Effectiveness of lifestyle-based weight loss interventions for adults with type 2 diabetes: A systematic review and meta-analysis

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ABSTRACT

Aims: This systematic review and meta-analysis consolidates recent evidence on the effectiveness of lifestyle-based, weight loss interventions for adults with type 2 diabetes.

Materials and methods: A literature search from January 2003 to July 2013 was conducted (PubMed, Embase, CINAHL and Web of Science). Eligible studies were randomized controlled trials evaluating weight loss interventions (diet and physical activity, with or without behavioral strategies) of ≥12-weeks duration, compared to usual care or other comparison intervention. Ten studies were included for review. Some heterogeneity was present in the sample, thus random-effects models were used to calculate pooled effects.

Results: Intervention duration ranged from 16-weeks to nine years, with all but one delivered via individual or group face-to-face sessions. From six studies comparing lifestyle intervention to usual care the pooled effect on weight (n=5,795) was -3.33kg (95% CI: -5.06, -1.60kg), and on HbA1c (n=5,784) was -0.29% (95% CI: -0.61, 0.03%), with both attenuated in sensitivity analyses. The pooled within-group effect on weight (n=3,063) from all ten lifestyle intervention groups was -5.33kg (95% CI: -7.33, -3.34kg), also attenuated in sensitivity analyses. No participant or intervention characteristic examined explained the heterogeneity. Only one study assessed whether intervention effects were maintained following the end-of-intervention.

Conclusions: Lifestyle-based weight loss intervention trials in type 2 diabetes achieve, on average, modest reductions in weight and HbA1c, but results were heavily influenced by one trial. Evidence-based approaches for improving the effectiveness of lifestyle-based interventions in type 2 diabetes are needed along with future studies reporting on maintenance and cost-effectiveness.

INTRODUCTION

The prevalence of type 2 diabetes continues to increase globally [1]. Recent estimates indicate that 11.3% of adults in the United States [2], 4.5% in the United Kingdom [3] and 7.4% in Australia [4] are affected by type 2 diabetes.

Obesity increases the risk of developing type 2 diabetes, and complicates management in those with the disease by increasing insulin resistance and blood glucose levels, and increasing risk of dyslipidemia, hypertension, cardiovascular disease and mortality [6]. Modest weight loss of 5-10% of total body weight is recommended for overweight or obese people with type 2 diabetes as it can improve glycemic control, reduce the need for diabetes medications, and improve cardiovascular risk factors [6,7,9].

While surgical and pharmacological interventions are effective at achieving significant weight loss [10], lifestyle-based interventions focusing on diet and physical activity remain the cornerstone of weight loss approaches [11,12]. However, current evidence suggests that lifestyle interventions for people with type 2 diabetes may not be effective for improving longer-term health outcomes such as all-cause mortality [15], thus further research is needed to better understand the effectiveness of such interventions.

A systematic review and meta-analysis published in 2004 [8] reviewed the long-term effectiveness of lifestyle-based weight loss intervention trials in adults with type 2 diabetes, suggesting such interventions achieve modest weight loss and improvements in hemoglobin A1c (HbA1c) at 1-2 years follow-up [8].

The aim of this systematic review and meta-analysis was to synthesize recent evidence from the previous 10 years on the effectiveness of lifestyle-based weight loss interventions on change in weight and HbA1c in adults with type 2 diabetes.

MATERIALS AND METHODS

The conduct and reporting of this review adhered to guidelines outlined in the Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) Statement [16].

Data Sources and Searches

A structured search of the following databases was conducted from January 2003 to July 2013: PubMed, Embase, Cumulative Index to Nursing and Allied Health Literature (CINAHL) and Web of Science (an example of the search strategy is shown in Appendix S1). Searches were limited to adults and English-language publications. A manual search of journals expected to have the highest relevance was also conducted from January 2003-July 2013: *Diabetes Care, the International Journal of Obesity and Related Metabolic Disorders, Obesity Research, Obesity, the American Journal of Clinical Nutrition,* and *the Journal of American Dietetic Association.* Reference lists of included studies were examined and authors were contacted if data were missing.

Study Selection

Following the search, two authors (COT and CLB) removed duplicates and screened titles and abstracts for relevant articles based on eligibility criteria. Studies were included if they: (1) reported on intervention outcomes from a randomized trial; (2) were conducted in adults with clinically diagnosed type 2 diabetes mellitus; (3) primarily focused on weight loss; (4) included a lifestyle-based only intervention as one of the study groups targeting weight loss through diet and physical activity, with or without explicitly defined behavioral strategies; and (5) had comparison groups which could be control/usual care or other intervention groups (e.g. pharmacological/surgical). Studies were excluded if: (1) intervention duration was less than 12-weeks; (2) weight change and HbA1c outcomes were not reported; (3) they were in abstract form or conference proceedings only; (4) focused on general diabetes self-management; and (5) primarily compared different dietary compositions. All decisions were checked with author MMR and uncertainty was resolved with discussion. Full text articles were retrieved for remaining records.

Data Extraction and Quality Assessment

Detailed information on methodology (e.g. study design, sample size and study assessments), participant characteristics (e.g. mean age, mean body mass index [BMI] and gender distribution), intervention details (e.g. intensity, frequency and duration of contact and mode of delivery) and the intervention effect (i.e. mean [SD] change from baseline to follow-up for weight and HbA1c outcomes) were extracted and tabulated. Attempts were made to contact authors if data were missing.

Methodological quality of studies was evaluated with an established quality score (0-10) [17,18]; using a tool adapted from the CONSORT statement for randomized controlled trials [19]. One point was awarded for each item scored as 'present' (✓) and zero points were awarded for each item scored as 'absent' (X) or 'unclear or inadequately described' (?). Each study was assigned a risk of bias category based on the following cut-offs for quality scores: high risk (0-3), moderate risk (4-7) and low risk (8-10). The methodological quality items included: (1) baseline results reported separately for each group; (2) randomization clearly described and adequately done (i.e. describes sequence generation and allocation concealment); (3) acceptable attrition (i.e. ≤20% for follow-up periods up to six months; or ≤30% for follow-up periods over six months); (4) assessor blinding; (5) weight outcomes assessed at least six months after baseline; (6) intention-to-treat analysis and an appropriate approach to missing data; (7) potential confounders including baseline level of behavior appropriately accounted for in analyses; (8) summary results presented with estimated effect size (between-group difference) and precision estimates; (9) power calculation reported and study adequately powered; and (10) weight was objectively measured. Two researchers independently assessed trials and discrepancies were discussed and verified.

Data Synthesis and Analysis

Meta-analyses were performed for changes in weight (kg) and HbA1c (%). Studies were included in between-group meta-analyses if they compared an intervention with usual care/brief diabetes education and either reported end-of-intervention effects (differences between groups and standard error) directly, or enough information to calculate these. Whenever possible, intervention effects were based on change from baseline, otherwise follow-up values were used. Lifestyle intervention groups from all studies were included in the within-group meta-analysis for change in weight (kg). Heterogeneity was tested using Cochran's Q test [20]. Publication bias was tested using Egger's test for small study effects [21] (Stata version 12.1; StataCorp LP, College Station, Texas). Meta-analyses were run in Review Manager (version 5.2). To calculate the pooled effects, random-effects (DerSimonian and Laird [22]) or fixed-effects models, as appropriate, were performed.

Sensitivity analyses were performed using the leave-one-out method to assess whether results remained stable, regardless of which studies were included/excluded from analyses, and excluding studies considered to have high risk of bias. To evaluate considerable heterogeneity, a post-hoc, random-effects meta-regression was performed (Stata version 12.1; StataCorp LP, College Station, Texas) to examine associations between age, sex, BMI, HbA1c, intervention duration (<12months vs. ≥12months), intervention delivery (individual vs. group-based contact; multidisciplinary team vs. individual facilitator), physical activity components (≥175mins/week goal vs. less; some supervised sessions vs. none), dietary components (meal replacement use vs. none; energy restriction vs. general reduction), and behavioral components (behavioral strategies used vs. none; self-monitoring; motivational interviewing), and changes in weight.

RESULTS

The search identified 2,506 records; 1,444 once duplicates were removed. Of these, 1,343 records were excluded based on title/abstract, leaving 101 full-text articles for review (Figure 1). Eleven individual studies (from 14 publications) met eligibility criteria, however one study was subsequently excluded as it targeted a highly specific sample of people with type 2 diabetes (i.e. also diagnosed with schizophrenia), leaving ten individual studies (from 13 publications) for review [10,23-31]. Appendix S2 shows detailed study, sample and intervention characteristics of included studies.

The ten studies recruited samples ranging from 27 to 5,145 participants. The reported mean age was, on average, 55 years (range, 47 to 60 years). The average proportion of female participants within studies was 59% (range, 37 to 100%). Mean baseline BMI was 35.7kg/m^2 (range, 30.0 to 38.2kg/m^2) and mean baseline HbA1c was 7.9% (range, 7.3 to 9.8%). Intervention duration ranged from 16-weeks to nine years. Nearly all (nine-of-ten) studies delivered their interventions via face-to-face individual [10,26,30] or group-based [24] sessions, or some combination [23,25,27,28,31]. One study delivered the intervention via the telephone [29]. Six studies compared lifestyle intervention to a control group, which received usual care or some form of brief diabetes education [24,25,27-29,31]. The other four studies compared lifestyle intervention to an intervention comparison group (i.e. no control) [10,23,26,30].

Risk of Bias within Studies

Appendix S3 displays the methodological quality score and risk of bias assessment. The median quality score was 6 (minimum-maximum: 1-9); only two studies were considered to have low risk of bias [29,31], six were considered to have moderate risk [10,23,24,26-28] and two were considered to have high risk [25,30].

Effectiveness of Lifestyle-based Interventions for People with Type 2 Diabetes

Appendix S4 shows results based on changes in weight and HbA1c from baseline.

Weight change

Compared with usual care/brief diabetes education (n=5,795), lifestyle intervention showed a statistically significantly greater reduction in weight, with a pooled effect of -3.33kg (95% CI: -5.06, -1.60kg), equivalent to approximately 3.3% of initial body weight (Figure 2A); however significant heterogeneity was observed (Q=53.70, p<0.001). The leave-one-out sensitivity analysis showed pooled effects were attenuated excluding the trial by Luley et al (-1.99kg [95% CI: -2.77, -1.21kg] [24]), (i.e. the single trial explaining the heterogeneity and with the largest intervention effect). Comparatively, further analysis showed pooled effects were considerably larger including the Look AHEAD trial's 1-year instead of 8-year weight change (-4.51kg [95% CI: -8.09, -0.93kg]) [33]. Excluding the one low quality study [25] did not alter the pooled effect observed.

Lifestyle intervention groups from all 10 studies (n=3,063) were included in the meta-analysis for within-group change in weight (Figure 2B). Lifestyle interventions, on average, achieved a statistically significant reduction in weight of -5.33kg (95% CI: -7.33, -3.34kg), equivalent to approximately 5.4% of initial body weight, however significant heterogeneity was observed (Q=381.04, p<0.001). The leave-one-out sensitivity analysis showed pooled effects were considerably smaller excluding the trial by Snel et al (-3.41kg [95% CI: -5.04, -1.79kg]) [30]. Excluding the two trials considered to have high risk of bias [25,30] resulted in similar attenuation of pooled effects. No single trial explained the heterogeneity, and meta-regression found no significant associations between the 14 participant or intervention characteristics examined and weight change (Appendix S5).

HbA1c change

Compared with usual care/brief diabetes education (n=5,784), lifestyle intervention showed a non-significant pooled trend toward a reduction in HbA1c of -0.29% (95% CI: -0.61, 0.03%; Figure 3); however significant heterogeneity was observed (Q=38.12, $p<0.001$). The leave-one-out sensitivity analysis showed pooled effects were considerably smaller excluding the trial by Luley et al (-0.10% [95% CI: -0.20, -0.01%], Q=1.20, p=0.877) [24]. Further analysis showed pooled effects were larger including the Look AHEAD trial's 1-year instead of end-of-intervention HbA1c change (-0.38% [95% CI: -0.67, -0.09%]) [33]. The pooled effect remained similar excluding the one low quality study [25].

Evidence for informing translation

Only one study [23] assessed whether improvements in outcomes were maintained following a period of no intervention contact; and did not report successful maintenance of outcomes [23]. None of the trials included reported on cost-effectiveness of the lifestyle interventions, although two are proposed [32,35].

DISCUSSION

This systematic review and meta-analysis synthesizes recent evidence on the effectiveness of lifestyle-based weight loss interventions for adults with type 2 diabetes over the previous decade. Compared with usual care or brief diabetes education, such interventions achieved modest reductions in weight and modest improvements in HbA1c. These results are remarkably similar to those found in an earlier review [8], which reported similarly modest declines in weight (-1.7kg, or equivalent to 3.1% of initial body weight) and HbA1c level (-0.3%), after 1-2 years of follow-up, compared with usual care or brief diabetes education.

Modest weight loss of at least 5% of body weight is encouraged for people with type 2 diabetes who are overweight or obese [36] and has been shown to reduce health risks [6,7,9,11]. Findings from pooled results of within-group change suggest that, lifestyle interventions may, on average, achieve this degree of weight loss. However, importantly there was considerable heterogeneity in the lifestyle interventions included, and the effects on weight loss were largely influenced by three studies [24,30,33]. None of the participant or intervention characteristics explored were associated with within-group weight changes, however this may be limited by the relatively small number of studies included [37].

Mean weight losses of at least 5% were achieved in only three lifestyle intervention groups and three comparison treatment groups; although one of these trials [26] included, the now withdrawn, sibutramine [38]. The remaining of these intervention protocols all differed considerably. The largest weight losses were observed with a short-term very low calorie diet (VLCD) (16 weeks), with and without the addition of exercise [30] and longer-term laparoscopic adjustable gastric banding (LAGB) surgery (24 months) [10]. The intervention by Luley et al [24], which achieved 11.3% mean weight loss after six-months required participants pay a fee to be involved (€150). This financial obligation may have impacted on weight loss through increased compliance [39], and possibly limited representativeness of the sample recruited. The Look AHEAD intervention also achieved weight loss ≥5% [31]. This highly resourced and intensive intervention encouraged the use of meal replacements (provided free of charge) [35]. Consumption of meal replacements was strongly associated with weight loss after one-year in the Look AHEAD intervention [40].

Improvements in glycemic control favorably improve health outcomes for people with type 2 diabetes by decreasing risk of diabetes complications [36,41]. While a 1% reduction in HbA1c has been associated with significant reductions in microvascular and macrovascular complications and diabetes-related mortality [41], smaller reductions in the order of 0.5% have also been associated with clinically meaningful improvements in cardiovascular disease risk factors [42]. Our meta-analysis revealed that lifestyle-based weight loss interventions reduced HbA1c on average by 0.29%; a magnitude similar to that observed in physical activity-only interventions in type 2 diabetes [43,44]. This review supports that larger reductions in HbA1c (in order to produce clinical benefit), are unlikely without substantial weight losses [12,13], or unless baseline HbA1c is >8%, as observed in other studies [45].

Of the treatment groups that achieved clinically meaningful mean weight losses (>5%), reductions in mean HbA1c of ≥1% were observed in the LAGB surgery and VLCD (with and without the addition of exercise) treatment groups only, where weight losses were, on average, >20% of initial body weight [10,30]. Bariatric surgery (i.e. gastric banding/bypass surgery) has been shown to induce diabetes remission in morbidly obese, type 2 diabetes patients, which may be maintained for over two years [46] and up to eight years [47]. However, bariatric surgery is only considered in patients with type 2 diabetes and BMI >35kg/m^2, where lifestyle and pharmacological therapy have been ineffective [36]. For adults with a BMI <35kg/m^2 and type 2 diabetes, bariatric surgery has shown some short-term benefits but long-term outcomes are unknown [48,49]; thus it is not currently recommended as part of routine medical care [36]. While VLCD treatment can achieve initial weight loss of a similar magnitude to bariatric surgery [50], maintenance of weight loss [50,51] is less successful than that observed following bariatric surgery [52].

Only one study assessed whether intervention effects were maintained following the end-of-intervention [23]; while a follow-up assessment is planned for an ongoing trial [32]. Aas et al [23] reported weight regain and HbA1c regression to baseline levels in the lifestyle intervention group 12-months after intervention completion. This finding needs to be interpreted with caution, however, as details on this follow-up assessment were poorly reported. It is surprising that there has been such limited attention to assessment of longer-term outcomes following lifestyle interventions. This is particularly important in the context of weight loss interventions, where studies in overweight and obese adults without chronic conditions have generally shown that 50% of initial weight lost is regained within the first year after intervention completion [53].

Longer-term findings from the Look AHEAD trial, where intervention contact continued over multiple years (albeit at a reduced frequency), showed that even with continued contact and ongoing resources, weight regain occurred following large initial weight loss [31]. Although, after almost 10 years follow-up, intervention participants maintained a mean weight loss of 6.0% of initial body weight [31]. Improvements in HbA1c observed after the first year of the Look AHEAD trial had also attenuated, such that at the final follow-up mean HbA1c levels in the intervention group were higher than baseline although still significantly lower than the control group [31]. The United Kingdom Prospective Diabetes Study noted that in both its intervention groups (conventional versus intensive therapy), although HbA1c reduced initially, it steadily increased even with ongoing therapy [47]. These results suggest that lifestyle-based interventions may delay inevitable progressive increases in HbA1c associated with advancing disease.

Limitations

There are a number of limitations with this review, including the restriction to studies published in English language. Studies included were heterogeneous with regard to their intervention components, comparison groups evaluated and outcomes reported. Thus random effects models were used for meta-analyses and attempts to contact corresponding authors were made, with few providing the additional data requested. The methodological quality of studies was moderate, and a number of methodological criteria were particularly poorly reported: randomization methods, assessor blinding, approaches to missing data and summary results presented with effect size and precision estimates. Future studies should pay specific attention to these in line with CONSORT guidelines [19].

Clinical implications

These results show that, despite greater understanding of mechanisms underlying obesity [54-56], lifestyle-based weight loss interventions over the past decade have continued to produce relatively modest results in terms of weight loss and glycemic control. Thus there remains an ongoing need to advance our efforts to effectively achieve and maintain weight loss and glycemic control in adults with type 2 diabetes. Bariatric surgery is touted as one such advancement; however limited health funding does not make this management approach viable on a population basis [52,57]. Effective and cost-effective non-surgical treatment options will therefore continue to be warranted.

In type 2 diabetes patients with a BMI $\geq 27 kg/m^2$, the addition of pharmacotherapy could be considered where lifestyle modification alone has been ineffective [58]. Newer diabetes medications, such as glucagon-like peptide 1 (GLP-1) receptor agonists, have the advantage of inducing weight loss, in addition to their glucose lowering effects, via their action on delaying gastric emptying and increasing satiety, and have been shown to result in weight loss of 1-4kg [59,60]. Future lifestyle-based trials in type 2 diabetes patients treated with GLP-1 receptor agonists may find greater effectiveness of these interventions in terms of initial weight loss and weight loss maintenance, as ongoing suppression of appetite may be needed to successfully maintain weight loss [61]. In the most recently published trial included in this review [29], only 4% of the sample were treated with a GLP-1 agent at baseline.

With a growing interest in personalized medicine [62] and the use of patients' genomic information to guide clinical care [62,63], future application of this information to lifestyle and behavior change interventions may be possible. Analysis of genetic markers in a subsample of participants from the Look AHEAD trial (n=3,899), found that none of the previously identified obesity risk single-nucleotide polymorphisms (SNPs), including the fat mass and obesity associated gene (*FTO*), were associated with weight loss at year 1 [64], although two novel regions (*ABCB11* and *TNFRSF11A*) were associated with weight loss in the lifestyle intervention group only: 1.16kg higher weight per minor allele for *ABCB11* rs484066 and 1.70kg lower weight per allele for *TNFRSF11A* rs17069904 [65]. In the Diabetes Prevention Program, which included adults at risk of type 2 diabetes, the only SNPs to show associations with weight loss were at *PPARG* and *MC4R* [66,67]. Further, evidence from a small number of trials suggests that obesity and diabetes-associated SNPs may moderate the effects of macronutrient composition of diets on weight loss [68]. Significant associations have also been observed for some obesity-associated SNPs and weight regain [66,68]. A move away from a one-size-fits-all approach to a more personalized approach for lifestyle and weight management in type 2 diabetes patients, may improve the effectiveness of lifestyle-based interventions.

Conclusions

Evidence-based and interdisciplinary approaches, drawing upon clinical/behavioral, pharmacological, and genomic evidence need exploration in future trials of lifestyle-based, weight loss interventions among those with type 2 diabetes to improve their effectiveness. Furthermore, future studies need to report on outcomes that are important for informing translation into practice such as cost-effectiveness and longer-term maintenance post-intervention.

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Author Contributions

COT, SPL and MMR conceived the study. COT and CLB conducted the literature search, and reviewed the abstracts and full-text articles. COT, CLB and MMR reviewed the study quality. CLB conducted the meta-analyses and meta-regression. All authors contributed to writing and reviewing the manuscript and approved the final manuscript.

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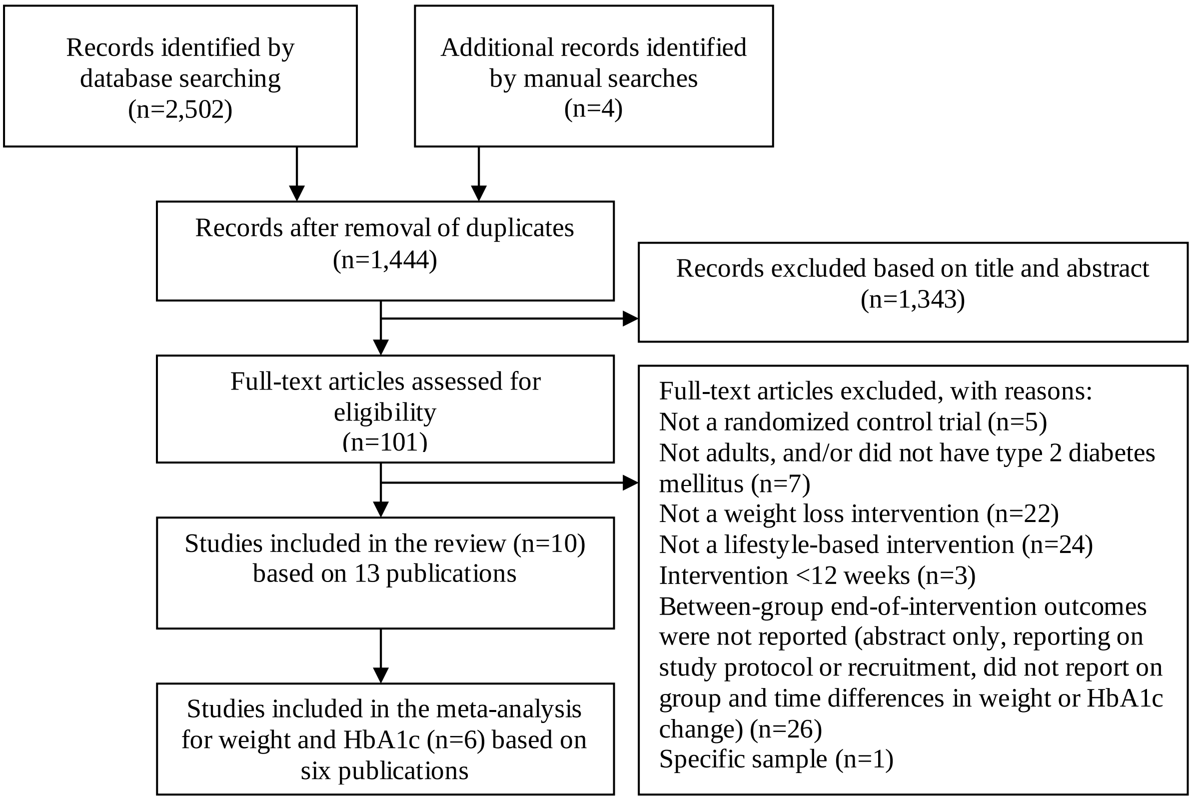

Figure 1. PRISMA flow of study selection through the review process

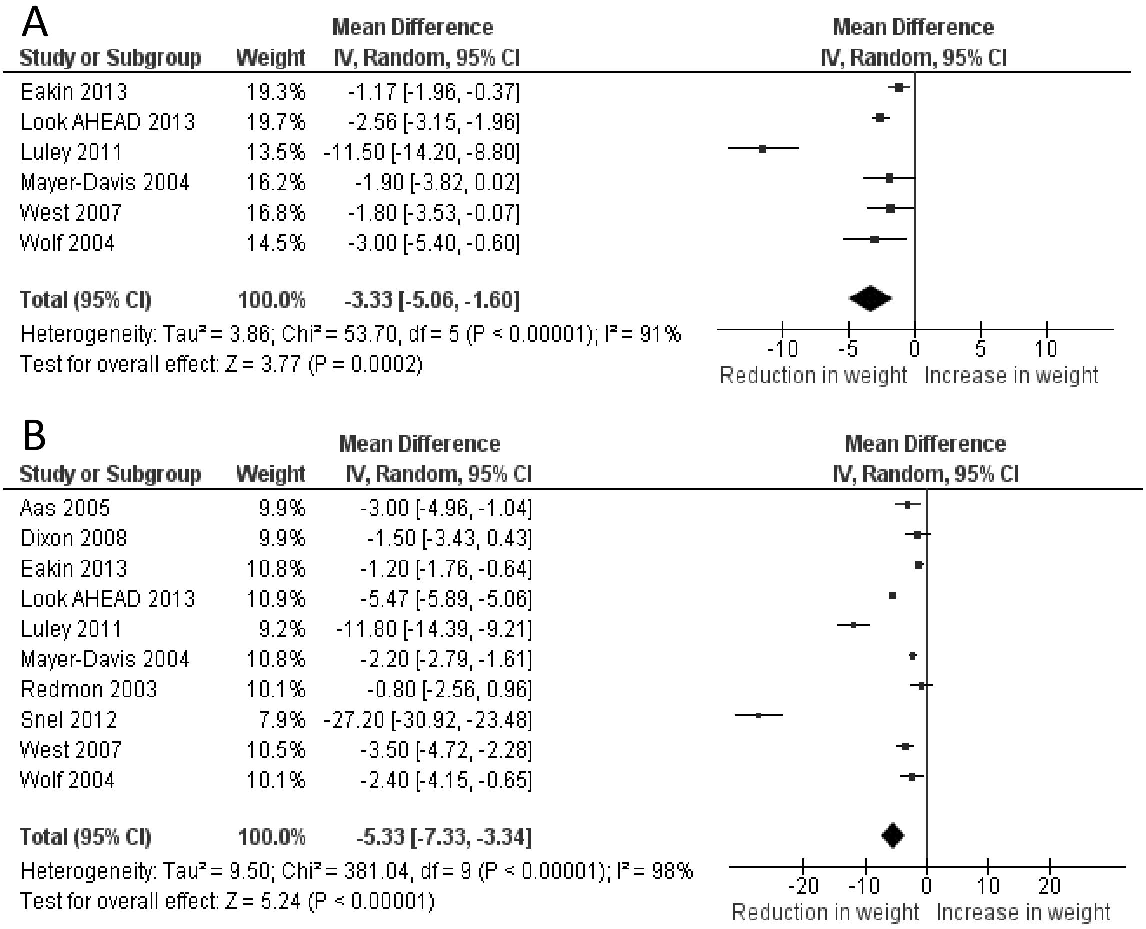

Figure 2. Meta-analysis results: Effect of lifestyle-based intervention trials versus usual care/brief diabetes education (n=6) on weight change (kg, A), and of lifestyle intervention (n=10) on within-group weight change (kg, B) in adults with type 2 diabetes

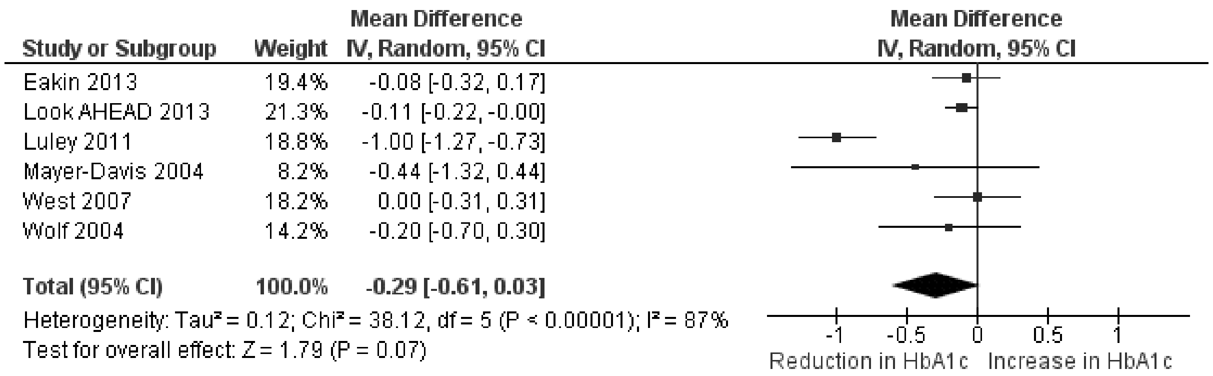

Figure 3. Meta-analysis results: Effect of lifestyle-based intervention trials versus usual care/brief diabetes education on HbA1c (%) in adults with type 2 diabetes