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Effect of Dietary Interventions on Blood Pressure: A Systematic Review and Meta-Analysis of Randomized Controlled Trials

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Effect of Dietary Interventions on Blood Pressure: A Systematic Review and Meta-Analysis of Randomized Controlled Trials

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Abstract

Effect of Dietary Interventions on Blood Pressure: A Systematic Review and Meta-Analysis of Randomized Controlled Trials
By Hawkins C. Gay

Importance: Previous studies have shown a beneficial effect of dietary strategies for blood pressure control, but their relative effectiveness is not well established.

Objective: To conduct a systematic review and meta-analysis of different dietary interventions on blood pressure control and assess their comparative effectiveness.

Data Sources: PubMed, EMBASE and Web of Science databases were searched to identify studies published between January 1, 1990 and February 28, 2015.

Study Selection: All studies met the following inclusion criteria: (i) randomized, controlled trial design; (ii) adult participants (≥ 19 years); (iii) dietary intervention aimed at improving health; (iv) control group receiving standard follow-up or advice only; (v) ability to collect or calculate mean difference in systolic or diastolic BP; and (vi) duration of at least six months. Exclusion criteria included the following: (i) secondary causes of hypertension; (ii) congestive heart failure; (iii) overlapping participants; (iv) intervention consisting of nutritional supplements only.

Data Extraction and Synthesis: Data was collected regarding study design, participant demographics and baseline characteristics, dietary details, and outcomes. The data were pooled using a random effects model.

Main Outcomes and Measures: Net differences in systolic and diastolic BP associated with various dietary interventions.

Results: 24 trials with 23,858 total participants were included. The overall pooled net effect of dietary intervention on systolic BP and diastolic BP was -3.07 mmHg (95% CI, -3.85 to -2.30; $P < 0.001$) and -1.81 mmHg (95% CI, -2.24 to -1.38; $P < 0.001$), respectively. The Dietary Approaches to Stop Hypertension diet had the largest effect and was associated with a net change in systolic BP of -7.62 mmHg (95% CI, -9.95 to -5.28; $P < 0.001$) and diastolic BP of -4.22 mmHg (95% CI, -5.88 to -2.57; $P < 0.001$). Low sodium; low sodium, high potassium; low sodium, low calorie; and low calorie diets also led to significantly lower systolic and diastolic BP, while the Mediterranean diet was associated with a significant reduction in diastolic BP but not systolic BP.

Conclusions and Relevance: Dietary modifications are associated with lower BP and could be useful as an alternative to pharmacologic therapy in some situations.

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BACKGROUND

Hypertension, or high blood pressure (BP), is a major public health concern as it is the principal risk factor for cardiovascular diseases (CVD), which are the leading causes of mortality in the United States and throughout the world (1). This disease affects roughly 77 million adults in the US (~33% of the population >20 years of age), and there is a higher prevalence among some race/ethnic groups; in particular, it is projected that up to 45% of African Americans are hypertensive. It is further estimated that only 53% of Americans with hypertension have their disease controlled to the level recommended in the most recent guidelines, which further increases the public health and economic burden of hypertension (2). Cumulatively, the annual direct and indirect costs associated with CVD in the US amount to almost $316 billion. Increased awareness, prevention, and treatment of hypertension could lead to significant cost savings within the healthcare industry (2).

Numerous observational epidemiologic studies have demonstrated the relationship between lifestyle factors (dietary components or patterns, physical activity or inactivity, tobacco and alcohol use) and the occurrence of hypertension (3-7). Furthermore, although many clinical trials have established the effectiveness of pharmacologic therapy, concerns about potential medication side effects and the total cost of prescription requirements have led to increased interest in behavioral interventions (8, 9). Current clinical guidelines recommend healthy lifestyle changes as the initial treatment for those with prehypertension, and also as a complementary aspect of pharmacologic therapy for all other stages (3, 9).

To date, there have been a number of clinical trials, meta-analyses and systematic reviews looking into the various lifestyle therapies aimed at controlling high blood pressure (10-18). Many studies have focused on specific elements within the diet, such as sodium and potassium, while more recent trials, including the Dietary Approaches to Stop Hypertension (DASH), have concentrated on participants adopting a more comprehensive nutritional program (17). Some dietary interventions are also aimed at total calorie reduction and weight loss, and therefore may have additional benefits beyond that provided by the change in nutritional components consumed. Although these studies have presented the positive effects associated with individual dietary programs for BP management, there has been a lack of research comparing these competing dietary modifications and measuring their relative effectiveness. The aim of this meta-analysis was to quantify the aggregated BP-lowering effects associated with dietary modifications, as well as to compare the relative BP changes observed between specific dietary patterns.

METHODS

The authors developed and wrote a protocol standardizing study processes before proceeding with the literature search and analysis. The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement was used to guide data extraction and reporting of results (19).

Study Selection

A systematic and comprehensive review of the literature was conducted utilizing PubMed (US National Library of Medicine), EMBASE (Elsevier B.V.) and Web of Science (Thomson Reuters) databases to identify relevant studies that were published within the last 25 years (after January 1, 1990). Search terms included "hypertension" and "life style" or "low salt" or "low sodium" or "diet" or "physical activity" or "exercise" or "weight loss" in all fields and with associated Medical Subject Headings (MeSH terms). The search was further limited to "humans" and "adults" and "randomized controlled trials" or "controlled clinical trials." Additional searches were conducted by manually reviewing references from eligible articles, relevant systematic reviews and meta-analyses, and through discussions with clinical experts.

Two investigators (HG and SR) independently screened all titles and abstracts to determine whether articles were eligible for inclusion in the meta-analysis. In cases of discordance of opinion, a third author was consulted to achieve consensus and resolve the discrepancy. Studies published between January 1, 1990 and February 28, 2015 fulfilling all of the following criteria were eligible for inclusion: (i) used a randomized, controlled trial design; (ii) enrolled adult participants (aged $\geq$ 19 years); (iii) tested an intervention that consisted of a dietary change aimed at improving health (though not specifically

blood pressure); (iv) had a comparison group following a standardized control diet, advice only, or regular follow up with no specialized intervention; (v) reported net change in SBP and/or DBP (or the information with which to calculate these data) and its associated variance, confidence intervals, or *P* value; and (vi) had a duration of at least six months. Reasons for exclusion included: (i) trials conducted in populations with secondary causes of hypertension, i.e. chronic kidney disease, renal vascular disease, or certain endocrine disorders; (ii) trials conducted exclusively in patients with congestive heart failure (these patients are regularly on multiple medications that affect blood pressure); (iii) trials with overlapping participants; (iv) trials of simple nutritional supplements (i.e. fish oil or docosahexaenoic acid) as opposed to alteration of dietary consumption; and (v) lack of an appropriate control group or a control that consisted of another dietary intervention. There was no sample size requirement for inclusion or exclusion.

Data Extraction

Original articles were retrieved to extract the following study characteristics using a standardized entry database: primary author, date of publication, title, country of origin, sample size, participant demographics, participant health status (i.e. diabetes, coronary artery disease, etc.), use of antihypertensive medication, dietary intervention details, any physical activity details, setting, duration of follow-up for all reported measurements, method of BP ascertainment, effect size, weight loss, and bias assessment. If BP measurements were reported at multiple points in time, data were analyzed for the period of longest follow-up. Some individual studies examined several unique dietary interventions versus a common control; when this was the case, each intervention was

considered as a separate comparison against the control group. In cases where incomplete data were presented in the published article, authors were contacted in an effort to obtain the missing information.

Studies were categorized into sub-classes of dietary intervention based on the approach examined in the trial. DASH diets followed a protocol that increased consumption of fruits, vegetables, low-fat dairy, whole grains, lean meats (fish and poultry), nuts and beans, as well as a reduced intake of red meat and fat. Mediterranean diets were characterized by reduced saturated fat consumption in favor of other monounsaturated and n-3 fatty acids from nuts, olive oil, and fish, as well as an increased amount of grains, vegetables, and fruits, with decreased levels of red meat. Low sodium diets entailed consuming below 2.3g (100 mmol/day) of total daily sodium. High potassium diets had this as a stated objective of the trial. Low fat diets required that less than 30% of total calories be consumed from fat. Low calorie diets adjusted the daily caloric intake to reduce weight by at least 4.5 kg or 5% of total body weight. When more than one dietary component was included in the comparison group, the study was categorized as a combined intervention, e.g. as a low sodium, high potassium diet.

Statistical Analysis

Net change in BP over the duration of follow-up, between intervention and control groups, was calculated by subtracting the change in the control group (from baseline to follow-up) from the change in the intervention arm (from baseline to follow-up): $(I_{fu} - I_b) - (C_{fu} - C_b)$. Treatment effects for each trial were weighted by the inverse of the variance (SE for the net change). If not reported directly, SEs were derived from the confidence intervals or *P* values of the net change, or by calculation from the

individual SD or SE of effects within parallel groups (assuming a correlation of 0.5 between variances at baseline and follow-up, as described by Follmann et al) (20). The overall estimated mean effect size of diet on blood pressure was pooled across trials using a random effects model to account for the heterogeneity between studies with regard to the intervention and study design, as well as participant ethnicity, age, sex, health status, and other important co-variables. Heterogeneity was quantitatively assessed using *Q* and I^2 statistics.

A number of pre-planned subgroup analyses were conducted based on current knowledge and the results of previous studies regarding BP behavior in these groups. These a priori sub-analyses involved examining differences in BP change by: pre-existing hypertensive status, antihypertensive use, age (<50 vs ≥50 years), gender (<50% vs ≥50% male), pre-existing diabetic status, study duration (<12 vs 12-24 vs >24 months), study sample size (<100 vs 100-1,000 vs >1,000 participants), BMI at baseline (<30 vs 30-35 vs >35 kg/m^2), the presence or absence of recommended physical activity, and whether BP reduction was considered a primary outcome of the trial. Pooled effect size for subgroups were determined using a random effects model, and analysis of variance (ANOVA) was used to determine the statistical significance of differences between subgroups. Additionally, meta-regression analyses were conducted to examine the impact of weight reduction (when reported) on net effect size, as weight loss has been shown to be independently correlated with BP change (11).

Comprehensive Meta-Analysis, version 3 (Biostat, Englewood, NJ), was used to perform the meta-regression and subgroup analyses, and Review Manager, version 5

(The Cochrane Collaboration, Nordic Cochrane Centre, Copenhagen, Denmark) was used for all other analyses.

Bias Assessment

The Review Manager risk of bias table was used to evaluate any potential methodological concerns amongst the included studies. Each trial was judged for: potential selection bias (random sequence allocation and allocation concealment), performance bias (blinding of participants and personnel), detection bias (blinding of outcome assessors), attrition bias (incomplete outcome data), and reporting bias (selective reporting). Within these categories, each trial was classified as low, high, or unclear on the risk of bias scale. The presence of publication bias was assessed via creation of funnel plots, by plotting the SE against the effect size for each study.

RESULTS

Selection Process and Study Characteristics

The initial search returned 3,201 studies once duplicates were removed. Figure 1 shows the number of studies identified and excluded at various stages of the selection process. Ultimately, 24 individual trials were included in the analysis. From these trials, there were a total of 39 comparison groups (39 unique intervention groups and 27 control groups) with 23,858 total participants.

Characteristics of the 24 trials with their respective interventions and participants are detailed in Table 1. Intervention arms varied in size from 11 to 2,570 participants (median of 129). Trial duration ranged from the minimum included length of 6 months to 48 months of follow-up (median of 12 months). 21 of the 36 comparison groups that reported sex distribution were predominantly male. 10 trials were conducted in the US and 14 were based internationally. Race distribution was not consistently reported in trials conducted outside of the US, while race was predominately white in all US studies. Comparison groups had a mean age range of 34 to 67 years (median of 45 years). There were 20 trials that reported hypertension status at baseline; among them, 14 comparisons were conducted in exclusively hypertensive patients with another 11 comparisons composed of a mix of hypertensive and normotensive patients. 10 studies with 14 comparison groups included patients who were taking blood pressure medication at baseline; in 4 of these comparison groups, 100% of participants were receiving an antihypertensive. The mean body mass was index (BMI) was in the overweight range (25 - <30) in 22 comparison groups and the obese range (≥30) for all others (14 comparison groups). There were 3 comparison groups with exclusively diabetic

participants and 14 comparisons composed entirely of non-diabetics. The average pre-treatment SBP and DBP ranged from 123.7 to 158.0 mmHg (mean of 136.2 mmHg) and 69.9 to 101.0 mmHg (mean of 85.7 mmHg), respectively.

Change in Blood Pressure

Forrest plots for the net change in SBP and DBP are presented in Figure 2. Net change in SBP and DBP varied from -12.10 to 7.00 mmHg and -9.32 to 0.20 mmHg, respectively. The overall pooled net effect (change in intervention minus change in control) of diet on SBP was -3.07 mmHg (95% CI, -3.85 to -2.30; $P < 0.001$) and DBP was -1.81 mmHg (95% CI, -2.24 to -1.38; $P < 0.001$).

Results varied when trials were grouped according to different dietary interventions, as detailed in Figure 3. The largest net effect (change in intervention minus change in control) on BP was seen in the DASH diet category, where there were 4 trials with a total of 5 comparison groups in which the pooled net change in SBP and DBP was -7.62 mmHg (95% CI, -9.95 to -5.28; $P < 0.001$) and -4.22 mmHg (95% CI, -5.88 to -2.57; $P < 0.001$), respectively. 5 comparison groups from 4 trials examined the effects of a Mediterranean diet, which led to a pooled net change of -1.17 mmHg (95% CI, -2.81 to 0.46; $P = 0.16$) in SBP and -1.44 mmHg (95% CI, -2.11 to -0.76; $P < 0.001$) in DBP. Low sodium diets (6 comparison groups) led to a pooled net decrease in SBP and DBP of -2.06 mmHg (95% CI, -3.50 to -0.68; $P = 0.005$) and -1.30 mmHg (95% CI, -2.37 to -0.23; $P = 0.02$), respectively. Low sodium combined with high potassium diets (5 comparison groups) decreased pooled net SBP by -3.14 mmHg (95% CI, -6.27 to -0.02; $P = 0.05$) and pooled net DBP by -2.01 mmHg (95% CI, -3.40 to -0.63; $P = 0.004$), whereas low sodium combined with low calorie diets (5 comparison groups) decreased

SBP by -2.39 mmHg (95% CI, -3.79 to -0.98; $P < -0.001$) and DBP by -1.33 mmHg (95% CI, -2.03 to -0.63; $P < 0.001$). Low calorie diets (some with low fat components) made up 13 comparison groups from 11 trials and reduced the pooled net SBP by -3.18 mmHg (95% CI, -4.24 to -2.11; $P < -0.001$) and DBP by -1.28 mmHg (95% CI, -1.88 to -0.69; $P < -0.001$).

Subgroup Analysis and Meta-Regression

Table 2 summarizes the pooled effects observed in different subgroups. All subgroups experienced statistically significant BP reductions except the following: (i) SBP, diabetics ($P = 0.16$); (ii) SBP, baseline BMI >35 ($P = 0.16$); and (iii) SBP, participant size >1,000 ($P = 0.08$). Larger BP reductions were noted in populations who had pre-existing hypertension at the beginning of the trial compared to those with a baseline BP in the normal range. This was statistically significant both for SBP ($P = 0.034$) and DBP ($P = 0.016$) reductions. Similarly, populations who were not already taking antihypertensive medications experienced significantly greater declines in mean BP, both for SBP ($P = 0.011$) and DBP ($P = 0.008$), than those including individuals receiving pharmacologic therapy. Groups with longer follow-up (>24 months) had a significantly smaller effect size then those with medium (21-24 months) and short (<12 month) follow-up, $P < 0.001$ for both SBP and DBP. Smaller trials (n < 100) had a larger net effect then studies of medium (n = 100-1,000) and large (n > 1,000) sizes; this effect was statistically significant for both SBP ($P <0.001$) and DBP ($P = 0.001$). There were significantly smaller net effects for both SBP ($P = 0.050$) and DBP ($P = 0.037$) in trials where the main outcome measure was BP reduction. Blood pressure change was not

significantly different based across participants of different age, gender, diabetes status, baseline BMI, or in trials which encouraged physical activity.

There were 30 comparison groups reporting net weight loss (change in intervention minus change in control) with a range of -16.00 to 1.4 kg and median of -2.90 kg. Meta-regression analysis (Figure 4) showed a significant relationship between mean weight loss and net change in both SBP ($P < 0.001$) and DBP ($P = 0.013$). Specifically, for every 1 kg of weight loss experienced, there was an associated 0.36 mmHg additional reduction in SBP (95% CI, 0.20 to 0.52) and a 0.13 mmHg reduction in DBP (95% CI, 0.03 to 0.24).

Bias Assessment

Funnel plots (Figure 5) of the SE versus the effect size for each study demonstrate that the distribution of the effect size estimates for individual comparison groups was approximately symmetrical around the pooled estimate. This suggests there is a low likelihood of publication bias influencing the results observed. Potential methodologic biases are detailed in Figure 6. Studies mostly generated low risk of bias, though some studies suffered from the standpoint that there was an inability to appropriately assess risk of bias in a number of categories.

DISCUSSION

This meta-analysis of 24 randomized controlled trials (RCTs), covering studies over a 25 year period and including over 23,000 participants, evaluated the pooled effect of various dietary interventions for BP control and showed significant reductions in both SBP and DBP. These effects were generally consistent across different types of diets and among various subgroups, however there were important differences. Though the overall effect was modest from an individual perspective, the range of the net change suggests that some patients may benefit to a greater degree than others. Furthermore, from a population standpoint, even relatively small reductions in BP can dramatically reduce the incidence of cardiovascular disease and mortality (21). The findings of this analysis have important clinical and public health implications, suggesting that dietary modifications are an effective method for controlling BP within the population and that certain approaches can be targeted to the individual based upon specific characteristics.

For all dietary interventions, compared to control groups, our study identified an incremental BP lowering effect of -3.07 mmHg and -1.81 mmHg for systolic and diastolic BP, respectively. Among the various diet sub-types, the DASH diet was associated with the greatest overall reduction in BP, with a SBP change of -7.62 mmHg and a DBP change of -4.22 mmHg. Importantly, this magnitude is similar to trials examining single drug therapies in mild hypertension, suggesting the DASH dietary pattern may be an alternative to medication initiation in early stage I hypertension (17, 22). Low sodium; low sodium, high potassium; low sodium, low calorie; and low calorie diets also showed significant BP lowering effects for both DBP and SBP. Furthermore, a recent meta-analysis conducted in 2014 by Yokoyama et al, found an association with

vegetarian diets and lower SBP and DBP, though the clinical trials included in that study were either too short for our analysis or conducted before 1990 (14). Interestingly, while the pooled effect of the Mediterranean diet significantly lowered DBP, its effect on SBP did not reach statistical significance. This is meaningful as a recent, major clinical trial showed that the Mediterranean diet was associated with lower incidence of cardiovascular events and death compared to a control diet (23). This finding, along with the results of our meta-analysis, suggest that there may be an alternative cardiovascular advantage beyond blood pressure control contributing to the mortality benefit of the Mediterranean diet, as has been proposed in other studies (24). Further investigation of this was beyond the scope of this analysis.

Subgroup evaluation indicated that blood pressure reduction was not as great in trials of longer duration. Specifically, trials that lasted longer than 24 months had a mean incremental SBP and DBP reduction of -1.36 mmHg and -0.96 mmHg, respectively, versus a SBP and DBP reduction of -5.25 mmHg and -2.95 mmHg, respectively, for trials that were shorter than 12 months. This is a finding that has been described in other analyses of lifestyle interventions and BP, such as that conducted by Whelton et al (13). A similar effect was also seen within individual trials, such as the PREMIER trial, which showed a declining level of BP reduction when participants were examined after 18 months of follow-up compared to the original trial of 6 months follow-up (25, 26). The most probable explanation for this finding is that of a declining adherence to the diet over time, and suggests that participant adherence is of primary importance in any lifestyle intervention program. We also found that larger ($n > 1,000$) and medium ($n = 100\text{-}1,000$) sized trials had lower effects on SBP and DBP than did smaller trials ($n < 100$). This

may be associated with the fact that the larger trials tended to be of longer duration. Trials conducted among participants with hypertension showed significantly greater mean changes in BP then those conducted in normotensive participants, which may reflect healthier baseline lifestyle practices among non-hypertensive individuals. Other studies have described a beneficial influence of physical activity level on BP reduction, however, in this analysis, there was no greater effect shown in trials that included a physical activity component versus those that did not (13). This likely reflects a similar level of physical activity between intervention and control groups as activity level was not a lifestyle component specifically under investigation for this analysis.

In our regression analysis, we detected an independent association of weight loss with BP reduction; this result was observed irrespective of baseline BMI, which had no correlation with the magnitude of the mean effect. Similar findings have been described in previous analyses and several biologically plausible explanations have been put forward (11). However, in our assessment of individual dietary sub-types, weight loss was not associated with BP reduction among low sodium or low sodium, high potassium diets; this is a probable reflection of the intricate involvement of these electrolytes in renal BP regulation, which likely has many influences other than weight (27).

Strengths of the study include the fact that only RCTs were incorporated in the analysis, thereby adding to the robustness of the clinical evidence and limiting potential confounding factors. Three large databases were used to complete the literature search, enhancing the comprehensive nature of the review and breadth of the included the studies. However, there are some important limitations to point out. As explained, there were greater reductions in BP revealed among studies with shorter duration and smaller

size. Not all interventions were equally distributed across the follow-up or sample size spectrum, and this allows for the possibility of bias within our dietary sub-analysis. For example, the DASH dietary intervention was associated with the largest mean effect size for both SBP and DBP, however, it is important to note that all of the studies included in this category were short-term (<6 months) trials and this may partially explain the size of the effect. In addition, there was a lack of information available to perform sub-analyses based on race, which may interact in important ways with some dietary interventions, such as sodium reduction. There are likely additional cardiovascular benefits of the different dietary patterns, such as the Mediterranean diet, that are not fully explained by their effect on blood pressure; these may have important and relevant implications and further research is needed in this area. Although the overall reductions in SBP and DBP were only moderate on an individual basis, these results should be interpreted on a population scale where even slight decreases in BP can substantially reduce the mortality and morbidity related to cardiovascular disease (21, 28).

CONCLUSION

In conclusion, this meta-analysis provides important evidence that dietary interventions offer significant benefits with regard to blood pressure control, and that different dietary patterns may be more effective than others. The public health and clinical implications of this research are important, and healthcare providers should consider these when giving dietary recommendations. The DASH intervention, which contains many aspects of the various approaches (low sodium recommendation and high potassium, low fat food groups) may be the most appropriate initial recommendation when BP control is the principle objective, although weight loss and other factors are certainly relevant. This is true for patients who are in the prehypertension range as well as those already taking antihypertensive medications. Adherence to any lifestyle modification is of primary importance and should always be addressed and evaluated. Additional studies are needed to assess the long-term mortality and morbidity effects from blood pressure reduction through dietary intervention.

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Tables and Figures

Table 1. Study design and baseline characteristics of randomized controlled trials of dietary interventions for BP.

Study*	Year	Country	*N*ǂ	Duration (mos)	Age (y)	Male (%)	BMI	HTN Trmt (%)¥	Baseline BP SBP (mmHg)	Baseline BP DBP (mmHg)	Intervention
DPP Group[29]	2005	US	1,079	36	51	32.0	33.9	17.0	123.7	78.6	*Low Calorie, Low Fat*
HPT Group[30a]	1990	US	125	36	38	75.2	29.0	0.0	125.3	83.0	*Low Calorie*
HPT Group[30b]	1990	US	196	36	39	63.3	27.0	0.0	124.0	82.6	*Low Sodium*
HPT Group[30c]	1990	US	195	36	38	65.1	26.0	0.0	124.1	82.3	*Low Sodium, High Potassium*
HPT Group[30d]	1990	US	129	36	39	65.1	29.0	0.0	124.4	82.6	*Low Sodium, Low Calorie*
Look AHEAD Group[31]	2007	US	2,570	12	59	40.7	35.9	75.3	128.2	69.9	*Low Calorie, Low Fat*
PREMIER Group[25a]	2003	US	269	6	50	42.8	33.3	0.0	134.9	84.6	*DASH Dietary Program*
PREMIER Group[25b]	2003	US	268	6	50	35.1	33.0	0.0	135.5	85.0	*Low Sodium, Low Calorie*
TOHP I Group[32a]	1992	US	327	18	43	70.9	27.1	0.0	124.8	83.7	*Low Sodium*
TOHP I Group[32b]	1992	US	308	18	43	72.7	29.5	0.0	124.3	83.7	*Low Calorie*
TOHP II Group[33a]	1997	US	594	36	44	64.8	30.9	0.0	127.7	86.1	*Low Sodium*
TOHP II Group[33b]	1997	US	595	36	43	63.0	31.0	0.0	127.6	86.0	*Low Calorie, Low Fat*
TOHP II Group[33c]	1997	US	597	36	44	68.8	30.9	0.0	127.4	86.0	*Low Sodium, Low Calorie, Low Fat*
Anderssen et al.[34]	1995	Norway	55	12	45	NR	29.5	0.0	132.8	87.5	*DASH Dietary Program*
Azadbakht et al.[35a]	2005	Iran	11	6	42	100.0	29.8	0.0	145.0	87.0	*DASH Dietary Program*
Azadbakht et al.[35b]	2005	Iran	27	6	42	0.0	29.8	0.0	143.0	85.0	*DASH Dietary Program*
Azadbakht et al.[35c]	2005	Iran	11	6	41	100.0	29.9	0.0	143.0	88.0	*Low Calorie*
Azadbakht et al.[35d]	2005	Iran	27	6	41	0.0	29.9	0.0	144.0	85.0	*Low Calorie*
Coppell et al.[36]	2010	New Zealand	52	6	57	38.0	35.1	84.0	131.9	79.8	*Low Calorie, Low Fat*
Esposito et al.[37]	2004	Italy	90	24	44	54.0	27.9	0.0	134.0	85.0	*Mediterranean Dietary Program*
Esposito et al.[38]	2003	Italy	60	24	34	0.0	35.0	0.0	124.0	85.0	*Mediterranean Dietary Program*
Geleijnse et al.[39]	1994	Netherlands	49	24	66	53.1	27.1	0.0	158.0	89.8	*Low Sodium, High Potassium*
Hjelstuen et al.[40]	2007	Norway	51	12	54	100.0	29.5	100.0	137.6	87.7	*Low Calorie, Low Fat*
Jalkanen et al.[41]	1991	Finland	25	12	49	50.0	NR	37.5	152.0	101.0	*Low Calorie*
Jula et al.[42a]	1990	Finland	32	12	44	100.0	28.5	0.0	147.3	98.2	*Low Sodium, High Potassium*
Jula et al.[42b]	1990	Finland	15	12	44	0.0	26.2	0.0	154.1	98.3	*Low Sodium, High Potassium*
Kastarinen et al.[43]	2002	Finland	360	24	54	48.0	28.9	48.0	149.0	91.0	*Low Sodium*
Langford et al.[44a]	1991	US	79	6	51	55.7	NR	64.6	144.9	94.4	*Low Sodium, High Potassium*
Langford et al.[44b]	1991	US	90	6	49	58.9	NR	65.6	143.2	94.0	*Low Calorie*
Makela et al.[45]	2008	Finland	40	6	44	70.0	27.3	0.0	149.9	98.0	*Low Sodium*
Marquez-Celedonio et al.[46]	2009	Mexico	46	6	44	NR	30.9	0.0	133.0	87.6	*DASH Dietary Program*
Mattila et al.[47]	2003	Finland	368	12	50	46.1	29.4	63.8	139.5	90.5	*Low Sodium, Low Calorie, Low Fat*
Toledo et al.[48a]	2013	Spain	2,441	48	67	41.7	29.9	68.0	148.0	83.0	*Mediterranean Dietary Program (EVOO)*
Toledo et al.[48b]	2013	Spain	2,367	48	67	46.1	29.7	68.4	149.0	83.0	*Mediterranean Dietary Program (Nuts)*
Toobert et al.[49]	2003	US	163	6	61	0.0	35.3	NR	136.1	79.3	*Mediterranean Dietary Program*
Watkins et al.[50]	2003	US	21	6	NR	NR	33.4	NR	139.0	96.0	*Low Calorie, Low Fat*
Whelton et al.[51a]	1998	US	340	30	67	50.9	27.9	100.0	127.3	71.3	*Low Sodium*
Whelton et al.[51b]	1998	US	147	30	66	49.0	31.0	100.0	128.6	70.7	*Low Calorie*
Whelton et al.[51c]	1998	US	147	30	66	56.0	31.2	100.0	127.6	71.3	*Low Sodium, Low Calorie*

* a, b, c, and d indicate different comparison groups within the same individual trial.

ǂ number of participants in each strata (excludes controls, as these were typically the same between strata of the same trial).

¥ % of participants taking an antihypertensive medication at the start of the trial.

BMI recorded in kg/m^2.

Table 2. Average net change in systolic and diastolic blood pressure by defined study design and participant characteristic subgroups.

	Systolic Blood Pressure					Diastolic Blood Pressure				
	Comp. Groups*	Mean Difference	95% Confidence Interval	Int.ǂ *P* Value	ANOVA¥ *P* Value	Comp. Groups*	Mean Difference	95% Confidence Interval	Int.ǂ *P* Value	ANOVA¥ *P* Value
Hypertensive Status					0.034					0.016
Hypertensive	14	-3.31	[-4.86, -1.77]	<0.001		14	-2.24	[-3.16, -1.32]	<0.001	
Normotensive	11	-1.56	[-2.05, -1.06]	<0.001		11	-0.97	[-1.44, -0.51]	<0.001	
Antihypertensive Meds					0.011					0.008
Yes	14	-1.87	[-3.01, -0.73]	<0.001		14	-1.18	[-1.46, -0.91]	<0.001	
No	23	-3.83	[-4.80, -2.86]	0.001		23	-2.07	[-2.67, -1.48]	<0.001	
Age					0.211					0.305
<50 years	22	-3.52	[-4.59, -2.44]	<0.001		22	-1.97	[-2.65, -1.29]	<0.001	
≥50 years	16	-2.48	[-3.70, -1.27]	<0.001		16	-1.54	[-2.00, -1.07]	<0.001	
Gender					0.877					0.793
≥ 50% Male	21	-2.84	[-3.80, -1.88]	<0.001		21	-1.63	[-2.24, -1.03]	<0.001	
< 50% Male	15	-2.96	[-4.17, -1.76]	<0.001		15	-1.76	[-2.44, -1.08]	<0.001	
Diabetic Status					0.686					0.197
Diabetic	3	-2.14	[-5.14, 0.86]	0.163		3	-1.20	[-1.73, -0.68]	<0.001	
Non-Diabetic	14	-2.80	[-4.01, -1.60]	<0.001		14	-1.73	[-2.68, -1.28]	<0.001	
Study Duration					<0.001					<0.001
<12 months	13	-5.25	[-7.16, -3.35]	<0.001		13	-2.95	[-4.40, -1.51]	<0.001	
12-24 months	13	-3.27	[-4.34, -2.20]	<0.001		13	-1.92	[-2.36, -1.47]	<0.001	
>24 months	13	-1.36	[-1.99, -0.73]	<0.001		13	-0.96	[-1.31, -0.61]	<0.001	
Intervention Sample Size					<0.001					0.001
<100	18	-5.02	[-6.32, -3.72]	<0.001		18	-2.76	[-3.55, -1.97]	<0.001	
100-1000	17	-2.05	[-2.65, -1.45]	<0.001		17	-1.17	[-1.55, -0.80]	<0.001	
>1000	4	-1.77	[-3.77, 0.22]	0.082		4	-1.23	[-1.73, -0.73]	<0.001	
Baseline BMI					0.299					0.117
<30	22	-3.63	[-4.75, -2.51]	<0.001		22	-2.03	[-2.62, -1.45]	<0.001	
30-35	11	-2.58	[-3.45, -1.70]	<0.001		11	-1.63	[-2.34, -0.91]	<0.001	
>35	3	-2.14	[-5.14, 0.86]	0.163		3	-1.20	[-1.73, -0.68]	<0.001	
BP Primary Outcome					0.050					0.037
Yes	24	-2.47	[-3.46, -1.49]	<0.001		24	-1.45	[1.93, -0.97]	<0.001	
No	15	-4.15	[-5.51, -2.79]	<0.001		15	-2.44	[-3.25, -1.64]	<0.001	
Physical Activity Encouraged					0.299					0.737
Yes	21	-2.70	[-3.23, -2.08]	<0.001		21	-1.68	[-2.09, -1.26]	<0.001	
No	18	-3.54	[-4.99, -2.09]	<0.001		18	-1.83	[-2.60, -1.06]	<0.001	

* The number of included comparison groups may not total 39 as a result of missing data.

ǂ P value reflects effect of dietary intervention vs. control within each specific subgroup.

¥ P value reflects intra-category varience in mean effect as determined through ANOVA methodology.

Figure 1. Process of study selection for meta-analysis.

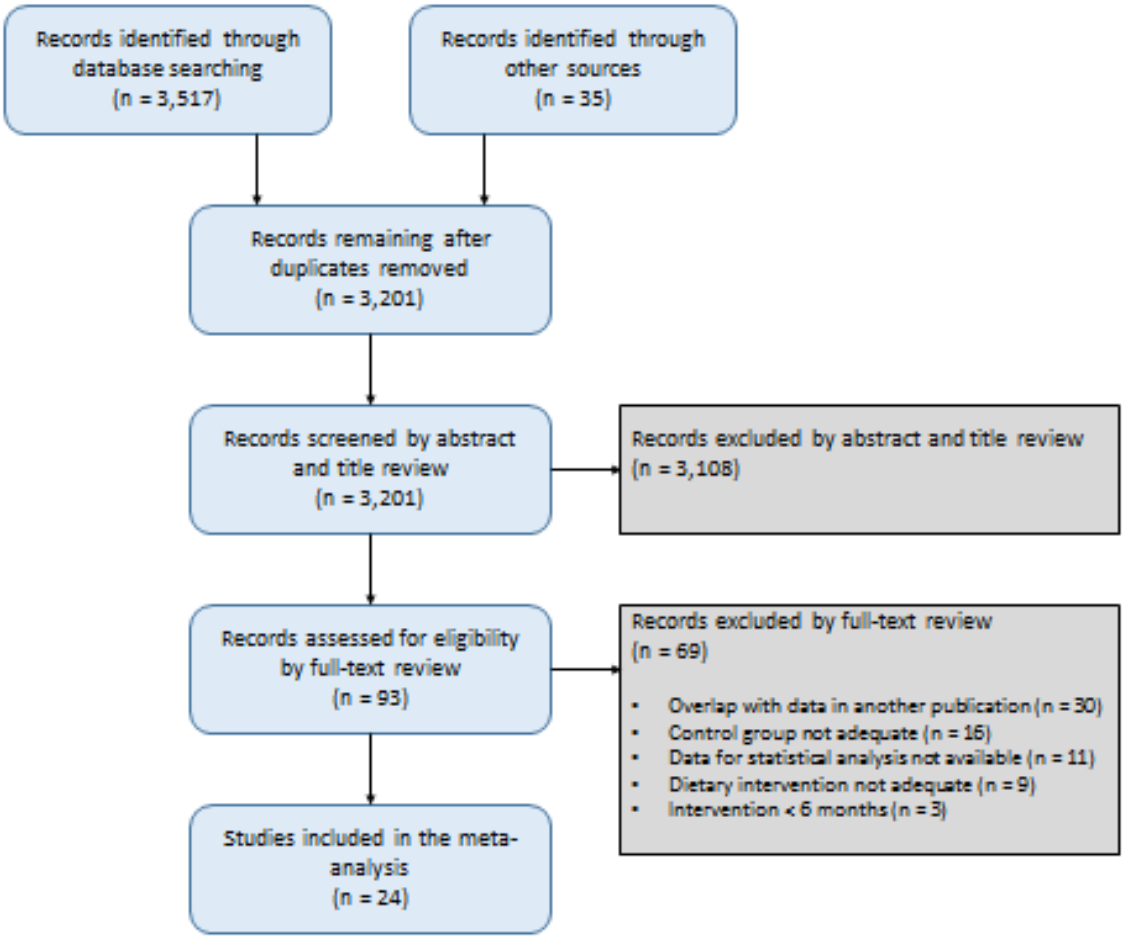
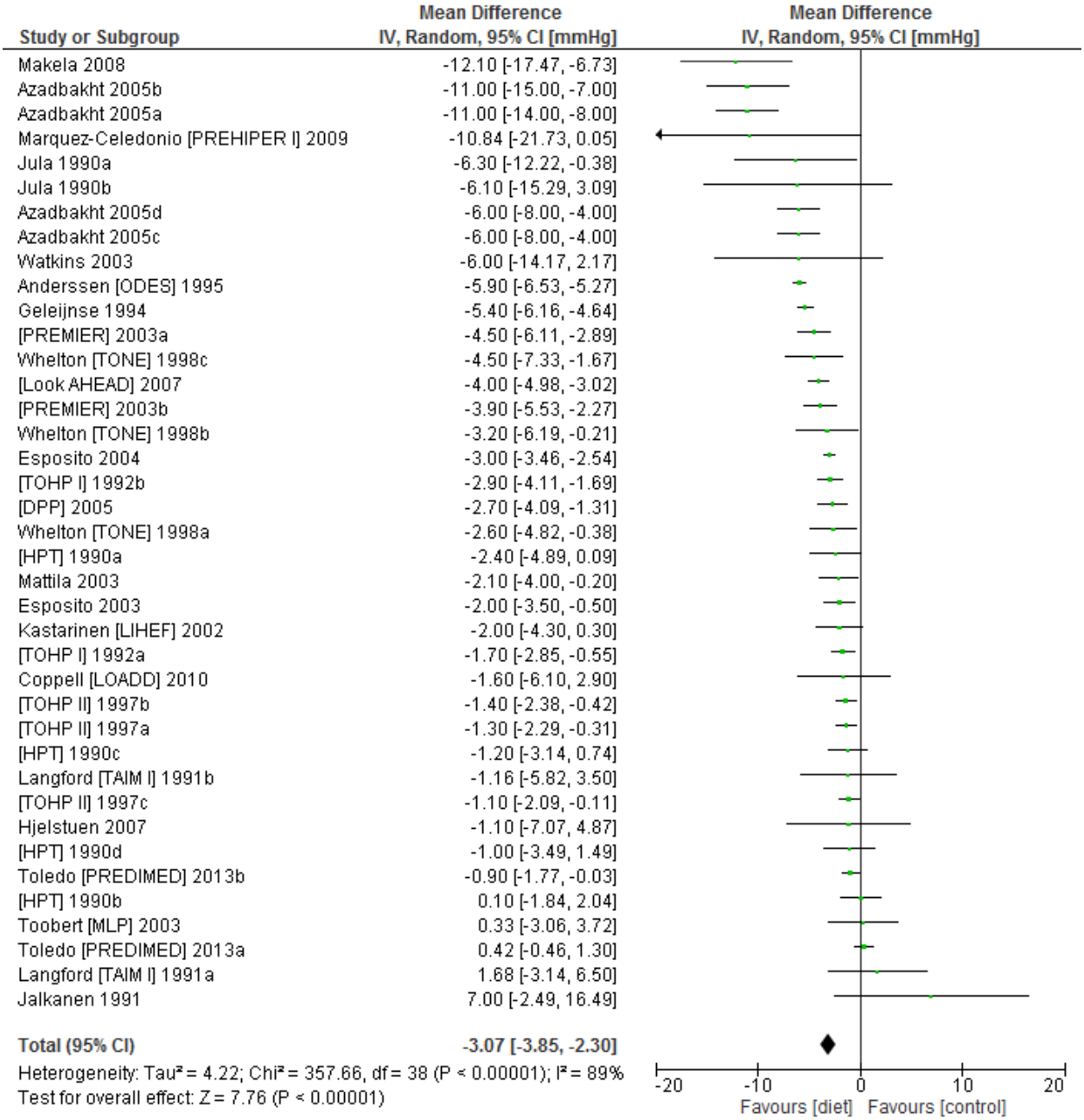


Figure 2. Average net change in (a) SBP and (b) DBP, and corresponding 95% confidence intervals related to all diets

A.



B.

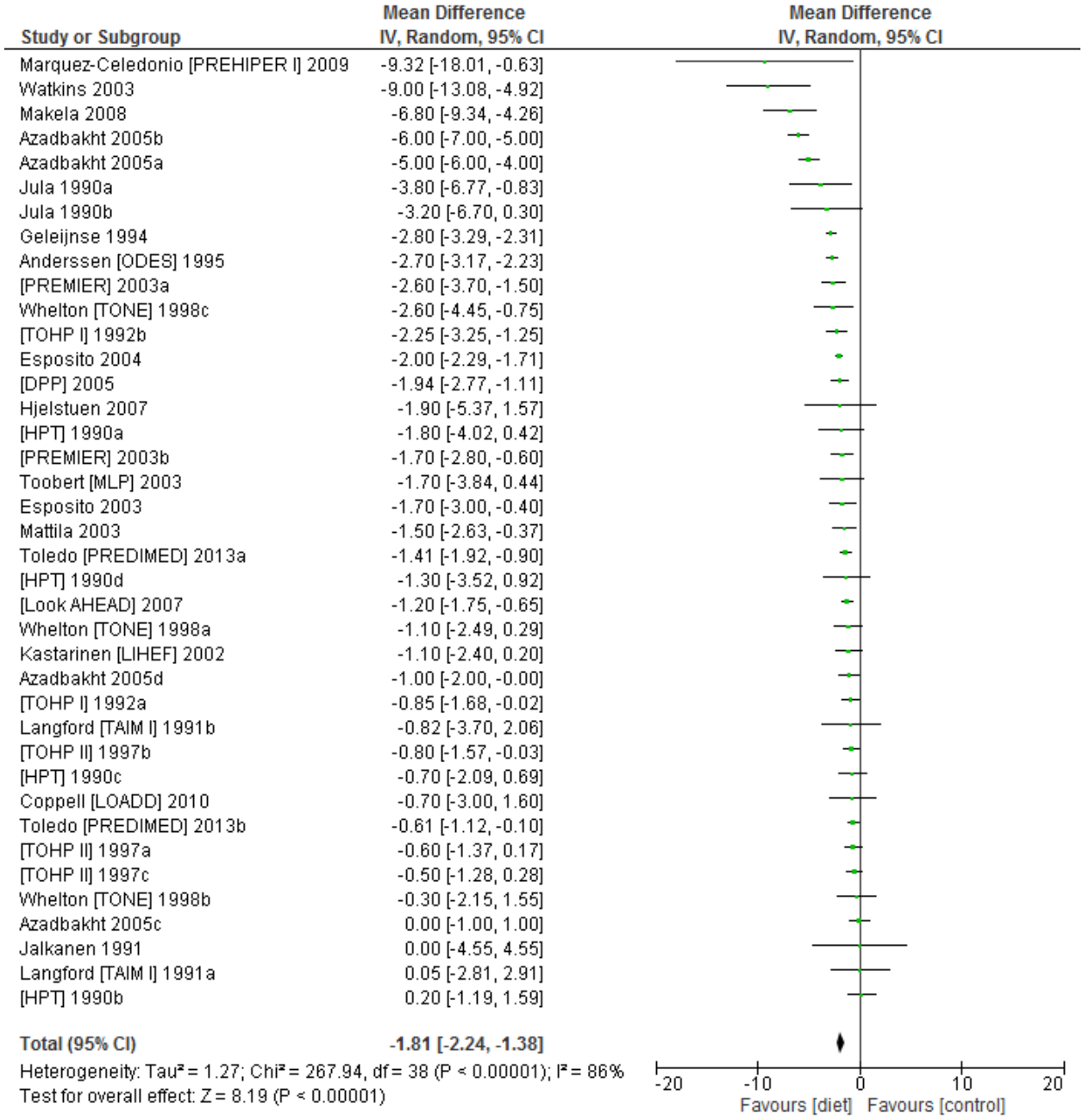
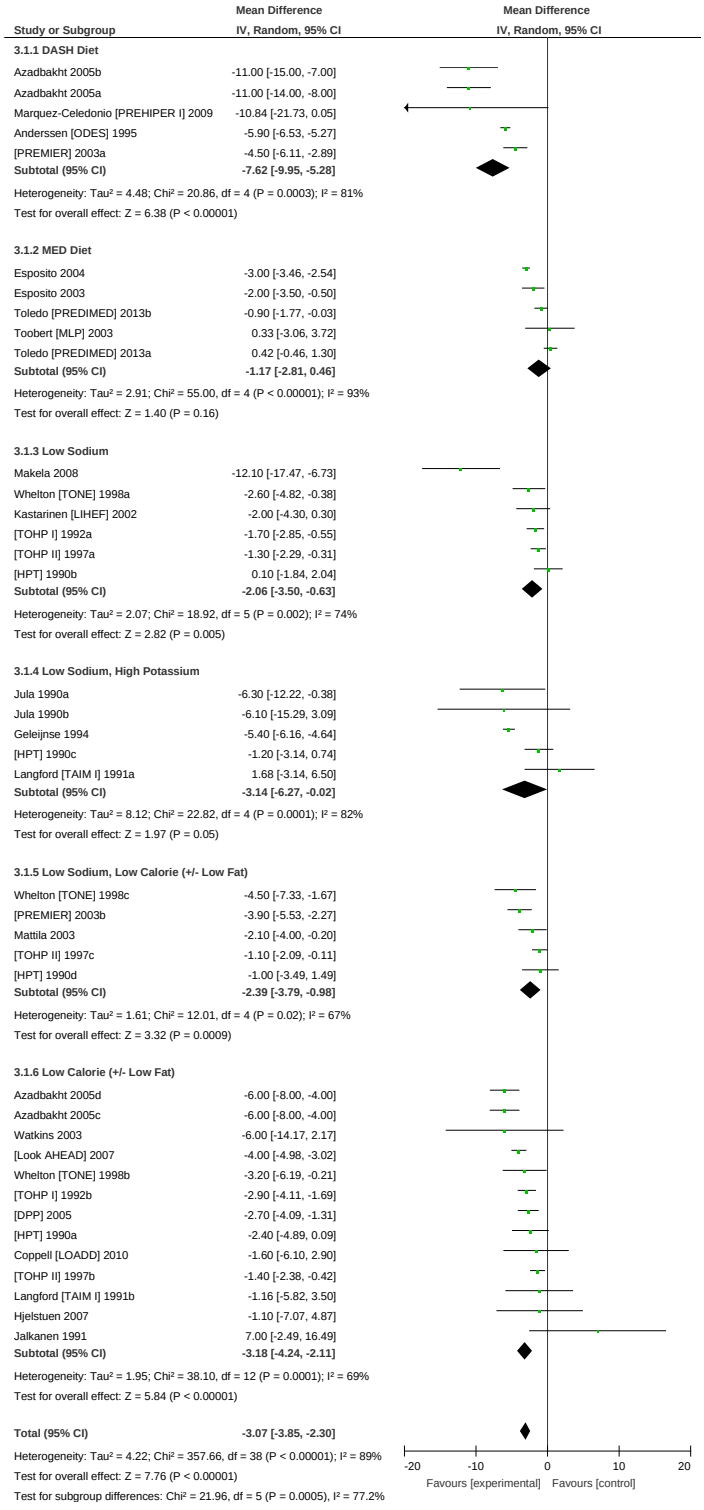

Study or Subgroup
Mean Difference
IV, Random, 95% CI
Mean Difference
IV, Random, 95% CI
Marquez-Celedonio [PREHIPER I] 2009 -9.32 [-18.01, -0.63]
Watkins 2003 -9.00 [-13.08, -4.92]
Makela 2008 -6.80 [-9.34, -4.26]
Azadbakht 2005b -6.00 [-7.00, -5.00]
Azadbakht 2005a -5.00 [-6.00, -4.00]
Jula 1990a -3.80 [-6.77, -0.83]
Jula 1990b -3.20 [-6.70, 0.30]
Geleijnse 1994 -2.80 [-3.29, -2.31]
Anderssen [ODES] 1995 -2.70 [-3.17, -2.23]
[PREMIER] 2003a -2.60 [-3.70, -1.50]
Whelton [TONE] 1998c -2.60 [-4.45, -0.75]
[TOHP I] 1992b -2.25 [-3.25, -1.25]
Esposito 2004 -2.00 [-2.29, -1.71]
[DPP] 2005 -1.94 [-2.77, -1.11]
Hjelstuen 2007 -1.90 [-5.37, 1.57]
[HPT] 1990a -1.80 [-4.02, 0.42]
[PREMIER] 2003b -1.70 [-2.80, -0.60]
Toobert [MLP] 2003 -1.70 [-3.84, 0.44]
Esposito 2003 -1.70 [-3.00, -0.40]
Mattila 2003 -1.50 [-2.63, -0.37]
Toledo [PREDIMED] 2013a -1.41 [-1.92, -0.90]
[HPT] 1990d -1.30 [-3.52, 0.92]
[Look AHEAD] 2007 -1.20 [-1.75, -0.65]
Whelton [TONE] 1998a -1.10 [-2.49, 0.29]
Kastarinen [LIHEF] 2002 -1.10 [-2.40, 0.20]
Azadbakht 2005d -1.00 [-2.00, -0.00]
[TOHP I] 1992a -0.85 [-1.68, -0.02]
Langford [TAIM I] 1991b -0.82 [-3.70, 2.06]
[TOHP II] 1997b -0.80 [-1.57, -0.03]
[HPT] 1990c -0.70 [-2.09, 0.69]
Coppell [LOADD] 2010 -0.70 [-3.00, 1.60]
Toledo [PREDIMED] 2013b -0.61 [-1.12, -0.10]
[TOHP II] 1997a -0.60 [-1.37, 0.17]
[TOHP II] 1997c -0.50 [-1.28, 0.28]
Whelton [TONE] 1998b -0.30 [-2.15, 1.55]
Azadbakht 2005c 0.00 [-1.00, 1.00]
Jalkanen 1991 0.00 [-4.55, 4.55]
Langford [TAIM I] 1991a 0.05 [-2.81, 2.91]
[HPT] 1990b 0.20 [-1.19, 1.59]
Total (95% CI) -1.81 [-2.24, -1.38]
Heterogeneity: Tau² = 1.27; Chi² = 267.94, df = 38 (P < 0.00001); I² = 86%
Test for overall effect: Z = 8.19 (P < 0.00001)
-20
-10
0
10
20
Favours [diet]
Favours [control]

Figure 3. Average net change in (a) systolic blood pressure and (b) diastolic blood pressure, and corresponding 95% confidence intervals by diet type.

A.



B.

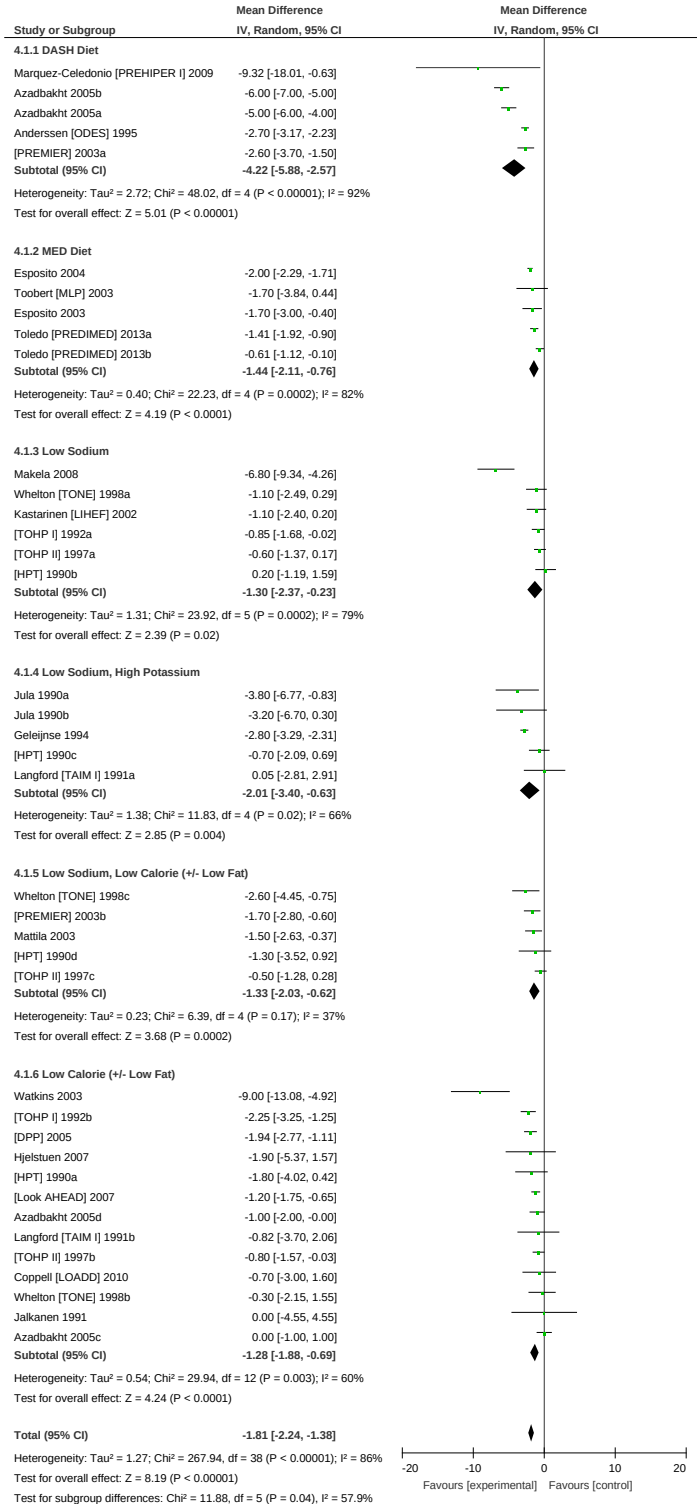
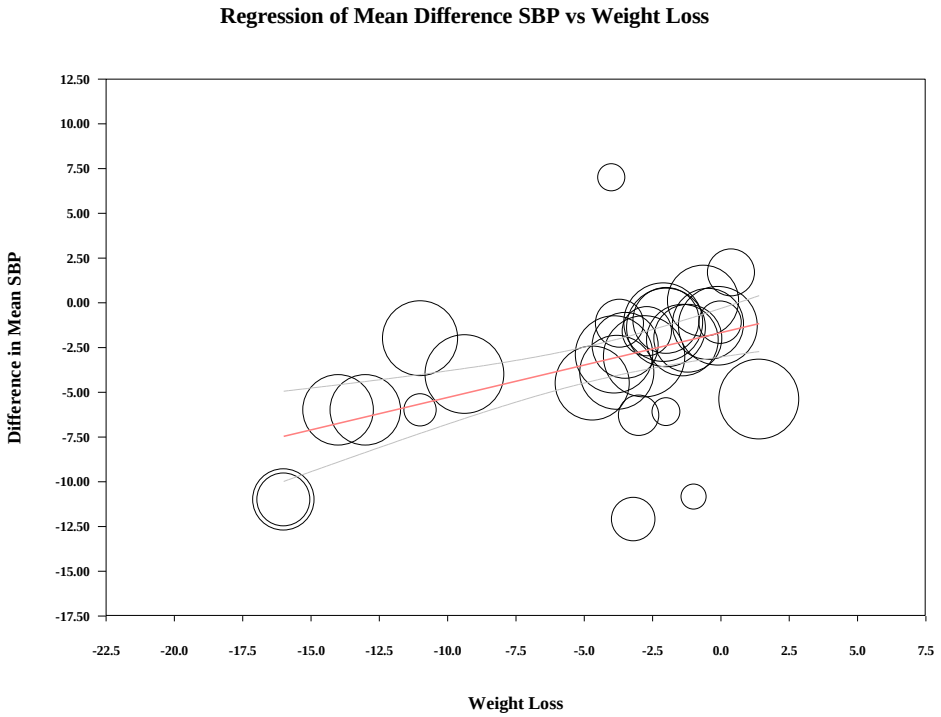


Figure 4. Meta-regression analysis of mean difference in (a.) SBP vs weight loss and (b.) DBP vs. weight loss, in the 30 trials with data available for weight loss.

A.



B.

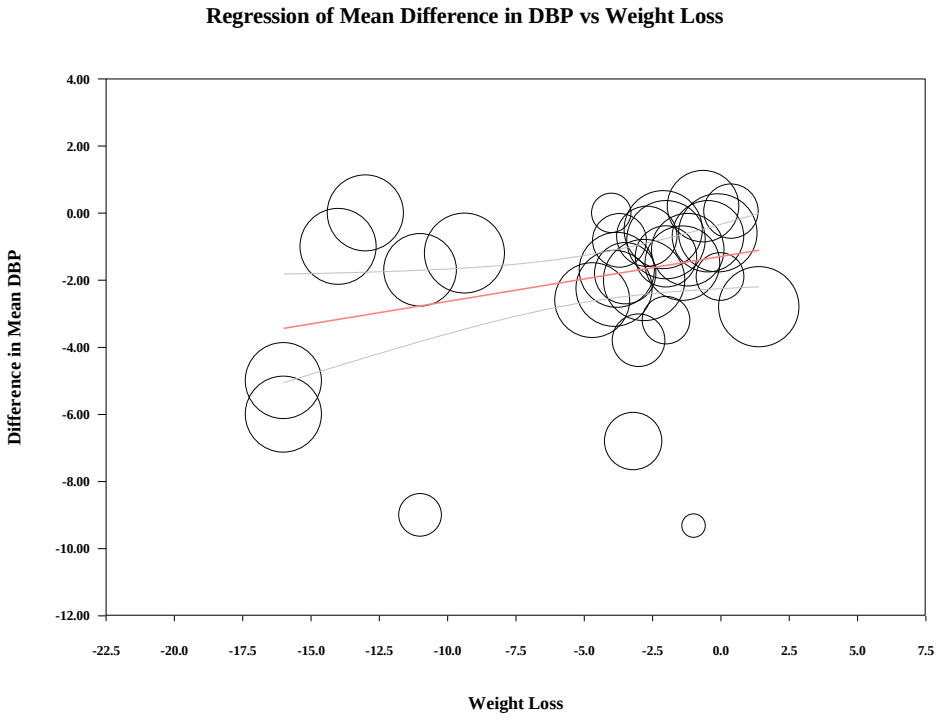
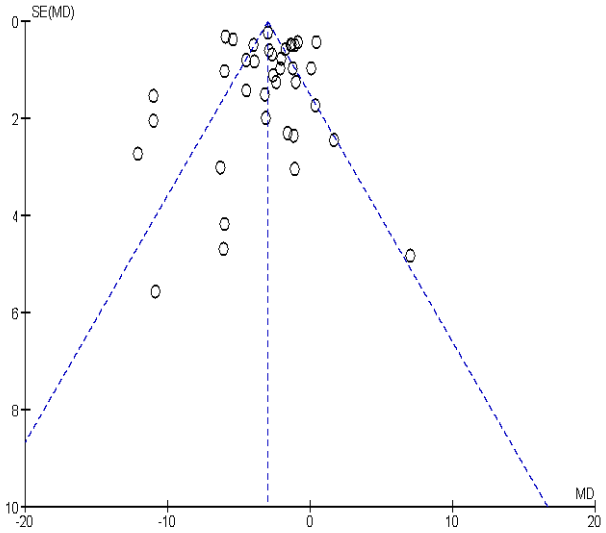


Figure 5. Funnel plots of (a) systolic blood pressure and (b) diastolic blood pressure in randomized controlled trials, plotted as net change in effect vs. SE of the net change.

A.



B.

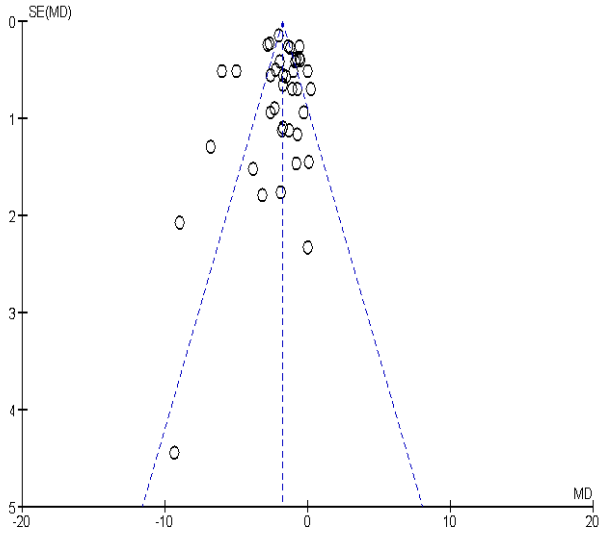


Figure 6. Risk of bias summary.