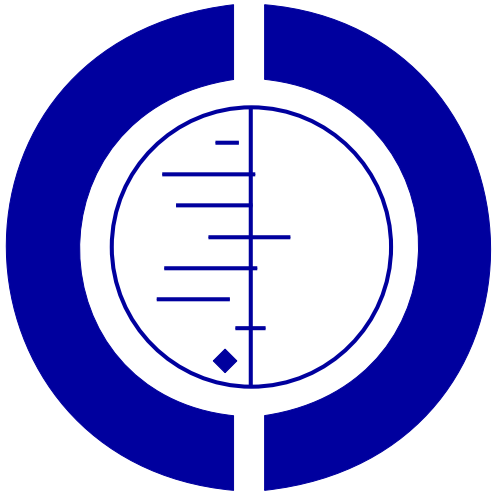
Alpha-glucosidase inhibitors for type 2 diabetes mellitus (Review)

Van de Laar FA, Lucassen PLBJ, Akkermans RP, Van de Lisdonk EH, Rutten GEHM, Van Weel C



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ABSTRACT

Background
Alpha-glucosidase inhibitors such as acarbose or miglitol, have the potential to improve glycemic control in type 2 diabetes mellitus. The true value of these agents, especially in relation to diabetes related mortality and morbidity, has never been investigated in a systematic literature review and meta-analysis.

Objectives
To assess the effects of alpha-glucosidase inhibitors s in patients with type 2 diabetes mellitus.

Search strategy
We searched *The Cochrane Library*, MEDLINE, EMBASE, Current Contents, LILACS, databases of ongoing trials, reference lists of reviews on the topic of alpha-glucosidase inhibitors and we contacted experts and manufacturers for additional trials. Date of most recent search: December 2003 (Current Contents) and April 2003 (other databases).

Selection criteria
Randomised controlled trials of at least 12 weeks duration comparing alpha-glucosidase inhibitor monotherapy in patients with type 2 diabetes with any other intervention and that included at least one of the following outcomes: mortality, morbidity, quality of life, glycemic control, lipids, insulin levels, body weight, adverse events.

Data collection and analysis
Two reviewers read all abstracts, assessed quality and extracted data independently. Discrepancies were resolved by consensus or by the judgement of a third reviewer. A statistician checked all extracted data entrance in the database. We attempted to contact all authors for data clarification.

Main results
We included 41 trials (8130 participants), 30 investigated acarbose, seven miglitol, one trial voglibose and three trials compared different alpha-glucosidase inhibitors. Study duration was 24 weeks in most cases and only two studies lasted amply longer than one year. We found only few data on mortality, morbidity and quality of life. Acarbose had a clear effect on glycemic control compared to placebo: glycated haemoglobin -0.8% (95% confidence interval -0.9 to -0.7), fasting blood glucose -1.1 mmol/L (95% confidence interval -1.4 to -0.9), post-load blood glucose -2.3 mmol/L (95% confidence interval -2.7 to -1.9). The effect on glycated haemoglobin by acarbose was not dose-dependent. We found a decreasing effect on post-load insulin and no clinically relevant effects on lipids or body weight. Adverse effects were mostly of gastro-intestinal origin and dose dependent. Compared to sulphonylurea, acarbose decreased fasting and post-load insulin levels by -24.8 pmol/L (95% confidence interval -43.3 to -6.3) and -133.2 pmol/L (95% confidence interval -184.5 to -81.8) respectively and acarbose caused more adverse effects.

Authors' conclusions

It remains unclear whether alpha-glucosidase inhibitors influence mortality or morbidity in patients with type 2 diabetes. Conversely, they have a significant effect on glycemic control and insulin levels, but no statistically significant effect on lipids and body weight. These effects are less sure when alpha-glucosidase inhibitors are used for a longer duration. Acarbose dosages higher than 50 mg TID offer no additional effect on glycated hemoglobin but more adverse effects instead. Compared to sulphonylurea, alpha-glucosidase inhibitors lower fasting and post-load insulin levels and have an inferior profile regarding glycemic control and adverse effects.

SYNOPSIS

Alpha-glucosidase inhibitors lower blood sugars, have no effect on lipids and there is no evidence for an effect on morbidity and mortality.

Alpha-glucosidase inhibitors may be used for patients with type 2 diabetes. They delay the absorbance of carbohydrates ('complex form of sugar') in the gut. In this review we present data from meta-analyses that show (among other things) a decrease in glycated haemoglobin, fasting and post-load blood glucose and post-load insulin. But we found no evidence for an effect on mortality or morbidity. We found clues that with higher dosages the effect on glycated haemoglobin, in contrast to post-load blood glucose, remains the same. This might be because a lower compliance due to increasing side-effects.

BACKGROUND

Diabetes mellitus is a metabolic disorder resulting from a defect in insulin secretion, insulin action, or both. As a result there is a disturbance of carbohydrate, fat and protein metabolism. Long-term complications of diabetes mellitus include retinopathy, nephropathy, neuropathy and increased risk of cardiovascular disease. For a detailed overview of diabetes mellitus, please see under 'Additional information' of the Metabolic and Endocrine Disorders Group on The Cochrane Library (see 'About the Cochrane Collaboration', 'Collaborative Review Groups', 'Cochrane Metabolic and Endocrine Disorders Group'). For an explanation of methodological terms, see the main Glossary on The Cochrane Library.

Alpha-glucosidase inhibitors

One therapeutic option in the treatment of type 2 diabetes mellitus are alpha-glucosidase inhibitors, reversible inhibitors of alpha-glucosidase, an enzyme present in the brush border of the small intestine. alpha-glucosidase inhibitors delay absorption of complex carbohydrates and thus inhibit postprandial glucose peaks thereby leading to decreased postprandial insulin levels.

Currently, four alpha-glucosidase inhibitors exist: acarbose, miglitol, voglibose and emiglitate. Of these, acarbose is by far the most prescribed drug. In most guidelines it is not a drug of first choice but used as an addition to other drugs for type 2 diabetes when treatment goals are not met, or in case of contra-indications for other medications (EDPG 1999; Rutten 2000). The price of acarbose and miglitol is approximately $72 per month for 100 mg tablets, three times daily.

Because of its lowering effect on the postprandial elevation of insulin levels, a beneficial effect on body weight is to be expected. Further, a positive effect on hypertriglyceridaemia has been reported (Reaven 1990). Abdominal discomfort like flatulence, diarrhoea and stomachache are the most frequently occurring adverse effects of alpha-glucosidase inhibitors. Because of their specific working mechanism hypoglycaemic adverse events do not occur. They do not increase insulin output potentially leading to hypoglycaemia.

Recently, alpha-glucosidase inhibitors have been put in a new light as a result of a study on the efficacy of acarbose in patients with impaired glucose tolerance (IGT) (Chiasson 2002; Chiasson 2003). This study showed that acarbose could prevent or delay the development of IGT into type 2 diabetes. Moreover, it showed a reduced risk of cardiovascular disease and hypertension in the acarbose treated group, but the conclusions of this study are heavily debated (Kaiser 2004).

Existing evidence

Systematic reviews

Some reviews have been published recently on the topic of acarbose (Breuer 2003; Laube 2002) and miglitol (Campbell 2000; Scott 2000), these reviews were not performed systematically with respect to one or more of the following items: literature search, inclusion criteria of studies and quality assessment. In none of these reviews a meta-analysis was performed.

A recent meta-analysis of seven trials with acarbose in the treatment of type 2 diabetes suggested a significant decrease in the occurrence of myocardial infarction (Hazard ratio 0.32, 95% CI 0.14 to 0.80) (Hanefeld 2004). However, we do not support the conclusions of this meta-analysis because the study was subject to publication bias, heterogeneity, detection bias and confounding (Van de Laar 2004b).

RCTs

Several randomised clinical trials evaluating the efficacy of alpha-glucosidase inhibitors as monotherapy or as a combination with other agents have been published. Most of these evaluated the efficacy of acarbose. One major trial reported a decrease in glycated haemoglobin of 0.6% when acarbose was given as sole therapy and compared to placebo (Coniff 1995).

Another large (n = 1946) randomised clinical trial, performed within the United Kingdom Prospective Diabetes Study (UKPDS), investigated acarbose versus placebo given in addition to diet, (combined) oral antidiabetic medication or insulin therapy (Holman 1999). At the three-years endpoint, 39% of the patients in the acarbose group and 58% in the placebo group were still taking the study medication. The intention-to-treat analysis showed, that compared with placebo during three years, acarbose lowered glycated haemoglobin by 0.2% (p = 0.003). When only the proportion of patients that continued to take the study medication was considered, this difference was 0.5%. The clinical relevance of this finding remains unclear, especially when considering that even in the per-protocol analysis for most patients using acarbose glycated haemoglobin remained higher than 8.0%. Further, data on other important outcomes like morbidity and mortality are not available from this study. Adverse effects were mostly of gastrointestinal origin (flatulence, stomachache) and were reported to resolve after a short while.

The scope of the current review was to assess the value of monotherapy with alpha-glucosidase inhibitors in the treatment of type 2 diabetes mellitus with respect to patient-oriented outcomes such as morbidity, mortality and quality of life. Further we investigated the value of alpha-glucosidase inhibitors with respect to parameters related to glucose and lipid metabolism, body weight and adverse events. We sought studies that compared alpha-glucosidase inhibitors with placebo or any other intervention. In the future, the review will be regularly updated to include relevant new trials.

OBJECTIVES

To assess the effects of alpha-glucosidase inhibitors primarily on mortality, morbidity and quality of life in patients with type 2 diabetes mellitus, and secondly, the effects on parameters representing glucose and lipid metabolism (that is glycated haemoglobin, glucose, insulin and cholesterol).

CRITERIA FOR CONSIDERING STUDIES FOR THIS REVIEW

Types of studies

Only randomised controlled trials with a minimum duration of three months were eligible for inclusion in this review. Because the common adverse effects of alpha-glucosidase inhibitors make true blinding difficult, both blinded and non-blinded studies were included. We included studies published in any language and all identified trials, published or unpublished, were investigated.

Types of participants

Patients with existing or newly diagnosed type 2 diabetes mellitus. Changes in diagnostic criteria (ADA 1997; ADA 1999; NDDG 1979; WHO 1980; WHO 1985; WHO 1998) may have produced variability in the clinical characteristics of the patients included as well as in the results obtained. These differences will be considered and explored in a sensitivity analysis.

Types of intervention

Monotherapy with alpha-glucosidase inhibitors (acarbose, miglitol, voglibose, emiglitate) compared with any other intervention:
1. Placebo;
2. Sulphonylurea (for example, glibenclamide);
3. Thiazolidinedione (for example, pioglitazone);
4. Meglitinide (for example, nateglinide);
5. Biguanide (for example, metformin);
6. Insulin;
7. Any other pharmacological intervention;
8. A non-pharmacological intervention (for example, diet therapy).

Types of outcome measures

Main outcome measures
1. Mortality: diabetes-related mortality (death from myocardial infarction, stroke, renal disease, or sudden death, death from hyperosmolar nonketotic coma), total mortality;
2. Diabetes-related complications: vascular complications (angina pectoris, myocardial infarction, stroke, peripheral vascular disease, amputation), neuropathy, retinopathy, nephropathy, erectile dysfunction, hyperosmolar nonketotic dysregulation;
3. Quality of life, assessed with a validated instrument.

Additional outcome measures
4. Glycaemic control: glycated haemoglobin levels, fasting and post-load blood glucose levels;
5. Plasma lipids (triglycerides, total-, high-density lipoprotein (HDL)- and low-density lipoprotein (LDL)-cholesterol);
6. Fasting and post-load insulin and C-peptide levels;
7. Body weight (or body mass index);
8. Adverse effects (i.e. diarrhoea, stomachache, flatulence).

Specific patient co-variates thought to be effect modifiers
9. Compliance.

Timing of outcome measurement
We assessed a possible influence of treatment duration in a sensitivity analysis.

SEARCH STRATEGY FOR IDENTIFICATION OF STUDIES

See: Metabolic and Endocrine Disorders Group search strategy

Electronic searches
We used the following sources for the identification of trials:

- The Cochrane Central Register of Controlled Trials (CENTRAL) (2003, issue 3);
- MEDLINE (up to April 2003) using the search terms listed below and combined with the MEDLINE search strategy for randomised controlled trials from the Cochrane Metabolic and Endocrine Disorders Group (see review group search strategy), without language restriction;
- EMBASE (up to April 2003);
- LILACS (www.bireme.br/bvs/I/ibd.htm) from up to April 2003;
- Current Contents (up to December 2003).
- Handsearching: checking references of existing reviews, checking abstract books and poster displays on congresses or meetings attended by the first author. The internet was searches non-systematically by using different combinations of (brand)names for alpha-glucosidase inhibitors.

Databases of ongoing trials (latest access April 2003):

- Current Controlled Trials (http://www.controlled-trials.com - with links to other databases of ongoing trials);
- UK National Research Register (http://www.update-software.com/National/nrr-frame.html);
- USA - CenterWatch Clinical Trials Listing Service (http://www.CenterWatch.com/);
- USA - National Institutes of Health (http://clinicalstudies.info.nih.gov/).

All records from each database that seemed eligible after assessing the title and/or abstract were imported to a bibliographic database, Reference Manager (Version 10, ISI ResearchSoft), checked for duplicates and merged into one core database. The content of that database was exported to the Review Manager computer program (Revman 4.2.3, The Cochrane Collaboration).

The described search strategy has been used for MEDLINE. For use with EMBASE and Current Contents this strategy was slightly adapted because these databases were only available with different browsers. The necessary alterations in search string were done in such a way that the search became more sensitive (that is yielded a higher number of 'hits'). In CENTRAL, LILACS and the databases of ongoing trials we searched with the various text words for the alpha-glucosidase inhibitors and their brand names. For the detailed search strategy see under 'Additional tables' (Table 02).

Handsearching
We searched reference lists of relevant trials and alpha-glucosidase inhibitor reviews and selected possible references that were not already in our database.

Other search strategies
Authors of relevant identified studies and other experts were contacted by mail in order to obtain additional references, unpublished trials, and ongoing trials or to obtain missing data not reported in the original trials. Similarly, manufacturers and patent holders (Bayer AG, Sanofi-Synthelabo, Pfizer, Takeda) were contacted in order to retrieve information on alpha-glucosidase inhibitors trials, published and unpublished.

METHODS OF THE REVIEW

Trial selection
Two reviewers (FVDL and PL) independently checked the titles, abstract sections and keywords of every record retrieved. Full articles were retrieved for further assessment when the information given suggested that the study: 1) included patients with diabetes mellitus, 2) compared alpha-glucosidase inhibitors with placebo or any other active intervention, 3) assessed one or more relevant predefined clinical outcome measure, 4) used random allocation to the comparison groups. In case of any doubt regarding these criteria from the information given in the title and abstract, the full article was retrieved for clarification. Interrater agreement for study selection was measured using the kappa statistic (Cohen 1960). Differences in opinion were resolved by a third party (EVDL) and when resolving the disagreement was not possible, the article was added to those 'awaiting assessment' and the authors were contacted for clarification. If the authors provided no clarification, the review group editorial base was consulted.

Quality assessment of trials
The two reviewers assessed each trial independently. Possible disagreement was resolved with consensus, or with consultation of a third reviewer (EVDL) in case of disagreement. In particular, the following quality criteria were assessed:

Minimisation of selection bias:

- Randomisation procedure: the randomisation procedures were scored adequate if the resulting sequences were unpredictable (that is computer generated schemes, tables of random numbers, coin tossing).
- Allocation concealment: allocation concealment was scored adequate if participating patients and investigators could not foresee the assignment (that is by central randomisation remote from trial site, sequentially numbered and sealed radio-opaque envelopes).

Minimisation of performance bias:

- Method of blinding: blinding was considered adequate if the two (or more) interventions were similar in size, colour and shape or when a double-dummy method was applied. Because of the sometimes-obvious adverse effects of alpha-glucosidase inhibitors, true blinding was difficult. For trials that reported blinding of patients for medications, we also investigated whether blinding was checked; for example by asking patient and investigator afterwards about the medication they suspected to be supplied.

Minimisation of attrition bias:

- Handling of drop-outs: handling of drop-outs was considered adequate if studies gave a complete description of all patients failing to participate until the end of the trial and if the data were analysed on intention-to-treat (ITT) basis, that means with all randomised patients included.
- Quantity of dropouts: overall dropout rate less than 15% was considered adequate.
- Selective dropout: a difference in dropout rate the in main treatment groups less than 10% was considered adequate.

Minimisation of detection bias:

- Method of blinding outcome-assessment: this item was considered less relevant for studies with laboratory data or death as main outcomes or if the (blinded) investigator was also outcome assessor. If applicable, outcome assessment was considered adequate if the outcome assessors were completely blind for the intervention.

We explored the influence of individual quality criteria in a sensitivity analysis (see under 'sensitivity analyses').

Based on these criteria, studies were broadly subdivided into the following three categories adapted from the Cochrane Handbook criteria (see Cochrane Handbook):
A - All quality criteria met (1. adequate randomisation and allocation concealment, 2. adequate blinding, 3. adequate ITT analysis and/or both drop-out rate less than 15% and selective drop-out less than 10%): low risk of bias.
B - One or more quality criteria only partially met (1. adequate randomisation or adequate allocation concealment, 2. mentioning of blinding but exact method unclear, 3. inadequate/unclear ITT analysis but drop-out less than 15% or selective drop-out less than 10%): moderate risk of bias.
C - One or more quality criteria not met (1. inadequate randomisation and allocation concealment, 2. inadequate or no blinding, 3. inadequate ITT and drop-out rate equal to or more than 15% and selective drop-out equal to or more than 10%): high risk of bias.

This adapted classification was also used as the basis of a sensitivity analysis.

Data extraction

Two reviewers extracted data on intervention and outcomes independently, using a pre-tested data extraction form that was adapted from a standard form provided by the review group. The data extraction form included the following items:

- General information: author, type of publication (including the existence of duplicate or multiple publications), year of publication, language, country were the study was conducted, setting (general practice, hospital or outpatient / rural, city, developed / developing world / single or multi-centre), the stated aim of the study published, sponsor(s), ethics approval;
- Study characteristics: parallel or cross-over, type of control groups (placebo, other medication etc.), existence of run-in and/or wash-out period, description of possible carry-over effect (for cross-over studies), method, type and quality of randomisation, method and quality of allocation concealment, method and quality of blinding, information about handling of drop-outs, withdrawals and losses to follow-up, numbers of and reasons for drop-out, existence of possible sub-groups, method of assessment of compliance;
- Participants: description of diagnostic criteria for type 2 diabetes mellitus, inclusion and exclusion criteria,
- Interventions: specification of a possible reinforcement of diet therapy, the nature, dose and regimen (including: fixed or titrated dose, step-up dosage scheme) of alpha-glucosidase inhibitor(s) and control interventions, duration of intervention and follow-up;
- Baseline characteristics and measurements: numbers of patients, sex, age, ethnicity, socio-economic status and duration of diabetes, existence of significant differences at baseline, baseline glycated haemoglobin, fasting and post-load blood glucose, plasma lipids (triglycerides, total-, HDL- and LDL-cholesterol), height, weight and body mass index (BMI), fasting and post-load insulin and C-peptide (standard deviations if applicable), specifications (including reference ranges) of all laboratory measurements, type of post-load test, time between fasting and post-load measurements, centralisation of laboratory measurements;
- Outcomes: total and disease specific deaths and morbidity, quality of life (including method of assessment), mean changes (standard deviation, SD) of the following values: glycated haemoglobin, fasting and post-load blood glucose, lipids, fasting and post-load insulin / C-peptide, body weight, BMI, occurrence of adverse events (total and gastro-intestinal), compliance.

When more than onde publication was available from a study, all articles were abstracted and scores separately and the collected data was synthesized. In case of contradictorily findings, the author was contacted for clarification.

Differences in data extraction were resolved by consensus, referring back to the original article. If necessary, information was sought from the authors of the original studies.
If necessary, data were also extracted from graphical figures: two reviewers (FVDL and PL) calculated the data independently and if both outcomes were not similar, a third reviewer (EVDL) recalculated the data. A statistician checked all extracted data for errors, after transfer to the database.

Data analysis
Data were summarised statistically if available and of sufficient quality. The table of comparison was first divided in all possible comparisons (that is acarbose versus placebo / voglibose versus sulphonylurea), then sub-divided into all possible outcomes (that is death, glycated haemoglobin adverse events) and finally, within the outcomes sub-groups were made for the different dosages. Outcomes were calculated per sub-group and for all sub-groups together.

Dichotomous data were expressed as odds ratios (OR), but in some cases the relative risk (RR) was also calculated in addition to the OR since its interpretation is easier, especially if the outcome was a negative event, for example death. We calculated the risk difference (RD) and we converted the RD into the number needed to treat (NNT) or the number needed to harm (NNH) taking into account the time of follow-up.

Continuous data were expressed as weighted mean differences (WMD) and an overall WMD was calculated. The actual measure of effect of all continuous variables were the differences from baseline to endpoint. The standard deviations of these differences were essential for the data to be included in the meta-analysis. When the standard deviation (SD) of the difference was not reported we first asked the authors to provide these data. If the SDs were not provided we estimated the SD of the difference with the following formula:

SDpaireddifference = ??(SD1)2 + (SD2)2 - 2 x r x SD1 x SD2].

SDpaireddifference = standard deviation of the difference (pre- / post-treatment)
SD1 = Standard deviation of the pre-treatment value, SD2 = Standard deviation of the post-treatment value, r = correlation coefficient. We used a conservative correlation coefficient of 0.4.

Overall results were calculated based on the random effects model. Heterogeneity was statistically tested by using the Z score and the Chi square statistic with significance set at $p < 0.10$. Possible sources of heterogeneity were assessed by subgroup, sensitivity and meta-regression analyses as described below. Small study bias was tested for using the funnel plot or other corrective analytical methods depending on the number of clinical trials included in the systematic review (Begg 1994; Egger 1997; Hedges 1992). Quantification of the effect of heterogeneity will be assessed by means of I squared, ranging from 0-100% including its 95% confidence interval (Higgins 2002). I squared demonstrates the percentage of total variation across studies due to heterogeneity and will be used to judge the consistency of evidence.

The analyses were done with the computer program RevMan Analyses 1.0.2 in Review Manager 4.2.3 (2003, The Cochrane Collaboration).

Subgroup analyses
Significant main outcome measures were explored by subgroup analyses in order to explore differences in effect as follows:

1) Glycated haemoglobin level at baseline (subdividing into three groups: less than 7%, 7 to 9%, more than 9%);
2) Age (based on mean age of total randomised group);
3) Gender (subdivided in two groups, based on data: less than 45% female, equal or more than 45% female);
4) Body mass index (BMI) (Normal: male less than 27, female less than 25; overweight: male 27 to 30, female 25 to 30; obese: more than 30);
5) Different kind of diets or exercise schedules used;
6) Duration of intervention (less than 24 weeks, 24 weeks, more than 24 weeks);

Sensitivity analyses
The sensitivity of the analysis for a number of factors was determined by comparing the results of the meta-analysis for studies with and without certain characteristics. Data from a minimum of five studies had to be available for both groups to be considered. The following factors were investigated:

1) Comparing published and unpublished studies;
2) Comparing studies with and without (or with unknown) quality characteristics: adequate randomisation, adequate allocation concealment, adequate method of blinding, adequate ITT analyses. Further, comparing studies with an overall drop-out rate equal to or more than 15% and less than 15%, difference of drop-out rates less than 10% and equal to or more than 10% between the main treatment groups. In addition, the overall score for quality based on the adapted Cochrane criteria was used so that studies with score A and B were compared with studies with C;
3) Repeating the analysis excluding trials using the following filters: diagnostic criteria, language of publication, source of funding (industry versus other or no sponsoring) or country;
4) Repeating the analyses using different measures of effect size (relative risk, risk difference) and different statistical models (fixed and random effects models);

Meta-regression analyses
We used meta-regression analyses (in SAS proc MIXED, version 8.0) to explore the influence of characteristics of study population and study design on the outcomes. We studied the dependent variables glycated haemoglobin, fasting and post-load glucose, fasting and post-load insulin, total cholesterol, triglycerides and adverse effects. The independent variables were similar to the pre-defined sub-groups (baseline glycated haemoglobin, age, gender, baseline BMI, and duration of treatment). In addition we studied

duration of diabetes at baseline, the use of a fixed dose and the use of a step-up dosage regimen. The weight of each trial was equal to the inverse sum of the within trial variance and the residual between trial variance, in order to perform a random effects analysis. To gain sufficient power, data from at least 10 studies had to be available to calculate results from the meta-regression.

DESCRIPTION OF STUDIES

Trials identified (See study flow diagram Figure 02)
* CENTRAL: 262 records were retrieved and assessed on the basis of title and/or abstract (Issue 3 2003), 59 records were initially included. Ten records were excluded after the full article had been read. So 49 records were finally included in the review.
* MEDLINE: 328 records found (April 2003), 43 records initially included, 34 records finally included in the review.
* Embase: 567 records found (April 2003), 50 records initially included, 40 records finally included in the review.
* Current Contents (December 2003): 260 records found, 27 records initially included, 23 records finally included in the review.
* LILACS: 13 records found, one records initially but excluded after further scrutiny.

Experts: We obtained 14 references as a result of correspondence with experts: seven references after a general mailing to 27 experts with a request for additional references (six out of 27 forms were returned), and another seven references as a result of contacts which we established searching for missing or additional data. Two references were already in our possession (one study performed by our group but that was not published at that time (Van de Laar 2004a) and an article referring to two trials (Fölsch 1990, using data from Hoffmann 1990 and Spengler 1992).
We included nine (out of these 16) references in the final review.

Manufacturers: Bayer, the developer of acarbose and miglitol, sent us 23 references, 17 were initially included and 16 were finally included in the review. The developer and patent holder of voglibose (Takeda) and the patent holders of miglitol (Pfizer and Sanofi-Synthelabo) did not reply to our letters.

Handsearch: 22 possibly eligible references were found by handsearching (checking references of existing reviews, browsing on the internet, posters on congresses etc.). Seventeen references were initially included, of which 14 references were finally included in the review.

Databases of ongoing trials (see table Characteristics of ongoing trials): in addition three studies were identified as ongoing studies in trial registers. All attempts to retrieve reports or data from these studies, failed so far.

Interrater agreement
Interrater kappa for agreement on inclusion, calculated on basis of the first 852 titles and / or abstracts read by the two reviewers (FVDL and PL) was good: 0.74 (95% confidence interval 0.67 to 0.81). All differences in opinion were resolved by consensus.

Missing data
Because none of the articles contained all the study data we required for the quality assessment and meta-analyses, we attempted to contact all corresponding authors. For one study we could not retrieve contact information (Hillebrand 1987). For 22 out of 41 studies we received additional data about design, quality and/or outcomes. For 12 studies the authors delegated the reply to representatives of Bayer Germany, USA or Italy because the data-files were kept by this firm. Studies for which we received additional data are indicated in the table 'Characteristics of included studies' and the reference list (published and unpublished data).

Excluded studies
Fifteen studies were excluded after reading the full article (see Figure 02). The most common reason was that patients used anti-diabetic medication in addition to the study medication. See table 'Charcteristics of excluded studies' for further details.

Included studies
Fourty-one studies with 8130 participants, described in 69 articles, abstracts, posters or unpublished documents were finally included in the review. Details are given in the Table of included studies.
Thirty-five studies were published as journal articles, three studies as abstract only (Campbell 1998; Hillebrand 1987; Rybka 1999) and two studies were found by their poster presentation (Holmes 2001; Kawamori 2003), one study done by our own group was accepted for publication during the review process (Van de Laar 2004a).
Four studies were performed in general practice, for one study the patients were recruited in general practice but all study related activities were done in so-called 'study-centres' (Drent 2002), patients from 34 studies were characterised as 'outpatients' and for two studies the setting was not reported.
Thirty-nine studies had a parallel design and two were crossover studies (Gentile 1999, Hillebrand 1987). Thirty-three studies were double-blinded, five studies were not blinded and three studies with three treatment groups were not blinded with respect to one treatment arm (metformin and glibenclamide).
Nineteen studies compared acarbose with placebo, four of which compared two or more doses with placebo. Eleven studies compared acarbose with other anti-diabetic medication and in most cases also with placebo. Miglitol was studied in comparison with placebo in three studies, one of which with four different dosages. In four studies miglitol was compared with other anti-diabetic medication (and placebo eventually). Two three-arm studies compared acarbose with miglitol and placebo (one study) or glibenclamide (one study). One study compared miglitol and voglibose (and placebo) and one trial studied voglibose versus diet and glyburide (a sulphonylurea). We found no studies with emiglitate.
Study duration was 24 weeks (21 studies), 16 weeks (seven studies), one year (four studies), 12 weeks (four studies), three years (two

studies), 30 weeks, 36 weeks or 56 weeks (all one study).
Two studies reported data on mortality (Coniff 1995; Johnston 1998) and one crossover study reported that no patients had died (Gentile 1999). Two studies reported data on morbidity (Holman 1999; Johnston 1998) and one study reported quality of life as an outcome (Meneilly 2000), but none of these data were primary efficacy measures.

Measurement of post-load blood glucose, insulin and c-peptide
There are several methods to determine the patients' response to a glucose load. The 'load' may consist of simple glucose (like in an oral Glucose Tolerance Test, oGTT), a standardised or ad libitum meal, or a standardised portion of carbohydrates. Studies may also differ in the time-interval used for the test and if the study drug was given prior to the test. We assessed all those differences and described them in a table (Table 01). Most studies used some form of test-meal with carbohydrates, except for two studies which used an OGTT (Hotta 1993; Van de Laar 2004a). In two studies the type of test was unclear (Hillebrand 1987; Rybka 1999).
For two studies, the only post-load measurement was at a 2-hours interval (Hotta 1993; Pagano 1995) and six studies reported both one and two hour values (Chiasson 2001; Coniff 1994; Coniff 1995; Coniff 1995b; Kawamori 2003; Santeusanio 1993), all other studies that measured post-load values for glucose, insulin and/or C-peptide used an 1-hour interval. Therefore, we chose to report the 1-hour values for post-load glucose, insulin and C-peptide, and to use the 2-hour outcomes if 1-hour data were not available. As a sensitivity analysis, we repeated the analysis with the opposite method: using the 2-hour values, and the 1-hour values for studies that did not report 2-hour measurements.

METHODOLOGICAL QUALITY

See table quality of studies in Figure 01.

Methodological quality
With respect to selection bias 11 studies had both an adequate randomisation and allocation concealment. The risk of attrition bias was low in 14 studies: one study had adequate ITT; one study had both adequate ITT analysis and low total / selective drop-out (less than 15% total drop-out, less than 10% difference between groups); 12 studies had low total / selective drop-out. Blinding (performance bias) was adequate in 22 studies.
The overall quality was roughly assessed on a three point scale according to the Cochrane handbook: five studies scored A (low risk of bias) and five studies B (moderate risk of bias). The other 31 studies scored C (high risk of bias).

Missing data
In a number of cases it was reported that certain outcomes (that is fasting blood glucose, triglycerides) were investigated, but the results were not or insufficiently reported (that is standard deviations missing). This was especially striking for a study with acarbose, that was of long duration and with a large number of participants (Campbell 1998). Data from this trial could not be used because the main outcome measure was the time until patients with good control on diet alone needed additional medication. Data from a large study of long duration investigating miglitol could not be used as no measures of variance were reported for the main outcomes (that are standard deviations) (Johnston 1998). Our written request for these data, has not been answered so far.
One large study (603 participants) comparing miglitol and acarbose was published as an abstract only (Rybka 1999). Attempts to contact the author failed so far.

RESULTS

Heterogeneity
Statistical tests for heterogeneity yielded statistically significant results in many cases. Studies were homogenous with respect to the fact that all participants were described as having type 2 diabetes and that they used the test drug as mono therapy for at least three months. But studies could differ with respect to country (and thus dietary habits), age, severity and duration of diabetes. These possible sources for heterogeneity were investigated in the subgroup and meta-regression analyses.

Effects of the intervention

Mortality, morbidity, quality of life
Three studies reported the occurrence of death (Coniff 1995; Holman 1999; Johnston 1998). No statistically or clinically significant differences in outcomes were found.
One 3-year study reported data on morbidity as relative risks (Holman 1999). The relative risk for acarbose users compared with placebo for "any diabetes-related end point" was 1.0 (95% confidence interval 0.8 to 1.2) and for microvascular disease 0.9 (95% confidence interval 0.6 to 1.4). The outcome for the subgroup actually receiving acarbose monotherapy was not reported.
One 56-weeks study that compared 25 mg and 50 mg TID miglitol with glyburide and placebo, reported the number of cardiovascular events in the table of adverse effects (Johnston 1998). The percentage of occurrence of any cardiovascular event was 19%, 17%, 22% and 29% for miglitol 25 mg TID, miglitol 50 mg TID, placebo and glyburide respectively. Statistical significance was reached for the comparison miglitol 50 mg and glyburide.

Glycemic control

Glycated haemoglobin, alpha-glucosidase inhibitors versus placebo
alpha-glucosidase inhibitors had a clear beneficial effect on glycemic control compared to placebo. Glycated haemoglobin was considered the primary measurement in most studies. The results of the meta-analysis for overall effect of alpha-glucosidase inhibitor on glycated haemoglobin compared to placebo was -0.8% (95% confidence interval -0.9 to -0.6, 28 comparisons) for acarbose and

-0.7% (95% confidence interval -0.9 to -0.4, seven comparisons) for miglitol. For voglibose, data from only one comparison were available: -0.5% (95% confidence interval -0.6 to -0.3). We did not see a clear dose dependency of the effect on glycated haemoglobin with respect to acarbose. Effect sizes for the subgroups for dosage 25 mg (n = 1 study), 50 mg (n = 2), 100 mg (n = 17), 200 mg (n = 4) and 300 mg (n = 2) TID were -0.5%, -0.9%, -0.8%, -0.8% and -0.8% respectively.
For miglitol, there seemed to be a dose dependent effect on glycated haemoglobin, but data from only seven comparisons, of which four originating from the same multi-arm study (Drent 2002), were available.

Fasting and post-load blood glucose, alpha-glucosidase inhibitors versus placebo
We also found a beneficial effect on fasting blood glucose for acarbose compared to placebo in a meta-analysis with 28 comparisons: -1.1 mmol/L (95% confidence interval -1.4 to -0.8). For miglitol and voglibose two and one comparisons were available in the meta-analysis with fasting blood glucose as outcome. These analyses resulted in a mean decrease in fasting blood glucose of -0.5 mmol/L (miglitol, 95% confidence interval -0.9 to -0.2) and -0.6 mmol/L (voglibose, 95% confidence interval -1.0 to -0.2).
The influence on (1-hour) post-load blood glucose was more profound. Overall effect on post-load blood glucose was -2.3 mmol/L (95% confidence interval -2.7 to -1.9, 22 comparisons). The subgroups for dosage showed a dose dependent pattern. For miglitol and voglibose only very limited data were available: miglitol -2.7 mmol/L 95% confidence interval -5.5 to 0.1, two comparisons), voglibose -2.4 mmol/L (95% -3.0 to -1.8, one comparison).
In contrast to the effect on glycated haemoglobin, the forest plots for the comparison acarbose versus placebo and the outcome fasting and post-load blood glucose suggested a dose dependency of the treatment effect.
Because not all studies used similar methods for the measurement of post-load blood glucose we repeated the analyses replacing 1-hour post-load data by 2-hour values (if available). We found no differences in that analysis compared with the meta-analysis in which we primarily used the 1-hour values.

Alpha-glucosidase inhibitors versus other medication
Studies that compared an alpha-glucosidase inhibitor with other interventions than placebo were scarce. Pooling of results was only possible for the comparison acarbose with sulphonylurea, as data from eight comparisons were available. For other comparisons, pooling was not possible because of lack of studies (metformin and nateglinide, both one study). The overall comparison acarbose versus sulphonylureas yielded a non-significant trend for sulphonylureas with respect to glycated haemoglobin (0.4%, 95% confidence interval -0.0 to 0.8). The results in the subgroup 'Acarbose 100 mg TID versus Glibenclamide 3.5 mg TID' were not consistent with the other comparisons (overall test for heterogeneity p < 0.00001). Leaving the entire sub-group out of the analysis would give an overall effect of 0.6% (95% confidence interval 0.3 to 1.0) in favour of sulphonylurea with a non-significant chi-square test for heterogeneity (p = 0.15). In the comparison acarbose versus sulphonylurea one study seemed to be an outlier (Kovacevic 1997), but the results of that study were again in line with the comparisons with other sulphonylurea. For most comparisons acarbose versus sulphonylurea, acarbose was given as a fixed dose and the sulphonylurea individually adjusted, mostly sub-maximal.
The result for fasting blood glucose showed a similar pattern: superiority for sulphonylurea except for the subgroup 'Acarbose 100 mg TID vs. Glibenclamide 3.5 mg TID'. Overall effect 0.7 mmol/L (95% confidence interval 0.2 to 1.2) in favour of sulphonylurea. Without the deviating sub-group: 1.2 mmol/L (95% confidence interval 0.6 to 1.8) in favour of sulphonylurea.
The outcome post-load blood glucose yielded no statistically significant differences between acarbose and sulphonylurea.

Results from studies not included in the meta-analyses:
In a four-arm study comparing miglitol 25 mg TID, miglitol 50 mg TID, glyburide maximum 20 mg QD or placebo, glycated haemoglobin decreased by 0.5%, 0.4%, 0.9% and 0.0% respectively (Johnston 1998). Similarly fasting blood glucose decreased by 0.7 mmol/L, 1.1 mmol/L, 1.7 mmol/L and 0.1 mmol/L and one hour post-load blood glucose decreased by 2.4 mmol/L, 3.2 mmol/L, 1.8 mmol/L and 0.0 mmol/L respectively.
One study with 603 participants and of 24 weeks duration (Rybka 1999) reported a placebo subtracted decrease of glycated haemoglobin of 0.4%, 0.5% and 0.4% respectively for miglitol 50 mg TID, miglitol 100 mg TID and acarbose 100 mg TID.

Plasma lipids
We found no effects of acarbose compared to placebo on total, HDL- and LDL-cholesterol. There was no statistically significant effect on triglycerides: -0.1 mmol/L (21 comparisons, 95% confidence interval -0.2 to 0.0). With respect to the comparison with sulphonylurea no statistically significant differences were found.
Very few comparisons (arcabose versus metformin etc.) were available.

Fasting and post-load insulin and c-peptide
The 25 studies that assessed pancreatic function mostly used insulin levels for this purpose. We found that acarbose had no statistically significant effect on fasting insulin levels compared to placebo and a non-statistically significant decreasing effect on post-load insulin levels (fasting insulin: -1 pmol/L (15 comparisons, 95% confidence interval -8 to 7), post-load insulin: -41 pmol/L (13 comparisons, 95% confidence interval -61 to -19)). For miglitol and voglibose only a limited number of comparisons were available and no statistically significant differences were found.
Compared to sulphonylurea, acarbose had a statistically significant decreasing effect on fasting insulin (seven comparisons, -25 pmol/L, 95% confidence interval -43 to -6) and post-load insulin as well (seven comparisons, -133 pmol/L, 95% confidence interval -185 to -82). Only one study compared miglitol with a sulphonylurea and found an opposite result: fasting insulin 28 pmol/L

increase compared to sulphonylurea (Pagano 1995). Post-load insulin was not measured in that study.

Body weight and Body Mass Index

Compared to placebo, alpha-glucosidase inhibitors had minimal effects on body weight. There were no statistically significant differences for body weight in the meta-analysis for acarbose versus placebo, but BMI decreased slightly in favour of acarbose: -0.2 kg/m2 (13 comparisons, 95% confidence interval -0.3 to -0.1).

The reported advantage for alpha-glucosidase inhibitors on body weight compared to sulphonylurea could not be confirmed: no significant differences were found.

Adverse events

Most studies reported the total number of adverse events and although it became clear from most reports that by far the most adverse effects were of gastro-intestinal origin, the number of patients with gastro-intestinal adverse effects were rarely reported exactly.

Compared to placebo, patients treated with acarbose reported significantly more adverse effects: OR 3.4 (or relative risk 1.4) (23 comparisons, 95% confidence interval 3.4 to 4.4). There was a dose dependent increase in adverse effects in the range 25 mg TID to 200 mg TID. When the sub-group for studies that applied a fixed dosage scheme (in contrast to studies with an individually titrated dose) was considered, the dose dependency was more clear: ORs for adverse events were 1.6, 2.9, 4.1, 7.0 and 8.3 for the dosages 25, 50, 100, 200 and 300 mg TID respectively. Most studies reported that the adverse events mainly consisted of gastro-intestinal symptoms. The meta-analysis on gastro-intestinal adverse events yielded a similar result: OR 3.30 (or relative risk 1.8) (four comparisons, 95% confidence interval 2.2 to 4.7). The comparison miglitol versus placebo resulted in similar figures: all adverse events OR 4.0 (seven comparisons, 95% confidence interval 1.7 to 9.5).

Compared to sulphonylurea, patients treated with acarbose had more adverse effects: OR 4.0 (seven comparisons, 95% confidence interval 2.0 to 7.8). Only two studies provided data for the comparison miglitol versus sulphonylurea: OR 1.3 (95% confidence interval 0.7 to 2.4).

Sensitivity analyses

We compared outcomes of meta-analyses between studies with and without certain characteristics. The results were considered of possible interest when the 95% confidence intervals of the two groups in the analysis (for example results from studies with adequate randomisation versus inadequate randomisation) did not overlap, or when one group yielded a statistically significant result whereas the other did not. At least five studies had to be in each groups to be considered, this was only the case for the comparison acarbose versus placebo.

1. Unpublished versus published studies

By the time the analyses were done, one study that was initially included as unpublished study was published (Van de Laar 2004a). All other studies were published in some form. Some studies were published otherwise than as a journal article: letter-to-the-editor (Calle-Pascual 1996) or congress abstract (Campbell 1998, Hillebrand 1987, Holmes 2001, Kawamori 2003, Rybka 1999). Because data from three of these studies could not be included in the meta-analysis, sensitivity analysis was not possible.

2. Quality criteria

Randomisation: studies with inadequate or unclear randomisation showed a beneficial effect of acarbose on total cholesterol: -0.3 (95% CI -0.5 to -0.0) versus 0.0 (95% CI -0.1 to 0.1) for studies with adequate randomisation. No other differences between studies with adequate and inadequate/unclear randomisation were found.

Allocation concealment: the studies with adequate allocation concealment showed a slightly more profound effect on glycaemic control although not statistically significant: glycated haemoglobin -0.8% (adequate allocation concealment) versus -0.7 (not adequate or unclear).

Blinding: we found no differences between studies with no or inadequate blinding and studies with adequate blinding.

ITT adequate: only two studies were considered to have done adequate ITT analyses, therefore sensitivity analyses were not possible.

Total dropout rate: studies with a total dropout rate less than 15% showed a beneficial effect on post-load insulin levels compared to studies with a total dropout rate equal to or more than 15%: -52 (95% confidence interval -77 to -29) versus -18 (95% confidence interval -55 to 19). No other differences between studies with high or low drop-out rates were found.

Selective drop-out (difference in drop-out between treatment groups): we found no differences between studies with selective dropout rate less than 10% or equal to or more than 10%.

Overall quality: studies with a overall quality A or B (high) showed a beneficial effect on post-load insulin levels compared to studies with an overall quality score of C (low): -46 (95% confidence interval -64 to -29) versus -8 (95% confidence interval -68 to 52). No other differences were found.

3. Other

Diagnostic criteria

Eight studies referred to the WHO criteria from 1985 (WHO 1985), three studies to the criteria from the National Diabetes Data group 1979 (NDDG 1979), two studies referred to WHO criteria of unknown data, one study referred to both ADA guidelines from 1997 (ADA 1997) and WHO guidelines from 1987 (unknown origin, no reference given), one study used the so-called UKPDS protocol (Holman 1999) and one study referred to diagnostic criteria of the Japan Diabetes Society. Twenty-five studies did not refer to specific diagnostic criteria of type 2 diabetes. Although most studies referred diagnostic criteria (that is fasting blood glucose more than 7.8 mmol/L), it was often not clear whether these criteria were used for the trial selection or for the original diagnosis. Sensitivity analysis was not possible with these data.

Language of publication
For most included studies the primary publication was in English, with exception of one study in Russian (Dedov 1995) and one in the Italian language (Gentile 1999). Thus, sensitivity analysis was not performed.

Source of funding
For one study the authors made clear that it was not sponsored (Calle-Pascual 1996), two study were sponsored by fundings other than a pharmaceutical company (Gentile 1999, Haffner 1997), for five studies possible sponsoring was not specified and all other studies were sponsored by a pharmaceutical company. Accordingly, sensitivity analysis was not performed.

Country
Twenty-five studies were conducted in Europe (including one Russian study), nine studies in the USA or Canada, six studies in Asia (including one Turkish study) and one study was performed in New Zealand and Australia.
European studies versus non-European studies: studies that were conducted in Europe showed a tendency towards a greater effect on glycated haemoglobin (-0.9%, 95% confidence interval -1.0 to -0.7) compared to non-European studies (-0.7%, 95% confidence interval -0.8 to -0.5). On the other hand, the effect on post-load blood glucose was significantly less than for the non-European studies: -1.9 mmol/L (95% confidence interval -2.2 to -1.5) for the European studies versus -3.3 mmol/L (95% CI -4.2 to -2.3) for the non-European studies. These differences could not be fully explained when the Asian studies were excluded from the analyses. We also compared the Asian studies with non-Asian studies separately because of the high carbohydrate food habits in Asia. The analyses with Asian studies only yielded a lower effect on glycated haemoglobin compared with the analyses with non-Asian studies (-0.5% versus -0.8%) but in the Asian group only three comparisons were available.

4. Different statistical models
We repeated the analyses for all outcomes using a fixed effects model. This yielded similar results with only two exceptions: 1) the effect on fasting insulin levels in the comparison acarbose versus placebo was statistically significant with a fixed effects model (5 pmol/L in favour of placebo, 95% confidence interval 1 to 10) 2) the effect on body weight in the comparison acarbose versus sulphonylurea was statistically significant with a fixed effects model (-1.4 in favour of acarbose, 95% confidence interval -1.9 to -0.9).

Sub-group analyses (Tables available on request)

- Subgroups baseline glycated haemoglobin: Subgroup 1a (acarbose - placebo), Subgroup 1b (tables available on request) (acarbose - sulphonylurea). The effects on glycated haemoglobin and post-load insulin tended to be more profound with higher baseline glycated haemoglobin.
- Subgroups gender: Subgroup 2a, Subgroup 2b (tables available on request). No significant differences between studies with less and more or equal than 45% female participants were observed.
- Subgroups baseline BMI: Subgroup 3a, Subgroup 3b (tables available on request). No significant differences between studies in patients with different mean baseline BMI values were observed.
- Subgroups study duration: Subgroup 4a, Subgroup 4b (tables available on request). We found a tendency towards a lower effect in studies that lasted longer than 24 weeks. The effect on glycated haemoglobin was -0.8%, -0.8% and -0.5% for studies less than 24, 24 and more than 24 weeks respectively. However only three studies were included in the latter (more than 24 weeks) categorie.

In addition to the pre-defined sub-groups, we also investigated the following subgroups: different duration of diabetes (mean duration of diabetes less or equal/more than 55 months), groups with a step-up dose regimen versus studies that administered the full dose at once and studies that used a fixed dosage scheme versus studies with an individually titrated scheme.

- Subgroups mean duration of diabetes: Subgroup 5a, Subgroup 5b (tables available on request). No significant differences between studies in patients with a mean duration of diabetes less or equal/more 55 months were observed.
- Subgroups step-up dosage versus no step-up dosages: Studies investigating acarbose versus placebo that used a step-up dosing schedule, tended to result in less effect on glycated haemoglobin, fasting and post-load blood glucose than studies that gave the full dose at once. On the other hand, the latter studies reported more adverse effects. The 95% confidence intervals for fasting blood glucose and adverse effects in both groups did not overlap indicating statistical significance (Subgroup 6a).

This effect was also found in the comparison acarbose versus sulphonylurea. (Subgroup 6b) (tables available on request)

- Subgroups fixed dose versus individually titrated: Subgroup 7a, Subgroup 7b (tables available on request). Studies that used a fixed dose showed more profound effect on glycated haemoglobin (-0.8% versus -0.5%) with no different effect on fasting blood glucose.

Meta-regression analyses (Tables available on request)
For the comparison acarbose versus placebo, sufficient data were available to perform meta-regression analyses.
Glycated haemoglobin: regression coefficient for mean baseline glycated Hb was -0.12, indicating a decrease in outcome value of 0.12% per 1% increase of baseline glycated Hb. The use of a fixed dosage yielded a regression coefficient of -0.32 (95% CI -0.69 to 0.04) and a step-up dosage scheme regression coefficient of 0.36 (95% CI 0.06 to 0.66), thus having an increasing influence

on glycated haemoglobin (Metaregression 1, table available on request).

Fasting blood glucose: use of a step-up dosages scheme had a deteriorating effect on the outcome: correlation coefficient 0.62 (95% CI 0.05 to 1.19) (Metaregression 2, table available on request).

Post-load blood glucose: no statistically significant effects were found (Metaregression 3, table available on request).
Total cholesterol: no statistically significant effects were found (Metaregression 4, table available on request).
Triglycerides: no statistically significant effects were found (Metaregression 5, table available on request).
Fasting insulin: no statistically significant effects were found (Metaregression 6, table available on request).
Post-load insulin: no statistically significant effects were found (Metaregression 7, table available on request)
Body weight: no statistically significant effects were found (Metaregression 8, table available on request).
Total adverse effects: The use of a step-up dosing scheme had a statistically significant decreasing effect on the occurrence of adverse effects (regression coefficient 0.50, 95% CI 0.29 to 0.88) (Metaregression 9, table available on request).

DISCUSSION

Summary

In this systematic review, we found no statistically significant effect for an effect of alpha-glucosidase inhibitors on mortality, morbidity and quality of life in patients with type 2 diabetes mellitus. Compared to placebo, alpha-glucosidase inhibitors reduce glycated hemoglobin (0.8% acarbose, 0.7% miglitol), fasting and postprandial blood glucose (acarbose: fasting glucose 1.1 mmol/L, post-load blood glucose 2.3 mmol/L) and post-load insulin. We found no clinically relevant effects on plasma lipids and body weight. We found no dose dependency for the effect on glycated haemoglobin for acarbose. alpha-glucosidase inhibitors caused significant more adverse effects, especially of gastro-intestinal origin. It should be noted that the data of the largest and longest studies could not be used for meta-analyses. Compared to sulphonylurea alpha-glucosidase inhibitors were inferior with respect to glycemic control and adverse effects, the extent of this effect differed with the sulphonylurea used. On the contrary, alpha-glucosidase inhibitors had a decreasing effect on fasting and post-load insulin levels compared to sulphonylurea. Of the three alpha-glucosidase inhibitors investigated, acarbose, miglitol and voglibose, most data and best outcomes were obtained for acarbose.

Comparison with existing literature

Although this is the first systematic review concerning alpha-glucosidase inhibitor monotherapy, some reviews have been published recently about acarbose (Breuer 2003; Laube 2002) or miglitol (Campbell 2000; Scott 2000). The quality of those reviews is limited: selection criteria for the studies were insufficiently specified and there was no mention of the criteria used to assess the validity of individual trials. Further, these reviews did not present explicit methods on data extraction, assessment of heterogeneity or subgroup analyses. Both reviews on acarbose referred also to a 'meta-analysis' of older date (Lebovitz 1998), which calculated the mean outcomes on glycemic control for 13 studies, using outcomes for single treatment arms (baseline minus endpoint) as well as placebo extracted outcomes in a non-transparent way.
Our results are roughly in line with the previous reviews with respect to the overall effect on glycemic control compared to placebo, but there are relevant differences and additional findings. First, we found no dose-dependency of acarbose on glycated haemoglobin in the meta-analysis. Remarkably, the effect on fasting and post-load blood glucose appeared to be dose dependent. This discrepancy might be explained by a better compliance of patients that were using the lower dosages, because higher dosages induce more adverse effects. Prior to their visit to the study centre, it is more likely that patients took their study medication and thus achieving good fasting and post-load glucose values. Only for glycated haemoglobin, the effect of low compliance will show up. Secondly, we could not find relevant effects on lipid levels, especially triglycerides. Thirdly, we also could not confirm the optimistic view on adverse effects reported in the previous reviews. Twenty out of 41 included studies were subject to a skewed drop-out pattern (? 10% difference per treatment group) and 25 studies had a total drop-out rate that was ? 15%, in most cases this was caused by adverse effects. Finally, the previous reviews are optimistic about the glucose lowering capacities of alpha-glucosidase inhibitors compared to other agents such as sulphonylurea. We confirm a clear beneficial effect with respect to fasting and post-load insulin levels. But overall, the effects on glycemic control are inferior to sulphonylurea. For glycated haemoglobin this is not statistically significant, but most studies that compare acarbose with sulphonylurea use inappropriate comparators (that is too low dose for sulphonylurea or using an individually titrated dosage versus a fixed dosage). Therefore, we feel that a conclusion that sulphonylurea have superior glucose lowering properties, is justified. In addition, alpha-glucosidase inhibitors cause more adverse effects.
The three-years trial performed within the UKPDS (Holman 1999) was one of the main studies included in the review. The effects regarding glycated hemoglobin obtained in this trial alone (a decrease of 0.2%) are considerably less profound than those from the meta-analysis. This discrepancy with the results from the meta-analysis, point in the direction of a possible overestimation of the effect in the long (3 years) term.

Strengths of the review

This is the first high-quality systematic review and meta-analysis on the topic of alpha-glucosidase inhibitors. It offers an up-to-date and most complete overview of all randomised trials concerning alpha-glucosidase inhibitor monotherapy, because it is the result of an extensive search, including grey literature and unpublished studies. In addition, maximum efforts have been done to minimise

missing or incomplete data by attempting to contact all authors. This has been successful in 22 out of 41 cases.

Although we included a high number of studies, the data are remarkably consistent and heterogeneity is limited. Statistical tests for heterogeneity are less reliable when a high number of studies are involved and further scrutiny by sub-group analysis and meta-regression analysis yielded few possible sources for heterogeneity. The use of a fixed dose (instead of an individually titrated dosage) may cause a more profound effect with respect to glycemic control but causes also more adverse effects. The same applies to giving the full dose at once, instead of using a step-up scheme.

Although this review presents a possibly confusing amount of data and figures, we feel that completeness is one of the strengths of a Cochrane systematic review. The way we presented these data, subdivided in types of alpha-glucosidase inhibitor, controls and outcome measures, makes it possible for the reader to find whatever specific piece of information on alpha-glucosidase inhibitor monotherapy he or she needs.

This review will be regularly updated, leaving the possibility open to add information or to correct possible errors. In fact, this is a plea for anyone who is aware of such additional data or errors in the data presented here, to report this to the authors.

Limitations of the review

Our main research question was not answered with the trials we included in this review so far. Only few studies reported data on morbidity and mortality on a reliable and consistent way. It is not likely that in the (near) future a randomised trial of long enough duration will be conducted with acarbose monotherapy to investigate mortality and morbidity. This raises the question whether our review, with its strict inclusion criteria and high demands for outcome data, overshoots the mark. Maybe with broader inclusion criteria, that is inclusion of (high quality) observational studies, we would have gained data to study a possible influence on mortality and morbidity. The use of observational data does not necessarily lead to biased outcomes (Concato 2000). Still, we feel that for the evaluation of medical interventions, well designed randomised trials are the first choice. To improve systematic reviews in the future, we strongly plea for the integration of outcome measures such as death or morbidity into all trials that evaluate medical interventions for patients with chronic diseases. Even if the trial is underpowered for that outcome, the data might always be of value for a meta-analysis. The question of including observational studies in a future update of this review is still open to us.

Despite an exhaustive and thorough search, including requests to experts and manufacturers, we still cannot rule out publication bias. For the three trials that we found in a database for ongoing trials, we were not able to reveal outcome data or additional information about the design despite the fact that one trial ended six years ago (Whitby 1998) and the others in 2003 (Holman 2003; Sa-adu 2003). Another clue for possible publication bias was that we, despite maximum efforts to retrieve unpublished data, discovered three previously unpublished studies coincidentally (Bayer 2003; Bayer 2003a; Campbell 1998) that were used for a study on a congress poster (Hanefeld 2003). Altogether, we still think that the overall risk for publication bias is limited because the funnel plots do not point at small study bias and because of the exhaustive search. Still, we welcome unpublished data for future updates.

Not all papers reported outcomes in a way that could contribute to meta-analyses. This problem was partially solved by asking authors for additional data, imputing the standard deviation of the mean difference (see under methods, data analysis) or using data from graphical figures. As an example, data from only four of the 32 studies investigating glycated haemoglobin in relation to the use of acarbose, suited for use in the meta-analysis directly; for twelve studies additional data had to be obtained from the authors to complete all blanks; for twelve studies we had to calculate the SD of the mean difference from the baseline and endpoint SDs and for four studies the data could not be used at all. Unfortunately, one of those four studies was of long duration (3 years) and had a high number of participants (Campbell 1998). In summary, we used the most precise data in about half of the cases (16 out of 32) and we had to use less precise figures in 12 out of 32 cases. Because we used a conservative correlation coefficient of 0.4, this will most probably have made the confidence interval larger. The influence of the missing data from the largest studies was discussed under 'existing literature'.

Only nine out of the 41 studies lasted longer than 24 weeks, and only two studies were amply longer than one year (Holman 1999; Campbell 1998). For one of those two studies data could not be included in the meta-analyses (Campbell 1998). The importance of long-term studies is evident, especially for a chronic disease such as type 2 diabetes. In the subgroup analysed for study duration, we found clues that the effect of alpha-glucosidase inhibitors decrease with time, This was mostly due to the UKPDS study un which a decrease of only 0.2% was found after three years of treatment (Holman 1999). Therefore, we feel that the results from our study should be interpreted with caution when applied to the long-term treatment with alpha-glucosidase inhibitors of patients with type 2 diabetes.

Research funded by pharmaceutical companies is more likely to produce results favouring the tested drug; this is often due to inappropriate comparators or small study bias (Lexchin 2003). In this review at least 33 studies were sponsored by a pharmaceutical company, including one study in which the sponsor was the producer of the comparison drug (Holmes 2001). We suppose that this will cause a slight overestimation of the results, especially concerning the studies that compare alpha-glucosidase inhibitors with other medication. In fact, this is probable in the comparison acarbose versus sulphonylurea (glycated haemoglobin) where acarbose is dosed in a fixed way and the comparison drugs are individually adjusted (Coniff 1995; Hoffmann 1990; Hoffmann 1994; Kovacevic 1997; Rosenthal 2002; Salman 2001) or very low dosed (Haffner 1997). In one study both treatment arms used an individually adjusted dosage scheme (Van de Laar 2004a). For the comparison with placebo the influence of this 'bias by sponsor-

ing' is less sure as it would be similar to publication bias like we discussed before.

Applicability

The results from this review are relevant for physicians dealing with patients with type 2 diabetes and for the developers of treatment guidelines. Data of beneficial effects on mortality or complications from diabetes mellitus are not available at the moment. Alpha-glucosidase-inhibitors inhibit post-pranidal glucose peaks thereby leading to decreased post-load insulin levels. Further, alpha-glucosidase inhibitors lower post-load insulin levels, especially when compared to sulphonylurea. There are no additional advantages with respect to the lipid profile or body weight. Most evidence is available for acarbose, which has also the best results for most outcomes. The importance of these findings and the exact place of alpha-glucosidase inhibitors in the treatment of type 2 diabetes mellitus, has to be judged in view of other evidence regarding the clinical importance of (post-load) hyperglycaemia and hyperinsulinaemia.

This review investigated alpha-glucosidase inhibitors as monotherapy. Although, from a theoretical point of view, it seems logical that alpha-glucosidase inhibitors offer similar potentials in addition to other antidiabetic therapies, this cannot be concluded from this review. Evidence for the possible efficacy for alpha-glucosidase inhibitors as add-on therapy might be derived from a systematic review that is currently going on (Navarro 2003).

AUTHORS' CONCLUSIONS

Implications for practice

In patients with type 2 diabetes, alpha-glucosidase inhibitor monotherapy inhibit post-prandial glucose peaks thereby leading to decreased post-load insulin levels. There are no advantages with respect to lipid metabolism or body weight. Compared to sulphonylurea, alpha-glucosidase inhibitors have less favourable effects with respect to glycemic control and adverse effects but they lower fasting and post-load insulin levels compared to sulphonylurea. For all outcomes, the largest evidence base exists for acarbose.

Implications for research

New studies that investigate alpha-glucosidase inhibitors on proxy indicators such as glycaemic control, lipids, insulin, body weight would be redundant. Large randomised controlled trials of long duration that investigate mortality, morbidity and quality of life as primary endpoints are necessary. In addition studies comparing alpha-glucosidase inhibitors with other glucose lowering agents (especially metformin and thiazilodines) are of use. When these trials are not available, inclusion of well-designed observational studies in this review may be considered.

POTENTIAL CONFLICT OF INTEREST

FvdL, PL, EvdL, GR and CvW conducted and published a trial that was sponsored by Bayer (Van de Laar 2004a).

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* *Indicates the major publication for the study*

TABLES

Characteristics of included studies

Study	**Braun 1996**
Methods	DESIGN: karallel study RANDOMISATION PROCEDURE: unclear BLINDING: double-blind DURATION: 24 weeks
Participants	COUNTRY: Germany SETTING: general practice NUMBER: randomised: AGI 80, CONTROL 72, analysed: AGI 42, CONTROL 44 SEX (F/M): AGI 16/26, CONTROL 20/24 AGE (YEARS (MEAN)): analysed patients: AGI 60, CONTROL 61 DURATION OF DIABETES (MONTHS (MEAN)): analysed patients: AGI 16, CONTROL 17
Interventions	Dietary reinforcement: unclear AGI: acarbose, week 1-2 50 mg TID, week 3-24 100 mg TID CONTROL: placebo TID
Outcomes	1. Mortality: ND 2. Diabetes related complications: ND 3. Quality of life: ND 4. Glycaemic control: glycated haemoglobin (HbA1c), fasting & post-load blood glucose

	5. Lipids: total cholesterol, HDL-cholesterol, triglycerides 6. Insulin levels: ND 7. Weight: body weight 8. Adverse effects: yes
Notes	Sponsor: oharmaceutical Author contacted: chief of department replied, data not in file, original authors were no longer working there Study retrieved: CENTRAL, EMBASE, manufacturer
Allocation concealment	B

Study	**Buchanan 1988**
Methods	DESIGN: parallel study RANDOMISATION PROCEDURE: unclear BLINDING: double-blind DURATION: 16 weeks
Participants	COUNTRY: Scotland SETTING: outpatient NUMBER: randomised 28, analysed 20 (AGI 9, CONTROL 11) SEX (F/M): AGI 3/6, CONTROL 3/8 AGE (YEARS (MEAN, SD)): analysed patients: AGI 60,1 (6,8), CONTROL 57,6 (8,2) DURATION OF DIABETES (MONTHS (MEAN, SD)): analysed patients: AGI 44,9 (28,6), CONTROL 50,6 (30,1)
Interventions	Dietary reinforcement: unclear; high complex carbohydrates / low-fat diet generally advised. AGI: acarbose, week 0-2 50 mg TID, week 3-8 100 mg TID, week 9-12: 200-100-100 mg, week 13-16 200-100-200 mg, in case of adverse effects patients were instructed to reduce the dosage of acarbose to that which could be tolerated. CONTROL: placebo TID
Outcomes	1. Mortality: ND 2. Diabetes related complications: ND 3. Quality of life: ND 4. Glycaemic control: glycated haemoglobin (HbA1), fasting blood glucose 5. Lipids: total cholesterol, triglycerides 6. Insulin levels: ND 7. Weight: body weight 8. Adverse effects: yes
Notes	Sponsor: pharmaceutical Author contacted: co-author replied but could not give detailed answers Study retrieved: CENTRAL, MEDLINE, EMBASE
Allocation concealment	B

Study	**Calle-Pascual 1996**
Methods	DESIGN: parallel study RANDOMISATION PROCEDURE: unclear BLINDING: double-blind DURATION: 16 weeks
Participants	COUNTRY: Spain SETTING: outpatient NUMBER: randomised AGI 20, control 20; dropout AGI 3/20, control 4/20 SEX: data missing AGE: data missing

Characteristics of included studies (*Continued*)

	DURATION OF DIABETES: data missing
Interventions	Dietary reinforcement: yes, patients included in a behaviour modification program. AGI: acarbose, week 1-4 50 mg TID, week 5-16 100 mg TID CONTROL: placebo
Outcomes	1. Mortality: ND 2. Diabetes related complications: ND 3. Quality of life: ND 4. Glycaemic control: glycated haemoglobin (HbA1c), fasting blood glucose 5. Lipids: total- and HDL-cholesterol, triglycerides 6. Insulin levels: fasting insulin 7. Weight: bodyweight, BMI 8. Adverse effects: yes
Notes	Sponsor: not sponsored Author contacted: additional data on design, quality and outcomes send by author Study retrieved: CENTRAL, MEDLINE, EMBASE Short report, published as letter to the editor
Allocation concealment	B

Study	**Campbell 1998**
Methods	DESIGN: parallel study RANDOMISATION PROCEDURE: adequate BLINDING: double-blind DURATION: 3 years
Participants	COUNTRY: UK SETTING: general practice NUMBER: randomised: 789 (baseline data: AGI 236, CONTROL1 254, CONTROL2 243) SEX (F/M): AGI 87/150, CONTROL1 98/156, CONTROL2 71/172 AGE (YEARS (MEAN)): AGI 62, CONTROL1 62, CONTROL2 62 DURATION OF DIABETES (MONTHS (MEAN)): AGI 34.7, CONTROL1 37.8, CONTROL2 41.6
Interventions	Dietary reinforcement: unclear AGI: acarbose 100 MG TID CONTROL1: placebo CONTROL2: acarbose 50 mg TID
Outcomes	1. Mortality: ND 2. Diabetes related complications: ND 3. Quality of life: ND 4. Glycaemic control: glycated haemoglobin (HbA1c) 5. Lipids: ND 6. Insulin levels: ND 7. Weight: ND 8. Adverse effects: yes
Notes	Sponsor: Pharmaceutical Author contacted: addtional data on design, quality and outcomes via manufacturer. The sparse outcome data of insufficient quality to be included in meta-analysis Study retrieved: handsearch Published as an abstract only. Patients were followed-up and an interim analysis was planned when the HbA1c progressed to >= 8.0 on two consecutive visits or > 10.6% at any time. Therefore the results are not suitable for meta-analysis.

Characteristics of included studies (*Continued*)

Allocation concealment	B

Study	**Chan 1998**
Methods	DESIGN: parallel study RANDOMISATION PROCEDURE: unclear BLINDING: double-blind DURATION: 24 weeks
Participants	COUNTRIES: China, Taiwan, Hong Kong, Philippines, Korea, Singapore, Malaysia SETTING: outpatient NUMBER: randomised AGI 63, CONTROL 63, analysed AGI 59, CONTROL 62 SEX (F/M): AGI 31/32, CONTROL 31/32 AGE (YEARS (MEAN, SD)): randomised patients: AGI 52,8 (10,2), CONTROL 54,0 (10,0) DURATION OF DIABETES (MONTHS (MEAN, SD)): randomised patients: AGI 32,4 (42), CONTROL 25,2 (40,8)
Interventions	Dietary reinforcement: unclear AGI: acarbose, week 1-4 50 mg TID, week 5-24 100 mg TID CONTROL: placebo TID
Outcomes	1. Mortality: ND 2. Diabetes related complications: ND 3. Quality of life: ND 4. Glycaemic control: glycated haemoglobin (HbA1c), fasting & post-load blood glucose 5. Lipids: total-, HDL- & LDL-cholesterol, triglycerides 6. Insulin levels: fasting & post-load insulin 7. Weight: body weight, BMI 8. Adverse effects: yes
Notes	Sponsor: pharmaceutical Author contacted: no reply Study retrieved: CENTRAL, MEDLINE, EMBASE, Current Contents
Allocation concealment	B

Study	**Chiasson 1994**
Methods	DESIGN: parallel study RANDOMISATION PROCEDURE: unclear BLINDING: double-blind DURATION: 1 year
Participants	COUNTRY: Canada SETTING: outpatient NUMBER: 354 patients randomised, 77 treated with diet alone; 67 (of 77) analysed SEX (F/M): 29/48 AGE (YEARS (MEAN, SD)): all randomised patients in diet-only group 57,2 (9.7) DURATION OF DIABETES (MONTHS (MEAN, SD)): all randomised patients in diet-only group 62,4 (63,6)
Interventions	Dietary reinforcement: yes, according to Canadian Association Nutritional guidelines (1993). AGI: acarbose 50, 100 or 200 mg TID, dose adjusted according to blood glucose values and / or tolerance, main target to achieve a postprandial blood glucose < 12 mmol/l CONTROL: placebo
Outcomes	1. Mortality: ND 2. Diabetes related complications: ND

	3. Quality of life: ND 4. Glycaemic control: glycated haemoglobin (HbA1c), fasting & 90 minutes post-load blood glucose 5. Lipids: ND 6. Insulin levels: ND 7. Weight: ND 8. Adverse effects: ND
Notes	Sponsor: pharmaceutical Author contacted: author requested us to send questions again, no reply since Study retrieved: CENTRAL, MEDLINE, EMBASE, Current Contents, manufacturer, handsearch For this review the reported data from the 'diet only' subgroup is used.
Allocation concealment	B

Study	**Chiasson 2001**
Methods	DESIGN: parallel study RANDOMISATION PROCEDURE: unclear BLINDING: double-blind DURATION: 36 weeks
Participants	COUNTRY: Canada SETTING: outpatient NUMBER: total: randomised 324, analysed 318; AGI 82, CONTROL1 83, CONTROL2 83, CONTROL3 76 SEX (F/M): AGI 18/64, CONTROL1 27/56, CONTROL2 22/61, CONTROL3 17/59 AGE (YEARS (MEAN, SD)): AGI 57,3 (9,0), CONTROL1 57,7 (9,9), CONTROLl2 57,9 (8,6), CONTROL3 58,9 (7,9) DURATION OF DIABETES (MONTHS (MEAN, SD)): AGI 62,4 (56,4), CONTROL1 61,2 (58,8), CONTROL2 90,0 (88,8), CONTROL3 73,2 (66,0)
Interventions	Dietary reinforcement: yes, 'well-balanced weight-reducing diet' (reference Diabetes Care 1994, 17(5) 490-519). AGI: miglitol, week 1-4 25 mg TID, week 5-12 50 mg TID, week 13-36 100 mg TID CONTROL1: placebo CONTROL2: metformin 500 mg TID CONTROL4: combination of miglitol 100 mg TID and metformin 500 mg TID
Outcomes	1. Mortality: ND 2. Diabetes related complications: ND 3. Quality of life: ND 4. Glycaemic control: glycated haemoglobin (HbA1c), fasting & post-load blood glucose 5. Lipids: ND 6. Insulin levels: fasting & post-load insulin 7. Weight: body weight 8. Adverse effects: any AE, gastrointestinal AE
Notes	Sponsor: pharmaceutical Author contacted: author requested us to send questions again, no reply since (4 months) Study retrieved: CENTRAL, MEDLINE, EMBASE, Current Contents
Allocation concealment	B

Study	**Coniff 1994**
Methods	DESIGN: parallel study RANDOMISATION PROCEDURE: adequate BLINDING: double-blind

Characteristics of included studies (*Continued*)

	DURATION: 24 weeks
Participants	COUNTRY: USA SETTING: outpatient NUMBER: randomised: AGI 105, CONTROL 107; analysed: AGI 91, CONTROL 98 SEX (F/M): analysed group: AGI 50/41, CONTROL 45/53 AGE (YEARS (MEAN, SD)): analysed group: AGI 56,0 (9,5), CONTROL 55,6 (9,9) DURATION OF DIABETES (MONTHS (MEDIAN, RANGE)): analysed group: AGI 48 (6-396), CONTROL 36 (6-252)
Interventions	Dietary reinforcement: yes, standard diabetic diet containing at least 50% carbohydrates. AGI: acarbose titrated to a maximum of 300 mg TID: dose in- or decreased according to fasting blood glucose and tolerance (cut-off point fasting blood glucose > 11.1 mmol/l) CONTROL: placebo TID
Outcomes	1. Mortality: ND 2. Diabetes related complications: ND 3. Quality of Life: ND 4. Glycaemic control: glycated haemoglobin (HbA1c), fasting & post-load blood glucose 5. Lipids: triglycerides, total-, HDL- & LDL-cholesterol 6. Insulin levels: ND 7. Weight: body weight 8. Adverse effects: yes
Notes	Sponsor: pharmaceutical Author contacted: additional data on design, quality and outcomes via manufacturer Study retrieved: CENTRAL, MEDLINE, EMBASE, manufacturer, handsearch
Allocation concealment	A

Study	**Coniff 1995**
Methods	DESIGN: parallel study RANDOMISATION PROCEDURE: adequate BLINDING: double-blind DURATION: 24 weeks
Participants	COUNTRY: USA SETTING: outpatient NUMBER: randomised: AGI 76, CONTROL1 72, CONTROL2 72, CONTROL3 70; analysed: AGI 67, CONTROL1 62, CONTROL2 66, CONTROL3 60 SEX (F/M): analysed group: AGI 41/26, CONTROL1 30/32, CONTROL2 29/37, CONTROL3 29/31 AGE (YEARS (MEAN)): analysed group: AGI 56,2, CONTROL1 56,3, CONTROL2 55,4, CONTROL3 55,7 DURATION OF DIABETES (MONTHS (MEAN, SD)):
Interventions	Dietary reinforcement: yes, standard diabetic diet with 50% energy as carbohydrates. AGI: acarbose 200 mg TID CONTROL1: placebo CONTROL2: tolbutamide, individually adjusted in steps of 250 mg TID, maximum dose unclear CONTROL4: acarbose & tolbutamide combination (data not used in this review)
Outcomes	1. Mortality: yes 2. Diabetes related complications: ND 3. Quality of life: ND 4. Glycaemic control: glycated haemoglobin (HbA1c), fasting & post-load blood glucose 5. Lipids: triglycerides, total-, HDL- & LDL-cholesterol 6. Insulin levels: fasting & post-load insulin

	7. Weight: body weight 8. Adverse effects: yes
Notes	Sponsor: pharmaceutical Author contacted: additional data on design, quality and outcomes via manufacturer Study retrieved: CCRCT, Medline, Embase, manufacturer
Allocation concealment	A

Study	**Coniff 1995b**
Methods	DESIGN: parallel study RANDOMISATION PROCEDURE: adequate BLINDING: double-blind DURATION: 16 weeks
Participants	COUNTRY: USA SETTING: outpatient NUMBER: randomised: AGI 73, CONTROL1 73, CONTROL2 72, CONTROL3 72; analysed: AGI 58, CONTROL1 64, CONTROL2 54, CONTROL3 53 SEX (F/M): analysed group: AGI 28/30, CONTROL1 27/37, CONTROL2 22/32, CONTROL3 22/31 AGE (YEARS (MEAN)): analysed group: AGI 55, CONTROL1 54, CONTROL2 56, CONTROL3 54 DURATION OF DIABETES (MONTHS (MEAN)): analysed group: AGI 72, CONTROL1 60, CONTROL2 60, CONTROL3 60
Interventions	Dietary reinforcement: yes, weight stable ADA diet (1979): 50% carbohydrate, 30% fat, 20% protein. AGI: acarbose 100 mg TID CONTROL1: placebo TID CONTROL2: acarbose, week 1-2 100 mg TID, week 3-16 200 mg TID CONTROL3: acarbose, week 1-2 100 mg TID, week 3-4 200 mg TID, week 5-16 300 mg TID
Outcomes	1. Mortality: ND 2. Diabetes Related Complications: ND 3. Quality of Life: ND 4. Glycaemic control: glycated haemoglobin (HbA1c), fasting & post-load blood glucose 5. Lipids: total cholesterol, triglycerides 6. Insulin levels: fasting & post-load insulin levels 7. Weight: body weight 8. Adverse effects: yes
Notes	Sponsor: pharmaceutical Author contacted: additional data on design, quality and outcomes via manufacturer Study retrieved: CENTRAL, MEDLINE, EMBASE, manufacturer
Allocation concealment	A

Study	**Dedov 1995**
Methods	DESIGN: parallel study RANDOMISATION PROCEDURE: unclear BLINDING: double-blind DURATION: 24 weeks
Participants	COUNTRY: Russia SETTING: outpatient NUMBER: randomised 180 patients, analysed 155 (AGI 82, CONTROL 73). Baseline values are given for 161 patients SEX (F/M): baseline group AGI 50/33, CONTROL 50/28 AGE (YEARS (MEAN, SD)): baseline group AGI 52,6 (9,5), CONTROL 49,2 (9,5)

Characteristics of included studies (*Continued*)

	DURATION OF DIABETES: ND
Interventions	Dietary reinforcement: unclear AGI: acarbose, week 1-2 50 mg TID, week 3-24 wk 100 mg TID CONTROL: placebo TID
Outcomes	1. Mortality: ND 2. Diabetes related complications: ND 3. Quality of life: ND 4. Glycaemic control: glycated haemoglobin (HbA1), fasting & post-load blood glucose 5. Lipids: ND 6. Insulin levels: ND 7. Weight: body weight 8. Adverse effects: yes
Notes	Sponsor: not specified Author contacted: no reply Study retrieved: CENTRAL, EMBASE
Allocation concealment	B

Study	**Delgado 2002**
Methods	DESIGN: parallel study RANDOMISATION PROCEDURE: unclear BLINDING: double-blind DURATION: 16 weeks
Participants	COUNTRY: Switzerland SETTING: outpatient NUMBER: AGI 9, CONTROL 8 SEX (F/M): AGI 3/6, CONTROL 3/5 AGE: ND DURATION OF DIABETES (MONTHS (MEAN, SD)): all patients 26 (6)
Interventions	Dietary reinforcement: yes, for details article referred to article in French (Journeés de diabétologie Hôtel Dieu 1998: 51-69). AGI: acarbose, week 1-2 50 mg once daily, week 3-16 50 mg BID CONTROL1: placebo BID
Outcomes	1. Mortality: ND 2. Diabetes related complications: ND 3. Quality of life: ND 4. Glycaemic control: glycated haemoglobin (HbA1c), fasting & post-load blood glucose 5. Lipids: total cholesterol, HDL-cholesterol, triglycerides 6. Insulin levels: Reaven's triple test 7. Weight: body weight, BMI 8. Adverse effects: ND
Notes	Sponsor: Not specified Author contacted: no reply Study retrieved: CENTRAL, MEDLINE, EMBASE, Current Contents, handsearch Study mainly about insulin insulin resistance & secretion
Allocation concealment	B

Study	**Drent 2002**
Methods	DESIGN: parallel study

Characteristics of included studies (*Continued*)

	RANDOMISATION PROCEDURE: unclear BLINDING: double-blind DURATION: 24 weeks
Participants	COUNTRY: The Netherlands SETTING: patients recruited in general practice, study performed in 'study centres' NUMBER: 599 enrolled, 468 randomised, 384 analysed (AGI 71, CONTROL1 87, CONTROL2 84, CONTROL3 58, CONTROL4 84) SEX (F/M): AGI 34/37, CONTROL1 38/49, CONTROL2 37/47, CONTROL3 21/37, CONTROL4 43/41 AGI (YEARS (MEAN, SD)): AGI 63 (11), CONTROL1 63 (11), CONTROL2 63 (9), CONTROL3 64 (10), CONTROL4 64 (10) DURATION OF DIABETES (MONTHS (MEAN)): AGI 36, CONTROL1 30, CONTROL2 48, CONTROL3 46, CONTROL4 41.5
Interventions	Dietary reinforcement: when patients were not using diet, advice was given during screening period, ADA/EASD guidelines, at least 40% carbohydrates . AGI: miglitol, week 1-2 50 mg TID, week 3-24 100 mg TID CONTROL1: placebo TID CONTROL2: miglitol 50 mg TID CONTROL3: miglitol, week 1-2 100 mg TID, week 3-24 200 mg TID CONTROL4: miglitol 25 mg TID
Outcomes	1. Mortality: ND 2. Diabetes related complications: ND 3. Quality of life: ND 4. Glycaemic control: glycated haemoglobin (HbA1c), fasting & post-load blood glucose 5. Lipids: "blood lipids" 6. Insulin levels: fasting & post-load insulin 7. Weight: weight & BMI 8. Adverse effects: yes
Notes	Sponsor: pharmaceutical Author contacted: additional data on design, quality and outcomes send by author Study retrieved: CENTRAL, MEDLINE, EMBASE, Current Contents (2nd reference via author)
Allocation concealment	A

Study	**Fischer 1998**
Methods	DESIGN: parallel study RANDOMISATION PROCEDURE: unclear BLINDING: double-blind DURATION: 24 weeks
Participants	COUNTRY: Germany, Austria, Croatia, Hungary, Italy SETTING: outpatient NUMBER: randomised 495, analysed 420 (AGI 25 mg 86, AGI 50 mg 88, AGI 100 mg 78, AGI 200 mg 87, CONTROL 81) SEX (F/M): AGI 25 mg 40/46, AGI 50 mg 45/43, AGI 100 mg 32/46, AGI 200 mg 43/44, CONTROL 38/43 AGE (YEARS (MEAN, SD)): analysed group: AGI 25 mg 58,5 (8,4), AGI 50 mg 55,5 (9,6), AGI 100 mg 56,8 (9,4), AGI 200 mg 59,4 (8,6), CONTROL 52,7 (8,7) DURATION OF DIABETES (MONTHS (MEDIAN)): AGI 25 mg 26, AGI 50 mg 20, AGI 100 mg 17, AGI 200 mg 21, CONTROL 24
Interventions	Dietary reinforcement: yes, ADA nutritional recommendations 1986

	AGI: acarbose divided in 4 groups: 25 mg, 50 mg, 100 mg (week 1-2 50 mg TID) and 200 mg TID (week 1-2 100 mg TID) CONTROL: placebo TID
Outcomes	1. Mortality: ND 2. Diabetes related complications: ND 3. Quality of life: ND 4. Glycaemic control: glycated haemoglobin (HbA1c), fasting blood glucose 5. Lipids: ND 6. Insulin levels: ND 7. Weight: body weight 8. Adverse effects: yes
Notes	Sponsor: pharmaceutical Author contacted: additional data on design, quality and outcomes via manufacturer Study retrieved: CENTRAL, MEDLINE, EMBASE, Current Contents, manufacturer
Allocation concealment	A

Study	**Gentile 1999**
Methods	DESIGN: cross-over study RANDOMISATION PROCEDURE: unclear BLINDING: double-blind DURATION: 2 x 12 weeks
Participants	COUNTRY: Italy SETTING: outpatient NUMBER: 76 SEX (F/M): 33/43 AGE: ND DURATION OF DIABETES (MONTHS (MEAN, SD)): 110,4 (49,2)
Interventions	Dietary reinforcement: unclear, general advice 60% carbohydrates, 20-22% fat, 18-20% protein. AGI: acarbose, week 1 50 mg TID, week 2-12 100 mg TID CONTROL: placebo
Outcomes	1. Mortality: ND 2. Diabetes related complications: ND 3. Quality of life: ND 4. Glycaemic control: glycated haemoglobin, fasting blood glucose 5. Lipids: ND 6. Insulin levels: ND 7. Weight: ND 8. Adverse effects: yes
Notes	Sponsor: “Fundi MURST”, not clear whether this is a pharmaceutical sponsor Author contacted: no reply Study retrieved: CENTRAL, MEDLINE, EMBASE This study is done with patients suffering from non-alcoholic liver cirrhosis
Allocation concealment	B

Study	**Haffner 1997**
Methods	DESIGN: parallel study RANDOMISATION PROCEDURE: unclear BLINDING: double-blind DURATION: 16 weeks

Characteristics of included studies (*Continued*)

Participants	COUNTRY: Germany SETTING: outpatient NUMBER: 77 patients randomised and analysed (AGI 25, CONTROL1 25, CONTROL2 27) SEX (F/M): AGI 6/19, CONTROL1 8/17, CONTROL2 11/16 AGI (YEARS (MEAN, SD)): AGI 59.4 (28), CONTROL1 58.6 (31.5), CONTROL2 58.1 (36.4) DURATION OF DIABETES (MONTHS (MEAN, SD)): AGI 94.0 (59.9), CONTROL1 77.3 (53.5), CONTROL2 69.5 (49.9)
Interventions	Dietary reinforcement: yes, body weight stable, 15% protein, 35% fat, 50% carbohydrates AGI: acarbose 100 mg TID CONTROL1: placebo TID CONTROL2: glibenclamide 1 mg TID
Outcomes	1. Mortality: ND 2. Diabetes related complications: ND 3. Quality of life: ND 4. Glycaemic control: glycated haemoglobin (HbA1c), fasting & post-load blood glucose 5. Lipids: triglycerides, total & HDL-cholesterol 6. Insulin levels: fasting & post-load insulin 7. Weight: weight & BMI 8. Adverse effects: ND
Notes	Sponsor: non-industry (National Heart Lung and Blood Institute) Author contacted: no reply Study retrieved: CENTRAL, MEDLINE, EMBASE, Current Contents, handsearch
Allocation concealment	B

Study	**Hanefeld 1991**
Methods	DESIGN: parallel study RANDOMISATION PROCEDURE: adequate BLINDING: double-blind DURATION: 24 weeks
Participants	COUNTRY: Germany SETTING: outpatient NUMBER: randomised 100, analysed 94; AGI 47, CONTROL 47 SEX (F/M): AGI 24/23, CONTROL 22/25 AGE (YEARS (MEAN)): analysed patients AGI 60, CONTROL 59 DURATION OF DIABETES (MONTHS (MEAN)): analysed patients AGI 70, CONTROL 49
Interventions	Dietary reinforcement: yes, specification diet unclear. AGI: acarbose 100 mg TID CONTROL: placebo
Outcomes	1. Mortality: ND 2. Diabetes related Complications: ND 3. Quality of life: ND 4. Glycaemic control: glycated haemoglobin (HbA1), fasting & 1 hour post-load blood glucose 5. Lipids: triglycerides, total- and HDL-cholesterol 6. Insulin levels: fasting & 1 hour post-load insulin 7. Weight: body weight 8. Adverse effects: yes
Notes	Sponsor: pharmaceutical Author contacted: additional data on design, quality and outcomes via manufacturer Study retrieved: CENTRAL, MEDLINE, EMBASE, manufacturer

Characteristics of included studies (*Continued*)

Allocation concealment	A

Study	**Hillebrand 1987**
Methods	DESIGN: cross-over study RANDOMISATION PROCEDURE: unclear BLINDING: double-blind DURATION: treatment periods of 12 weeks
Participants	COUNTRY: Germany SETTING: outpatient NUMBER: 76 SEX (F/M): 33/43 AGE: ND DURATION OF DIABETES (MONTHS (MEAN, SD)): 110,4 (49,2)
Interventions	Dietary reinforcement: unclear AGI: acarbose 200 mg BID CONTROL1: miglitol 200 mg BID CONTROL2: glibenclamide 7 mg once daily
Outcomes	1. Mortality: ND 2. Diabetes related complications: ND 3. Quality of life: ND 4. Glycaemic control: glycated haemoglobin (HbA1), fasting & post-load blood glucose 5. Lipids: ND 6. Insulin levels: ND 7. Weight: ND 8. Adverse effects: yes
Notes	Sponsor: not specified Author contacted: authors could not be retrieved Study retrieved: handsearch Published as abstract only.
Allocation concealment	B

Study	**Hoffmann 1990**
Methods	DESIGN: parallel study RANDOMISATION PROCEDURE: adequate BLINDING: no blinding DURATION: 24 weeks
Participants	COUNTRY: Germany SETTING: outpatient NUMBER: 95 patients included; AGI 48, CONTROL 47 SEX (F/M): AGI 30/18, CONTROL 26/21 AGE (YEARS (MEAN, SD)): AGI 61.8 (5.6), CONTROL 61.2 (5.5) DURATION OF DIABETES (MONTHS (MEAN (SD)): AGI 22.4 (16.2), CONTROL 30.7 (29.2)
Interventions	Dietary reinforcement: yes, normocaloric diet of 1500 kcal with 120 g carbohydrates, 50 g protein, 55 g fat AGI: acarbose, week 1-4 50 mg TID, week 5-25 100 mg TID (for one patient dose reduced to 100 mg BID) CONTROL: glibenclamide 3,5 mg administered individually 1-3 times per day
Outcomes	1. Mortality: ND 2. Diabetes related complications: ND 3. Quality of life: ND

	4. Glycaemic control: glycated haemoglobin (HbA1), fasting & post-load blood glucose 5. Lipids: triglycerides, total-, HDL and LDL-cholesterol 6. Insulin levels: ND 7. Weight: body weight, Broca index 8. Adverse effects: yes
Notes	Sponsor: pharmaceutical Author contacted: additional data on design, quality and outcomes via manufacturer Study retrieved: CENTRAL, experts
Allocation concealment	B

Study	**Hoffmann 1994**
Methods	DESIGN: parallel study RANDOMISATION PROCEDURE: adequate BLINDING: double-blind regarding comparison acarbose / placebo, glibenclamide single-blind DURATION: 24 weeks
Participants	COUNTRY: Germany SETTING: outpatient NUMBER: 96 patients randomised, 85 analysed for efficacy (AGI 28, control1 30, control2 27) SEX (F/M): AGI 15/13, CONTROL1 18/12, CONTROL2 14/13 AGE (YEARS (MEAN, SD)): analysed patients: AGI 58,8 (6,9), CONTROL1 56,9 (6,7), CONTROL2 59,9 (5,7) DURATION OF DIABETES (MONTHS (MEAN, SD)): analysed patients: AGI 12,7 (10,8), CONTROL1 12,1 (10,8), CONTROL2 17,6 (13,1)
Interventions	Dietary reinforcement: yes, 50% carbohydrates, 35% fat, 15% protein. AGI: acarbose 100 mg TID CONTROL1: placebo TID CONTROL2: glibenclamide 3,5 mg administered individually 1-3 times per day
Outcomes	1. Mortality: ND 2. Diabetes related complications: ND 3. Quality of life: ND 4. Glycaemic control: glycated haemoglobin (HbA1c), fasting & post-load blood glucose 5. Lipids: triglycerides, total- and HDL-cholesterol 6. Insulin levels: fasting & post-load insulin 7. Weight: body weight, BMI 8. Adverse effects: yes
Notes	Sponsor: pharmaceutical Author contacted: additional data on design, quality and outcomes via manufacturer Study retrieved: CENTRAL, MEDLINE, EMBASE, manufacturer
Allocation concealment	A

Study	**Hoffmann 1997**
Methods	DESIGN: parallel study RANDOMISATION PROCEDURE: adequate BLINDING: double blind regarding comparison acarbose / placebo, metformin single-blind DURATION: 24 weeks
Participants	COUNTRY: Germany SETTING: outpatient NUMBER: 96 patients randomised; 94 analysed for efficacy (AGI 31, CONTROL1 32, CONTROL2 31) SEX (F/M): AGI 25/6, CONTROL1 20/12, CONTROL2 17/14

Characteristics of included studies (*Continued*)

	AGE (YEARS (MEAN, SD)): analysed patients: AGI 58,9 (9,4), CONTROL1 60,2 (8,6), CONTROL2 55,9 (7,8) DURATION OF DIABETES (MONTHS (MEAN, SD)): analysed patients: AGI 36,9 (27,2), CONTROL1 43,2 (33,9), CONTROL2 25,0 (17,4)
Interventions	Dietary reinforcement: yes, 50% carbohydrates, 35% fat, 15% protein AGI: acarbose 100 mg TID CONTROL1: placebo TID CONTROL2: metformin 850 mg BID
Outcomes	1. Mortality: ND 2. Diabetes related complications: ND 3. Quality of life: ND 4. Glycaemic control: glycated haemoglobin (HbA1c), fasting post-load blood glucose 5. Lipids: triglycerides, total-, HDL- & LDL-cholesterol 6. Insulin levels: fasting & post-load insulin 7. Weight: body weight 8. Adverse effects: yes
Notes	Sponsor: pharmaceutical Author contacted: additional data on design, quality and outcomes via manufacturer Study retrieved: CENTRAL, MEDLINE, EMBASE, Current Contents, manufacturer
Allocation concealment	A

Study	**Holman 1999**
Methods	DESIGN: parallel study RANDOMISATION PROCEDURE: adequate BLINDING: double-blind DURATION: 3 years
Participants	COUNTRY: England SETTING: outpatient, part of the United Kingdom Prospective Diabetes Study NUMBER: 1946 patients randomised, total 1624 analysed (intention-to-treat): diet only group randomised 256, diet only group analysed (HbA1c) AGI 83, CONTROL 107. SEX (F/M): AGI 36/84, CONTROL 38/98 AGE (YEARS (MEAN, SD)): AGI 60.0 (8.2), CONTROL 60.9 (9.0) DURATION OF DIABETES (MONTHS (MEAN, SD)): AGI 82.6 (33.3), CONTROL 91.3 (34.9)
Interventions	Dietary reinforcement: no (dietary advice according to UKPDS protocol) AGI: acarbose, 50 mg once, BID & TID at two-week intervals; 4 months after start dosage increased in 3 weeks period with 50 mg per step to 100 mg TID. In case of side effects patients were allowed to reduce the dose. CONTROL: placebo
Outcomes	1. Mortality: yes 2. Diabetes related complications: yes 3. Quality of life: ND 4. Glycaemic control: glycated haemoglobin (HbA1c) 5. Lipids: ND 6. Insulin levels: ND 7. Weight: body weight, BMI 8. Adverse effects: yes
Notes	Sponsor: pharmaceutical Author contacted: additional data on design, quality and outcomes send by authors Study retrieved: CENTRAL, MEDLINE, EMBASE, Current Contents, Manufacturer

	For this review the reported data from the 'diet only' subgroup is used.
Allocation concealment	A

Study	**Holmes 2001**
Methods	DESIGN: parallel study RANDOMISATION PROCEDURE: adequate BLINDING: double-blind DURATION: 24 weeks
Participants	COUNTRY: Germany, France and Spain SETTING: outpatient NUMBER: 260 patients entered run-in period, 179 randomised (AGI 92, CONTROL 87). analysed (for HbA1c) AGI 90, CONTROL 85 SEX (F/M): randomised group AGI 33/59; CONTROL 30/57 AGE (YEARS (MEAN, SD)): randomised patients AGI 60,6 (10.2); CONTROL 64.3 (10.4) DURATION OF DIABETES (MONTHS (MEAN (SD)): randomised patients AGI 53.9 (62.4 or 64.4); CONTROL 63.4 (66.5)
Interventions	Dietary reinforcement: no ("patients continued with their normal dietary habits'). AGI: acarbose, week 0-4 50 mg TID, week 4-8 100 mg TID, in case of side-effects to be reduced to 50 mg CONTROL: nateglinide 120 mg TID
Outcomes	1. Mortality: ND 2. Diabetes related complications: ND 3. Quality of life: ND 4. Glycaemic control: glycated haemoglobin (HbA1c), fasting blood glucose 5. Lipids: ND 6. Insulin levels: ND 7. Weight: body weight 8. Adverse effects: yes
Notes	Sponsor: pharmaceutical Author contacted: additional data on design, quality and outcomes send by author Study retrieved: handsearch
Allocation concealment	A

Study	**Hotta 1993**
Methods	DESIGN: parallel study RANDOMISATION PROCEDURE: unclear BLINDING: double-blind DURATION: 24 weeks
Participants	COUNTRY: Japan SETTING: outpatient NUMBER: randomised: AGI 20, CONTROL 20, analysed: AGI 16, CONTROL 15, (baseline values given for 37 patients) SEX (F/M): AGI 5/14, CONTROL 4/14 AGE (YEARS (MEAN)): AGI 49,8, CONTROL 47,9 DURATION OF DIABETES (MONTHS (MEAN)): AGI 55,2, CONTROL 57,6
Interventions	Dietary reinforcement: yes, specification unclear AGI: acarbose 100 mg TID CONTROL: placebo TID
Outcomes	1. Mortality: ND

	2. Diabetes related complications: ND 3. Quality of life: ND 4. Glycaemic control: glycated haemoglobin (HbA1c), fasting & post-load blood glucose 5. Lipids: total- & HDL-cholesterol, triglycerides 6. Insulin levels: ND 7. Weight: body weight 8. Adverse effects: yes
Notes	Sponsor: pharmaceutical Author contacted: additional data on design, quality and outcomes send by author Study retrieved: CENTRAL, MEDLINE, EMBASE, manufacturer, (2nd reference via author)
Allocation concealment	A

Study	**Johnston 1998**
Methods	DESIGN: parallel study RANDOMISATION PROCEDURE: unclear BLINDING: double-blind DURATION: 56 weeks
Participants	COUNTRY: USA SETTING: outpatient NUMBER: randomised: AGI 102, CONTROL1 104, CONTROL2 104, CONTROL3 101, analysed: AGI 85, CONTROL1 95, CONTROL2 92, CONTROL3 92 SEX (F/M): analysed patients: AGIN24/61, CONTROL1 35/60, CONTROL2 33/59, CONTROL3 26/66 AGE (YEARS (MEAN, SD)): analysed group: AGI 67,8 (5,5), CONTROL1 67,2 (5,8), CONTROL2 67,7 (5,8), CONTROL3 68,5 (5,8) DURATION OF DIABETES (MONTHS (MEAN, SD)): AGI 81,6 (88,8), CONTROL1 90 (93,6), CONTROL2 86,4 (92,4), CONTROL3 84 (92,4)
Interventions	Dietary reinforcement: yes, ADA approved diet >= 50% carbohydrates AGI: miglitol 50 mg TID CONTROL1: miglitol 25 mg TID CONTROL2: glyburide 20 mg once daily, step up & individually titrated: every 2 weeks increase: 2,5/5/7,5/10/15/20 mg CONTROL4: placebo TID and once daily
Outcomes	1. Mortality: yes 2. Diabetes related complications: yes 3. Quality of life: ND 4. Glycaemic control: glycated haemoglobin (HbA1c), fasting & post-load blood glucose 5. Lipids: triglycerides 6. Insulin levels: fasting & post-load insulin 7. Weight: BMI 8. Adverse effects: yes
Notes	Sponsor: pharmaceutical Author contacted: Bayer replied that the data from this study was transferred to Pfizer. Pfizer didn't reply to our requests do far. Study retrieved: CENTRAL, MEDLINE, EMBASE, Current Contents
Allocation concealment	B

Study	**Johnston 1998a**
Methods	DESIGN: parallel study RANDOMISATION PROCEDURE: unclear

Characteristics of included studies (*Continued*)

	BLINDING: double-blind DURATION: 52 weeks, main outcomes measured at 26 weeks
Participants	COUNTRY: USA SETTING: outpatient NUMBER: total randomised: AGI 254, CONTROL 131, diet only group 55 (AGI), 14 (CONTROL); analysed: AGI 19, CONTROL 10 SEX: no data for diet only group AGE: no data for diet only group DURATION OF DIABETES: no data for diet only group
Interventions	Dietary reinforcement: yes, at least 50% carbohydrates, intended to maintain weight. AGI: miglitol 50 mg: when tolerant the patient increased the dose to 100/150/200 TID at wk 13/26 and 39 respectively. Backtitration allowed (in case of intolerance). CONTROL: placebo TID
Outcomes	1. Mortality: ND 2. Diabetes related complications: ND 3. Quality of life: ND 4. Glycaemic control: glycated haemoglobin (HbA1c) 5. Lipids: no data for diet only group 6. Insulin levels: no data for diet only group 7. Weight: no data for diet only group 8. Adverse effects: yes
Notes	Sponsor: pharmaceutical Author contacted: Bayer replied that the data from this study was transferred to Pfizer. Pfizer didn't reply to our requests so far. Study retrieved: CENTRAL, MEDLINE, EMBASE, Current Contents Both patients using diet only and patients receiving additional sulphonylurea therapy were included in this study.
Allocation concealment	B

Study	**Johnston 1998b**
Methods	DESIGN: parallel study RANDOMISATION PROCEDURE: unclear BLINDING: double-blind DURATION: 52 weeks, primary efficacy criterion measured at 28 weeks
Participants	COUNTRY: USA SETTING: outpatient NUMBER: total randomised: AGI 229, CONTROL 116; valid for efficacy diet only group: AGI 32, CONTROL 13; analysed for HbA1c: AGI 30, CONTROL 9 SEX (F/M): diet only group valid for efficacy: AGI 12/20, CONTROL 7/6 AGE (YEARS (MEAN, SD)): diet only group valid for efficacy: AGI 57,3 (10,2), CONTROL 54,9 (12,6) DURATION OF DIABETES (MONTHS (MEAN, SD)): diet only group valid for efficacy: AGI 57,6 (95,0), CONTROL 30 (38,9)
Interventions	Dietary reinforcement: yes, overweight patients received counselling to produce gradual (1 lb./week) weight loss. AGI: miglitol, week 1-12 50 mg TID, week 12-52 100 mg TID. In case of intolerance to be decreased to 50 mg CONTROL: placebo TID
Outcomes	1. Mortality: ND 2. Diabetes related complications: ND

	3. Quality of life: ND 4. Glycaemic control: glycated haemoglobin (HbA1c) 5. Lipids: no data for diet only group 6. Insulin levels: no data for diet only group 7. Weight: no data for diet only group 8. Adverse effects: no data for diet only group
Notes	Sponsor: pharmaceutical Author contacted: Bayer replied that the data from this study was transferred to Pfizer. Pfizer didn't reply to our requests so far. Study retrieved: CENTRAL, MEDLINE, EMBASE, Current Contents Study among African-American patients. Both patients using diet only and patients receiving additional sulphonylurea therapy were included in this study.
Allocation concealment	B

Study	**Kawamori 2003**
Methods	DESIGN: parallel study RANDOMISATION PROCEDURE: unclear BLINDING: double-blind DURATION: 12 weeks
Participants	COUNTRY: Japan SETTING: unclear NUMBER: 445 patients enrolled, efficacy data for 396 patients (AGI1 158, AGI2 154, CONTROL 84) SEX: Data missing AGE: Data missing DURATION OF DIABETES: Data missing
Interventions	Dietary reinforcement: unclear AGI1: miglitol 50 mg TID AGI2: voglibose 0.2 mg TID CONTROL: placebo
Outcomes	1. Mortality: ND 2. Diabetes related complications: ND 3. Quality of life: ND 4. Glycaemic control: glycated haemoglobin (HbA1c), fasting & post-load blood glucose 5. Lipids: ND 6. Insulin levels: post-load insulin 7. Weight: ND 8. Adverse effects: yes
Notes	Sponsor: not specified Author contacted: no additional data before study was published as journal article Study retrieved: handsearch Data extracted from a congress abstract and a copy of a poster presentation. Authors refused to give more data before this study was published.
Allocation concealment	B

Study	**Kovacevic 1997**
Methods	DESIGN: parallel study RANDOMISATION PROCEDURE: unclear BLINDING: double-blind with respect to acarbose and placebo, single blind with respect to glibenclamide DURATION: 24 weeks

Characteristics of included studies (*Continued*)

Participants	COUNTRY: Croatia SETTING: outpatient NUMBER: randomised: AGI 34, CONTROL1 34, CONTROL2 34; analysed AGI 33, CONTROL1 31, CONTROL2 33 SEX (F/M): total group 55/47; analysed AGI 16/17, CONTROL1 18/13, CONTROL2 20/13 AGE (YEARS (MEAN, SD)): total group 57,5 (8,1), analysed AGI 58.42 (7.76), CONTROL1 59.35 (8.61), CONTROL2 54.73 (7.80) DURATION OF DIABETES (MONTHS (MEAN)): total group 54
Interventions	Dietary reinforcement: yes, 40-50% carbohydrates, 35-40% fat, 15% protein AGI: acarbose 100 mg TID CONTROL1: placebo TID CONTROL2: glibenclamide 3.5 mg adjusted individually, maximum TID
Outcomes	1. Mortality: ND 2. Diabetes related complications: ND 3. Quality of life: ND 4. Glycaemic control: glycated haemoglobin (HbA1c), fasting & post-load blood-glucose 5. Lipids: tot cholesterol, HDL and triglycerides 6. Insulin levels: fasting & post-load insulin 7. Weight: BMI 8. Adverse effects: yes
Notes	Sponsor: pharmaceutical Author contacted: additional data on design, quality and outcomes send by author Study retrieved: CENTRAL, EMBASE, manufacturer
Allocation concealment	A

Study	**Meneilly 2000**
Methods	DESIGN: parallel study RANDOMISATION PROCEDURE: unclear BLINDING: double-blind DURATION: 12 months
Participants	COUNTRY: Canada SETTING: outpatient NUMBER: AGI 93, CONTROL 99 SEX (F/M): AGI 28/65, CONTROL 39/60 AGE (YEARS (MEAN, SD)): AGI 69.7 (4,8), CONTROL 70.3 (5,0) DURATION OF DIABETES (MONTHS (MEAN, SD)): AGI 69,6 (81,6), CONTROL 57,6 (60)
Interventions	Dietary reinforcement: yes, advised to maintain diet to ensure that calorie intake was consistent throughout the study. AGI: acarbose, week 1: 50 mg once daily, week 2: 50 mg BID, week 3: 50 mg TID, week 4-52 titrated upward to 100 mg TID when post-load blood glucose > 12 mmol/l, downtitrated in case of intolerance. CONTROL: placebo TID
Outcomes	1. Mortality: ND 2. Diabetes related complications: ND 3. Quality of life: SF 36 & Boyer quality of life rating instrument 4. Glycaemic control: glycated haemoglobin (HbA1c), fasting & post-load blood glucose 5. Lipids: ND 6. Insulin levels: fasting & post-load insulin 7. Weight: body weight 8. Adverse effects: yes

Characteristics of included studies (*Continued*)

Notes	Sponsor: pharmaceutical Author contacted: no reply Study retrieved: CENTRAL, MEDLINE, EMBASE, Current Contents, manufacturer, handsearch Study conducted in older patients
Allocation concealment	B

Study	**Pagano 1995**
Methods	DESIGN: parallel study RANDOMISATION PROCEDURE: unclear BLINDING: double-blind DURATION: 24 weeks
Participants	COUNTRY: Italy SETTING: outpatient NUMBER: 100 patients randomised, 96 patients completed study: AGI 49, CONTROL 47. Primary efficacy data for 90 patients SEX (F/M): AGI 16/33, CONTROL 23/24 AGE (YEARS (MEAN, SD)): patients that completed study: AGI 57 (8.4), CONTROL 59 (7.5) DURATION OF DIABETES (MONTHS (MEAN, SD)): patients that completed study: AGI 60 (48.3), CONTROL 84 (64.4)
Interventions	Dietary reinforcement: yes, 30 kcal per Kg of ideal body weight per day (60% carbohydrates, 25% fat, 15% protein, 30g dietary fibres). AGI: miglitol, week 1-6 50 mg TID, week 7-24 100 mg TID CONTROL: glibenclamide week 1-6 2,5 mg BID, week 7-24 5 mg BID, 1 placebo tablet to ensure blinding.
Outcomes	1. Mortality: ND 2. Diabetes related complications: ND 3. Quality of life: ND 4. Glycaemic control: glycated haemoglobin (HbA1c), fasting & post-load blood glucose 5. Lipids: total-, HDL-cholesterol, triglycerides 6. Insulin levels: fasting insulin 7. Weight: body weight 8. Adverse effects: yes
Notes	Sponsor: pharmaceutical Author contacted: additional data on design, quality and outcomes send by author Study retrieved: CENTRAL, MEDLINE, EMBASE
Allocation concealment	A

Study	**Rosenthal 2002**
Methods	DESIGN: parallel study RANDOMISATION PROCEDURE: adequate BLINDING: no blinding DURATION: 24 weeks
Participants	COUNTRY: Germany SETTING: general practice NUMBER: selected: AGI 39, CONTROL 37, analysed: AGI 32, CONTROL 31 SEX: data missing AGE (YEARS (MEAN, SD)): AGI 57.4 (8.6), CONTROL 57.7 (10.5) DURATION OF DIABETES (MONTHS (MEAN, SD)): AGI 20.2 (31.2), CONTROL 35.6 (44.8)
Interventions	Dietary reinforcement: no AGI: acarbose, 50 mg TID, uptitrated to 100 mg TID (exact scheme not reported)

	CONTROL: glibenclamide, maximum 10.5 mg daily (7 mg - 0 - 3.5 mg), step-up scheme as long as fasting blood glucose remained > 8.9 mmol/l
Outcomes	1. Mortality: ND 2. Diabetes related complications: ND 3. Quality of life: ND 4. Glycaemic control: glycated haemoglobin (HbA1c), fasting & post-load blood-glucose 5. Lipids: total cholesterol, HDL, triglycerides 6. Insulin levels: fasting & post-load insulin 7. Weight: body weight, BMI 8. Adverse effects: yes
Notes	Sponsor: pharmaceutical Author contacted: additional data on design, quality and outcomes via manufacturer Study retrieved: EMBASE, Current Contents, manufacturer, (2 additional references via authors) Main outcome is blood pressure. According to the statistical report, the changes for lipids are calculated with standardised values (using a linear transformation to the interval [0,1] with respect to normal range), and therefore cannot be used for the meta-analysis.
Allocation concealment	B

Study	**Rybka 1999**
Methods	DESIGN: parallel study RANDOMISATION PROCEDURE: unclear BLINDING: double-blind DURATION: 24 weeks
Participants	COUNTRY: multiple European countries, not further specification SETTING: unclear NUMBER: 603 patients included SEX: data missing AGE: data missing DURATION OF DIABETES: data missing
Interventions	Dietary reinforcement: yes, specifications unclear AGI: acarbose 100 mg TID CONTROL1: placebo CONTROL2: miglitol 50 mg TID CONTROL3: miglitol 100 mg TID
Outcomes	1. Mortality: ND 2. Diabetes related complications: ND 3. Quality of life: ND 4. Glycaemic control: glycated haemoglobin (HbA1c), fasting & post-load blood glucose 5. Lipids: ND 6. Insulin levels: ND 7. Weight: body weight 8. Adverse effects: yes
Notes	Sponsor: pharmaceutical Author contacted: no reply Study retrieved: handsearch Published as an abstract. A non-systematic review on miglitol cited this study also as an unpublished document (Scott 2000). Bayer referred to Pfizer being the current owner of this data, but wen received no reply from Pfizer so far.

Allocation concealment	B

Study	**Salman 2001**
Methods	DESIGN: parallel study RANDOMISATION PROCEDURE: adequate BLINDING: no blinding DURATION: 24 weeks
Participants	COUNTRY: Turkey SETTING: outpatient NUMBER: randomised 72; analysed: AGI 27, CONTROL 30 SEX (F/M): analysed patients: AGI 10/17, CONTROL 14/16 AGE (YEARS (MEAN, SD)): analysed group: AGI 52,6 (9,1), CONTROL 56,1 (8,7) DURATION OF DIABETES (MONTHS (MEAN, SD)): analysed group: AGI 50,4 (40,8), CONTROL 56,4 (67,2)
Interventions	Dietary reinforcement: patients under dietary recommendations for at least 3 months, controlled for diet compliance before study inclusion. AGI: acarbose, week 1 to 4 every week 50 mg increase to 100 mg BID, week 4-24 100 mg TID, dose reduced to 100 mg BID in case of adverse events CONTROL: gliclazide maximum 80 mg BID, depending on degree of glycemic control; in general maximum dose was not recommended
Outcomes	1. Mortality: ND 2. Diabetes related complications: ND 3. Quality of life: ND 4. Glycaemic Control: glycated haemoglobin (HbA1c), fasting & post-load blood glucose 5. Lipids: triglycerides, total-, HDL- & LDL-cholesterol 6. Insulin levels: fasting & post-load insulin, fasting & post-load C-peptide 7. Weight: body weight, BMI 8. Adverse effects: yes
Notes	Sponsor: pharmaceutical Author contacted: additional data on design, quality and outcomes send by author Study retrieved: CENTRAL, MEDLINE, EMBASE, Current Contents, manufacturer
Allocation concealment	A

Study	**Santeusanio 1993**
Methods	DESIGN: parallel study RANDOMISATION PROCEDURE: adequate BLINDING: double-blind DURATION: 16 weeks
Participants	COUNTRY: Italy SETTING: outpatient NUMBER: randomised: AGI 27, CONTROL1 29, CONTROL2 28; evaluated in ITT-analysis: AGI 23, CONTROL1 23, CONTROL2 18 SEX (F/M): ITT: AGI 8/15, CONTROL1 7/16, CONTROL2 8/10 AGE (YEARS (MEAN, SD)): ITT: AGI 53,8 (11,0), CONTROL1 55,5 (11,5), CONTROL2 58,9 (9,8) DURATION OF DIABETES (MONTHS (MEAN, SD)): ITT: AGI 60,6 (57,6), CONTROL1 46,4 (51,6), CONTROL2 46,4 (36,0)
Interventions	Dietary reinforcement: yes, iso-caloric diet to maintain stable body weight (50-55% carbohydrates, <30% lipids, 15-20% protein and <10 g/1000 kcal as fibre). AGI: acarbose m100 mg TID

Characteristics of included studies (*Continued*)

	CONTROL1: placebo TID CONTROL2: acarbose 50 mg TID
Outcomes	1. Mortality: ND 2. Diabetes related complications: ND 3. Quality of life: ND 4. Glycaemic control: glycated haemoglobin (HbA1c), fasting & post-load blood glucose 5. Lipids: ND 6. Insulin levels: fasting & post-load insulin 7. Weight: ND 8. Adverse effects: yes
Notes	Sponsor: pharmaceutical Author contacted: additional data on design, quality and outcomes via manufacturer Study retrieved: CENTRAL, MEDLINE, EMBASE, Current Contents, manufacturer, handsearch
Allocation concealment	B

Study	**Scott 1999**
Methods	DESIGN: parallel study RANDOMISATION PROCEDURE: unclear BLINDING: double-blind DURATION: 16 weeks
Participants	COUNTRY: New Zealand / Australia SETTING: outpatient NUMBER: AGI 53, CONTROL 52 SEX (F/M): AGI 20/33, CONTROL 18/34 AGE (YEARS (MEAN, SD)): AGI 56 (9), CONTROL 57 (8) DURATION OF DIABETES (MONTHS (MEAN, SD)): AGI 21 (15), CONTROL 26 (17)
Interventions	Dietary reinforcement: yes, 'conforming to current recommendations for type 2 diabetes' AGI: acarbose, week 1-2 50 mg TID, wk 3-16 100 mg TID, dose reduced to 50 mg TID in case of adverse events CONTROL: placebo TID
Outcomes	1. Mortality: ND 2. Diabetes related complications: ND 3. Quality of life: ND 4. Glycaemic control: glycated haemoglobin (HbA1c), fasting blood glucose 5. Lipids: triglycerides, total- and HDL-cholesterol 6. Insulin levels: fasting insulin 7. Weight: ND 8. Adverse effects: yes
Notes	Sponsor: pharmaceutical Author contacted: author replied that he passed our queries through to Bayer Australia, but we received no reply from Bayer Australia since. Study retrieved: CENTRAL, MEDLINE, EMBASE, Current Contents
Allocation concealment	A

Study	**Segal 1997**
Methods	DESIGN: parallel study RANDOMISATION PROCEDURE: unclear BLINDING: double-blind DURATION: 24 weeks

Characteristics of included studies (*Continued*)

Participants	COUNTRY: Germany, Austria, Israel, Czech Republic SETTING: outpatient NUMBER: randomised 201, ITT 186, PP 119 (AGI 40, CONTROL 37, CONTROL2 42) SEX (F/M): PP: AGI 18/22, CONTROL1 14/23, CONTROL2 18/24 AGE (YEARS (MEAN)): PP: AGI 61, CONTROL1 56, CONTROL2 59 DURATION OF DIABETES (MONTHS (MEAN, SD)): ND
Interventions	Dietary reinforcement: no AGI: miglitol, week 1-4 50 mg TID, week 5-25 100 mg TID CONTROL1: glibenclamide 3,5 mg once or twice daily CONTROL2: placebo TID
Outcomes	1. Mortality: ND 2. Diabetes related complications: ND 3. Quality of life: ND 4. Glycaemic control: glycated haemoglobin (HbA1c), fasting & post-load glucose 5. Lipids: ND 6. Insulin levels: ND 7. Weight: body weight 8. Adverse effects: yes
Notes	Sponsor: pharmaceutical Author contacted: no reply Study retrieved: CENTRAL, MEDLINE, EMBASE, Current Contents
Allocation concealment	B

Study	**Spengler 1992**
Methods	DESIGN: Parallel study RANDOMISATION PROCEDURE: adequate BLINDING: no blinding DURATION: 24 weeks
Participants	COUNTRY: Germany SETTING: outpatient NUMBER: randomised 72, analysed: AGI 26, CONTROL 29 SEX (F/M): AGI 15/11, CONTROL 18/11 AGE (YEARS (MEAN, SD)): analysed: AGI 59 (5), CONTROL 60 (7) DURATION OF DIABETES (MONTHS (MEDIAN)): analysed: AGI 12.0, CONTROL 8.4
Interventions	Dietary reinforcement: unclear AGI: acarbose, week 1-2 50 mg TID, week 3-24 100 mg TID CONTROL: glibenclamide maximum 3,5 mg TID
Outcomes	1. Mortality: ND 2. Diabetes related complications: ND 3. Quality of life: ND 4. Glycaemic control: glycated haemoglobin (HbA1c), fasting & post-load blood glucose 5. Lipids: ND 6. Insulin levels: ND 7. Weight: body weight 8. Adverse effects: yes
Notes	Sponsor: pharmaceutical Author contacted: additional data on design, quality and outcomes via manufacturer Study retrieved: CENTRAL, MEDLINE, EMBASE, experts (1 additional reference via author)

	For all outcomes except body weight, geometric means are reported; true means not available from articles and statistical reports.
Allocation concealment	B

Study	**Takami 2002**
Methods	DESIGN: parallel study RANDOMISATION PROCEDURE: unclear BLINDING: no blinding DURATION: 3 months
Participants	COUNTRY: Japan SETTING: outpatient NUMBER: Analysed: AGI 12, CONTROL1 11, CONTROL2 9 SEX (F/M): AGI 3/9, CONTROL1 4/7, CONTROL2 3/10 AGE (YEARS (MEAN, SD)): total group (n=36!) men 48,7 (8,3), women 55,0 (7,8) DURATION OF DIABETES: Newly diagnosed patients
Interventions	Dietary reinforcement: yes, 30 kcal/Kg of ideal body weight per day, 60% carbohydrate, 20% fat, 20% protein. AGI: voglibose 0,3 mg TID CONTROL1: diet therapy CONTROL2: glyburide 1,25 mg once daily
Outcomes	1. Mortality: ND 2. Diabetes related complications: ND 3. Quality of life: ND 4. Glycaemic control: glycated haemoglobin (HbA1c), fasting bloodglucose 5. Lipids: Total & HDL-cholesterol, triglycerides 6. Insulin levels: fasting insulin 7. Weight: weight & BMI 8. Adverse effects: ND
Notes	Sponsor: not specified Author contacted: no reply Study retrieved: CENTRAL, MEDLINE, Current Contents, handsearch 36 'study subjects', 32 randomised and 4 patients assigned to diet group after random phase to 'facilitate analysis of correlations between the changes in abdominal adipose tissue and glycemic control with diet'.
Allocation concealment	B

Study	**Van de Laar 2004a**
Methods	DESIGN: Parallel study RANDOMISATION PROCEDURE: adequate BLINDING: double-blind DURATION: 30 weeks
Participants	COUNTRY: The Netherlands SETTING: general practice NUMBER: randomised: AGI 48, CONTROL 48, ITT: AGI 32, CONTROL 43 SEX (F/M): ITT: AGI 16/16, CONTROL 20/23 AGE (YEARS (MEAN, SD)): ITT: AGI 58.6 (7.7), CONTROL 58.6 (7.1) DURATION OF DIABETES (MONTHS (MEDIAN)): analysed: AGI 12.0, CONTROL 8.4
Interventions	Dietary reinforcement: yes, advice tailored to individual food habits by dietician with access to current recommendations AGI: acarbose, maximum dosage schedule at week 0, 2, 4 and 6-30 was (mg): 50 - 0 - 0, 50 - 0 - 50, 50 - 50 - 50 and 100 - 100 - 100 respectively CONTROL: tolbutamide, maximum dosage schedule at week 0, 2, 4 and 6-30 (mg) was 500 - 0 - 0, 500 - 0 - 500, 500 - 500 - 500 and 1000 - 500 - 500 respectively.

Characteristics of included studies (*Continued*)

Outcomes	1. Mortality: ND 2. Diabetes related complications: ND 3. Quality of Life: ND 4. Glycaemic Control: glycated haemoglobin (HbA1c), fasting & post-load blood glucose 5. Lipids: triglycerides, total-, LDL- & HDL-cholesterol 6. Insulin levels: fasting & post-load insulin 7. Weight: BMI 8. Adverse effects: yes
Notes	Sponsor: pharmaceutical Author contacted: data possessed by authors review Study retrieved: experts Equivalence study
Allocation concealment	A

Study	**Zheng 1995**
Methods	DESIGN: parallel study RANDOMISATION PROCEDURE: unclear BLINDING: double-blind DURATION: 24 weeks
Participants	COUNTRY: China SETTING: outpatient NUMBER: AGI 39, CONTROL 38 SEX (F/M): AGI 19/20, CONTROL 18/20 AGE (YEARS (MEAN, SD)): AGI 49.6 (6.9), CONTROL 49.0 (6.6) DURATION OF DIABETES (MONTHS (MEAN, SD)): AGI 49.2 (33.6), CONTROL 50.4 (43.2)
Interventions	Dietary reinforcement: unclear ('diet and level of activity had to remain stable) AGI: acarbose, week 1-3 50 mg TID, wk 4-24 100 mg TID CONTROL: placebo
Outcomes	1. Mortality: ND 2. Diabetes related complications: ND 3. Quality of life: ND 4. Glycaemic control: glycated haemoglobin (HbA1c), fasting & post-load blood glucose 5. Lipids: triglycerides, total- and HDL-cholesterol 6. Insulin levels: fasting & post-load insulin 7. Weight: BMI 8. Adverse effects: yes
Notes	Sponsor: pharmaceutical Author contacted: no reply Study retrieved: CENTRAL
Allocation concealment	B

BID = two times per day; BMI = body mass index; CENTRAL = Cochrane Central Register of Controlled Trials; HDL = high-density lipoprotein; ITT = intention-to-treat analysis; LDL = low-density lipoprotein; ND = no reported data; PP = per protocol analysis; TID = three times per day,
For interventions the maximum dosage is given
For outcomes: Outome measures that are reported are given

Characteristics of excluded studies

Bachmann 2003	Use of additional anti-diabetic medication
Bayer 2003	Use of additional anti-diabetic medication
Bayer 2003a	Use of additional anti-diabetic medication, included patients with type 1 and type 2 diabetes
Coniff 1995a	Falsely included on basis of Embase search (excluded from Medline search) acarbose given as additional therapy (added to insulin therapy)
De Leiva 1993	Use of additional anti-diabetic medication, reported data does not allow subgroup analysis of AGI only group

Characteristics of excluded studies (*Continued*)

Escobar-Jimenez 1995	Use of additional anti-diabetic medication, reported data does not allow subgroup analysis of AGI only group
Fujita 2001	Use of additional anti-diabetic medication, reported data does not allow subgroup analysis of AGI only group
Hasche 1999	Use of additional medication, reported data does not allow subgroup analysis of AGI only group
Holman 1991	Duration of AGI treatment < 12 wk (4 wk)
Ikeda 1998	Use of additional anti-diabetic medication, reported data does not allow subgroup analysis of AGI only group
Jenney 1993	No randomisation; Acarbose not given as monotherapy
Rosak 2002	Study duration < 12 wk (1 day)
Rosenbaum 2002	Us of additional anti-diabetic medication, reported data does not allow subgroup analysis of AGI only group
Soonthornpun 1998	Use of additional anti-diabetic medication
Wang 2000	Patients with impaired glucose tolerance (in stead of type 2 diabetes mellitus)

Characteristics of ongoing studies

Study	**Holman 2003**
Trial name or title	Early Diabetes Intervention Study (EDIT)
Participants	Subjects were selected on the basis of two consecutive fasting plasma glucose values of 5.5 to 7.7 mmol/l. They all underwent OGTTs at entry into the study but if the 2-h glucose was found to be in the diabetic range (i.e. 11.1 or above) they were not excluded, provided that the fasting remained below 7.8 mmol/l.
Interventions	Acarbose (50mg TID), metformin (500mg TID) and placebo; Design: prospective, parallel group, double blind, double dummy, randomised, factorial design, multicentre study; Duration 6 years
Outcomes	Progression to frank diabetes; Glycaemic reduction
Starting date	01 / 04 / 1998; end date: 30 / 04 / 2003
Contact information	Dr Rury Holman Diabetes Research Laboratories Radcliffe Infirmary Woodstock Rd Oxford OX2 6HE UK rury.holman@dtu.ox.ac.uk
Notes	A subgroup of 106 patients had postprandial blood glucose in the diabetic range (> 11.1 mmol/l, but fasting blood glucose < 7.8 mmol/l). Data from this sub-group might be possible included in the review

Study	**Sa-adu 2003**
Trial name or title	A one-year multicentre, international, randomised, double-blind comparison of Mitiglinide (10to40mgTID) and Acarbose (50mgODto100mgTID) administered orally for the treatment of elderly type 2 diabetic patients
Participants	Elderly type 2 diabetic patients suboptimally controlled with diet alone.
Interventions	Mitiglinide (10 to 40 mg TID) and Acarbose (50 mg OD to 100 mg TID); Design: comparative, randomised, double blind, parallel group phase III
Outcomes	HbA1c
Starting date	01 /12 / 2--1; end date: 01/ 06 / 2003
Contact information	Prof Alan Sinclair, The University of Warwick; Dr Alfa Sa-adu Care of the Elderly

Characteristics of ongoing studies (*Continued*)

	Watford General Hospital Vicarage Road Watford Herts WD18 0HB UK Telephone: 01923 217227 E-mail: a.saadu.btinternet.com
Notes	Two e-mails to prof. Sinclair were not answered. Dr Sa-adu replied that he was not a contributor to this study and that recruitment was taken to East European Countries.

Study	**Whitby 1998**
Trial name or title	A long-term study to investigate the effects of acarbose (glucobay) in preventing or delaying deterioration in glycaemic status in non-insulin diabetes will controlled on diet alone.
Participants	Non-insulin dependent diabetics, either newly diagnosed or well controlled on diet alone.
Interventions	Acarbose versus placebo
Outcomes	Not specified
Starting date	28 / 09 / 1993; end date: 31 / 07 / 1996
Contact information	Dr Robert E J Ryder Department of Diabetes City Hospital Dudley Road Birmingham West Midlands B18 7QH England Telephone: 0121 554 3801 Dr R J Whitby Linden Medical Centre Linden Ave Kettering NN15 7NX Northants
Notes	Dr Ryder and dr. Whitby were contacted. Dr Ryder referred to prof. Holman as leading investigator, but Professor Holman did not reply to our e-mails regarding questions about this study.

TID = three times per day

ADDITIONAL TABLES

Table 01. Methods post-load glucose / insulin measurement

Study	Type of test	Interval	Data used	Medication given?
Braun 1996	Breakfast ('no special meals')	1 hour	1 hour glucose	unclear
Buchanan 1988	No post-load test			

Table 01. Methods post-load glucose / insulin measurement (*Continued*)

Study	Type of test	Interval	Data used	Medication given?
Calle-Pascual 1996	No post-load test			
Campbell 1998	No post-load test			
Chan 1998	Individually tailored meal recommended by dietician (60% carbohydrate, <30% fat, 12-20% protein)	1 hour	1 hour glucose & insulin	yes (at least at 24 weeks measurement)
Chiasson 1994	Standard breakfast: 450 kcal, 55% carbohydrates, 30.5% lipids, 14.5% protein	1, 1.5 and 2 hours measured	Data not reported	yes
Chiasson 2001	Standardised liquid test breakfast (55% carbohydrate, 30% fat, and 15% protein; providing ~450 kcal)	1, 1.5 and 2 hours measured and reported	1 hour (2 hours value in sensitivity analysis) glucose & insulin	yes
Coniff 1994	Breakfast, 2520 kJ, with 50% carbohydrates, 30% fat, 20% protein.	1, 1.5 and 2 hours measured and reported	1 hour (2 hours value in sensitivity analysis) glucose	yes
Coniff 1995	Full-meal tolerance test: 600 kcal breakfast (50% carbohydrate, 30% fat, 20% protein	1, 1.5 and 2 hours measured and reported	1 hour (2 hours value in sensitivity analysis) glucose & insulin	yes
Coniff 1995b	Standardised meal tolerance test, 600-kcal breakfast of 50% carbohydrates (75g), 30% fat (20g), 20% protein (30g)	1, 1.5 and 2 hours measured and reported	1 hour (2 hours value in sensitivity analysis) glucose & insulin	yes
Dedov 1995	Post-load test performed, type of test unclear	1 hour	1 hour glucose	unclear
Delgado 2002	Post-load test performed, type of test unclear	Not reported	post-load glucose	unclear
Drent 2002	White bread, margarine, diet jam and cheese, 1556 kJ, 49% carbohydrate, 40% fat, 11% protein, 2,5 g fibre.	1, 1.5 and 2 hours measured	Data not reported	yes
Fischer 1998	Test meal 1562 kJ, 49% carbohydrate, 40% fat, 11% protein (80 g white bread, 10g spread, 25g diet jam, 20 g 45% fat cheese)	1 hour measured and reported (2 hours value measured but not reported adequately)	1 hour glucose	yes

Table 01. Methods post-load glucose / insulin measurement (*Continued*)

Study	Type of test	Interval	Data used	Medication given?
Gentile 1999	Home cooked breakfast, lunch and diner	2 hours (after diner also after 4 hours) measured, not reported adequately	Data not reported	unclear
Haffner 1997	Standardised breakfast (370 kcal; 49% carbohydrates, 40 % fat, 11% protein)	1 hour measured and reported	1 hour glucose & insulin	unclear
Hanefeld 1991	Testmeal: 400 kcal (50% carbohydrates, 35% fat, 15% protein)	1 hour measured and reported (2, 3, 4 and 5 hours also measured but not reported)	1 hour glucose & insulin	yes
Hillebrand 1987	Unclear	Measurement at 11 AM and 5 AM, interval not clear	Data not adequately reported	unclear
Hoffmann 1990	Standard breakfast: 80 g bread, 20g low fat spread, 25g marmalade, 20 g cheese (45% fat), 1 egg	1 hour measured and reported	1 hour glucose	yes
Hoffmann 1994	Standardised breakfast: 1,569 kJ (372 Kcal), 49% energy as (mainly complex) carbohydrates, 40% fat, 11% protein	1 hour measured and reported	1 hour glucose & insulin	yes
Hoffmann 1997	Standardised breakfast: 1,569 kJ (372 Kcal), 49% energy as (mainly complex) carbohydrates, 40% fat, 11% protein	1 hour measured and reported	1 hour glucose & insulin	yes
Holman 1999	No post-load test			
Holmes 2001	No post-load test			
Hotta 1993	75 grams Oral Glucose Tolerance Test	0.5, 1, 2 and 3 hours measured	2 hours glucose, 0.5, 1 and 3 hours not reported adequately	yes
Johnston 1998	Standardised test meal: 480 calories, 51% carbohydrates	1, 1.5 and 2 hours measured	Data not reported adequately	unclear
Johnston 1998a	Standard 483 kcal, 51% carbohydrate mixed-meal breakfast	2 hours measured	Data not reported adequately	unclear
Johnston 1998b	Standard 438 kcal, 51% carbohydrate, 14% protein, 35% fat meal	2 hours measured	Data not reported adequately	unclear
Kawamori 2003	'meal-loading test'	1 and 2 hours measured	1 hour (2 hours value	unclear

Table 01. Methods post-load glucose / insulin measurement (*Continued*)

Study	Type of test	Interval	Data used	Medication given?
		and reported	in sensitivity analysis) glucose & insulin	
Kovacevic 1997	Full meal tolerance test: 80 g white bread; 10 g butter, 25 g diet marmalade (with 23% fructose); 20 g cheese (45% fat); 250 ml coffee or tea	1 hour measured and reported	1 hour glucose & insulin	unclear
Meneilly 2000	400 ml Ensure ™ with fibre (450 kcal, 55% carbohydrate, 30% fat and 15% protein)	1, 1.5 and 2 hours measured	Data not reported adequately	yes
Pagano 1995	Standard breakfast, with 125 g fruit juice, 75 g ham and 80 g white bread (590 kcal, 44% carbohydrates, 41% lipids, 15% protein)	0.5, 1,2 and 3 hours measured and reported, 0.5, 1, and 3 hours measured	2 hour glucose, 0.5, 1 and 3 hours not reported adequately	yes (not with respect to glibencamide)
Rosenthal 2002	Standard breakfast: 80g bread, 20 g low fat spread, 25 g marmalade, 20 g cheese (45%), 1 egg	1 hour measured and reported	1 hour glucose & insulin	yes
Rybka 1999	Unclear	1 hour measured	Data not reported adequately	unclear
Salman 2001	Breakfast which was prepared by an experienced dietician according to individual needs	1.5 hours measured and reported	1.5 hours glucose, insulin & c-peptide	no
Santeusanio 1993	Mixed meal test, consisting 440 calories, as 30% protein, 20% lipid and 50% carbohydrate	1, 2 and 3 hours measured and reported (0.5 hours not reported)	1 hour (2 hours value in sensitivity analysis) glucose & insulin	unclear
Scott 1999	Standardised breakfast meal (1.6 MJ)	1 and 2 hours measured	Data not reported adequately	unclear
Segal 1997	Standardised breakfast test meal (372 kcal; 49% carbohydrate, 40% fat, 11% protein)	1 and 2 hour measured	Data not reported adequately	unclear
Spengler 1992	Standard breakfast: 80 g, 20 g low fat spread, 25 g marmelade, 20 g cheese, 1 egg	1 hour measured	Data not reported adequately	yes

Table 01. Methods post-load glucose / insulin measurement (*Continued*)

Study	Type of test	Interval	Data used	Medication given?
Takami 2002	No post-load test			
Van de Laar 2004a	75 grams Oral Glucose Tolerance Test	1 hour mesured and reported	1 hour glucose & insulin	no
Zheng 1995	'meal'	1 hour measured and reported	1 hour glucose & insulin	unclear

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Comparison 01. Acarbose versus placebo

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Change in glycated haemoglobin (%)	28	2831	Weighted Mean Difference (Random) 95% CI	-0.77 [-0.90, -0.64]
02 Change in fasting blood glucose (mmol/l)	28	2838	Weighted Mean Difference (Random) 95% CI	-1.09 [-1.36, -0.83]
03 Change in post-load blood glucose (mmol/l)	22	2238	Weighted Mean Difference (Random) 95% CI	-2.32 [-2.73, -1.92]
04 Change in total cholesterol (mmol/l)	23	2133	Weighted Mean Difference (Random) 95% CI	0.00 [-0.10, 0.09]
05 Change in HDL-cholesterol (mmol/l)	14	924	Weighted Mean Difference (Random) 95% CI	0.00 [-0.04, 0.04]
06 Change in LDL-cholesterol (mmol/l)	4	402	Weighted Mean Difference (Random) 95% CI	-0.08 [-0.41, 0.25]
07 Change in triglycerides (mmol/l)	21	1969	Weighted Mean Difference (Random) 95% CI	-0.09 [-0.18, 0.00]
08 Change in fasting insulin levels (pmol/l)	15	1264	Weighted Mean Difference (Random) 95% CI	-0.52 [-7.90, 6.86]
09 Change in post-load insulin levels (pmol/l)	13	1050	Weighted Mean Difference (Random) 95% CI	-40.82 [-60.64, -21.01]
10 Change in fasting C-peptide levels (nmol/l)	1	94	Weighted Mean Difference (Random) 95% CI	-0.05 [-0.18, 0.08]
11 Change in post-load C-peptide levels (nmol/l)	1	94	Weighted Mean Difference (Random) 95% CI	-0.10 [-0.34, 0.14]
12 Change in body weight (Kg)	16	1451	Weighted Mean Difference (Random) 95% CI	-0.13 [-0.46, 0.20]
13 Change in body mass index (Kg/m2)	14	1430	Weighted Mean Difference (Random) 95% CI	-0.17 [-0.25, -0.08]
15 Total deaths	2	385	Odds Ratio (Random) 95% CI	1.11 [0.29, 4.22]
16 Disease related deaths	1	129	Odds Ratio (Random) 95% CI	Not estimable
20 Occurence of morbidity (total)	0	0	Odds Ratio (Random) 95% CI	Not estimable
21 Occurence of morbidity (disease specific)	0	0	Odds Ratio (Random) 95% CI	Not estimable
30 Occurence of adverse effects	23	3819	Odds Ratio (Random) 95% CI	3.37 [2.60, 4.36]
31 Occurence of gastro-intestinal adverse effects	4	1442	Odds Ratio (Random) 95% CI	3.30 [2.31, 4.71]
50 Quality of life	0	0	Weighted Mean Difference (Random) 95% CI	Not estimable

90 Change in post-load blood glucose (mmol/l) (2-hours)	22	2243	Weighted Mean Difference (Random) 95% CI	-2.27 [-2.67, -1.88]
91 Change in post-load insulin levels (pmol/l) (2-hours)	13	1057	Weighted Mean Difference (Random) 95% CI	-38.83 [-58.77, -18.89]

Comparison 02. Acarbose versus sulphonylurea (SU)

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Change in glycated haemoglobin (%)	8	596	Weighted Mean Difference (Random) 95% CI	0.38 [-0.02, 0.77]
02 Change in fasting blood glucose (mmol/l)	8	596	Weighted Mean Difference (Random) 95% CI	0.69 [0.16, 1.23]
03 Change in post-load blood glucose (mmol/l)	8	591	Weighted Mean Difference (Random) 95% CI	-0.10 [-0.43, 0.22]
04 Change in total cholesterol (mmol/l)	7	499	Weighted Mean Difference (Random) 95% CI	-0.09 [-0.23, 0.05]
05 Change in HDL-cholesterol (mmol/l)	7	485	Weighted Mean Difference (Random) 95% CI	0.02 [-0.02, 0.06]
06 Change in LDL-cholesterol (mmol/l)	4	312	Weighted Mean Difference (Random) 95% CI	0.10 [-0.07, 0.27]
07 Change in triglycerides (mmol/l)	8	591	Weighted Mean Difference (Random) 95% CI	0.01 [-0.18, 0.20]
08 Change in fasting insulin levels (pmol/l)	7	486	Weighted Mean Difference (Random) 95% CI	-24.78 [-43.30, -6.26]
09 Change in post-load insulin levels (pmol/l)	7	483	Weighted Mean Difference (Random) 95% CI	-133.17 [-184.53, -81.82]
10 Change in fasting C-peptide levels (nmol/l)	1	57	Weighted Mean Difference (Random) 95% CI	-0.18 [-0.51, 0.15]
11 Change in post-load C-peptide levels (nmol/l)	1	57	Weighted Mean Difference (Random) 95% CI	-0.36 [-0.94, 0.22]
12 Change in body weight (Kg)	5	397	Weighted Mean Difference (Random) 95% CI	-1.90 [-4.01, 0.21]
13 Change in body mass index (Kg/m2)	4	230	Weighted Mean Difference (Random) 95% CI	-0.39 [-0.83, 0.05]
15 Total deaths	1	133	Odds Ratio (Random) 95% CI	0.32 [0.01, 8.08]
16 Disease related deaths	1	133	Odds Ratio (Random) 95% CI	0.32 [0.01, 8.08]
30 Occurence of adverse effects	7	607	Odds Ratio (Random) 95% CI	3.95 [2.00, 7.80]
31 Occurence of gastro-intestinal adverse effects	1	145	Odds Ratio (Random) 95% CI	7.70 [3.64, 16.31]
90 Change in post-load blood glucose (mmol/l) (2 hours)	8	591	Weighted Mean Difference (Random) 95% CI	0.06 [-0.42, 0.53]
91 Change in post-load insulin levels (pmol/l) (2 hours)	7	484	Weighted Mean Difference (Random) 95% CI	-115.84 [-152.52, -79.15]

Comparison 03. Acarbose versus Metformin

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Change in glycated haemoglobin (%)	1	62	Weighted Mean Difference (Random) 95% CI	-0.25 [-0.61, 0.11]
02 Change in fasting blood glucose (mmol/l)	1	62	Weighted Mean Difference (Random) 95% CI	-0.39 [-0.74, -0.04]

03 Change in post-load blood glucose (mmol/l)	1	62	Weighted Mean Difference (Random) 95% CI	-0.42 [-0.79, -0.05]
04 Change in total cholesterol (mmol/l)	1	62	Weighted Mean Difference (Random) 95% CI	-0.94 [-1.66, -0.22]
05 Change in HDL-cholesterol (mmol/l)	1	62	Weighted Mean Difference (Random) 95% CI	0.24 [-0.02, 0.50]
06 Change in LDL-cholesterol (mmol/l)	1	62	Weighted Mean Difference (Random) 95% CI	-0.94 [-1.52, -0.36]
07 Change in triglycerides (mmol/l)	1	62	Weighted Mean Difference (Random) 95% CI	-0.28 [-0.80, 0.24]
08 Change in fasting insulin levels (pmol/l)	1	61	Weighted Mean Difference (Random) 95% CI	33.80 [-28.24, 95.84]
09 Change in post-load insulin levels (pmol/l)	1	61	Weighted Mean Difference (Random) 95% CI	115.30 [-13.22, 243.82]
12 Change in body weight (Kg)	1	62	Weighted Mean Difference (Random) 95% CI	-0.30 [-5.45, 4.85]
30 Occurence of adverse effects	1	64	Odds Ratio (Random) 95% CI	15.00 [3.06, 73.58]

Comparison 04. Acarbose versus nateglinide / repaglinide

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Change in glycated haemoglobin (%)	1	179	Weighted Mean Difference (Random) 95% CI	0.03 [-0.19, 0.25]
02 Change in fasting blood glucose (mmol/l)	1	175	Weighted Mean Difference (Random) 95% CI	-0.02 [-1.10, 1.06]
12 Change in body weight (Kg)	1	169	Weighted Mean Difference (Random) 95% CI	-0.68 [-1.30, -0.06]
30 Occurence of adverse effects	1	179	Odds Ratio (Random) 95% CI	1.92 [1.05, 3.50]
31 Occurence of gastro-intestinal adverse effects	1	179	Odds Ratio (Random) 95% CI	3.22 [1.66, 6.24]

Comparison 05. Miglitol versus placebo

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Change in glycated haemoglobin (%)	7	1088	Weighted Mean Difference (Random) 95% CI	-0.68 [-0.93, -0.44]
02 Change in fasting blood glucose (mmol/l)	2	398	Weighted Mean Difference (Random) 95% CI	-0.52 [-0.88, -0.16]
03 Change in post-load blood glucose (mmol/l)	2	398	Weighted Mean Difference (Random) 95% CI	-2.70 [-5.54, 0.14]
08 Change in fasting insulin levels (pmol/l)	1	162	Weighted Mean Difference (Random) 95% CI	-18.20 [-57.01, 20.61]
09 Change in post-load insulin levels (pmol/l)	2	398	Weighted Mean Difference (Random) 95% CI	-16.62 [-39.23, 6.00]
12 Change in body weight (Kg)	1	162	Weighted Mean Difference (Random) 95% CI	0.27 [-0.50, 1.04]
15 Total deaths	2	408	Odds Ratio (Random) 95% CI	2.97 [0.31, 28.80]
16 Disease related deaths	2	408	Odds Ratio (Random) 95% CI	2.94 [0.12, 73.07]
30 Occurence of adverse effects	7	1304	Odds Ratio (Random) 95% CI	4.01 [1.69, 9.52]
31 Occurence of gastro-intestinal adverse effects	2	428	Odds Ratio (Random) 95% CI	3.12 [1.62, 6.02]
90 Change in post-load blood glucose (mmol/l) (2-hours)	2	398	Weighted Mean Difference (Random) 95% CI	-1.66 [-2.25, -1.07]

91 Change in post-load insulin levels (pmol/l) (2-hours)	2	398	Weighted Mean Difference (Random) 95% CI	-15.69 [-38.63, 7.24]

Comparison 06. Miglitol versus sulphonylurea (SU)

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Change in glycated haemoglobin (%)	1	90	Weighted Mean Difference (Random) 95% CI	0.40 [-0.16, 0.96]
02 Change in fasting blood glucose (mmol/l)	1	90	Weighted Mean Difference (Random) 95% CI	0.27 [-0.74, 1.28]
03 Change in post-load blood glucose (mmol/l)	1	88	Weighted Mean Difference (Random) 95% CI	-0.60 [-3.43, 2.23]
04 Change in total cholesterol (mmol/l)	1	88	Weighted Mean Difference (Random) 95% CI	0.08 [-0.29, 0.45]
05 Change in HDL-cholesterol (mmol/l)	1	86	Weighted Mean Difference (Random) 95% CI	-0.01 [-0.26, 0.24]
07 Change in triglycerides (mmol/l)	1	89	Weighted Mean Difference (Random) 95% CI	-0.04 [-0.40, 0.32]
08 Change in fasting insulin levels (pmol/l)	1	90	Weighted Mean Difference (Random) 95% CI	-44.75 [-53.72, -35.78]
12 Change in body weight (Kg)	1	90	Weighted Mean Difference (Random) 95% CI	0.46 [-0.48, 1.40]
15 Total deaths	2	414	Odds Ratio (Random) 95% CI	0.50 [0.09, 2.76]
16 Disease related deaths	2	414	Odds Ratio (Random) 95% CI	0.63 [0.08, 5.14]
30 Occurence of adverse effects	2	232	Odds Ratio (Random) 95% CI	1.29 [0.69, 2.41]

Comparison 07. Miglitol versus metformin

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Change in glycated haemoglobin (%)	1	161	Weighted Mean Difference (Random) 95% CI	0.87 [0.56, 1.18]
02 Change in fasting blood glucose (mmol/l)	1	161	Weighted Mean Difference (Random) 95% CI	1.00 [0.18, 1.82]
03 Change in post-load blood glucose (mmol/l)	1	161	Weighted Mean Difference (Random) 95% CI	0.70 [-0.43, 1.83]
08 Change in fasting insulin levels (pmol/l)	1	161	Weighted Mean Difference (Random) 95% CI	-1.10 [-30.04, 27.84]
09 Change in post-load insulin levels (pmol/l)	1	161	Weighted Mean Difference (Random) 95% CI	-48.30 [-94.38, -2.22]
12 Change in body weight (Kg)	1	161	Weighted Mean Difference (Random) 95% CI	0.37 [-0.50, 1.24]
17 Occurence of gastro-intestinal side-effects	1	165	Odds Ratio (Random) 95% CI	1.59 [0.83, 3.05]
30 Occurence of adverse effects	1	165	Odds Ratio (Random) 95% CI	1.69 [0.39, 7.31]
90 Change in post-load blood glucose (mmol/l) (2 hours)	1	161	Weighted Mean Difference (Random) 95% CI	0.80 [-0.45, 2.05]
91 Change in post-load insulin levels (pmol/l) (2-hours)	1	161	Weighted Mean Difference (Random) 95% CI	-67.20 [-115.65, -18.75]

Comparison 08. Voglibose versus placebo

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Change in glycated haemoglobin (%)	1	238	Weighted Mean Difference (Random) 95% CI	-0.47 [-0.63, -0.31]
02 Change in fasting blood glucose (mmol/l)	1	234	Weighted Mean Difference (Random) 95% CI	-0.60 [-0.97, -0.23]
03 Change in post-load blood glucose (mmol/l)	1	234	Weighted Mean Difference (Random) 95% CI	-2.40 [-2.97, -1.83]
08 Change in post-load insulin levels (pmol/l)	1	234	Weighted Mean Difference (Random) 95% CI	-12.90 [-37.06, 11.26]
30 Occurence of adverse effects	1	263	Odds Ratio (Random) 95% CI	1.15 [0.67, 1.97]
31 Occurence of gastro-intestinal adverse effects	1	263	Odds Ratio (Random) 95% CI	1.62 [0.96, 2.75]
90 Change in post-load blood glucose (mmol/l) (2 hours)	1	234	Weighted Mean Difference (Random) 95% CI	-1.70 [-2.37, -1.03]

Comparison 09. Voglibose versus diet therapy

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Change in glycated haemoglobin (%)	1	23	Weighted Mean Difference (Random) 95% CI	0.00 [-1.15, 1.15]
02 Change in fasting blood glucose (mmol/l)	1	23	Weighted Mean Difference (Random) 95% CI	-2.40 [-4.58, -0.22]
04 Change in total cholesterol (mmol/l)	1	23	Weighted Mean Difference (Random) 95% CI	-0.70 [-1.64, 0.24]
05 Change in HDL-cholesterol (mmol/l)	1	23	Weighted Mean Difference (Random) 95% CI	-0.40 [-0.81, 0.01]
08 Change in fasting insulin levels (pmol/l)	1	23	Weighted Mean Difference (Random) 95% CI	6.00 [-19.22, 31.22]
12 Change in body weight (Kg)	1	23	Weighted Mean Difference (Random) 95% CI	0.20 [-4.99, 5.39]
13 Change in body mass index (Kg/m2)	1	23	Weighted Mean Difference (Random) 95% CI	0.00 [-2.26, 2.26]

Comparison 10. .Voglibose versus sulphonylurea (SU)

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Change in glycated haemoglobin (%)	1	21	Weighted Mean Difference (Random) 95% CI	1.30 [-0.45, 3.05]
02 Change in fasting blood glucose (mmol/l)	1	21	Weighted Mean Difference (Random) 95% CI	-0.50 [-3.15, 2.15]
04 Change in total cholesterol (mmol/l)	1	21	Weighted Mean Difference (Random) 95% CI	0.10 [-1.13, 1.33]
05 Change in HDL-cholesterol (mmol/l)	1	21	Weighted Mean Difference (Random) 95% CI	-0.20 [-0.59, 0.19]
08 Change in fasting insulin levels (pmol/l)	1	21	Weighted Mean Difference (Random) 95% CI	-11.80 [-25.49, 1.89]
12 Change in body weight (Kg)	1	21	Weighted Mean Difference (Random) 95% CI	0.60 [-9.73, 10.93]

13 Change in body mass index (Kg/m2)	1	21	Weighted Mean Difference (Random) 95% CI	0.00 [-2.40, 2.40]

Comparison 11. Miglitol versus voglibose

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Change in glycated haemoglobin (%)	1	312	Weighted Mean Difference (Random) 95% CI	-0.13 [-0.24, -0.02]
02 Change in fasting blood glucose (mmol/l)	1	306	Weighted Mean Difference (Random) 95% CI	0.00 [-0.31, 0.31]
03 Change in post-load blood glucose (mmol/l)	1	306	Weighted Mean Difference (Random) 95% CI	-1.70 [-2.27, -1.13]
09 Change in post-load insulin levels (pmol/l)	1	306	Weighted Mean Difference (Random) 95% CI	-2.90 [-30.04, 24.24]
30 Occurence of adverse effects	1	348	Odds Ratio (Random) 95% CI	1.53 [0.96, 2.45]
31 Occurence of gastro-intestinal adverse effects	1	348	Odds Ratio (Random) 95% CI	1.41 [0.93, 2.16]
90 Change in post-load blood glucose (mmol/l) (2 hours)	1	312	Weighted Mean Difference (Random) 95% CI	0.00 [-0.61, 0.61]

INDEX TERMS

Medical Subject Headings (MeSH)

Acarbose [therapeutic use]; Diabetes Mellitus, Type 2 [drug therapy]; Enzyme Inhibitors [therapeutic use]; Glucosamine [analogs & derivatives]; Hypoglycemic Agents [therapeutic use]; Inositol [analogs & derivatives]; Randomized Controlled Trials; alpha-Glucosidases [antagonists & inhibitors]

Medical MeSH check words

Humans

COVER SHEET

Title	Alpha-glucosidase inhibitors for type 2 diabetes mellitus
Authors	Van de Laar FA, Lucassen PLBJ, Akkermans RP, Van de Lisdonk EH, Rutten GEHM, Van Weel C
Contribution of author(s)	FLORIS VAN DE LAAR: Protocol development, searching for trials, abstract assessment for eligibility, quality assessment of trials, data extraction, data entry, data analysis, review development PETER LUCASSEN: Protocol development, abstract assessment for eligibility, quality assessment of trials, data extraction, data analysis, review development REINIER AKKERMANS: (double) data entry, data analysis, review development ELOY VAN DE LISDONK: Quality assessment of trials (referee), data analysis, translation Italian articles, review development GUY RUTTEN: Protocol development, data analysis (advisor), review development CHRIS VAN WEEL: Protocol development, data analysis (advisor), review development
Issue protocol first published	2002/2
Review first published	2005/2
Date of most recent amendment	25 May 2005

Date of most recent SUBSTANTIVE amendment	23 February 2005
What's New	We received additional data for the Holman (1999) study on september 1st 2004. The information is added. (see Table of included studies, comparions tables and study quality)
Date new studies sought but none found	Information not supplied by author
Date new studies found but not yet included/excluded	Information not supplied by author
Date new studies found and included/excluded	Information not supplied by author
Date authors' conclusions section amended	Information not supplied by author
Contact address	Floris Van de Laar M.D. GP / investigator Department of General Practice, 229 HAG Radboud University Nijmegen Medical Centre P.O. Box 9101 Nijmegen 6500 HB NETHERLANDS E-mail: f.vandelaar@hag.umcn.nl Tel: + 31 24 3614411 Fax: + 31 24 3541862
DOI	10.1002/14651858.CD003639.pub2
Cochrane Library number	CD003639
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GRAPHS AND OTHER TABLES

Fig. 1.

Fig. 2.

Fig. 3. Comparison 01. Acarbose versus placebo

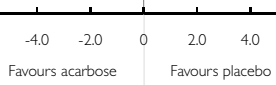
01.01 Change in glycated haemoglobin (%)

Review: Alpha-glucosidase inhibitors for type 2 diabetes mellitus

Comparison: 01 Acarbose versus placebo

Outcome: 01 Change in glycated haemoglobin (%)

Study	Acarbose N	Acarbose Mean(SD)	Placebo N	Placebo Mean(SD)	Weighted Mean Difference (Random) 95% CI	Weight (%)	Weighted Mean Difference (Random) 95% CI
01 Acarbose 25 mg TID							
Fischer 1998	92	0.00 (1.07)	86	0.48 (1.49)		4.7	-0.48 [-0.86, -0.10]
Subtotal (95% CI)	92		86			4.7	-0.48 [-0.86, -0.10]
Test for heterogeneity: not applicable							
Test for overall effect z=2.45 p=0.01							
02 Acarbose 50 mg BID							
Delgado 2002	9	-0.10 (1.40)	8	0.00 (2.90)		0.3	-0.10 [-2.31, 2.11]
Subtotal (95% CI)	9		8			0.3	-0.10 [-2.31, 2.11]
Test for heterogeneity: not applicable							
Test for overall effect z=0.09 p=0.9							
05 Acarbose 50 mg TID							
Fischer 1998	91	-0.40 (1.18)	86	0.48 (1.49)		4.6	-0.88 [-1.28, -0.48]
Santeusanio 1993	18	-0.59 (0.68)	22	0.33 (0.88)		3.8	-0.92 [-1.40, -0.44]
Subtotal (95% CI)	109		108			8.4	-0.90 [-1.20, -0.59]
Test for heterogeneity chi-square=0.02 df=1 p=0.90 I^2 =0.0%							
Test for overall effect z=5.72 p<0.00001							
10 Acarbose 100 mg TID							
Braun 1996	42	-2.50 (1.80)	44	-1.10 (2.10)		1.9	-1.40 [-2.23, -0.57]
Calle-Pascual 1996	17	-0.30 (0.90)	16	-0.03 (1.50)		1.8	-0.27 [-1.12, 0.58]
Chan 1998	59	-0.70 (1.20)	62	-0.27 (1.10)		4.4	-0.43 [-0.84, -0.02]
Coniff 1995b	57	-0.46 (0.98)	62	0.35 (1.02)		5.0	-0.81 [-1.17, -0.45]
Dedov 1995	82	-2.17 (1.80)	73	-1.61 (2.10)		2.8	-0.56 [-1.18, 0.06]
Fischer 1998	89	-0.26 (1.43)	86	0.48 (1.49)		4.2	-0.74 [-1.17, -0.31]
Haffner 1997	25	0.00 (1.60)	25	0.70 (1.40)		1.9	-0.70 [-1.53, 0.13]
Hanefeld 1991	47	-0.65 (1.30)	47	-0.08 (1.40)		3.3	-0.57 [-1.12, -0.02]
Hoffmann 1994	28	-0.98 (0.45)	30	0.16 (0.39)		6.6	-1.14 [-1.36, -0.92]
Hoffmann 1997	31	-1.10 (0.79)	32	0.30 (0.27)		5.7	-1.40 [-1.69, -1.11]
Holman 1999	83	0.16 (1.78)	107	0.35 (1.56)		3.8	-0.19 [-0.67, 0.29]
Hotta 1993	16	-1.38 (1.75)	13	-0.42 (1.30)		1.2	-0.96 [-2.07, 0.15]



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Study	Acarbose N	Acarbose Mean(SD)	Placebo N	Placebo Mean(SD)	Weighted Mean Difference (Random) 95% CI	Weight (%)	Weighted Mean Difference (Random) 95% CI
Kovacevic 1997	33	-0.70 (0.90)	31	0.20 (1.60)		2.7	-0.90 [-1.54, -0.26]
Meneilly 2000	80	-0.30 (1.00)	94	0.30 (1.00)		5.6	-0.60 [-0.90, -0.30]
Santeusanio 1993	22	-0.73 (0.96)	22	0.33 (0.88)		3.3	-1.06 [-1.60, -0.52]
Scott 1999	41	-0.14 (0.90)	42	0.25 (1.20)		4.0	-0.39 [-0.85, 0.07]
Zheng 1995	39	-0.94 (2.20)	38	-0.46 (2.40)		1.3	-0.48 [-1.51, 0.55]
Subtotal (95% CI)	791		824			59.5	-0.76 [-0.95, -0.56]
Test for heterogeneity chi-square=45.01 df=16 p=0.0001 I² =64.5%							
Test for overall effect z=7.55 p<0.00001							
19 Acarbose 200-100-200							
Buchanan 1988	9	1.10 (3.50)	11	1.60 (3.90)		0.2	-0.50 [-3.75, 2.75]
Subtotal (95% CI)	9		11			0.2	-0.50 [-3.75, 2.75]
Test for heterogeneity: not applicable							
Test for overall effect z=0.30 p=0.8							
20 Acarbose 200 mg TID							
Chiasson 1994	30	-0.40 (1.50)	37	0.50 (1.30)		2.5	-0.90 [-1.58, -0.22]
Coniff 1995	65	-0.54 (1.05)	62	0.04 (1.02)		5.0	-0.58 [-0.94, -0.22]
Coniff 1995b	54	-0.30 (1.03)	62	0.35 (1.02)		4.8	-0.65 [-1.02, -0.28]
Fischer 1998	90	-0.59 (1.24)	86	0.48 (1.49)		4.5	-1.07 [-1.48, -0.66]
Subtotal (95% CI)	239		247			16.7	-0.77 [-1.00, -0.53]
Test for heterogeneity chi-square=3.69 df=3 p=0.30 I² =18.8%							
Test for overall effect z=6.40 p<0.00001							
30 Acarbose 300 mg TID							
Coniff 1994	87	-0.06 (1.12)	96	0.53 (1.08)		5.4	-0.59 [-0.91, -0.27]
Coniff 1995b	53	-0.65 (1.02)	62	0.35 (1.02)		4.8	-1.00 [-1.37, -0.63]
Subtotal (95% CI)	140		158			10.2	-0.78 [-1.18, -0.38]
Test for heterogeneity chi-square=2.67 df=1 p=0.10 I² =62.5%							
Test for overall effect z=3.83 p=0.0001							
Total (95% CI)	1389		1442			100.0	-0.77 [-0.90, -0.64]
Test for heterogeneity chi-square=55.87 df=27 p=0.0009 I² =51.7%							
Test for overall effect z=11.61 p<0.00001							

Fig. 4. Comparison 01. Acarbose versus placebo

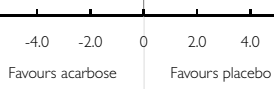
01.02 Change in fasting blood glucose (mmol/l)

Review: Alpha-glucosidase inhibitors for type 2 diabetes mellitus

Comparison: 01 Acarbose versus placebo

Outcome: 02 Change in fasting blood glucose (mmol/l)

Study	Acarbose N	Acarbose Mean(SD)	Placebo N	Placebo Mean(SD)	Weighted Mean Difference (Random) 95% CI	Weight (%)	Weighted Mean Difference (Random) 95% CI
01 Acarbose 25 mg TID							
Fischer 1998	90	-0.33 (1.82)	87	-0.04 (1.96)		5.0	-0.29 [-0.85, 0.27]
Subtotal (95% CI)	90		87			5.0	-0.29 [-0.85, 0.27]
Test for heterogeneity: not applicable							
Test for overall effect z=1.02 p=0.3							
02 Acarbose 50 mg BID							
Delgado 2002	9	-0.60 (1.50)	8	-0.90 (1.40)		2.3	0.30 [-1.08, 1.68]
Santeusanio 1993	18	-1.24 (1.29)	22	0.41 (2.04)		3.2	-1.65 [-2.69, -0.61]
Subtotal (95% CI)	27		30			5.6	-0.73 [-2.64, 1.18]
Test for heterogeneity chi-square=4.90 df=1 p=0.03 I^2 =79.6%							
Test for overall effect z=0.75 p=0.5							
05 Acarbose 50 mg TID							
Fischer 1998	92	-1.00 (1.82)	87	-0.04 (1.96)		5.0	-0.96 [-1.51, -0.41]
Subtotal (95% CI)	92		87			5.0	-0.96 [-1.51, -0.41]
Test for heterogeneity: not applicable							
Test for overall effect z=3.39 p=0.0007							
10 Acarbose 100 mg TID							
Braun 1996	42	-2.40 (2.40)	44	-1.10 (2.70)		3.1	-1.30 [-2.38, -0.22]
Calle-Pascual 1996	17	-0.70 (1.90)	16	0.10 (2.90)		1.8	-0.80 [-2.48, 0.88]
Chan 1998	59	-0.37 (1.50)	62	0.41 (2.00)		4.7	-0.78 [-1.41, -0.15]
Coniff 1995b	51	-0.33 (2.66)	57	1.04 (2.73)		3.3	-1.37 [-2.39, -0.35]
Dedov 1995	83	-1.90 (1.70)	73	-1.70 (1.50)		5.2	-0.20 [-0.70, 0.30]
Fischer 1998	86	-0.63 (1.87)	87	-0.04 (1.96)		5.0	-0.59 [-1.16, -0.02]
Haffner 1997	25	-0.90 (3.60)	25	0.60 (2.70)		1.7	-1.50 [-3.26, 0.26]
Hanefeld 1991	47	-1.40 (1.90)	47	-0.60 (2.20)		3.9	-0.80 [-1.63, 0.03]
Hoffmann 1994	28	-1.20 (0.89)	30	0.16 (0.67)		5.6	-1.36 [-1.77, -0.95]
Hoffmann 1997	31	-1.39 (0.81)	32	0.46 (0.53)		5.8	-1.85 [-2.19, -1.51]
Holman 1999	102	0.03 (3.08)	115	0.06 (3.65)		3.7	-0.03 [-0.93, 0.87]
Hotta 1993	16	-0.71 (1.85)	15	-0.04 (1.29)		3.0	-0.67 [-1.79, 0.45]



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Study	Acarbose N	Acarbose Mean(SD)	Placebo N	Placebo Mean(SD)	Weighted Mean Difference (Random) 95% CI	Weight (%)	Weighted Mean Difference (Random) 95% CI
Kovacevic 1997	33	-1.90 (3.00)	31	-0.70 (3.80)		1.8	-1.20 [-2.88, 0.48]
Meneilly 2000	80	-0.30 (1.90)	94	0.40 (2.00)		4.9	-0.70 [-1.28, -0.12]
Santeusanio 1993	22	-1.35 (2.54)	22	0.41 (2.04)		2.4	-1.76 [-3.12, -0.40]
Scott 1999	41	-0.46 (2.00)	42	0.90 (2.20)		3.7	-1.36 [-2.26, -0.46]
Zheng 1995	39	-3.17 (2.30)	38	-0.49 (2.70)		3.0	-2.68 [-3.80, -1.56]
Subtotal (95% CI)	802		830			62.6	-1.07 [-1.41, -0.72]
Test for heterogeneity chi-square=54.54 df=16 p=<0.0001 I^2 =70.7%							
Test for overall effect z=6.02 p<0.00001							
19 Acarbose 200-100-200							
Buchanan 1988	9	0.90 (3.80)	11	-0.70 (5.00)		0.4	1.60 [-2.26, 5.46]
Subtotal (95% CI)	9		11			0.4	1.60 [-2.26, 5.46]
Test for heterogeneity: not applicable							
Test for overall effect z=0.81 p=0.4							
20 Acarbose 200 mg TID							
Chiasson 1994	30	-0.70 (2.20)	37	1.40 (2.40)		3.0	-2.10 [-3.20, -1.00]
Coniff 1995	67	-1.11 (3.17)	62	0.12 (3.24)		3.0	-1.23 [-2.34, -0.12]
Coniff 1995b	49	-0.92 (2.73)	57	1.04 (2.73)		3.2	-1.96 [-3.00, -0.92]
Fischer 1998	89	-1.27 (2.10)	87	-0.04 (1.96)		4.8	-1.23 [-1.83, -0.63]
Subtotal (95% CI)	235		243			14.1	-1.49 [-1.92, -1.06]
Test for heterogeneity chi-square=2.89 df=3 p=0.41 I^2 =0.0%							
Test for overall effect z=6.74 p<0.00001							
30 Acarbose 300 mg TID							
Coniff 1994	91	-0.28 (2.92)	97	0.58 (2.92)		3.9	-0.86 [-1.70, -0.02]
Coniff 1995b	50	-0.98 (2.66)	57	1.04 (2.73)		3.3	-2.02 [-3.04, -1.00]
Subtotal (95% CI)	141		154			7.2	-1.40 [-2.54, -0.27]
Test for heterogeneity chi-square=2.96 df=1 p=0.09 I^2 =66.3%							
Test for overall effect z=2.42 p=0.02							
Total (95% CI)	1396		1442			100.0	-1.09 [-1.36, -0.83]
Test for heterogeneity chi-square=79.39 df=27 p=<0.0001 I^2 =66.0%							
Test for overall effect z=8.08 p<0.00001							

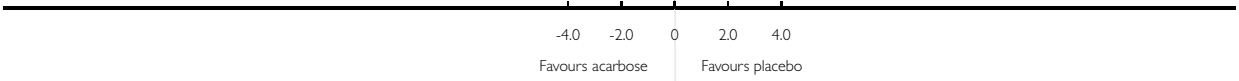


Fig. 5. Comparison 01. Acarbose versus placebo

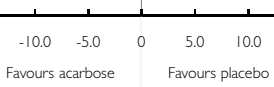
01.03 Change in post-load blood glucose (mmol/l)

Review: Alpha-glucosidase inhibitors for type 2 diabetes mellitus

Comparison: 01 Acarbose versus placebo

Outcome: 03 Change in post-load blood glucose (mmol/l)

Study	Acarbose N	Acarbose Mean(SD)	Placebo N	Placebo Mean(SD)	Weighted Mean Difference (Random) 95% CI	Weight (%)	Weighted Mean Difference (Random) 95% CI
01 Acarbose 25 mg TID							
Fischer 1998	89	-1.34 (2.55)	87	0.02 (2.74)		5.9	-1.36 [-2.14, -0.58]
Subtotal (95% CI)	89		87			5.9	-1.36 [-2.14, -0.58]
Test for heterogeneity: not applicable							
Test for overall effect z=3.41 p=0.0007							
02 Acarbose 50 mg BID							
Delgado 2002	9	-1.50 (1.60)	8	0.30 (1.40)		3.9	-1.80 [-3.23, -0.37]
Subtotal (95% CI)	9		8			3.9	-1.80 [-3.23, -0.37]
Test for heterogeneity: not applicable							
Test for overall effect z=2.47 p=0.01							
05 Acarbose 50 mg TID							
Fischer 1998	92	-1.71 (2.86)	87	0.02 (2.74)		5.8	-1.73 [-2.55, -0.91]
Santeusanio 1993	18	-0.80 (3.50)	22	0.20 (3.20)		2.5	-1.00 [-3.10, 1.10]
Subtotal (95% CI)	110		109			8.3	-1.63 [-2.40, -0.87]
Test for heterogeneity chi-square=0.40 df=1 p=0.53 I^2 =0.0%							
Test for overall effect z=4.19 p=0.00003							
10 Acarbose 100 mg TID							
Braun 1996	42	-3.20 (2.50)	44	-1.40 (2.50)		5.0	-1.80 [-2.86, -0.74]
Chan 1998	59	-0.77 (2.60)	62	0.65 (2.90)		5.2	-1.42 [-2.40, -0.44]
Coniff 1995b	51	-2.31 (3.31)	56	1.36 (3.39)		4.3	-3.67 [-4.94, -2.40]
Dedov 1995	82	-3.20 (2.20)	73	-2.50 (2.00)		6.3	-0.70 [-1.36, -0.04]
Fischer 1998	87	-1.48 (2.69)	87	0.02 (2.74)		5.8	-1.50 [-2.31, -0.69]
Haffner 1997	25	-2.40 (6.40)	25	-0.10 (7.40)		1.0	-2.30 [-6.14, 1.54]
Hanefeld 1991	47	-3.70 (2.30)	47	-0.80 (2.60)		5.2	-2.90 [-3.89, -1.91]
Hoffmann 1994	28	-1.80 (0.74)	30	0.03 (1.01)		6.9	-1.83 [-2.28, -1.38]
Hoffmann 1997	31	-2.36 (0.74)	32	0.01 (0.36)		7.3	-2.37 [-2.66, -2.08]
Hotta 1993	16	-2.69 (3.22)	15	-0.21 (2.93)		2.4	-2.48 [-4.65, -0.31]
Kovacevic 1997	33	-4.70 (3.70)	31	-1.70 (4.20)		2.7	-3.00 [-4.94, -1.06]
Santeusanio 1993	22	-2.00 (3.00)	22	0.20 (3.20)		3.0	-2.20 [-4.03, -0.37]



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Study	Acarbose N	Acarbose Mean(SD)	Placebo N	Placebo Mean(SD)	Weighted Mean Difference (Random) 95% CI	Weight (%)	Weighted Mean Difference (Random) 95% CI
Zheng 1995	39	-5.82 (3.60)	38	-0.40 (3.50)		3.5	-5.42 [-7.01, -3.83]
Subtotal (95% CI)	562		562			58.6	-2.26 [-2.79, -1.73]
Test for heterogeneity chi-square=52.37 df=12 p=<0.0001 I^2 =77.1%							
Test for overall effect z=8.35 p<0.00001							
20 Acarbose 200 mg TID							
Coniff 1995	67	-2.82 (3.71)	62	-0.61 (3.93)		4.2	-2.21 [-3.53, -0.89]
Coniff 1995b	51	-2.50 (3.39)	56	1.36 (3.39)		4.3	-3.86 [-5.15, -2.57]
Fischer 1998	88	-2.40 (2.96)	87	0.02 (2.74)		5.7	-2.42 [-3.26, -1.58]
Subtotal (95% CI)	206		205			14.2	-2.78 [-3.72, -1.85]
Test for heterogeneity chi-square=4.07 df=2 p=0.13 I^2 =50.9%							
Test for overall effect z=5.83 p<0.00001							
30 Acarbose 300 mg TID							
Coniff 1994	90	-1.70 (3.70)	95	1.07 (3.91)		4.9	-2.77 [-3.87, -1.67]
Coniff 1995b	50	-3.17 (3.31)	56	1.36 (3.39)		4.3	-4.53 [-5.81, -3.25]
Subtotal (95% CI)	140		151			9.2	-3.62 [-5.34, -1.89]
Test for heterogeneity chi-square=4.20 df=1 p=0.04 I^2 =76.2%							
Test for overall effect z=4.11 p=0.00004							
Total (95% CI)	1116		1122			100.0	-2.32 [-2.73, -1.92]
Test for heterogeneity chi-square=80.59 df=21 p=<0.0001 I^2 =73.9%							
Test for overall effect z=11.28 p<0.00001							

Fig. 6. Comparison 01. Acarbose versus placebo

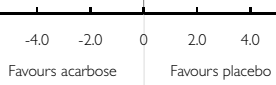
01.04 Change in total cholesterol (mmol/l)

Review: Alpha-glucosidase inhibitors for type 2 diabetes mellitus

Comparison: 01 Acarbose versus placebo

Outcome: 04 Change in total cholesterol (mmol/l)

Study	Acarbose N	Acarbose Mean(SD)	Placebo N	Placebo Mean(SD)	Weighted Mean Difference (Random) 95% CI	Weight (%)	Weighted Mean Difference (Random) 95% CI
01 Acarbose 25 mg TID							
Fischer 1998	92	0.03 (0.98)	87	-0.09 (0.96)		7.1	0.12 [-0.16, 0.40]
Subtotal (95% CI)	92		87			7.1	0.12 [-0.16, 0.40]
Test for heterogeneity: not applicable							
Test for overall effect z=0.83 p=0.4							
02 Acarbose 50 mg BID							
Delgado 2002	9	0.20 (1.20)	8	0.50 (1.10)		0.7	-0.30 [-1.39, 0.79]
Subtotal (95% CI)	9		8			0.7	-0.30 [-1.39, 0.79]
Test for heterogeneity: not applicable							
Test for overall effect z=0.54 p=0.6							
05 Acarbose 50 mg TID							
Fischer 1998	91	-0.06 (0.94)	87	-0.09 (0.96)		7.3	0.03 [-0.25, 0.31]
Santeusanio 1993	18	-0.03 (0.81)	22	0.06 (0.91)		2.7	-0.09 [-0.62, 0.44]
Subtotal (95% CI)	109		109			10.0	0.00 [-0.24, 0.25]
Test for heterogeneity chi-square=0.15 df=1 p=0.70 I^2 =0.0%							
Test for overall effect z=0.03 p=1							
10 Acarbose 100 mg TID							
Braun 1996	41	-0.90 (1.10)	42	-0.30 (1.00)		3.6	-0.60 [-1.05, -0.15]
Calle-Pascual 1996	17	-0.05 (1.10)	16	0.13 (1.00)		1.6	-0.18 [-0.90, 0.54]
Chan 1998	59	0.13 (0.50)	62	-0.04 (5.40)		0.5	0.17 [-1.18, 1.52]
Coniff 1995b	56	0.15 (0.70)	62	-0.06 (0.70)		8.2	0.21 [-0.04, 0.46]
Fischer 1998	89	0.32 (1.00)	87	-0.09 (0.96)		6.9	0.41 [0.12, 0.70]
Haffner 1997	17	0.05 (0.93)	16	-0.04 (0.86)		2.1	0.09 [-0.52, 0.70]
Hanefeld 1991	47	0.10 (0.90)	47	0.10 (0.90)		5.0	0.00 [-0.36, 0.36]
Hoffmann 1994	28	-0.59 (1.34)	30	0.01 (1.67)		1.4	-0.60 [-1.38, 0.18]
Hoffmann 1997	31	-0.85 (1.67)	32	-0.05 (1.37)		1.5	-0.80 [-1.56, -0.04]
Hotta 1993	16	0.04 (0.68)	13	0.12 (0.57)		3.6	-0.08 [-0.54, 0.38]
Kovacevic 1997	33	-0.30 (1.10)	31	0.00 (1.80)		1.5	-0.30 [-1.04, 0.44]
Santeusanio 1993	22	0.05 (1.01)	22	0.06 (0.91)		2.4	-0.01 [-0.58, 0.56]



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Study	Acarbose N	Acarbose Mean(SD)	Placebo N	Placebo Mean(SD)	Weighted Mean Difference (Random) 95% CI	Weight (%)	Weighted Mean Difference (Random) 95% CI
Scott 1999	41	-0.04 (1.40)	42	0.28 (1.30)		2.3	-0.32 [-0.90, 0.26]
Subtotal (95% CI)	497		502			40.7	-0.10 [-0.30, 0.11]
Test for heterogeneity chi-square=25.95 df=12 p=0.01 I^2 =53.8%							
Test for overall effect z=0.90 p=0.4							
19 Acarbose 200-100-200							
Buchanan 1988	9	-0.10 (1.20)	11	0.20 (1.80)		0.5	-0.30 [-1.62, 1.02]
Subtotal (95% CI)	9		11			0.5	-0.30 [-1.62, 1.02]
Test for heterogeneity: not applicable							
Test for overall effect z=0.44 p=0.7							
20 Acarbose 200 mg TID							
Coniff 1995	64	-0.21 (0.79)	58	-0.13 (0.80)		7.2	-0.08 [-0.36, 0.20]
Coniff 1995b	51	-0.09 (0.71)	62	-0.06 (0.70)		7.9	-0.03 [-0.29, 0.23]
Fischer 1998	88	-0.04 (1.00)	87	-0.09 (0.96)		6.9	0.05 [-0.24, 0.34]
Subtotal (95% CI)	203		207			21.9	-0.02 [-0.18, 0.14]
Test for heterogeneity chi-square=0.40 df=2 p=0.82 I^2 =0.0%							
Test for overall effect z=0.27 p=0.8							
30 Acarbose 300 mg TID							
Coniff 1994	80	0.09 (0.63)	95	0.14 (0.64)		11.0	-0.05 [-0.24, 0.14]
Coniff 1995b	53	0.09 (0.70)	62	-0.06 (0.70)		8.1	0.15 [-0.11, 0.41]
Subtotal (95% CI)	133		157			19.1	0.03 [-0.16, 0.22]
Test for heterogeneity chi-square=1.51 df=1 p=0.22 I^2 =33.9%							
Test for overall effect z=0.31 p=0.8							
Total (95% CI)	1052		1081			100.0	0.00 [-0.10, 0.09]
Test for heterogeneity chi-square=29.29 df=22 p=0.14 I^2 =24.9%							
Test for overall effect z=0.10 p=0.9							

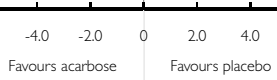


Fig. 7. Comparison 01. Acarbose versus placebo

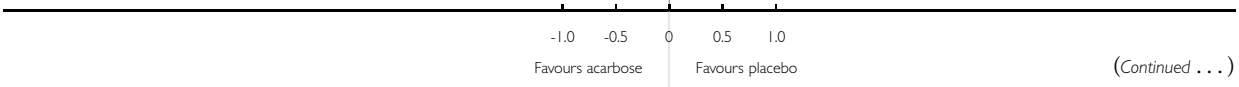
01.05 Change in HDL-cholesterol (mmol/l)

Review: Alpha-glucosidase inhibitors for type 2 diabetes mellitus

Comparison: 01 Acarbose versus placebo

Outcome: 05 Change in HDL-cholesterol (mmol/l)

Study	Acarbose N	Acarbose Mean(SD)	Placebo N	Placebo Mean(SD)	Weighted Mean Difference (Random) 95% CI	Weight (%)	Weighted Mean Difference (Random) 95% CI
02 Acarbose 50 mg BID							
Delgado 2002	9	0.00 (0.30)	8	0.10 (0.30)		1.8	-0.10 [-0.39, 0.19]
Subtotal (95% CI)	9		8			1.8	-0.10 [-0.39, 0.19]
Test for heterogeneity: not applicable							
Test for overall effect z=0.69 p=0.5							
05 Acarbose 50 mg TID							
Santeusanio 1993	17	-0.05 (0.31)	21	0.04 (0.29)		3.9	-0.09 [-0.28, 0.10]
Subtotal (95% CI)	17		21			3.9	-0.09 [-0.28, 0.10]
Test for heterogeneity: not applicable							
Test for overall effect z=0.92 p=0.4							
10 Acarbose 100 mg TID							
Braun 1996	41	0.10 (0.30)	42	0.10 (0.50)		4.6	0.00 [-0.18, 0.18]
Calle-Pascual 1996	17	0.11 (0.30)	16	-0.03 (0.90)		0.7	0.14 [-0.32, 0.60]
Chan 1998	59	-0.02 (0.30)	62	-0.03 (0.30)		11.8	0.01 [-0.10, 0.12]
Haffner 1997	17	0.01 (0.30)	16	0.00 (0.26)		4.0	0.01 [-0.18, 0.20]
Hoffmann 1994	28	0.09 (0.44)	30	0.15 (0.64)		1.9	-0.06 [-0.34, 0.22]
Hoffmann 1997	31	0.23 (0.63)	31	-0.15 (0.40)		2.2	0.38 [0.12, 0.64]
Hotta 1993	16	0.06 (0.18)	12	0.15 (0.17)		8.2	-0.09 [-0.22, 0.04]
Kovacevic 1997	33	0.10 (0.30)	31	0.00 (0.40)		4.8	0.10 [-0.07, 0.27]
Santeusanio 1993	22	0.02 (0.30)	21	0.04 (0.29)		4.7	-0.02 [-0.20, 0.16]
Scott 1999	41	0.00 (0.30)	42	0.06 (0.30)		8.4	-0.06 [-0.19, 0.07]
Subtotal (95% CI)	305		303			51.2	0.01 [-0.06, 0.07]
Test for heterogeneity chi-square=12.58 df=9 p=0.18 I^2 =28.5%							
Test for overall effect z=0.25 p=0.8							
20 Acarbose 200 mg TID							
Coniff 1995	58	0.07 (0.23)	51	0.06 (0.24)		16.4	0.01 [-0.08, 0.10]
Subtotal (95% CI)	58		51			16.4	0.01 [-0.08, 0.10]
Test for heterogeneity: not applicable							
Test for overall effect z=0.22 p=0.8							



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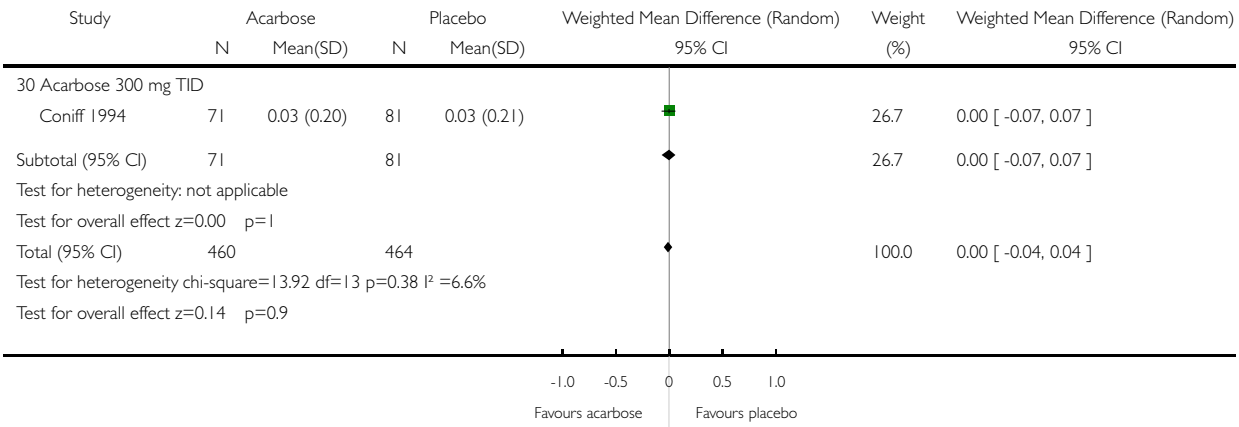


Fig. 8. Comparison 01. Acarbose versus placebo

01.06 Change in LDL-cholesterol (mmol/l)

Review: Alpha-glucosidase inhibitors for type 2 diabetes mellitus

Comparison: 01 Acarbose versus placebo

Outcome: 06 Change in LDL-cholesterol (mmol/l)

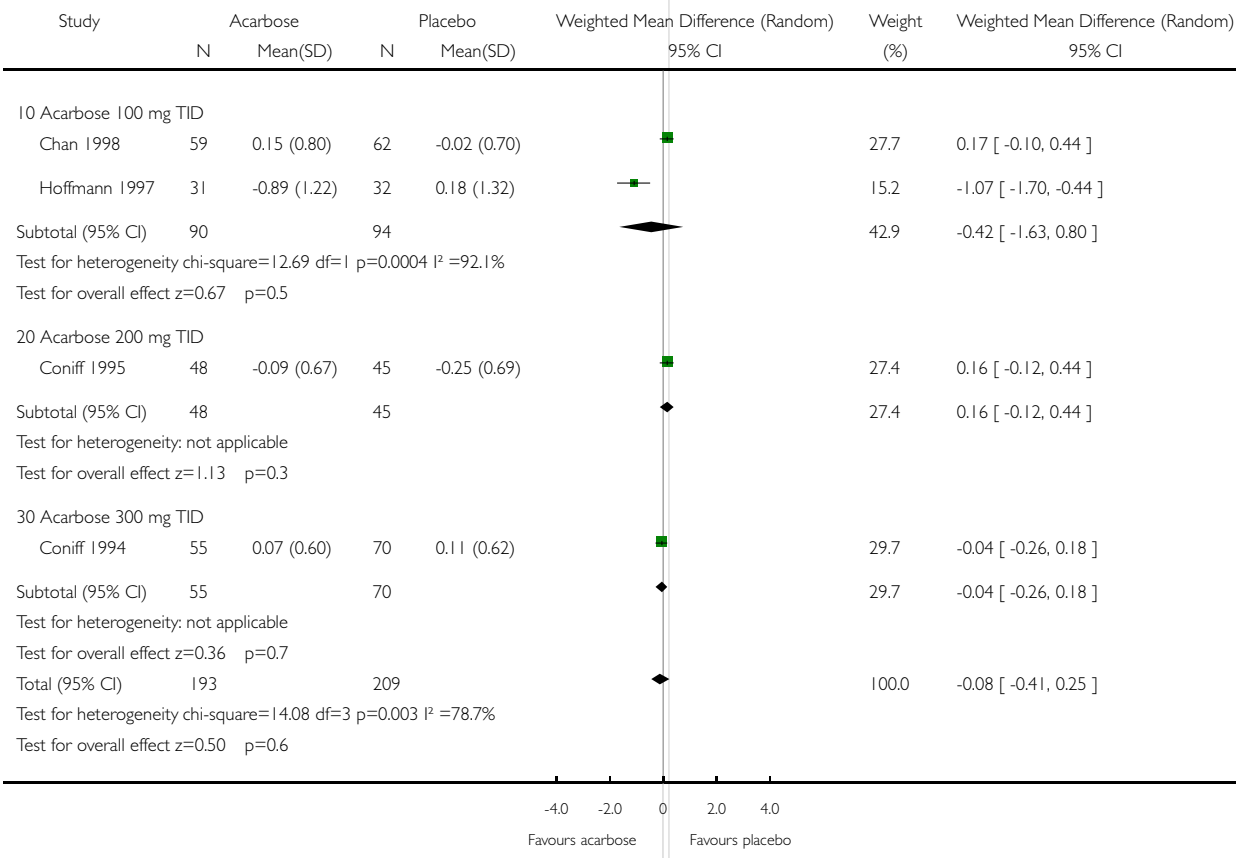


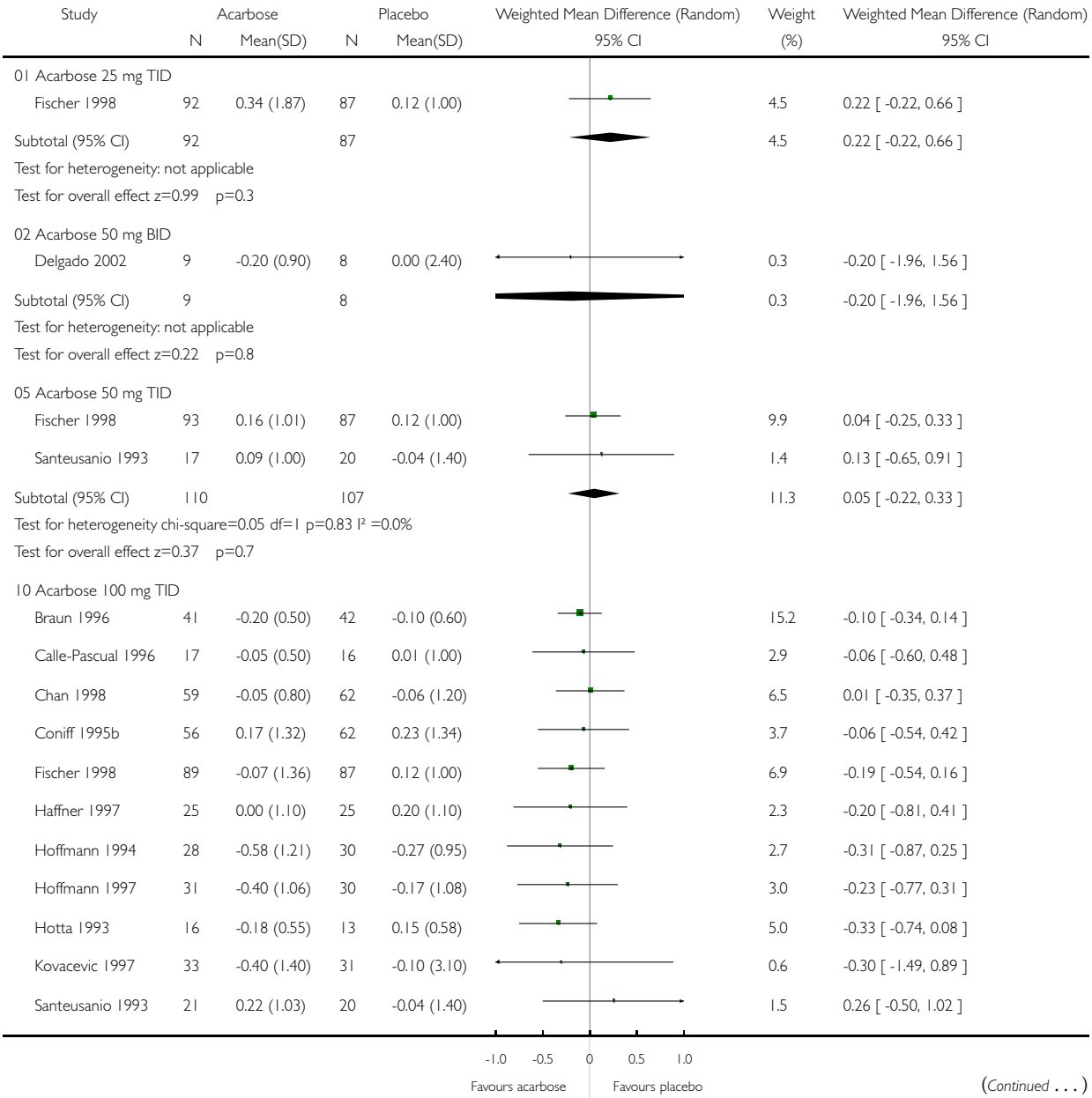
Fig. 9. Comparison 01. Acarbose versus placebo

01.07 Change in triglycerides (mmol/l)

Review: Alpha-glucosidase inhibitors for type 2 diabetes mellitus

Comparison: 01 Acarbose versus placebo

Outcome: 07 Change in triglycerides (mmol/l)



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Study	Acarbose N	Acarbose Mean(SD)	Placebo N	Placebo Mean(SD)	Weighted Mean Difference (Random) 95% CI	Weight (%)	Weighted Mean Difference (Random) 95% CI
Subtotal (95% CI)	416		418			50.2	-0.13 [-0.26, 0.00]
Test for heterogeneity chi-square=3.47 df=10 p=0.97 I² =0.0%							
Test for overall effect z=1.96 p=0.05							
19 Acarbose 200-100-200							
Buchanan 1988	9	0.20 (0.60)	11	-0.20 (2.00)		0.6	0.40 [-0.85, 1.65]
Subtotal (95% CI)	9		11			0.6	0.40 [-0.85, 1.65]
Test for heterogeneity: not applicable							
Test for overall effect z=0.63 p=0.5							
20 Acarbose 200 mg TID							
Coniff 1995	64	-0.49 (1.87)	58	-0.31 (1.90)		1.9	-0.18 [-0.85, 0.49]
Coniff 1995b	51	0.02 (1.34)	62	0.23 (1.34)		3.5	-0.21 [-0.71, 0.29]
Fischer 1998	90	-0.24 (1.80)	87	0.12 (1.00)		4.7	-0.36 [-0.79, 0.07]
Subtotal (95% CI)	205		207			10.1	-0.27 [-0.57, 0.02]
Test for heterogeneity chi-square=0.30 df=2 p=0.86 I² =0.0%							
Test for overall effect z=1.84 p=0.07							
30 Acarbose 300 mg TID							
Coniff 1994	80	0.12 (0.70)	95	0.18 (0.71)		19.5	-0.06 [-0.27, 0.15]
Coniff 1995b	53	0.20 (1.33)	62	0.23 (1.34)		3.6	-0.03 [-0.52, 0.46]
Subtotal (95% CI)	133		157			23.0	-0.06 [-0.25, 0.14]
Test for heterogeneity chi-square=0.01 df=1 p=0.91 I² =0.0%							
Test for overall effect z=0.56 p=0.6							
Total (95% CI)	974		995			100.0	-0.09 [-0.18, 0.00]
Test for heterogeneity chi-square=9.42 df=20 p=0.98 I² =0.0%							
Test for overall effect z=1.88 p=0.06							

Fig. 10. Comparison 01. Acarbose versus placebo

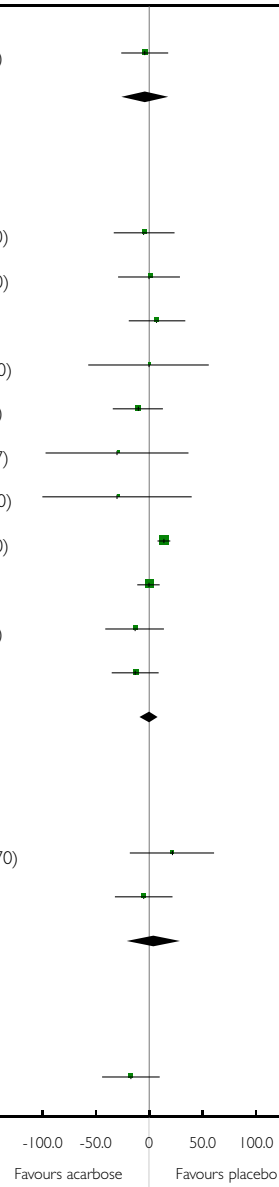
01.08 Change in fasting insulin levels (pmol/l)

Review: Alpha-glucosidase inhibitors for type 2 diabetes mellitus

Comparison: 01 Acarbose versus placebo

Outcome: 08 Change in fasting insulin levels (pmol/l)

Study	Acarbose N	Acarbose Mean(SD)	Placebo N	Placebo Mean(SD)	Weighted Mean Difference (Random) 95% CI	Weight (%)	Weighted Mean Difference (Random) 95% CI
05 Acarbose 50 mg TID							
Santeusanio 1993	10	13.40 (19.40)	14	16.90 (35.10)		7.7	-3.50 [-25.47, 18.47]
Subtotal (95% CI)	10		14			7.7	-3.50 [-25.47, 18.47]
Test for heterogeneity: not applicable							
Test for overall effect z=0.31 p=0.8							
10 Acarbose 100 mg TID							
Calle-Pascual 1996	17	-14.20 (39.00)	16	-10.10 (45.00)		5.2	-4.10 [-32.91, 24.71]
Chan 1998	59	-10.70 (103.00)	62	-11.60 (50.00)		5.1	0.90 [-28.18, 29.98]
Coniff 1995b	57	14.64 (72.60)	63	6.74 (73.50)		6.0	7.90 [-18.27, 34.07]
Haffner 1997	25	10.00 (92.00)	25	10.00 (110.00)		1.6	0.00 [-56.21, 56.21]
Hanefeld 1991	47	0.00 (50.00)	47	10.00 (66.00)		7.0	-10.00 [-33.67, 13.67]
Hoffmann 1994	28	-33.56 (139.81)	30	-4.31 (118.67)		1.2	-29.25 [-96.22, 37.72]
Hoffmann 1997	31	-7.60 (123.80)	32	21.70 (157.90)		1.1	-29.30 [-99.24, 40.64]
Kovacevic 1997	33	-14.40 (11.90)	31	-28.90 (14.00)		20.8	14.50 [8.11, 20.89]
Meneilly 2000	80	-9.00 (39.00)	94	-9.00 (30.00)		16.5	0.00 [-10.48, 10.48]
Santeusanio 1993	14	4.10 (38.70)	14	16.90 (35.10)		5.6	-12.80 [-40.17, 14.57]
Zheng 1995	39	-7.50 (50.80)	38	4.90 (47.60)		7.7	-12.40 [-34.38, 9.58]
Subtotal (95% CI)	430		452			77.7	0.07 [-8.60, 8.73]
Test for heterogeneity chi-square=16.94 df=10 p=0.08 I^2 =41.0%							
Test for overall effect z=0.02 p=1							
20 Acarbose 200 mg TID							
Coniff 1995	65	-3.20 (112.80)	62	-25.30 (114.70)		3.0	22.10 [-17.49, 61.69]
Coniff 1995b	52	1.87 (74.00)	63	6.74 (73.50)		5.7	-4.87 [-31.96, 22.22]
Subtotal (95% CI)	117		125			8.7	4.59 [-20.63, 29.82]
Test for heterogeneity chi-square=1.21 df=1 p=0.27 I^2 =17.6%							
Test for overall effect z=0.36 p=0.7							
30 Acarbose 300 mg TID							
Coniff 1995b	53	-9.61 (73.70)	63	6.74 (73.50)		5.8	-16.35 [-43.24, 10.54]



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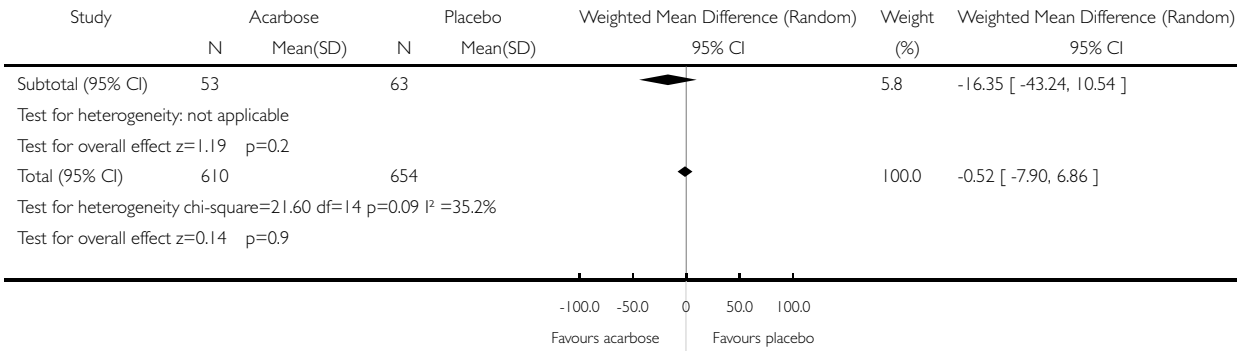


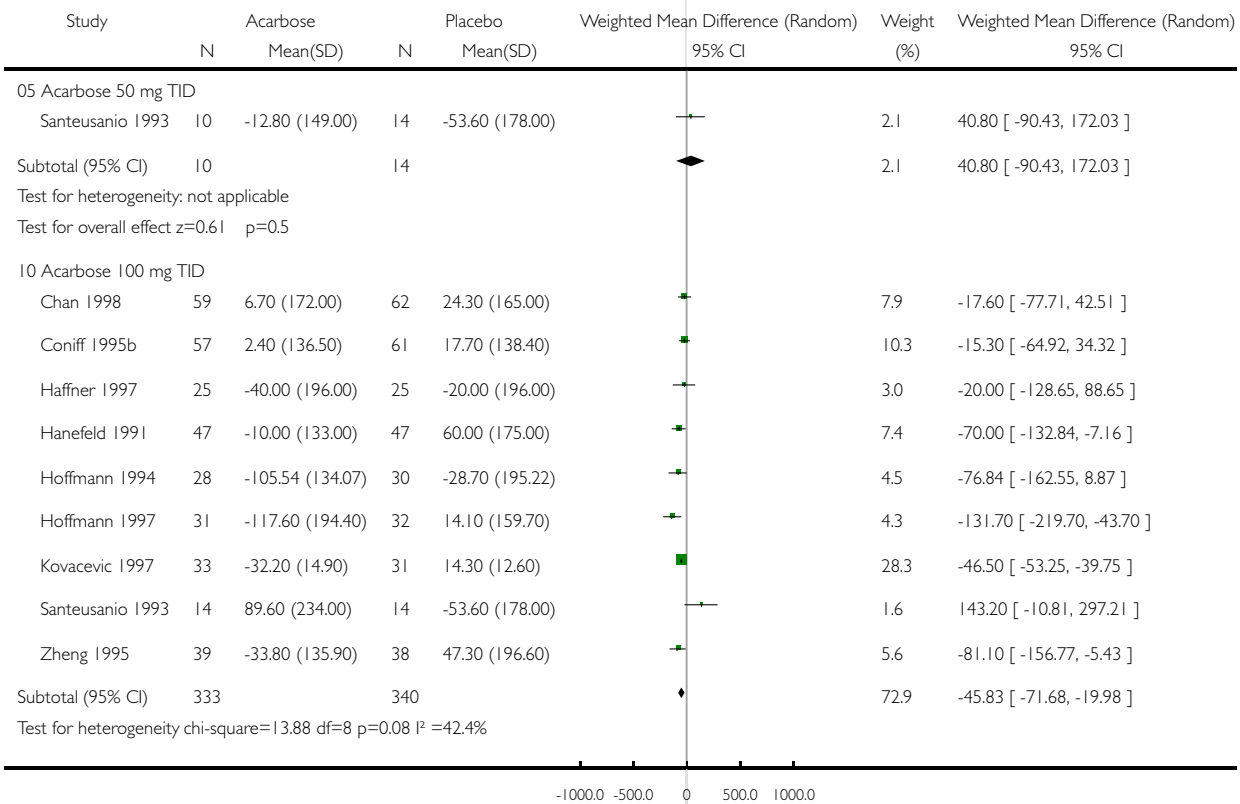
Fig. 11. Comparison 01. Acarbose versus placebo

01.09 Change in post-load insulin levels (pmol/l)

Review: Alpha-glucosidase inhibitors for type 2 diabetes mellitus

Comparison: 01 Acarbose versus placebo

Outcome: 09 Change in post-load insulin levels (pmol/l)



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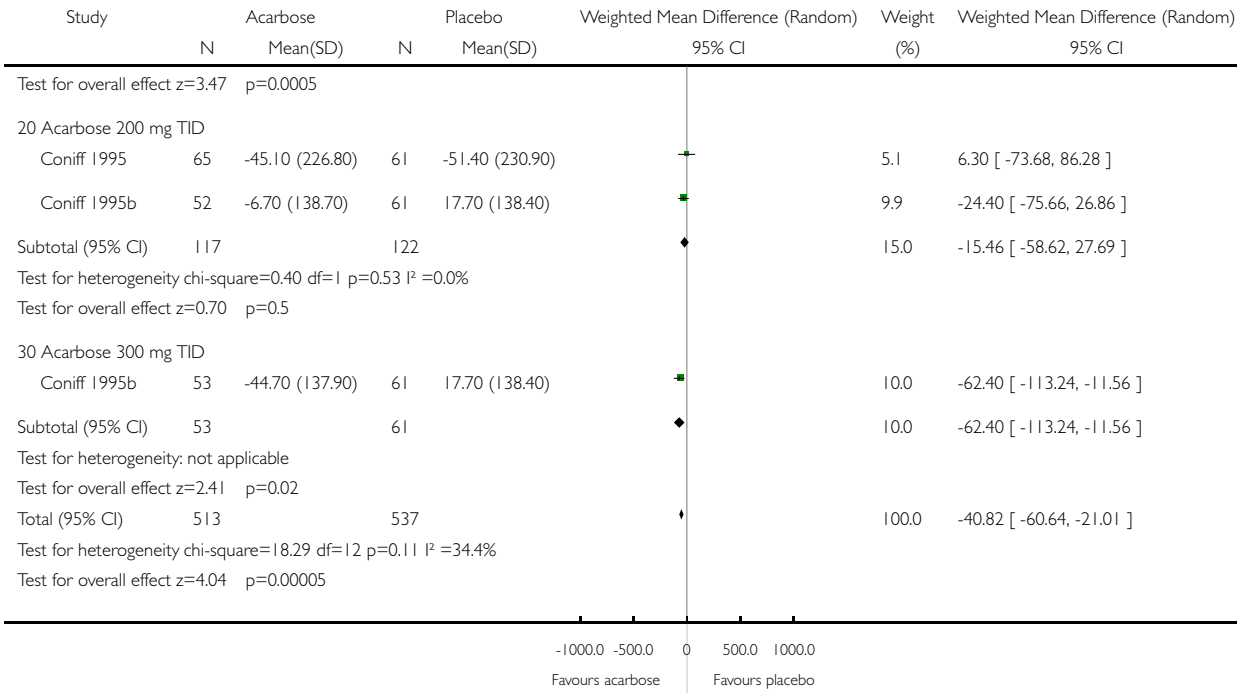


Fig. 12. Comparison 01. Acarbose versus placebo

01.10 Change in fasting C-peptide levels (nmol/l)

Review: Alpha-glucosidase inhibitors for type 2 diabetes mellitus

Comparison: 01 Acarbose versus placebo

Outcome: 10 Change in fasting C-peptide levels (nmol/l)

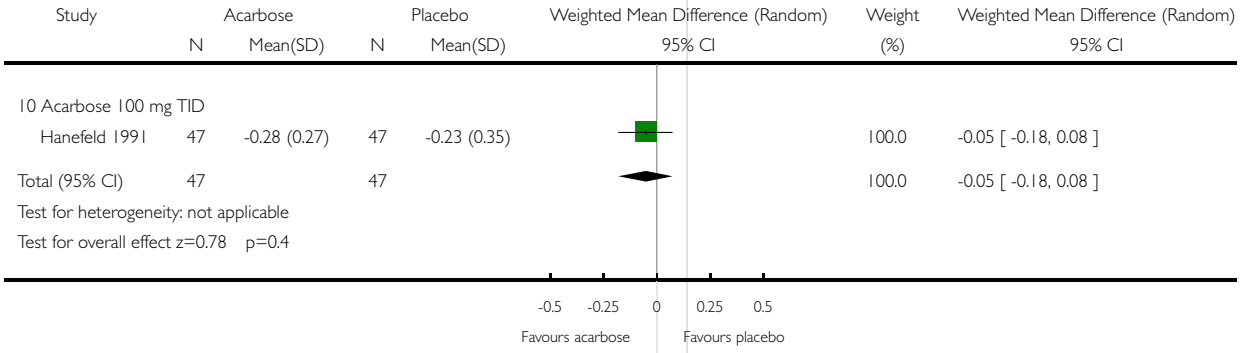


Fig. 13. Comparison 01. Acarbose versus placebo

01.11 Change in post-load C-peptide levels (nmol/l)

Review: Alpha-glucosidase inhibitors for type 2 diabetes mellitus

Comparison: 01 Acarbose versus placebo

Outcome: 11 Change in post-load C-peptide levels (nmol/l)

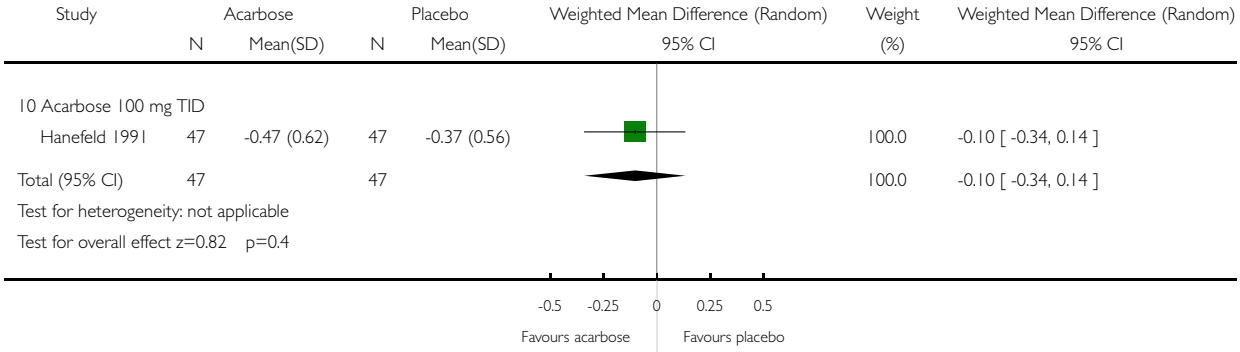


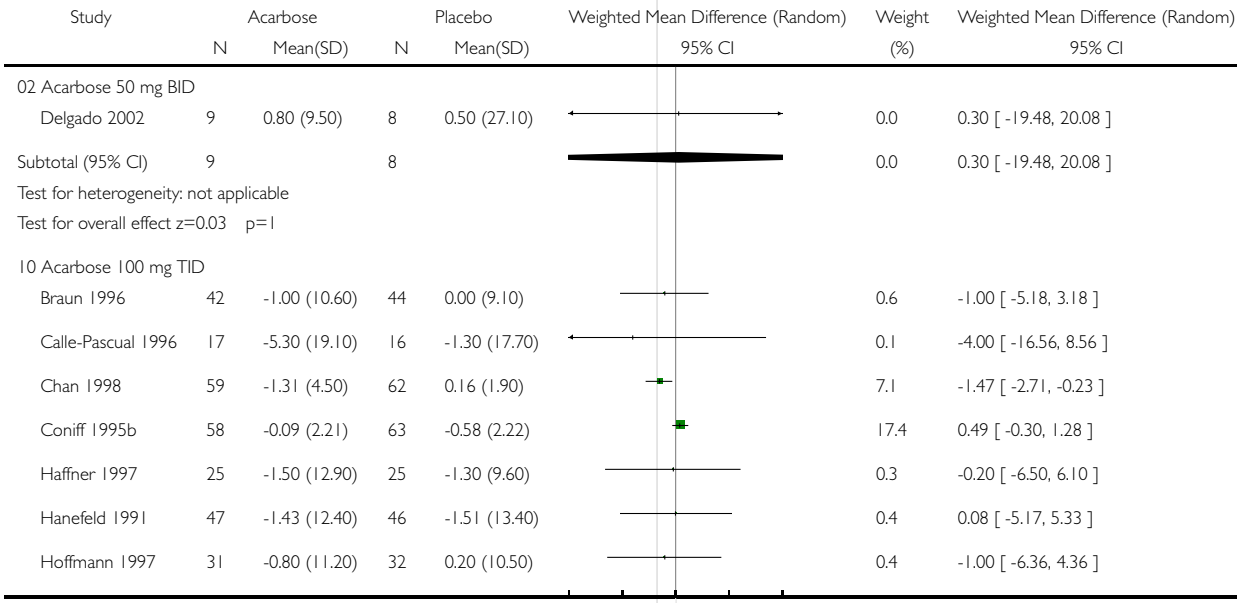
Fig. 14. Comparison 01. Acarbose versus placebo

01.12 Change in body weight (Kg)

Review: Alpha-glucosidase inhibitors for type 2 diabetes mellitus

Comparison: 01 Acarbose versus placebo

Outcome: 12 Change in body weight (Kg)



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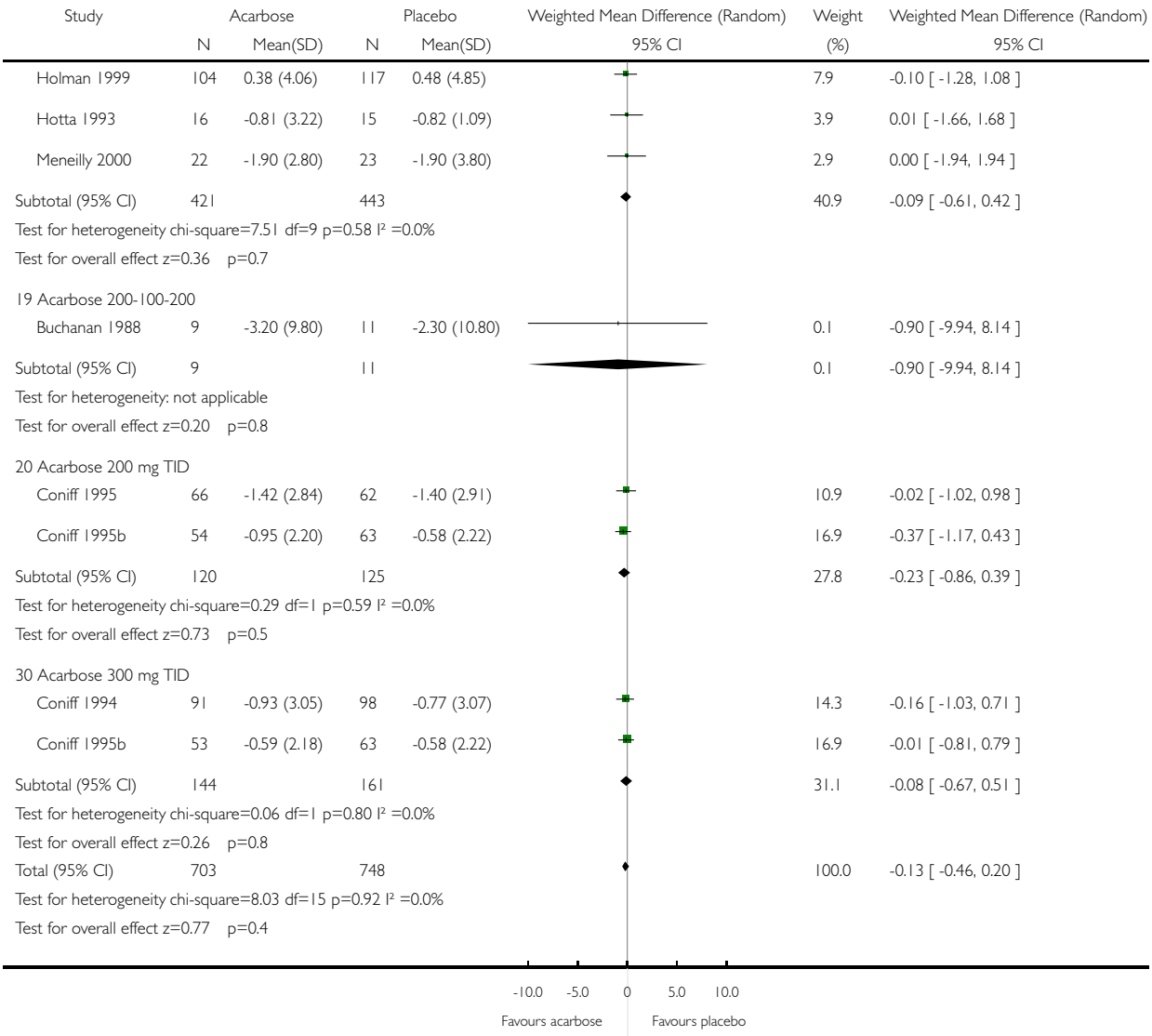


Fig. 15. Comparison 01. Acarbose versus placebo

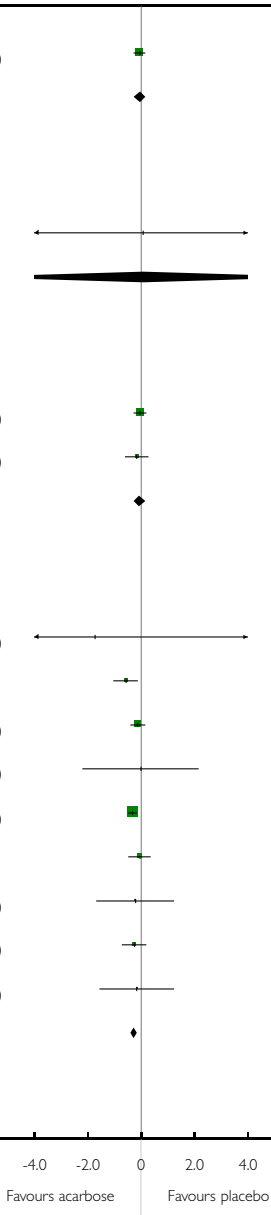
01.13 Change in body mass index (Kg/m2)

Review: Alpha-glucosidase inhibitors for type 2 diabetes mellitus

Comparison: 01 Acarbose versus placebo

Outcome: 13 Change in body mass index (Kg/m2)

Study	Acarbose N	Acarbose Mean(SD)	Placebo N	Placebo Mean(SD)	Weighted Mean Difference (Random) 95% CI	Weight (%)	Weighted Mean Difference (Random) 95% CI
01 Acarbose 25 mg TID							
Fischer 1998	90	-0.15 (0.60)	87	-0.12 (0.87)		15.7	-0.03 [-0.25, 0.19]
Subtotal (95% CI)	90		87			15.7	-0.03 [-0.25, 0.19]
Test for heterogeneity: not applicable							
Test for overall effect z=0.27 p=0.8							
02 Acarbose 50 mg BID							
Delgado 2002	9	0.20 (5.10)	8	0.10 (8.40)		0.0	0.10 [-6.61, 6.81]
Subtotal (95% CI)	9		8			0.0	0.10 [-6.61, 6.81]
Test for heterogeneity: not applicable							
Test for overall effect z=0.03 p=1							
05 Acarbose 50 mg TID							
Fischer 1998	92	-0.15 (0.75)	87	-0.13 (0.87)		13.5	-0.02 [-0.26, 0.22]
Santeusanio 1993	18	-0.25 (0.57)	22	-0.11 (0.89)		3.7	-0.14 [-0.60, 0.32]
Subtotal (95% CI)	110		109			17.2	-0.05 [-0.26, 0.17]
Test for heterogeneity chi-square=0.21 df=1 p=0.65 I^2 =0.0%							
Test for overall effect z=0.42 p=0.7							
10 Acarbose 100 mg TID							
Calle-Pascual 1996	17	-2.20 (9.30)	16	-0.50 (8.30)		0.0	-1.70 [-7.71, 4.31]
Chan 1998	59	-0.52 (1.60)	62	0.04 (0.70)		3.9	-0.56 [-1.00, -0.12]
Fischer 1998	87	-0.22 (0.98)	87	-0.12 (0.87)		10.1	-0.10 [-0.38, 0.18]
Haffner 1997	25	-0.50 (4.10)	25	-0.50 (3.80)		0.2	0.00 [-2.19, 2.19]
Hoffmann 1994	28	-0.42 (0.27)	30	-0.12 (0.35)		29.8	-0.30 [-0.46, -0.14]
Holman 1999	104	0.12 (1.45)	117	0.16 (1.67)		4.5	-0.04 [-0.45, 0.37]
Kovacevic 1997	33	-0.80 (3.00)	31	-0.60 (3.00)		0.4	-0.20 [-1.67, 1.27]
Santeusanio 1993	22	-0.35 (0.67)	22	-0.11 (0.89)		3.5	-0.24 [-0.71, 0.23]
Zheng 1995	39	-0.31 (2.70)	38	-0.18 (3.50)		0.4	-0.13 [-1.53, 1.27]
Subtotal (95% CI)	414		428			52.8	-0.25 [-0.37, -0.13]
Test for heterogeneity chi-square=4.70 df=8 p=0.79 I^2 =0.0%							
Test for overall effect z=4.11 p=0.00004							



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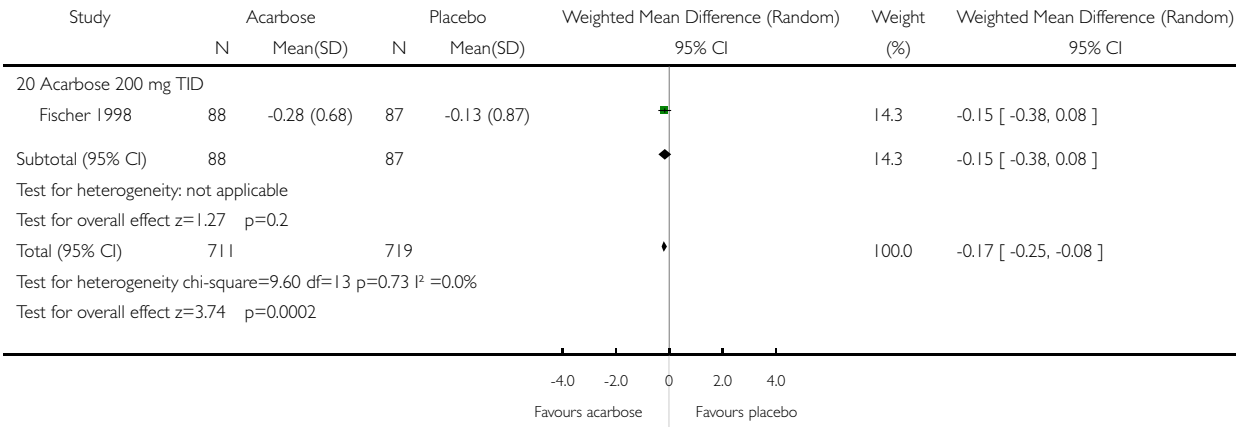


Fig. 16. Comparison 01. Acarbose versus placebo

01.15 Total deaths

Review: Alpha-glucosidase inhibitors for type 2 diabetes mellitus

Comparison: 01 Acarbose versus placebo

Outcome: 15 Total deaths

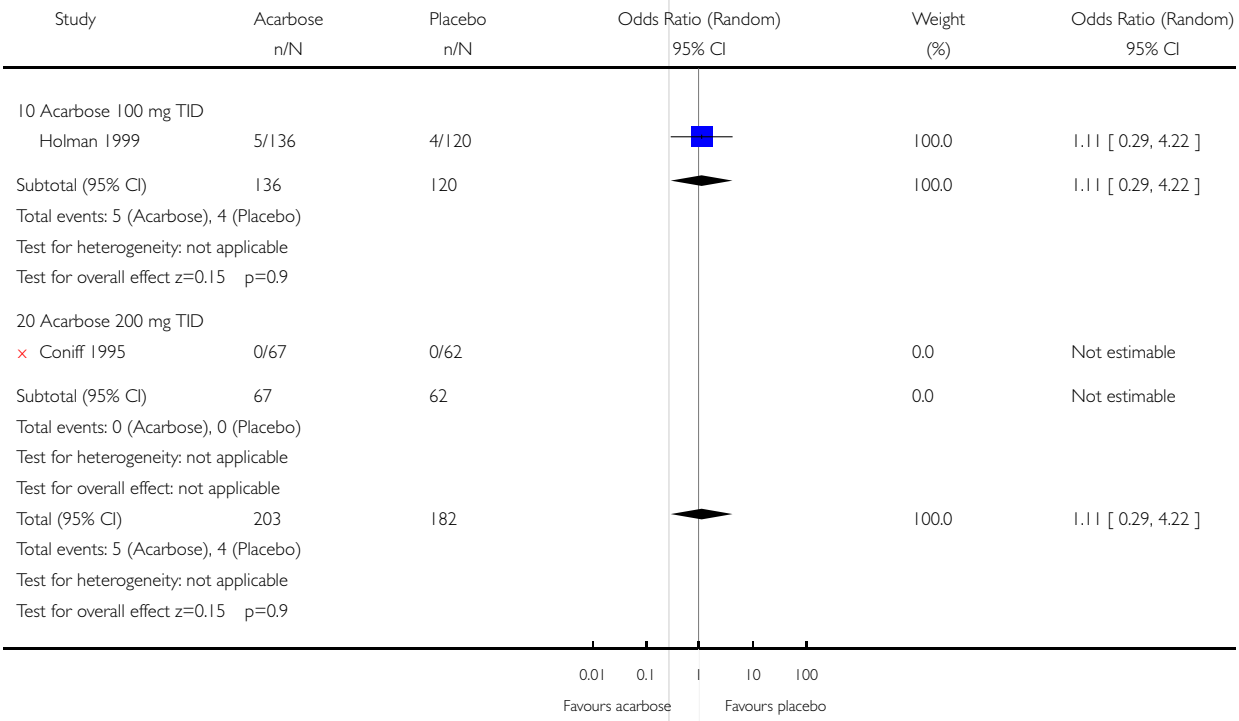


Fig. 17. Comparison 01. Acarbose versus placebo

01.16 Disease related deaths

Review: Alpha-glucosidase inhibitors for type 2 diabetes mellitus

Comparison: 01 Acarbose versus placebo

Outcome: 16 Disease related deaths

Study	Acarbose n/N	Placebo n/N	Odds Ratio (Random) 95% CI	Weight (%)	Odds Ratio (Random) 95% CI
20 Acarbose 200 mg TID					
× Coniff 1995	0/67	0/62		0.0	Not estimable
Total (95% CI)	67	62		0.0	Not estimable
Total events: 0 (Acarbose), 0 (Placebo)					
Test for heterogeneity: not applicable					
Test for overall effect: not applicable					

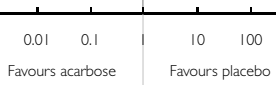


Fig. 18. Comparison 01. Acarbose versus placebo

01.20 Occurence of morbidity (total)

Review: Alpha-glucosidase inhibitors for type 2 diabetes mellitus

Comparison: 01 Acarbose versus placebo

Outcome: 20 Occurence of morbidity (total)

Study	Acarbose n/N	Placebo n/N	Odds Ratio (Random) 95% CI	Weight (%)	Odds Ratio (Random) 95% CI
20 Acarbose 200 mg TID					
Total (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Acarbose), 0 (Placebo)					
Test for heterogeneity: not applicable					
Test for overall effect: not applicable					

Fig. 19. Comparison 01. Acarbose versus placebo

01.21 Occurence of morbidity (disease specific)

Review: Alpha-glucosidase inhibitors for type 2 diabetes mellitus

Comparison: 01 Acarbose versus placebo

Outcome: 21 Occurence of morbidity (disease specific)

Study	Acarbose n/N	Placebo n/N	Odds Ratio (Random) 95% CI	Weight (%)	Odds Ratio (Random) 95% CI
20 Acarbose 200 mg TID					
Total (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Acarbose), 0 (Placebo)					
Test for heterogeneity: not applicable					
Test for overall effect: not applicable					

Fig. 20. Comparison 01. Acarbose versus placebo

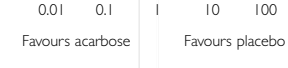
01.30 Occurence of adverse effects

Review: Alpha-glucosidase inhibitors for type 2 diabetes mellitus

Comparison: 01 Acarbose versus placebo

Outcome: 30 Occurence of adverse effects

Study	Acarbose n/N	Placebo n/N	Odds Ratio (Random) 95% CI	Weight (%)	Odds Ratio (Random) 95% CI
01 Acarbose 25 mg TID					
Fischer 1998	46/102	33/97		7.1	1.59 [0.90, 2.83]
Subtotal (95% CI)	102	97		7.1	1.59 [0.90, 2.83]
Total events: 46 (Acarbose), 33 (Placebo)					
Test for heterogeneity: not applicable					
Test for overall effect z=1.59 p=0.1					
05 Acarbose 50 mg TID					
Campbell 1998	248/259	242/263		5.7	1.96 [0.92, 4.14]
Fischer 1998	59/99	33/97		7.0	2.86 [1.60, 5.11]
Santeusanio 1993	9/28	9/29		3.6	1.05 [0.34, 3.22]
Subtotal (95% CI)	386	389		16.2	2.11 [1.29, 3.47]
Total events: 316 (Acarbose), 284 (Placebo)					
Test for heterogeneity chi-square=2.55 df=2 p=0.28 I^2 =21.6%					
Test for overall effect z=2.95 p=0.003					
10 Acarbose 100 mg TID					
Braun 1996	21/55	4/57		3.4	8.18 [2.58, 25.92]



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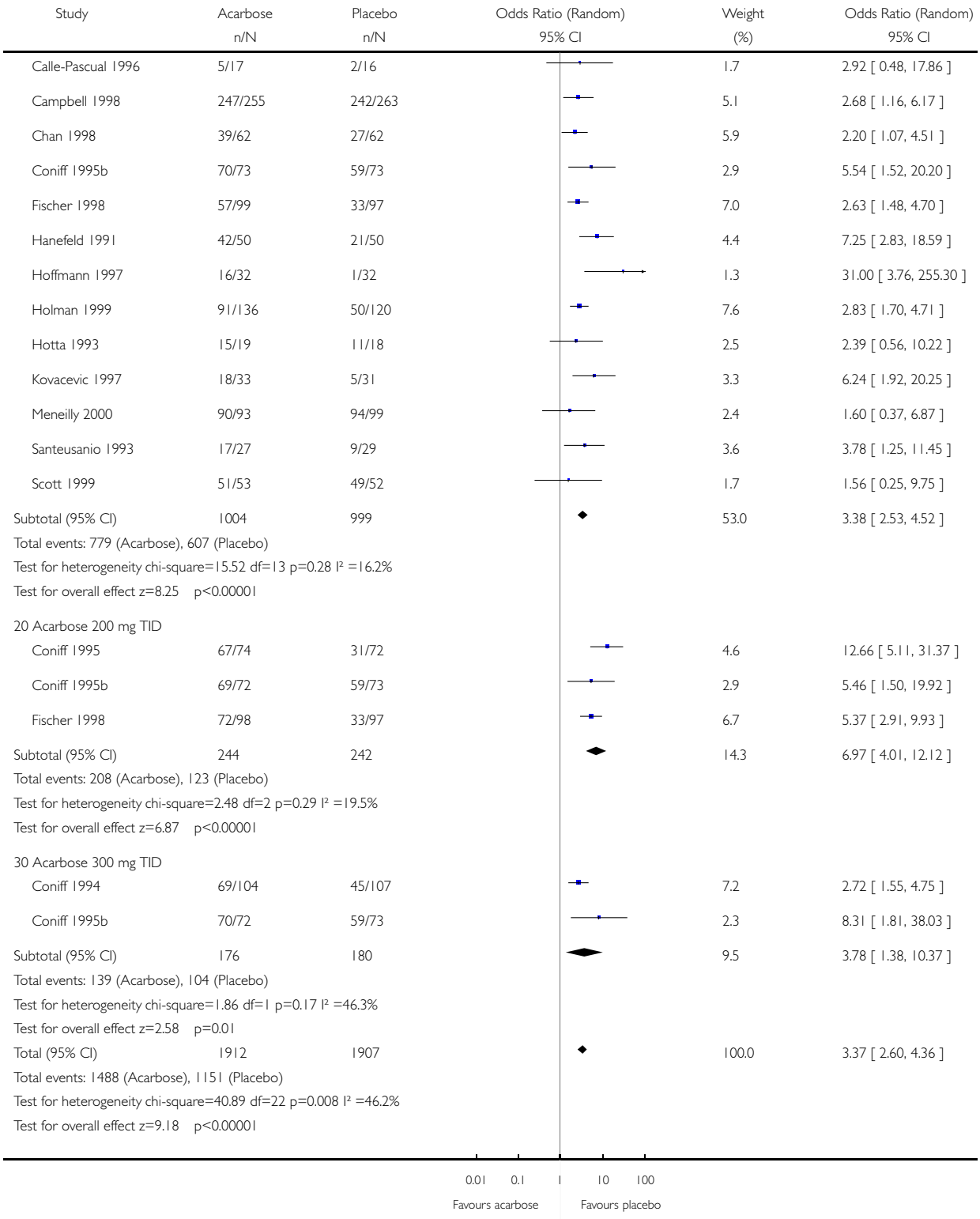


Fig. 21. Comparison 01. Acarbose versus placebo

01.31 Occurence of gastro-intestinal adverse effects

Review: Alpha-glucosidase inhibitors for type 2 diabetes mellitus

Comparison: 01 Acarbose versus placebo

Outcome: 31 Occurence of gastro-intestinal adverse effects

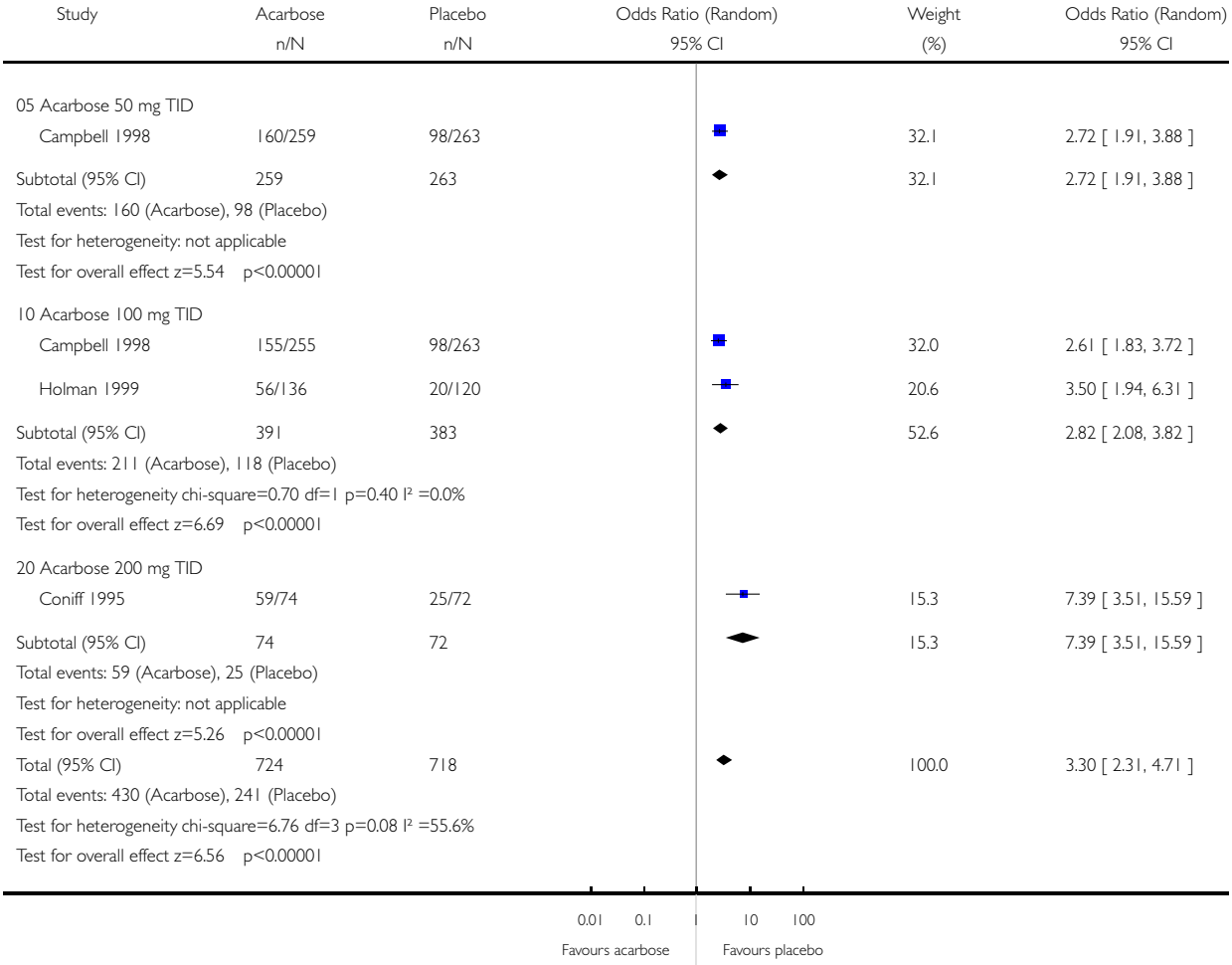


Fig. 22. Comparison 01. Acarbose versus placebo

01.50 Quality of life

Review: Alpha-glucosidase inhibitors for type 2 diabetes mellitus

Comparison: 01 Acarbose versus placebo

Outcome: 50 Quality of life

Study	Acarbose N Mean(SD)	Placebo N Mean(SD)	Weighted Mean Difference (Random) 95% CI	Weight (%)	Weighted Mean Difference (Random) 95% CI
Total (95% CI)	0	0		0.0	Not estimable
Test for heterogeneity: not applicable					
Test for overall effect: not applicable					

Fig. 23. Comparison 01. Acarbose versus placebo

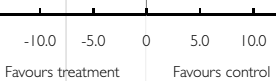
01.90 Change in post-load blood glucose (mmol/l) (2-hours)

Review: Alpha-glucosidase inhibitors for type 2 diabetes mellitus

Comparison: 01 Acarbose versus placebo

Outcome: 90 Change in post-load blood glucose (mmol/l) (2-hours)

Study	Treatment N	Mean(SD)	Control N	Mean(SD)	Weighted Mean Difference (Random) 95% CI	Weight (%)	Weighted Mean Difference (Random) 95% CI
01 Acarbose 25 mg TID							
Fischer 1998	89	-1.34 (2.55)	87	0.02 (2.74)		6.2	-1.36 [-2.14, -0.58]
Subtotal (95% CI)	89		87			6.2	-1.36 [-2.14, -0.58]
Test for heterogeneity: not applicable							
Test for overall effect z=3.41 p=0.0007							
02 Acarbose 50 mg BID							
Delgado 2002	9	-1.50 (1.60)	8	0.30 (1.40)		4.0	-1.80 [-3.23, -0.37]
Subtotal (95% CI)	9		8			4.0	-1.80 [-3.23, -0.37]
Test for heterogeneity: not applicable							
Test for overall effect z=2.47 p=0.01							
03 Acarbose 50 mg TID							
Fischer 1998	92	-1.71 (2.86)	87	0.02 (2.74)		6.0	-1.73 [-2.55, -0.91]
Santeusanio 1993	18	-1.41 (2.87)	22	-0.54 (3.28)		2.8	-0.87 [-2.78, 1.04]
Subtotal (95% CI)	110		109			8.8	-1.60 [-2.35, -0.84]
Test for heterogeneity chi-square=0.66 df=1 p=0.42 I^2 =0.0%							
Test for overall effect z=4.15 p=0.00003							



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Study	Treatment N	Treatment Mean(SD)	Control N	Control Mean(SD)	Weighted Mean Difference (Random) 95% CI	Weight (%)	Weighted Mean Difference (Random) 95% CI
04 Acarbose 100 mg TID							
Braun 1996	42	-3.20 (2.50)	44	-1.40 (2.50)		5.1	-1.80 [-2.86, -0.74]
Chan 1998	59	-0.77 (2.60)	62	0.65 (2.90)		5.4	-1.42 [-2.40, -0.44]
Coniff 1995b	52	-2.15 (3.95)	57	1.23 (4.05)		3.7	-3.38 [-4.88, -1.88]
Dedov 1995	82	-3.20 (2.20)	73	-2.50 (2.00)		6.6	-0.70 [-1.36, -0.04]
Fischer 1998	87	-1.48 (2.69)	87	0.02 (2.74)		6.1	-1.50 [-2.31, -0.69]
Haffner 1997	25	-2.40 (6.40)	25	-0.10 (7.40)		0.9	-2.30 [-6.14, 1.54]
Hanefeld 1991	47	-3.70 (2.30)	47	-0.80 (2.60)		5.4	-2.90 [-3.89, -1.91]
Hoffmann 1994	28	-1.80 (0.74)	30	0.03 (1.01)		7.4	-1.83 [-2.28, -1.38]
Hoffmann 1997	31	-2.36 (0.74)	32	0.01 (0.36)		7.8	-2.37 [-2.66, -2.08]
Hotta 1993	16	-2.69 (3.22)	15	-0.21 (2.93)		2.4	-2.48 [-4.65, -0.31]
Kovacevic 1997	33	-4.70 (3.70)	31	-1.70 (4.20)		2.7	-3.00 [-4.94, -1.06]
Santeusanio 1993	22	-2.92 (4.11)	22	-0.54 (3.28)		2.3	-2.38 [-4.58, -0.18]
Zheng 1995	39	-5.82 (3.60)	38	-0.40 (3.50)		3.5	-5.42 [-7.01, -3.83]
Subtotal (95% CI)	563		563			59.4	-2.22 [-2.75, -1.70]
Test for heterogeneity chi-square=49.35 df=12 p=<0.0001 I^2 =75.7%							
Test for overall effect z=8.31 p<0.00001							
05 Acarbose 200 mg TID							
Coniff 1995	67	-3.16 (4.38)	61	-0.76 (4.47)		3.7	-2.40 [-3.94, -0.86]
Coniff 1995b	51	-2.79 (4.05)	57	1.23 (4.05)		3.7	-4.02 [-5.55, -2.49]
Fischer 1998	88	-2.40 (2.96)	87	0.02 (2.74)		5.9	-2.42 [-3.26, -1.58]
Subtotal (95% CI)	206		205			13.3	-2.83 [-3.78, -1.88]
Test for heterogeneity chi-square=3.42 df=2 p=0.18 I^2 =41.6%							
Test for overall effect z=5.82 p<0.00001							
06 Acarbose 300 mg TID							
Coniff 1994	91	-2.11 (4.18)	96	0.69 (4.18)		4.7	-2.80 [-4.00, -1.60]
Coniff 1995b	50	-3.19 (3.94)	57	1.23 (4.05)		3.7	-4.42 [-5.94, -2.90]
Subtotal (95% CI)	141		153			8.4	-3.54 [-5.12, -1.96]
Test for heterogeneity chi-square=2.70 df=1 p=0.10 I^2 =63.0%							
Test for overall effect z=4.39 p=0.00001							
Total (95% CI)	1118		1125			100.0	-2.27 [-2.67, -1.88]
Test for heterogeneity chi-square=72.36 df=21 p=<0.0001 I^2 =71.0%							
Test for overall effect z=11.27 p<0.00001							

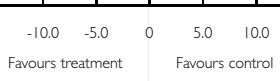


Fig. 24. Comparison 01. Acarbose versus placebo

01.91 Change in post-load insulin levels (pmol/l) (2-hours)

Review: Alpha-glucosidase inhibitors for type 2 diabetes mellitus

Comparison: 01 Acarbose versus placebo

Outcome: 91 Change in post-load insulin levels (pmol/l) (2-hours)

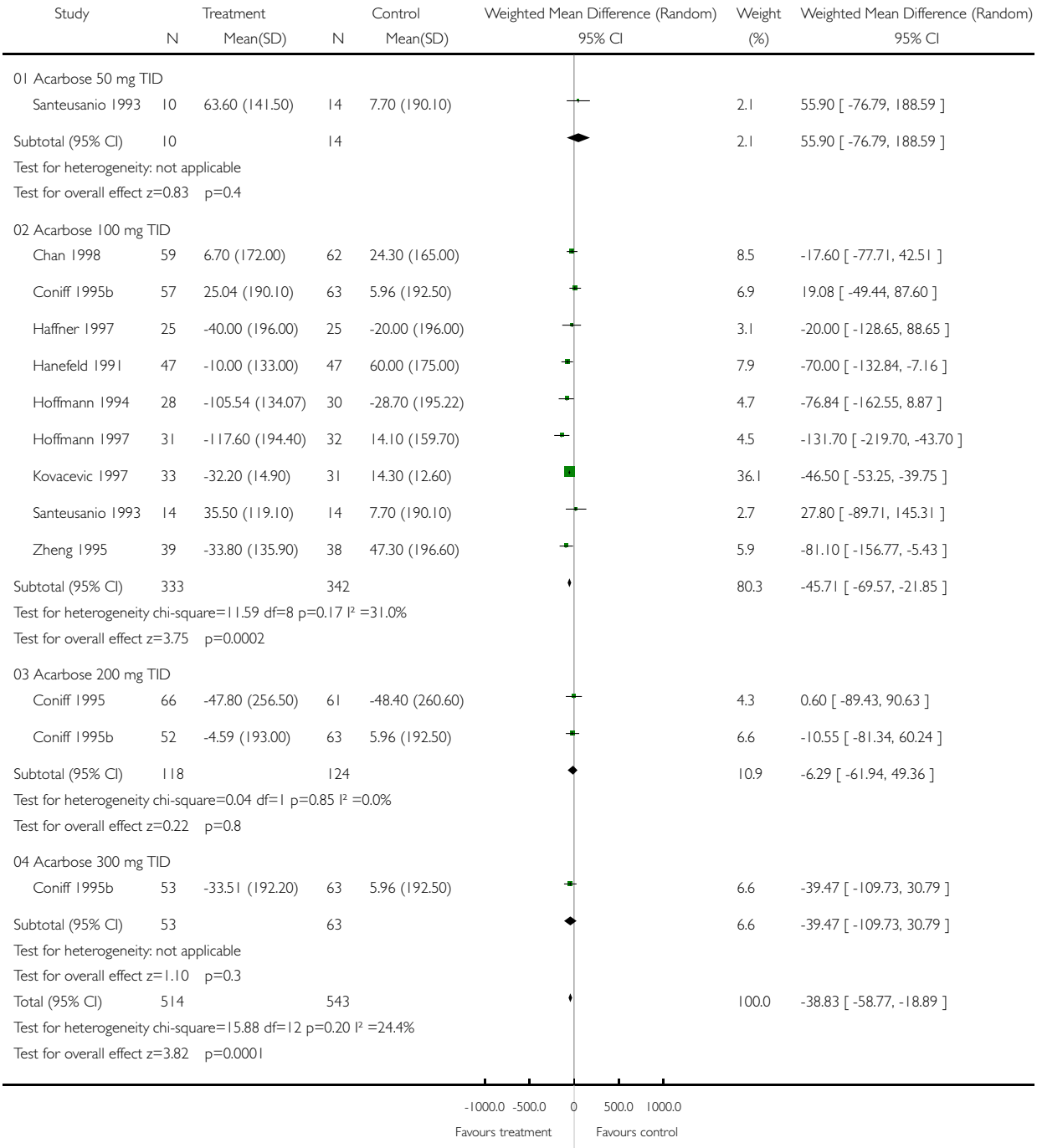


Fig. 25. Comparison 02. Acarbose versus sulphonylurea (SU)

02.01 Change in glycated haemoglobin (%)

Review: Alpha-glucosidase inhibitors for type 2 diabetes mellitus

Comparison: 02 Acarbose versus sulphonylurea (SU)

Outcome: 01 Change in glycated haemoglobin (%)

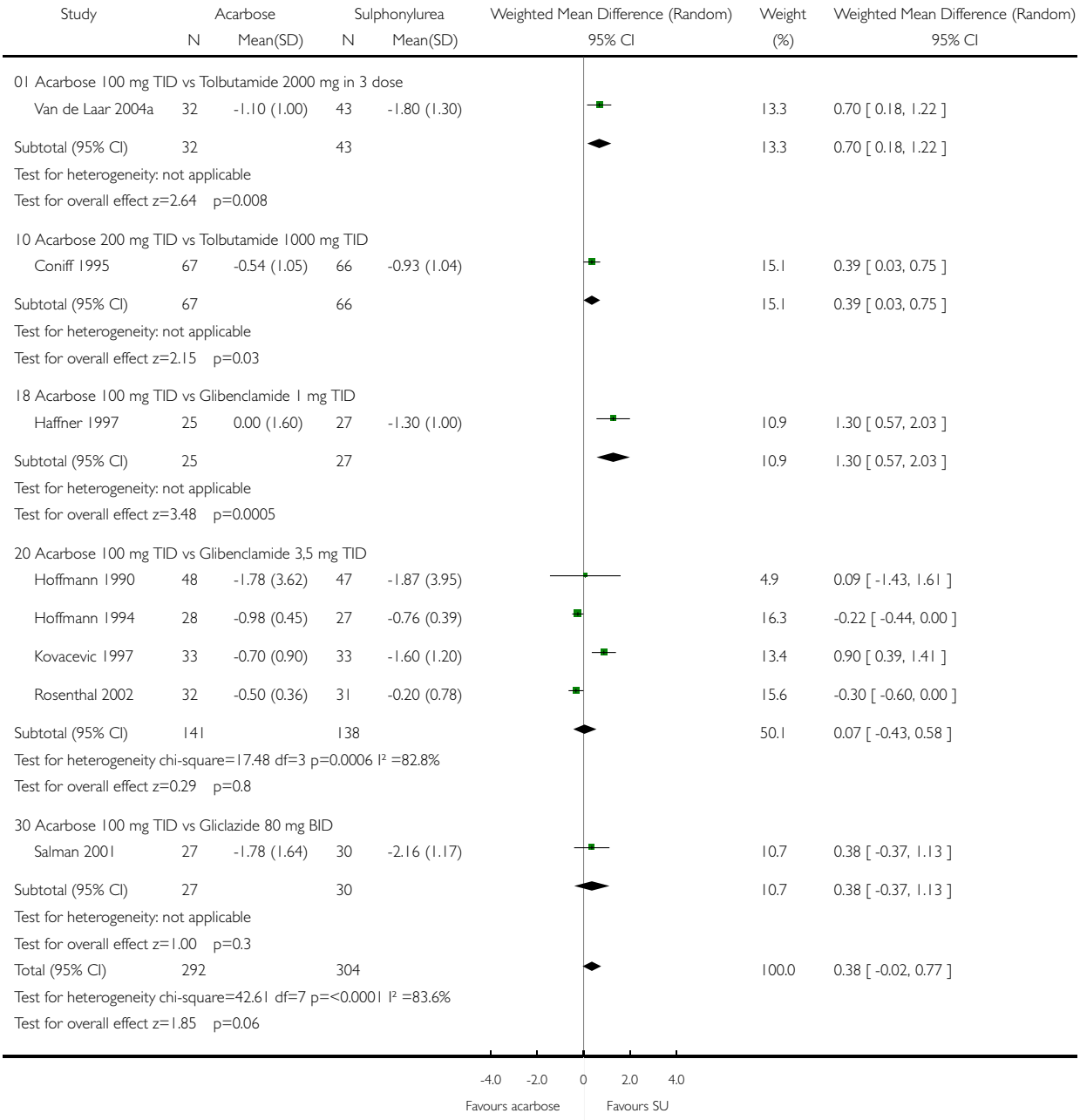


Fig. 26. Comparison 02. Acarbose versus sulphonylurea (SU)

02.02 Change in fasting blood glucose (mmol/l)

Review: Alpha-glucosidase inhibitors for type 2 diabetes mellitus

Comparison: 02 Acarbose versus sulphonylurea (SU)

Outcome: 02 Change in fasting blood glucose (mmol/l)

Study	Acarbose N	Acarbose Mean(SD)	Sulphonylurea N	Sulphonylurea Mean(SD)	Weighted Mean Difference (Random) 95% CI	Weight (%)	Weighted Mean Difference (Random) 95% CI
01 Acarbose 100 mg TID vs Tolbutamide 2000 mg in 3 dose							
Van de Laar 2004a	32	-1.50 (2.10)	43	-2.90 (2.60)		12.3	1.40 [0.34, 2.46]
Subtotal (95% CI)	32		43			12.3	1.40 [0.34, 2.46]
Test for heterogeneity: not applicable							
Test for overall effect z=2.58 p=0.01							
10 Acarbose 200 mg TID vs Tolbutamide 1000 mg TID							
Coniff 1995	67	-1.11 (3.17)	66	-2.02 (3.13)		12.2	0.91 [-0.16, 1.98]
Subtotal (95% CI)	67		66			12.2	0.91 [-0.16, 1.98]
Test for heterogeneity: not applicable							
Test for overall effect z=1.67 p=0.1							
18 Acarbose 100 mg TID vs Glibenclamide 1 mg TID							
Haffner 1997	25	-0.90 (3.60)	27	-3.40 (3.00)		6.4	2.50 [0.69, 4.31]
Subtotal (95% CI)	25		27			6.4	2.50 [0.69, 4.31]
Test for heterogeneity: not applicable							
Test for overall effect z=2.71 p=0.007							
20 Acarbose 100 mg TID vs Glibenclamide 3,5 mg TID							
Hoffmann 1990	48	-1.70 (1.20)	47	-1.70 (0.90)		20.9	0.00 [-0.43, 0.43]
Hoffmann 1994	28	-1.20 (0.89)	27	-1.25 (0.89)		20.3	0.05 [-0.42, 0.52]
Kovacevic 1997	33	-1.90 (3.00)	33	-4.00 (4.00)		7.0	2.10 [0.39, 3.81]
Rosenthal 2002	32	-0.70 (2.40)	31	-0.90 (2.50)		10.8	0.20 [-1.01, 1.41]
Subtotal (95% CI)	141		138			58.8	0.20 [-0.29, 0.69]
Test for heterogeneity chi-square=5.56 df=3 p=0.14 I^2 =46.1%							
Test for overall effect z=0.79 p=0.4							
30 Acarbose 100 mg TID vs Gliclazide 80 mg BID							
Salman 2001	27	-1.93 (2.80)	30	-2.62 (1.93)		10.3	0.69 [-0.57, 1.95]
Subtotal (95% CI)	27		30			10.3	0.69 [-0.57, 1.95]
Test for heterogeneity: not applicable							
Test for overall effect z=1.07 p=0.3							
Total (95% CI)	292		304			100.0	0.69 [0.16, 1.23]
Test for heterogeneity chi-square=18.68 df=7 p=0.009 I^2 =62.5%							
Test for overall effect z=2.54 p=0.01							

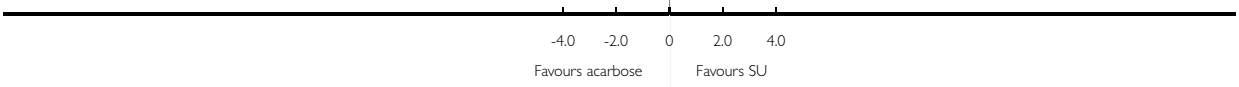


Fig. 27. Comparison 02. Acarbose versus sulphonylurea (SU)

02.03 Change in post-load blood glucose (mmol/l)

Review: Alpha-glucosidase inhibitors for type 2 diabetes mellitus

Comparison: 02 Acarbose versus sulphonylurea (SU)

Outcome: 03 Change in post-load blood glucose (mmol/l)

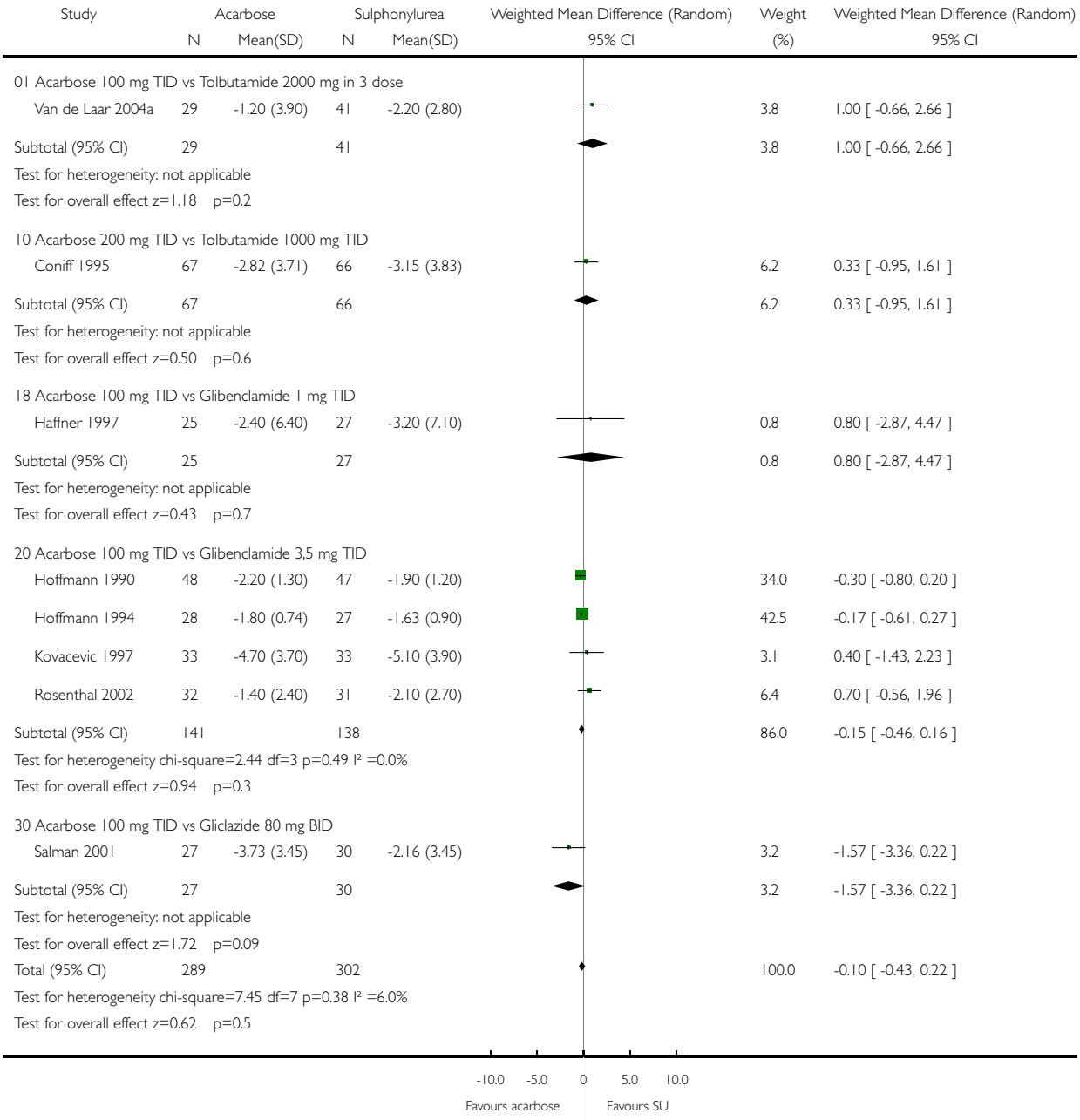


Fig. 28. Comparison 02. Acarbose versus sulphonylurea (SU)

02.04 Change in total cholesterol (mmol/l)

Review: Alpha-glucosidase inhibitors for type 2 diabetes mellitus

Comparison: 02 Acarbose versus sulphonylurea (SU)

Outcome: 04 Change in total cholesterol (mmol/l)

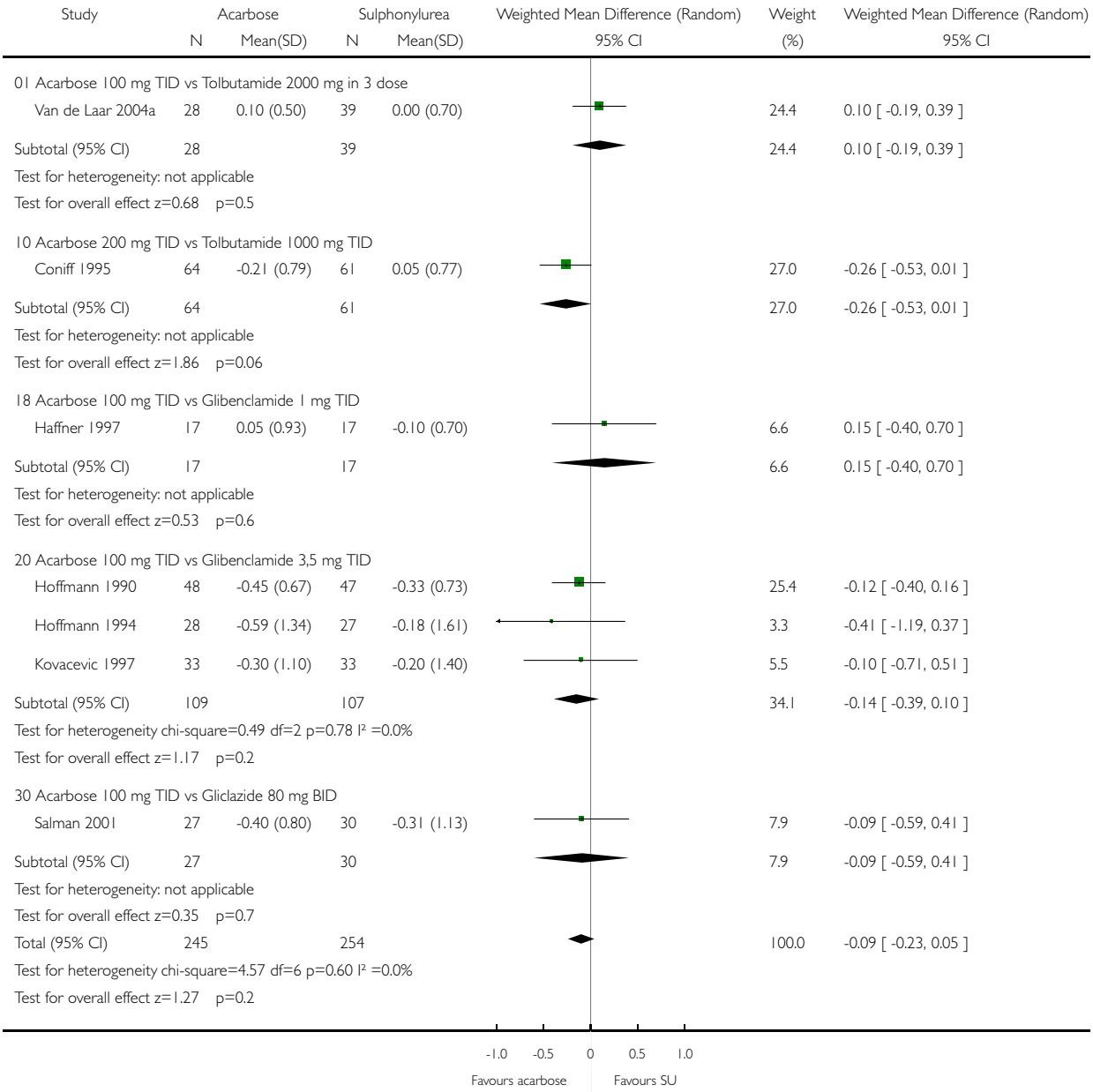


Fig. 29. Comparison 02. Acarbose versus sulphonylurea (SU)

02.05 Change in HDL-cholesterol (mmol/l)

Review: Alpha-glucosidase inhibitors for type 2 diabetes mellitus

Comparison: 02 Acarbose versus sulphonylurea (SU)

Outcome: 05 Change in HDL-cholesterol (mmol/l)

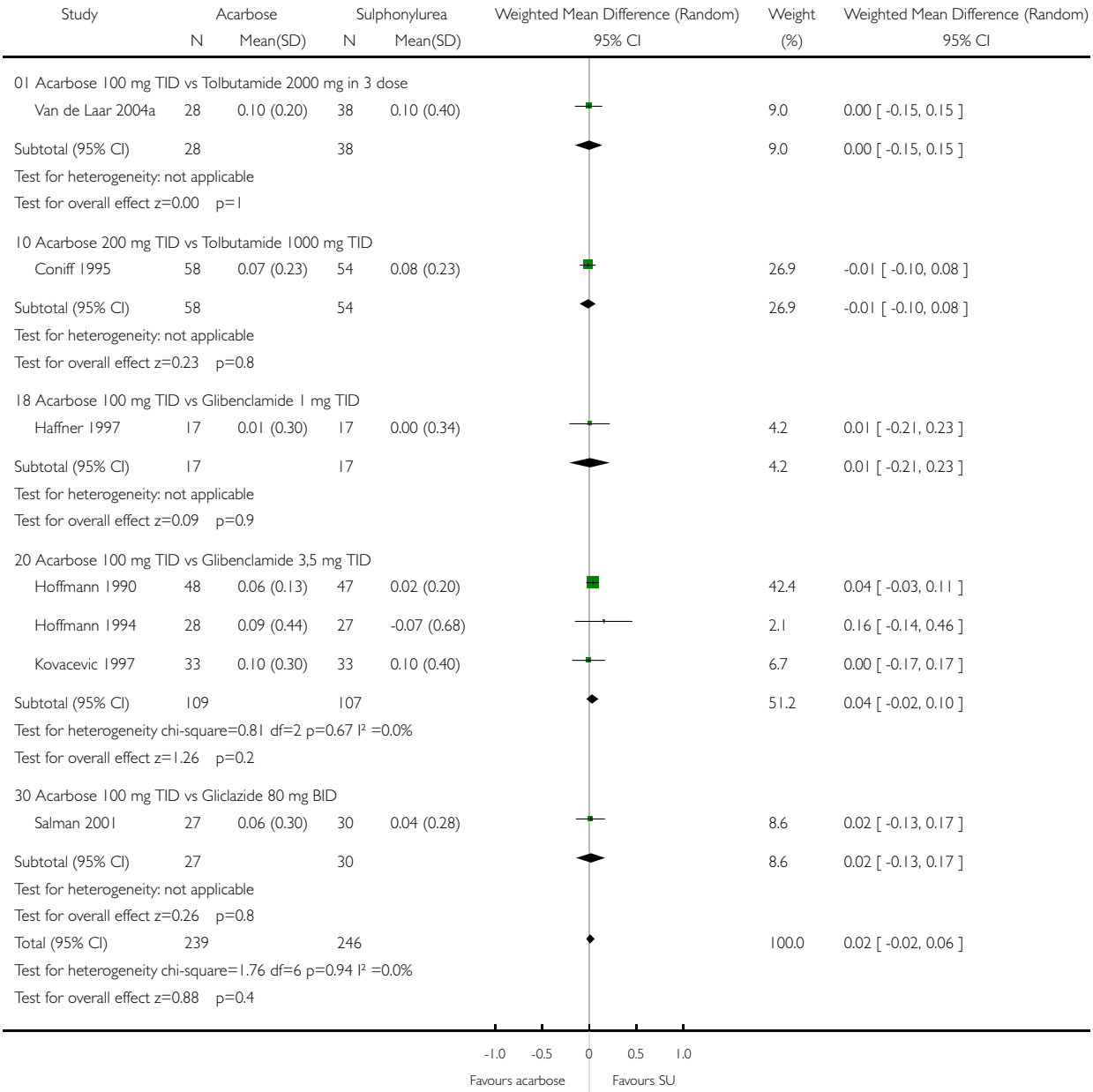


Fig. 30. Comparison 02. Acarbose versus sulphonylurea (SU)

02.06 Change in LDL-cholesterol (mmol/l)

Review: Alpha-glucosidase inhibitors for type 2 diabetes mellitus

Comparison: 02 Acarbose versus sulphonylurea (SU)

Outcome: 06 Change in LDL-cholesterol (mmol/l)

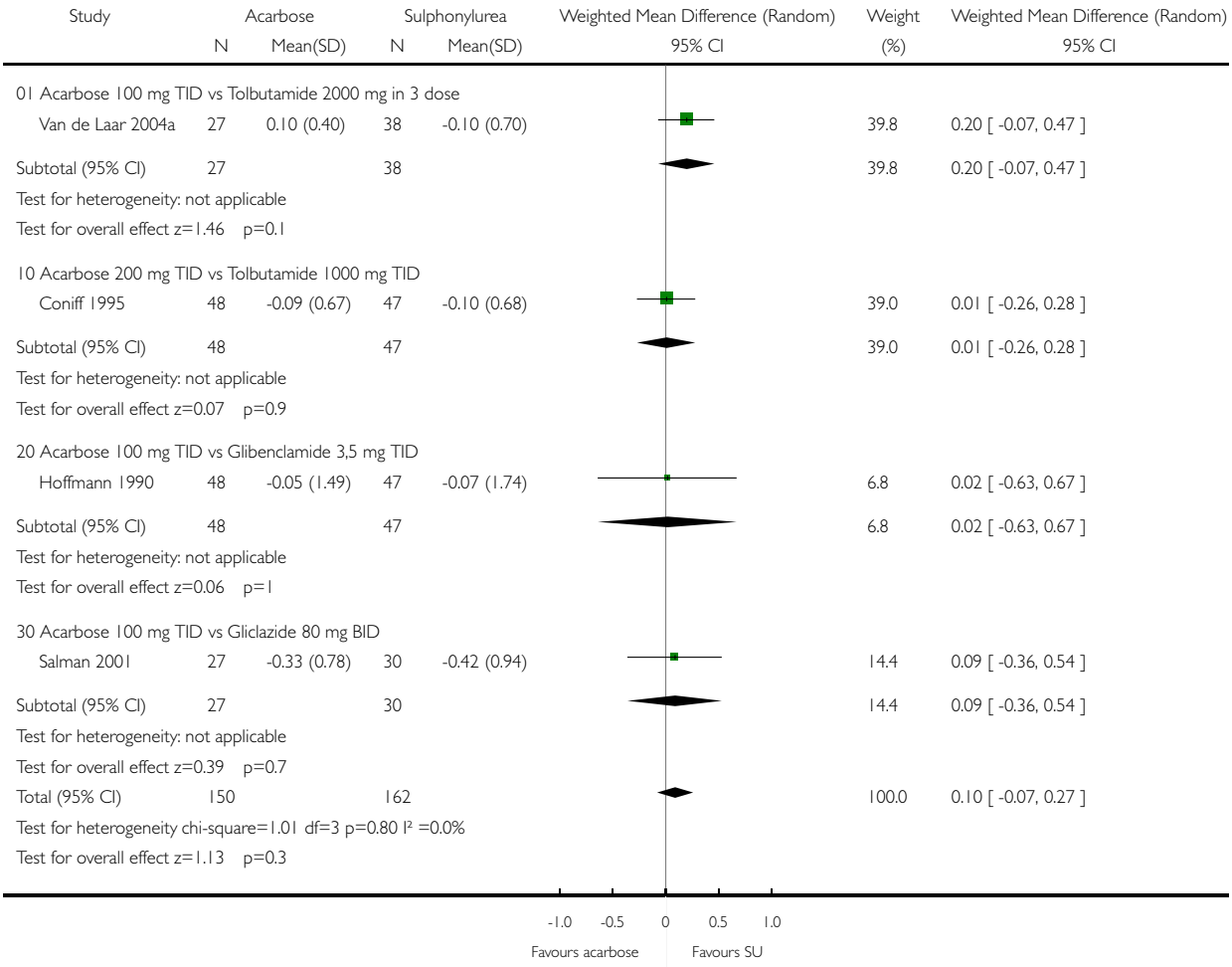


Fig. 31. Comparison 02. Acarbose versus sulphonylurea (SU)

02.07 Change in triglycerides (mmol/l)

Review: Alpha-glucosidase inhibitors for type 2 diabetes mellitus

Comparison: 02 Acarbose versus sulphonylurea (SU)

Outcome: 07 Change in triglycerides (mmol/l)

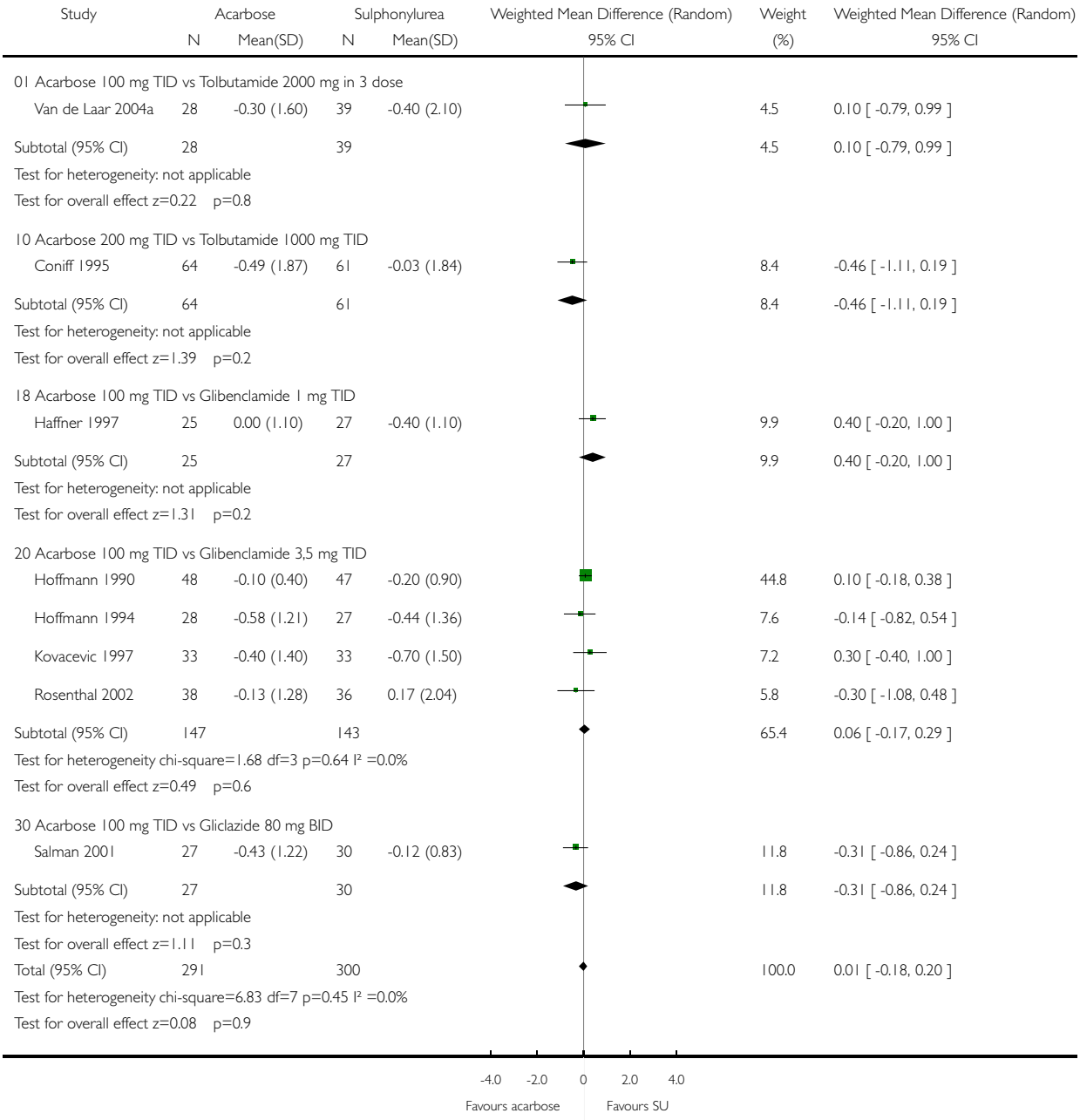


Fig. 32. Comparison 02. Acarbose versus sulphonylurea (SU)

02.08 Change in fasting insulin levels (pmol/l)

Review: Alpha-glucosidase inhibitors for type 2 diabetes mellitus

Comparison: 02 Acarbose versus sulphonylurea (SU)

Outcome: 08 Change in fasting insulin levels (pmol/l)

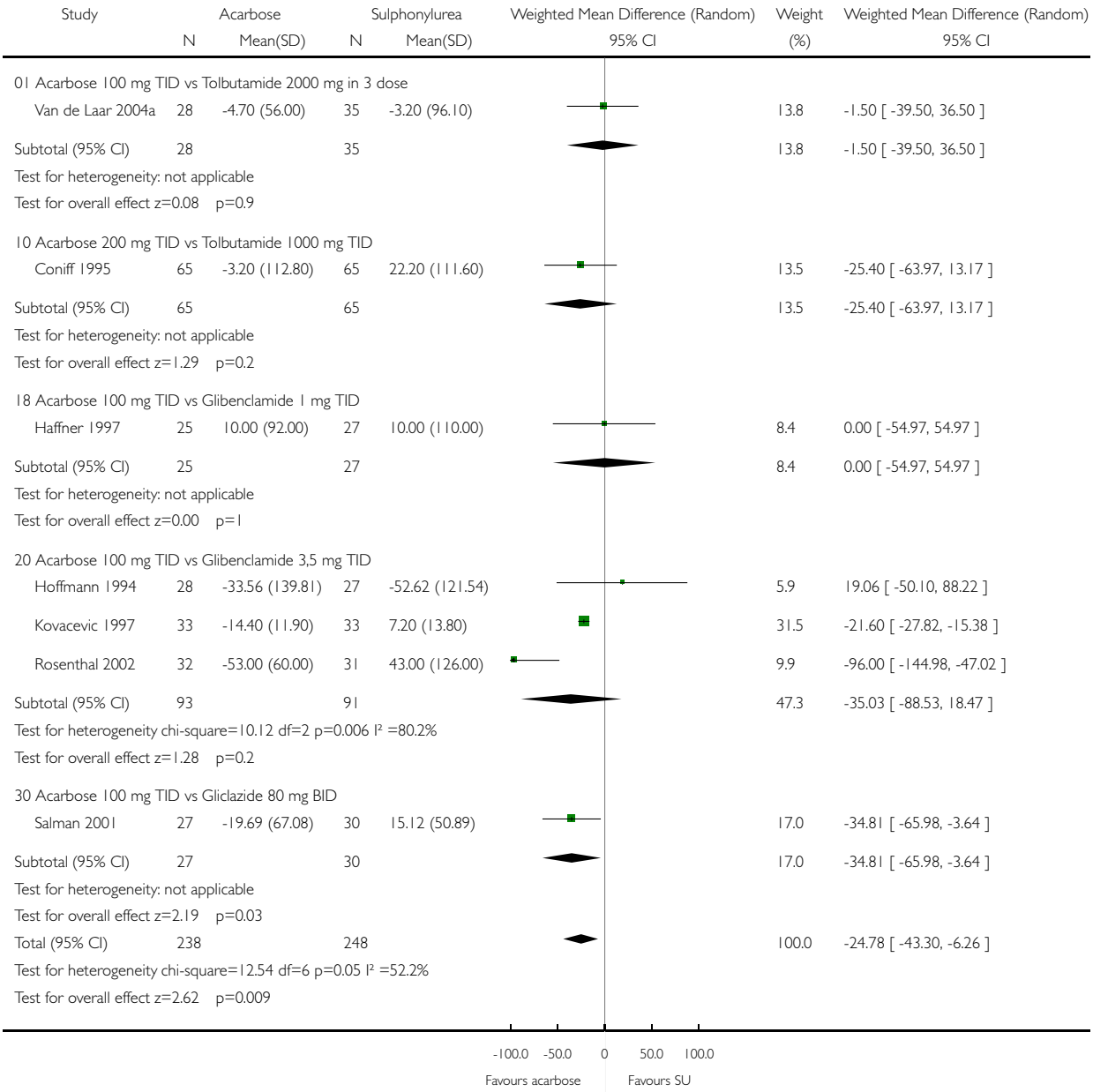


Fig. 33. Comparison 02. Acarbose versus sulphonylurea (SU)

02.09 Change in post-load insulin levels (pmol/l)

Review: Alpha-glucosidase inhibitors for type 2 diabetes mellitus

Comparison: 02 Acarbose versus sulphonylurea (SU)

Outcome: 09 Change in post-load insulin levels (pmol/l)

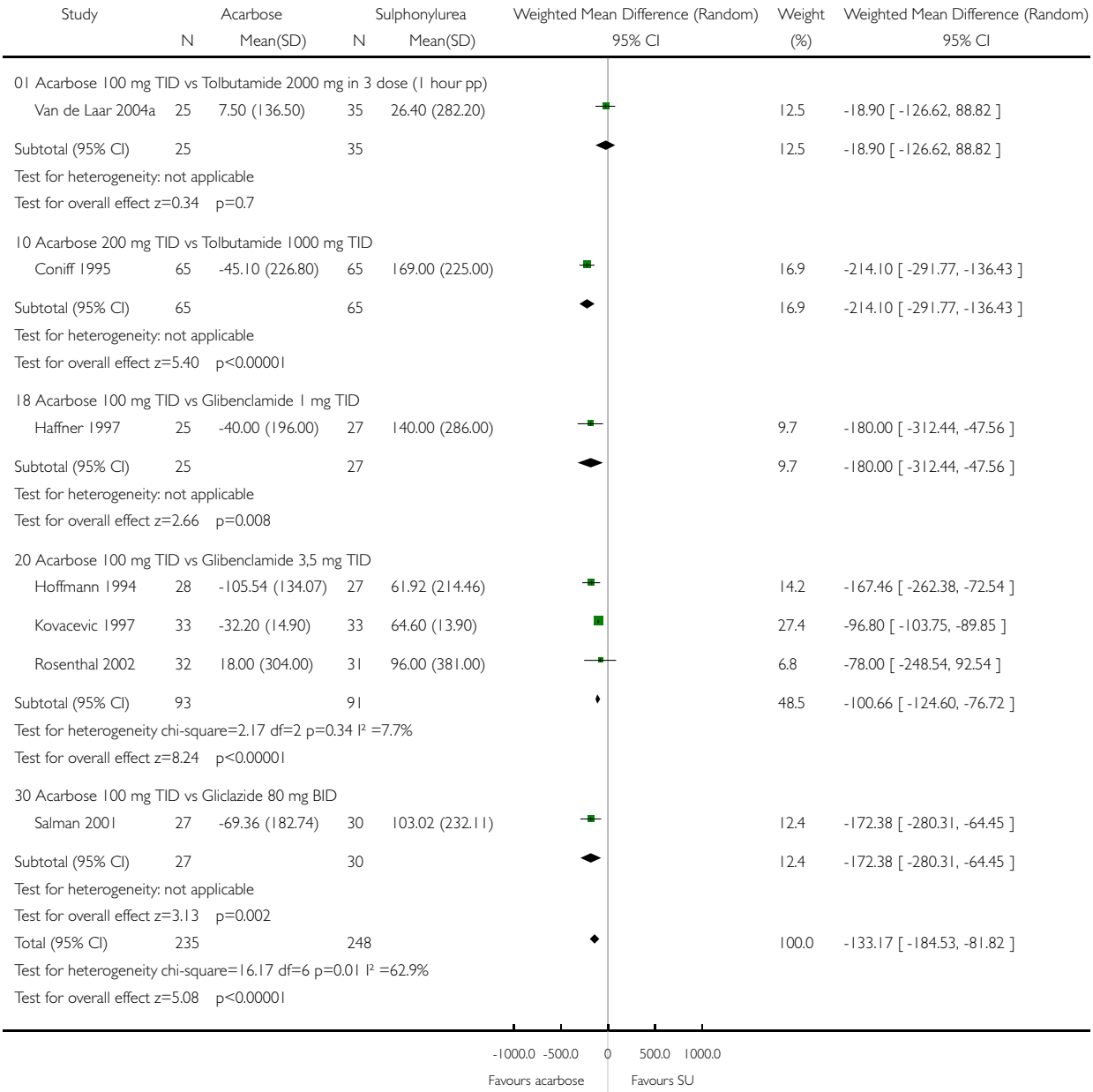


Fig. 34. Comparison 02. Acarbose versus sulphonylurea (SU)

02.10 Change in fasting C-peptide levels (nmol/l)

Review: Alpha-glucosidase inhibitors for type 2 diabetes mellitus

Comparison: 02 Acarbose versus sulphonylurea (SU)

Outcome: 10 Change in fasting C-peptide levels (nmol/l)

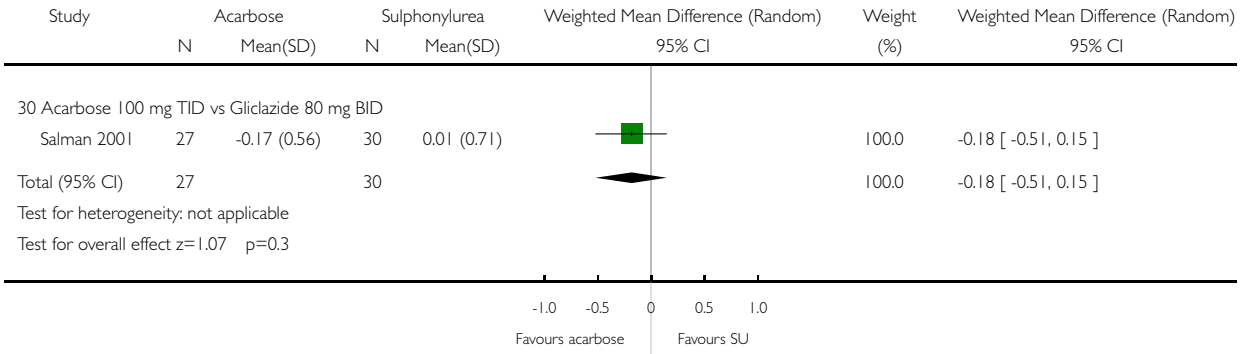


Fig. 35. Comparison 02. Acarbose versus sulphonylurea (SU)

02.11 Change in post-load C-peptide levels (nmol/l)

Review: Alpha-glucosidase inhibitors for type 2 diabetes mellitus

Comparison: 02 Acarbose versus sulphonylurea (SU)

Outcome: 11 Change in post-load C-peptide levels (nmol/l)

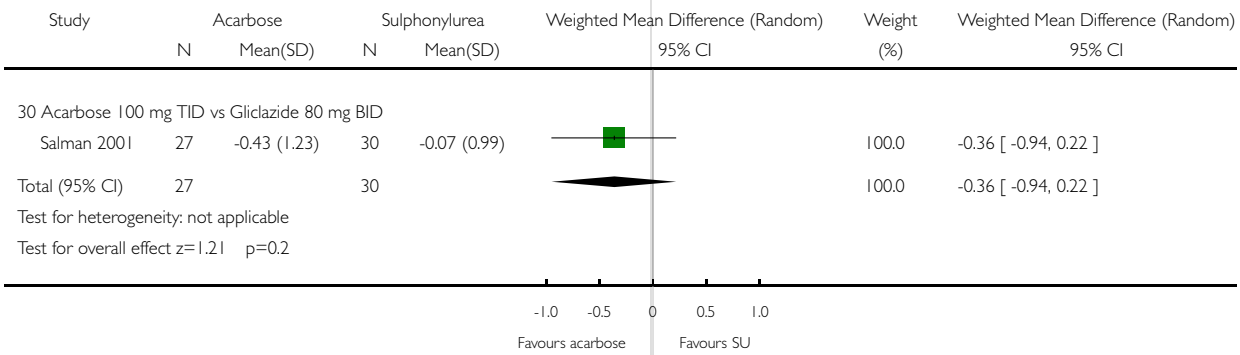


Fig. 36. Comparison 02. Acarbose versus sulphonylurea (SU)

02.12 Change in body weight (Kg)

Review: Alpha-glucosidase inhibitors for type 2 diabetes mellitus

Comparison: 02 Acarbose versus sulphonylurea (SU)

Outcome: 12 Change in body weight (Kg)

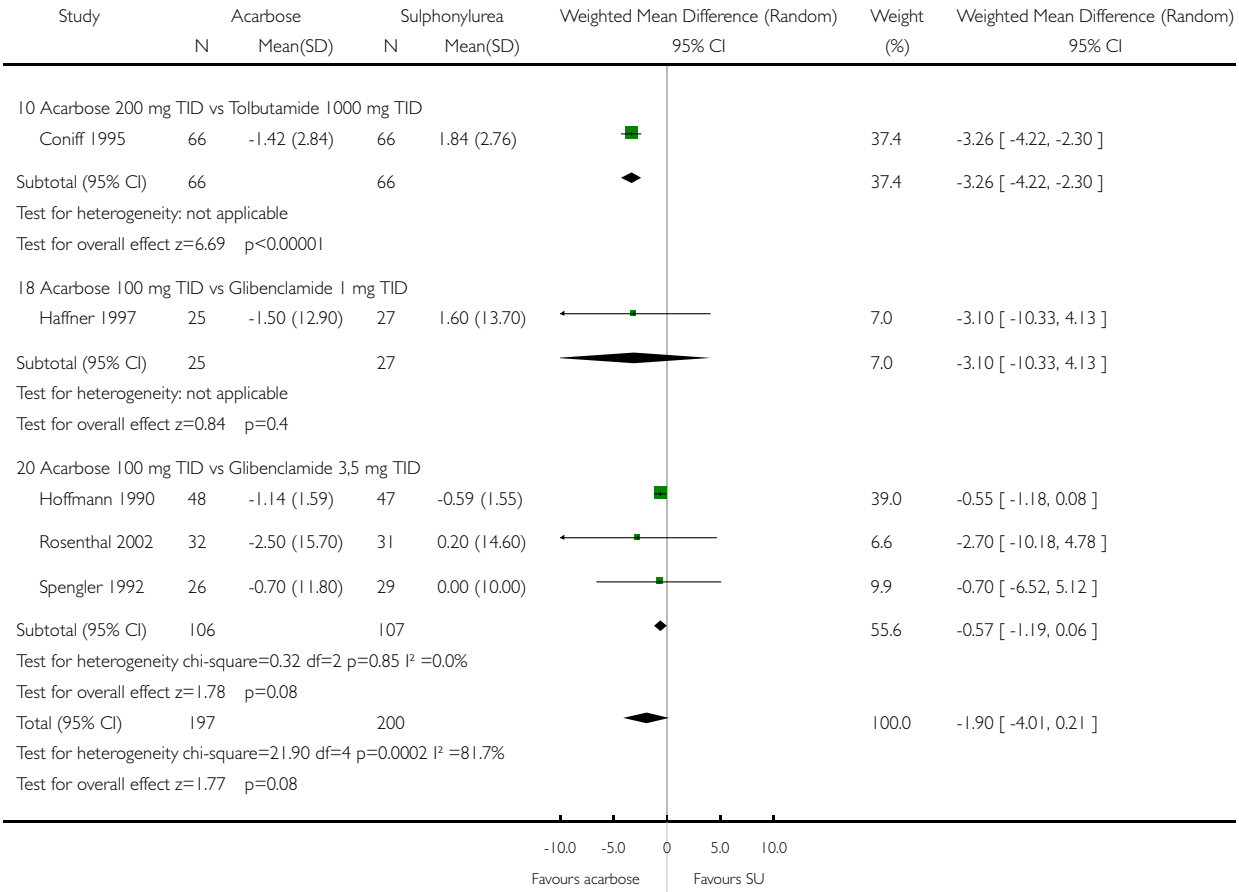


Fig. 37. Comparison 02. Acarbose versus sulphonylurea (SU)

02.13 Change in body mass index (Kg/m2)

Review: Alpha-glucosidase inhibitors for type 2 diabetes mellitus

Comparison: 02 Acarbose versus sulphonylurea (SU)

Outcome: 13 Change in body mass index (Kg/m2)

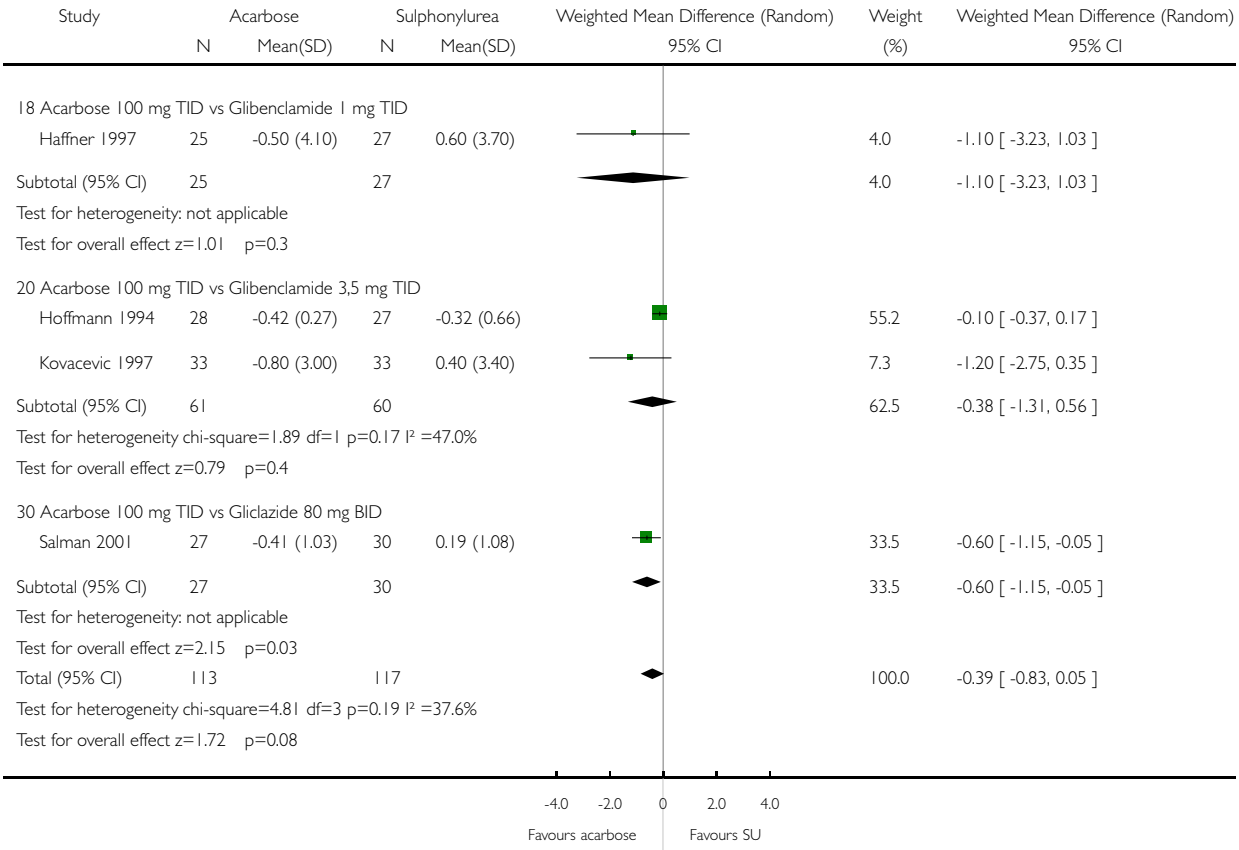


Fig. 38. Comparison 02. Acarbose versus sulphonylurea (SU)

02.15 Total deaths

Review: Alpha-glucosidase inhibitors for type 2 diabetes mellitus

Comparison: 02 Acarbose versus sulphonylurea (SU)

Outcome: 15 Total deaths

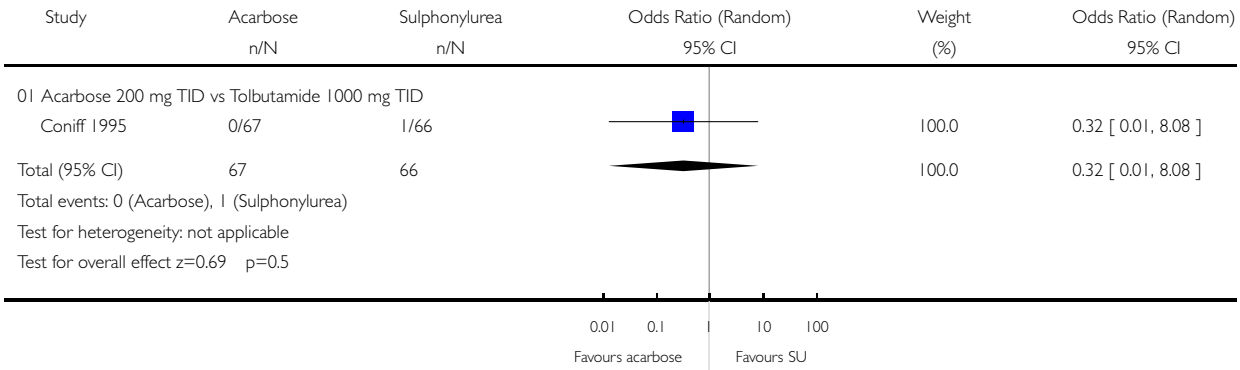


Fig. 39. Comparison 02. Acarbose versus sulphonylurea (SU)

02.16 Disease related deaths

Review: Alpha-glucosidase inhibitors for type 2 diabetes mellitus

Comparison: 02 Acarbose versus sulphonylurea (SU)

Outcome: 16 Disease related deaths

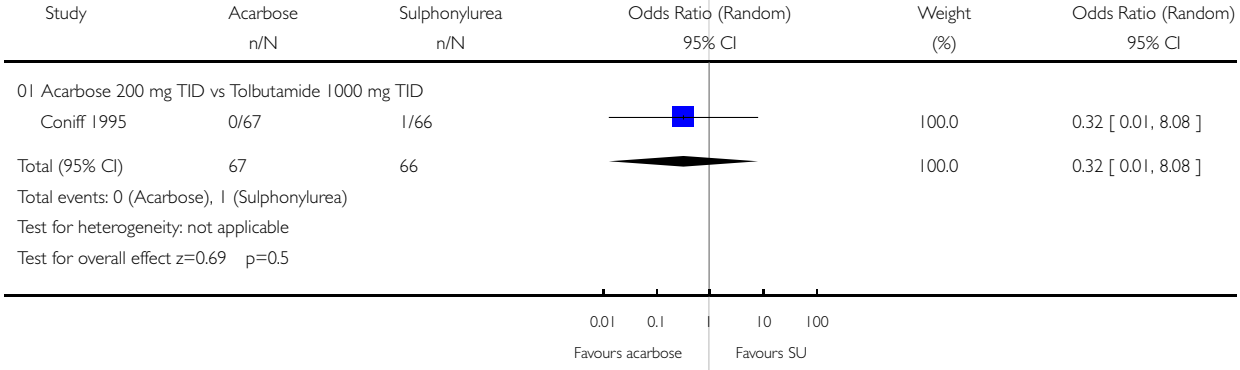


Fig. 40. Comparison 02. Acarbose versus sulphonylurea (SU)

02.30 Occurence of adverse effects

Review: Alpha-glucosidase inhibitors for type 2 diabetes mellitus

Comparison: 02 Acarbose versus sulphonylurea (SU)

Outcome: 30 Occurence of adverse effects

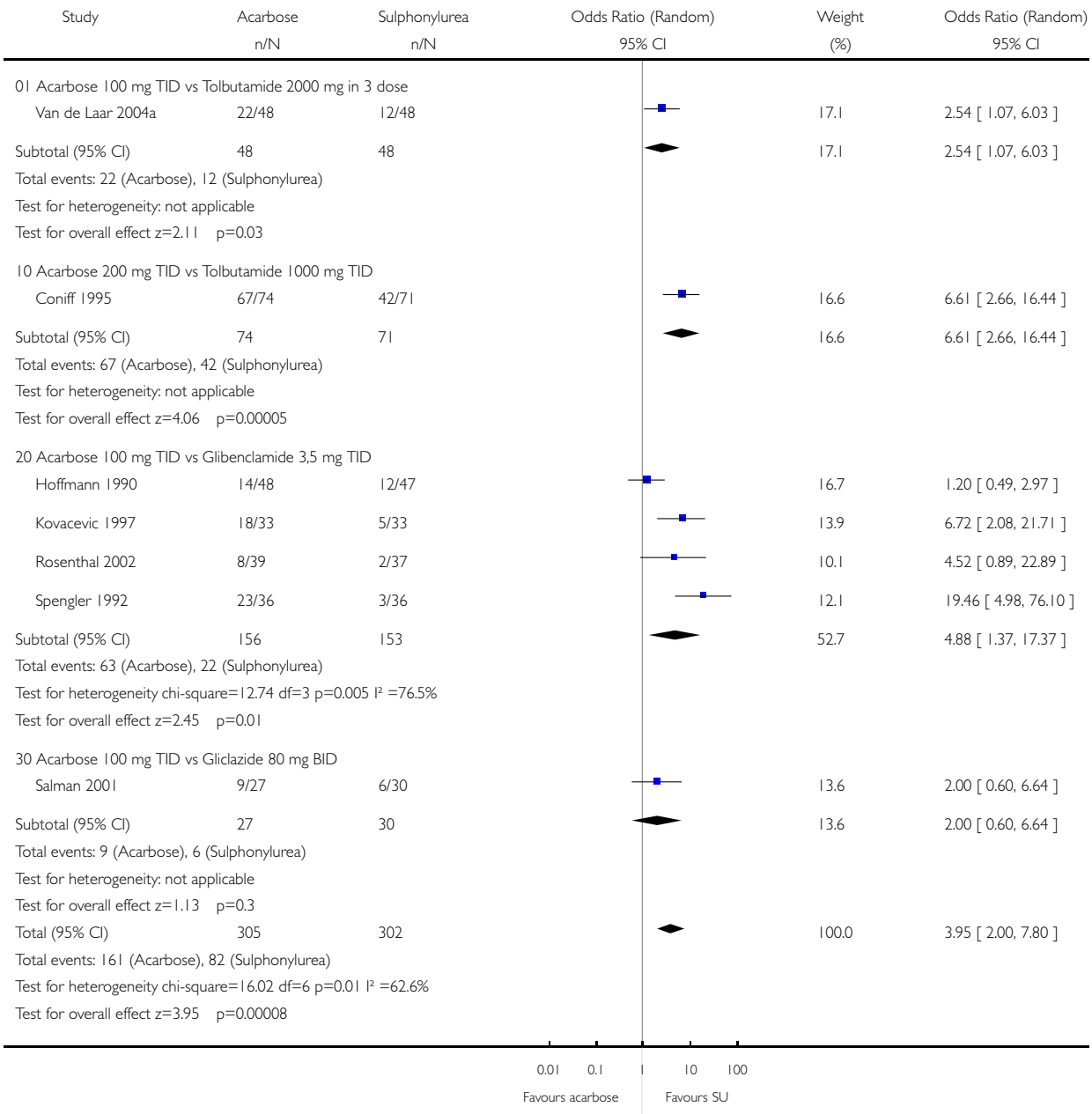


Fig. 41. Comparison 02. Acarbose versus sulphonylurea (SU)

02.31 Occurence of gastro-intestinal adverse effects

Review: Alpha-glucosidase inhibitors for type 2 diabetes mellitus

Comparison: 02 Acarbose versus sulphonylurea (SU)

Outcome: 31 Occurence of gastro-intestinal adverse effects

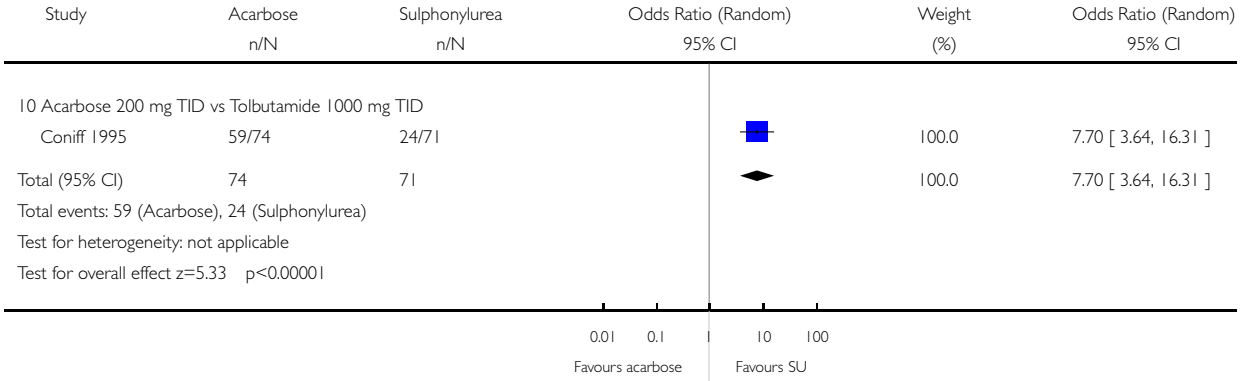


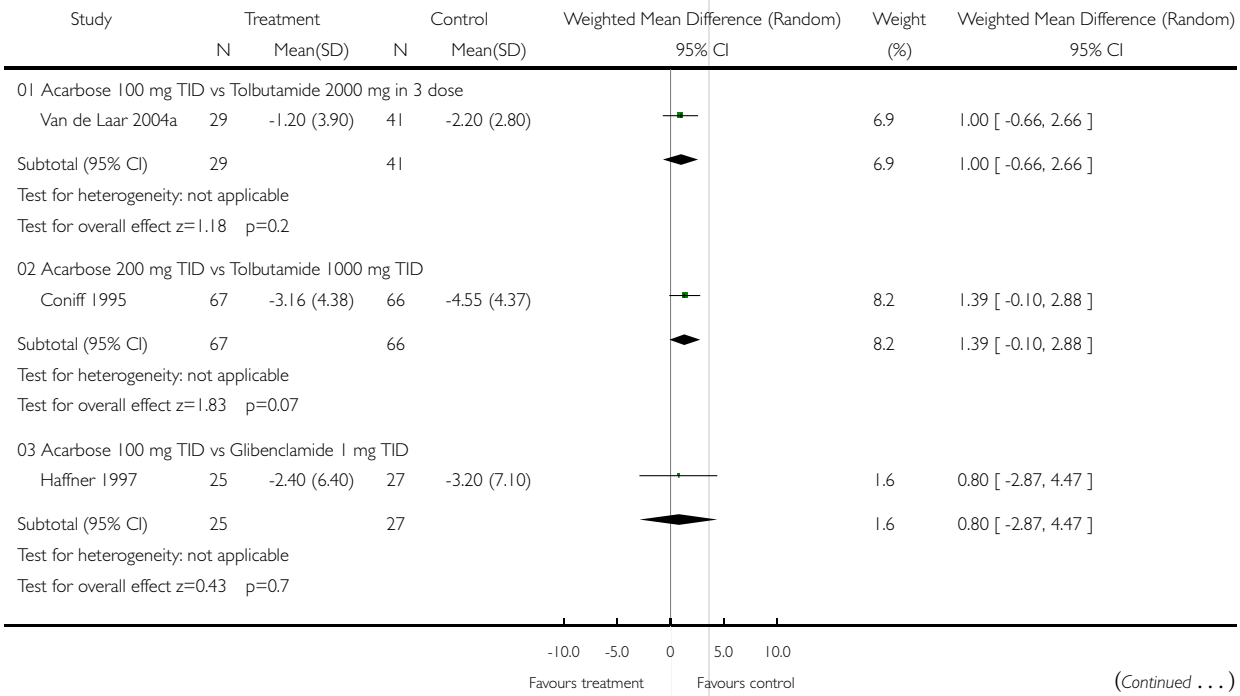
Fig. 42. Comparison 02. Acarbose versus sulphonylurea (SU)

02.90 Change in post-load blood glucose (mmol/l) (2 hours)

Review: Alpha-glucosidase inhibitors for type 2 diabetes mellitus

Comparison: 02 Acarbose versus sulphonylurea (SU)

Outcome: 90 Change in post-load blood glucose (mmol/l) (2 hours)



(*Continued . . .*)

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Study	Treatment N	Treatment Mean(SD)	Control N	Control Mean(SD)	Weighted Mean Difference (Random) 95% CI	Weight (%)	Weighted Mean Difference (Random) 95% CI
04 Acarbose 100 mg TID vs Glibenclamide 3,5 mg TID							
Hoffmann 1990	48	-2.20 (1.30)	47	-1.90 (1.20)		29.1	-0.30 [-0.80, 0.20]
Hoffmann 1994	28	-1.80 (0.74)	27	-1.63 (0.90)		31.7	-0.17 [-0.61, 0.27]
Kovacevic 1997	33	-4.70 (3.70)	33	-5.10 (3.90)		5.8	0.40 [-1.43, 2.23]
Rosenthal 2002	32	-1.40 (2.40)	31	-2.10 (2.70)		10.7	0.70 [-0.56, 1.96]
Subtotal (95% CI)	141		138			77.2	-0.15 [-0.46, 0.16]
Test for heterogeneity chi-square=2.44 df=3 p=0.49 I^2 =0.0%							
Test for overall effect z=0.94 p=0.3							
05 Acarbose 100 mg TID vs Gliclazide 80 mg BID							
Salman 2001	27	-3.73 (3.45)	30	-2.16 (3.45)		6.0	-1.57 [-3.36, 0.22]
Subtotal (95% CI)	27		30			6.0	-1.57 [-3.36, 0.22]
Test for heterogeneity: not applicable							
Test for overall effect z=1.72 p=0.09							
Total (95% CI)	289		302			100.0	0.06 [-0.42, 0.53]
Test for heterogeneity chi-square=10.88 df=7 p=0.14 I^2 =35.7%							
Test for overall effect z=0.24 p=0.8							

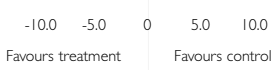


Fig. 43. Comparison 02. Acarbose versus sulphonylurea (SU)

02.91 Change in post-load insulin levels (pmol/l) (2 hours)

Review: Alpha-glucosidase inhibitors for type 2 diabetes mellitus

Comparison: 02 Acarbose versus sulphonylurea (SU)

Outcome: 91 Change in post-load insulin levels (pmol/l) (2 hours)

Study	Treatment N	Treatment Mean(SD)	Control N	Control Mean(SD)	Weighted Mean Difference (Random) 95% CI	Weight (%)	Weighted Mean Difference (Random) 95% CI
01 Acarbose 100 mg TID vs Tolbutamide 2000 mg in 3 dose (1 hour pp)							
Van de Laar 2004a	25	7.50 (136.50)	35	26.40 (282.20)		9.3	-18.90 [-126.62, 88.82]
Subtotal (95% CI)	25		35			9.3	-18.90 [-126.62, 88.82]
Test for heterogeneity: not applicable							
Test for overall effect z=0.34 p=0.7							
02 Acarbose 200 mg TID vs Tolbutamide 1000 mg TID							
Coniff 1995	66	-47.80 (256.50)	65	100.20 (254.50)		12.8	-148.00 [-235.51, -60.49]
Subtotal (95% CI)	66		65			12.8	-148.00 [-235.51, -60.49]
Test for heterogeneity: not applicable							
Test for overall effect z=3.31 p=0.0009							
03 Acarbose 100 mg TID vs Glibenclamide 1 mg TID							
Haffner 1997	25	-40.00 (196.00)	27	140.00 (286.00)		6.6	-180.00 [-312.44, -47.56]
Subtotal (95% CI)	25		27			6.6	-180.00 [-312.44, -47.56]
Test for heterogeneity: not applicable							
Test for overall effect z=2.66 p=0.008							
04 Acarbose 100 mg TID vs Glibenclamide 3,5 mg TID							
Hoffmann 1994	28	-105.54 (134.07)	27	61.92 (214.46)		11.3	-167.46 [-262.38, -72.54]
Kovacevic 1997	33	-32.20 (14.90)	33	64.60 (13.90)		46.4	-96.80 [-103.75, -89.85]
Rosenthal 2002	32	18.00 (304.00)	31	96.00 (381.00)		4.2	-78.00 [-248.54, 92.54]
Subtotal (95% CI)	93		91			62.0	-100.66 [-124.60, -76.72]
Test for heterogeneity chi-square=2.17 df=2 p=0.34 I^2 =7.7%							
Test for overall effect z=8.24 p<0.00001							
05 Acarbose 100 mg TID vs Gliclazide 80 mg BID							
Salman 2001	27	-69.36 (182.74)	30	103.02 (232.11)		9.3	-172.38 [-280.31, -64.45]
Subtotal (95% CI)	27		30			9.3	-172.38 [-280.31, -64.45]
Test for heterogeneity: not applicable							
Test for overall effect z=3.13 p=0.002							
Total (95% CI)	236		248			100.0	-115.84 [-152.52, -79.15]
Test for heterogeneity chi-square=8.84 df=6 p=0.18 I^2 =32.1%							
Test for overall effect z=6.19 p<0.00001							

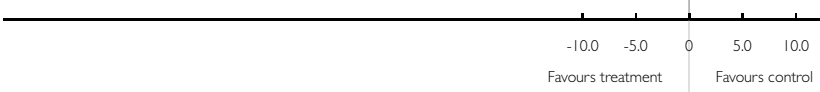


Fig. 44. Comparison 03. Acarbose versus Metformin

03.01 Change in glycated haemoglobin (%)

Review: Alpha-glucosidase inhibitors for type 2 diabetes mellitus

Comparison: 03 Acarbose versus Metformin

Outcome: 01 Change in glycated haemoglobin (%)

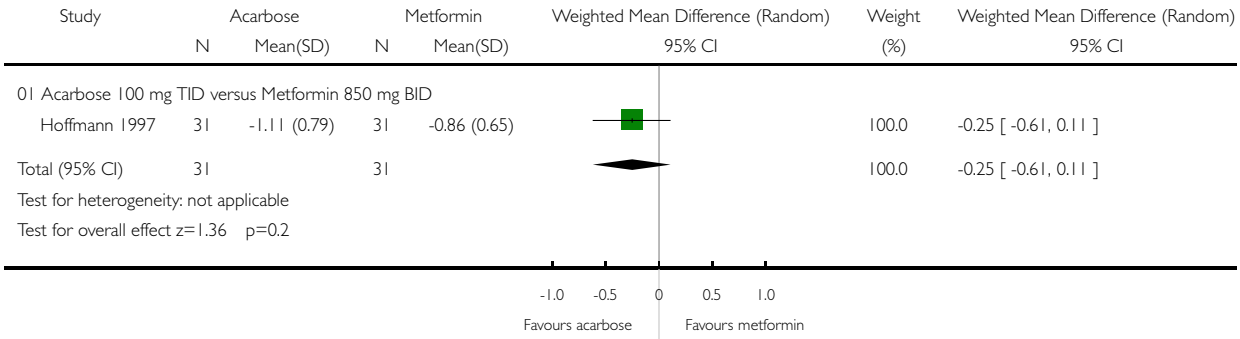


Fig. 45. Comparison 03. Acarbose versus Metformin

03.02 Change in fasting blood glucose (mmol/l)

Review: Alpha-glucosidase inhibitors for type 2 diabetes mellitus

Comparison: 03 Acarbose versus Metformin

Outcome: 02 Change in fasting blood glucose (mmol/l)

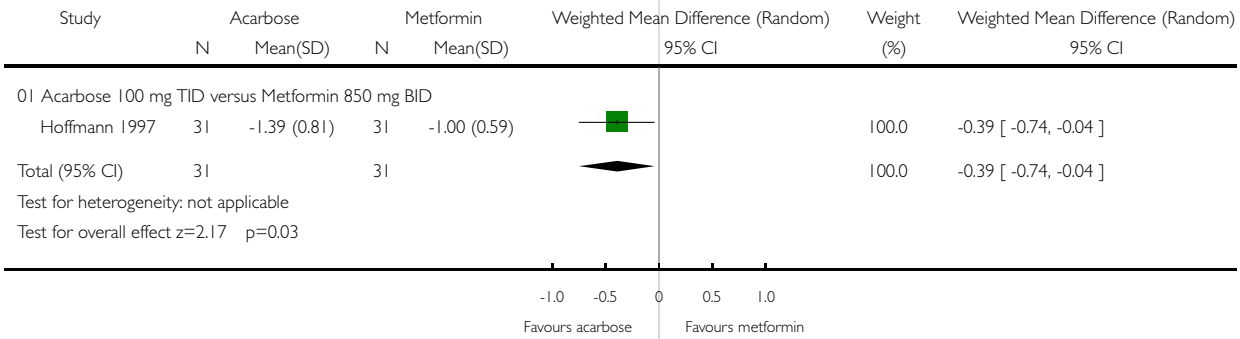


Fig. 46. Comparison 03. Acarbose versus Metformin

03.03 Change in post-load blood glucose (mmol/l)

Review: Alpha-glucosidase inhibitors for type 2 diabetes mellitus

Comparison: 03 Acarbose versus Metformin

Outcome: 03 Change in post-load blood glucose (mmol/l)

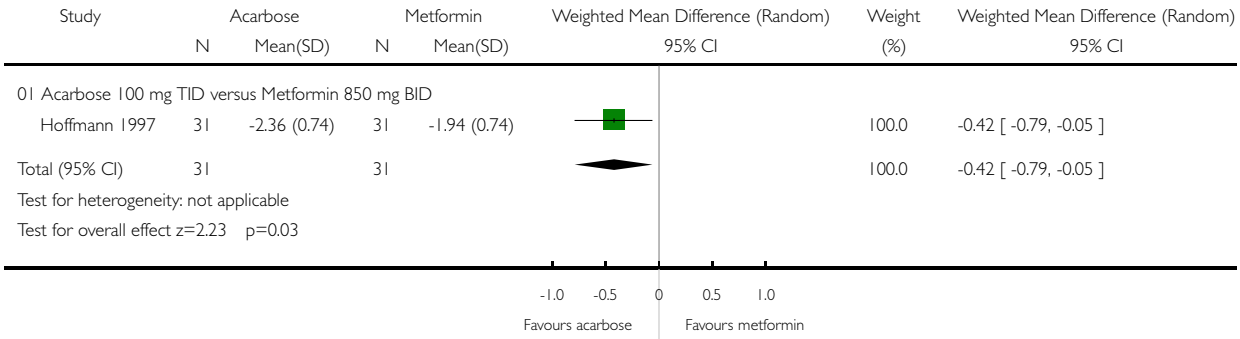


Fig. 47. Comparison 03. Acarbose versus Metformin

03.04 Change in total cholesterol (mmol/l)

Review: Alpha-glucosidase inhibitors for type 2 diabetes mellitus

Comparison: 03 Acarbose versus Metformin

Outcome: 04 Change in total cholesterol (mmol/l)

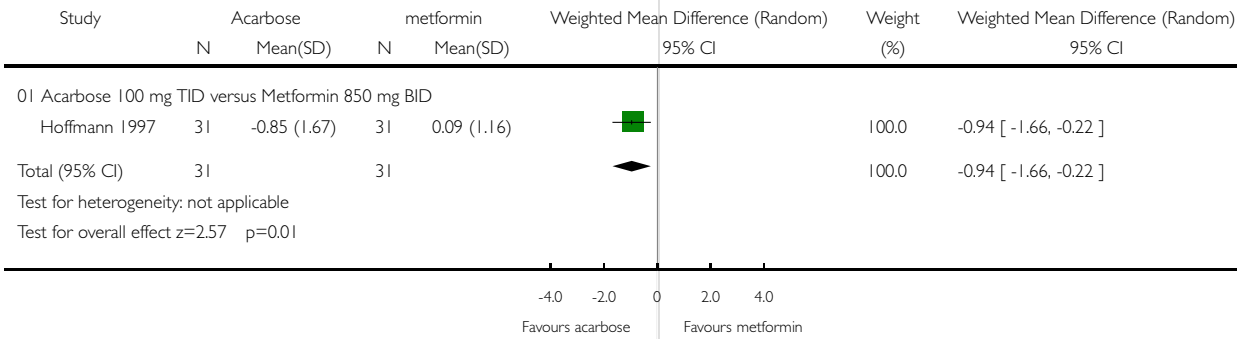


Fig. 48. Comparison 03. Acarbose versus Metformin

03.05 Change in HDL-cholesterol (mmol/l)

Review: Alpha-glucosidase inhibitors for type 2 diabetes mellitus

Comparison: 03 Acarbose versus Metformin

Outcome: 05 Change in HDL-cholesterol (mmol/l)

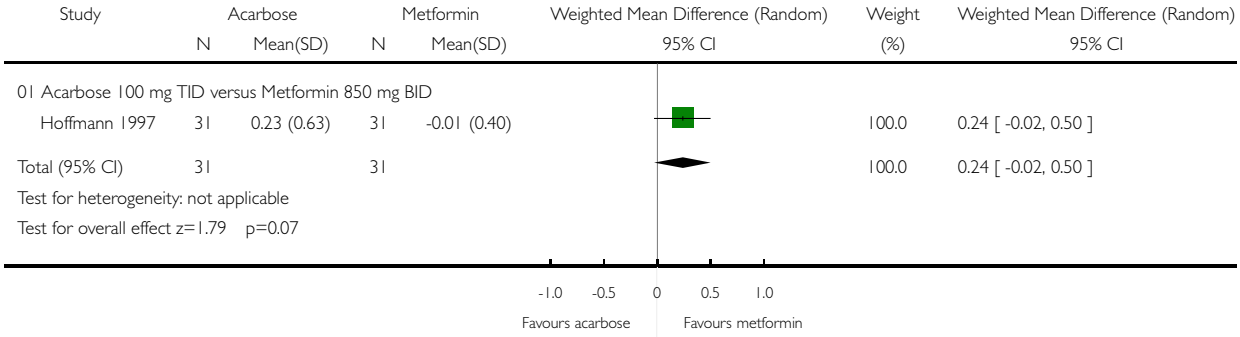


Fig. 49. Comparison 03. Acarbose versus Metformin

03.06 Change in LDL-cholesterol (mmol/l)

Review: Alpha-glucosidase inhibitors for type 2 diabetes mellitus

Comparison: 03 Acarbose versus Metformin

Outcome: 06 Change in LDL-cholesterol (mmol/l)

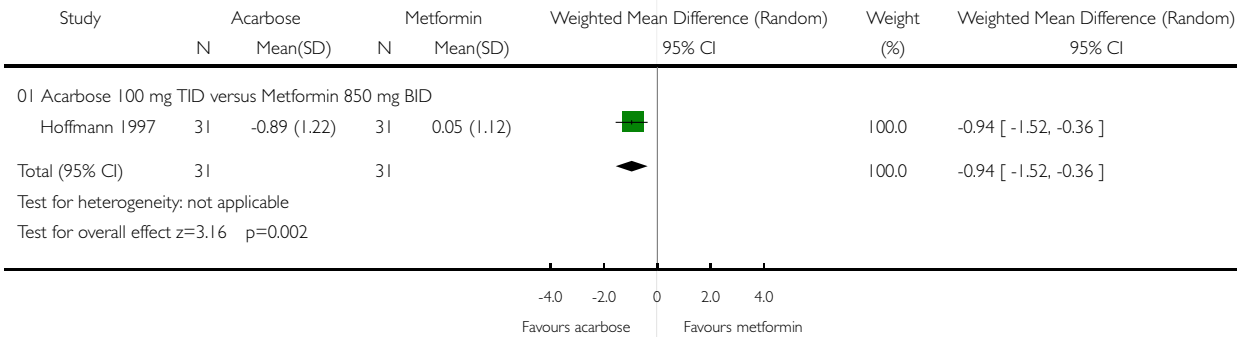


Fig. 50. Comparison 03. Acarbose versus Metformin

03.07 Change in triglycerides (mmol/l)

Review: Alpha-glucosidase inhibitors for type 2 diabetes mellitus

Comparison: 03 Acarbose versus Metformin

Outcome: 07 Change in triglycerides (mmol/l)

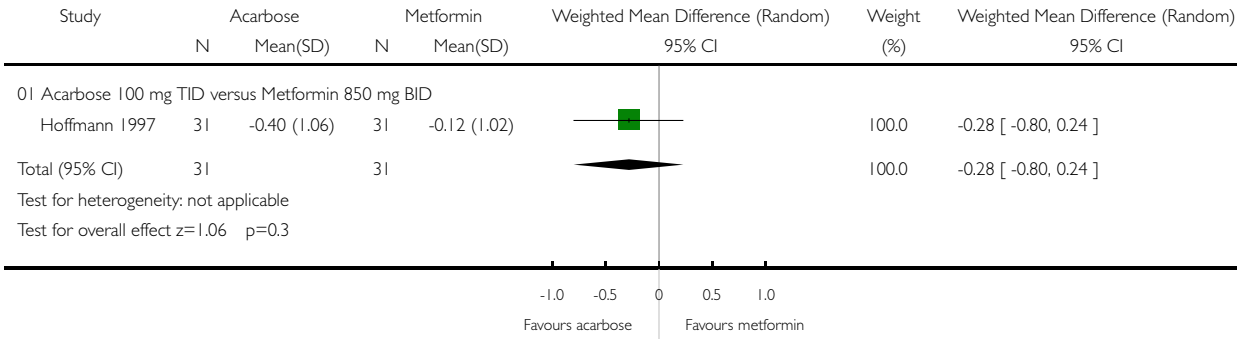


Fig. 51. Comparison 03. Acarbose versus Metformin

03.08 Change in fasting insulin levels (pmol/l)

Review: Alpha-glucosidase inhibitors for type 2 diabetes mellitus

Comparison: 03 Acarbose versus Metformin

Outcome: 08 Change in fasting insulin levels (pmol/l)

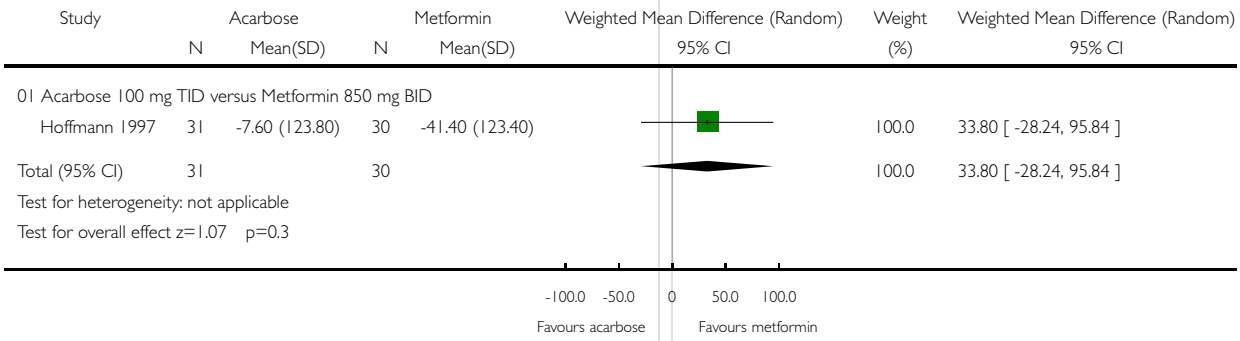


Fig. 52. Comparison 03. Acarbose versus Metformin

03.09 Change in post-load insulin levels (pmol/l)

Review: Alpha-glucosidase inhibitors for type 2 diabetes mellitus

Comparison: 03 Acarbose versus Metformin

Outcome: 09 Change in post-load insulin levels (pmol/l)

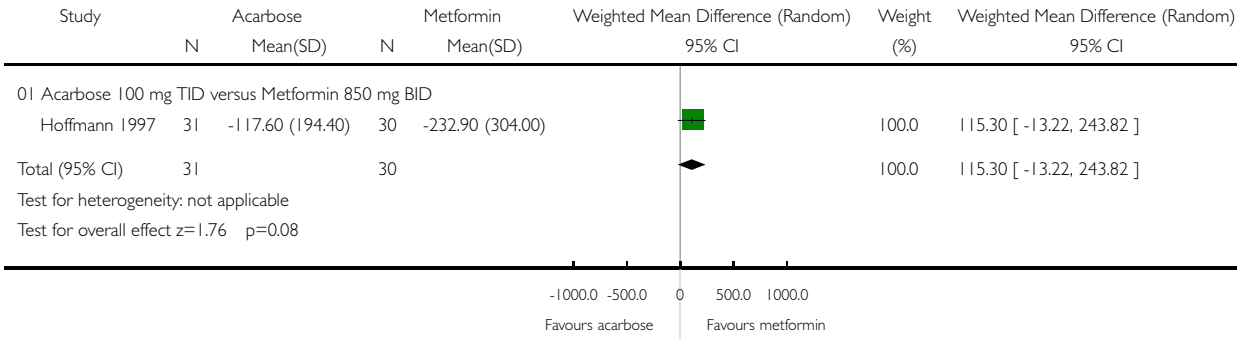


Fig. 53. Comparison 03. Acarbose versus Metformin

03.12 Change in body weight (Kg)

Review: Alpha-glucosidase inhibitors for type 2 diabetes mellitus

Comparison: 03 Acarbose versus Metformin

Outcome: 12 Change in body weight (Kg)

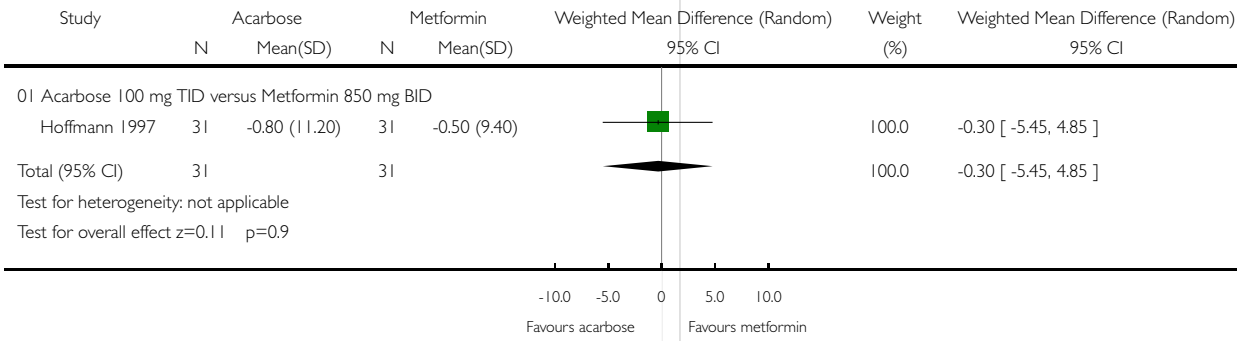


Fig. 54. Comparison 03. Acarbose versus Metformin

03.30 Occurence of adverse effects

Review: Alpha-glucosidase inhibitors for type 2 diabetes mellitus

Comparison: 03 Acarbose versus Metformin

Outcome: 30 Occurence of adverse effects

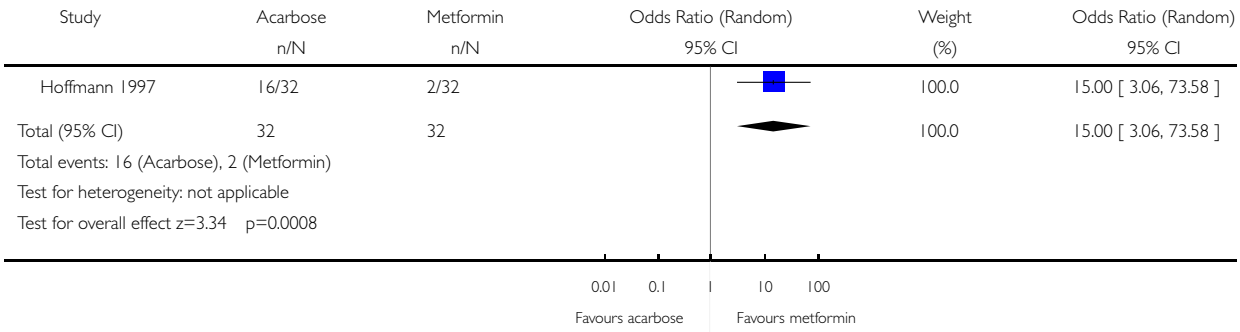


Fig. 55. Comparison 04. Acarbose versus nateglinide / repaglinide

04.01 Change in glycated haemoglobin (%)

Review: Alpha-glucosidase inhibitors for type 2 diabetes mellitus

Comparison: 04 Acarbose versus nateglinide / repaglinide

Outcome: 01 Change in glycated haemoglobin (%)

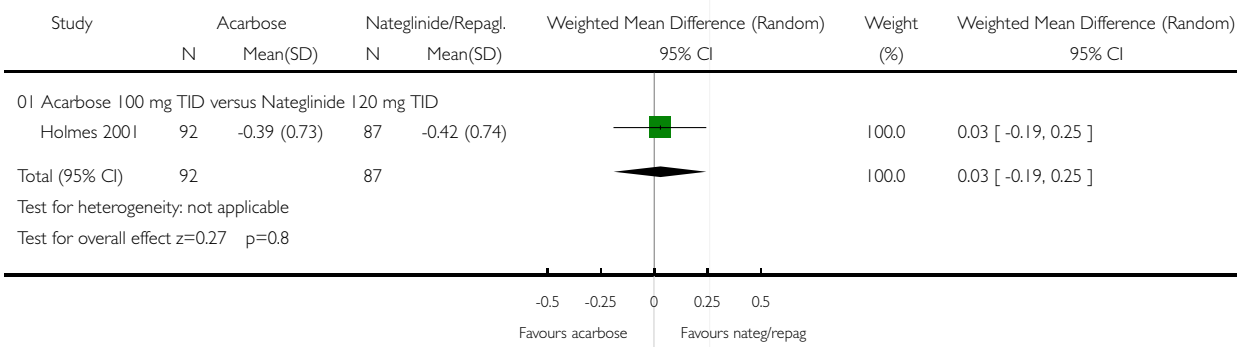


Fig. 56. Comparison 04. Acarbose versus nateglinide / repaglinide

04.02 Change in fasting blood glucose (mmol/l)

Review: Alpha-glucosidase inhibitors for type 2 diabetes mellitus

Comparison: 04 Acarbose versus nateglinide / repaglinide

Outcome: 02 Change in fasting blood glucose (mmol/l)

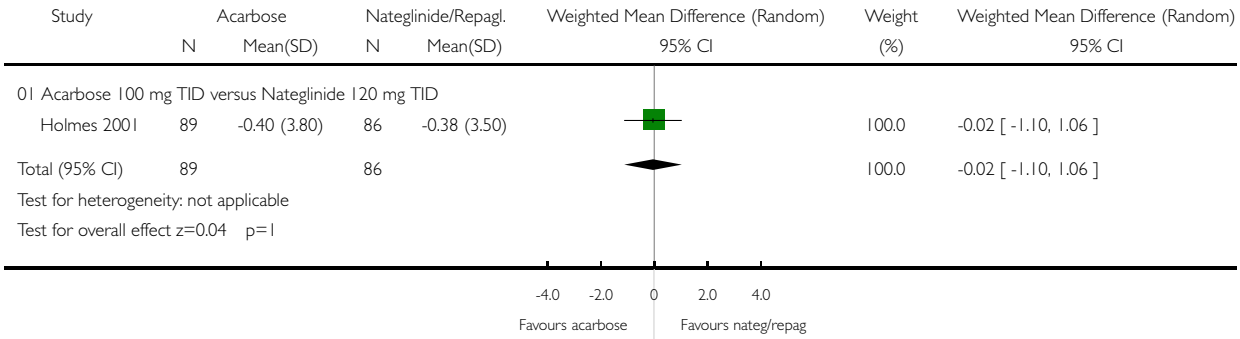


Fig. 57. Comparison 04. Acarbose versus nateglinide / repaglinide

04.12 Change in body weight (Kg)

Review: Alpha-glucosidase inhibitors for type 2 diabetes mellitus

Comparison: 04 Acarbose versus nateglinide / repaglinide

Outcome: 12 Change in body weight (Kg)

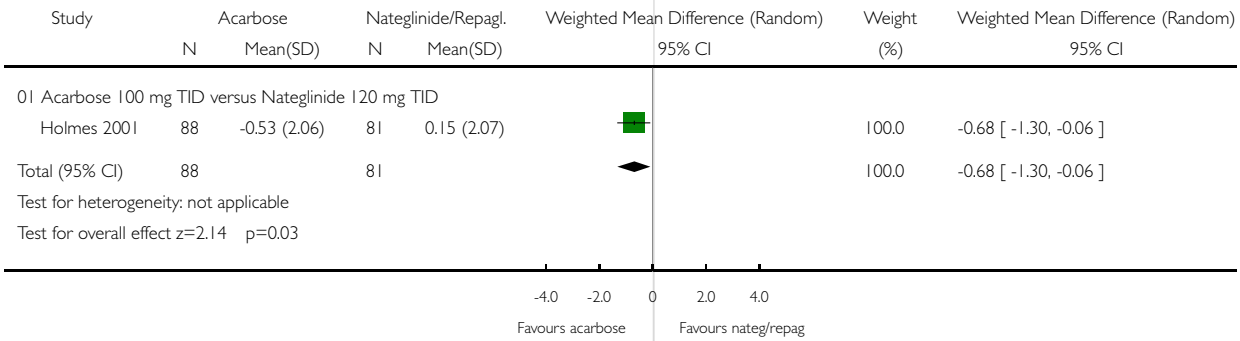


Fig. 58. Comparison 04. Acarbose versus nateglinide / repaglinide

04.30 Occurence of adverse effects

Review: Alpha-glucosidase inhibitors for type 2 diabetes mellitus

Comparison: 04 Acarbose versus nateglinide / repaglinide

Outcome: 30 Occurence of adverse effects

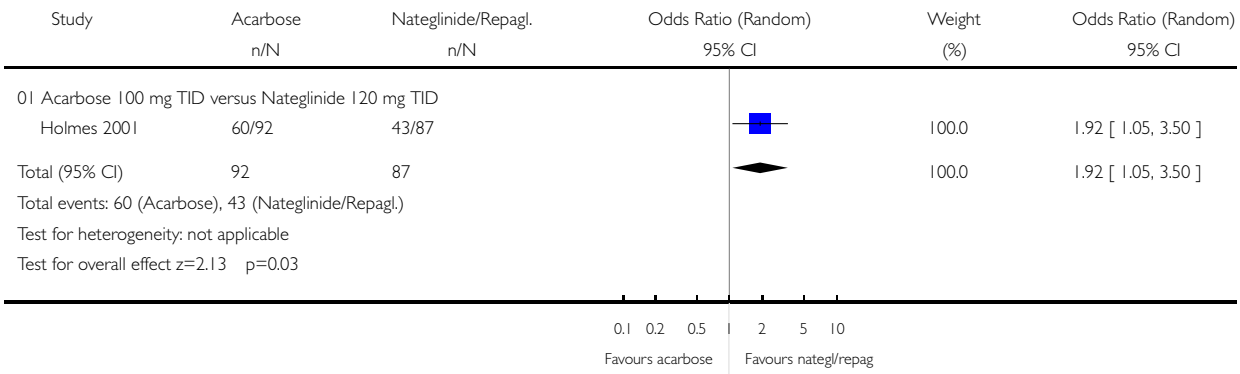


Fig. 59. Comparison 04. Acarbose versus nateglinide / repaglinide

04.31 Occurence of gastro-intestinal adverse effects

Review: Alpha-glucosidase inhibitors for type 2 diabetes mellitus

Comparison: 04 Acarbose versus nateglinide / repaglinide

Outcome: 31 Occurence of gastro-intestinal adverse effects

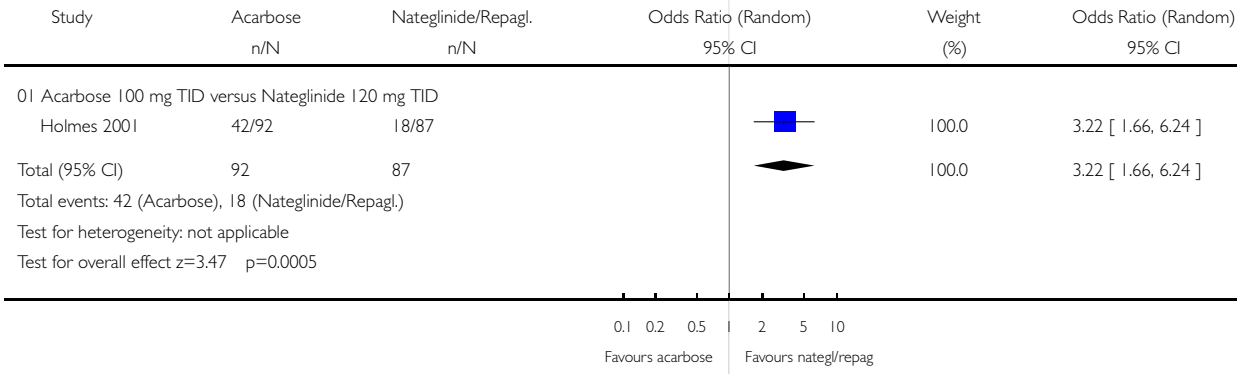


Fig. 60. Comparison 05. Miglitol versus placebo

05.01 Change in glycated haemoglobin (%)

Review: Alpha-glucosidase inhibitors for type 2 diabetes mellitus

Comparison: 05 Miglitol versus placebo

Outcome: 01 Change in glycated haemoglobin (%)

Study	Miglitol N	Miglitol Mean(SD)	Placebo N	Placebo Mean(SD)	Weighted Mean Difference (Random) 95% CI	Weight (%)	Weighted Mean Difference (Random) 95% CI
02 Miglitol 25 mg TID							
Drent 2002	84	-0.06 (1.00)	87	0.40 (1.50)		15.1	-0.46 [-0.84, -0.08]
Subtotal (95% CI)	84		87			15.1	-0.46 [-0.84, -0.08]
Test for heterogeneity: not applicable							
Test for overall effect z=2.37 p=0.02							
05 Miglitol 50 mg TID							
Drent 2002	84	0.02 (1.50)	87	0.40 (1.50)		13.2	-0.38 [-0.83, 0.07]
Kawamori 2003	158	-0.35 (0.50)	84	0.25 (0.64)		21.5	-0.60 [-0.76, -0.44]
Subtotal (95% CI)	242		171			34.7	-0.58 [-0.72, -0.43]
Test for heterogeneity chi-square=0.82 df=1 p=0.37 I^2 =0.0%							
Test for overall effect z=7.59 p<0.00001							
10 Miglitol 100 mg TID							
Chiasson 2001	80	0.02 (0.90)	82	0.38 (1.10)		17.2	-0.36 [-0.67, -0.05]
Drent 2002	71	-0.46 (0.90)	87	0.40 (1.50)		15.2	-0.86 [-1.24, -0.48]
Johnston 1998b	30	-0.84 (1.10)	9	1.00 (1.80)		3.4	-1.84 [-3.08, -0.60]
Subtotal (95% CI)	181		178			35.8	-0.79 [-1.35, -0.22]
Test for heterogeneity chi-square=7.97 df=2 p=0.02 I^2 =74.9%							
Test for overall effect z=2.71 p=0.007							
20 Miglitol 200 mg TID							
Drent 2002	58	-0.86 (1.00)	87	0.40 (1.50)		14.4	-1.26 [-1.67, -0.85]
Subtotal (95% CI)	58		87			14.4	-1.26 [-1.67, -0.85]
Test for heterogeneity: not applicable							
Test for overall effect z=6.07 p<0.00001							
Total (95% CI)	565		523			100.0	-0.68 [-0.93, -0.44]
Test for heterogeneity chi-square=19.30 df=6 p=0.004 I^2 =68.9%							
Test for overall effect z=5.44 p<0.00001							

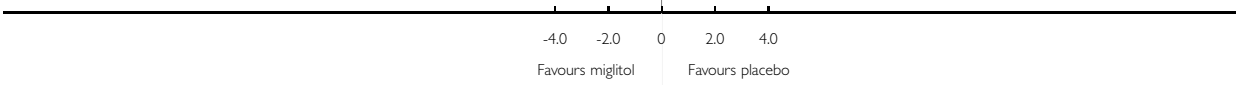


Fig. 61. Comparison 05. Miglitol versus placebo

05.02 Change in fasting blood glucose (mmol/l)

Review: Alpha-glucosidase inhibitors for type 2 diabetes mellitus

Comparison: 05 Miglitol versus placebo

Outcome: 02 Change in fasting blood glucose (mmol/l)

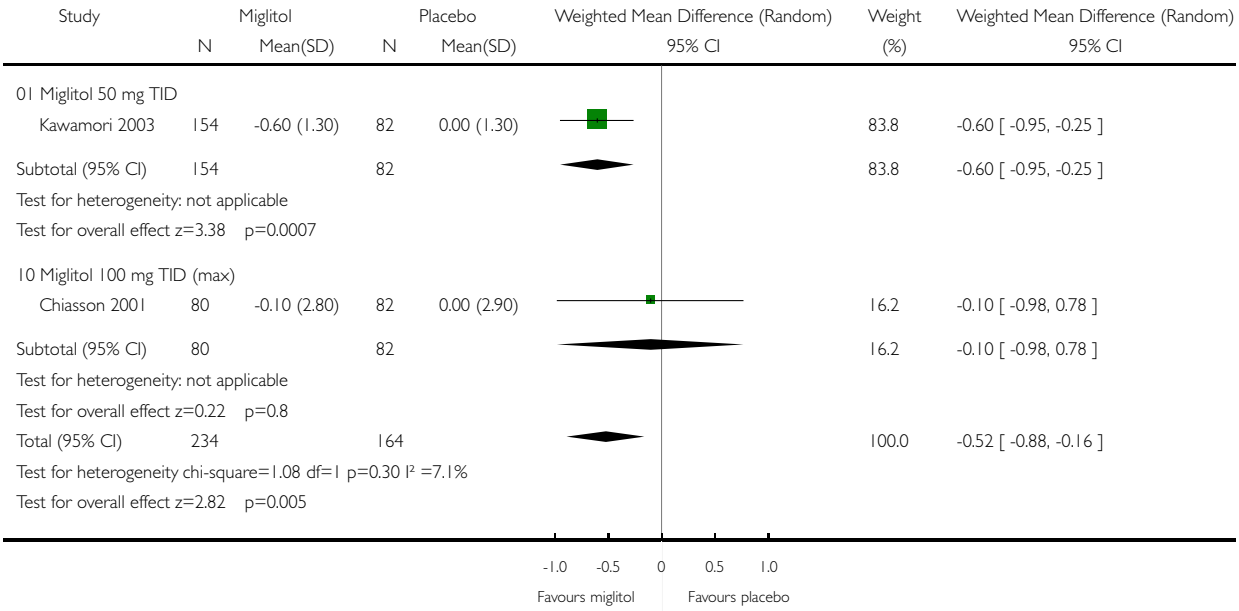


Fig. 62. Comparison 05. Miglitol versus placebo

05.03 Change in post-load blood glucose (mmol/l)

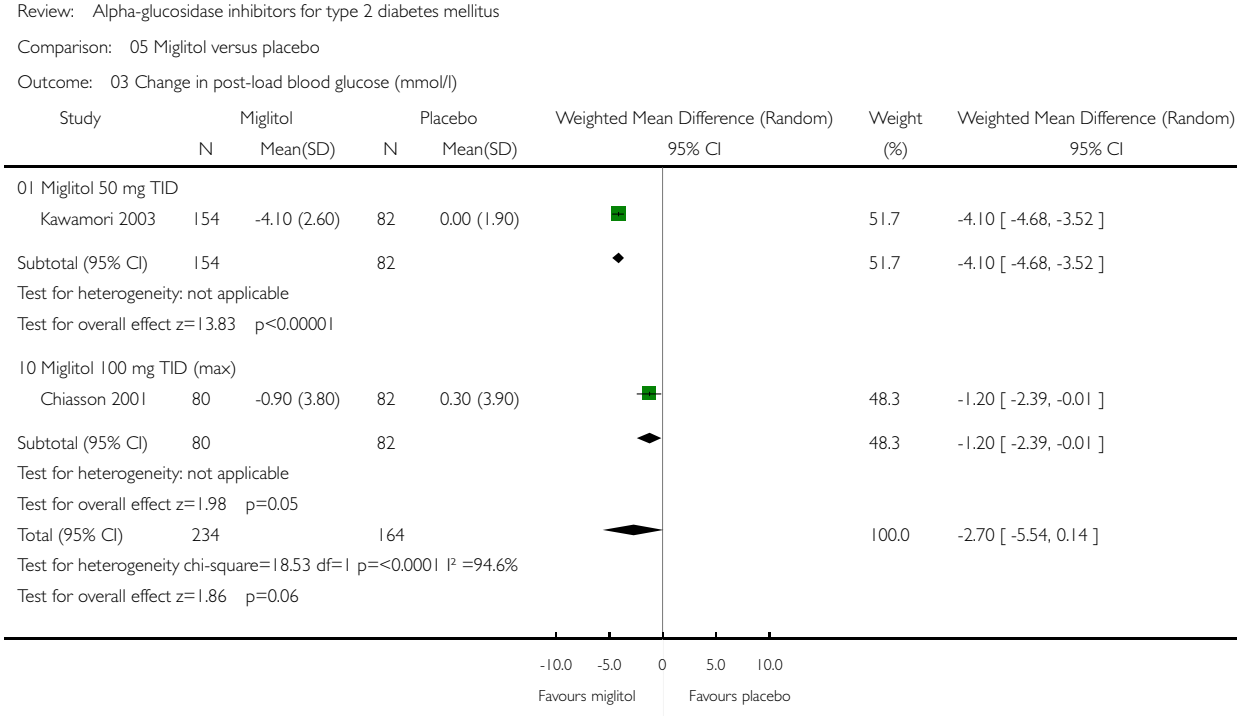


Fig. 63. Comparison 05. Miglitol versus placebo

05.08 Change in fasting insulin levels (pmol/l)

Review: Alpha-glucosidase inhibitors for type 2 diabetes mellitus

Comparison: 05 Miglitol versus placebo

Outcome: 08 Change in fasting insulin levels (pmol/l)

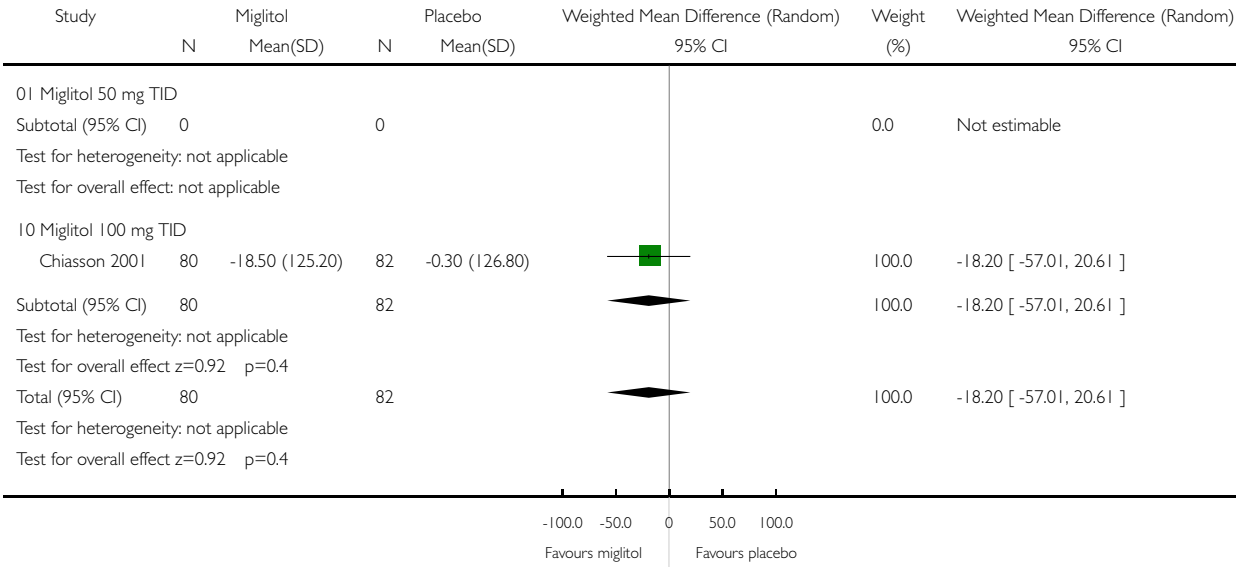


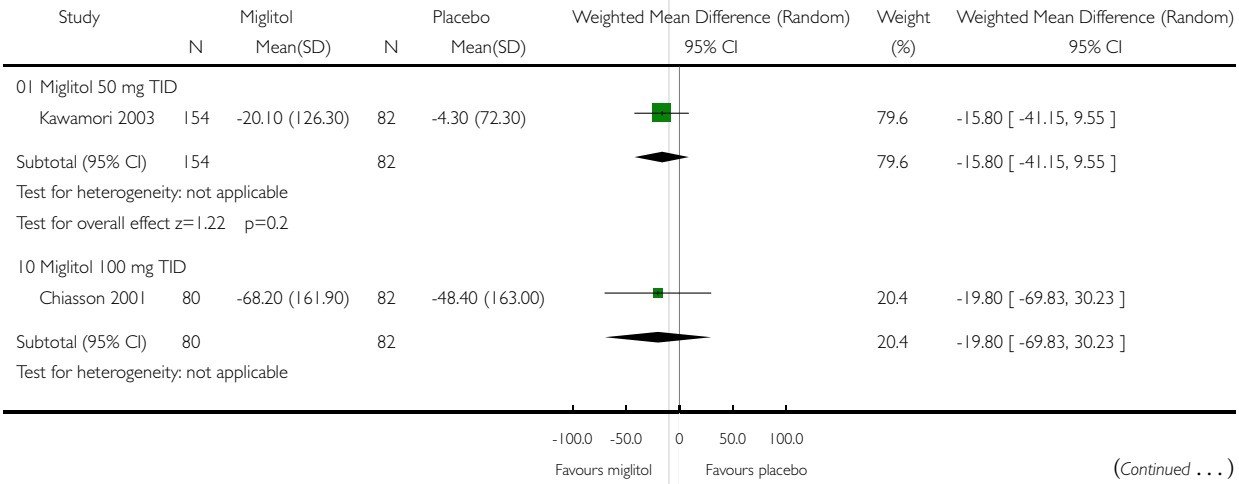
Fig. 64. Comparison 05. Miglitol versus placebo

05.09 Change in post-load insulin levels (pmol/l)

Review: Alpha-glucosidase inhibitors for type 2 diabetes mellitus

Comparison: 05 Miglitol versus placebo

Outcome: 09 Change in post-load insulin levels (pmol/l)



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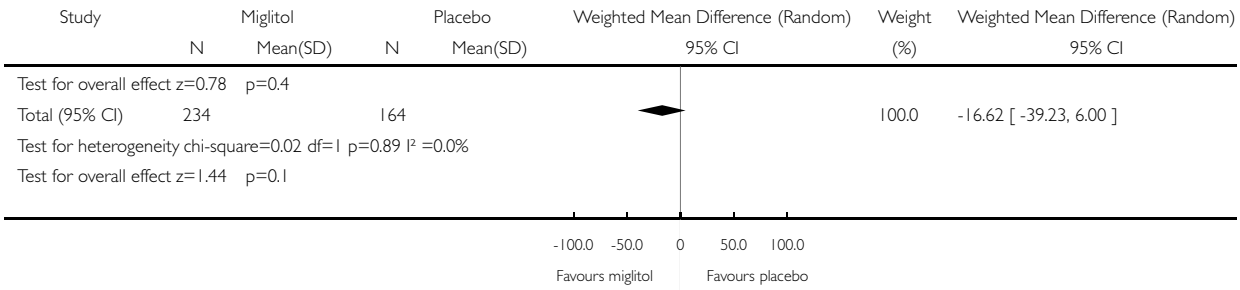

Fig. 65. Comparison 05. Miglitol versus placebo

05.12 Change in body weight (Kg)

Review: Alpha-glucosidase inhibitors for type 2 diabetes mellitus

Comparison: 05 Miglitol versus placebo

Outcome: 12 Change in body weight (Kg)

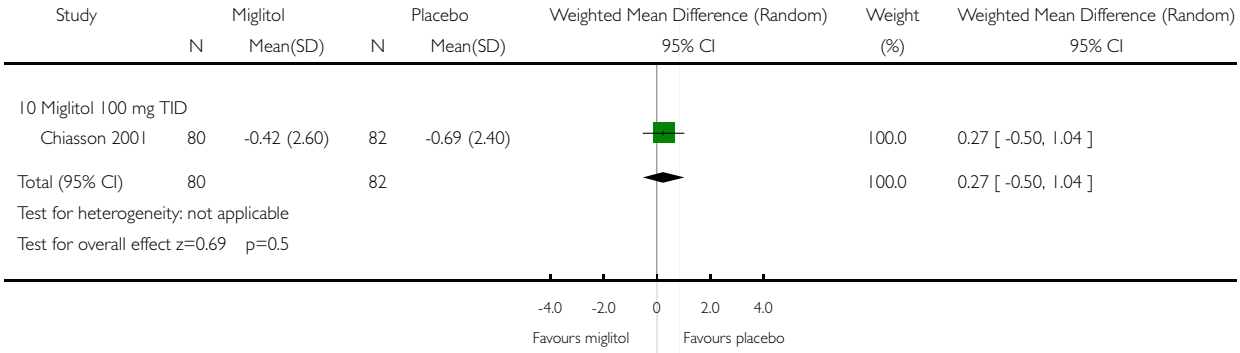

Fig. 66. Comparison 05. Miglitol versus placebo

05.15 Total deaths

Review: Alpha-glucosidase inhibitors for type 2 diabetes mellitus

Comparison: 05 Miglitol versus placebo

Outcome: 15 Total deaths

Study	Miglitol n/N	Placebo n/N	Odds Ratio (Random) 95% CI	Weight (%)	Odds Ratio (Random) 95% CI
02 Miglitol 25 mg TID					
Johnston 1998	1/104	0/101		50.0	2.94 [0.12, 73.07]
Subtotal (95% CI)	104	101		50.0	2.94 [0.12, 73.07]
Total events: 1 (Miglitol), 0 (Placebo)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.66 p=0.5					
05 Miglitol 50 mg TID					
Johnston 1998	1/102	0/101		50.0	3.00 [0.12, 74.52]
Subtotal (95% CI)	102	101		50.0	3.00 [0.12, 74.52]
Total events: 1 (Miglitol), 0 (Placebo)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.67 p=0.5					
Total (95% CI)	206	202		100.0	2.97 [0.31, 28.80]
Total events: 2 (Miglitol), 0 (Placebo)					
Test for heterogeneity chi-square=0.00 df=1 p=0.99 I^2 =0.0%					
Test for overall effect z=0.94 p=0.3					

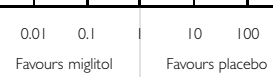

Fig. 67. Comparison 05. Miglitol versus placebo

05.16 Disease related deaths

Review: Alpha-glucosidase inhibitors for type 2 diabetes mellitus

Comparison: 05 Miglitol versus placebo

Outcome: 16 Disease related deaths

Study	Miglitol n/N	Placebo n/N	Odds Ratio (Random) 95% CI	Weight (%)	Odds Ratio (Random) 95% CI
02 Miglitol 25 mg TID					
Johnston 1998	1/104	0/101		100.0	2.94 [0.12, 73.07]
Subtotal (95% CI)	104	101		100.0	2.94 [0.12, 73.07]
Total events: 1 (Miglitol), 0 (Placebo)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.66 p=0.5					
05 Miglitol 50 mg TID					
× Johnston 1998	0/102	0/101		0.0	Not estimable
Subtotal (95% CI)	102	101		0.0	Not estimable
Total events: 0 (Miglitol), 0 (Placebo)					
Test for heterogeneity: not applicable					
Test for overall effect: not applicable					
Total (95% CI)	206	202		100.0	2.94 [0.12, 73.07]
Total events: 1 (Miglitol), 0 (Placebo)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.66 p=0.5					

Fig. 68. Comparison 05. Miglitol versus placebo

05.30 Occurence of adverse effects

Review: Alpha-glucosidase inhibitors for type 2 diabetes mellitus

Comparison: 05 Miglitol versus placebo

Outcome: 30 Occurence of adverse effects

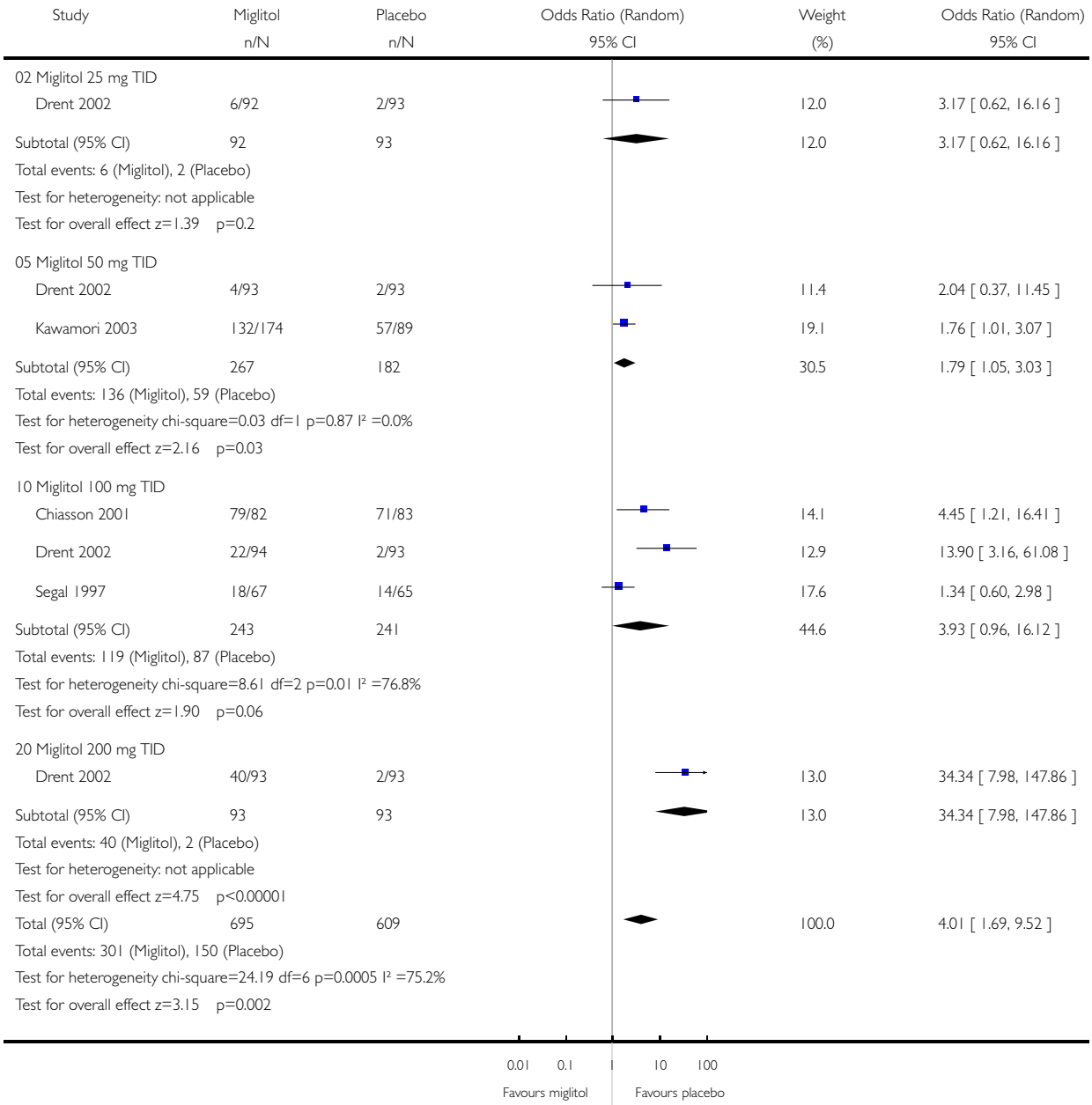

Fig. 69. Comparison 05. Miglitol versus placebo

05.31 Occurence of gastro-intestinal adverse effects

Review: Alpha-glucosidase inhibitors for type 2 diabetes mellitus

Comparison: 05 Miglitol versus placebo

Outcome: 31 Occurence of gastro-intestinal adverse effects

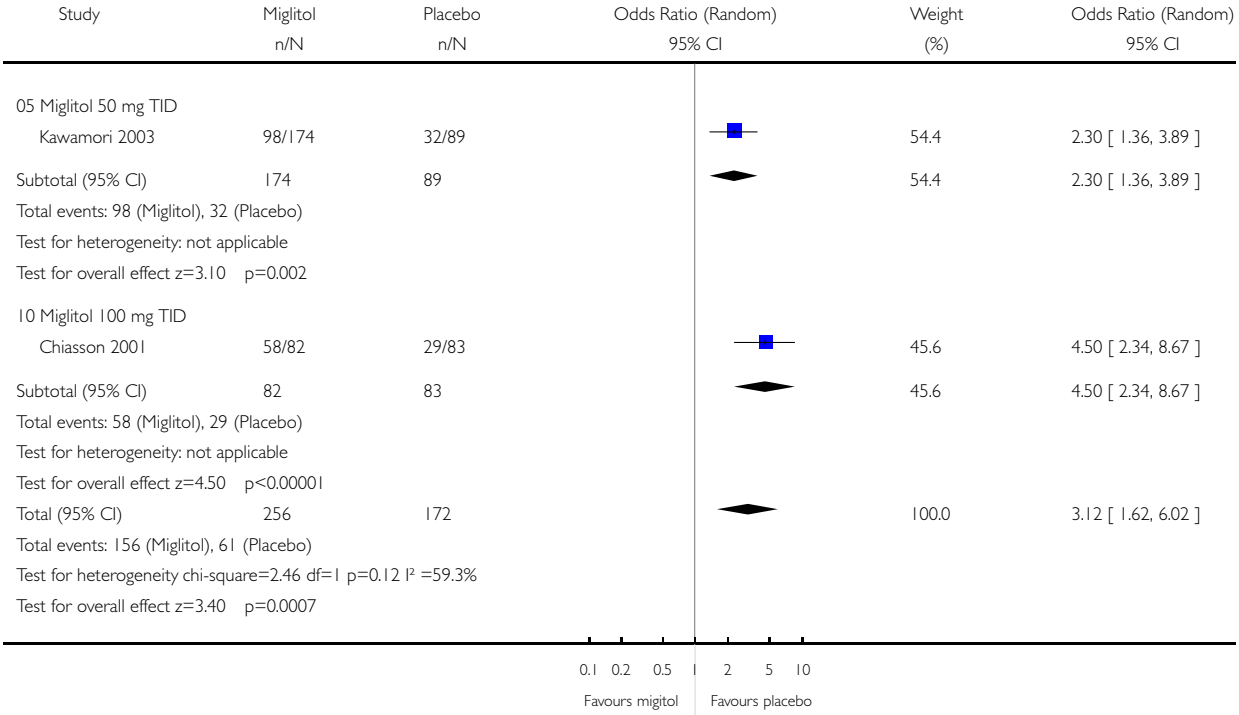

Fig. 70. Comparison 05. Miglitol versus placebo

05.90 Change in post-load blood glucose (mmol/l) (2-hours)

Review: Alpha-glucosidase inhibitors for type 2 diabetes mellitus

Comparison: 05 Miglitol versus placebo

Outcome: 90 Change in post-load blood glucose (mmol/l) (2-hours)

Study	Treatment N	Treatment Mean(SD)	Control N	Control Mean(SD)	Weighted Mean Difference (Random) 95% CI	Weight (%)	Weighted Mean Difference (Random) 95% CI
01 Miglitol 50 mg TID							
Kawamori 2003	154	-1.50 (2.70)	82	0.20 (2.30)		79.9	-1.70 [-2.36, -1.04]
Subtotal (95% CI)	154		82			79.9	-1.70 [-2.36, -1.04]
Test for heterogeneity: not applicable							
Test for overall effect z=5.08 p<0.00001							
02 Miglitol 100 mg TID (max)							
Chiasson 2001	80	-1.30 (4.20)	82	0.20 (4.30)		20.1	-1.50 [-2.81, -0.19]
Subtotal (95% CI)	80		82			20.1	-1.50 [-2.81, -0.19]
Test for heterogeneity: not applicable							
Test for overall effect z=2.25 p=0.02							
Total (95% CI)	234		164			100.0	-1.66 [-2.25, -1.07]
Test for heterogeneity chi-square=0.07 df=1 p=0.79 I^2 =0.0%							
Test for overall effect z=5.55 p<0.00001							

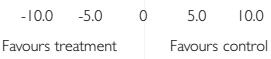

Fig. 71. Comparison 05. Miglitol versus placebo

05.91 Change in post-load insulin levels (pmol/l) (2-hours)

Review: Alpha-glucosidase inhibitors for type 2 diabetes mellitus

Comparison: 05 Miglitol versus placebo

Outcome: 91 Change in post-load insulin levels (pmol/l) (2-hours)

Study	Treatment N	Treatment Mean(SD)	Control N	Control Mean(SD)	Weighted Mean Difference (Random) 95% CI	Weight (%)	Weighted Mean Difference (Random) 95% CI
01 Miglitol 50 mg TID							
Kawamori 2003	154	-20.10 (126.30)	82	-4.30 (72.30)		81.8	-15.80 [-41.15, 9.55]
Subtotal (95% CI)	154		82			81.8	-15.80 [-41.15, 9.55]
Test for heterogeneity: not applicable							
Test for overall effect z=1.22 p=0.2							
02 Miglitol 100 mg TID							
Chiasson 2001	80	-63.60 (177.10)	82	-48.40 (172.10)		18.2	-15.20 [-68.99, 38.59]
Subtotal (95% CI)	80		82			18.2	-15.20 [-68.99, 38.59]
Test for heterogeneity: not applicable							
Test for overall effect z=0.55 p=0.6							
Total (95% CI)	234		164			100.0	-15.69 [-38.62, 7.24]
Test for heterogeneity chi-square=0.00 df=1 p=0.98 I^2 =0.0%							
Test for overall effect z=1.34 p=0.2							

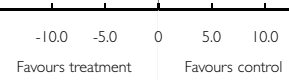

Fig. 72. Comparison 06. Miglitol versus sulphonylurea (SU)

06.01 Change in glycated haemoglobin (%)

Review: Alpha-glucosidase inhibitors for type 2 diabetes mellitus

Comparison: 06 Miglitol versus sulphonylurea (SU)

Outcome: 01 Change in glycated haemoglobin (%)

Study	Miglitol N	Miglitol Mean(SD)	Sulphonylurea N	Sulphonylurea Mean(SD)	Weighted Mean Difference (Random) 95% CI	Weight (%)	Weighted Mean Difference (Random) 95% CI
01 Miglitol 100 mg TID versus Glibenclamide 5 mg BID							
Pagano 1995	45	-0.78 (1.40)	45	-1.18 (1.30)		100.0	0.40 [-0.16, 0.96]
Total (95% CI)	45		45			100.0	0.40 [-0.16, 0.96]
Test for heterogeneity: not applicable							
Test for overall effect z=1.40 p=0.2							

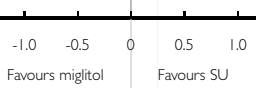

Fig. 73. Comparison 06. Miglitol versus sulphonylurea (SU)

06.02 Change in fasting blood glucose (mmol/l)

Review: Alpha-glucosidase inhibitors for type 2 diabetes mellitus

Comparison: 06 Miglitol versus sulphonylurea (SU)

Outcome: 02 Change in fasting blood glucose (mmol/l)

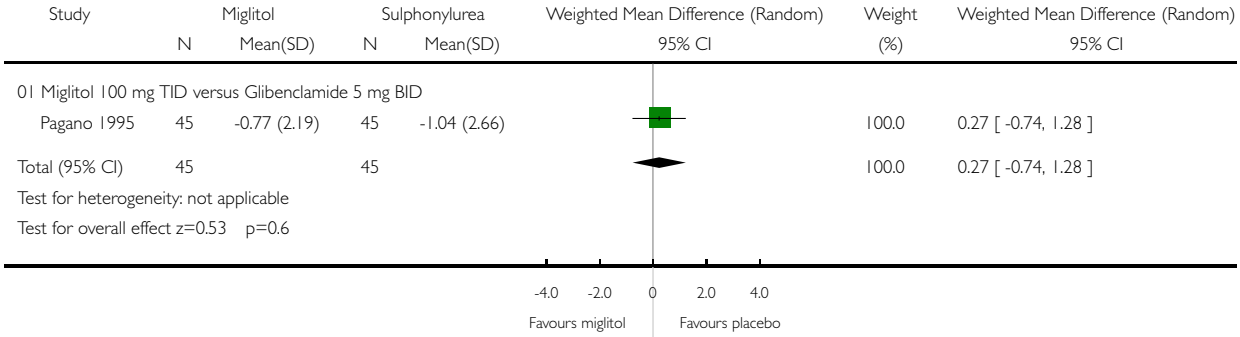

Fig. 74. Comparison 06. Miglitol versus sulphonylurea (SU)

06.03 Change in post-load blood glucose (mmol/l)

Review: Alpha-glucosidase inhibitors for type 2 diabetes mellitus

Comparison: 06 Miglitol versus sulphonylurea (SU)

Outcome: 03 Change in post-load blood glucose (mmol/l)

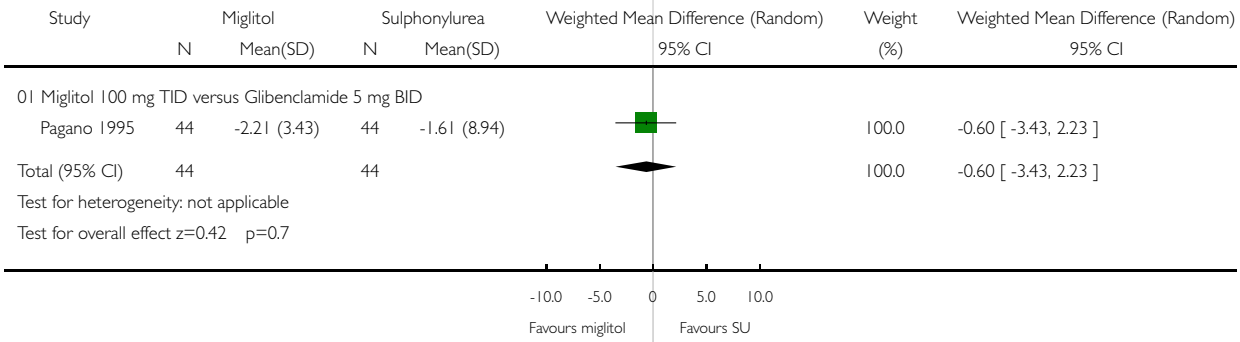

Fig. 75. Comparison 06. Miglitol versus sulphonylurea (SU)

06.04 Change in total cholesterol (mmol/l)

Review: Alpha-glucosidase inhibitors for type 2 diabetes mellitus

Comparison: 06 Miglitol versus sulphonylurea (SU)

Outcome: 04 Change in total cholesterol (mmol/l)

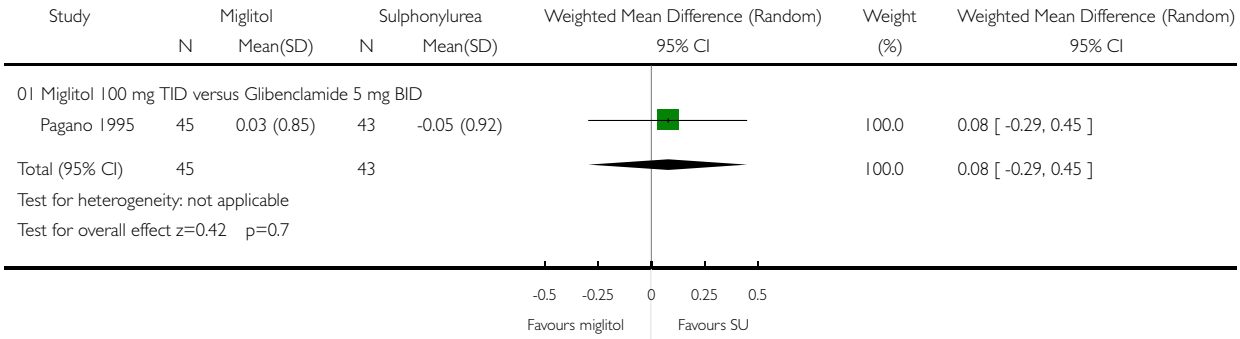

Fig. 76. Comparison 06. Miglitol versus sulphonylurea (SU)

06.05 Change in HDL-cholesterol (mmol/l)

Review: Alpha-glucosidase inhibitors for type 2 diabetes mellitus

Comparison: 06 Miglitol versus sulphonylurea (SU)

Outcome: 05 Change in HDL-cholesterol (mmol/l)

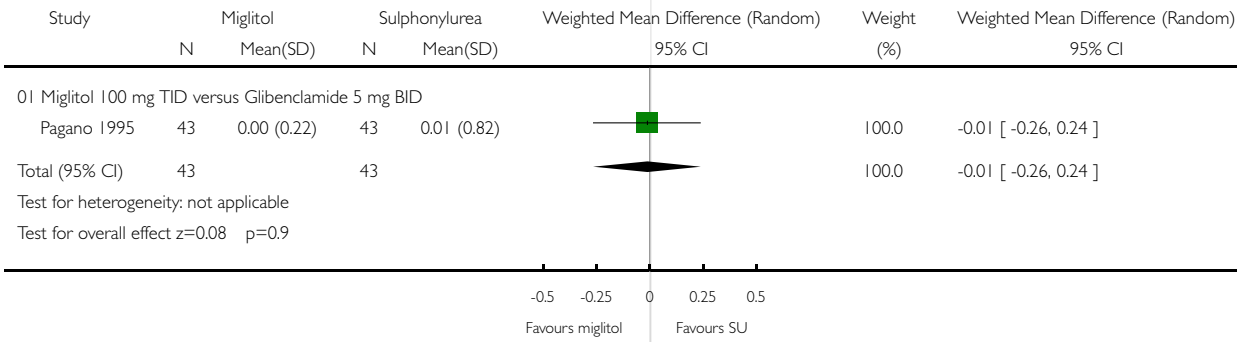

Fig. 77. Comparison 06. Miglitol versus sulphonylurea (SU)

06.07 Change in triglycerides (mmol/l)

Review: Alpha-glucosidase inhibitors for type 2 diabetes mellitus

Comparison: 06 Miglitol versus sulphonylurea (SU)

Outcome: 07 Change in triglycerides (mmol/l)

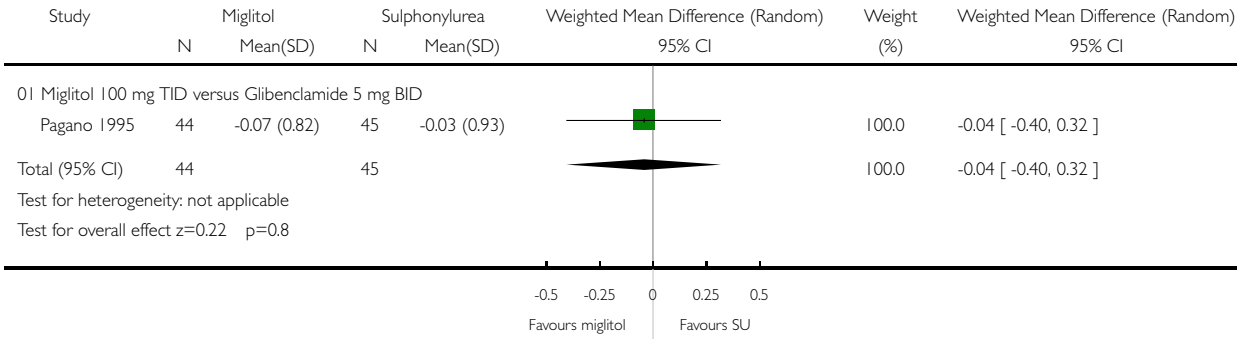

Fig. 78. Comparison 06. Miglitol versus sulphonylurea (SU)

06.08 Change in fasting insulin levels (pmol/l)

Review: Alpha-glucosidase inhibitors for type 2 diabetes mellitus

Comparison: 06 Miglitol versus sulphonylurea (SU)

Outcome: 08 Change in fasting insulin levels (pmol/l)

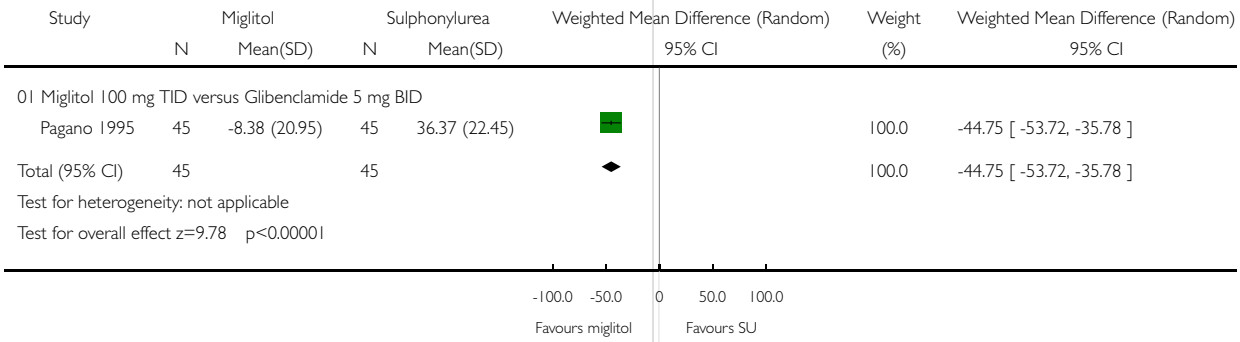

Fig. 79. Comparison 06. Miglitol versus sulphonylurea (SU)

06.12 Change in body weight (Kg)

Review: Alpha-glucosidase inhibitors for type 2 diabetes mellitus
Comparison: 06 Miglitol versus sulphonylurea (SU)
Outcome: 12 Change in body weight (Kg)

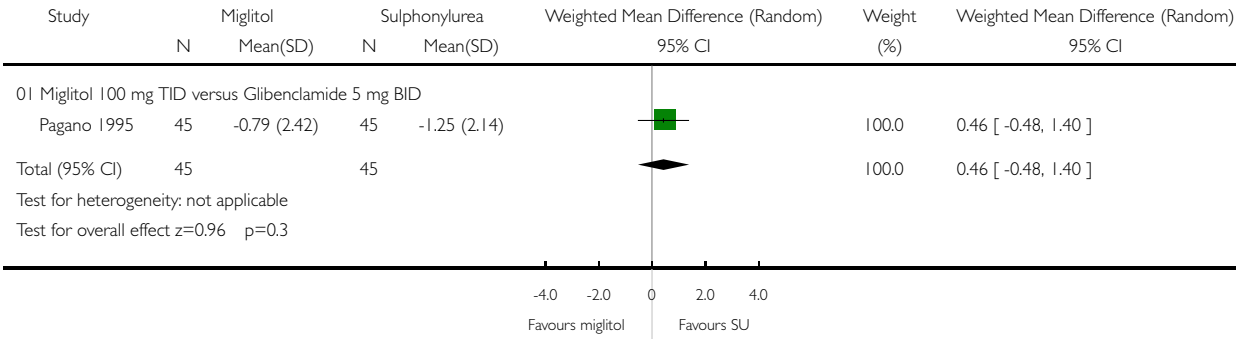

Fig. 80. Comparison 06. Miglitol versus sulphonylurea (SU)

06.15 Total deaths

Review: Alpha-glucosidase inhibitors for type 2 diabetes mellitus
Comparison: 06 Miglitol versus sulphonylurea (SU)
Outcome: 15 Total deaths

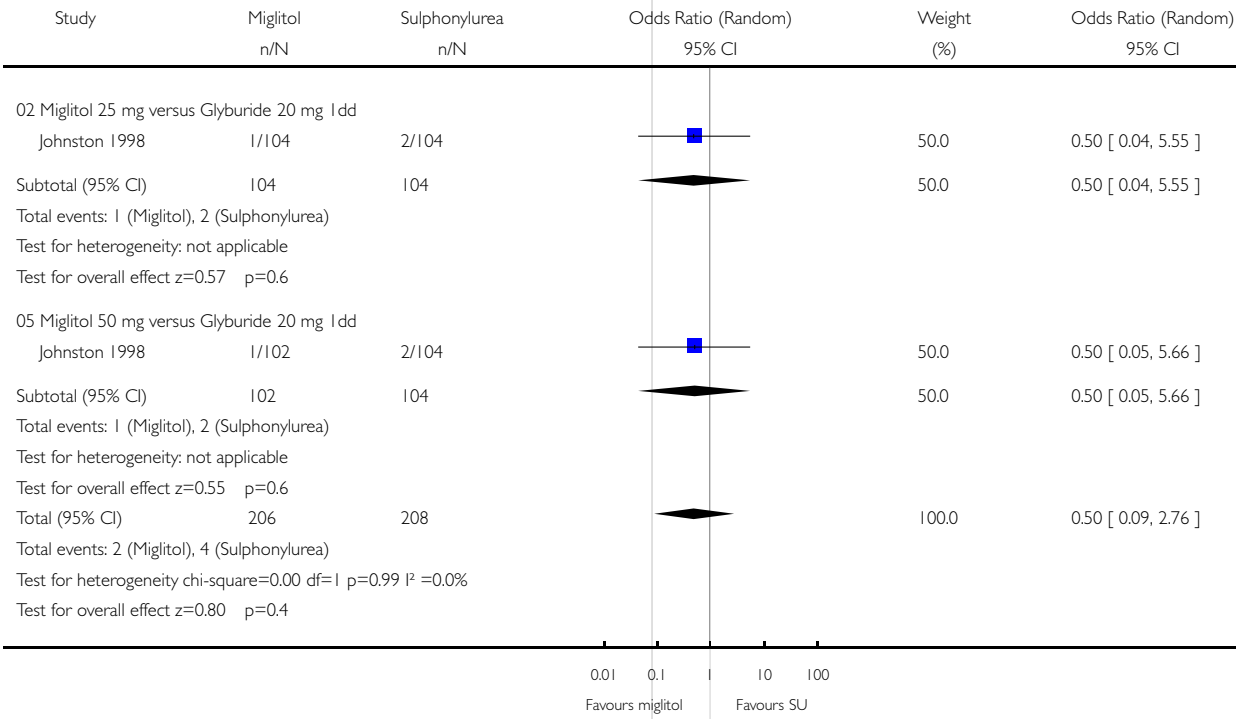

Fig. 81. Comparison 06. Miglitol versus sulphonylurea (SU)

06.16 Disease related deaths

Review: Alpha-glucosidase inhibitors for type 2 diabetes mellitus

Comparison: 06 Miglitol versus sulphonylurea (SU)

Outcome: 16 Disease related deaths

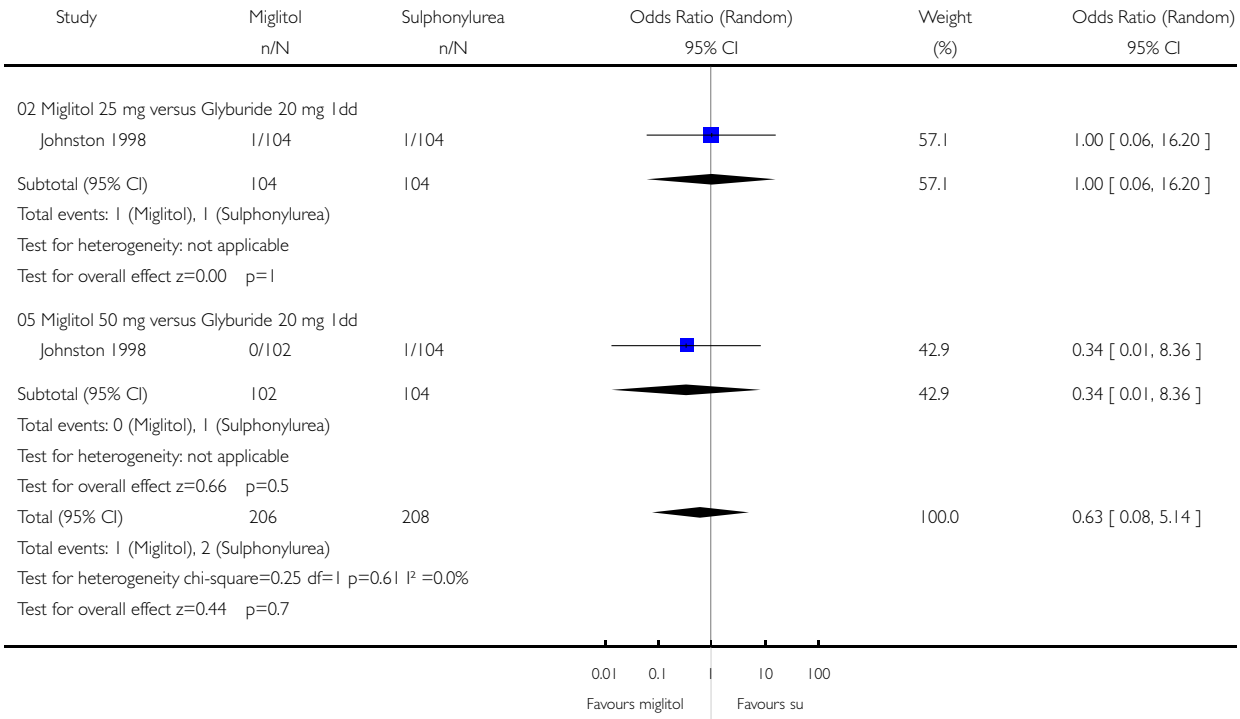

Fig. 82. Comparison 06. Miglitol versus sulphonylurea (SU)

06.30 Occurence of adverse effects

Review: Alpha-glucosidase inhibitors for type 2 diabetes mellitus

Comparison: 06 Miglitol versus sulphonylurea (SU)

Outcome: 30 Occurence of adverse effects

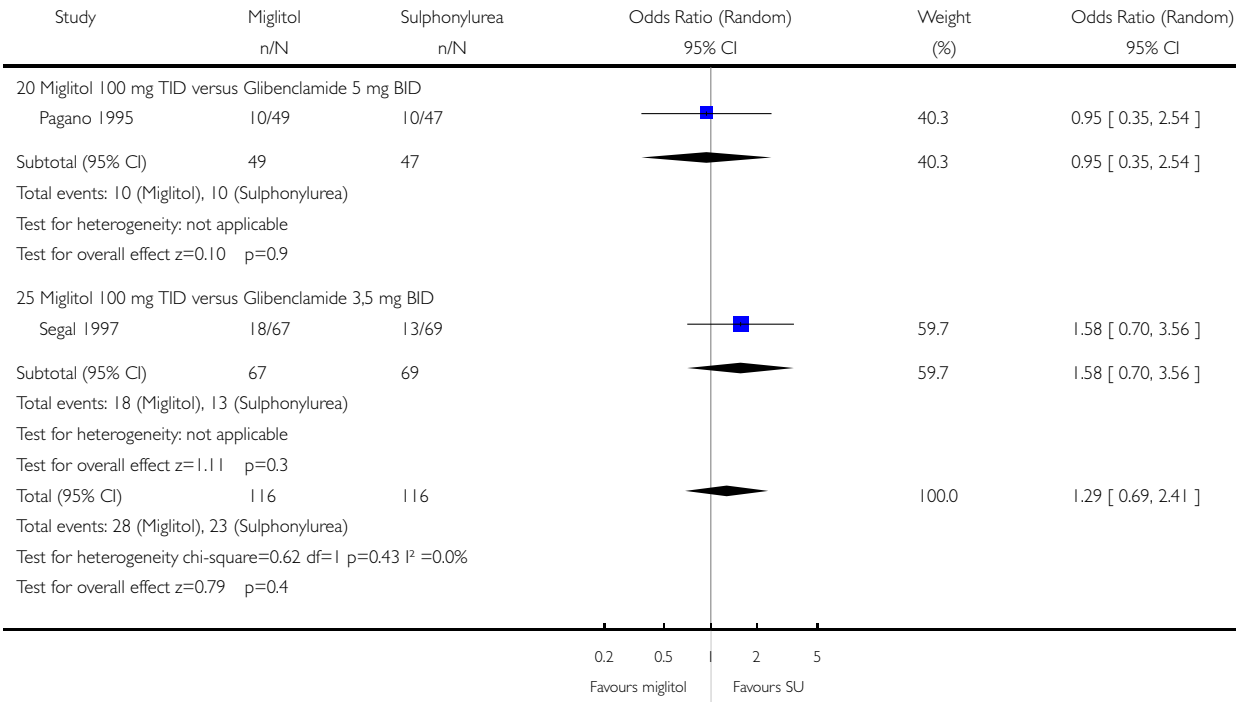

Fig. 83. Comparison 07. Miglitol versus metformin

07.01 Change in glycated haemoglobin (%)

Review: Alpha-glucosidase inhibitors for type 2 diabetes mellitus

Comparison: 07 Miglitol versus metformin

Outcome: 01 Change in glycated haemoglobin (%)

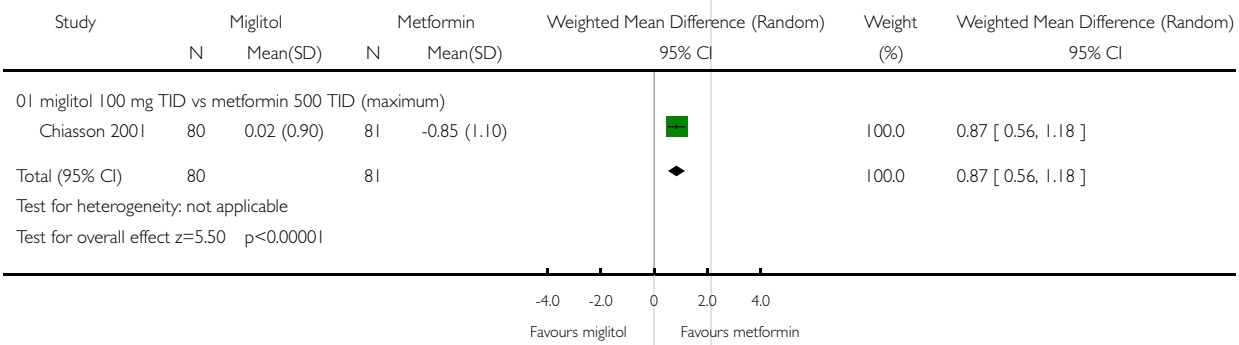

Fig. 84. Comparison 07. Miglitol versus metformin

07.02 Change in fasting blood glucose (mmol/l)

Review: Alpha-glucosidase inhibitors for type 2 diabetes mellitus

Comparison: 07 Miglitol versus metformin

Outcome: 02 Change in fasting blood glucose (mmol/l)

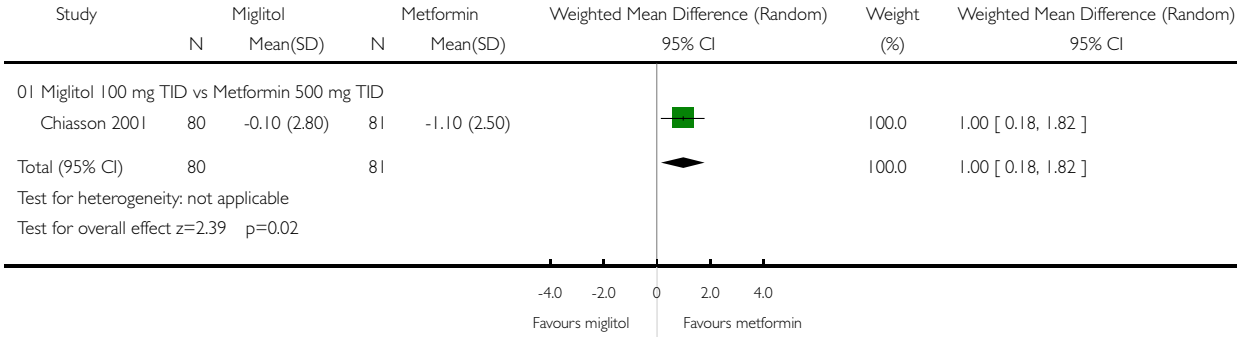

Fig. 85. Comparison 07. Miglitol versus metformin

07.03 Change in post-load blood glucose (mmol/l)

Review: Alpha-glucosidase inhibitors for type 2 diabetes mellitus

Comparison: 07 Miglitol versus metformin

Outcome: 03 Change in post-load blood glucose (mmol/l)

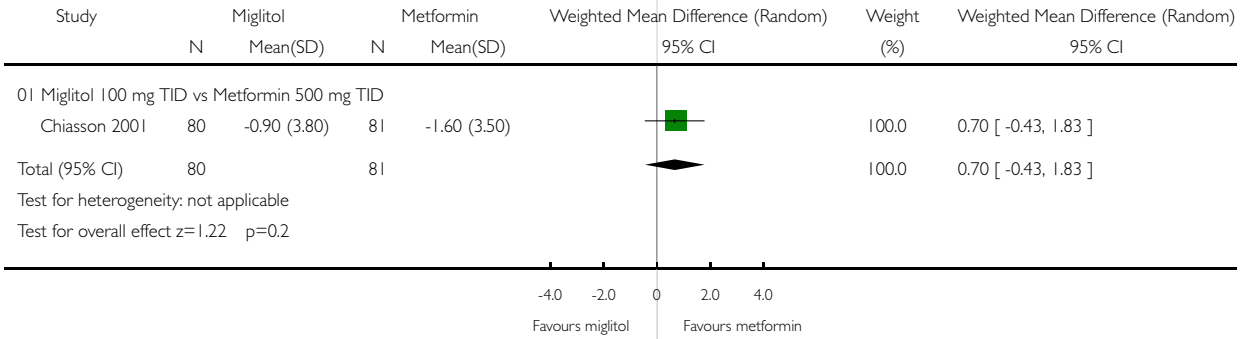

Fig. 86. Comparison 07. Miglitol versus metformin

07.08 Change in fasting insulin levels (pmol/l)

Review: Alpha-glucosidase inhibitors for type 2 diabetes mellitus

Comparison: 07 Miglitol versus metformin

Outcome: 08 Change in fasting insulin levels (pmol/l)

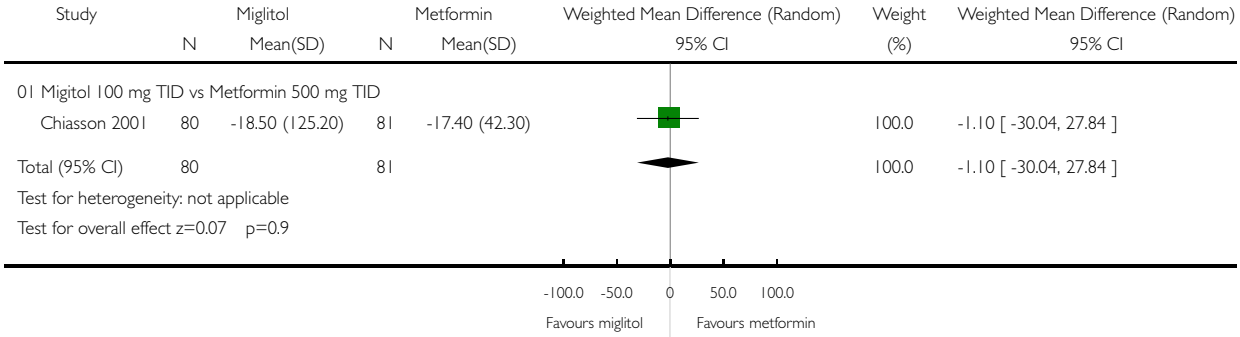

Fig. 87. Comparison 07. Miglitol versus metformin

07.09 Change in post-load insulin levels (pmol/l)

Review: Alpha-glucosidase inhibitors for type 2 diabetes mellitus

Comparison: 07 Miglitol versus metformin

Outcome: 09 Change in post-load insulin levels (pmol/l)

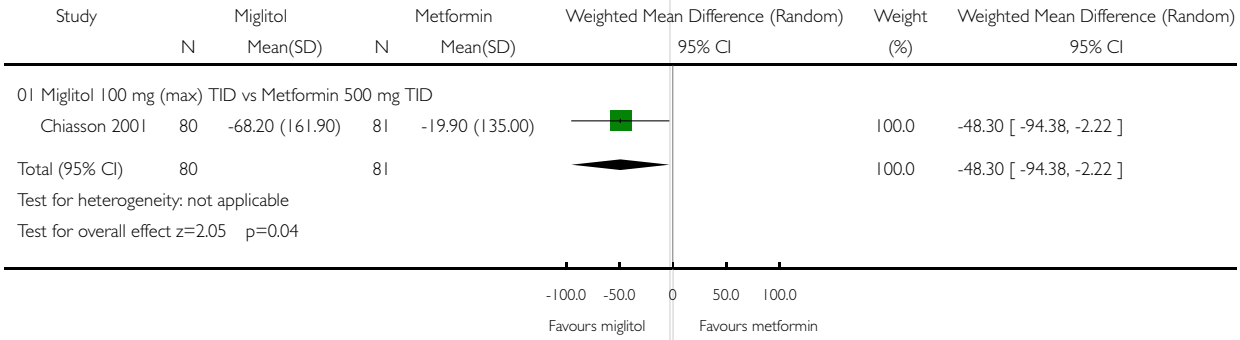

Fig. 88. Comparison 07. Miglitol versus metformin

07.12 Change in body weight (Kg)

Review: Alpha-glucosidase inhibitors for type 2 diabetes mellitus

Comparison: 07 Miglitol versus metformin

Outcome: 12 Change in body weight (Kg)

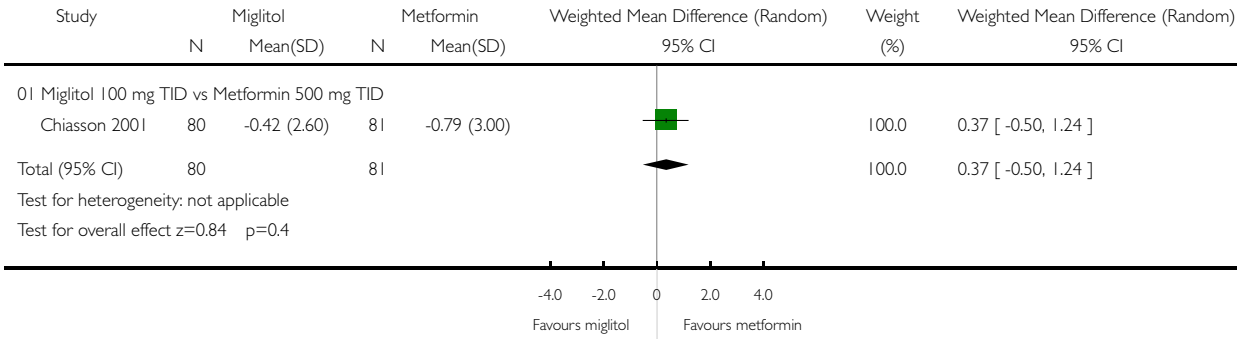

Fig. 89. Comparison 07. Miglitol versus metformin

07.17 Occurence of gastro-intestinal side-effects

Review: Alpha-glucosidase inhibitors for type 2 diabetes mellitus

Comparison: 07 Miglitol versus metformin

Outcome: 17 Occurence of gastro-intestinal side-effects

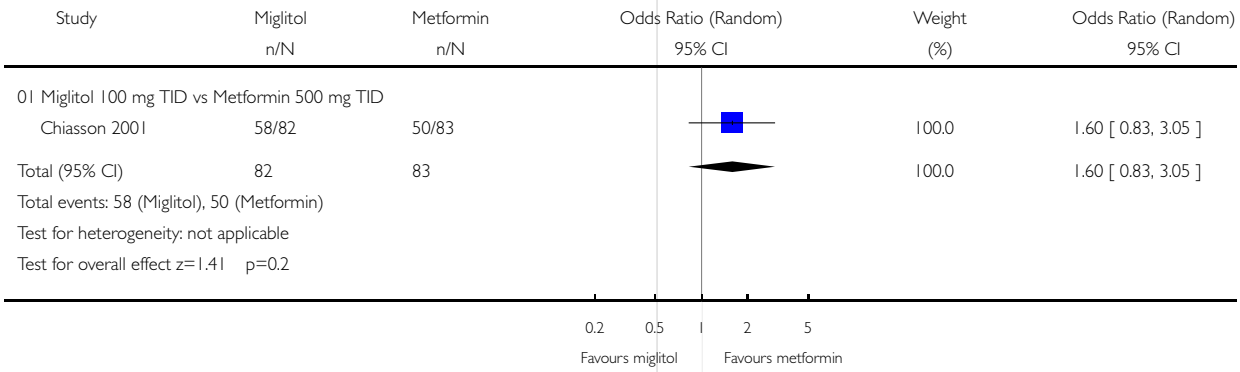

Fig. 90. Comparison 07. Miglitol versus metformin

07.30 Occurence of adverse effects

Review: Alpha-glucosidase inhibitors for type 2 diabetes mellitus

Comparison: 07 Miglitol versus metformin

Outcome: 30 Occurence of adverse effects

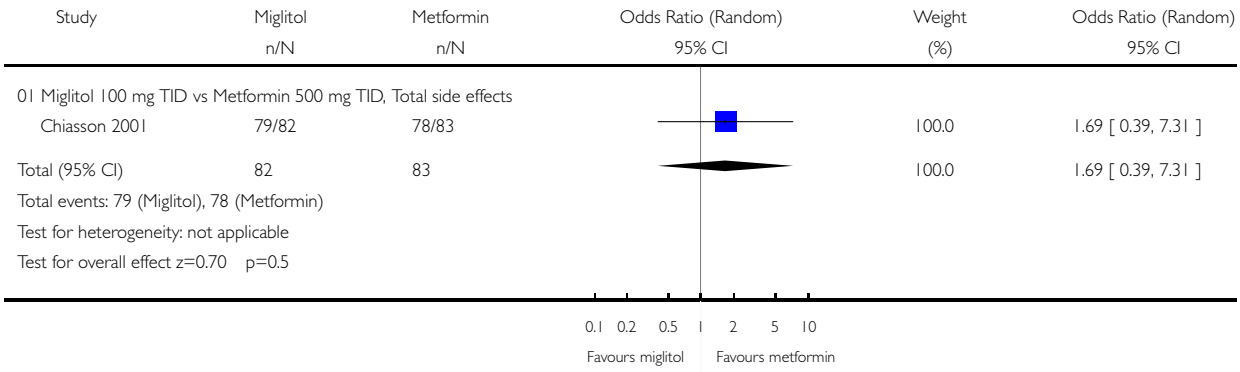

Fig. 91. Comparison 07. Miglitol versus metformin

07.90 Change in post-load blood glucose (mmol/l) (2 hours)

Review: Alpha-glucosidase inhibitors for type 2 diabetes mellitus

Comparison: 07 Miglitol versus metformin

Outcome: 90 Change in post-load blood glucose (mmol/l) (2 hours)

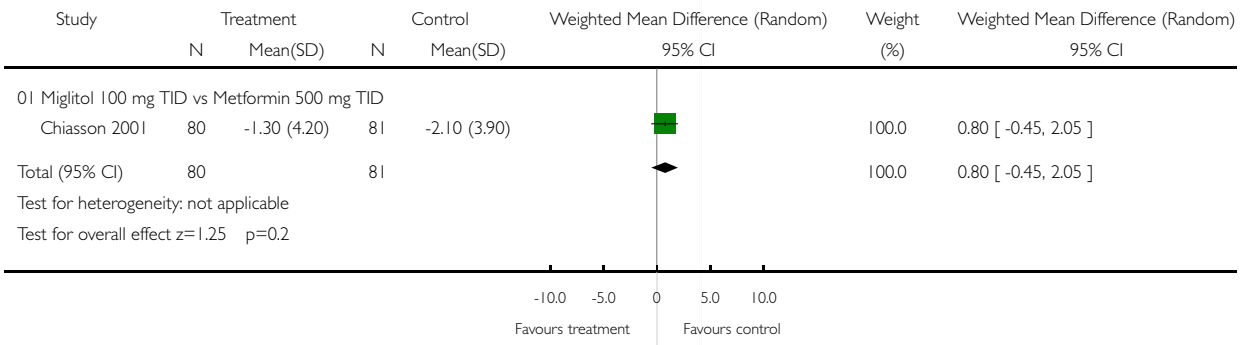

Fig. 92. Comparison 07. Miglitol versus metformin

07.91 Change in post-load insulin levels (pmol/l) (2-hours)

Review: Alpha-glucosidase inhibitors for type 2 diabetes mellitus

Comparison: 07 Miglitol versus metformin

Outcome: 91 Change in post-load insulin levels (pmol/l) (2-hours)

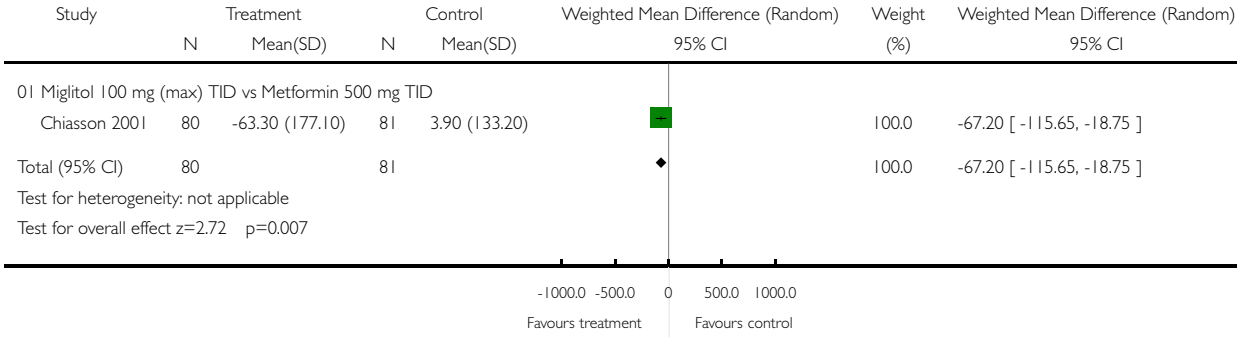

Fig. 93. Comparison 08. Voglibose versus placebo

08.01 Change in glycated haemoglobin (%)

Review: Alpha-glucosidase inhibitors for type 2 diabetes mellitus

Comparison: 08 Voglibose versus placebo

Outcome: 01 Change in glycated haemoglobin (%)

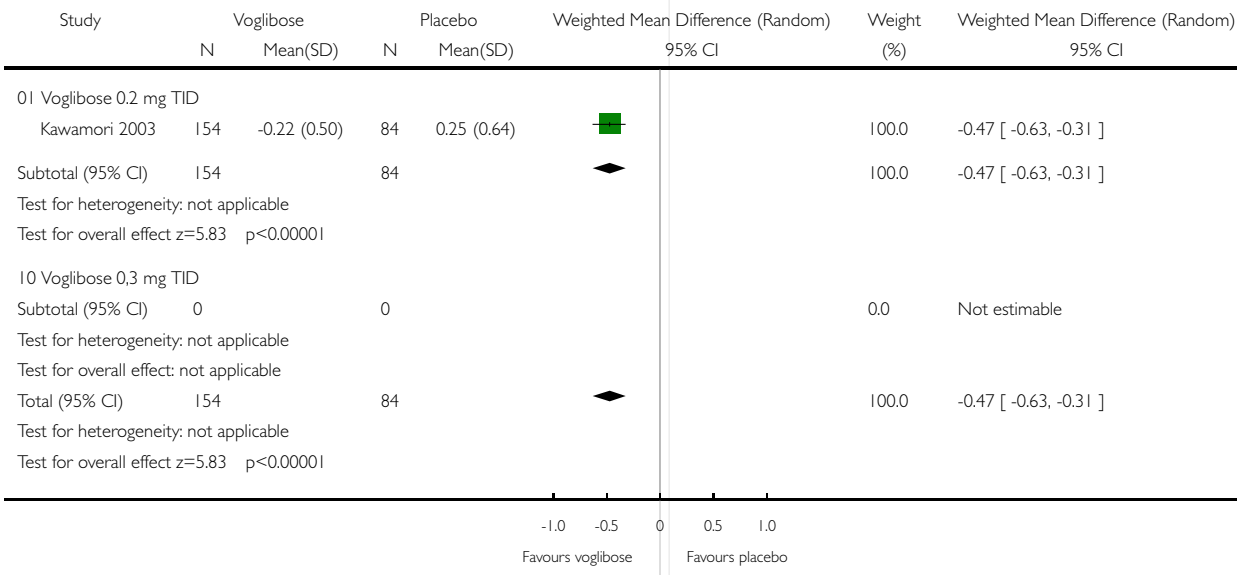

Fig. 94. Comparison 08. Voglibose versus placebo

08.02 Change in fasting blood glucose (mmol/l)

Review: Alpha-glucosidase inhibitors for type 2 diabetes mellitus

Comparison: 08 Voglibose versus placebo

Outcome: 02 Change in fasting blood glucose (mmol/l)

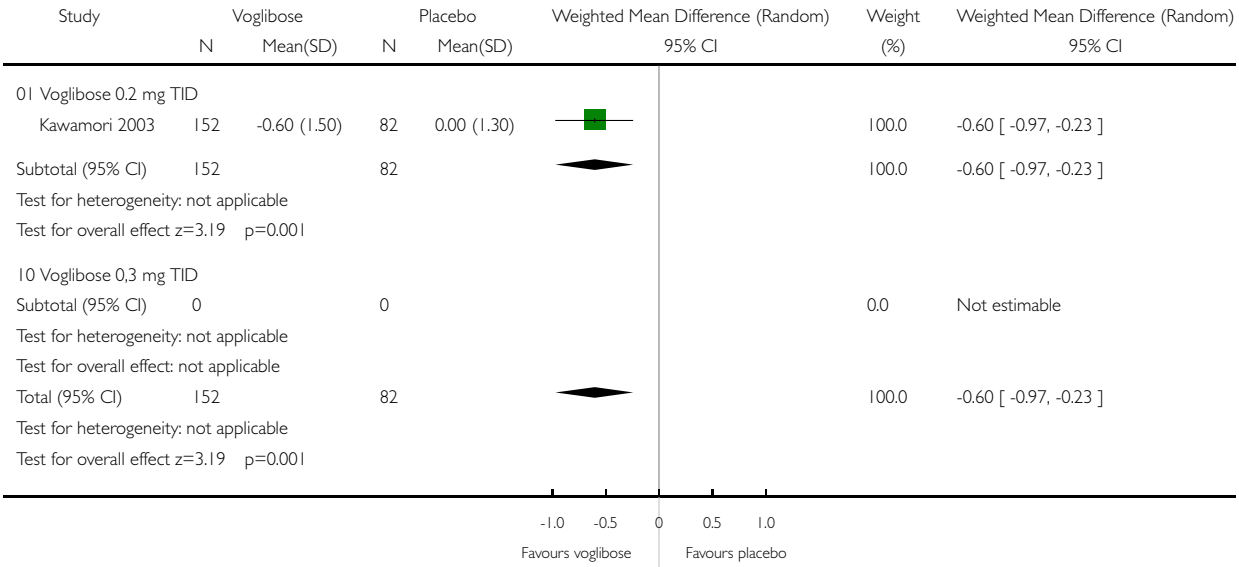

Fig. 95. Comparison 08. Voglibose versus placebo

08.03 Change in post-load blood glucose (mmol/l)

Review: Alpha-glucosidase inhibitors for type 2 diabetes mellitus

Comparison: 08 Voglibose versus placebo

Outcome: 03 Change in post-load blood glucose (mmol/l)

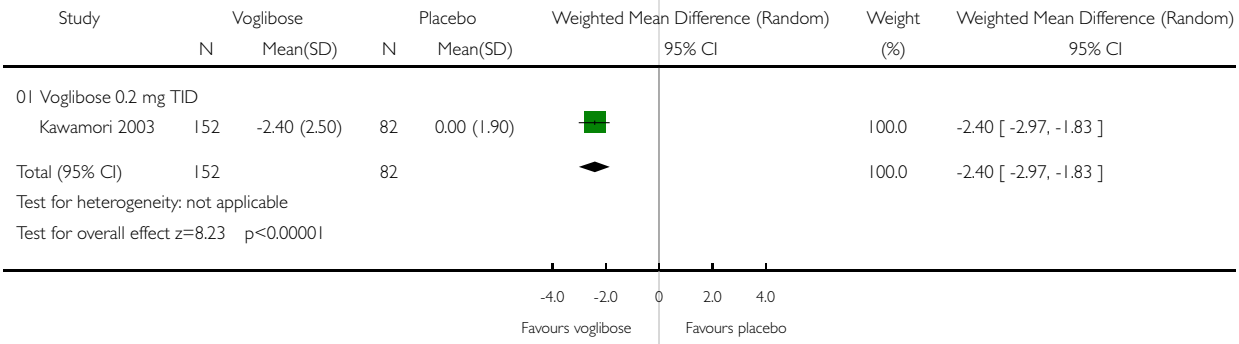

Fig. 96. Comparison 08. Voglibose versus placebo

08.08 Change in post-load insulin levels (pmol/l)

Review: Alpha-glucosidase inhibitors for type 2 diabetes mellitus

Comparison: 08 Voglibose versus placebo

Outcome: 08 Change in post-load insulin levels (pmol/l)

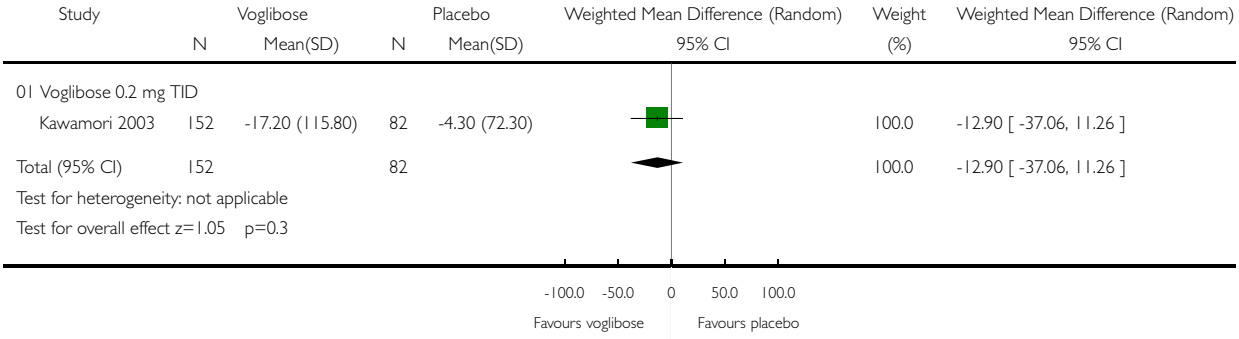

Fig. 97. Comparison 08. Voglibose versus placebo

08.30 Occurence of adverse effects

Review: Alpha-glucosidase inhibitors for type 2 diabetes mellitus

Comparison: 08 Voglibose versus placebo

Outcome: 30 Occurence of adverse effects

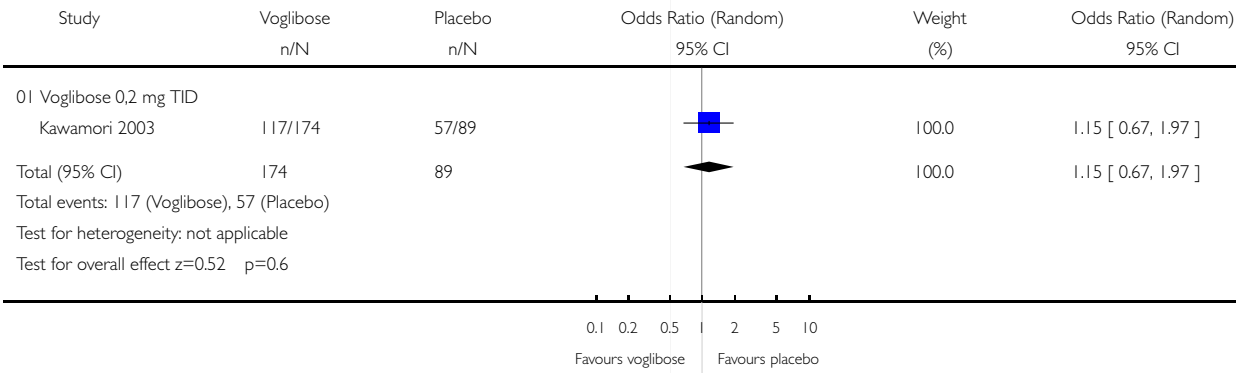

Fig. 98. Comparison 08. Voglibose versus placebo

08.31 Occurence of gastro-intestinal adverse effects

Review: Alpha-glucosidase inhibitors for type 2 diabetes mellitus

Comparison: 08 Voglibose versus placebo

Outcome: 31 Occurence of gastro-intestinal adverse effects

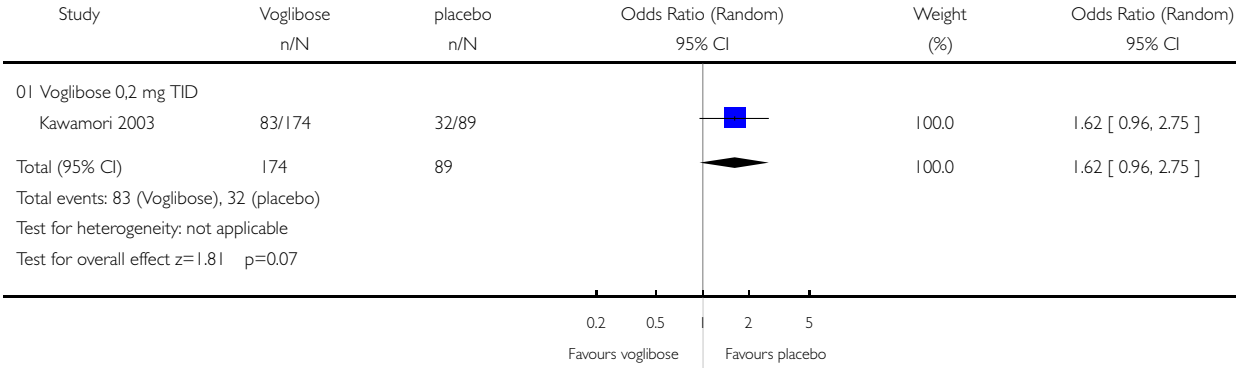

Fig. 99. Comparison 08. Voglibose versus placebo

08.90 Change in post-load blood glucose (mmol/l) (2 hours)

Review: Alpha-glucosidase inhibitors for type 2 diabetes mellitus

Comparison: 08 Voglibose versus placebo

Outcome: 90 Change in post-load blood glucose (mmol/l) (2 hours)

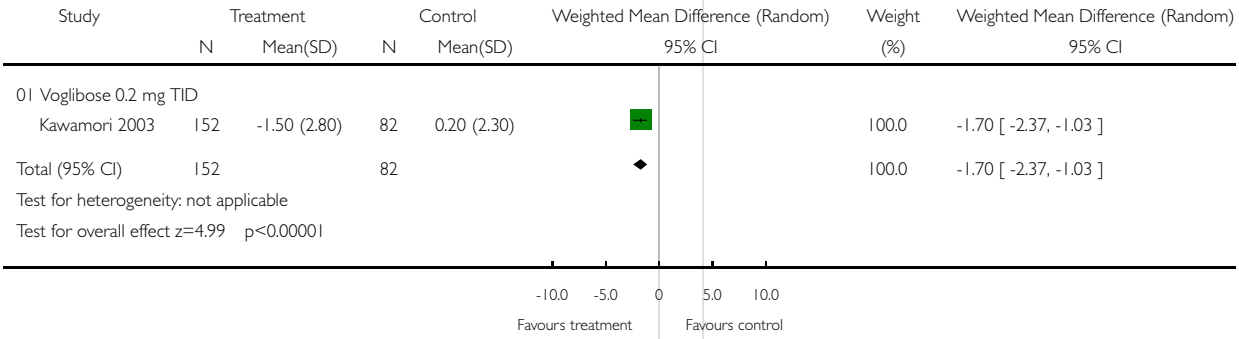

Fig. 100. Comparison 09. Voglibose versus diet therapy

09.01 Change in glycated haemoglobin (%)

Review: Alpha-glucosidase inhibitors for type 2 diabetes mellitus

Comparison: 09 Voglibose versus diet therapy

Outcome: 01 Change in glycated haemoglobin (%)

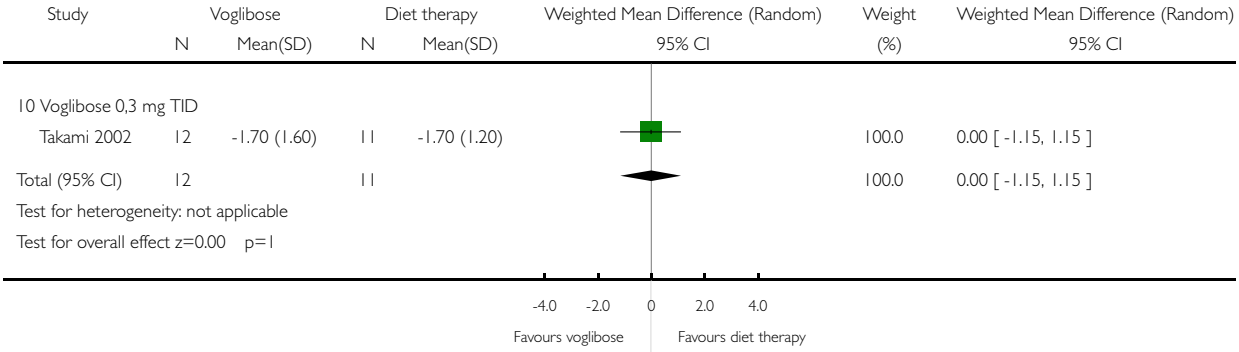

Fig. 101. Comparison 09. Voglibose versus diet therapy

09.02 Change in fasting blood glucose (mmol/l)

Review: Alpha-glucosidase inhibitors for type 2 diabetes mellitus

Comparison: 09 Voglibose versus diet therapy

Outcome: 02 Change in fasting blood glucose (mmol/l)

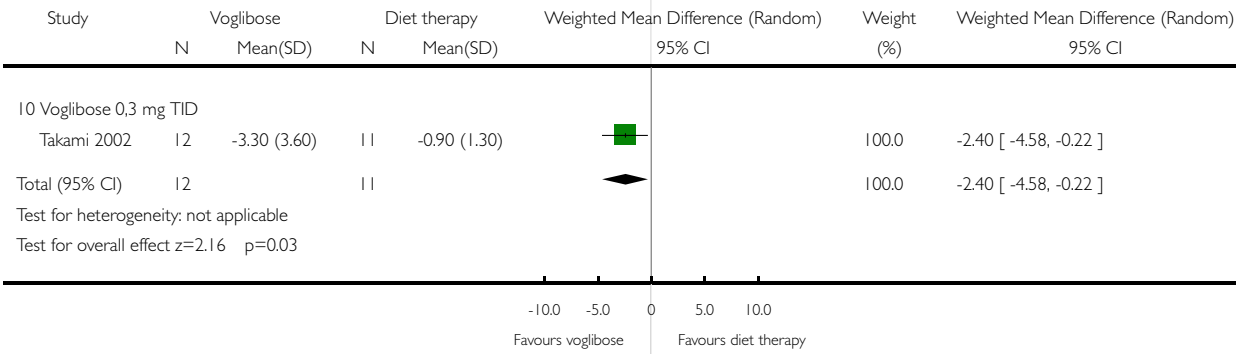

Fig. 102. Comparison 09. Voglibose versus diet therapy

09.04 Change in total cholesterol (mmol/l)

Review: Alpha-glucosidase inhibitors for type 2 diabetes mellitus

Comparison: 09 Voglibose versus diet therapy

Outcome: 04 Change in total cholesterol (mmol/l)

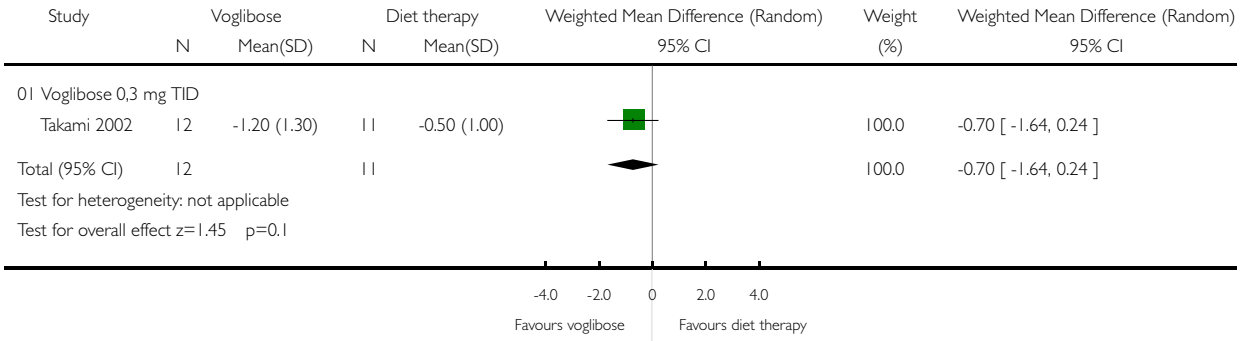

Fig. 103. Comparison 09. Voglibose versus diet therapy

09.05 Change in HDL-cholesterol (mmol/l)

Review: Alpha-glucosidase inhibitors for type 2 diabetes mellitus

Comparison: 09 Voglibose versus diet therapy

Outcome: 05 Change in HDL-cholesterol (mmol/l)

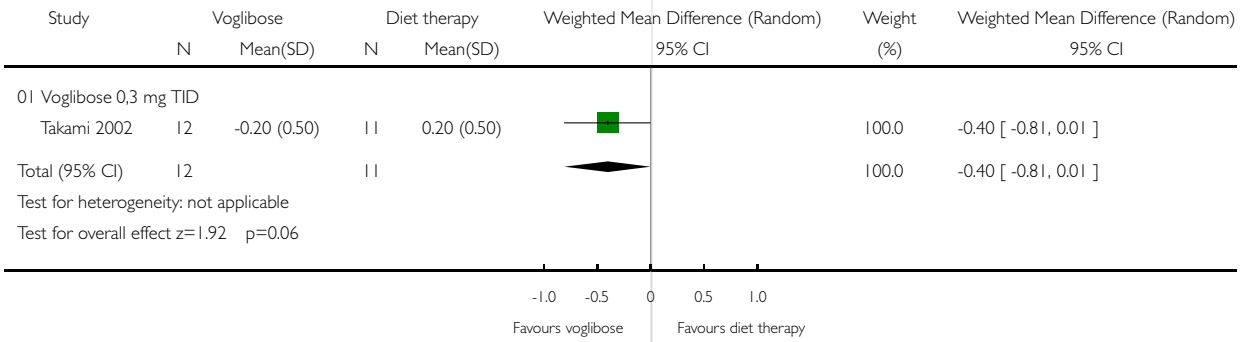

Fig. 104. Comparison 09. Voglibose versus diet therapy

09.08 Change in fasting insulin levels (pmol/l)

Review: Alpha-glucosidase inhibitors for type 2 diabetes mellitus

Comparison: 09 Voglibose versus diet therapy

Outcome: 08 Change in fasting insulin levels (pmol/l)

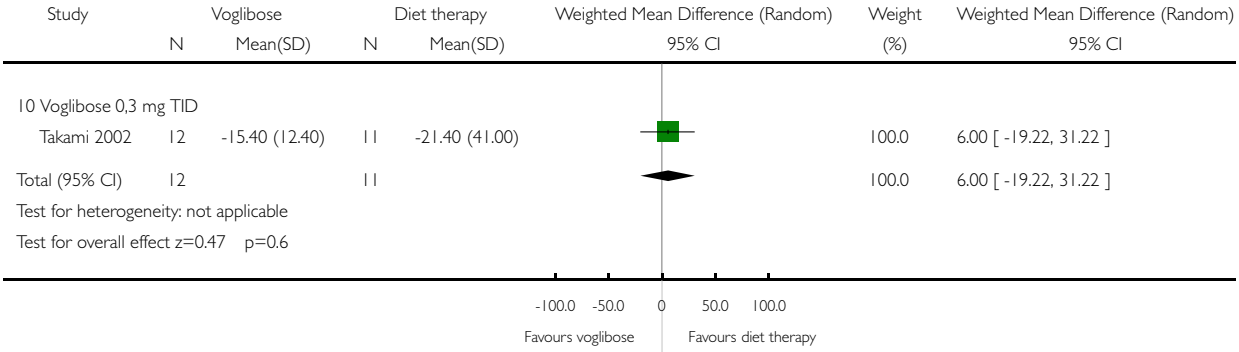

Fig. 105. Comparison 09. Voglibose versus diet therapy

09.12 Change in body weight (Kg)

Review: Alpha-glucosidase inhibitors for type 2 diabetes mellitus

Comparison: 09 Voglibose versus diet therapy

Outcome: 12 Change in body weight (Kg)

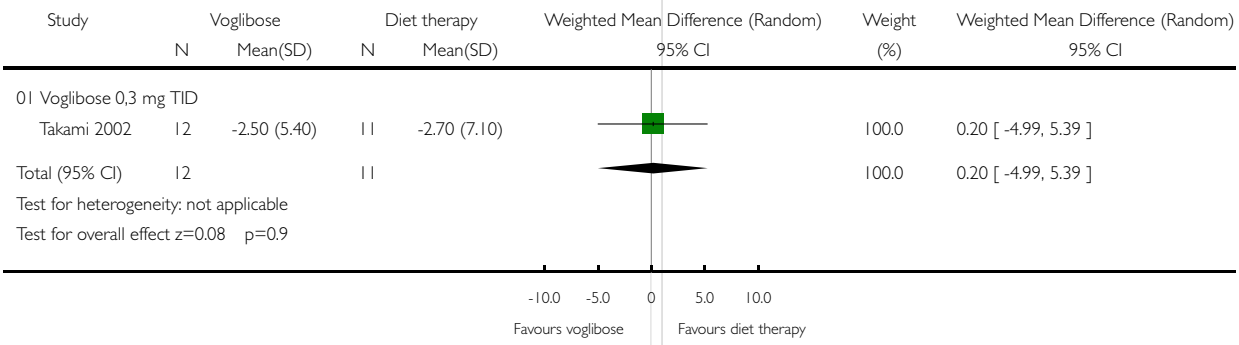

Fig. 106. Comparison 09. Voglibose versus diet therapy

09.13 Change in body mass index (Kg/m2)

Review: Alpha-glucosidase inhibitors for type 2 diabetes mellitus

Comparison: 09 Voglibose versus diet therapy

Outcome: 13 Change in body mass index (Kg/m2)

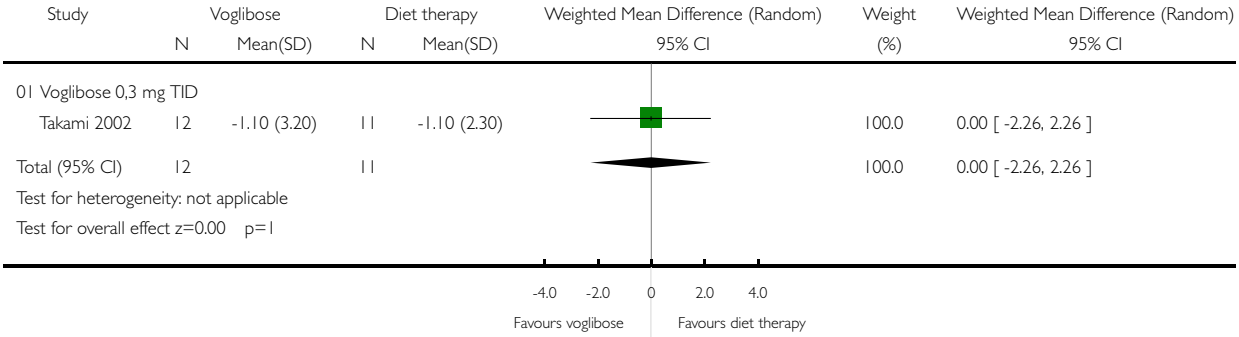

Fig. 107. Comparison 10. .Voglibose versus sulphonylurea (SU)

10.01 Change in glycated haemoglobin (%)

Review: Alpha-glucosidase inhibitors for type 2 diabetes mellitus

Comparison: 10 .Voglibose versus sulphonylurea (SU)

Outcome: 01 Change in glycated haemoglobin (%)

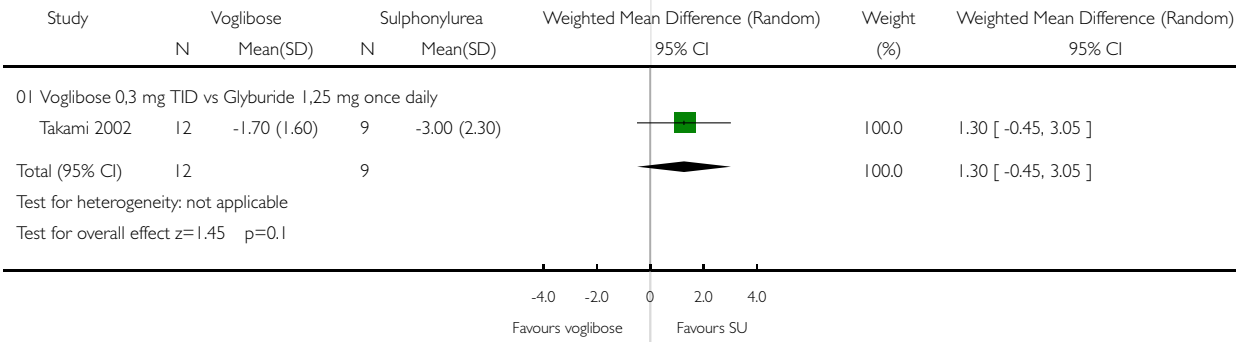

Fig. 108. Comparison 10. .Voglibose versus sulphonylurea (SU)

10.02 Change in fasting blood glucose (mmol/l)

Review: Alpha-glucosidase inhibitors for type 2 diabetes mellitus

Comparison: 10 .Voglibose versus sulphonylurea (SU)

Outcome: 02 Change in fasting blood glucose (mmol/l)

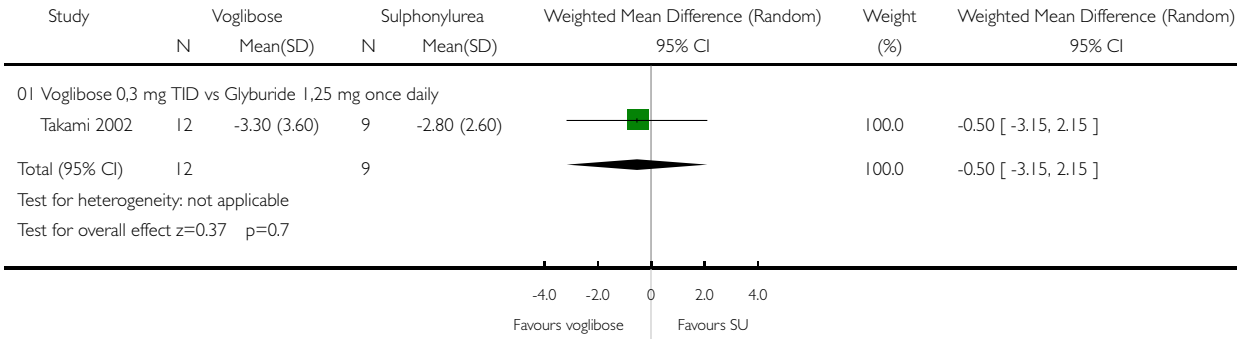

Fig. 109. Comparison 10. .Voglibose versus sulphonylurea (SU)

10.04 Change in total cholesterol (mmol/l)

Review: Alpha-glucosidase inhibitors for type 2 diabetes mellitus

Comparison: 10 .Voglibose versus sulphonylurea (SU)

Outcome: 04 Change in total cholesterol (mmol/l)

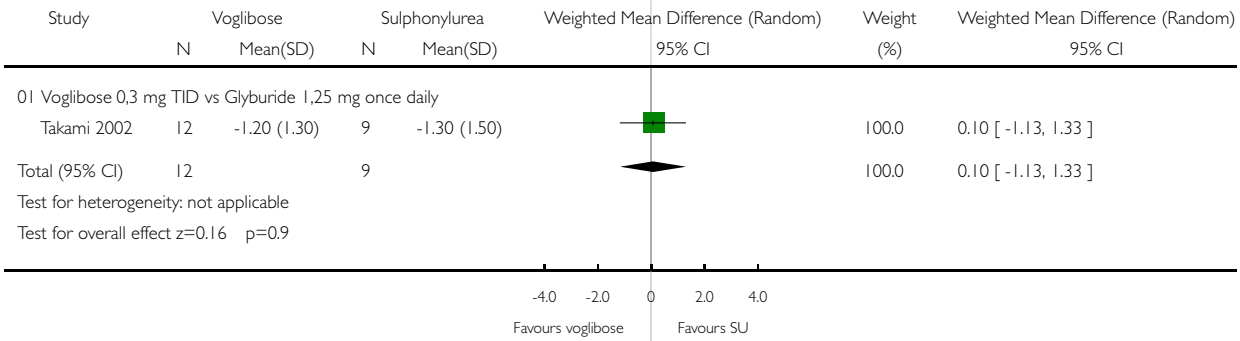

Fig. 110. Comparison 10. .Voglibose versus sulphonylurea (SU)

10.05 Change in HDL-cholesterol (mmol/l)

Review: Alpha-glucosidase inhibitors for type 2 diabetes mellitus

Comparison: 10 .Voglibose versus sulphonylurea (SU)

Outcome: 05 Change in HDL-cholesterol (mmol/l)

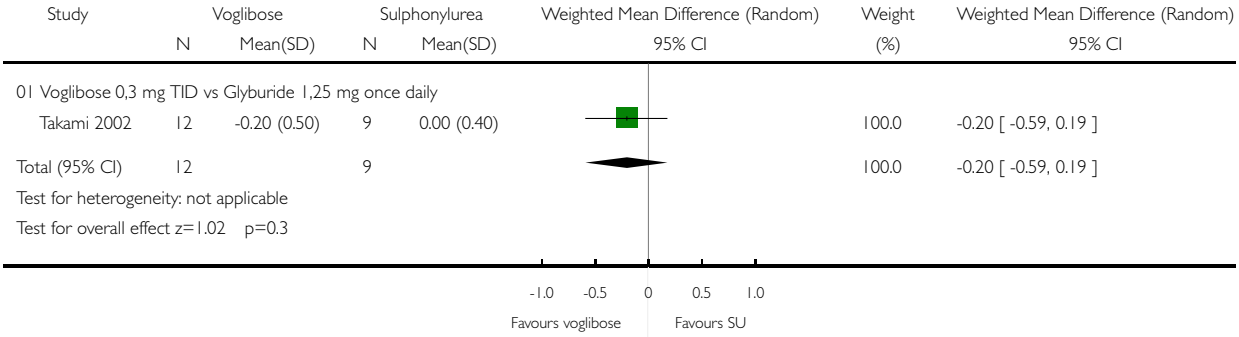

Fig. 111. Comparison 10. .Voglibose versus sulphonylurea (SU)

10.08 Change in fasting insulin levels (pmol/l)

Review: Alpha-glucosidase inhibitors for type 2 diabetes mellitus

Comparison: 10 .Voglibose versus sulphonylurea (SU)

Outcome: 08 Change in fasting insulin levels (pmol/l)

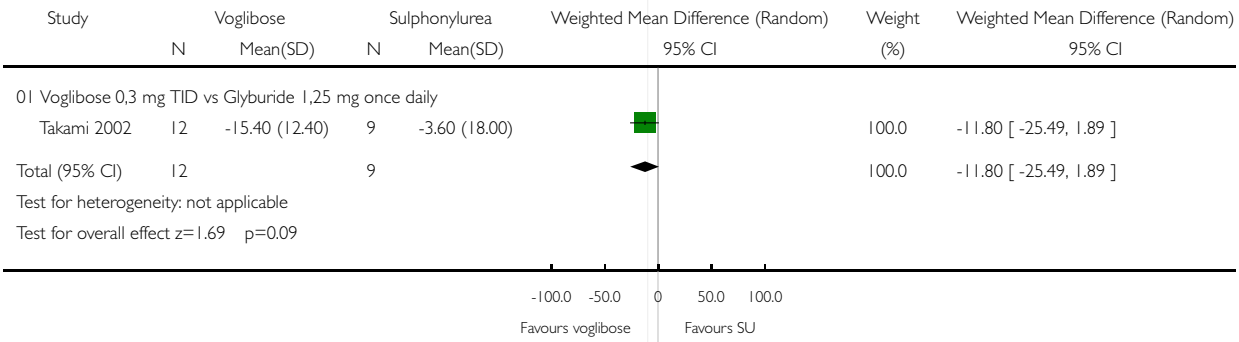

Fig. 112. Comparison 10. .Voglibose versus sulphonylurea (SU)

10.12 Change in body weight (Kg)

Review: Alpha-glucosidase inhibitors for type 2 diabetes mellitus

Comparison: 10 .Voglibose versus sulphonylurea (SU)

Outcome: 12 Change in body weight (Kg)

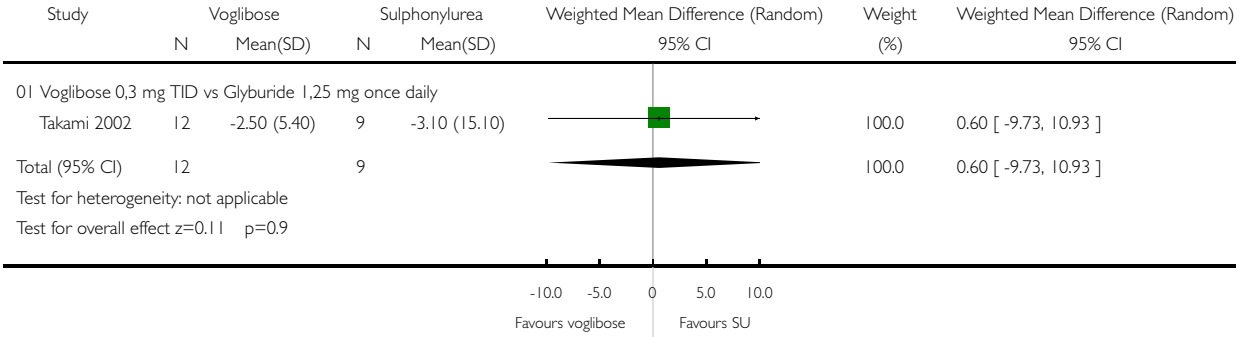

Fig. 113. Comparison 10. .Voglibose versus sulphonylurea (SU)

10.13 Change in body mass index (Kg/m2)

Review: Alpha-glucosidase inhibitors for type 2 diabetes mellitus

Comparison: 10 .Voglibose versus sulphonylurea (SU)

Outcome: 13 Change in body mass index (Kg/m2)

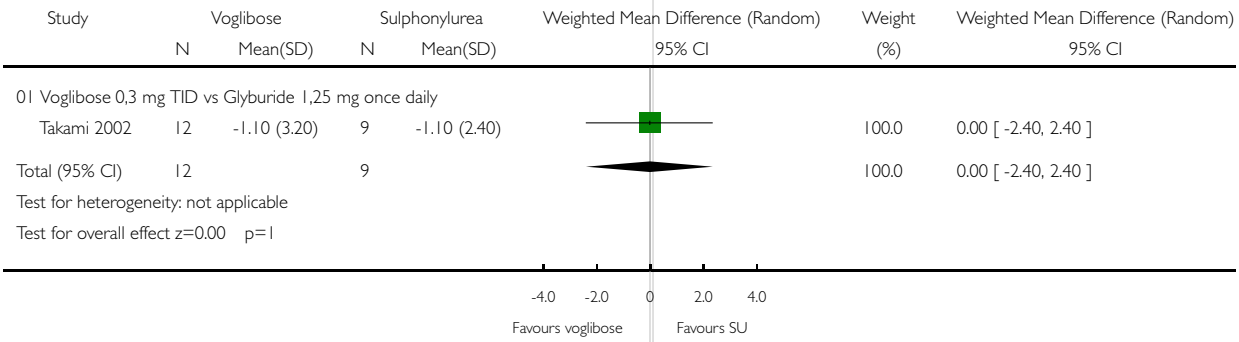

Fig. 114. Comparison 11. Miglitol versus voglibose

11.01 Change in glycated haemoglobin (%)

Review: Alpha-glucosidase inhibitors for type 2 diabetes mellitus

Comparison: 11 Miglitol versus voglibose

Outcome: 01 Change in glycated haemoglobin (%)

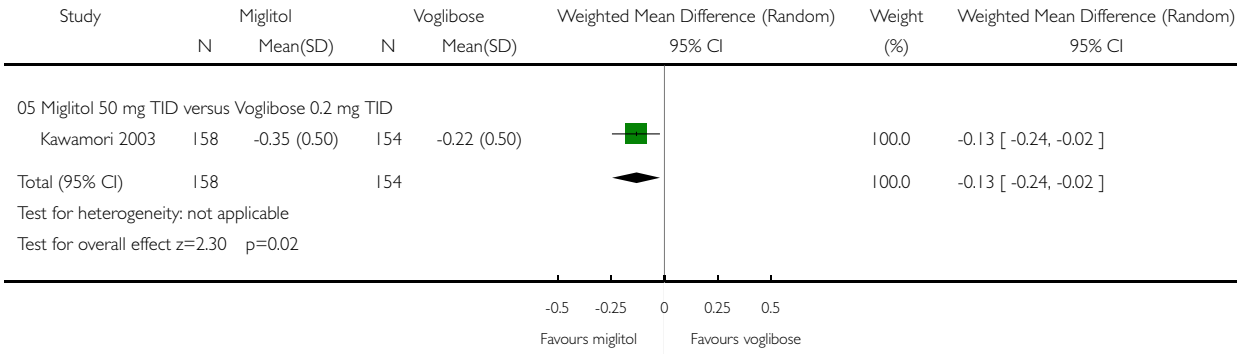

Fig. 115. Comparison 11. Miglitol versus voglibose

11.02 Change in fasting blood glucose (mmol/l)

Review: Alpha-glucosidase inhibitors for type 2 diabetes mellitus

Comparison: 11 Miglitol versus voglibose

Outcome: 02 Change in fasting blood glucose (mmol/l)

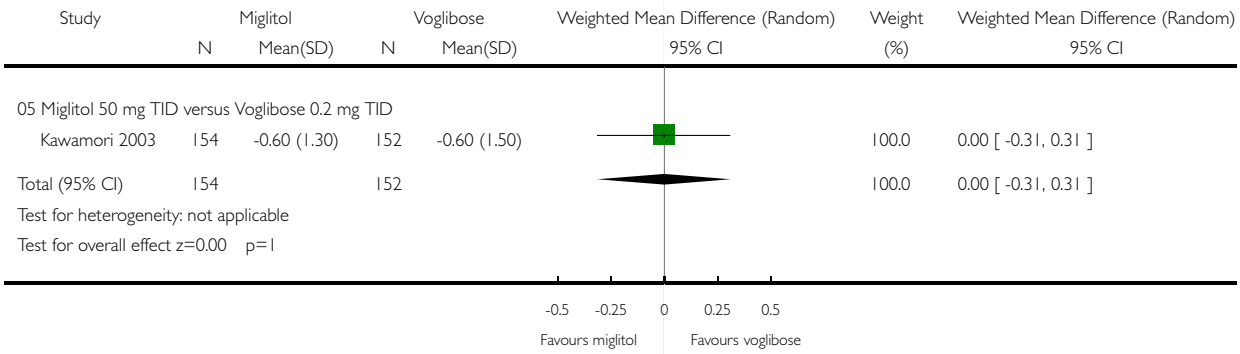

Fig. 116. Comparison 11. Miglitol versus voglibose

11.03 Change in post-load blood glucose (mmol/l)

Review: Alpha-glucosidase inhibitors for type 2 diabetes mellitus

Comparison: 11 Miglitol versus voglibose

Outcome: 03 Change in post-load blood glucose (mmol/l)

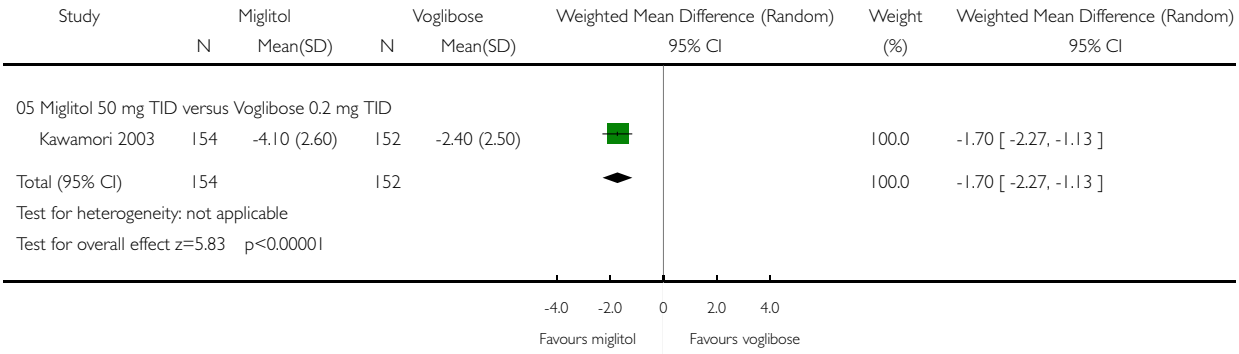

Fig. 117. Comparison 11. Miglitol versus voglibose

11.09 Change in post-load insulin levels (pmol/l)

Review: Alpha-glucosidase inhibitors for type 2 diabetes mellitus

Comparison: 11 Miglitol versus voglibose

Outcome: 09 Change in post-load insulin levels (pmol/l)

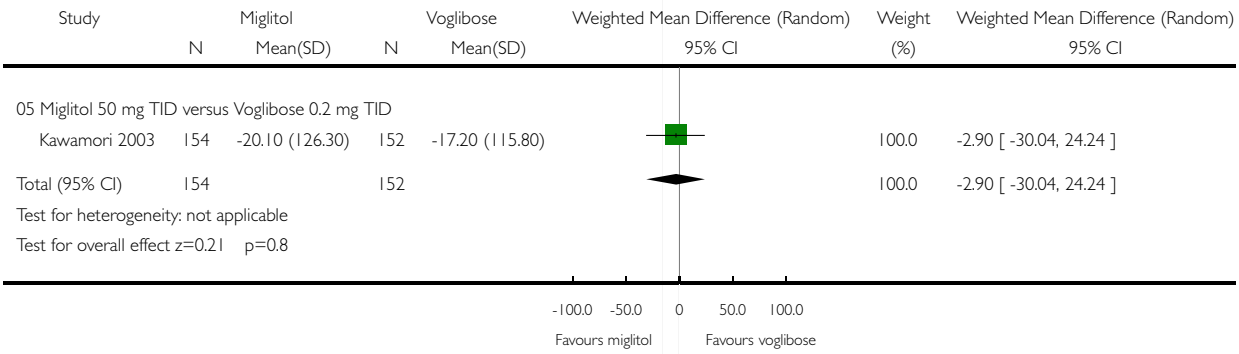

Fig. 118. Comparison 11. Miglitol versus voglibose

11.30 Occurence of adverse effects

Review: Alpha-glucosidase inhibitors for type 2 diabetes mellitus

Comparison: 11 Miglitol versus voglibose

Outcome: 30 Occurence of adverse effects

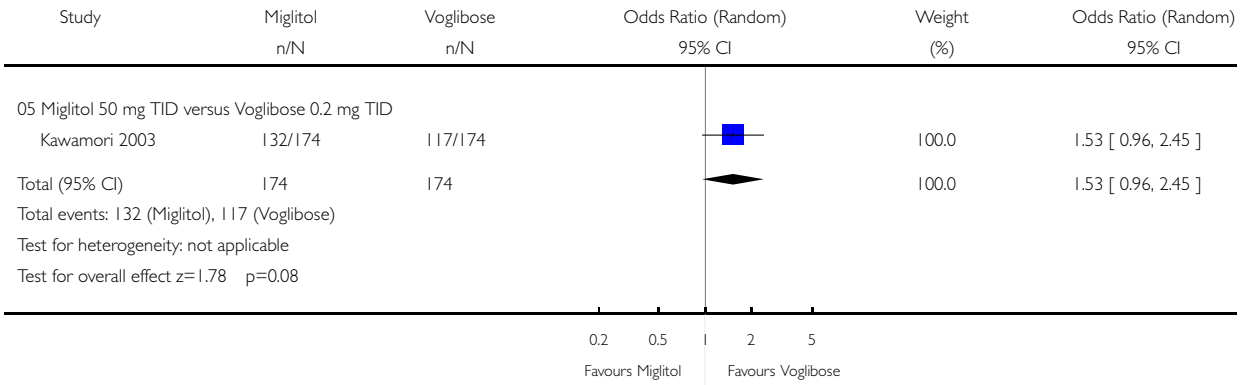

Fig. 119. Comparison 11. Miglitol versus voglibose

11.31 Occurence of gastro-intestinal adverse effects

Review: Alpha-glucosidase inhibitors for type 2 diabetes mellitus

Comparison: 11 Miglitol versus voglibose

Outcome: 31 Occurence of gastro-intestinal adverse effects

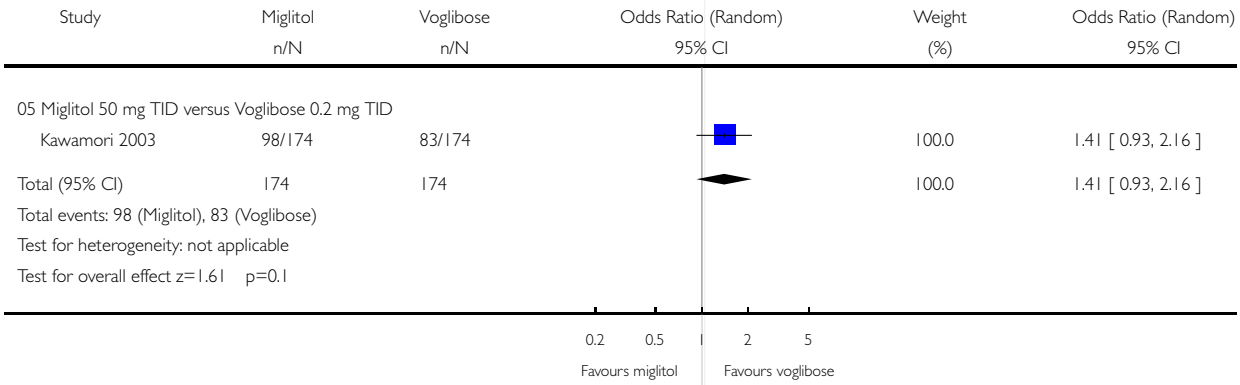

Fig. 120. Comparison 11. Miglitol versus voglibose

11.90 Change in post-load blood glucose (mmol/l) (2 hours)

Review: Alpha-glucosidase inhibitors for type 2 diabetes mellitus

Comparison: 11 Miglitol versus voglibose

Outcome: 90 Change in post-load blood glucose (mmol/l) (2 hours)