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## Chinese herbal medicines for people with impaired glucose tolerance or impaired fasting blood glucose

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### Abstract

**Background**—Around 308 million people worldwide are estimated to have impaired glucose tolerance (IGT); 25% to 75% of these will develop diabetes within a decade of initial diagnosis. At diagnosis, half will have tissue-related damage and all have an increased risk for coronary heart disease.

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**Declarations of interest** Suzanne Grant is currently undertaking a randomised controlled trial of Chinese herbal medicines to treat impaired glucose tolerance or impaired fasting blood glucose. There are no other known potential conflicts of interest.

**Objectives**—The objective of this review was to assess the effects and safety of Chinese herbal medicines for the treatment of people with impaired glucose tolerance or impaired fasting glucose (IFG).

**Search strategy**—We searched the following databases: *The Cochrane Library*, PubMed, EMBASE, AMED, a range of Chinese language databases, SIGLE and databases of ongoing trials.

**Selection criteria**—Randomised clinical trials comparing Chinese herbal medicines with placebo, no treatment, pharmacological or non-pharmacological interventions in people with IGT or IFG were considered.

**Data collection and analysis**—Two authors independently extracted data. Trials were assessed for risk of bias against key criteria: random sequence generation, allocation concealment, blinding of participants, outcome assessors and intervention providers, incomplete outcome data, selective outcome reporting and other sources of bias.

**Main results**—This review examined 16 trials lasting four weeks to two years involving 1391 participants receiving 15 different Chinese herbal medicines in eight different comparisons. No trial reported on mortality, morbidity or costs. No serious adverse events like severe hypoglycaemia were observed. Meta-analysis of eight trials showed that those receiving Chinese herbal medicines combined with lifestyle modification were more than twice as likely to have their fasting plasma glucose levels return to normal levels (i.e. fasting plasma glucose <7.8 mmol/L and 2hr blood glucose <11.1 mmol/L) compared to lifestyle modification alone (RR 2.07; 95% confidence interval (CI) 1.52 to 2.82). Those receiving Chinese herbs were less likely to progress to diabetes over the duration of the trial (RR 0.33; 95% CI 0.19 to 0.58). However, all trials had a considerable risk of bias and none of the specific herbal medicines comparison data was available from more than one study. Moreover, results could have been confounded by rates of natural reversion to normal glucose levels.

**Authors' conclusions**—The positive evidence in favour of Chinese herbal medicines for the treatment of IGT or IFG is constrained by the following factors: lack of trials that tested the same herbal medicine, lack of details on co-interventions, unclear methods of randomisation, poor reporting and other risks of bias.

## Plain language summary

### Chinese herbal medicines for people with impaired glucose tolerance or impaired fasting blood glucose

Around 308 million people worldwide are reported to have 'impaired glucose tolerance'. These individuals show higher than normal blood sugar (glucose) levels, but do not meet diagnostic criteria for having type 1 or type 2 diabetes. This may provide a window in which to prevent or delay the onset of diabetes and its complications like cardiovascular disease. Within a decade of the initial diagnosis 'impaired glucose tolerance' 25% to 75% are estimated to progress to diabetes.

This review examined 16 randomised controlled trials of 15 different Chinese herbal medicines. The trials lasted from four weeks to two years (average nine months) and involved altogether 1391 participants. Death from any cause, diabetic complications and economic outcomes were not investigated. No serious adverse events were reported.

The available evidence suggests that Chinese herbal medicines are able to lower and normalise high blood glucose. Due to considerable distortions (bias) in the trials, further high-quality and rigorously evaluated studies are required before any conclusions can

confidently be reached about the effects of Chinese herbal medicines for the treatment of impaired glucose tolerance and the delay of diabetes onset.

## Background

### Description of the condition

In 2007, an estimated 308 million had impaired glucose tolerance (IGT) or about 7.5% of the age group 20 to 79 years. More than 80% live in developing countries (IDF 2008). This is projected to rise to 418 million, or 8.1% by 2025. Around 10% of people with combined impaired fasting glucose (IFG) and IGT will progress to diabetes per year. The progression rate from isolated IGT to diabetes is estimated at 3.7% per year (Engberg 2009). The predicted cumulative 5 to 6 year incidence of development of type 2 diabetes for people with either IGT or IFG is 20% to 34%, those with both IGT and IFG have a progression rate of 38% to 65% (ADA 2003).

IGT and IFG are frequently present for many years until health checks reveal raised plasma glucose levels, or diabetic symptoms develop. By the time a diagnosis of type 2 diabetes is made around half of all people have diabetes related tissue damage. Even after diagnosis, management of type 2 diabetes is not easy. Achieving and maintaining normal glucose levels is difficult, leading to long-term complications. Coronary heart disease has been shown to be more prevalent in people with impaired glucose tolerance compared to those with normal glucose tolerance and is likely to develop before the onset of diabetes or symptoms (Haller 1998).

The concept of IGT was first introduced by the World Health Organisation (WHO) in 1979. Criteria for diagnosing IGT and IFG were revised by the WHO in 1999 (Unwin 2002). People with IGT show abnormal fasting plasma glucose and abnormal two-hour post-load plasma glucose values. People with IFG only however, demonstrate an abnormal fasting plasma glucose. Currently, the criteria for IGT and IFG are as follows (plasma venous glucose concentrations):

- IGT - fasting blood glucose less than 7.0 mmol/L and two-hour post-load blood glucose 7.8 to 11.0 mmol/L (WHO 1999);
- IFG - fasting blood glucose 6.1 to 6.9 mmol/L (two-hour post-load blood glucose less than 7.8 mmol/L, if measured) (ADA 1999; WHO 1999). In 2003, the American Diabetes Association (ADA) recommended to change these criteria to 5.6 to 6.9 mmol/L (ADA 2003).

The pathophysiology of the progression to type 2 diabetes is complex and still not fully understood. The progression seems to be governed by two processes: 1) a decline in sensitivity to the action of insulin, and 2) dysfunction and eventual exhaustion of beta-cell function (Polonsky 1996). Beta-cell dysfunction starts some 10 to 12 years prior to the presentation of type 2 diabetes (Davies 2004). This provides a window of opportunity to prevent or delay development of type 2 diabetes, and potentially diminish the risk of cardiovascular and other complications.

'Lifestyle' modification is the ideal method of delaying or preventing diabetes as it also reduces cardiovascular risk profile (DPP Research GP 2002). A systematic review concluded that lifestyle education was clearly effective for reducing two-hour plasma glucose and the incidence of type 2 diabetes over one year (Yamaoka 2005). Not all individuals however, will be able to undertake the intensive lifestyle interventions prescribed in these trials. Long-term adherence to the interventions described is a potentially limiting factor (Padwal 2005).

Pharmacological interventions have been employed to delay or prevent the onset of diabetes. Several studies have measured the effects of various interventions in people with IGT on the development of type 2 diabetes mellitus. Therapy with metformin (a biguanide), troglitazone (a thiazolidinedione, see below), or acarbose (an alpha-glucosidase inhibitor) have reduced the progression of IGT to diabetes mellitus by 31%, 49% and 25%, respectively. Metformin is probably the most extensively used pharmacological treatment for people with prediabetes to date. It improves peripheral and liver sensitivity to insulin, reduces basal liver glucose production and increases insulin-stimulated uptake and utilisation of glucose by peripheral tissues (AHFS 1999). The 'Diabetes Prevention Program' found that while metformin reduced the incidence of diabetes by 31% compared to placebo, the efficacy of metformin was variable among subgroups (DPP Research GP 2002). Metformin is less effective in those over 60 years of age, those with a body mass index (BMI) less than 35 kg/m<sup>2</sup>, and those with a fasting plasma glucose (FPG) below 6.1 mmol/L. Gastrointestinal symptoms including diarrhoea, flatulence, nausea and vomiting occurred in 77 of every 100 persons on metformin in the study.

Troglitazone, which was withdrawn from the market due to an increased incidence of drug-induced hepatic damage, markedly reduced the incidence of diabetes during its limited period of use, but this action did not persist (Knowler 2005). Whether other thiazolidinedione drugs used for longer periods can safely prevent or delay diabetes remains to be determined.

The class of drugs called alpha-glucosidase inhibitors are also sometimes used where blood sugar levels are not being stabilized through diet and exercise, or where metformin is not suitable or tolerated. The main alpha-glucosidase inhibitor currently used is acarbose. Acarbose prevents the degradation of complex carbohydrates into glucose, the carbohydrates will remain in the intestine. In the colon, bacteria will digest the complex carbohydrates, thereby causing gastrointestinal side effects such as flatulence (78% of people) and diarrhoea (14% of people). A systematic review of acarbose in people with IGT found that the use of acarbose reduces the incidence of type 2 diabetes, but the effects on glycaemic control are limited (Van de Laar 2006).

### Description of the intervention

Chinese herbal medicines include the use of plant, animal and mineral substances in preparations administered as pills, teas and powders. Chinese herbal medicines have long been used for the treatment of IGT and IFG and diabetes in China, Korea and Japan, with strong supportive anecdotal evidence for their efficacy (Liu 2004) and may offer a safe and effective alternative. These herbal medicines tend to be complex formulas combining two or more herbs.

### How the intervention might work

Pharmacological studies of the Chinese herbal formulas for the treatment of diabetes indicate that the mechanisms of action of these interventions might be multifactorial. It has been suggested that herbs containing polysaccharides restore the function of the pancreatic tissues causing increased insulin output by the beta-cells. Other herbs have been thought to enhance the microcirculation, increase the availability of insulin and facilitate the metabolism in insulin dependent processes (Jia 2003; Yu 2006). Herbal formulas that exert such a combined effect on insulin and blood glucose control in people with diabetes have relevance to IGT and IFG.

**Adverse effects of the intervention—**The chronic nature of prediabetes and diabetes means that people are potentially on treatments for a long period of time which increases the

likelihood of adverse effects (ADA 2003). Chinese herbal medicines have a long history of being used to treat diabetes and prediabetes in broad and varied population groups. As a consequence there is an accumulated knowledge of the safety in the use for many of the herbal substances. However, all medicinal agents have potentially unexpected effects including toxicity, and herbals are no different. Adverse effects of herbal medications may be intrinsic such as predictable toxicity, overdosage, interaction with other pharmaceutical or idiopathic (allergy, anaphylaxis etc). They may also be extrinsic, relating to misidentification, contamination, lack of standardisation and so on (Bensoussan 1996).

### Why it is important to do this review

A Cochrane review of herbal medicines for type 2 diabetes reviewed 66 randomised controlled trials and demonstrated that some herbal medicines with hypoglycaemic effects may be beneficial in type 2 diabetes (Liu 2004). However, no systematic review on the efficacy of Chinese herbal medicines in people with IGT or IFG has been undertaken. In view of the high proportion of people with IGT that go on to develop overt diabetes, and potentially cardiovascular disease, there is considerable interest in exploring therapeutic approaches that will reduce the risk of diabetes in individuals with IGT with minimal or no adverse effects where lifestyle modifications have failed and pharmacological treatment is inappropriate.

### Objectives

To assess the effects and safety of Chinese herbal medicines for the treatment of people with impaired glucose tolerance or impaired fasting glucose.

### Methods

#### Criteria for considering studies for this review

**Types of studies**—Randomised clinical trials were included irrespective of blinding, publication status or language.

**Types of participants**—People with impaired glucose tolerance (IGT) or impaired fasting glucose (IFG), existing or newly diagnosed.

#### Types of interventions

**Intervention:** Chinese herbal medicines involving extracts from herbs, single or mixture herbal preparations regardless of their compositions or forms or Chinese herbal medicines combined with a pharmacological intervention.

#### Control

- placebo;
- no treatment;
- pharmacological compounds (for example biguanides such as metformin, sulphonylureas);
- non-pharmacological interventions (for example diet, exercise)

Co-interventions were allowed as long as all arms of the randomised trial received the same co-intervention(s). Only interventions performed for a minimum duration of four weeks were included.

## Types of outcome measures

### Primary outcomes

- glycaemic control: glycosylated haemoglobin levels A1c (HbA1c), fasting and post-load blood glucose levels;
- incidence of type 2 diabetes mellitus: as diagnosed with at the time of the diagnosis prevailing diagnostic criteria (for example, ADA 1997; ADA 1999; WHO 1985; WHO 1999);
- adverse effects.

### Secondary outcomes

- morbidity related to impaired glucose metabolism, the metabolic syndrome or type 2 diabetes: vascular complications (angina pectoris, myocardial infarction, stroke, peripheral vascular disease, amputation), neuropathy, retinopathy, nephropathy, erectile dysfunction, hyperosmolar nonketotic dysregulation);
- mortality: mortality related to impaired glucose metabolism, the metabolic syndrome or type 2 diabetes (death from myocardial infarction, stroke, renal disease, or sudden death, death from hyperosmolar nonketotic coma), death from any cause;
- insulin: fasting and post-load insulin;
- insulin sensitivity;
- plasma lipids (triglycerides, total-, high-density lipoprotein (HDL)- and low-density lipoprotein (LDL)-cholesterol);
- blood pressure (diastolic and systolic blood pressure);
- body weight (or body mass index);
- inflammatory markers (for example, C-reactive protein);
- quality of life (using a validated instrument);
- costs.

*Covariates, effect modifiers and confounders:* Compliance.

*Timing of outcome measurement:* Possible influence of treatment duration was addressed in a sensitivity analysis.

## Search methods for identification of studies

**Electronic searches**—We searched the following sources for the identification of trials:

- The Cochrane Library
- PubMed (contains MEDLINE and a number of additional life science journals);
- EMBASE;
- Allied and Complementary Medicine Database (AMED);
- Chinese Biomedical Literature Database (CBM);
- Chinese Medical Current Contents (CMCC);

- Traditional Chinese Medical Literature Analysis and Retrieval System (TCMLARS);
- Chinese Dissertation Database (CDDDB);
- Chinese Academic Conference Papers (CACP);
- China Medical Academic Conference (CMAC);
- The System for Information on Grey Literature in Europe (SIGLE).

The Centralised Information Service For Complementary Medicine (CISCOM) was not searched as the database was not operating when the search was finished (February 2009).

Databases of ongoing trials:

- 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/>).

We combined three different search strategies as follows:

- for IGT and IFG we used the strategy from a previous systematic review of western medicine for IGT and IFG (Van de Laar 2006);
- for Chinese herbal medicines we employed strategies used for other Cochrane reviews of Chinese herbal medicines;
- for controlled trials we used a sensitive validated search strategy (Robinson 2002).

All the above databases were searched from the available date of inception until the latest issue (Feb 2009). For a detailed MEDLINE search strategy please see under Appendix 1.

**Searching other resources**—The authors of significant publications or experts in the relevant field were contacted for potential studies. We telephoned authors who had published two or more papers on clinical trials of prediabetes (three authors). When we contacted authors to collect details on included and excluded studies they were asked if they had participated in any other clinical trials of Chinese herbal medicines and IGT. Details of contact are provided in the tables of included and excluded studies. Relevant pharmaceutical companies which produced relevant products, were to be checked and contacted. However none were contacted, the products on the market are aimed at type 2 diabetes not prediabetes.

We searched the reference lists of included trials to identify additional trials. Studies published in any language were included.

## Data collection and analysis

**Selection of studies**—To determine the studies to be assessed further, two authors independently scanned the abstract, title or both sections of every record retrieved. All potentially relevant articles were investigated as full text. Where information was ambiguous or missing in the article the author was contacted where possible. If the author could not be contacted, the decision to include the trial was resolved by consensus. An

adapted PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) (Liberati 2009) flow-chart of study selection is attached.

**Dealing with duplicate publications:** In the case of duplicate publications and companion papers of a primary study, we tried to maximise yield of information by simultaneous evaluation of all available data. In cases of doubt, the original publication (usually the oldest version) obtained priority.

**Data extraction and management—**For studies that fulfilled the inclusion criteria, two authors abstracted relevant population and intervention characteristics using standard data extraction templates (for details see Characteristics of included studies), with any disagreements resolved by discussion, or if required by a third party. Any relevant missing information on the trial was sought from the original author(s) of the article.

**Assessment of risk of bias in included studies—**Two authors independently assessed the risk of bias of each of the included studies against key criteria: random sequence generation; allocation concealment; blinding of participants, outcome assessors and intervention providers; incomplete outcome data; selective outcome reporting; and other sources of bias. Studies that did not adequately meet these criteria were considered at high risk of bias. These methods have been updated since the publication of the protocol for this review to reflect guidance from the Cochrane Collaboration (Higgins 2008).

#### **Measures of treatment effect**

**Dichotomous data:** Dichotomous data were expressed as relative risk (RR) ratios rather than odds ratios (OR). This method has been changed since the publication of the protocol to reflect the approach used by other studies in this modality of treatment. It is also a more easily understood statistic in presenting these outcomes.

**Continuous data:** Weighted mean differences (WMD) and 95% confidence intervals (CI) were calculated for continuous data using a random-effects model. A random-effects model was used in preference to a fixed-effect model due to the expected heterogeneity of the trials. The actual measure of effect of all continuous variables was the differences from baseline to endpoint. The standard deviations (SD) of these differences were essential for the data to be included in the meta-analysis. All SDs of the difference were reported, and it was not necessary to impute SDs.

**Time-to-event data:** We planned to summarise time-to-event data using use methods of survival analysis and express the treatment effect as a hazard ratio.

**Unit of analysis issues—**Data were summarised statistically if they were available, sufficiently similar and of sufficient quality. Statistical analysis was performed according to the statistical guidelines referenced in the newest version of the Cochrane Handbook for Systematic Reviews of Interventions (Higgins 2008).

**Dealing with missing data—**Relevant missing data were obtained from authors, where possible. Important numerical data such as screened, eligible and randomised participants as well as intention-to-treat (ITT) and per-protocol (PP) population were evaluated. Drop-outs, misses to follow-up and withdrawn study participants were also investigated where possible. Issues of last-observation-carried-forward (LOCF), ITT and PP were critically appraised and compared to specification of primary outcome parameters and power calculation.



**Assessment of heterogeneity**—In the event of substantial clinical or methodological or statistical heterogeneity, study results were not combined in meta-analysis. Heterogeneity was identified by visual inspection of the forest plots, by using a standard  $\chi^2$ -test and a significance level of  $\alpha=0.1$ . Heterogeneity was also examined with  $I^2$  (Higgins 2002), where  $I^2$  values of 75% and more indicate a considerable level of heterogeneity (Higgins 2003). When heterogeneity was found, we attempted to determine potential reasons for it by examining individual study characteristics and those of subgroups of the main body of evidence.

**Assessment of reporting biases**—Funnel plots were used to assess for the potential existence of small study bias. There are a number of explanations for the asymmetry of a funnel plot. Therefore, we planned to carefully interpret results (Lau 2006).

**Data synthesis**—Data concerning details of study population, intervention and outcomes were extracted independently by two reviewers using a standard data extraction form. The standard data extraction form included at least the following items:

- general information: published/unpublished, title, authors, source, contact address, country, urban/rural, language of publication, year of publication, duplicate publications, sponsoring, setting;
- trial characteristics: design, duration, randomisation (and method), allocation concealment (and method), blinding (participants, people administering treatment, outcome assessors), check of blinding;
- intervention(s): placebo included, intervention(s) (single herb or compound of herbs, dose, route, timing, mode of treatment, expertise of the practitioner), comparison intervention(s) (dose, route, timing), co-medication(s) (dose, route, timing);
- participants: sampling (random / convenience), exclusion criteria, total number and number in comparison groups, sex, age, baseline characteristics, diagnostic criteria, duration of diabetes, similarity of groups at baseline (including any co-morbidity), assessment of compliance, withdrawals / losses to follow-up (reasons / description), subgroups;
- outcomes: outcomes specified above, any other outcomes assessed, other events, length of follow-up, quality of reporting of outcomes;
- results: for outcomes and times of assessment (including a measure of variation), if necessary converted to measures.

**Subgroup analysis and investigation of heterogeneity**—Subgroup analyses were to be performed if one of the primary outcome parameters demonstrated statistically significant differences between treatment groups. The following subgroup analyses were planned:

- glycosylated haemoglobin A1c (HbA1c) level at baseline (subdivided into groups, based on data);
- age (subdivided into groups, based on data);
- gender;
- body mass index (BMI) (subdivided into groups, based on data);
- duration of intervention (subdivided into groups, based on data).

**Sensitivity analysis**—We planned to perform sensitivity analyses in order to explore the influence of the following factors on effect size:

- repeating the analysis excluding unpublished studies;
- repeating the analysis taking account of risk of bias, as specified above;
- repeating the analysis excluding any very long or large studies to establish how much they dominate the results;
- repeating the analysis excluding studies using the following filters: diagnostic criteria, language of publication, source of funding (industry versus other), country.

The robustness of the results was also to be tested by repeating the analysis using different measures of effects size (relative risk, odds ratio etc.) and different statistical models (fixed- and random-effects models).

## Results

### Description of studies

**Results of the search**—The initial search identified 1926 records, from these 83 full papers were identified for further examination. If there was unclear information in the title or abstract, the full article was retrieved for clarification. The other studies were excluded on the basis of their abstracts because they were not relevant to the question under study, obvious duplicates were removed. After screening the full text of the 83 selected papers, 16 studies finally met the inclusion criteria (Figure 1), and one study is awaiting classification (Liu DQ 2007).

**Included studies**—There were 16 randomised clinical trials included in this review. They reported random allocations of participants with impaired glucose tolerance (IGT) to Chinese herbal medicines versus controls. Nine studies randomised participants to receive Chinese herbal medicines with a co-intervention of lifestyle modification versus a control of lifestyle modification alone (Fan GJ 2004; Hao AZ 2004; Li CP 2004; Tang QZ 2007; Yang B 2004; Yao Z 2001; Wei AS 2001; Zeng YH 2006; Zhou DY 2003). Three trials compared Chinese herbal medicines with placebo (Hioki C 2004; Fang ZH 2007; Wang BQ 2008), two of these trials included a co-intervention of a lifestyle intervention. Two trials compared Chinese herbal medicines with the biguanide metformin (Qu LX 2002; Shi J 2005). There was one three-arm trial comparing *Jian pi zhi shen huo xue* with lifestyle modification versus the alpha-glucosidase inhibitor, acarbose versus lifestyle modification alone (Tang QZ 2007). One trial compared *Jinqi jiangtang* and basic IGT education with basic IGT education alone (Wang YX 2005). Finally, there was a single trial that compared *Yi qi yang yin huo xue* with a co-intervention of an antihypertensive medication (vasodilator) versus the same antihypertensive medication alone (Lu X 2005). The details of the trials are listed under ‘Characteristics of included studies’.

The duration of the trials ranged from four weeks to two years (mean 9.3 months). Of the 16 included trials, eight trials ran for over 12 months (Fan GJ 2004; Li CP 2004; Tang QZ 2007; Wang BQ 2008; Wang YX 2005; Wei AS 2001; Zeng YH 2006; Zhou DY 2003). There were three large trials (more than 100 participants) that ran for over 12 months (Tang QZ 2007; Wang YX 2005; Zeng YH 2006).

All trials had a parallel design. Fourteen trials were two-armed and two were three-armed (Tang QZ 2007; Zeng YH 2006). The third control arm of the Zeng YH 2006 trial was not included in the comparisons or this result section. The control arm had a simple education intervention differing to the co-intervention of the herbal medicine. This comparison did not

meet the inclusion criteria set for this review. Data from this arm are not included in the results section.

The trials were all conducted from 2001 onwards. One study is still awaiting classification.

**Participants:** The sixteen trials included 1391 participants. The average number of participants in the trials was 87, ranging from 42 to 168.

Mean age of the participants was 52, ranging from 44 to 66 years (missing data from Fang ZH 2007). This is consistent with population prevalence which shows that the 40 to 59 years age group currently has the greatest number of persons with impaired glucose tolerance and diabetes (IDF 2008).

There were 719 males and 659 females (no gender data available on 13 withdrawals). One trial (Hioki C 2004) chose to enrol female participants only (n = 81). The aim of this study was primarily to assess insulin resistance and visceral adiposity. One other trial (Hao AZ 2004) had an over-representation of males to females (121 : 47). The overall ratio of the trials is not consistent with the population prevalence of diabetes and prediabetes which shows a female predominance with females ranging 10% higher than males for diabetes, and females ranging 20% higher than males for impaired glucose tolerance (IDF 2008).

Two trials enrolled obese or overweight participants only (Hioki C 2004; Shi J 2005). Three studies (Yang B 2004; Zeng YH 2006; Zhou DY 2003) included participants with a mean body mass index (BMI) in the healthy weight range (ranging from 20.8 to 24.3). Five studies (Tang QZ 2007; Wang BQ 2008; Wang YX 2005; Wei AS 2001; Yao Z 2001) included participants with a mean BMI in the obese range (ranging from 25.3 to 27.2).

One trial enrolled hypertensive participants only (Qu LX 2002).

With regard to ethnicity, all trial participants, with the exception of one trial which involved Japanese women (Hioki C 2004), were Chinese.

All trials included participants with impaired glucose tolerance, only with the exception of one trial (Wang YX 2005) which involved those with impaired fasting tolerance (IFG) in addition to those with IGT.

All trials recruited outpatients from hospitals or clinics.

For an overview of the study populations of the trials, like randomised individuals, intention-to-treat populations and participants finishing the study, please refer to Table 1.

**Diagnosis:** The diagnostic criteria used in the trials were mainly based on the WHO criteria. Eight trials used WHO 1999 and three trials used WHO 1985 criteria (Yao Z 2001; Zeng YH 2006; Zhou DY 2003). Four trials used the American Diabetes Association (ADA 1997) criteria (Fang ZH 2007; Lu X 2005; Qu LX 2002; ; Yang B 2004). One trial used a combination of the WHO 1999 and the ADA 1997 criteria (Wang YX 2005). The ADA criteria rely on a fasting plasma glucose level equal or greater than 6.1 mmol/L and less than 7.0 mmol/L. This differs from the WHO 1999 criteria which uses both a fasting plasma glucose less than 7.0 mmol/L AND a 2hr blood glucose after oral glucose tolerance test (oGTT) equal or greater than 7.8 and less than 11.0. The WHO 1985 criteria had a slightly higher range for including people as IGT - fasting plasma glucose less than 7.8 mmol/L. The different diagnostic criteria were subjected to a sensitivity analysis but no significant differences were detected (see Appendix 2).

**Interventions:** Fifteen Chinese herbal medicine interventions were examined in the 16 randomised trials (see Characteristics of included studies). Chinese herbal medicine *Jinqi jiangtang* was tested in two trials (Wang YX 2005; Zhou DY 2003). The trials all tested compounds of complex herbal formulas (see Table 2 'Preparation and compositions of the Chinese herbal medicines'). Preparations of herbs were as decoctions, pills, capsules or granules.

The herbal composition of the interventions varied. However, some individual herbs were prevalent in the different formulas. *Astragalus membranecus* was present in 10 of the 15 interventions for which the ingredients were known. Where *Astragalus membranecus* was a major part of the formula (either in amounts equal or greater than 20 g or only one of six herbs) it was analysed in a separate analysis. Other commonly used herbs included *Shan yao* (eight of the 15 interventions) and *Ge gen* (four of the 15 interventions).

The 16 trials had eight distinct comparisons:

- nine trials compared nine Chinese herbal medicines with lifestyle modification as a control and co-intervention (*Jiangtang bushen* decoction (Fan GJ 2004), *Jinqi jiangtang* pills (Zhou DY 2003), *Liu wei di huang wan* pills (Zeng YH 2006), *Qimai jiangtang yin* decoction (Li CP 2004), *Tang kang yin* decoction (Yang B 2004), *Tang Heng I* ( Yao Z 2001), *Xiaoke huayu* tablets (Hao AZ 2004), *Xiaoke yuye* decoction (Wei AS 2001) and *Jian pi zhi shen huo xue* (Tang QZ 2007);
- two trials compared Chinese herbal formulas with a placebo with lifestyle modification as a co-intervention: *Bofu-tsusho-san* (Hioki C 2004) and *Dan zhi jiang tang jiao* (Fang ZH 2007);
- one trial compared *Qiwei tangping* capsules with a placebo (Wang BQ 2008);
- one trial compared *Tang ping san* with metformin, with a lifestyle modification as co-intervention (Qu LX 2002);
- one trial compared *Fufang cangzhu* decoction with metformin (Shi J 2005);
- one trial compared *Jian pi zhi shen huo xue* with acarbose (Tang QZ 2007);
- one trial compared *Yi qi yang yin huo xue* combined with an antihypertensive medication with an antihypertensive medication alone (Lu X 2005);
- one trial compared *Jinqi jiangtang* pills with a basic education on IGT as a co-intervention and as a control (Wang YX 2005).

Tang QZ 2007 and Zeng YH 2006 were three-arm trials. Tang QZ 2007 compared a *Jian pi zhi shen huo xue* plus lifestyle modification versus acarbose plus lifestyle modification versus lifestyle modification alone. Zeng YH 2006 compared *Liu wei di huang tang* plus lifestyle modification versus lifestyle modification alone versus a control receiving a diabetes educational pamphlet only.

Lifestyle modification typically involved diet, exercise and education about the disease. In most cases the specific nature of this intervention was poorly documented with the exception of Hioki C 2004 and Zeng YH 2006.

The studies yielded widely differing estimates of effect (a high level of heterogeneity) when results were pooled on most outcomes. This was expected with a review that includes a range of Chinese herbal medicine interventions composed of differing herbs and formulations.

**Outcomes:** The outcomes reported were mainly metabolic parameters including fasting blood glucose (reported in all studies except Qu LX 2002), 2hr fasting glucose (reported in all studies) and 'normalisation of fasting blood glucose' (reported in 10 studies). Normalisation was defined as fasting blood glucose <7.0 mmol/L and 2hr oGTT ≤7.8 mmol/L according to WHO 1999 criteria for all trials except Yao Z 2001, which used the ADA 1997 criteria for normal glucose tolerance of fasting blood glucose less than 6.1 mmol/L. Outcomes on normalisation of blood glucose were recorded as dichotomous data.

Ten studies measured the incidence of diabetes (Fan GJ 2004; Hao AZ 2004; Li CP 2004; Tang QZ 2007; Zhou DY 2003; Wang BQ 2008; Wang YX 2005; Wei AS 2001; Yao Z 2001). Incidence of diabetes refers to the number of participants that have converted to diabetes by the completion of the trial. Eight of the ten trials reporting on this outcome used WHO 1999 criteria to define diabetes (FPG >7.0 mmol/L and 2hr oGTT >11.0 mmol/L).

Four studies measured glycosylated haemoglobin A1c (HbA1c) (Hao AZ 2004; Hioki C 2004; Tang QZ 2007; Wei AS 2001). Zeng YH nominated HbA1c as an outcome but did not report the data.

Eleven studies measured lipids, either total cholesterol, triglycerides or both. Five studies measured HDL-cholesterol. Nine studies measured fasting insulin.

No study investigated mortality, morbidity or cost effectiveness. Lu X 2005 was the only study to measure quality of life. Adverse effects were reported in two of the studies. Other outcomes measured were body mass index (BMI), waist-hip-ratio (WHR) and blood pressure.

**Excluded studies**—Most of the references identified by the search update were excluded at the first screening step by one reviewer, as they were clearly irrelevant (see Characteristics of excluded studies). The most frequent reasons for exclusion at this level were: article was a review or a commentary; studies of people with diabetes; and clearly non-randomised design.

The full text of 83 studies was retrieved. Sixty-six studies had to be excluded after careful evaluation of the full publication. Seventeen studies were excluded due to inadequate methods of randomisation (odd-even, alternation, and based on clinician's decision). Sixteen studies were non-randomised trials and 15 were case series. A further 18 studies were excluded as they did not meet the review criteria for the population group, outcomes, duration or intervention. Of these, five studies were excluded due large sampling discrepancies indicating there was no true randomisation. In each case we were unable to contact the authors to resolve the discrepancy. One study was excluded as it was a duplicate.

### **Risk of bias in included studies**

Most published reports of trials were lacking in details of trial methodology (see Figure 2). We tried to contact all primary trial authors to clarify randomisation methods. When details were obtained (through phone calls) it was apparent that eleven of the trials had used an adequate sequence generation. The method was not reported for five trials and we were unable to contact the trial authors (Hao AZ 2004; Li CP 2004; Qu LX 2002; Wang YX 2005; Yao Z 2001).

Most of the trials provided data on important baseline characteristics of the intervention and control groups to judge the comparability of the two groups.

Three trials (Fang ZH 2007; Hioki C 2004; Wang BQ 2008) could be considered as having a low risk of bias reporting adequate sequence generation, adequate allocation concealment, participants blinded, all participants accounted for and no other apparent bias.

**Allocation**—Allocation concealment was adequate in only five trials (Fang ZH 2007; Hioki C 2004; Wang BQ 2008; Wei AS 2001; Zeng YH 2006). It was unclear in nine trials and not adequate in two.

**Blinding**—Participants were blinded in three trials (Fang ZH 2007; Hioki C 2004; Wang BQ 2008). The lack of blinding in the other trials could have resulted in an over- or underestimation of the outcomes as it may have affected the behaviour of the participants.

**Incomplete outcome data**—Attrition was low or adequately accounted for in most trials.

**Selective reporting**—In all trials but one (Zeng YH 2006), nominated and expected outcomes were reported. As no trials reviewed had published protocols of their data collection or analysis it is not known if some outcomes were not published.

**Other potential sources of bias**—Some authors were contacted by phone for further information on methods of randomisation, sequence generation, allocation concealment and, in some cases, clarify data issues. Authors were relying on recall and this may have led to some bias.

Six trials clearly reported the number of drop-outs and withdrawals (Fan GJ 2004; Hioki C 2004; Tang QZ 2007; Wang BQ 2008; Wang YX 2005; Wei AS 2001), although ITT analysis was not implemented; nor was it used in any of the other included trials. Reasons for drop-outs or withdrawals were not always clear.

Small study and reporting bias were considered. It is possible that the results are biased as it is possible that studies with negative outcomes have not been published. Outcomes for the first comparison group of studies were explored through funnel plots (see Figure 5 and Figure 6). However, these cannot be considered reliable as there were fewer than 10 studies; in addition funnel plot asymmetry may occur by chance. A sensitivity analysis was conducted to determine if the positive results of the small trial of Tang Heng I (Yao Z 2001) had influenced the meta-analysis of normalisation of fasting blood glucose (RR 1.99; 95% confidence interval (CI) 1.47 to 2.71 versus RR 2.07; 95% CI 1.52 to 2.82).

## Effects of interventions

There were no outcome data in any of the trials on death from any cause, morbidity, diabetes complications, or costs. No serious adverse events or hypoglycaemic episodes were reported.

We were only able to perform meta-analyses on two outcomes in this review and these should be interpreted cautiously. This is mainly due to issues of heterogeneity and because none of the specific herbal medicines comparison data was available from more than one study.

**Herbal medicine plus lifestyle modification versus lifestyle modification alone**—Nine trials involving 792 participants compared herbal medicines along with lifestyle intervention with lifestyle intervention alone (Fan GJ 2004; Hao AZ 2004; Li CP 2004; Tang QZ 2007; Wei AS 2001; Yang B 2004; Yao Z 2001; Zeng YH 2006; Zhou DY 2003). The average number of trial participants was 50, ranging from 42 to 168 participants. Average trial duration was 8.3 months, ranging from one month to 24 months

Nine different herbal medicines were investigated: *Jiangtang Bushen* decoction, *Xiaoke huaya* tablet, *Qimai jiangtang yin* decoction, *Jinqi jiangtang* tablets, *Xiaoke yuye* decoction, *Liu wei di huang tang*, *Tang kang yin* decoction, *Tang Heng I* decoction and *Jian pi zhi shen huo xue*.

In all trials, with the exception of Zeng YH 2006, the lifestyle intervention was poorly documented.

**Normalisation of fasting blood glucose and incidence of diabetes:** Normalisation of fasting blood glucose refers to the number of participants who returned to normal blood glucose range at the end of the trial.

Eight trials involving 625 participants reported on the normalisation of fasting blood glucose levels following the intervention.

Of the eight trials analysed, those receiving the Chinese herbal intervention were more than twice as likely (RR 2.07; 95% confidence interval (CI) 1.52 to 2.82) to have normalised their fasting blood glucose compared to those receiving lifestyle modification only (Figure 3).

The incidence of diabetes refers to the number of participants who had progressed to type 2 diabetes according to WHO or ADA criteria by the end of the trial.

Eight trials reported on the incidence of diabetes in the groups (Figure 4). There was a significant difference in the incidence of diabetes in favour of the Chinese herbal medicines following Tang Keng Yin tablets (Yang B 2004). When the results of the eight trials were pooled there was a significant difference found in favour of the Chinese herbal medicines compared to the lifestyle intervention alone (RR 0.33; 95% CI 0.19 to 0.58). All except three of these trials had a duration of more than 12 months (Yang B 2004 ran for one month, Hao AZ 2004 ran for two months, and Yao Z 2001 for three months).

In the pooling of results on these two measures there was no considerable statistical heterogeneity among the comparisons (normalisation of fasting blood glucose:  $I^2 = 66\%$ ; incidence of diabetes:  $I^2 = 0\%$ ). It is important to note that there was clinical heterogeneity. The Chinese herbal medicines used in the clinical trials analysed are wide ranging in their ingredients. These ingredients are used for a variety of different clinical purposes. However, they may still be considered as 'class' or 'group' of oral hypoglycaemic herbal medicines. But any pooled effect size should be interpreted only as crude indicator of the overall direction of the findings. Nevertheless, these findings show that participants receiving Chinese herbal medicines were less likely to develop diabetes and more likely to have normal blood glucose than those in the control group.

**Fasting blood glucose and 2hr blood glucose after an oral glucose tolerance test (oGTT):** Fasting blood glucose refers to the fasting plasma glucose (FPG) levels (mmol/L) measured in all nine trials in this comparison (continuous data).

In four of the nine trials, the Chinese herbal medicines combined with lifestyle modification were significantly better at reducing fasting blood glucose levels than lifestyle modification alone. *Jinqi jiangtang* tablets (Zhou DY 2003) showed a significant reduction (MD  $-0.58$  mmol/L; 95% CI  $-0.74$  to  $-0.42$ ), as did Hao AZ 2004 (MD  $-1.40$  mmol/L; 95% CI  $-1.72$  to  $-1.08$ ), Yang B 2004 (MD  $-0.21$  mmol/L; 95% CI  $-0.33$  to  $-0.09$ ), and Zeng YH 2006 (MD  $-0.31$  mmol/L; 95% CI  $-0.58$  to  $-0.04$ ). There was no significant difference of fasting blood glucose in the trials of *Jiangtang Bushen* decoction (Fan GJ 2004), *Qimai jiangtang*

*Yin* ( Li CP 2004), *Jian pi zhi shen huo xue* (Tang QZ 2007), *Xiaoke yuye* ( Wei AS 2001), and *Tang heng I* ( Yao Z 2001).

Two hour fasting blood glucose refers to blood glucose levels (mmol/L) measured after an oGTT. Six of the nine trials in this comparison reported significantly better results for reducing 2hr fasting blood glucose levels than the lifestyle modification control. There was no significant difference in the trials of *Jiangtang bushen* decoction (Fan GJ 2004) *Tang Heng I* decoction (Yao Z 2001) and *Liu wei di huang tang* (Zeng YH 2006).

When these studies were pooled, considerable heterogeneity was found among the studies ( $I^2 = 90\%$ ). This may be due to the type of the intervention, the duration of the intervention or both which prevented a meaningful meta-analysis of these outcomes.

**Glycosylated haemoglobin A1c (HbA1c):** Only three studies reported HbA1c outcomes. *Xiaoke huayu tablets* (MD  $-0.6\%$ ; 95% CI  $-1.0$  to  $-0.3$ ) ( Hao AZ 2004), *Xiaoke Yuye decoction* ( Wei AS 2001) (MD  $-0.9\%$ ; 95% CI  $-1.4$  to  $-0.3$ ) and *Jian pi zhi shen huo xue* (MD  $-0.1\%$ ; 95% CI  $-0.1$  to  $0.0$ ) ( Tang QZ 2007) combined with lifestyle modification were all statistically significant in reducing HbA1c compared to the control of lifestyle modification alone. No meta-analysis was conducted due to considerable statistical heterogeneity ( $I^2 = 88\%$ ).

**Insulin:** In the six trials that measured insulin levels, significantly lower levels were detected in those taking *Jiangtang bushen* decoction (Fan GJ 2004), *Qimai jiangtang* decoction (Li CP 2004), and *Jinqi jiangtang* tablets (Zhou DY 2003). No significant differences in insulin levels were found in those participants taking *Tang Kang Yin* (Yang B 2004) and *Tang Heng I* decoction (Yao Z 2001) compared with the lifestyle modification control group. In the trial of *Jian pi zhi shen huo xue* (Tang QZ 2007) insulin levels of the lifestyle modification control group were significantly lower than those in the Chinese herbal intervention group.

Insulin active index (IAI), a measure of insulin sensitivity, was assessed in one trial of *Qimai jiangtang yin* ( Li CP 2004). No significant differences were detected.

**Lipids:** Cholesterol outcomes were measured in seven trials (Fan GJ 2004; Hao AZ 2004; Tang QZ 2007; Wei AS 2001; Yang B 2004; Zeng YH 2006; Zhou DY 2003). Triglycerides were also measured in these seven trials. High density lipoprotein (HDL) cholesterol was measured in two trials (Tang QZ 2007; Zhou DY 2003).

One trial that measured all three outcomes, *Jian pi zhi shen huo xue* ( Tang QZ 2007) showed a significant improvement in reducing total cholesterol (MD  $-0.73$  mmol/L; 95% CI  $-1.15$  to  $-0.31$ ), HDL-cholesterol (MD  $0.30$  mmol/L; 95% CI  $0.10$  to  $0.50$ ) and triglycerides (MD  $-0.31$  mmol/L; 95% CI  $-0.52$  to  $-0.10$ ) for the combined intervention of Chinese herbal medicines with lifestyle interventions.

*Jiangtang bushen tang* ( Fan GJ 2004), *Tang kang yin* ( Yang B 2004), *Liu wei di huang tang* ( Zeng YH 2006), and *Xiaoke huayu pian* (Wei AS 2001) also all showed a significant improvement compared to the control in reducing total cholesterol and triglycerides.

**Body mass index (BMI):** Five trials comparing herbal medicine with lifestyle modification with lifestyle modification alone measured BMI. *Xiaoke yuye* decoction (Wei AS 2001), *Tang kang yin* decoction (Yang B 2004) , and *Liu wei di huang* capsule (Zeng YH 2006) all demonstrated a significant improvement in BMI. There was no significant improvement in



BMI in those taking *Jinqi jiangtang pian* (Zhou DY 2003) and *Jiangtang bushen tang* (Fan GJ 2004).

**Blood pressure:** Two trials (Zeng YH 2006; Zhou DY 2003) in this comparison group examined blood pressure. *Liu wei di huang* capsules were statistically significantly more effective than the control group in reducing diastolic (MD -3 mm Hg; 95% CI -4 to -1) and systolic (MD -4 mm Hg; CI 95% -7 to -1) blood pressure. The diastolic blood pressure data for *Jinqi Jiangtang pian* were unusual in favour of lifestyle intervention alone (MD 20 mm Hg; 95% CI 19 to 21) and we were unable to contact the author to clarify any reporting anomaly. There were no significant differences in the systolic blood pressure (MD -0.4 mm Hg; 95% CI -3 to 2).

**Subgroup analysis: Astragalus membranecus and FBG:** *Astragalus membranecus* was present as a main ingredient in five of the trials and it was analysed in a subgroup analysis. In three of these trials with *Astragalus membranecus* there was a significant difference of combined herbal medicine with lifestyle interventions in FBG compared to the control (Wang YX 2005; Zhou DY 2003). However, the remaining three trials did not detect a significant difference (Fan GJ 2004; Li CP 2004; Tang QZ 2007).

**Herbal medicine plus lifestyle modification versus placebo plus lifestyle modification**—Two trials compared a Chinese herbal medicine with placebo with the co-intervention of lifestyle modification.

*Danzhi jiangtang jiao* capsules (Fang ZH 2007) combined with lifestyle modification were significantly better than a placebo and lifestyle modification in improving 2hr-oGTT blood glucose (MD -1.44 mmol/L; 95% CI -2.01 to -0.87). But there was no significant difference between the groups in reducing fasting blood glucose (MD -0.40 mmol/L; 95% CI -0.83 to -0.03). Triglycerides and insulin levels also showed significant reductions .

*Bofu-Tsusho-San* (Hioki C 2004) significantly improved fasting blood glucose (MD -0.28 mmol/L; 95% CI -46 to -0.10) but not 2hr-oGTT blood glucose (MD -0.12 mmol/L; 95% CI -0.60 to 0.36). There was no significant difference in the HbA1c between those taking *Bofu-Tsusho-San* and the control group. There was no significant difference in cholesterol levels found in the trial of *Bofu-Tsusho-San*, and while *Bofu-Tsusho-San* did not show an improvement in total cholesterol outcomes it demonstrated a significant difference in increasing HDL-cholesterol (MD 0.25 mmol/L; 95% CI 0.12 to 0.38).

**Herbal medicine plus lifestyle modification versus metformin plus lifestyle modification**—There was no significant difference in the 2-hr glucose tolerance test levels between *Tangping san* plus lifestyle modification and metformin plus lifestyle modification at the end of the three months intervention. No other outcomes were reported for *Tangping San* (Qu LX 2002).

**Herbal medicine versus placebo**—Compared with placebo, those taking *Qi wei tang ping* capsules (Wang BQ 2008) showed significantly better results for fasting blood glucose and 2hr-oGTT blood glucose. There was a significant higher level of normalisation of fasting blood glucose compared to placebo (RR 2.94, 95% CI 1.47 to 5.87). There was no significant difference in BMI or waist-to-hip ratio in the herbal medicine group compared to those taking placebo.

**Herbal medicine versus metformin**—There was no significant difference between *Fufang cangzhu* decoction and metformin in reducing fasting blood glucose, cholesterol,

triglycerides, insulin, weight, or waist-to-hip ratio (Shi J 2005). We were unable to ascertain if this comparison was constructed as a non-inferiority trial.

#### **Herbal medicine plus lifestyle modification versus acarbose plus lifestyle modification**

—There was no significant difference between the *Jian pi zhi shen huo xue* (Tang QZ 2007) and acarbose in any of the outcome measures (FBG, 2hr-oGTT blood glucose, insulin, lipids or HbA1c). There was also no significant difference between *Jian pi zhi shen huo xue* and acarbose regarding the normalisation of fasting blood glucose (Tang QZ 2007).

#### **Herbal medicine plus antihypertensive medication versus antihypertensive medication alone**

—The Chinese herbal medicine, *Yi qi yang yin huo xue* combined with antihypertensive medication was significantly better than the antihypertensive medication alone in reducing fasting blood glucose (one trial, MD  $-0.96$  mmol/L, 95% CI  $-1.55$  to  $-0.37$ ). *Yi qi yang yin huo xue* was also significantly better than the control in reducing cholesterol, triglycerides and increasing HDL-cholesterol. There was no significant difference between *Yi qi yang yin huo xue* and the control in regard to systolic or diastolic blood pressure. This trial also evaluated quality of life using an instrument comprised of eight scales designed for hypertension based on a study of an American hypertensive population (Testa 1989) and validated for a Chinese population (Du 1994). The trial found that on the five of the eight scales: physical symptoms distress scale, sexual symptoms distress scale, sleep dysfunction scale, positive symptom scale and working performance, there was a significant difference in favour of the herbal medicine group (Lu X 2005). There was no significant difference in the measures of life satisfaction scale, social participation scale and general well-being adjustment scale. However, it was difficult to disentangle the effects of the various compound on quality of life. This study reported that there were no adverse renal or liver findings and in ECG tests.

**Herbal medicine plus basic education versus basic education alone**—In this comparison one study compared *Jinqi jiangtang* tablets with a control with a co-intervention of basic education about IGT (Wang YX 2005). This did not involve diet or exercise instruction. Normalisation of blood glucose was significant (RR 10.80; 95% CI 3.47 to 33.66) as was the incidence of diabetes (RR 0.44; 95% CI 0.22 to 0.87) and reduction of fasting blood glucose (MD  $-0.88$ ; 95% CI  $-1.14$  to  $-0.62$ ) and 2-hr oGTT. There was a significant reduction in triglycerides but not total cholesterol in the intervention group compared to the control.

**Adverse events:** Five of 17 trials reported outcomes for adverse events. In the trial of *Bufo-Tsusho-San* there were four withdrawals; three from the treatment group for non-compliance because of loose bowels. In Wang BQ there were two instances of abdominal discomfort, one participant from each group (Wang BQ 2008). In the two other studies recording outcomes for adverse events none were reported (Wei AS 2001; Lu X 2005). In the trial of *Jinqi Jiangtang* (Wang YX 2005) three cases in the intervention group developed mild gastro-intestinal symptoms in the early stage of taking the Chinese herbal medicine. These resolved after one to two weeks.

## Discussion

### Summary of main results

Sixteen randomised trials were included in this review. There was considerable clinical heterogeneity in the interventions of the included studies. In the 16 studies lasting four

weeks to two years there were eight different comparisons, with 15 unique herbal formulations investigated.

In this systematic review we found evidence from eight trials that Chinese herbal medicines combined with lifestyle modification were significantly better at normalising blood glucose levels than lifestyle modification alone (RR 2.07; 95% CI 1.52 to 2.82). In a meta-analysis of eight trials, those receiving Chinese herbs were also more likely to have a reduced incidence of diabetes (RR 0.33; 95% CI 0.19 to 0.58). In the pooling of the results for the meta-analyses of the two measures of normalising blood glucose and incidence of diabetes there was no considerable statistical heterogeneity among the comparisons ( $I^2 = 66%$  and  $I^2 = 0%$ , respectively). It is important to note that there is a clinical difference in the herbal composition of these interventions and likely a difference in the active components. But these Chinese herbal medicines are not completely dissimilar. They form part of a 'group' of herbal medicines with hypoglycaemic effects designed to normalised elevated blood glucose and prevent diabetes. The population groups according to age, gender and ethnicity were similar. However, any pooled effect size should be interpreted only as a crude indicator of the overall direction of the findings. Further, all of these trials had a high risk of bias. Specifically, none of these trials were blinded and three of the trials reported unclear randomisation procedures. Nevertheless, these findings indicate that participants receiving Chinese herbs were less likely to develop diabetes and more likely to have normal blood glucose than those in the control group. The result therefore provides guidance for future research not for specific clinical practice.

*Xiaoke huayu tablets* ( Hao AZ 2004), *Xiaoke yuye decoction* ( Wei AS 2001) and *Jian pi zhi shen huo xue* ( Tang QZ 2007) combined with lifestyle modification were all statistically significant in reducing glycosylated haemoglobin A1c (HbA1c) compared to the control of lifestyle modification alone.

Compared with placebo and lifestyle modification, *Danzhi jiangtang jiao* capsules (Fang ZH 2007) with lifestyle modification were significantly better at reducing 2hr blood glucose after oral glucose tolerance testing (oGTT). *Bofu-Tsusho-San* (Hioki C 2004) combined with lifestyle modification was significantly better at reducing fasting blood glucose (FBG).

Compared with placebo alone, *Qiweitang ping* (Wang BQ 2008) was significantly better at normalising blood glucose, reducing FBG and 2hr-oGTT blood glucose.

Three trials compared Chinese herbal medicines with a pharmaceutical control. However, these were not clearly specified as non-inferiority or equivalence trials. Compared with metformin, *Fufang cangzhu* (Shi J 2005) showed no significant difference in reducing FBG. Compared to metformin combined with lifestyle modification, *Tangping san* (Qu LX 2002) combined with lifestyle modification showed no significant differences in reducing 2hr-oGTT blood glucose.

There was no significant difference between *Jian pi zhi shen huo xue* (Tang QZ 2007) compared to acarbose, with both groups receiving lifestyle modification, on any of the outcome measures.

In a trial of an antihypertensive pharmaceutical the combination of *Yi Qi Yang Yin Huo Xue* (Lu X 2005) with the antihypertensive drug was significantly better at reducing FBG, cholesterol, triglycerides and HDL-cholesterol than the antihypertensive drug alone.

Some of the Chinese herbal medicines showed potential for improving cholesterol and triglycerides along with normalising FBG. *Jian pi zhi shen huo xue*, *Jiangtang bushen tang*,

*Tang kang yin*, *Liu wei di huang tang*, and *Xiaoke huayu pian* all showed a significant improvement compared to the control in reducing total cholesterol and triglycerides.

### Overall completeness and applicability of evidence

The age and gender of participants in the included trials was representative of the general global population showing IGT (IDF 2008). Although all but one trial were conducted in a Chinese population this is not thought to impact on the applicability of the interventions to other populations.

### Quality of the evidence

Thirteen of the 16 trials included in this review demonstrated a risk of bias in at least two of several key criteria: random sequence generation; allocation concealment; blinding of participants, outcome assessors and intervention providers; incomplete outcome data; selective outcome reporting; and other sources of bias (see Figure 2).

Details of sequence generation and concealment allocation were only reported in one of the published papers. Trial authors were contacted to clarify details. We found that nine trials had used adequate sequence generation methods (Fan GJ 2004; Fang ZH 2007; Hioki C 2004; Lu X 2005; Wang BQ 2008; Wei AS 2001; Yang B 2004; Zeng YH 2006; Zhou DY 2003). Allocation concealment was less frequently understood or adequately performed, with only five of the trial authors providing satisfactory details when questioned (Fang ZH 2007; Hioki C 2004; Wang BQ 2008; Wei AS 2001; Zeng YH 2006). Empirical evidence suggests that failure to meet these criteria, such as adequate allocation concealment, is associated with overestimates of effect.

In clarifying risk of bias with authors it was apparent that the concept of randomisation was not always fully understood. Of the 83 full papers retrieved, 34 claimed to be randomised but after contacting authors only 17 of these were truly randomised (50%). This is lower than the findings of a Cochrane review of Chinese herbal medicines for the treatment of common cold which found more than 95% of the authors misunderstood the concept of randomisation (Wu 2007).

Overall only three of the 16 included trials were well designed and had a fairly low risk of bias (Fang ZH 2007; Hioki C 2004; Wang BQ 2008). The insufficient number of trials prohibited us from performing meaningful sensitivity analyses to clarify robustness of the review results to the exclusion of trials with inadequate methodology.

The double-blind, placebo controlled trial of *Dan zhi jiang tang jiao* (Fang ZH 2007) reported a significant improvement in 2 hr-oGTT blood glucose, insulin and triglycerides but there was no significant difference in fasting blood glucose. The method of sequence generation and allocation concealment was not reported in the trial but deemed adequate after an interview with one of the authors.

A second double-blind trial compared *Bofu-Tsusho-San* plus lifestyle modification versus placebo plus lifestyle modification in 81 people over six months. People randomised to *Bofu-Tsusho-San* plus lifestyle modification demonstrated a significantly improved fasting blood glucose but not 2hr-oGTT blood glucose (Hioki C 2004). There was no significant difference in glycosylated haemoglobin A1c (HbA1c) between those taking *Bofu-Tsusho-San* and the control group.

The third double-blind trial, comparing *Qi wei jiangtang yin* with placebo, demonstrated a significant improvement in the rate of normalisation of fasting blood glucose, reduction of fasting blood glucose, and 2hr-oGTT (Wang BQ 2008) in those randomised to the placebo

group. This trial had a duration of 24 months and a low risk of bias as well as an adequately powered sample. However, as there are no other trials of this herbal medicine in this population group, these results cannot be seen as definitive.

There were few trials ( $n = 4$ ) that collected HbA1c data. This will be an important outcome measure to collect in future trials. According to the American Diabetes Association Expert Committee on the Diagnosis of Diabetes, the European Association for the Study of Diabetes, and the International Diabetes Federation, the HbA1c will become the preferred diagnostic test for diabetes (ADA 2009).

In many of the trials it is possible that the statistical power may not have been adequate. Several studies have reported rates of natural reversion to normal glucose levels of one third to one half for participants identified with IGT (Forrest 1988; Riccardi 1985). Moreover, rates of reversion to normal glucose levels appeared independent of the duration of follow-up, with a range of two months to 10 years (Rambod 2009). The rate of reversion needs to be built into statistical calculations of the power required to detect a difference in blood glucose and other outcomes.

Twelve of the 16 trials had lifestyle modifications as a co-intervention, all but two trials failed to provide any details on the nature of this intervention. Without thorough details, replication of the trials to build evidence for these interventions is not possible. Further this operates as a potentially confounding factor and calls into question the veracity of the results.

Overall the positive evidence in favour of Chinese herbal medicines for the treatment of impaired glucose tolerance is constrained by the following factors: a lack of trials that tested the same medicine, lack of details on co-interventions, unclear methods of randomisation, poor reporting and other risks of bias.

### **Potential biases in the review process**

We have tried to reduce bias by contacting all trial authors to clarify the methods of randomisation. In this way we were able to eliminate trials that were only quasi-randomised. Nonetheless we were unable to contact the authors of five of the included trials to clarify the methods of randomisation (Hao AZ 2004; Li CP 2004; Qu LX 2002; Wang YX 2005).

### **Agreements and disagreements with other studies or reviews**

As far as we are aware of, no systematic review has been done with a focus on Chinese herbal medicines for people with impaired glucose tolerance or impaired fasting glucose.

## **Authors' conclusions**

### **Implications for practice**

The available evidence suggests that some Chinese herbal medicines could be considered as a potential treatment in people with impaired glucose tolerance and reduce the incidence of diabetes. Given the sources of potential bias further evidence is required to confirm these trends. A separate systematic review on the efficacy of lifestyle education concluded that lifestyle education was clearly effective for reducing two-hour plasma glucose after an oral glucose tolerance test and the incidence of type 2 diabetes over one year (Yamaoka 2005). Our review adds to this growing body of evidence, in 80% of the included trials lifestyle modification was used as a co-intervention.

## Implications for research

Further trials are required before any conclusions can confidently be reached about the effects of Chinese herbal medicines for the treatment of impaired glucose tolerance and the delay of diabetes onset.

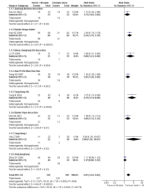
Future trials need to be designed in such a way as to address the risk of bias identified in the trials reviewed here. It is essential that such trials have adequate methods of randomisation and allocation concealment and that these methods are clearly reported. Ideally, future trials will involve a control of a pharmacological nature or be placebo-controlled. The Chinese herbal medicines and the control intervention need to be manufactured in such a way that participants and intervention providers can be blinded. If a lifestyle modification is to be used as a co-intervention or control this should be described in detail. The rate of reversion to normal blood glucose needs to be built into statistical calculations of the power of the trial required to detect a difference in blood glucose and other outcomes. Along with fasting blood glucose outcomes, other measurements of efficacy and safety should include glycosylated haemoglobin A1c (HbA1c), health-related quality of life, death from any cause, diabetic complications, economic outcomes and adverse events.

All future Chinese herbal medicines trials should be reported according to the elaborated CONSORT statement for reporting randomised controlled trials of herbal medicines (Gagnier 2006).

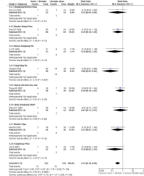
## Graphs

### 1 - Herbal medicine plus lifestyle modification versus lifestyle modification alone

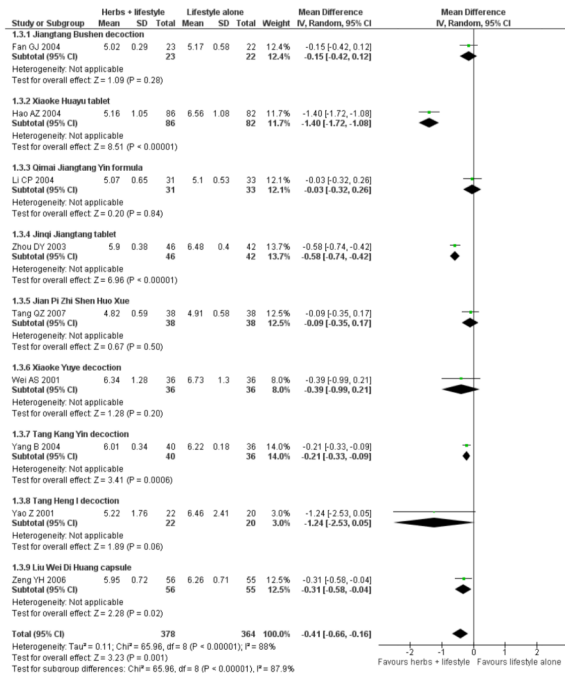
#### 1.1 Normalisation of fasting blood glucose at trial completion (n)—



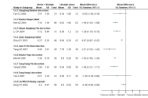
#### 1.2 Incidence of diabetes (n)—



#### 1.3 Fasting blood glucose (mmol/L)—



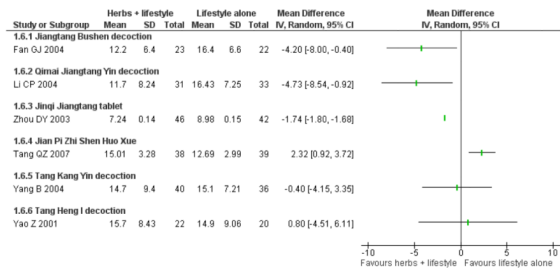
**1.4 2hr fasting blood glucose (mmol/L) [ after oral glucose tolerance test]—**



**1.5 HbA1c (%)—**



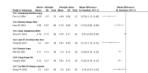
**1.6 Insulin (µU/ml)—**



**1.7 IAI (insulin sensitivity)—**



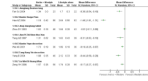
**1.8 Total cholesterol (mmol/L)—**



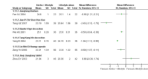
**1.9 Lipids: HDL (mmol/L)—**



### 1.10 Triglycerides (mmol/L)—



### 1.11 Body Mass Index (kg/m<sup>2</sup>)—



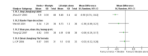
### 1.12 Diastolic blood pressure (mmHg)—



### 1.13 Systolic Blood Pressure (mmHg)—



### 1.14 Main ingredient Astragalus membranecus (≥30g): Fasting blood glucose (mmol/ml)—



## 2 - Herbal medicine plus lifestyle modification versus placebo plus lifestyle modification

### 2.1 Reduction in fasting blood glucose (mmol/L)—



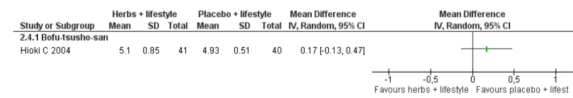
### 2.2 Reduction in 2hr fasting blood glucose after oral glucose tolerance test—



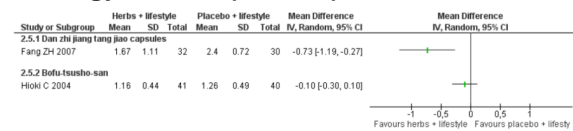
### 2.3 Reduction in HbA1c (%)—



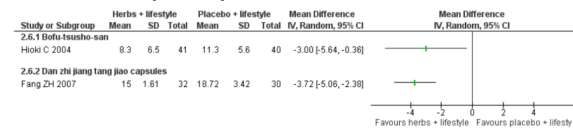
### 2.4 Total cholesterol (mmol/L)—



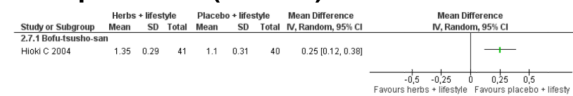
### 2.5 Triglycerides (mmo/L)—



### 2.6 Insulin (mu/L)—



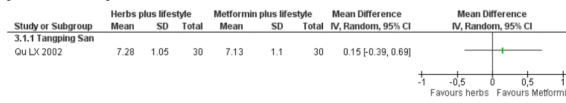
### 2.7 Lipids: HDL (mmol/L)—





### 3 - Herbal medicine plus lifestyle modification versus metformin plus lifestyle modification

#### 3.1 Reduction in 2 hr fasting blood glucose after oral glucose tolerance test (mmol/L)—

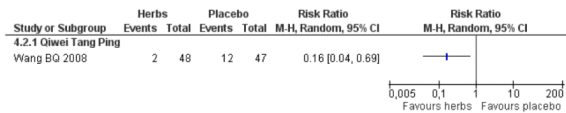


### 4 - Herbal medicine versus placebo

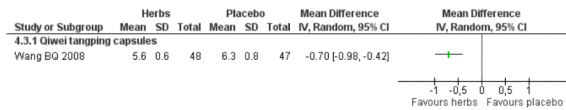
#### 4.1 Normalisation of fasting blood glucose (n)—



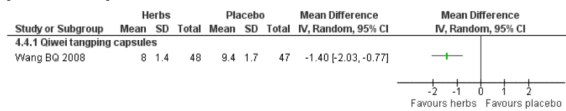
#### 4.2 Incidence of diabetes (n)—



#### 4.3 Reduction in fasting blood glucose (mmol/L)—



#### 4.4 Reduction in 2hr fasting blood glucose after orale glucose tolerance test (mmol/L)—



#### 4.5 Body mass index (kg/m<sup>2</sup>)—



#### 4.6 Waist-to-hip ratio (WHR)—

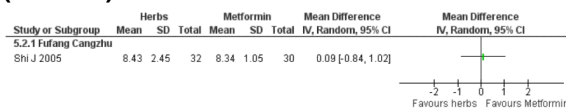


### 5 - Herbal medicine versus metformin

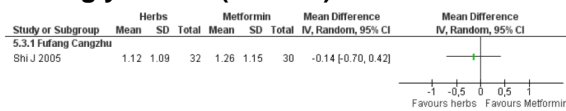
#### 5.1 Reduction in fasting blood glucose (mmol/L)—



#### 5.2 Reduction in 2hr fasting blood glucose after orale glucose tolerance test (mmol/L)—



#### 5.3 Triglycerides (mmol/L)—



#### 5.4 Total cholesterol—

6.5 HbA1c (%)—

### 5.5 Insulin (mU/L)—

6.4 Incidence of diabetes (n)—

### 5.6 Waist-to-hip ratio (WHR)—

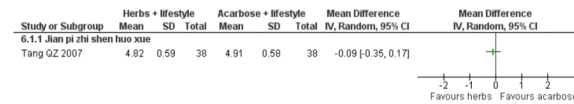
6.3 Normalisation of blood glucose (n)—

### 5.7 Weight (kg)—

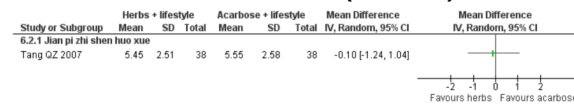
6.2 2hr-Glucose tolerance (mmol/L)—

## 6 - Herbal medicine plus lifestyle modification versus acarbose plus lifestyle modification

### 6.1 Reduction in fasting blood glucose (mmol/L)—



### 6.2 2hr-Glucose tolerance (mmol/L)—



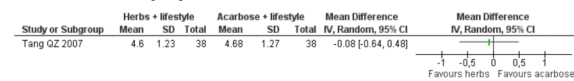
### 6.3 Normalisation of blood glucose (n)—

6.1 Reduction in fasting blood glucose (mmol/L)—

### 6.4 Incidence of diabetes (n)—

6.2 2hr-Glucose tolerance (mmol/L)—

### 6.5 HbA1c (%)—



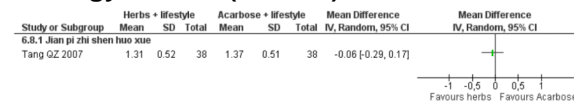
### 6.6 Insulin (FINS mmol/L)—

6.3 Normalisation of blood glucose (n)—

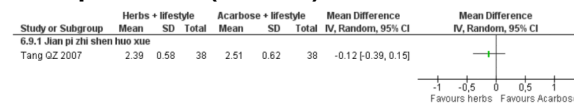
### 6.7 Total cholesterol (mmol/L)—



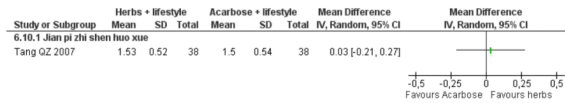
### 6.8 Triglycerides (mmol/L)—



### 6.9 Lipids: LDL (mmol/L)—



### 6.10 Lipids: HDL (mmol/L)—



## 7 - Herbal medicine plus antihypertensive medication versus antihypertensive medication alone

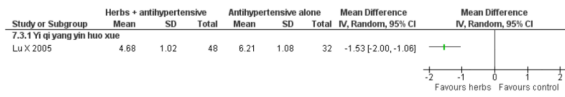
### 7.1 Reduction in fasting glucose (mmol/L)—



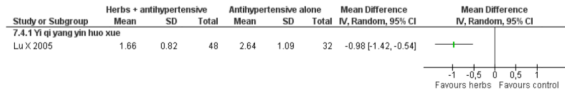
### 7.2 Reduction in 2hr blood glucose after oral glucose tolerance test (mmol/L)—



### 7.3 Total cholesterol (mmol/L)—



### 7.4 Triglycerides (mmol/L)—



### 7.5 Lipids: HDL (mmol/L)—



### 7.6 Systolic Blood Pressure (Kpa)—



### 7.7 Diastolic blood pressure (kpa)—



## 8 - Herbal medicine versus basic education (diabetes pamphlet)

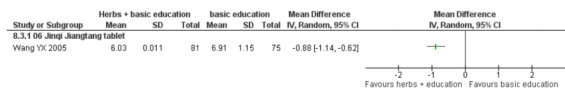
### 8.1 Normalisation of fasting blood glucose at trial completion (n)—



### 8.2 Incidence of diabetes (n)—



### 8.3 Fasting blood glucose (mmol/L)—



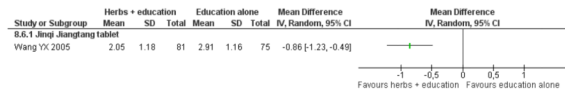
### 8.4 2hr fasting blood glucose (mmol/L) [ after oral glucose tolerance test]—



### 8.5 Total cholesterol (mmol/L)—



### 8.6 Triglycerides (mmol/L)—



## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

## Acknowledgments

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## Published notes

### Characteristics of studies

#### Characteristics of included studies

Fan GJ 2004

<b>Methods</b>	Parallel randomised controlled trial
<b>Participants</b>	<p>SETTING: Outpatients at Guangxi TCM College Affiliated No.1 Hospital, China</p> <p>WHO PARTICIPATED: 45 (M/F 21/24; 23 in the treatment group, age 54.6 yrs; 22 in the control, age 57.45 yrs)</p> <p>INCLUSION CRITERIA: IGT diagnosed by WHO criteria (WHO 1999)</p> <p>EXCLUSION CRITERIA: &lt;35 yrs, BMI &lt;19 kg/m, serious liver or kidney disorders, hypertension, IGT induced by other organic diseases, drugs or stress.</p> <p>CO-MORBIDITIES: none reported</p> <p>CO-MEDICATIONS: none reported</p>
<b>Interventions</b>	<p>INTERVENTION: Jiangtang bushen tang (gou qi 10g, chuan duan xu 10g, nu zhen zi 15g, han lian cao 15g, di gu pi 15g, sheng huang qi 15g, sheng di huang 15g, ge gen 12g, huang lian 5g, sang bai pi 10g, zhi mu 6g) plus diet and exercise; Dosage: 1 decoction every two days</p> <p>CONTROL: lifestyle modification</p>
<b>Outcomes</b>	<p>FBG (mmol/L), 2hr-GTT (mmol/L), Triglycerides (mmol/L), total cholesterol (mmol/L), BMI (kg/m<sup>2</sup>), fasting insulin (mmol/L), TCM symptoms;</p> <p>Outcomes assessed at baseline, 3 months, 6 months and 12 months.</p>
<b>Study details</b>	<p>DURATION OF INTERVENTION: 12 months</p> <p>DURATION OF FOLLOW-UP: 12 months</p> <p>RUN-IN PERIOD: none</p>
<b>Publication details</b>	<p>LANGUAGE OF PUBLICATION: Chinese</p> <p>COMMERCIAL FUNDING: No</p> <p>NON-COMMERCIAL FUNDING: Not reported</p> <p>PUBLICATION STATUS (PEER REVIEW JOURNAL): Yes</p> <p>PUBLICATION STATUS (JOURNAL SUPPLEMENT): No</p> <p>PUBLICATION STATUS (ABSTRACT): Yes</p>

<b>Stated aim of study</b>	“To evaluate the intervention effect of diet, exercise and Jiangtang Bushen Recipe (JBR, a Chinese herbal recipe) in preventing the progress of patients with impaired glucose tolerance (IGT) to diabetes mellitus (DM) type 2.”
<b>Notes</b>	

Risk of bias table

Item	Authors' judgement	Support for judgement
Adequate sequence generation?	Yes	Quote from phone call: “numbers randomisation from random table”
Allocation concealment?	Unclear	Phone call: Participants did not know the group to which they were to be allocated. No information provided about whether researchers knew the allocation.
Blinding?	No	No blinding of participants, intervention provider or outcomes assessor.
Incomplete outcome data addressed?	Yes	All participants are reported. Six withdrawals are explained. One participant left the intervention as they did not want to take the decoction, the other withdrawal did not give a reason. There were four withdrawals from the control where contact was lost.
Free of selective reporting?	Unclear	No protocol provided but all nominated and expected outcomes are reported.
Free of other bias?	Yes	None identified.

Fang ZH 2007

<b>Methods</b>	Parallel placebo controlled randomised trial
<b>Participants</b>	SETTING: Outpatient and inpatients, No 1 Affiliated Hospital of An Hui University of Chinese Medicine, China WHO PARTICIPATED: 62 (in treatment group M/F 18/14; age 40-67 yrs; in the control group M/F 17/13, age 39-65 yrs) INCLUSION CRITERIA: IGT diagnosed by ADA criteria (ADA 1997) and traditional Chinese medicine (TCM) diagnosis of qi and yin deficiency or blood stagnation EXCLUSION CRITERIA: None reported CO-MORBIDITIES: none reported CO-MEDICATIONS: none report
<b>Interventions</b>	INTERVENTION: Dan zhi jiang tang jiao capsules: mu dan pi, shui zhi, tu si zi, ze xie, huang jing, tai zi shen plus liu wei di huang tang oral, 5 capsules (0.35g per capsule) 3 time per day after meals plus lifestyle modification (diet & lifestyle advice) CONTROL: placebo plus lifestyle modification (diet & lifestyle advice)
<b>Outcomes</b>	FBG (mmol/L), 2hr-GTT (mmol/L), insulin (mu/L), triglycerides (mmol/L), traditional Chinese medicine patterns and symptoms. Outcomes were assessed at baseline and trial completion (12 wks).

<b>Study details</b>	DURATION OF INTERVENTION: 12 weeks DURATION OF FOLLOW-UP: 12 weeks RUN-IN PERIOD: none
<b>Publication details</b>	LANGUAGE OF PUBLICATION: Chinese COMMERCIAL FUNDING: no NON-COMMERCIAL FUNDING: no PUBLICATION STATUS (PEER REVIEW JOURNAL): yes PUBLICATION STATUS (JOURNAL SUPPLEMENT): no PUBLICATION STATUS (ABSTRACT): yes
<b>Stated aim of study</b>	To observe the intervention effects of Dan zhi jiang tang jiao on IGT.
<b>Notes</b>	

Risk of bias table

Item	Authors' judgement	Support for judgement
Adequate sequence generation?	Yes	Quote (from the report): "the randomly divided into two groups". Quote (from phone interview): numbers generated through a random table
Allocation concealment?	Yes	Concealed envelopes with random numbers were used.
Blinding?	Yes	From phone interview: participants were blinded with the use of a placebo and provided with the same diet & lifestyle advice as the treatment group; clinicians were blinded also; not known if the assessors were blinded.
Incomplete outcome data addressed?	Yes	No missing participants or withdrawals.
Free of selective reporting?	Unclear	No protocol provided but all nominated outcomes reported, reported TCM patterns and symptoms also.
Free of other bias?	Yes	None identified.

## Hao AZ 2004

<b>Methods</b>	Parallel placebo-controlled randomised trial
<b>Participants</b>	SETTING: Outpatients at the General Hospital of the People's Liberation Army, China WHO PARTICIPATED: n=168 (in treatment group M/F 62/24; mean age 55.6 yrs, duration of disease 1mth -2yrs; in the control group M/F 59/23, mean age 53.8, duration of disease 1mth-2yrs). INCLUSION CRITERIA: IGT (WHO 1999) and hypertension plus high total cholesterol or high triglycerides or low HDL. EXCLUSION CRITERIA: IGT due to endocrinological disorders, liver disease, drugs, stress. CO-MORBIDITIES: hypertension, hypercholesteremia or high triglycerides or low high

	density lipoprotein (HDL). CO-MEDICATIONS: none reported
<b>Interventions</b>	INTERVENTION: Xiaoke huaya tablet (Zhi My, Gui Jian Yu etc), dosage: 0.5g three times per day plus lifestyle modification (diet & exercise) CONTROL: lifestyle modification (diet & exercise alone)
<b>Outcomes</b>	FBG (mmol/L), 2hr-GTT (mmol/L), HbA1c (%), triglycerides (mmol/L), total cholesterol (mmol/L), normalisation of FBG (n), incidence of diabetes (n) Outcomes were measured at baseline and trial completion (8 wks).
<b>Study details</b>	DURATION OF INTERVENTION: 8 weeks DURATION OF FOLLOW-UP: 8 weeks RUN-IN PERIOD: none
<b>Publication details</b>	LANGUAGE OF PUBLICATION: Chinese COMMERCIAL FUNDING: No NON-COMMERCIAL FUNDING: Yes (Translational Funding Project) PUBLICATION STATUS (PEER REVIEW JOURNAL): Yes PUBLICATION STATUS (JOURNAL SUPPLEMENT): No PUBLICATION STATUS (ABSTRACT): Yes
<b>Stated aim of study</b>	Quote "to validate the therapeutic effects of Xiaoke Huaya tablet in the impaired glucose tolerance population"
<b>Notes</b>	

Risk of bias table

Item	Authors' judgement	Support for judgement
Adequate sequence generation?	Unclear	Randomisation method not mentioned in paper and unable to contact author.
Allocation concealment?	Unclear	Allocation concealment not mentioned in paper and unable to contact author.
Blinding?	No	Participants were not blinded. It is not clear if the outcome assessor or intervention providers were blinded. Unable to contact author.
Incomplete outcome data addressed?	Yes	All participants reported. No withdrawals.
Free of selective reporting?	Unclear	No protocol but all nominated and expected outcomes reported.
Free of other bias?	Yes	None identified.

Hioki C 2004

<b>Methods</b>	Parallel placebo-controlled randomised trial
<b>Participants</b>	SETTING: Outpatients at the Obesity Clinic of Kyoto Prefectural University, Japan WHO PARTICIPATED: n= 81 (44 in treatment group mean age 52.6 yrs, mean weight 90.8 kg, mean BMI 36.7; in the 41 in control group mean age 54.8, mean weight 90.3, mean BMI 36.1)

	<p>INCLUSION CRITERIA: IGT (WHO 1999) and obese</p> <p>EXCLUSION CRITERIA: People with kidney, heart and/or liver disease, any metabolic or endocrine disease, psychiatric disorders and cancer.</p> <p>CO-MORBIDITIES: obesity</p> <p>CO-MEDICATIONS: none reported</p>
<b>Interventions</b>	<p>INTERVENTION: Bofu-tsusho-san (Scutellariae Radix, Glycyrrhizae Radix, Platycodi Radix, Gypsum Fibrosum, Atractylodis Rhizoma, Rhei Rhizoma, Schizonepetae Spica, Gardeniae Fructus, Paeoniae Radix, Cnidium Rhizoma, Angelicae Radix, Menthae Herba, Ledebourieliae Radix, Ephedrae Herba, Forsythiae Fructus, Zingiberis Rhizoma, Talcum, Natrium Sulphuricum), dry extract, three times a day (t.i.d) 30 mins before meals, for 24 wks plus lifestyle modification (diet &amp; exercise).</p> <p>CONTROL: placebo three times a day (t.i.d) 30 mins before meals, for 24wks plus lifestyle modification (diet &amp; exercise)</p> <p>Lifestyle modification for all participants involved a diet of 1200 kcal/day, analysed based on food ingestion records, and exercise (5000 steps/day) determined by pedometer recordings.</p>
<b>Outcomes</b>	<p>FBG (mg/dL), 2hr-GTT (mg/dL), HbA1c (%), triglycerides (mg/dL), HDL (mg/dL), LDL (mg/dL), total cholesterol (mg/dL), fasting insulin (<math>\mu</math>U/mL), 2hr insulin (<math>\mu</math>U/mL), insulin AUC, HOMA-IR.</p> <p>Outcomes for all measures were assessed at baseline, 12 weeks, and 24 weeks.</p> <p>Note: For FBG mg/dL &amp; 2hr-GTT conversion to mmol/L: mg/dl of glucose to mmol/l, divided by 18.</p> <p>For total cholesterol, HDL, LDL mg/dL conversion to mmol/L: convert mg/dl of HDL or LDL cholesterol to mmol/l, divided by 38.67.</p> <p>For triglycerides mg/dL conversion to mmol/L: mg/dl of triglycerides to mmol/l, divide by 89.</p>
<b>Study details</b>	<p>DURATION OF INTERVENTION: 24 weeks</p> <p>DURATION OF FOLLOW-UP: 24 weeks</p> <p>RUN-IN PERIOD: after 2 months of lifestyle modification (diet and exercise therapy as described above), the active drug or placebo was introduced.</p>
<b>Publication details</b>	<p>LANGUAGE OF PUBLICATION: English and Japanese</p> <p>COMMERCIAL FUNDING: no</p> <p>NON-COMMERCIAL FUNDING: This study was supported, in part, by a Grant-in-Aid (No.14571106; to TY) for Scientific Research from the Ministry of Education, Culture, Sports, Science and Technology of Japan.</p> <p>PUBLICATION STATUS (PEER REVIEW JOURNAL): yes</p> <p>PUBLICATION STATUS (JOURNAL SUPPLEMENT): no</p> <p>PUBLICATION STATUS (ABSTRACT): yes</p>
<b>Stated aim of study</b>	The aim of the study was to determine whether BF was effective in decreasing visceral adiposity and insulin resistance.
<b>Notes</b>	

Risk of bias table

Item	Authors' judgement	Support for judgement
Adequate sequence generation?	Yes	Randomisation by random number table
Allocation concealment?	Yes	As a placebo controlled study it is likely that allocation was concealed.



Item	Authors' judgement	Support for judgement
Blinding?	Yes	Participants were blinded (placebo controlled), outcome assessors blinded.
Incomplete outcome data addressed?	Yes	All withdrawals are explained and all participant data included. Four withdrawals; 3 from treatment group for non-compliance because of loose bowels; 1 withdrew from control for non-compliance. The data of these subjects was excluded from the analysis. The baseline data of all 85 subjects was not significantly different from those of the 81 women.
Free of selective reporting?	Unclear	No protocol provided but all nominated and expected outcomes are reported.
Free of other bias?	Yes	None identified.

## Li CP 2004

<b>Methods</b>	Parallel randomised controlled trial
<b>Participants</b>	<p>SETTING: inpatients and outpatients at Nanning TCM hospital, China</p> <p>WHO PARTICIPATED: n= 64; (28/36 (M/F); mean age 50.9yrs; 31 in treatment group; 33 in control group)</p> <p>INCLUSION CRITERIA: IGT (WHO 1999)</p> <p>EXCLUSION CRITERIA: People &lt;40yrs, BMI &lt;19kg/m, hypertension, IGT induced by other organic diseases, drugs or stress.</p> <p>CO-MORBIDITIES: none reported</p> <p>CO-MEDICATIONS: none reported</p>
<b>Interventions</b>	<p>INTERVENTION: Qimai jiangtang yin (huang qi 20g, ge gen 20g, mai dong 10g, nu zhen zi 10g, san qi 10g, yu jin 10g, sheng di huang 15g) decoction taken 1 dose (100ml) every two days in 1st and 2nd months plus lifestyle modification (diet &amp; lifestyle advice)</p> <p>CONTROL: Lifestyle modification (diet &amp; lifestyle advice)</p>
<b>Outcomes</b>	<p>FBG (mmol/L), 2hr GTT (mmol/L), fasting insulin, IAI, normalisation rate of IGT (n), incidence of diabetes</p> <p>Outcomes were measured at baseline and at trial completion (12 months).</p>
<b>Study details</b>	<p>DURATION OF INTERVENTION: 12 months</p> <p>DURATION OF FOLLOW-UP: 12 months</p> <p>RUN-IN PERIOD: none</p>
<b>Publication details</b>	<p>LANGUAGE OF PUBLICATION: Chinese</p> <p>COMMERCIAL FUNDING: no</p> <p>NON-COMMERCIAL FUNDING: no</p> <p>PUBLICATION STATUS (PEER REVIEW JOURNAL): yes</p> <p>PUBLICATION STATUS (JOURNAL SUPPLEMENT): no</p> <p>PUBLICATION STATUS (ABSTRACT): yes</p>
<b>Stated aim of study</b>	To observe the effect of Qimai jingtang yin on impaired glucose tolerance.
<b>Notes</b>	

Risk of bias table

Item	Authors' judgement	Support for judgement
Adequate sequence generation?	Unclear	Method not reported in published article and unable to contact authors to get further information.
Allocation concealment?	Unclear	Unable to contact authors to get further information.
Blinding?	No	Probably not as the control group were not taking a placebo.
Incomplete outcome data addressed?	Yes	All participant data reported.
Free of selective reporting?	Unclear	No protocol provided, but all nominated and expected outcomes reported.
Free of other bias?	Yes	None identified.

## Lu X 2005

<b>Methods</b>	Parallel randomised controlled trial (block randomisation, 3 participants in the intervention group : 2 in the control group)
<b>Participants</b>	SETTING: Outpatients presenting at Guigang City TCM Hospital, China  WHO PARTICIPATED: 80 (48 in treatment group, M/F 29/19, mean age 48.08 yrs; 32 in control group, M/F 19/13, mean age 47.62 yrs)  INCLUSION CRITERIA: IGT (ADA 1997): FBG $\geq$ and less than 7.0 AND 2-hr TT (75g) $\geq$ 7.8<11.1 PLUS either hypertension systolic $\geq$ 18.7kpa and/or diastolic $\geq$ 12.0; OR total cholesterol $\geq$ 5.7mmol/L OR triglycerides $\geq$ 2.26 mmol/L OR HDL $\leq$ 1.04 mmol/L.  EXCLUSION CRITERIA: none reported  CO-MORBIDITIES: primary hypertension  CO-MEDICATIONS: none reported
<b>Interventions</b>	INTERVENTION: Yi qi yang yin huo xue (Huang qi, Dang gui, Shan yao, Sang bai pi, Sang ye, Sang zhi) 100 ml per dose, 3 times per day, plus Beijing Jiang Ya No. 0 tablets (Blood pressure lowering medication: Pterofen 12.5 mg, Dihydralazine Sulfate 12.5 mg, reserpine 0.1 mg)  CONTROL: Beijing Jiang Ya No. 0 tablets (Blood pressure lowering medication: Pterofen 12.5 mg, Dihydralazine Sulfate 12.5 mg, reserpine 0.1 mg)
<b>Outcomes</b>	Blood pressure, fasting blood glucose (mmol/L), 2hr-GTT (mmol/L), total cholesterol (mmol/L), triglycerides (mmol/L), HDL (mmol/L), and quality of life assessment (Chinese scale, Du 1994).  Outcomes were measured at baseline and trial completion (28d)  This study reported that there were no adverse findings in renal, liver, and ECG tests.
<b>Study details</b>	DURATION OF INTERVENTION: 28 days  DURATION OF FOLLOW-UP: 28 days  RUN-IN PERIOD: none
<b>Publication details</b>	LANGUAGE OF PUBLICATION: Chinese  COMMERCIAL FUNDING: No  NON-COMMERCIAL FUNDING: No  PUBLICATION STATUS (PEER REVIEW JOURNAL): yes  PUBLICATION STATUS (JOURNAL SUPPLEMENT): no

	PUBLICATION STATUS (ABSTRACT): yes
<b>Stated aim of study</b>	“To observe the influences of combination of Chinese and western therapies on the life quality and blood-fat [lipids] of primary hypertension patients with declined glucose tolerance.”
<b>Notes</b>	

Risk of bias table

Item	Authors' judgement	Support for judgement
Adequate sequence generation?	Yes	Phone call: random table used randomisation sequence
Allocation concealment?	Unclear	No information in the report or from phone call.
Blinding?	No	Noticeably different interventions provided, blinding is unlikely and not mentioned.
Incomplete outcome data addressed?	Yes	No withdrawals or exclusions, all participant data reported.
Free of selective reporting?	Unclear	Nominated and expected outcomes were reported but no protocol was available.
Free of other bias?	Yes	None identified.

Qu LX 2002

<b>Methods</b>	Parallel randomised controlled trial
<b>Participants</b>	<p>SETTING: inpatients and outpatients at Huaian County Hospital</p> <p>WHO PARTICIPATED: n=60 (30 in treatment group, M/F 21/9, mean age 48yrs and 30 in control group, M/F 17/13, mean age 49yrs)</p> <p>INCLUSION CRITERIA: IGT (ADA 1997)</p> <p>EXCLUSION CRITERIA: none reported</p> <p>CO-MORBIDITIES: none reported</p> <p>CO-MEDICATIONS: none reported</p>
<b>Interventions</b>	<p>INTERVENTION: Tang ping san (Huang Qi 30g, Shan Yao 10g, Sheng Di Huang 10g, Shu Di Huang 10g, Gou Qi Zi 10g, He Shou Wu 10g, Xian Ling Pi 10g, Dan Shen 30g, Ze Xie 10g, Sang Ye 10g), oral, decoction, once per day (b.i.d), plus lifestyle modification (diet &amp; lifestyle advice)</p> <p>CONTROL: Metformin, oral, 0.25g per dose, three times a day (t.i.d), plus lifestyle modification (diet &amp; lifestyle advice)</p>
<b>Outcomes</b>	2hr-GTT (mmol/L) measured at baseline, at trial completion (3 months) and at follow-up (6 months)
<b>Study details</b>	<p>DURATION OF INTERVENTION: 12 weeks</p> <p>DURATION OF FOLLOW-UP: 3 months</p> <p>RUN-IN PERIOD: none</p>
<b>Publication details</b>	<p>LANGUAGE OF PUBLICATION: Chinese</p> <p>COMMERCIAL FUNDING: No</p> <p>NON-COMMERCIAL FUNDING: Yes (Scientific research funding by Municipal Government).</p>

	PUBLICATION STATUS (PEER REVIEW JOURNAL): Yes PUBLICATION STATUS (JOURNAL SUPPLEMENT): no PUBLICATION STATUS (ABSTRACT): no
<b>Stated aim of study</b>	Quote "to observe the treatment of impaired glucose with Tangping san".
<b>Notes</b>	

Risk of bias table

Item	Authors' judgement	Support for judgement
Adequate sequence generation?	Unclear	The method of randomisation was not stated. We were unable to contact the author about the method used.
Allocation concealment?	Unclear	Comment: unable to contact the author about the method used.
Blinding?	No	Comment: both received an intervention but of a different nature (powder vs pill). It's likely that participants and intervention providers knew the intervention they were receiving.
Incomplete outcome data addressed?	Yes	All participants data reported.
Free of selective reporting?	Unclear	No protocol but all expected and nominated outcomes reported.
Free of other bias?	Yes	None reported.

Shi J 2005

<b>Methods</b>	Parallel randomised controlled trial
<b>Participants</b>	SETTING: Inpatients and outpatients at Liyuan Hospital, China WHO PARTICIPATED: 62 people (32 in intervention group, M/F 17/15, mean age 65.3 yrs, mean disease duration 3.1yrs, mean weight 82.3kg; 30 in control group, M/F 15/15, mean age 66.1 yrs, mean disease duration 3.6yrs, mean weight 82.1kg) INCLUSION CRITERIA: IGT according to WHO,1998 EXCLUSION CRITERIA: none reported CO-MORBIDITIES: none reported CO-MEDICATIONS: none reported
<b>Interventions</b>	INTERVENTION: Fufang cangzhu decoction (cang zhu 15g, yi yi ren 24g, sang shen 20g, shan yao 30g, huang bai 10g, li zhi hue 20g, di long 10g) oral, decoction, 150ml, bid CONTROL: metformin 0.25g, oral, tablet, tid
<b>Outcomes</b>	FBG (mmol/L), 1hr-GTT (mmol/L), 2hr-GTT (mmol/L), weight (kg), waist-hip ratio (WHR), triglycerides (mmol/L), total cholesterol (mmol/L), fasting insulin (mU/L) All outcomes measured at baseline and at trial completion (8 weeks).
<b>Study details</b>	DURATION OF INTERVENTION: 8 weeks DURATION OF FOLLOW-UP: 8 weeks RUN-IN PERIOD: none

<b>Publication details</b>	LANGUAGE OF PUBLICATION: Chinese COMMERCIAL FUNDING: no NON-COMMERCIAL FUNDING: no PUBLICATION STATUS (PEER REVIEW JOURNAL): yes PUBLICATION STATUS (JOURNAL SUPPLEMENT): no PUBLICATION STATUS (ABSTRACT): yes
<b>Stated aim of study</b>	Quote "To observe therapeutic effect of Fufang Cangzhu Decoction on senile obesity or overweight with impaired glucose tolerance (IGT)".
<b>Notes</b>	

Risk of bias table

Item	Authors' judgement	Support for judgement
Adequate sequence generation?	Yes	The authors were interviewed by phone and stated that the randomisation was done by use of a random table.
Allocation concealment?	Unclear	No details provided on allocation concealment.
Blinding?	No	Assessors blinded; participants could not be blinded as one group was taking capsule and the other a decoction. Intervention provider not blinded.
Incomplete outcome data addressed?	Yes	All participants reported. No withdrawals.
Free of selective reporting?	Unclear	All expected and nominated outcomes reported.
Free of other bias?	Yes	None reported.

Tang QZ 2007

<b>Methods</b>	Parallel randomised controlled trial, three arms: Chinese herbal medicines plus diet & lifestyle vs acarbose plus diet & lifestyle vs diet & lifestyle
<b>Participants</b>	SETTING: outpatients at the Intergrated Medicine Hospital of Guangdong Province, China WHO PARTICIPATED: 120 participants (40 in intervention I, M/F 24/16, mean age 53.5yrs; 40 in intervention II, M/F 20/20, mean age 54.8yrs; 40 in the control, M/F 22/18, mean age 50.6yrs) INCLUSION CRITERIA: IGT WHO 1999 EXCLUSION CRITERIA: <35yrs, BMI <19, hypertension level 3, severe liver or kidney diseases, other endocrine diseases, any IGT caused by medication or high levels of stress. CO-MORBIDITIES: none stated CO-MEDICATIONS: none stated
<b>Interventions</b>	INTERVENTION I: Jian Pi Zhi Shen Huo Xue (shan yao 30g, shan zha 30g, huang qi 20g, fu ling 20g, shan zhu yu 15g, tao ren 10g) plus diet & lifestyle once per day. INTERVENTION II: Acarbose 50mg per dose, three times a day plus diet & lifestyle CONTROL: diet & lifestyle alone
<b>Outcomes</b>	BMI (kg/m <sup>2</sup> ), FBG (mmol/L), 2hr-GTT (mmol/L), HbA1c (%), triglycerides (mmol/L), total cholesterol (mmol/L), HDL (mmol/L), LDL (mmol/L), FINS (mmol/L), ISI,

	normalisation of blood glucose (n), incidence of diabetes (n) All outcomes assessed at baseline, 6 months and at trial completion (12 months).
<b>Study details</b>	DURATION OF INTERVENTION: 12 months. After 6 months a 2hr-GTT to check if participants had progressed to diabetes which was the endpoint, if normal GT or still IGT one or more treatment courses given. DURATION OF FOLLOW-UP: 12 months RUN-IN PERIOD: none
<b>Publication details</b>	LANGUAGE OF PUBLICATION: Chinese COMMERCIAL FUNDING: no NON-COMMERCIAL FUNDING: no PUBLICATION STATUS (PEER REVIEW JOURNAL): yes PUBLICATION STATUS (JOURNAL SUPPLEMENT): no PUBLICATION STATUS (ABSTRACT): yes
<b>Stated aim of study</b>	Quote "to study the method of strengthen the spleen, nourish the kidney and activate the blood method for the treatment of impaired glucose tolerance."
<b>Notes</b>	

Risk of bias table

Item	Authors' judgement	Support for judgement
Adequate sequence generation?	Yes	A random table was used to divide the sample into 3 groups (40 in each group).
Allocation concealment?	Unclear	No information provided in the report on allocation concealment.
Blinding?	No	Not reported, unlikely given the design of the trial consisting of a chinese herbal powder, western pharmaceutical tablet and a group taking no medication.
Incomplete outcome data addressed?	Yes	No missing data. 5 withdrawals: 2 from intervention I; reason given: could not continue with medication; 2 from intervention II reason given: could not continue with medication; 1 from the control; reason given: participant left the area.
Free of selective reporting?	Unclear	No protocol provided and all nominated outcomes reported.
Free of other bias?	Yes	None reported.

## Wang BQ 2008

<b>Methods</b>	Parallel randomised controlled trial
<b>Participants</b>	SETTING: China WHO PARTICIPATED: 95 participants (48 in intervention, M/F 32/16, mean age 53.5yrs; 47 in control, M/F 29/18, mean age 53.5yrs) INCLUSION CRITERIA: IGT (WHO 1999); >30yrs<60yrs; not taking any medication that influences glucose levels for at least one month; willingness to comply with the trial and examination;

	<p>EXCLUSION CRITERIA: Level 3 hypertension; serious heart, liver or kidney dysfunction; mental diseases; allergic condition; pregnancy or lactation.</p> <p>DIAGNOSTIC CRITERIA: IGT WHO 1999</p> <p>CO-MORBIDITIES: none stated</p> <p>CO-MEDICATIONS: none stated</p>
<b>Interventions</b>	<p>INTERVENTION: Qiweitangping capsule (huang qi, huang qin, zi su zi, dang shen, da huang, da zao, shu di huang, chai hu, dan shen, yu jin, yin chen, tian hua fen, shi gao, che qian zi, shan yao, we wei zi, shan zhu yu, zhi mu, gou qi zi, ge gen, bai he, gua lou, wu yao, di huang, hua jiao, wang bu liu xing, gan cao) 3 capsule twice daily</p> <p>CONTROL: placebo 3 capsules twice daily oral</p>
<b>Outcomes</b>	<p>FBG (mmol/L), 2hr-GTT (mmol/L), BMI (kg/m<sup>2</sup>), WHR</p> <p>All outcomes were measured at baseline and trial completion (24 months).</p> <p>Adverse effects: one participant from treatment and one from the control developed abdominal discomfort. Both were resolved without any treatment</p>
<b>Study details</b>	<p>DURATION OF INTERVENTION: 24 months</p> <p>DURATION OF FOLLOW-UP: 24 months</p> <p>RUN-IN PERIOD: none</p>
<b>Publication details</b>	<p>LANGUAGE OF PUBLICATION: Chinese</p> <p>COMMERCIAL FUNDING: no</p> <p>NON-COMMERCIAL FUNDING: no</p> <p>PUBLICATION STATUS (PEER REVIEW JOURNAL): yes</p> <p>PUBLICATION STATUS (JOURNAL SUPPLEMENT): no</p> <p>PUBLICATION STATUS (ABSTRACT): yes</p>
<b>Stated aim of study</b>	<p>Quote "To observe the intervention effects of Qiweitangping capsule on impaired glucose tolerance (IGT) and on the morbidity of diabetes mellitus (DM)and the effect of conversing IFF to normal glucose tolerance (NGT) "</p>
<b>Notes</b>	

Risk of bias table

Item	Authors' judgement	Support for judgement
Adequate sequence generation?	Yes	SAS was used to generate the allocation sequence.
Allocation concealment?	Yes	Both the participant and the intervention provider did not know the allocation groups.
Blinding?	Yes	Participants, doctor and outcomes assessor all blinded.
Incomplete outcome data addressed?	Yes	All participant data reported. 5 withdrawals.
Free of selective reporting?	Unclear	No protocol reported but all expected and nominated outcome measures were reported.
Free of other bias?	Yes	None identified.

## Wang YX 2005

<b>Methods</b>	Parallel randomised controlled trial
<b>Participants</b>	<p>SETTING: Tianjin No. 1 Zhong Xin Hospital outpatients, China</p> <p>WHO PARTICIPATED: n=159 (81 in the intervention group, M/F 40/41; 78 in the control group, M/F 37/41)</p> <p>INCLUSION CRITERIA: IGT (WHO 1999) and/or IFG (ADA 1997)</p> <p>EXCLUSION CRITERIA: None reported</p> <p>CO-MORBIDITIES: None reported</p> <p>CO-MEDICATIONS: None reported</p>
<b>Interventions</b>	<p>INTERVENTION: Jinqi Jiangtang 4-7 tablets each dose, three times a day plus basic education (no diet or exercise)</p> <p>CONTROL (ROUTE, TOTAL DOSE/DAY, FREQUENCY): basic education alone (no diet or exercise)</p>
<b>Outcomes</b>	<p>Fasting blood glucose (mmol/L), 2hr-GTT (mmol/L), normalisation of glucose tolerance (n), total cholesterol (mmol/L), triglycerides (mmol/L), systolic blood pressure (mm/Hg), diastolic blood pressure (mm/Hg)</p> <p>Adverse effects: 3 cases in the intervention group developed mild GIT symptoms in the early stage of taking the Chinese herbal medicine. These resolved after one to two weeks. No other adverse effects were observed.</p>
<b>Study details</b>	<p>DURATION OF INTERVENTION: 2 years</p> <p>DURATION OF FOLLOW-UP: 2 years</p> <p>RUN-IN PERIOD: none</p>
<b>Publication details</b>	<p>LANGUAGE OF PUBLICATION: Chinese</p> <p>COMMERCIAL FUNDING: no</p> <p>NON-COMMERCIAL FUNDING: no</p> <p>PUBLICATION STATUS (PEER REVIEW JOURNAL): yes</p> <p>PUBLICATION STATUS (JOURNAL SUPPLEMENT): no</p> <p>PUBLICATION STATUS (ABSTRACT): no</p>
<b>Stated aim of study</b>	Quote "To observe the effect of Jinqi Jiangtang tablet on preventing patients with impaired glucose becoming diabetes"
<b>Notes</b>	

Risk of bias table

Item	Authors' judgement	Support for judgement
Adequate sequence generation?	Unclear	Stated as randomised but unable to contact the authors.
Allocation concealment?	Unclear	No information available in report.
Blinding?	No	Unlikely due to the nature of the medication intervention (tablets vs no medication).
Incomplete outcome data addressed?	Yes	Three withdrawals reported in the control group. All data for the other participants reported.



Item	Authors' judgement	Support for judgement
Free of selective reporting?	Unclear	No protocol provided but all expected and nominated outcomes reported.
Free of other bias?	Yes	None identified.

## Wei AS 2001

<b>Methods</b>	Parallel randomised controlled trial
<b>Participants</b>	<p>SETTING: Outpatients at the Foshan TCM Hospital, Guangdong Province, China</p> <p>WHO PARTICIPATED: n=72 (36 in the intervention group, M/F 19/13, mean age 46.3yrs; 36 in the control group, M/F 20/13, mean age 47.1yrs)</p> <p>INCLUSION CRITERIA: IGT (WHO 1999)</p> <p>EXCLUSION CRITERIA: none reported</p> <p>CO-MORBIDITIES: none reported</p> <p>CO-MEDICATIONS none reported</p>
<b>Interventions</b>	<p>INTERVENTION (ROUTE, TOTAL DOSE/DAY, FREQUENCY): Xiaoke Yuye (Huang qi, huang jing, he shou wu, zhi mu) 10ml three times per day, plus lifestyle modification (diet and exercise)</p> <p>CONTROL: lifestyle modification (diet and exercise)</p>
<b>Outcomes</b>	<p>Fasting blood glucose (mmol/L), 2hr-GTT (mmol/L), HbA1c (%), total cholesterol (mmol/L), BMI, normalisation of fasting blood glucose (n), incidence of diabetes (n)</p> <p>All outcomes were measured at baseline and at trial completion (24 months)</p> <p>No adverse effects in the treatment group.</p>
<b>Study details</b>	<p>DURATION OF INTERVENTION: 2 years</p> <p>DURATION OF FOLLOW-UP: 2 years</p> <p>RUN-IN PERIOD: none</p>
<b>Publication details</b>	<p>LANGUAGE OF PUBLICATION: Chinese</p> <p>COMMERCIAL FUNDING: no</p> <p>NON-COMMERCIAL FUNDING: no</p> <p>PUBLICATION STATUS (PEER REVIEW JOURNAL): yes</p> <p>PUBLICATION STATUS (JOURNAL SUPPLEMENT): no</p> <p>PUBLICATION STATUS (ABSTRACT): yes</p>
<b>Stated aim of study</b>	Quote "To observe the effects of Xiaoke yuye on patients with impaired glucose tolerance."
<b>Notes</b>	

## Risk of bias table

Item	Authors' judgement	Support for judgement
Adequate sequence generation?	Yes	Authors were interviewed by phone and stated that a random table was used.

Item	Authors' judgement	Support for judgement
Allocation concealment?	Yes	Allocation concealment not mentioned in the report. Information obtained from phone interview that numbers drawn from a sealed box designated the random number allocation.
Blinding?	No	No placebo so probably not blinded.
Incomplete outcome data addressed?	Yes	7 withdrawals reported, no reason given. Four in the intervention group and 3 in the control group. Baseline data reported included participants only. No difference at baseline.
Free of selective reporting?	Unclear	No protocol provided but all nominated outcomes reported.
Free of other bias?	Yes	None identified.

## Yang B 2004

<b>Methods</b>	Parallel randomised controlled trial
<b>Participants</b>	<p>SETTING: Hospital outpatients and patients recruited from general company check-up, Huabei Petroleum Two Hospital, Hebei, China</p> <p>WHO PARTICIPATED: n=76 (40 in the intervention group M/F 31/19, mean age 44.2yrs; 36 in the control M/F 23/13, mean age 43.9yrs)</p> <p>INCLUSION CRITERIA: IGT (ADA 1997): FBG &lt;7.0 and 2hr-GTT (75g) ≥7.8 &lt;11.1</p> <p>EXCLUSION CRITERIA: &lt;20yrs &lt;65yrs; IGT induced by other disorders, drugs or stress, pregnancy, serious liver, kidney or heart disorders.</p> <p>CO-MORBIDITIES: none reported</p> <p>CO-MEDICATIONS: none reported</p>
<b>Interventions</b>	<p>INTERVENTION: Tang Kang Yin decoction (ren shen 6g, huang lian 10g, nu zhen zi 15g, xia ku cao 30g, fan shi liu ye 30g) oral, 200ml, 2x/day, plus lifestyle modification (diet &amp; exercise)</p> <p>CONTROL: lifestyle modification (diet &amp; lifestyle)</p>
<b>Outcomes</b>	<p>Fasting blood glucose (mmol/L), 2hr-GTT (mmol/L), insulin (ng/ml), triglycerides (mmol/L), total cholesterol (mmol/L), BMI, normalisation of fasting blood glucose (n), incidence of diabetes (n)</p> <p>All outcomes were assessed at baseline and trial completion (30 days).</p>
<b>Study details</b>	<p>DURATION OF INTERVENTION: 30 days</p> <p>DURATION OF FOLLOW-UP: 30 days</p> <p>RUN-IN PERIOD: none</p>
<b>Publication details</b>	<p>LANGUAGE OF PUBLICATION: Chinese</p> <p>COMMERCIAL FUNDING: no</p> <p>NON-COMMERCIAL FUNDING: no</p> <p>PUBLICATION STATUS (PEER REVIEW JOURNAL): no</p> <p>PUBLICATION STATUS (JOURNAL SUPPLEMENT): no</p> <p>PUBLICATION STATUS (ABSTRACT): yes</p>
<b>Stated aim of study</b>	Quote "To observe the clinical effect of intervention of Tangganyin decoction on patients with Impaired glucose tolerance ( IGT )."

<b>Notes</b>	
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Risk of bias table

Item	Authors' judgement	Support for judgement
Adequate sequence generation?	Yes	The authors were interviewed by phone and stated that randomisation was conducted by using a random table from the internet.
Allocation concealment?	No	The intervention provider knew the which group each participant was to be allocated to.
Blinding?	No	Not stated in the report. From phone interview "participants and intervention provider were not blinded".
Incomplete outcome data addressed?	Yes	All participants reported. No withdrawals.
Free of selective reporting?	Unclear	No protocol provided but all expected and nominated outcomes reported.
Free of other bias?	Yes	None identified.

Yao Z 2001

<b>Methods</b>	Parallel randomised controlled trial
<b>Participants</b>	<p>SETTING: Hospital outpatients and patients recruited from general company check-up; Shugang Hospital, Shanghai, China</p> <p>WHO PARTICIPATED: 42 (22 in the intervention group, M/F 8/14; and 20 in the control group M/F 8/12)</p> <p>INCLUSION CRITERIA: IGT (WHO 1985)</p> <p>EXCLUSION CRITERIA: disorders that interfere with glucose metabolism</p> <p>CO-MORBIDITIES: none reported</p> <p>CO-MEDICATIONS: none reported</p>
<b>Interventions</b>	<p>INTERVENTION: Tangheng I, 2 bags twice a day for 3 mth splus lifestyle modification (diet &amp; exercise)</p> <p>CONTROL: lifestyle modification (diet and exercise) for 3 months</p>
<b>Outcomes</b>	<p>FBG (mmol/L), 2hr-GTT (mmol/L), insulin (ng/mL), BMI, systolic blood pressure (mmHg), diastolic blood pressure (mmHg)</p> <p>All outcomes were assessed at baseline and trial completion (3 months)</p>
<b>Study details</b>	<p>DURATION OF INTERVENTION: 3 months</p> <p>DURATION OF FOLLOW-UP: 3 months</p> <p>RUN-IN PERIOD: none</p>
<b>Publication details</b>	<p>LANGUAGE OF PUBLICATION: Chinese</p> <p>COMMERCIAL FUNDING: no</p> <p>NON-COMMERCIAL FUNDING: no</p> <p>PUBLICATION STATUS (PEER REVIEW JOURNAL): yes</p> <p>PUBLICATION STATUS (JOURNAL SUPPLEMENT): no</p> <p>PUBLICATION STATUS (ABSTRACT): yes</p>

<b>Stated aim of study</b>	Quote "To observe the intervention on 42 cases of impaired glucose with Tangheng I."
<b>Notes</b>	

Item	Authors' judgement	Support for judgement
Adequate sequence generation?	Unclear	Method not reported and unable to contact authors.
Allocation concealment?	Unclear	Method not reported and unable to contact authors.
Blinding?	No	No placebo so probably not blinded.
Incomplete outcome data addressed?	Yes	No missing data. No withdrawals.
Free of selective reporting?	Unclear	No protocol provided. All expected and nominated outcomes appropriately reported.
Free of other bias?	Yes	None identified.

## Zeng YH 2006

<b>Methods</b>	Parallel randomised controlled trial
<b>Participants</b>	<p>SETTING: Hospital outpatients, Guangdong Province People's Hospital, China</p> <p>WHO PARTICIPATED: n=166 (I: n=56, 29/27 m/f, mean age 53.12yrs; II: n=55 m/f 29/26, mean age 52.68yrs; Control: n=55, m/f 30/25, mean age 52.45yrs)</p> <p>INCLUSION CRITERIA: IGT (WHO 1985)</p> <p>EXCLUSION CRITERIA: none reported</p> <p>CO-MORBIDITIES: none reported</p> <p>CO-MEDICATIONS: none reported</p>
<b>Interventions</b>	<p>INTERVENTION 1: Liu wei di huang capsule, oral, 2 capsules bid, plus lifestyle modification involving a strict diet prescription, frequent diabetes lectures, moderate exercise.</p> <p>INTERVENTION 2: lifestyle modification as per intervention 1.</p> <p>CONTROL: pamphlet on diabetes only (no diet or exercise).</p>
<b>Outcomes</b>	FBG (mmol/L), 2-hr GTT (mmol/L), HbA1c (%), total cholesterol (mmol/L), triglycerides (mmol/L), BMI (kg/m <sup>2</sup> ), blood pressure
<b>Study details</b>	<p>DURATION OF INTERVENTION: 18 months</p> <p>DURATION OF FOLLOW-UP: 18 months</p> <p>RUN-IN PERIOD: none</p>
<b>Publication details</b>	<p>LANGUAGE OF PUBLICATION: Chinese</p> <p>COMMERCIAL FUNDING: no</p> <p>NON-COMMERCIAL FUNDING: no</p> <p>PUBLICATION STATUS (PEER REVIEW JOURNAL): yes</p> <p>PUBLICATION STATUS (JOURNAL SUPPLEMENT): no</p> <p>PUBLICATION STATUS (ABSTRACT): yes</p>

<b>Stated aim of study</b>	Quote "To study the effect of Liu wei di huang pill for the treatment of IGT to reduce the risk of CVD".
<b>Notes</b>	Two articles about this study, one reports only two groups (2000) and the other three groups (2006).

Risk of bias table

Item	Authors' judgement	Support for judgement
Adequate sequence generation?	Yes	The authors were interviewed by phone and advised that randomisation by a random table.
Allocation concealment?	Yes	Allocation unknown to groups and intervention provider until after allocation.
Blinding?	No	No placebo so not blinded.
Incomplete outcome data addressed?	No	HbA1c was nominated as a collected outcome but not reported. No withdrawals.
Free of selective reporting?	Unclear	A study protocol is not available but the published data includes all nominated and expected outcomes.
Free of other bias?	Yes	None identified.

Zhou DY 2003

<b>Methods</b>	Parallel randomised controlled trial
<b>Participants</b>	<p>SETTING: Outpatients, Zhejiang Province, Hangzhou Red Cross Hospital, China</p> <p>WHO PARTICIPATED: n=88 (46 in the intervention group M/F 18/28, mean age 55.6 yrs; 42 in the control M/F 17/25, mean age 54.0 yrs)</p> <p>INCLUSION CRITERIA: IGT (WHO 1985)</p> <p>EXCLUSION CRITERIA: none reported</p> <p>CO-MORBIDITIES: none reported</p> <p>CO-MEDICATIONS: none reported</p>
<b>Interventions</b>	<p>INTERVENTION: Jinqi Jiangtang tablet, oral, 7 tablets, 0.42g per tablet, three times per day, 30mins before meals plus lifestyle modification (diet and exercise)</p> <p>CONTROL: lifestyle modification (diet and exercise)</p>
<b>Outcomes</b>	<p>Fasting blood glucose (mmol/L), 2hr-GTT (mmol/L), fasting insulin, 2hr-insulin, triglycerides, total cholesterol, HDL, systolic blood pressure (kpa), diastolic blood pressure (kpa), normalisation of fasting blood glucose (n), incidence of diabetes (n)</p> <p>Blood pressure measurement converted as follows: 1 mmHg = 0.133 kPa</p> <p>All outcomes reported at baseline, 3 months, 6 months and trial completion (12 months)</p>
<b>Study details</b>	<p>DURATION OF INTERVENTION: 12 months</p> <p>DURATION OF FOLLOW-UP: 12 months</p> <p>RUN-IN PERIOD: none</p>
<b>Publication details</b>	<p>LANGUAGE OF PUBLICATION: Chinese</p> <p>COMMERCIAL FUNDING: no</p> <p>NON-COMMERCIAL FUNDING: no</p>

	PUBLICATION STATUS (PEER REVIEW JOURNAL): yes PUBLICATION STATUS (JOURNAL SUPPLEMENT): no PUBLICATION STATUS (ABSTRACT): no
<b>Stated aim of study</b>	To observe the effect of Jingqi Jiangtang tablet on non-overweight people with impaired glucose tolerance.
<b>Notes</b>	

Risk of bias table

Item	Authors' judgement	Support for judgement
Adequate sequence generation?	Yes	The authors were interviewed by phone and advised that randomisation by a random table
Allocation concealment?	No	Not mentioned in the report. From the phone interview: not adequate allocation concealment
Blinding?	No	No placebo so probably not blinded.
Incomplete outcome data addressed?	Yes	All participant data reported, no withdrawals.
Free of selective reporting?	Unclear	No protocol provided. All expected and nominated outcomes appropriately reported.
Free of other bias?	Yes	None identified.

ADA: American Diabetes Association; AUC: area under the curve; BMI: body-mass index; FBG: fasting blood glucose; GTT: (oral) glucose tolerance test; HbA1c: glycosylated haemoglobin A1c; HDL: high-density cholesterol; IGT: impaired glucose tolerance; M/F: male / female; LDL: low-density cholesterol; TCM: Traditional Chinese Medicine; t.i.d.: three times daily

## Characteristics of excluded studies

### An SH 2007a

Reason for exclusion	Quasi-randomised study comparing the effects of a Chinese herbal formula (ren shen 10g, huang qi 30g, sheng di huang 15g, shan yao 15, bai zhu 15g, ban xia 10g, fu ling 10g, cang zhu 10g, dang shen 12g, chi shao 10g, chuan xiong 10g, shan zha 10g, ge gen 10g, tian hua fen 15g) plus diet and lifestyle advice versus diet and lifestyle advice alone in 80 participants with impaired glucose tolerance over 4 months. The report stated that the study was randomised. Information obtained from phone interview indicated that allocation was based on clinician's decision.
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### An SH 2007b

Reason for exclusion	Quasi-randomised study comparing the effects of a Chinese herbal medicine formula (Shu di 20g, shan zhu yu 10g, shan yao 10g, ze xie 10g, mu dan pi 10g, fu ling 10g, ban xia 10g, chen pi 10g, dan shen 10g, gou qi zi 10g, shan zha 10g) versus metformin in 90 participants with impaired glucose tolerance over 4 months. The report stated that the study was randomised. Information obtained from phone interview indicated that allocation was based on clinician's decision.
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### Cai X 2001

Reason for exclusion	Non-randomised study of Ke Tang Ling in people with IGT.
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## Cai X 2002

Reason for exclusion	Non-randomised study of Ke Tang Ling in people with IGT. Possible duplicate of Cai X 2001.
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## Chen C 2005

Reason for exclusion	Trial comparing two herbal medicines in people with IGT. This study did not meet the review criteria as it was an ineligible comparison.
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## Chen G 2001

Reason for exclusion	Case series of 48 people with IGT taking Jianpi nichan tang.
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## Chen JM 2006

Reason for exclusion	Randomised study comparing the effects of Yuye Tang (Shanyao 30g, Shenghuangqi (raw Huangqi) 30g, Zhimu 10g, Jinei jin 6g, Gegen 10g, Wuweizi 6g, Tianhua fen 30g, Huanqin 10g) versus dimethylidiguanide tablets in people with impaired glucose tolerance over 8 wks. The study reported that it randomly divided the sample into two groups. There is a large sampling discrepancy between the control (n = 43) and intervention group (n = 72) implying this was not random. Method of randomisation not reported. Unable to contact the authors.
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## Chen Y 2005

Reason for exclusion	Non-randomised study of Jinqi jiangtang tablets (n = 42) versus metformin (n = 38) in 80 participants over 3 months.
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## Dai FF 2005

Reason for exclusion	A three-arm study comparing the effects of Ketangling granules (sheng di 10g, shu di 15g, huang jing 10g, huang lian 5g, huang bai 6g, tian hua fen 10g, ze xie 15g, dan shen 10g, chuan xiong 10g, zhi da huang 6g) plus diet & lifestyle modification (n = 32) compared to diet & lifestyle alone (n = 14) and compared to no intervention (n = 16) in people with impaired glucose tolerance. The discrepancy in sampling numbers indicates that it is unlikely that the study was truly randomised.
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## Ding P 2007

Reason for exclusion	Quasi-randomised three-arm study comparing the effects of a Chinese herbal formula (huang qi, huang jing, ge gen, zhe xie, chai hui, gui jian yu etc) in 66 people with impaired glucose tolerance over 3 months. The report stated that the study was randomised. Information obtained from phone interview indicated that allocation was based on alternation. No blinding.
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## Fan GJ 2003

Reason for exclusion	Case series of a chinese herbal medicine in people with IGT.
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## Fan JB 2000

Reason for exclusion	Case series of the effects of a chinese herbal medicine (ren shen 15g, ge gen 20g, bai zhu 10g, fu ling 30g, shan yao 30g, huang qi 30g, shan zhu yu 15g, shui zhi 10g, cang zhu 10, xuan shen 10g, tian hua fen 15g, huang lian 12g For obesity add ji nei jin 15g, shan zha 15g, yi mi 15g; For yin deficient heat add zhi mu 10g, sheng di huang 10g, and delete ren shen, huang qi) in 26 participants with impaired glucose tolerance.
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## Gao S 2007

Reason for exclusion	Case series of Huanyan kuguasu pills in people with IGT.
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## Gu HX 2005

Reason for exclusion	Case series.
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## He Y 2000

Reason for exclusion	Quasi-randomised study comparing the effects of Danshen injection plus xuezhi kang versus xuezhi kang (extract of cholestin, red yeast Chinese rice) in 62 participants with IGT over 4 weeks. The report stated that the study was randomised. Information obtained from phone interview indicated that allocation was based on the judgement of the clinician.
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## Hu XX 2001

Reason for exclusion	Case series of chinese herbal medicine in 60 people with IGT.
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## Huang JX 2003

Reason for exclusion	Quasi-randomised study comparing the effects of a Chinese herbal medicine (huang qi 20g, shan yao 20g, dan shen 20g, sheng di huang 20g, shu di huang 20g, tian hua fen 40g, fu ling 15g, chi shao 15g, chai hu 12g, shu da huang 10g, zhi shi 10g, huang qin 10g, qu mai 10g) versus metformin in 64 people over 12 months. The method of allocation to groups was inadequate.  From a phone call to the author it was ascertained that participants were allocated to the treatment according to the judgement of the clinician.
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## Huang SL 2005

Reason for exclusion	Quasi-randomised study comparing the effects of Xiao yang tang (tao ren 15g, mu dan pi 15g, dan shen 15g, xuan shen 15g, da huang 10g, yu jin 10g, chuan bei mu 10g, lai
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	fu zi 10g) versus metformin in 90 people with impaired glucose tolerance. The method of randomisation was alternation.  From a phone call it was determined that the participants were randomised on the basis of alternation.
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## Huang XP 2003

Reason for exclusion	Randomised study comparing yangxing tongmai tables versus metformin in 67 people with insulin resistance. The criteria for inclusion in the study included people with IGT, diabetes or abnormal ISI. These criteria do not match the required ones for this review.
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## Ji HM 2002

Reason for exclusion	Non-randomised study of Qiweibaizhu san and Gan cao shaoyao tang in 31 people with IGT.
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## Ju S 2007

Reason for exclusion	Non-randomised study of a Chinese herbal extract (berberine) in people with IGT and hyperlipedemia.
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## Kuang KA 2001

Reason for exclusion	Case series.
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## Li CL 2007

Reason for exclusion	Quasi-randomised study comparing the effects of Hu Ben Hui Ni (shu di 20g, shan zhu yu 10g, shan yao 10g, ze xie 10g, mu dan pi 10g, fu ling 10g, ban xia 10g, chen pi 10g, dan shen 10g, gou qi zi 10g, shan zha 10g) in 90 people with impaired glucose tolerance.  Report: "randomly divided into control group of 40 and treatment group of 42 cases. Phone interview: allocation was according to the preference of the participant.
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## Li HB 2002

Reason for exclusion	Duplicate of LI HB 2003
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## Li HB 2003

Reason for exclusion	Quasi-randomised study comparing the effect of Yiqi jianpi fang (dang shen 20g, ge gen 20g, huang qi 15g, fu ling 15g, bai zhu 15g, cang zhu 15g, tian hua fen 15g, shen qu 15g) plus captopril vs captopril alone in 64 participants with impaired glucose tolerance. The study duration was 21 days (<4wks).  The report stated that participants were randomly divided into treatment group A and control group B. From phone contact with the authors the subjects were divided into
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	groups according to ages and other characteristics by the clinician. Same study with more detailed information as Li HB 2002
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Lian JE 2004

Reason for exclusion	Case series.
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Liu DH 2001

Reason for exclusion	Case series of Jianpi sanjing tang in 31 people with IGT.
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Liu PY 2008

Reason for exclusion	This trial compared different herbal medicines.
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Lu YZ 2003

Reason for exclusion	Case series.
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Luo GB 2005

Reason for exclusion	Randomised study comparing Jiangtang bushen fang plus diet & lifestyle advice vs diet & lifestyle advice alone in 51 participants. Only TCM symptom outcomes were reported. These reported outcomes did not fall into our designated categories.
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Luo HX 2008

Reason for exclusion	Randomised study comparing Chinese herbal formula in 156 people with impaired glucose tolerance. Outcomes (FBG, 2hr-GTT, HbA1c and clinical signs and symptoms) were reported as grouped data only: absolutely effective, effective, not effective.
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Mao LH 2003

Reason for exclusion	Quasi-randomised study comparing Jinqi Jiangtang plus diet & exercise vs diet and exercise in 62 participants over 3 months. The report stated that the trial was "randomised". Contact with the author revealed that participants were "casually grouped".
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Meng FX 2000

Reason for exclusion	Randomised study comparing the effect of a chinese herbal decoction plus diet, exercise and education versus diet, exercise and education alone. The trial did not state if it was randomised. There is a sampling discrepancy, with 34 allocated to the treatment group and 22 to the control. Unable to contact the authors.
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## Niu ZY 2003

Reason for exclusion	Non-randomised study comparing Xuexi II capsules plus diet & exercise versus diet & exercise alone in 50 people with IGT.
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## Ouyang AJ 2003

Reason for exclusion	Randomised study observing Yi ming decoction plus insulin vs insulin alone in 131 in people with type 2 diabetes. This population group did not meet the criteria of this review.
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## Shi Y 2000

Reason for exclusion	Case series.
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## Sun BR 2005

Reason for exclusion	The study used a mixed intervention of Chinese herbs and western medicine and was quasi randomised.
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## Sun Y 2005

Reason for exclusion	Case series of 40 people with IGT.
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## Sun YW 2002

Reason for exclusion	This study included subjects with both IGT and diabetes.
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## Wang BH 2004

Reason for exclusion	Review of traditional methods of treating people with IGT.
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## Wang D 1999

Reason for exclusion	Participants were all diabetes type 2. This population group did not meet the criteria of this review.
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## Wang H 2002

Reason for exclusion	Non-randomised study comparing Liu wei di huang wan plus diet & exercise versus diet & exercise alone in 64 participants.
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## Wang H 2003

Reason for exclusion	Case series.
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## Wang H 2004

Reason for exclusion	Randomised study comparing Yiqi ziyin granules (Huang qi 10g, sang shen 10g, xuan shen 10g, tai zi shen 15g) plus diet & lifestyle advice versus diet & lifestyle advice alone in 61 participants. There is a discrepancy in the sampling, 41 in the treatment group versus 20 in the control group.
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## Wang J 2005

Reason for exclusion	Randomised study comparing the effect of Fufang Yin Yang huo chongji versus rosiglitazone in 90 or 60 participants. Participant numbers reported in the tables were 45 in each group and in the text 30 in each group is reported. Authors refused to provide any further information about the study.
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## Wang YF 2008

Reason for exclusion	Quasi-randomised study of Shenqi di huang tang plus diet & exercise versus metformin plus diet & exercise in 80 participants over two and a half years.
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## Wei Y 2008

Reason for exclusion	Quasi-randomised, parallel trial of Tang No. 1 granules plus education versus education alone in 140 people for 6 months. Randomisation was based on the visiting sequence of the participants.
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## Wu G 2007

Reason for exclusion	Review of traditional methods of treating people with IGT.
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## Wu S 2004

Reason for exclusion	Review of traditional methods of treating people with IGT.
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## Wu ZX 2006

Reason for exclusion	A review of traditional methods of treating people with IGT, not a clinical trial.
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## Xin XX 2007

Reason for exclusion	Randomised controlled trial of Jianpi bushen pill plus diet and exercise compared to multivitamin supplement and diet and exercise in 136 participants. The control intervention did not fall into the category of the inclusion criteria.
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## Xu YJ 2008

Reason for exclusion	Non-randomised parallel study of Chinese herbal medicine in combinations with vitamin C or pioglitazone in 150 participants (30 participants in 5 groups).
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## Xue LH 2008

Reason for exclusion	Quasi-randomised, parallel study comparing Jianpi Jiangtang Yin (fu ling 20g, huang qi 30g, cang zhu 15g, yi yi ren 25g, ge gen 15g, mai dong 15g, xuan shen 15g, san qi 15g, dang gui 15g, huang lian 10g. Additions: 1) 5 palm sweat, excessive thirst & drinking: zhi mu 20g, tian hua fen 15g; 2) vexation and irritability, insomnia: bai zi ren 20g, ye jiao teng 15g, huang lian 10g; 3) dizziness and swollen eyes, reddish complexion & ears: mu dan pi 15g, gou teng 15g vs diet and exercise in 160 participants. Method of randomisation was odd-even.
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## Yang E 2007

Reason for exclusion	Study of different methods of treating people with IGT.
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## Yang SJ 2001

Reason for exclusion	Non-randomised.
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## Yang WX 2007

Reason for exclusion	Review of traditional methods of treating people with IGT.
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## Yin B 2007

Reason for exclusion	Quasi-randomised study comparing Jinqi jiangtang tablets plus diet & lifestyle advice vs diet & lifestyle advice in 72 participants. (Randomisation based on age).
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## Yin L 2004

Reason for exclusion	A study of Shengmai injection into elderly people. There were no blood glucose outcomes reported.
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## Yu FH 2005

Reason for exclusion	Non-randomised trial of Jinqi jiangtang pills in people with IGT.
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## Yuan WL 2008

Reason for exclusion	Quasi-randomised (odd-even method) study comparing Chinese herbal medicine (Zhu ru 10g, zhi shi 12g, chen pi 12g, fa xia 12g, fu ling 10g, sheng jiang 5g, yu zhu 15g, dan shen 15g, ze xie 12g, gan cao 3g) plus vigorous exercise, diet and education vs vigorous exercise, diet and education alone in 72 participants.
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## Zhang L 2006

Reason for exclusion	Review of traditional methods of treating people with IGT.
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## Zhang RR 2005

Reason for exclusion	Randomised study comparing the effect of Jinqi jiangtang tablet vs placebo in 57 people. The trial objective was to assess efficacy of the herbal medicine on the excretion rate of microalbuminuria. No blood glucose outcomes were reported.
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## Zhang X 2003

Reason for exclusion	Non-randomised case series of a chinese herbal formula.
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## Zhou XL 2006

Reason for exclusion	Randomised study comparing Shen qi jiang tang ke li vs placebo in 60 participants with impaired glucose tolerance. The study duration was 14 days (<4 wks).
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## Zhou ZN 2001

Reason for exclusion	Quasi-randomised study comparing Huaqi Jiangtang vs diet and exercise in 72 participants with impaired glucose tolerance. Although the report stated the participants were randomised, from the phone interview the author advised that the allocation to treatment group was based on the preference of the participants.
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## Zhou ZN 2002

Reason for exclusion	Quasi-randomised study comparing the effects of Jinqi jiangtang tablet in 46 participants with impaired glucose tolerance. The method of randomisation was alternation. From phone interview it was revealed that the allocation to treatment group was based on the judgement of the clinician.
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IGT: impaired glucose tolerance

## Characteristics of studies awaiting classification

Liu DQ 2007

<b>Methods</b>	Parallel, randomised controlled trial
<b>Participants</b>	<p>SETTING: Outpatients, Hospital, China</p> <p>WHO PARTICIPATED: 160 (80 in treatment group, M/F 50/30, mean age 44.3 yrs; 80 in control group, M/F 48/32, mean age 44.1yrs)</p> <p>INCLUSION CRITERIA: IGT (WHO 1999).</p> <p>EXCLUSION CRITERIA: Excluded hyperthyroid, depression, cancer.</p> <p>CO-MORBIDITIES: none reported</p> <p>CO-MEDICATIONS: none reported</p>
<b>Interventions</b>	<p>INTERVENTION: Jie yu huo xue decoction (dang gui 15g, chai hu 15g, Yu Zhu 10g, huang qi 30g, chuan xiong 10g, chi shao 15g, san qi 3g, ge gen 15g, huang jing 15g, yu jin 15g, ren shen 25g, xia ku cao 10g) , oral, 100ml decoction per dose, 3 times per day; plus lifestyle modification (diet and lifestyle advice). This prescription was added to if the following symptoms were present:</p> <p>If heat in palms, thirst, increased drinking: + zhi mu 20g, wu wei zi 10g.</p> <p>if restlessness, tendency to anger, insomnia: + bai zi ren 20g, ye jiao teng 15g, huang lian 10g.</p> <p>if dizziness, stuffiness in eyes, reddish face &amp; ears with heat: +mu dan pi, gou teng 15g.</p> <p>CONTROL: Lifestyle modification (diet and lifestyle advice).</p>
<b>Outcomes</b>	<p>FBG (mmol/L), 2hr-GTT (mmol/L), normalisation of glucose levels (n).</p> <p>Outcomes were measured at baseline and at trial completion (12 months).</p>
<b>Notes</b>	<p>We are trying to contact the authors to clarify a discrepancy in the publication. The number randomised to the intervention group is reported as 80. In Table 1 of the published report, the incidence of diabetes gives different numbers for the intervention group with totals of 88 (42 normalised, 40 IGT, 6 diabetes mellitus).</p>

IGT: impaired glucose tolerance; FBG: fasting blood glucose; M/F: male/female

## Characteristics of ongoing studies

Footnotes

# Summary of findings tables

## Additional tables

### 1 Overview of study populations

stud y ID	intervention (I) control (C)	[n] screened	[n] randomised	[n] safety	[n] ITT	[n] finishing study	[%] of randomised participants finishing study	comments
Fan GJ 2004	I: Jiang tang bu shen plus diet & lifestyle modification C: diet & lifestyle modification	I: NR C: NRTotal: 51	I: 25 C: 26	I: NR C: NR	I: NR C: NR	I: 23 C: 22 Total: 45	I: 92 C: 85 Total: 88	
Fang ZH 2007	I: Dan zhi jiang tang jiao capsule plus diet & lifestyle modification C: diet & lifestyle modification	I: NR C: NRTotal: 62	I: 32 C: 30	I: NR C: NR	I: NR C: NR	I: 32 C: 30 Total: 62	I: 100 C: 100 Total: 100	
Hao AZ 2004	I: Xiaoke Huayu tablet plus diet & lifestyle modification C: diet & lifestyle modification	I: NR C: NRTotal: 168	I: 86 C: 82	I: NR C: NR	I: NR C: NR	I: 86 C: 82 Total: 168	I: 100 C: 100 Total: 100	
Hioki C 2004	I: Bofu-tsusho-san plus diet & exercise C: diet & exercise	I: NR C: NRTotal: 85	I: 44 C: 41	I: NR C: NR	I: NR C: NR	I: NR C: NR Total: NR	I: ? C: ? Total: ?	three participants withdrew from the intervention group due to loose bowels
Li CP 2004	I: Gimai jiangtang yin plus diet & lifestyle modification C: diet & lifestyle modification	I: NR C: NRTotal: 64	I: 31 C: 33	I: NR C: NR	I: NR C: NR	I: NR C: NR Total: NR	I: ? C: ? Total: ?	
Liu DQ 2007	I: Jie yu huo xue tang plus diet & lifestyle modification C: diet & lifestyle modification	I: NR C: NRTotal: 160	I: 80 C: 80	I: NR C: NR	I: NR C: NR	I: NR C: NR Total: NR	I: ? C: ? Total: ?	

LUX 2005	I: Chinese herbal medicines plus antihypertensive (vasodilator) medication C: antihypertensive (vasodilator) medication	I: NR C: NRTotal: 90	I: 40 C: 50	I: NR C: NR	I: NR C: NR	I: NR C: NR Total: NR	I: ? C: ? Total: ?	blocked randomisation (2 participants in the intervention group; 2 participants in the control group)
Du LX 2002	I: Tang gao san plus diet & lifestyle modification C: metformin plus diet & lifestyle modification	I: NR C: NRTotal: 90	I: 39 C: 51	I: NR C: NR	I: NR C: NR	I: NR C: NR Total: NR	I: ? C: ? Total: ?	
SHU 2005	I: Fufeng oingthu C: metformin	I: NR C: NRTotal: 92	I: 32 C: 60	I: NR C: NR	I: NR C: NR	I: NR C: NR Total: NR	I: ? C: ? Total: ?	
Tang QZ 2007	I: Chinese herbal medicines plus diet & lifestyle modification C1: acarbosae plus diet & lifestyle modification C2: diet & lifestyle modification	I: NR C1: NR C2: NR Total: NR	I: 40 C1: 41 C2: 40 Total: 120	I: NR C1: NR C2: NR	I: NR C1: NR C2: NR Total: NR	I: NR C1: NR C2: NR Total: NR	I: ? C1: ? C2: ? Total: ?	I1, C1: drop-outs due to not being able to continue the medication; C2 no reason was given
Wan BBO 2008	I: Qiwanggang capsule C: placebo	I: NR C: NRTotal: 100	I: 50 C: 50	I: NR C: NR	I: NR C: NR	I: NR C: NR Total: NR	I: ? C: ? Total: ?	
Wan g YX 2005	I: Jnai jiangtang plus diet & lifestyle modification C: diet & lifestyle modification	I: NR C: NRTotal: 159	I: 81 C: 78	I: NR C: NR	I: NR C: NR	I: NR C: NR Total: NR	I: ? C: ? Total: ?	
Wan AS 2001	I: Xiaoke Yuyi plus diet & lifestyle modification C: diet & lifestyle modification	I: NR C: NRTotal: 72	I: 36 C: 36	I: NR C: NR	I: NR C: NR	I: NR C: NR Total: NR	I: ? C: ? Total: ?	



Yang B 2004	I: Tang Kang Yin plus diet & lifestyle modification C: diet & lifestyle modification	I: 40 I: NR C: 36 C: NRT total 76	I: 40 I: NR C: 36 C: NR Total 76	I: NR C: NR Total NR	I: ? C: ? Total: ?
Yao Z 2001	I: Tangheng I plus diet & lifestyle modification C: diet & lifestyle modification	I: 22 I: NR C: 20 C: NRT total 42	I: 22 I: NR C: 20 C: NR Total 42	I: NR C: NR Total NR	I: ? C: ? Total: ?
Zeng YH 2000	I: Liu wei di huang capsule plus diet & lifestyle modification C: diet & lifestyle modification	I: 56 I: NR C: 55 C: NRT total 111	I: 56 I: NR C: 55 C: NR Total 111	I: NR C: NR Total NR	I: ? C: ? Total: ?
Zhou DY 2003	I: Jinqi jiangtang tablet plus diet & lifestyle modification C: diet & lifestyle modification	I: 46 I: NR C: 42 C: NRT total 88	I: 46 I: NR C: 42 C: NR Total 88	I: NR C: NR Total NR	I: ? C: ? Total: ?

?: unclear; ITT = intention-to-treat; NR: not reported

## 2 Preparation and composition of Chinese herbal medicines in the included trials

name of herbal formula	preparation	composition	study ID
Bofutushuo-san	powder	Scutellariae Radix, Glycyrrhizae Radix, Platycodi Radix, Gypsum Fibrosum, Atractylodis-Rhizoma, Rhei Rhizoma, Schizonepetae Spica, Gardeniae Fructus, Paeoniae Radix, Cnidium Rhizoma, Angelicae Radix, Menthae Herba, Ledebouriae Radix, Ephedrae Herba, Forsythiae Fructus, Zingiberis Rhizoma, Talcum, Natrium Sulphuricum	Hicki C 2004
Yi Qi Yang Yin Huo Xue	decoction	Astragali Radix 30g, Angelicae sinensis Radix 20g, Dioscoreae Rhizoma 20g, Mori Cortex 50g, Mori Folium 30g, Mori Ramulus 30g	Lu X 2005
Jian Pi Zhi Shen Huo Xue	powder	Dioscoreae Rhizoma, Crataegi Fructus 30g, Astragali Radix 20g, Poria 20g, Corni Fructus 15g, Persicae Semen 10g	Tang GZ 2007
Dan zhi jiang tang jiao	capsules	Moutan Cortex, Hirodu, Cuscutae Semen, Polygonati Rhizoma, Pseudostellariae Radix, plus Rehmanniae glutinosae, Corni of cinalis, Dioscoreae oppositae, Alismatis orientalis, Poriae cocos, Moutan radidis.	Fang ZH 2007
Fufang cangzhu	decoction	Atractylodis Rhizoma 15g, Coptidis Semen 24g, Mori Fructus 20g, Dioscoreae Rhizoma 30g, Phellodendri Cortex 10g, Litchi Semen 20g, Pheretima 10g	Shi J 2005
Jiangtang bushen tang	decoction	Cibotii Rhizoma 10g, Dipsaci Radix 10g, Ligustri lucidi Fructus 15g, Ecliptae Herba 15g, Lycii Cortex 15g, Astragali Radix 15g, Rehmanniae Radix 15g, Puerariae Radix 12g, Coptidis Rhizoma 5g, Mori Cortex 10g, Moutan Cortex 6g	Fan GJ 2004
Jie yu huo xue	decoction	Angelicae sinensis Radix 15g, Bupleuri Radix 15g, Polygonati odorati Rhizoma 10g, Astragali Radix 30g, Chuanxiong Rhizoma 10g, Paeoniae Radix rubra 15g, Notoginseng Radix 3g, Puerariae Radix 15g, Polygonati Rhizoma 15g, Curcumae Radix 15g, Ginseng Radix 25g, Prunellae Spica 10g, If heat in palms, thirst, increased drinking: + Anemarrhenae Rhizoma 20g, Schisandrae Fructus 10g; if restlessness, tendency to anger, insomnia: + Platycladi Semen 20g, Polygoni multiflori Caulis 15g, Coptidis Rhizoma 10g, If dizziness, stuffiness in eyes, reddish face & ears with heat: + Moutan Cortex 15g, Uncariae Ramulus cum Uncis 15g	Liu DQ 2007
Jinqi Jiangtang	pill	Astragali Radix, Lonicera Flos etc	Zhou DY 2003
Jinqi Jiangtang	pill	Astragali Radix, Lonicera Flos etc	Weng YX 2005
Liu wei di huang wan	pill	Rehmanniae glutinosae, Corni of cinalis, Dioscoreae oppositae, Alismatis orientalis, Poriae cocos, Moutan radidis.	Zeng YH 2006

Qimai jiangtang yin	decoction	Astragalii Radix 20g, Puerariae Radix 20g, Ophiopogonis Radix 10g, Ligustri lucidi Fructus 10g, Notoginseng Radix 10g, Curcumae Radix 10g, Rehmanniae Radix 25g	Li CP 2004
Qiwetangqing	capsule	Astragalii Radix, Scutellariae Radix, Perillae Fructus, Codonopsis Radix, Rhei Radix et Rhizoma, Jujubae Fructus, Rehmanniae Radix preparata, Bupleuri Radix, Salviae miltorhizae Radix, Curcumae Radix, Artemisiae scopariae Herba, Tricosanthi Radix, Cypsum fibrosus, Plantaginis Semen, Dioscoreae Rhizoma, Schisandriae Fructus, Comi Fructus, Anemarrhenae Rhizoma, Lycii Fructus, Puerariae Radix, Lili Bulbus, Glycyrrhizae Radix, Linderae Radix, Rehmanniae Radix, Zanthoxyli Pericarpium, Vaccariae Semen, Glycyrrhizae Radix	Wang BQ 2006
Tang Kang Yin	decoction	Ginseng Radix 6g, Coptidis Rhizoma 10g, Ligustri lucidi Fructus 15g, Prunellae Spica 30g, Alumen 30g	Yang B 2004
Tang jing san	powder	Astragalii Radix 30g, Dioscoreae Rhizoma 10g, Rehmanniae Radix 10g, Rehmanniae Radix preparata 10g, Lycii Fructus 10g, Polygoni multiflori Radix preparata 10g, Epimedii Herba 10g, Salviae miltorhizae 30g, Alismatis Rhizoma 10g, Mori Folium 10g	Gu LX 2002
Xiaoke huayu pian	tablet	Anemarrhenae Rhizoma, Euonymi Ramulus etc	Hao AZ 2004
Xiaoke yuye	decoction	Astragalii Radix, Polygonati Rhizoma, Polygoni multiflori Radix preparata, Anemarrhenae Rhizoma	Wei AS 2001

## Data and analyses

### 1 Herbal medicine plus lifestyle modification versus lifestyle modification alone

Outcome or Subgroup	Studies	Participants	Statistical Method	Effect Estimate
1.1 Normalisation of fasting blood glucose at trial completion (n)	8	625	Risk Ratio (IV, Random, 95% CI)	2.07 [1.52, 2.82]
1.1.1 Jiantang Bushen decoction	1	45	Risk Ratio (IV, Random, 95% CI)	1.72 [1.04, 2.86]
1.1.2 Xiaoke Huaya tablet	1	168	Risk Ratio (IV, Random, 95% CI)	2.54 [1.70, 3.79]
1.1.3 Qimai Jiangtang Yin decoction	1	64	Risk Ratio (IV, Random, 95% CI)	2.89 [1.41, 5.90]
1.1.4 Jian Pi Zhi Shen Huo Xue	1	77	Risk Ratio (IV, Random, 95% CI)	1.92 [1.28, 2.90]
1.1.5 Tang Kang Yin	1	76	Risk Ratio (IV, Random, 95% CI)	3.75 [1.74, 8.09]
1.1.6 Xiaoke Yuye decoction	1	65	Risk Ratio (IV, Random, 95% CI)	1.89 [1.14, 3.14]
1.1.7 Tang Heng I	1	42	Risk Ratio (IV, Random, 95% CI)	5.00 [1.26, 19.87]
1.1.8 Jinqi jiangtang	1	88	Risk Ratio (IV, Random, 95% CI)	1.17 [0.90, 1.53]
1.2 Incidence of diabetes (n)	8	632	Risk Ratio (M-H, Random, 95% CI)	0.33 [0.19, 0.58]
1.2.1 Jiangtang Bushen tang	1	45	Risk Ratio (M-H, Random, 95% CI)	0.32 [0.04, 2.84]
1.2.2 Xiaoke Huayu Pian	1	168	Risk Ratio (M-H, Random, 95% CI)	.36 [0.10, 1.30]
1.2.3 Qimai Jiangtang Yin	1	64	Risk Ratio (M-H, Random, 95% CI)	0.18 [0.02, 1.39]

Outcome or Subgroup	Studies	Participants	Statistical Method	Effect Estimate
1.2.4 Tang King Yin	1	76	Risk Ratio ( M-H , Random , 95% CI )	0.06 [0.01, 0.46]
1.2.5 Jian pi zhi shen huo xue	1	77	Risk Ratio ( M-H , Random , 95% CI )	0.59 [0.19, 1.84]
1.2.6 Jinqi Jiangtang tablet	1	88	Risk Ratio ( M-H , Random , 95% CI )	0.61 [0.11, 3.47]
1.2.7 Xiaoke Yuye	1	72	Risk Ratio ( M-H , Random , 95% CI )	0.33 [0.07, 1.54]
1.2.8 Tangheng I Plus	1	42	Risk Ratio ( M-H , Random , 95% CI )	0.18 [0.02, 1.43]
1.3 <u>Fasting blood glucose (mmol/L)</u>	9	742	Mean Difference ( IV , Random , 95% CI )	-0.41 [-0.66, -0.16]
1.3.1 Jiangtang Bushen decoction	1	45	Mean Difference ( IV , Random , 95% CI )	0.15 [ -0.42, 0.12]
1.3.2 Xiaoke Huayu tablet	1	168	Mean Difference ( IV , Random , 95% CI )	-1.40 [-1.72, -1.08]
1.3.3 Qimai Jiangtang Yin formula	1	64	Mean Difference ( IV , Random , 95% CI )	-0.03 [-0.32, 0.26]
1.3.4 Jinqi Jiangtang tablet	1	88	Mean Difference ( IV , Random , 95% CI )	-0.58 [-0.74, -0.42]
1.3.5 Jian Pi Zhi Shen Huo Xue	1	76	Mean Difference ( IV , Random , 95% CI )	-0.09 [-0.35, 0.17]
1.3.6 Xiaoke Yuye decoction	1	72	Mean Difference ( IV , Random , 95% CI )	-0.39 [-0.99, 0.21]
1.3.7 Tang Kang Yin decoction	1	76	Mean Difference ( IV , Random , 95% CI )	-0.21 [-0.33, -0.09]
1.3.8 Tang Heng I decoction	1	42	Mean Difference ( IV , Random , 95% CI )	-1.24 [-2.53, 0.05]
1.3.9 Liu Wei Di Huang capsule	1	111	Mean Difference ( IV , Random , 95% CI )	-0.31 [-0.58, -0.04]
1.4 <u>2hr fasting blood glucose (mmol/L) [ after oral glucose tolerance test]</u>	9		Mean Difference ( IV , Random , 95% CI )	No totals
1.4.1 Jiangtang Bushen decoction	1		Mean Difference ( IV , Random , 95% CI )	No totals
1.4.2 Xiaoke Huaye tablet	1		Mean Difference ( IV , Random , 95% CI )	No totals
1.4.3 Qimai Jiangtang Yin decoction	1		Mean Difference ( IV , Random , 95% CI )	No totals

Outcome or Subgroup	Studies	Participants	Statistical Method	Effect Estimate
1.4.4 Jinqi Jiangtang tablet	1		Mean Difference ( IV , Random , 95% CI )	No totals
1.4.5 Jian Pi Zhi Shen Huo Xue	1		Mean Difference ( IV , Random , 95% CI )	No totals
1.4.6 Xiaoke Yuye decoction	1		Mean Difference ( IV , Random , 95% CI )	No totals
1.4.7 Tang Kang Yin decoction	1		Mean Difference ( IV , Random , 95% CI )	No totals
1.4.8 Tang Heng I decoction	1		Mean Difference ( IV , Random , 95% CI )	No totals
1.4.9 Liu Wei Di Huang capsule	1		Mean Difference ( IV , Random , 95% CI )	No totals
1.5 <u>HbA1c (%)</u>	3	317	Mean Difference ( IV , Random , 95% CI )	-0.47 [-1.00, 0.06]
1.5.1 Xiaoke Huayu tablet	1	168	Mean Difference ( IV , Random , 95% CI )	-0.63 [-0.99, -0.27]
1.5.2 Jian Pi Zhi Shen Huo Xue	1	77	Mean Difference ( IV , Random , 95% CI )	-0.87 [-1.43, -0.31]
1.5.3 Xiaoke Yuye decoction	1	72	Mean Difference ( IV , Random , 95% CI )	-0.06 [-0.12, 0.00]
1.6 <u>Insulin (μU/ml)</u>	6		Mean Difference ( IV , Random , 95% CI )	No totals
1.6.1 Jiangtang Bushen decoction	1		Mean Difference ( IV , Random , 95% CI )	No totals
1.6.2 Qimai Jiangtang Yin decoction	1		Mean Difference ( IV , Random , 95% CI )	No totals
1.6.3 Jinqi Jiangtang tablet	1		Mean Difference ( IV , Random , 95% CI )	No totals
1.6.4 Jian Pi Zhi Shen Huo Xue	1		Mean Difference ( IV , Random , 95% CI )	No totals
1.6.5 Tang Kang Yin decoction	1		Mean Difference ( IV , Random , 95% CI )	No totals
1.6.6 Tang Heng I decoction	1		Mean Difference ( IV , Random , 95% CI )	No totals
1.7 <u>IAI (insulin sensitivity)</u>	1		Mean Difference ( IV , Random , 95% CI )	No totals
1.7.1 Qimai Jiangtang Yin decoction	1		Mean Difference ( IV , Random , 95% CI )	No totals

Outcome or Subgroup	Studies	Participants	Statistical Method	Effect Estimate
1.8 <u>Total cholesterol (mmol/L)</u>	7		Mean Difference ( IV , Random , 95% CI )	No totals
1.8.1 Jiangtang Bushen tang	1		Mean Difference ( IV , Random , 95% CI )	No totals
1.8.2 Xiaoke Huayu Pian	1		Mean Difference ( IV , Random , 95% CI )	No totals
1.8.3 Jinqi Jiangtang tablet	1		Mean Difference ( IV , Random , 95% CI )	No totals
1.8.4 Jian Pi Zhi Shen Huo Xue	1		Mean Difference ( IV , Random , 95% CI )	No totals
1.8.5 Xiaoke Yuye	1		Mean Difference ( IV , Random , 95% CI )	No totals
1.8.6 Tang Kang Yin	1		Mean Difference ( IV , Random , 95% CI )	No totals
1.8.7 Liu Wei Di Huang capsule	1		Mean Difference ( IV , Random , 95% CI )	No totals
1.9 <u>Lipids: HDL (mmol/L)</u>	2		Mean Difference ( IV , Random , 95% CI )	No totals
1.9.1 Jian Pi Zhi Shen Huo Xue	1		Mean Difference ( IV , Random , 95% CI )	No totals
1.9.2 Jinqi Jiangtang tablet	1		Mean Difference ( IV , Random , 95% CI )	No totals
1.10 <u>Triglycerides (mmol/L)</u>	7		Mean Difference ( IV , Random , 95% CI )	No totals
1.10.1 Jiangtang Bushen tang	1		Mean Difference ( IV , Random , 95% CI )	No totals
1.10.2 Xiaoke Huayu Pian	1		Mean Difference ( IV , Random , 95% CI )	No totals
1.10.3 Jinqi Jiangtang tablet	1		Mean Difference ( IV , Random , 95% CI )	No totals
1.10.4 Jian Pi Zhi Shen Huo Xue	1		Mean Difference ( IV , Random , 95% CI )	No totals
1.10.5 Xiaoke Yuye decoction	1		Mean Difference ( IV , Random , 95% CI )	No totals
1.10.6 Tang Kang Yin decoction	1		Mean Difference ( IV , Random , 95% CI )	No totals
1.10.7 Liu Wei Di Huang Wan	1		Mean Difference ( IV , Random , 95% CI )	No totals

Outcome or Subgroup	Studies	Participants	Statistical Method	Effect Estimate
1.11 <u>Body Mass Index (kg/m<sup>2</sup>)</u>	6		Mean Difference ( IV , Random , 95% CI )	No totals
1.11.1 Jiangtang Bushen	1		Mean Difference ( IV , Random , 95% CI )	No totals
1.11.2 Jian Pi Zhi Shen Huo Xue	1		Mean Difference ( IV , Random , 95% CI )	No totals
1.11.3 Xiaoke Yuye decoction	1		Mean Difference ( IV , Random , 95% CI )	No totals
1.11.4 Tang Kang Yin decoction	1		Mean Difference ( IV , Random , 95% CI )	No totals
1.11.5 Liu Wei Di Huang capsule	1		Mean Difference ( IV , Random , 95% CI )	No totals
1.11.6 Jinqi Jiangtang tablet	1		Mean Difference ( IV , Random , 95% CI )	No totals
1.12 <u>Diastolic blood pressure (mmHg)</u>	2		Mean Difference ( IV , Random , 95% CI )	No totals
1.12.1 Liu wei di huang wan	1		Mean Difference ( IV , Random , 95% CI )	No totals
1.12.2 Jinqi jiangtang tablets	1		Mean Difference ( IV , Random , 95% CI )	No totals
1.13 <u>Systolic Blood Pressure (mmHg)</u>	2		Mean Difference ( IV , Random , 95% CI )	No totals
1.13.1 Liu wei di huang wan	1		Mean Difference ( IV , Random , 95% CI )	No totals
1.13.2 Jinqi jiangtang tablets	1		Mean Difference ( IV , Random , 95% CI )	No totals
1.14 <u>Main ingredient Astragalus membranaceus (≥30g): Fasting blood glucose (mmol/ml)</u>	4		Mean Difference ( IV , Random , 95% CI )	No totals
1.14.1 Jinqi Jiangtang tablet	1		Mean Difference ( IV , Random , 95% CI )	No totals
1.14.2 Xiaoke Yuye decoction	1		Mean Difference ( IV , Random , 95% CI )	No totals
1.14.3 Shan yao, shan zha, huang qi etc	1		Mean Difference ( IV , Random , 95% CI )	No totals
1.14.4 Qimai Jiangtang Yin formula	1		Mean Difference ( IV , Random , 95% CI )	No totals
1.15 <u>Hypoglycaemic effects of herbal medicines with lifestyle modification compared lifestyle</u>	9		Other data	No numeric data

Outcome or Subgroup	Studies	Participants	Statistical Method	Effect Estimate
modification alone				

## 2 Herbal medicine plus lifestyle modification versus placebo plus lifestyle modification

Outcome or Subgroup	Studies	Participants	Statistical Method	Effect Estimate
2.1 <u>Reduction in fasting blood glucose (mmol/L)</u>	2		Mean Difference ( IV , Random , 95% CI )	No totals
2.1.1 Dan zhi jiang tang jiao capsules	1		Mean Difference ( IV , Random , 95% CI )	No totals
2.1.2 Bofu-tsusho-san	1		Mean Difference ( IV , Random , 95% CI )	No totals
2.2 <u>Reduction in 2hr fasting blood glucose after oral glucose tolerance test</u>	2		Mean Difference ( IV , Random , 95% CI )	No totals
2.2.1 Dan zhi jiang tang jiao capsules	1		Mean Difference ( IV , Random , 95% CI )	No totals
2.2.2 Bofu-tsusho-san	1		Mean Difference ( IV , Random , 95% CI )	No totals
2.3 <u>Reduction in HbA1c (%)</u>	1		Mean Difference ( IV , Random , 95% CI )	No totals
2.3.1 Bofu-tsusho-san	1		Mean Difference ( IV , Random , 95% CI )	No totals
2.4 <u>Total cholesterol (mmol/L)</u>	1		Mean Difference ( IV , Random , 95% CI )	No totals
2.4.1 Bofu-tsusho-san	1		Mean Difference ( IV , Random , 95% CI )	No totals
2.5 <u>Triglycerides (mmo/L)</u>	2		Mean Difference ( IV , Random , 95% CI )	No totals
2.5.1 Dan zhi jiang tang jiao capsules	1		Mean Difference ( IV , Random , 95% CI )	No totals
2.5.2 Bofu-tsusho-san	1		Mean Difference ( IV , Random , 95% CI )	No totals
2.6 <u>Insulin (mu/L)</u>	2		Mean Difference ( IV , Random , 95% CI )	No totals
2.6.1 Bofu-tsusho-san	1		Mean Difference ( IV , Random , 95% CI )	No totals
2.6.2 Dan zhi jiang tang jiao capsules	1		Mean Difference ( IV , Random , 95% CI )	No totals

Outcome or Subgroup	Studies	Participants	Statistical Method	Effect Estimate
2.7 <u>Lipids: HDL (mmol/L)</u>	1		Mean Difference ( IV , Random , 95% CI )	No totals
2.7.1 Bofu-tsusho-san	1		Mean Difference ( IV , Random , 95% CI )	No totals

### 3 Herbal medicine plus lifestyle modification versus metformin plus lifestyle modification

Outcome or Subgroup	Studies	Participants	Statistical Method	Effect Estimate
3.1 <u>Reduction in 2 hr fasting blood glucose after oral glucose tolerance test (mmol/L)</u>	1		Mean Difference ( IV , Random , 95% CI )	No totals
3.1.1 Tangping San	1		Mean Difference ( IV , Random , 95% CI )	No totals

### 4 Herbal medicine versus placebo

Outcome or Subgroup	Studies	Participants	Statistical Method	Effect Estimate
4.1 <u>Normalisation of fasting blood glucose (n)</u>	1		Risk Ratio ( M-H , Random , 95% CI )	No totals
4.1.1 Qiwei Tang Ping capsule	1		Risk Ratio ( M-H , Random , 95% CI )	No totals
4.2 <u>Incidence of diabetes (n)</u>	1		Risk Ratio ( M-H , Random , 95% CI )	No totals
4.2.1 Qiwei Tang Ping	1		Risk Ratio ( M-H , Random , 95% CI )	No totals
4.3 <u>Reduction in fasting blood glucose (mmol/L)</u>	1		Mean Difference ( IV , Random , 95% CI )	No totals
4.3.1 Qiwei tangping capsules	1		Mean Difference ( IV , Random , 95% CI )	No totals
4.4 <u>Reduction in 2hr fasting blood glucose after orale glucose tolerance test (mmol/L)</u>	1		Mean Difference ( IV , Random , 95% CI )	No totals
4.4.1 Qiwei tangping capsules	1		Mean Difference ( IV , Random , 95% CI )	No totals
4.5 <u>Body mass index (kg/m<sup>2</sup>)</u>	1		Mean Difference ( IV , Random , 95% CI )	No totals
4.5.1 Qiwei tangping capsules	1		Mean Difference ( IV , Random , 95% CI )	No totals



Outcome or Subgroup	Studies	Participants	Statistical Method	Effect Estimate
4.6 <u>Waist-to-hip ratio (WHR)</u>	1		Mean Difference ( IV , Random , 95% CI )	No totals
4.6.1 Qiwei tangping capsules	1		Mean Difference ( IV , Random , 95% CI )	No totals

## 5 Herbal medicine versus metformin

Outcome or Subgroup	Studies	Participants	Statistical Method	Effect Estimate
5.1 <u>Reduction in fasting blood glucose (mmol/L)</u>	1		Mean Difference ( IV , Random , 95% CI )	No totals
5.1.1 Fufang Cangzhu decoction	1		Mean Difference ( IV , Random , 95% CI )	No totals
5.2 <u>Reduction in 2hr fasting blood glucose after orale glucose tolerance test (mmol/L)</u>	1		Mean Difference ( IV , Random , 95% CI )	No totals
5.2.1 Fufang Cangzhu	1		Mean Difference ( IV , Random , 95% CI )	No totals
5.3 <u>Triglycerides (mmol/L)</u>	1		Mean Difference ( IV , Random , 95% CI )	No totals
5.3.1 Fufang Cangzhu	1		Mean Difference ( IV , Random , 95% CI )	No totals
5.4 <u>Total cholesterol</u>	1		Mean Difference ( IV , Random , 95% CI )	No totals
5.4.1 Fufang Cangzhu	1		Mean Difference ( IV , Random , 95% CI )	No totals
5.5 <u>Insulin (mU/L)</u>	1		Mean Difference ( IV , Random , 95% CI )	No totals
5.5.1 Fufang Cangzhu	1		Mean Difference ( IV , Random , 95% CI )	No totals
5.6 <u>Waist-to-hip ratio (WHR)</u>	1		Mean Difference ( IV , Random , 95% CI )	No totals
5.6.1 Fufang Cangzhu	1		Mean Difference ( IV , Random , 95% CI )	No totals
5.7 <u>Weight (kg)</u>	1		Mean Difference ( IV , Random , 95% CI )	No totals
5.7.1 Fufang Cangzhu	1		Mean Difference ( IV , Random , 95% CI )	No totals

## 6 Herbal medicine plus lifestyle modification versus acarbose plus lifestyle modification

Outcome or Subgroup	Studies	Participants	Statistical Method	Effect Estimate
6.1 <u>Reduction in fasting blood glucose (mmol/L)</u>	1		Mean Difference ( IV , Random , 95% CI )	No totals

Outcome or Subgroup	Studies	Participants	Statistical Method	Effect Estimate
6.1.1 Jian pi zhi shen huo xue	1		Mean Difference ( IV , Random , 95% CI )	No totals
6.2 <u>2hr-Glucose tolerance (mmol/L)</u>	1		Mean Difference ( IV , Random , 95% CI )	No totals
6.2.1 Jian pi zhi shen huo xue	1		Mean Difference ( IV , Random , 95% CI )	No totals
6.3 <u>Normalisation of blood glucose (n)</u>	1		Odds Ratio ( M-H , Random , 95% CI )	No totals
6.3.1 Jian pi zhi shen huo xue	1		Odds Ratio ( M-H , Random , 95% CI )	No totals
6.4 <u>Incidence of diabetes (n)</u>	1		Risk Ratio ( M-H , Random , 95% CI )	No totals
6.4.1 Jian pi zhi shen huo xue	1		Risk Ratio ( M-H , Random , 95% CI )	No totals
6.5 <u>HbA1c (%)</u>	1		Mean Difference ( IV , Random , 95% CI )	No totals
6.6 <u>Insulin (FINS mmol/L)</u>	1		Mean Difference ( IV , Random , 95% CI )	No totals
6.6.1 Jian pi zhi shen huo xue	1		Mean Difference ( IV , Random , 95% CI )	No totals
6.7 <u>Total cholesterol (mmol/L)</u>	1		Mean Difference ( IV , Random , 95% CI )	No totals
6.8 <u>Triglycerides (mmol/L)</u>	1		Mean Difference ( IV , Random , 95% CI )	No totals
6.8.1 Jian pi zhi shen huo xue	1		Mean Difference ( IV , Random , 95% CI )	No totals
6.9 <u>Lipids: LDL (mmol/L)</u>	1		Mean Difference ( IV , Random , 95% CI )	No totals
6.9.1 Jian pi zhi shen huo xue	1		Mean Difference ( IV , Random , 95% CI )	No totals
6.10 <u>Lipids: HDL (mmol/L)</u>	1		Mean Difference ( IV , Random , 95% CI )	No totals
6.10.1 Jian pi zhi shen huo xue	1		Mean Difference ( IV , Random , 95% CI )	No totals

## 7 Herbal medicine plus antihypertensive medication versus antihypertensive medication alone

Outcome or Subgroup	Studies	Participants	Statistical Method	Effect Estimate
7.1 <u>Reduction in fasting glucose (mmol/L)</u>	1		Mean Difference ( IV , Random , 95% CI )	No totals
7.1.1 Yi qi yang yin huo xue	1		Mean Difference ( IV , Random , 95% CI )	No totals
7.2 <u>Reduction in 2hr blood glucose after oral glucose tolerance test (mmol/L)</u>	1		Mean Difference ( IV , Random , 95% CI )	No totals
7.2.1 Yi qi yang yin huo xue	1		Mean Difference ( IV , Random , 95% CI )	No totals
7.3 <u>Total cholesterol (mmol/L)</u>	1		Mean Difference ( IV , Random , 95% CI )	No totals
7.3.1 Yi qi yang yin huo xue	1		Mean Difference ( IV , Random , 95% CI )	No totals
7.4 <u>Triglycerides (mmol/L)</u>	1		Mean Difference ( IV , Random , 95% CI )	No totals
7.4.1 Yi qi yang yin huo xue	1		Mean Difference ( IV , Random , 95% CI )	No totals
7.5 <u>Lipids: HDL (mmol/L)</u>	1		Mean Difference ( IV , Random , 95% CI )	No totals
7.5.1 Yi qi yang yin huo xue	1		Mean Difference ( IV , Random , 95% CI )	No totals
7.6 <u>Systolic Blood Pressure (kpa)</u>	1		Mean Difference ( IV , Random , 95% CI )	No totals
7.6.1 Yi qi yang yin huo xue	1		Mean Difference ( IV , Random , 95% CI )	No totals
7.7 <u>Diastolic blood pressure (kpa)</u>	1		Mean Difference ( IV , Random , 95% CI )	No totals
7.7.1 Yi qi yang yin huo xue	1		Mean Difference ( IV , Random , 95% CI )	No totals

## 8 Herbal medicine versus basic education (diabetes pamphlet)

Outcome or Subgroup	Studies	Participants	Statistical Method	Effect Estimate
8.1 <u>Normalisation of fasting blood glucose at trial completion (n)</u>	1		Risk Ratio ( IV , Random , 95% CI )	No totals
8.1.1 Jinqi Jiangtang tablet	1		Risk Ratio ( IV , Random , 95% CI )	No totals

Outcome or Subgroup	Studies	Participants	Statistical Method	Effect Estimate
8.2 <u>Incidence of diabetes (n)</u>	1		Risk Ratio ( M-H , Random , 95% CI )	No totals
8.2.1 Jinqi Jiangtang tablet	1		Risk Ratio ( M-H , Random , 95% CI )	No totals
8.3 <u>Fasting blood glucose (mmol/L)</u>	1		Mean Difference ( IV , Random , 95% CI )	No totals
8.3.1 06 Jinqi Jiangtang tablet	1		Mean Difference ( IV , Random , 95% CI )	No totals
8.4 <u>2hr fasting blood glucose (mmol/L) [ after oral glucose tolerance test]</u>	1		Mean Difference ( IV , Random , 95% CI )	No totals
8.4.1 Jinqi Jiangtang tablet	1		Mean Difference ( IV , Random , 95% CI )	No totals
8.5 <u>Total cholesterol (mmol/L)</u>	1		Mean Difference ( IV , Random , 95% CI )	No totals
8.5.1 Jinqi Jiangtang tablet	1		Mean Difference ( IV , Random , 95% CI )	No totals
8.6 <u>Triglycerides (mmol/L)</u>	1		Mean Difference ( IV , Random , 95% CI )	No totals
8.6.1 Jinqi Jiangtang tablet	1		Mean Difference ( IV , Random , 95% CI )	No totals

## Other data tables

### 1 Herbal medicine plus lifestyle modification versus lifestyle modification alone

#### 1.15 Hypoglycaemic effects of herbal medicines with lifestyle modification compared lifestyle modification alone

Study ID	Intervention	FBG levels (mmol/L)	2hr GTT FBG (mmol/L)	Normalisation of FBG: RR [95% CI]	HbA1c (%)
Fan GJ 2004	Jiantang bushen Tang	-0.15 [0.42, 0.12]	-0.83 [-1.84, 0.18]	1.72 [1.04, 2.86]	-
Hao AZ 2004	Xiaoke Huaya tablet	-1.40 [-1.72, -1.08]	-1.46 [-1.83, -1.09]	2.54 [1.70, 3.79]	-0.63 [-0.99, -0.27]
Li CP 2004	Qimai Jiangtang Yin formula	-0.03 [-0.32, 0.26]		2.89 [1.41, 5.90]	-
Tang QZ 2007	Shan yao, Shan zha, Huang qi etc	-0.09 [-0.35, 0.17]	-2.31 [-3.20, -1.42]	1.92 [1.28, 2.90]	-0.87 [-1.43, -0.31]
Wei AS 2001	Xiaoke Yuye decoction	-0.39 [0.99, 0.21]	-1.54 [-1.65, -1.43]	1.89 [1.14, 3.14]	-0.06 [-0.12, 0.00]

Study ID	Intervention	FBG levels (mmol/L)	2hr GTT FBG (mmol/L)	Normalisation of FBG: RR [95% CI]	HbA1c (%)
Yang B 2004	Tang Kang Yin decoction	-0.21 [-0.33, -0.09]	-1.66 [-2.21, -1.11]	-	-
Yao Z 2001	Tang Heng I	-1.24 [-2.53, 0.05]	-1.25 [-3.30, 0.80]	5.00 [1.26, 19.87]	-
Zeng YH 2006	Liu Wei Di Huang capsule	-1.19 [-1.46, -0.92]	-2.77 [-3.17, -2.37]	-	-
Zhou DY 2003	Jinqi Jiangtang tablet	-0.58 [-0.74, -0.42]	-0.57 [-0.67, -0.47]	-	-

## Feedback

## Appendices

### 1 MEDLINE search strategy

Electronic searches
Unless otherwise stated, search terms were free text terms; exp = exploded MeSH: Medical Subject Heading (Medline medical index term); the dollar sign (\$) stands for any character(s); the question mark (?) = substitute for one or no characters; ab = abstract; ti = title; ot = original title; pt = publication type; sh = MeSH: Medical subject heading (MEDLINE medical index term); adj = adjacency.
<b>I. Impaired glucose tolerance / impaired fasting blood glucose:</b>
1.exp Glucose Intolerance/
2.exp Diabetes Mellitus/pc [Prevention & Control]
3.exp Glucose Tolerance Test/
4.exp Insulin Resistance/
5.exp Metabolic Syndrome X/
6.IGT.ab,ti,ot.
7.glucose intoleranc\$.ab,ti,ot.
8.(glucose adj tolerance test\$).ab,ti,ot.
9.OGTT.ab,ti,ot.
10.insulin\$ resistanc\$.ab,ti,ot.
11.(impaired fasting and (blood or glucos\$ or gly?emia\$)).ab,ti,ot.
12.(impaired glucose and (toleranc\$ or stat\$ or respons\$ or control\$)).ab,ti,ot.
13.(impaired glucose and (regul\$ or metab\$ or homeost\$)).ab,ti,ot.
14.(reduced glucose and (metabol\$ or toleranc\$)).ab,ti,ot.
15.glucose intolerant\$.ab,ti,ot.
16.pr?ediabet\$.ab,ti,ot.
17.pr?e diabet\$.ab,ti,ot.
18.metabolic syndr\$.ab,ti,ot.
19.syndrom\$ X.ab,ti,ot.
20.(borderline or mild or chemical) adj diabet\$).ab,ti,ot.
21.((impaired insulin\$ or reduced insulin\$) adj secret\$).ab,ti,ot.

<b>Electronic searches</b>
22.or/1-21
<b>II. Chinese herbal medicines:</b>
23.exp Medicine, Oriental Traditional/
24.exp Drugs, Chinese Herbal/
25.exp Plants, Medicinal/
26.exp Plant Extracts/
27.exp Phytotherapy/
28.exp Medicine, Ayurvedic/
29.integrative medicin\$.ab,ti,ot.
30.(medicin\$ adj5 (chines\$ or oriental\$ or tibetan\$)).ab,ti,ot.
31.(herbal medicin\$ or medicin\$ herbal\$).ab,ti,ot.
32.(plant\$ medicin\$ or medicin\$ plant\$).ab,ti,ot.
33.plant\$ extract\$.ab,ti,ot.
34.phytotherap\$.ab,ti,ot.
35.medicine ayurvedic.ab,ti,ot.
36.(chinese adj (herb\$ or drug\$ or formul\$ or plant\$ or presri\$ or remed\$ or materia medica)).ab,ti,ot.
37.((herb\$ or drug\$ or formul\$ or plant\$ or presri\$ or remed\$ or materia medica) adj chinese).ab,ti,ot.
38.((chines\$ or oriental\$ or tibetan\$) adj medicine\$).ab,ti,ot.
39.or/23-38
<b>III. Impaired glucose tolerance/Impaired fasting blood glucose and Chinese herbal medicine:</b>
40.22 and 39
<b>IV. RCT / CCT (sensitive search):</b>
Part 1:
41.randomized controlled trial.pt.
42.controlled clinical trial.pt.
43.randomized controlled trials.sh.
44.random allocation.sh.
45.double-blind method.sh.
46.single-blind method.sh.
47.or/41-46
Part 2:
48.clinical trial.pt.
49.exp clinical trials/
50.(clinic\$ adj25 trial\$).ab,ti,ot.
51.((singl\$ or doubl\$ or trebl\$ or tripl\$) adj (mask\$ or blind\$)).ab,ti,ot.
52.placebos.sh.
53.placebo\$.ab,ti,ot.
54.random\$.ab,ti,ot.

<b>Electronic searches</b>
55.research design.sh.
56.(latin adj square).ab,ti,ot.
57.or/48-56
Part 3:
58.comparative study.pt.
59.exp evaluation studies/
60.follow-up studies.sh.
61.prospective studies.sh.
62.(control\$ or prospectiv\$ or volunteer\$).ab,ti,ot.
63.cross-over studies.sh.
64.or/58-63
65.47 or 57 or 64
<b>V. Meta-analyses, systematic reviews, health technology assessments:</b>
66.exp meta-analysis/
67.exp Review Literature/
68.meta-analysis.pt.
69.review.pt.
70.or/66-69
71.letter.pt.
72.comment.pt.
73.editorial.pt.
74.historical-article.pt.
75.or/71-74
76.70 not 75
77.((systematic\$ or quantitativ\$ or methodologic\$) adj (review\$ or overview\$)).ab,ti,ot.
78meta?anal\$.ab,ti,ot.
79.(integrativ\$ research review\$ or research integration\$).ab,ti,ot.
80.quantitativ\$ synthes\$.ab,ti,ot.
81.(pooling\$ or pooled analys\$ or mantel\$ haenszel\$).ab,ti,ot.
82.(peto\$ or der?simonian\$ or fixed effect\$ or random effect\$).ab,ti,ot.
83.or/77-82
84.76 or 83
<b>VI. Impaired glucose tolerance / impaired fasting blood glucose AND Chinese herbal medicine AND RCTs / CCTs:</b>
85.40 and 65
<b>VII. Impaired glucose tolerance / impaired fasting blood glucose AND Chinese herbal medicine AND systematic reviews:</b>
86.40 and 85
<b>VIII. VI OR VII:</b>
87.85 or 86

<b>Electronic searches</b>
88.limit 87 to animal
89.limit 87 to human
90.88 not 89
91.87 not 90

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## 2 Sensitivity analysis on diagnostic criteria

outcome	sensitivity analysis on diagnostic criteria	result
1.1 Normalisation of fasting blood glucose	Exclude WHO 1985 (Yao Z 2001)	RR 2.35 (95% CI 1.71 to 3.23) I <sup>2</sup> = 51%
1.2 Incidence of diabetes	Exclude WHO 1985 (Yao Z 2001; Zhou DY 2003)	RR 0.29 (95% CI 0.15 to 0.56) I <sup>2</sup> = 41%
1.3 Fasting blood glucose	Exclude ADA 1997 (Yang B 2004)	RR -0.64 (95% CI -0.94 to -0.35) I <sup>2</sup> = 90%
	Exclude WHO 1985 (Yao Z 2001; Zeng YH 2006; Zhou DY 2003)	RR -0.50 (95% CI -0.81 to -0.18) I <sup>2</sup> = 92%
	Exclude both WHO 1985 and ADA 1997	RR -0.54 (95% CI -0.93 to -0.16) I <sup>2</sup> = 92%

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#### Differences between protocol and review

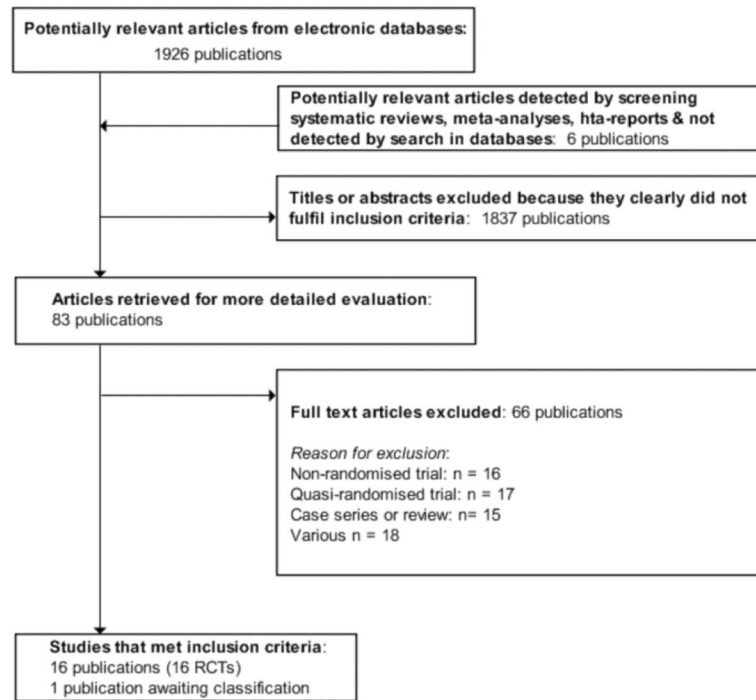
We chose to alter the way in which the assessment of methodological quality was conducted and focus on a risk of bias assessment as a more useful analysis of the individual trials rather than using the tool originally described in the protocol.

Rather than using fixed effect modelling for continuous data as per the protocol the authors determined that a random-effects model was more appropriate for the relatively heterogeneous nature of herbal medicines. It would not be expected that different herbal formulations would produce the same quantity but that the different interventions would produce a distribution in magnitude of effects on any given outcome.

Dichotomous data were expressed as relative risk (RR) ratios rather than odds ratios (OR). This method has been changed since the publication of the protocol to reflect the approach used by other studies in this modality of treatment. It is also a more easily understood statistic in presenting these outcomes.

A high level of statistical heterogeneity was found in the comparison of Chinese herbal medicines with lifestyle modification vs lifestyle modification alone on nearly all outcomes. For this reason subgroup analyses were undertaken. Due to the nature of the trials included the subgroup analyses varied from those set out in the trial protocol.

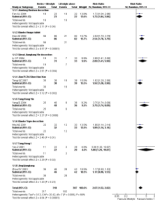
The database CISCOM was not searched as it is no longer active.



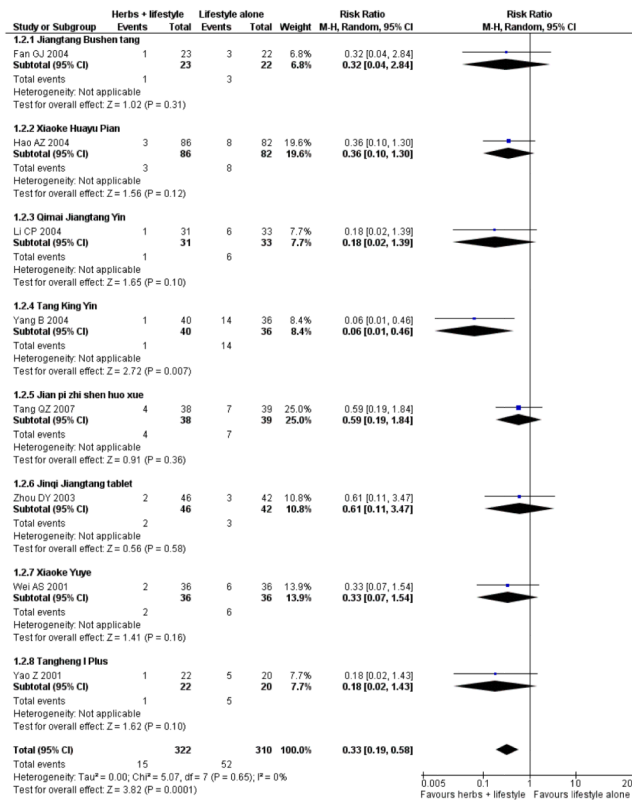
**Figure 1.** PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) flow-chart of study selection

	Adequate sequence generation?	Allocation concealment?	Blinding?	Incomplete outcome data addressed?	Free of selective reporting?	Free of other bias?
Fan GJ 2004	●	?	●	●	?	●
Fang ZH 2007	●	●	●	●	?	●
Hao AZ 2004	?	?	●	●	?	●
Hioki C 2004	●	●	●	●	?	●
Li CP 2004	?	?	●	●	?	●
Lu X 2005	●	?	●	●	?	●
Qu LX 2002	?	?	●	●	?	●
Shi J 2005	●	?	●	●	?	●
Tang QZ 2007	●	?	●	●	?	●
Wang BQ 2008	●	●	●	●	?	●
Wang YX 2005	?	?	●	●	?	●
Wei AS 2001	●	●	●	●	?	●
Yang B 2004	●	●	●	●	?	●
Yao Z 2001	?	?	●	●	?	●
Zeng YH 2006	●	●	●	●	?	●
Zhou DY 2003	●	●	●	●	?	●

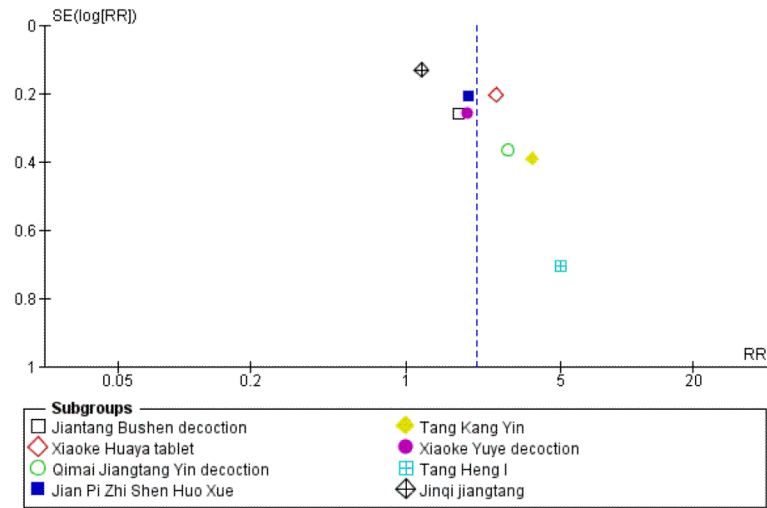
**Figure 2.** Risk of bias summary: review authors' judgements about each risk of bias item for each included study.



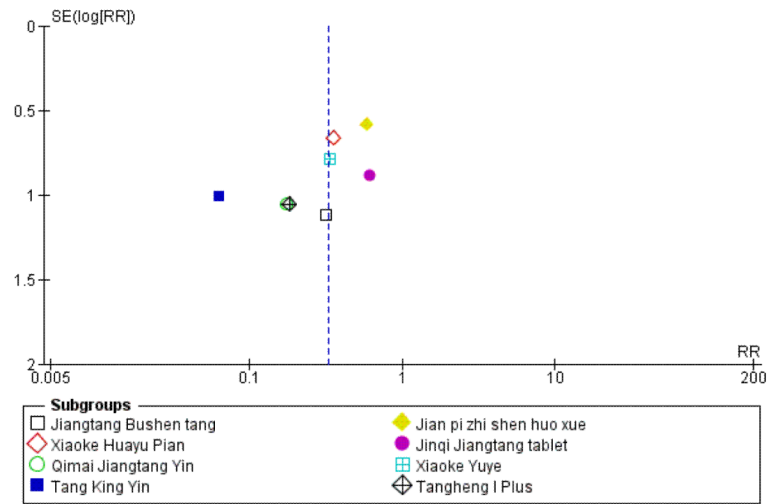
**Figure 3.** Forest plot of outcome 'normalisation of fasting blood glucose at trial completion' (herbal medicines plus lifestyle modification versus lifestyle modification alone)



**Figure 4.** Forest plot of outcome ‘diabetes incidence’ (herbal medicines plus lifestyle modification versus lifestyle modification alone)



**Figure 5.** Funnel plot of outcome 'normalisation of fasting blood glucose at trial completion' (herbal medicines plus lifestyle modification versus lifestyle modification alone)



**Figure 6.** Funnel plot of outcome 'diabetes incidence' (herbal medicines plus lifestyle modification versus lifestyle modification alone)