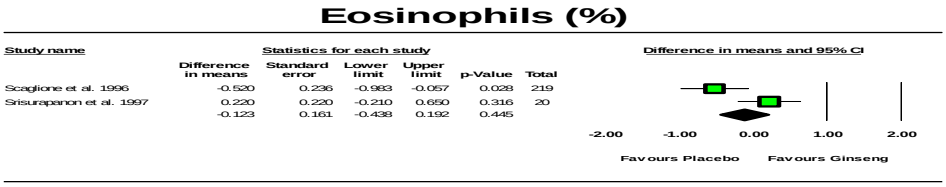


Table 7. Studies Included for Cognitive Function Endpoints

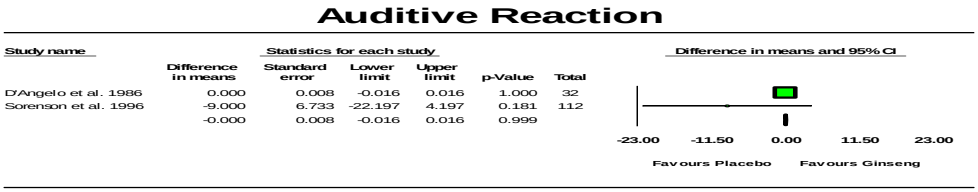
First Author, year (study #)	N	M	F	Mean age	Study Duration	Panax Ginseng Type used/Dose	Jadad's Score
Sorensen et.al. 1996 (33)	112	38	74	51.5+-8.5	8-9 weeks	Standardized P. ginseng extract/400mg	4
D'Angelo et.al. 1986 (34)	32	32	0	20-24	12 weeks	G115/200mg/day	4

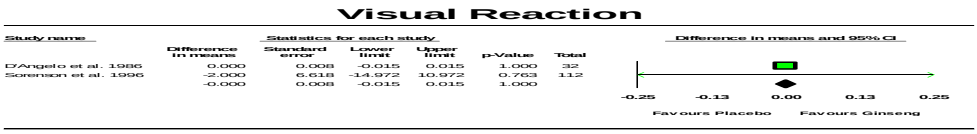
Studies excluded from final cognitive function endpoint final analysis.

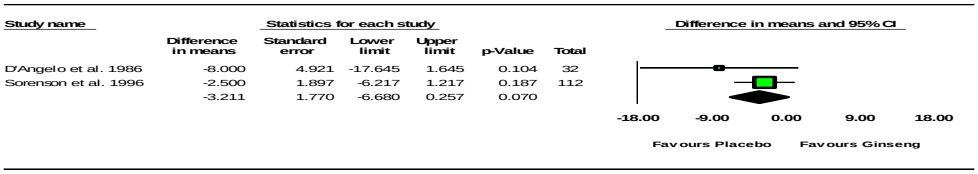
First Author, year (study #)	Reason for exclusion
Reay et.al. 2005 (35)	1day study duration
Kennedy et.al. 2001 (36)	1day study duration

N= number of patients, M= male, F = female.

Table 8. Results from the cognitive function endpoints.







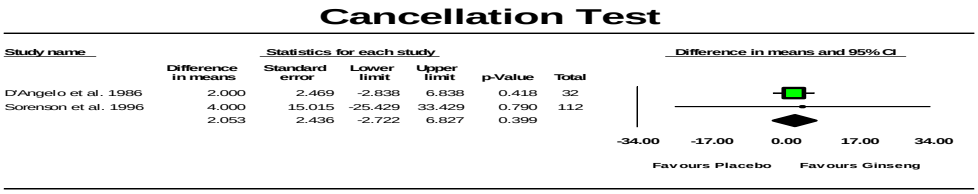


Table 9. Studies Included for Wellbeing Endpoints.

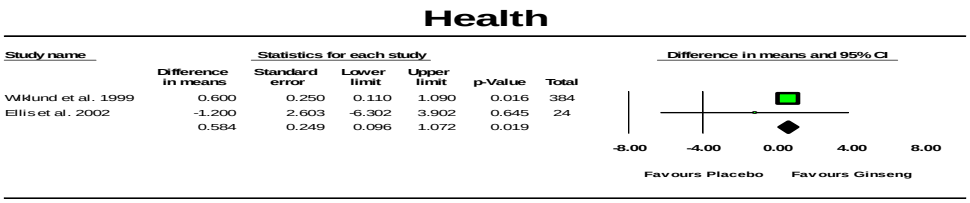
First Author, year (study #)	N	M	F	Mean age	Study Duration	Panax Ginseng Type used/Dose	Jadad's Score
Wiklund et al. 1999 (37)	384	-	384	53.6+-4.0	16 weeks	G115/200mg/day	4
Ellis et al. 2002 (38)	24	-	-	21.6+-2.7	8 weeks	G115/200mg/day	5

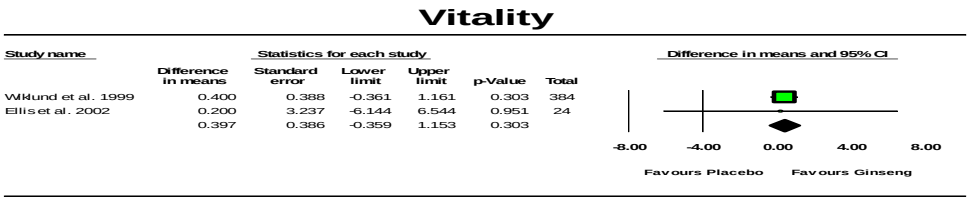
Studies excluded from final analysis for wellbeing endpoint.

First Author, year (study #)	Reason for exclusion
Cardinal et al. 2001(39)	No matching outcome with the studies included in the final analysis

N= number of patients; M= male; F = female

Table 10. Results from well being end points.





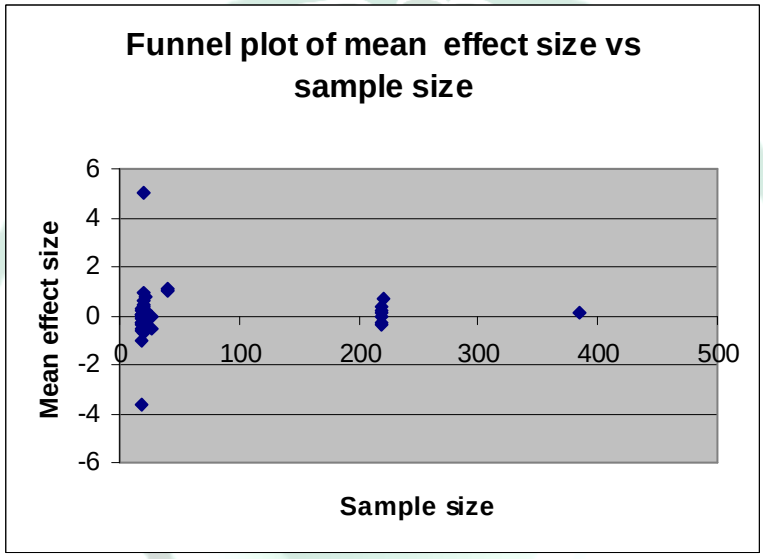


Figure 3: Funnel plot of mean effect size (all end-points) vs. sample size

Appendix

$$Q = \Sigma_{i=1}^{C} W_i (y_i - \bar{y})^2$$

Where,

C is the number of studies

$W_i = (n_{i1}\, n_{i2})/(n_{i1} + n_{i2})$ with n being the sample size for treatment group (1) and control group (2)

$y_i = (X_1 - X_2)/S$ with X_1 and X_2 are the average end-points for the treatment group and control group, respectively; S is the pooled standard deviation:

$$S = \{ [(n_{i1} - 1)(S_{i1})^2 + (n_{i2} - 1)(S_{i2})^2]/(n_{i1} + n_{i2} - 2)\}^{1/2}$$

$$\bar{y} = (\Sigma_{i=1}^{C} W_i\, y_i)/(\Sigma_{i=1}^{C} W_i)$$

The value of Q is compared to a χ^2 distribution with degrees of freedom of (C – 1) for significance ($\alpha = 0.05$).