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Chromium picolinate supplementation for overweight or obese adults (Review)

Tian H, Guo X, Wang X, He Z, Sun R, Ge S, Zhang Z

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Chromium picolinate supplementation for overweight or obese adults.
Cochrane Database of Systematic Reviews 2013, Issue 11. Art. No.: CD010063.
DOI: 10.1002/14651858.CD010063.pub2.

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[Intervention Review]

Chromium picolinate supplementation for overweight or obese adults

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Editorial group: Cochrane Metabolic and Endocrine Disorders Group.
Publication status and date: New, published in Issue 11, 2013.

Citation: Tian H, Guo X, Wang X, He Z, Sun R, Ge S, Zhang Z. Chromium picolinate supplementation for overweight or obese adults. *Cochrane Database of Systematic Reviews* 2013, Issue 11. Art. No.: CD010063. DOI: 10.1002/14651858.CD010063.pub2.

ABSTRACT

Background

Obesity is a global public health threat. Chromium picolinate (CrP) is advocated in the medical literature for the reduction of body weight, and preparations are sold as slimming aids in the USA and Europe, and on the Internet.

Objectives

To assess the effects of CrP supplementation in overweight or obese people.

Search methods

We searched *The Cochrane Library*, MEDLINE, EMBASE, ISI Web of Knowledge, the Chinese Biomedical Literature Database, the China Journal Fulltext Database and the Chinese Scientific Journals Fulltext Database (all databases to December 2012), as well as other sources (including databases of ongoing trials, clinical trials registers and reference lists).

Selection criteria

We included trials if they were randomised controlled trials (RCT) of CrP supplementation in people who were overweight or obese. We excluded studies including children, pregnant women or individuals with serious medical conditions.

Data collection and analysis

Two authors independently screened titles and abstracts for relevance. Screening for inclusion, data extraction and 'Risk of bias' assessment were carried out by one author and checked by a second. We assessed the risk of bias by evaluating the domains selection, performance, attrition, detection and reporting bias. We performed a meta-analysis of included trials using Review Manager 5.

Main results

We evaluated nine RCTs involving a total of 622 participants. The RCTs were conducted in the community setting, with interventions mainly delivered by health professionals, and had a short- to medium-term follow up (up to 24 weeks). Three RCTs compared CrP plus resistance or weight training with placebo plus resistance or weight training, the other RCTs compared CrP alone versus placebo. We focused this review on investigating which dose of CrP would prove most effective versus placebo and therefore assessed the results according to CrP dose. However, in order to find out if CrP works in general, we also analysed the effect of all pooled CrP doses versus placebo on body weight only.

Across all CrP doses investigated (200 µg, 400 µg, 500 µg, 1000 µg) we noted an effect on body weight in favour of CrP of debatable clinical relevance after 12 to 16 weeks of treatment: mean difference (MD) -1.1 kg (95% CI -1.7 to -0.4); P = 0.001; 392 participants; 6 trials; low-quality

evidence (GRADE)). No firm evidence and no dose gradient could be established when comparing different doses of CrP with placebo for various weight loss measures (body weight, body mass index, percentage body fat composition, change in waist circumference).

Only three studies provided information on adverse events (low-quality evidence (GRADE)). There were two serious adverse events and study dropouts in participants taking 1000 µg CrP, and one serious adverse event in an individual taking 400 µg CrP. Two participants receiving placebo discontinued due to adverse events; one event was reported as serious. No study reported on all-cause mortality, morbidity, health-related quality of life or socioeconomic effects.

Authors' conclusions

We found no current, reliable evidence to inform firm decisions about the efficacy and safety of CrP supplements in overweight or obese adults.

PLAIN LANGUAGE SUMMARY

Chromium picolinate supplementation for overweight or obese people

Review question

Are chromium supplements useful for reducing body weight in overweight or obese adults?

Background

Chromium is an essential nutrient (trace element) required for the normal metabolism of carbohydrate, protein and fat (i.e. the chemical reactions involved in breaking down these molecules to a form suitable for absorption by the body). Chromium increases the activity of insulin, and dietary supplementation with chromium has produced improvements in glucose metabolism which may lower blood glucose being important for overweight people with diabetes. It is generally believed that chromium may help to reduce a person's weight by decreasing the amount of fat in the body. Chromium is also said to suppress the appetite and stimulate the production of heat by the body, thus increasing energy expenditure. This may contribute to weight loss. Chromium picolinate is one of several chemical compounds of chromium sold as a nutritional supplement as a potential aid to weight loss.

Study characteristics

We included nine randomised controlled trials which compared the efficacy and safety of 8 to 24 weeks of chromium supplementation and placebo in overweight or obese adults (i.e. with a body mass index between 25 and 29.9 kg/m^2 defining being overweight and a body mass index of $30kg/m^2$ or more defining obesity). A total of 622 participants took part in the studies, 346 participants received chromium picolinate and 276 received placebo. The evidence is current to December 2012.

Key results

When the results obtained from the doses of chromium picolinate investigated (200 µg, 400 µg, 500 µg, 1000 µg) were pooled, study participants lost around 1 kg of body weight more than participants receiving placebo. We were unable to find good evidence that this potential weight loss effect increased with increasing dose of chromium picolinate. Only three of nine studies provided information on adverse events, so we were unable to determine whether chromium picolinate supplements are safe and whether any potential harms may increase with dose. In addition, the length of studies included was rather short (maximum of 24 weeks), so we were unable to determine any long-term effects of supplementation. No study reported whether supplementation was associated with increases in deaths from any cause or illnesses (such as myocardial infarction or stroke), or the health-related quality of life or socioeconomic effects of supplementation.

Quality of the evidence

The overall quality of evidence was considered low and we have inadequate information from which to draw conclusions about the efficacy and safety of chromium picolinate supplementation in overweight or obese adults.

SUMMARY OF FINDINGS

Summary of findings for the main comparison.

Chromium picolinate supplementation for overweight or obese adults

Population: overweight or obese adults

Settings: community volunteers and outpatients

Intervention: chromium picolinate

Comparison: placebo

Outcomes	Relative / absolute effect(s) (95% CI)	No of participants (studies)	Quality of the evidence (GRADE)	Comments
Health-related quality of life	See comment	See comment	See comment	Not investigated
Adverse events Follow-up: 8 weeks to 6 months	2 serious adverse events and study dropouts after 1000 µg chromium picolinate (2/15 participants); 1 serious adverse event after 400 µg chromium picolinate (1/39 participants); 1 serious adverse event (1/18 participants) and 2 study dropouts on placebo (2/58 participants)	189 (3)	⊕⊕⊖⊖ **low**[a]	Only 3/9 studies provided information on adverse events
Death from any cause	See comment	See comment	See comment	Not investigated
Morbidity	See comment	See comment	See comment	Not investigated
Weight loss [kg] Follow-up: 12 to 16 weeks	-1.1 (-1.7 to -0.4)	392 (6)	⊕⊕⊖⊖ **low**[b]	All chromium picolinate doses were pooled
Socioeconomic effects	See comment	See comment	See comment	Not investigated

*The basis for the **assumed risk** (e.g. the median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% CI) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: confidence interval; **RR:** risk ratio

GRADE Working Group grades of evidence
High quality: Further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality: We are very uncertain about the estimate.

[a]Downgraded by two levels owing to high risk of performance and detection bias, and inadequate reporting in most of the included studies
[b]Downgraded by two levels owing to indirectness and conflicting evidence between different studies of various doses of chromium picolinate and duration of treatment

BACKGROUND

Description of the condition

Obesity and overweight are common global health conditions. The prevalence of obesity and overweight has increased considerably in both developing and developed countries. The World Health Organization (WHO) have estimated that, globally in 2005, approximately 1.6 billion adults (aged 15 years or older) were overweight and that at least 400 million adults were obese (WHO 2006). The WHO projects that, by 2015, approximately 2.3 billion adults will be overweight and more than 700 million will be obese. Obesity is defined as the degree of fat storage associated with elevated health risks. However, because fat mass is difficult to measure, the pragmatic definition of obesity is based on body mass index (BMI). The WHO guidelines define a BMI of 18.5 to 24.9 kg/m^2 as normal, 25 to 29.9 kg/m^2 as grade 1 overweight and greater than 30 kg/m^2 as grade 2 overweight (obesity) (WHO 1995).

Obesity is a concern because of its implications for the health of an individual, as it increases the risk of many diseases and health conditions, including coronary heart disease (Rimm 1995; Whitlock 2002), type 2 diabetes (Colditz 1995), hypertension, dyslipidaemia (Denke 1994), sleep apnoea and respiratory problems (Naimark 1960).

Description of the intervention

Chromium is an essential trace element required for the normal metabolism of carbohydrate, protein and fat. Chromium is a cofactor necessary for the activity of insulin, and dietary supplementation with chromium has produced modest improvements in glucose metabolism, insulin sensitivity and body composition in human trials (Drake 2012). Organic chromium is a compound of trivalent chromium and it assists in efficient chromium absorption. Chromium picolinate (CrP) is advocated in the medical literature for the reduction of body weight (Murray 1998; Pizzorno 1999) and preparations are sold as slimming aids in the USA and Europe, and on the Internet.

Adverse effects of the intervention

In a narrative review, most of the reported side effects of CrP supplementation were non-specific and the most frequent complaints were watery stools, weakness, dizziness, headaches, nausea and vomiting (Kleefstra 2006). Overall, chromium was well tolerated. There were no serious adverse events. Also, the number of individuals reporting adverse events in the supplemented groups was not significantly different from that in placebo groups (John 2007; Stephen 2008).

How the intervention might work

It is generally believed that chromium may exert its effects on weight loss by decreasing fat levels in the body and through insulin-sensitising effects. CrP has been suggested to impact on neurotransmitters involved in the regulation of eating behaviour, mood and food cravings (Docherty 2005). Chromium may suppress the appetite and stimulate thermogenesis through sensitisation of insulin-sensitive glucoreceptors in the brain (Wang 2007). Body fat distribution is related to insulin sensitivity; peripheral fat is more insulin-sensitive than central fat found in the chest and abdomen (Kahn 2006).

Why it is important to do this review

Chromium may improve impaired glucose tolerance, reduce elevated blood lipid concentrations, and result in weight loss and improved body composition in some individuals, but results have been equivocal (Volpe 2001). A meta-analysis of 10 double-blind, placebo-controlled trials provided evidence of a relatively small reduction in body weight in overweight and obese individuals receiving CrP (Pittler 2003). However, because of the limited number of trials and participants, the clinical relevance of this effect is debatable and a lack of robustness means that the results have to be interpreted with caution. Since the publication of this meta-analysis, the results of many studies including large numbers of individual shave become available. A systematic review of all available randomised controlled trials (RCTs) is needed, which could help clinicians, individuals and others decide whether chromium is a useful weight loss tool for overweight and obese individuals.

OBJECTIVES

To assess the effects of CrP supplementation in overweight or obese people.

METHODS

Criteria for considering studies for this review

Types of studies

Randomised controlled trials (RCTs).

Types of participants

Adults (aged 18 years and older) defined as overweight or obese at baseline. We excluded studies including children, pregnant women or individuals with serious medical conditions.

Diagnostic criteria

Adults with a BMI between 25 and 29.9 kg/m^2 were considered overweight; those with a BMI of 30 kg/m^2 or higher were considered obese.

Types of interventions

We investigated the following comparisons of the intervention versus controls/comparators where the same letters indicate direct comparisons.

Intervention

- (a) Chromium picolinate (CrP)
- (b) CrP plus another treatment

Comparator

(a1) Placebo

(a2) Different CrP dosage

(b) Placebo plus another treatment

Concomitant treatments (e.g. diet or exercise) had to be identical between intervention and control groups.

Types of outcome measures

Primary outcomes

- Weight loss (e.g. BMI, waist circumference, percentage body fat).
- Adverse events (e.g. gastrointestinal, nervous system, metabolism).
- Health-related quality of life (measured with a validated instrument).

Secondary outcomes

- Death from any cause.
- Morbidity (e.g. cardiovascular outcomes such as myocardial infarction or stroke).
- Blood pressure.
- Lipids (e.g. total cholesterol, HDL-C, LDL-C and triglycerides).
- Fasting blood glucose.
- Socioeconomic effects.

Timing of outcome measurement

- Short-term: one to six weeks.
- Medium-term: more than 6 weeks to 12 weeks.
- Long-term: more than 12 weeks.

Search methods for identification of studies

Electronic searches

We searched the following sources from inception to the specified date to identify trials:

- *The Cochrane Library* (Issue 10, 2012).
- MEDLINE (to December 2012).
- EMBASE (to December 2012).
- ISI Web of Knowledge (to December 2012).
- Chinese Biomedical Literature Database (CBM) (to December 2012).
- China Journal full-text database (to December 2012).
- Chinese Scientific Journals full-text database (to December 2012).

We also searched databases of ongoing trials (www.ClinicalTrials.gov/) and the Current Controlled Trials metaRegister (www.controlled-trials.com/).

For detailed search strategies please see Appendix 1 (searches were not older than six months at the moment the final review draft was checked into the Cochrane Information Management System for editorial approval). We used PubMed's 'My NCBI' (National Center for Biotechnology Information) email alert service for the identification of newly published studies using a basic search strategy (see Appendix 1).

If we detected additional key words of relevance during any of the electronic or other searches we planned to modify the electronic search strategies to incorporate these terms. We included studies published in any language.

Searching other resources

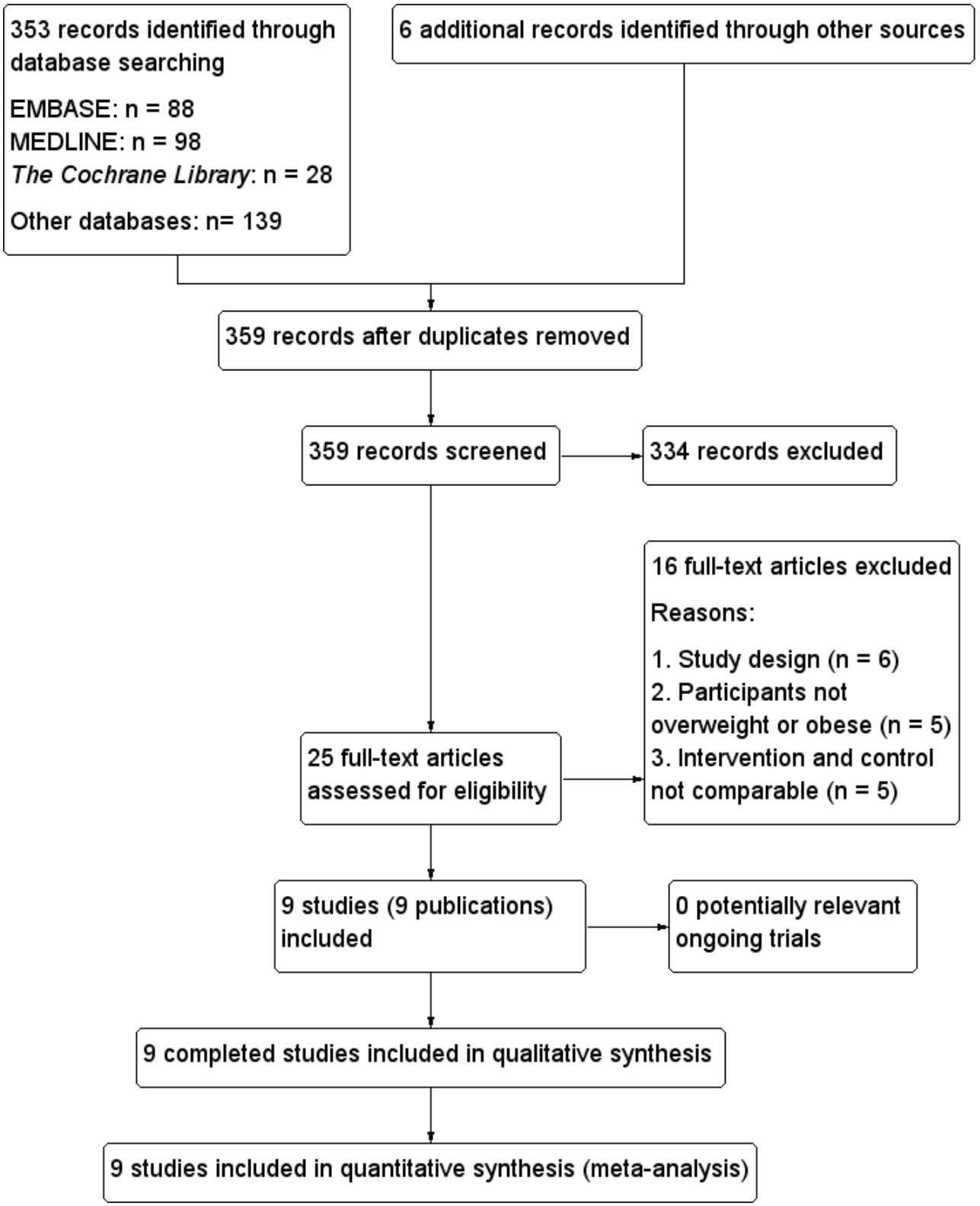
We tried to identify other potentially eligible trials or ancillary publications by searching the reference lists of retrieved included trials, (systematic) reviews, meta-analyses and health-technology assessment reports.

Data collection and analysis

Selection of studies

To identify the studies to be assessed further, two review authors (TH, GX) independently scanned the abstract or title, or both, of every record retrieved. We investigated the full text of all potentially relevant articles. Where there were differences in opinion between authors, these were resolved by a third author (ZZ). If resolution of disagreement was not possible, we intended to add the article to those 'awaiting assessment' and we contacted the trial authors for clarification. We present an adapted PRISMA (preferred reporting items for systematic reviews and meta-analyses) flow-chart showing the process of study selection (Figure 1) (Liberati 2009).

Figure 1. Study flow diagram.



Data extraction and management

For studies that fulfilled the inclusion criteria, two authors (TH, HZ) independently extracted relevant population and intervention characteristics using standard data extraction templates (for details see Table 1 and Appendix 2; Appendix 3; Appendix 4; Appendix 5; Appendix 6; Appendix 7; Appendix 8; Appendix 9); any disagreements were resolved by discussion or, if required, by a third author.

We sent an email request to contact authors of published studies to enquire whether they were willing to answer questions regarding their trials. We published the results of this survey in Appendix 10. Thereafter, we sought relevant missing information on the trial from the original author(s) of the article, if required.

We planned to provide information, including the trial identifier, about potentially relevant ongoing studies in the table 'Characteristics of ongoing studies'. We also intended to include specific data from the protocol of each included study, obtained from databases of ongoing trials or from publications of study designs, or both, in Appendix 6 ('Matrix of study endpoints (protocol/trial documents)').

Dealing with duplicate publications and companion papers

In the case of duplicate publications and companion papers of a primary study, we tried to maximise the yield of information by the simultaneous evaluation of all available data.

Assessment of risk of bias in included studies

Two authors (TH, JL) assessed each trial independently. We resolved possible disagreements by consensus, or by consultation with a third author (ZZ). In cases of disagreement, we consulted the rest of the group and made a judgement based on consensus.

We assessed risk of bias using *The Cochrane Collaboration*'s tool (Higgins 2011; Higgins 2011a) and adopted the following bias criteria.

- Random sequence generation (selection bias).
- Allocation concealment (selection bias).
- Blinding (performance bias and detection bias), separated for blinding of participants and personnel and blinding of outcome assessment.
- Incomplete outcome data (attrition bias).
- Selective reporting (reporting bias) - see Appendix 5.
- Other bias.

We judged 'Risk of bias' criteria as low, high or unclear, and evaluated individual bias items as described in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011). We present a 'Risk of bias' figure and a 'Risk of bias summary' figure.

We assessed the impact of individual bias domains on study results at endpoint and study levels.

For performance bias (blinding of participants and personnel), detection bias (blinding of outcome assessors) and attrition bias (incomplete outcome data) we intended to evaluate risk of bias separately for subjective and objective outcomes.

We defined the following endpoints as subjective outcomes.

- Adverse events.
- Health-related quality of life.

We defined the following outcomes as objective outcomes.

- Weight loss.
- Death from any cause.
- Blood pressure.
- Lipids.
- Fasting blood glucose.
- Socioeconomic effects.

Measures of treatment effect

We expressed dichotomous data as odds ratios (ORs) or risk ratios (RRs) with 95% confidence intervals (CIs). We expressed continuous data as mean differences (MDs) with 95% CIs.

Unit of analysis issues

We took into account the level at which randomisation occurred, such as cross-over trials, cluster-randomised trials and multiple observations for the same outcome.

Dealing with missing data

We tried our best to obtain relevant missing data from authors if feasible, and carefully performed evaluations of important numerical data, such as screened, randomised participants as well as intention-to-treat (ITT), as-treated and per-protocol (PP) populations. We investigated attrition rates (e.g. dropouts, losses to follow-up and withdrawals), and critically appraised issues of missing data and imputation methods (e.g. last observation carried forward (LOCF)).

Assessment of heterogeneity

In the event of substantial clinical, methodological or statistical heterogeneity, our intention was not to report study results as meta-analytically pooled effect estimates.

We identified heterogeneity by visual inspection of the forest plots and by using a standard Chi^2 test with a significance level of $\alpha = 0.1$, in view of the low power of this test. We specifically examined heterogeneity using the I^2 statistic, which quantifies inconsistency across studies to assess the impact of heterogeneity on the meta-analysis (Higgins 2002; Higgins 2003), where an I^2 statistic of 75% or more indicates a considerable level of inconsistency (Higgins 2011).

If heterogeneity was found, we intended to attempt to determine potential reasons for it by examining individual study and subgroup characteristics.

We expected the following characteristics to introduce clinical heterogeneity:

- Sex.
- Age.
- Chromium doses.
- Body mass index (BMI).
- Duration of treatment.

Assessment of reporting biases

We planned to use funnel plots when we included 10 or more studies for a given outcome, in order to assess small study effects. As there could be several explanations for funnel plot asymmetry we planned to interpret results carefully (Sterne 2011).

Data synthesis

We planned, unless there was good evidence for homogeneity across studies, to primarily summarise data at low risk of bias by means of a random-effects model (Wood 2008). We intended to

interpret random-effects meta-analyses giving due consideration to the whole distribution of effects, ideally by presenting a prediction interval (Higgins 2009). A prediction interval specifies a predicted range for the true treatment effect in an individual study (Riley 2011). In addition, we performed statistical analyses according to the statistical guidelines contained in the newest version of the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011).

Subgroup analysis and investigation of heterogeneity

We planned to carry out the following subgroup analyses of our primary outcome parameter(s) (see above) and investigate any interactions:

- Dose (depending on data).
- Duration of intervention (depending on data).

Sensitivity analysis

We planned to perform sensitivity analyses in order to explore the influence of the following factors on effect sizes.

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

We also planned to test the robustness of the results by repeating the analysis using different measures of effect size (RR, OR etc.) and different statistical models (fixed-effect and random-effects models).

RESULTS

Description of studies

For a detailed description of studies, see the 'Characteristics of included studies' and 'Characteristics of excluded studies' sections.

Results of the search

The initial search identified 359 records; from these, 25 full text papers were identified for further examination. We excluded the other studies on the basis of their titles or abstracts because they did not meet the inclusion criteria, were not relevant to the question under study or were a duplicate report (see Figure 1). After screening the full text of the selected publications, nine studies (nine publications) met the inclusion criteria. All studies were published in English. We contacted all authors of included studies and received no reply.

Included studies

A detailed description of the characteristics of included studies is presented elsewhere (see 'Characteristics of included studies' and Appendix 2; Appendix 3; Appendix 4; Appendix 5; Appendix 6; Appendix 7; Appendix 8; Appendix 9).

The following is a succinct overview.

Comparisons

Three studies evaluated CrP plus resistance training (RT) or weight training versus placebo with RT or weight training (Campbell 1999; Joseph 1999; Volpe 2001). The other studies investigated CrP alone versus placebo.

Overview of study populations

A total of 622 participants were included in the nine trials, 346 participants were randomised to CrP and 276 to placebo. A total of 320 (93%) participants receiving CrP and 256 (93%) participants receiving placebo finished the study.The individual total sample sizes ranged from 18 to 154.

Study design

All studies were RCTs. All trials adopted a parallel-group superiority design and all used a placebo control. No trial was multicentred. In terms of blinding, five studies were double-blinded for participants and personnel (Joseph 1999; Kaats 1996; Kaats 1998; Kleefstra 2006; Yazaki 2010). Outcome assessors were blinded in four studies (Joseph 1999; Kaats 1996; Kaats 1998; Kleefstra 2006). Studies were performed between the years 1996 and 2010. The duration of interventions ranged from eight weeks to six months, with a mean study period of 12 weeks. Only two trials had a duration of intervention longer than 24 weeks (Kleefstra 2006; Yazaki 2010); durations in the other trials were 16 weeks (Iqbal 2009), 12 weeks (Campbell 1999; Joseph 1999; Volpe 2001), 10 weeks (Kaats 1996), 13 weeks (Kaats 1998) and 8 weeks (Anton 2008).

Settings

All of the studies were conducted in the USA. Two studies had an outpatient setting (Kleefstra 2006; Iqbal 2009); the other studies included community volunteers.

Participants

The participating population comprised overweight and obese adults only (see Appendix 3 and Appendix 4). Females were recruited more often than males in four trials (Iqbal 2009; Kaats 1996; Kaats 1998; Kleefstra 2006); one trial recruited more male than female participants (Joseph 1999). Two trials included only women (Anton 2008; Volpe 2001) and one trial only men (Campbell 1999). Four trials reported age as a range of values (Campbell 1999; Iqbal 2009; Volpe 2001; Yazaki 2010), whereas five trials reported age as a mean value (Anton 2008; Joseph 1999; Kaats 1996; Kaats 1998; Kleefstra 2006). All trials included participants from economically developed countries. Two trials reported the ethnic proportion of participants (Anton 2008; Iqbal 2009). One trial included participants with diabetes mellitus reporting insulin treatment before the start of the trial (Kleefstra 2006). Across all studies, mean baseline BMI at baseline ranged from 28.4 to 37.8 kg/m^2.

No trial reported participant comorbidities, six trials provided detail about cointerventions in participants (Anton 2008; Campbell 1999; Joseph 1999; Kaats 1998; Volpe 2001; Yazaki 2010) and one trial provided details of the concomitant medications used by participants (Kleefstra 2006). Criteria for entry into the individual studies are outlined in the 'Characteristics of included studies' section.

Diagnosis

Participants were diagnosed as overweight or obese according to BMI criteria. In all the studies, participants had a BMI greater than 25 kg/m^2.

Interventions

No study had a titration period. CrP was applied by the oral route and varied in dosing schedule between one and two times a day. The daily dose of chromium varied between 0.4 mg and 1 mg, with an average daily dose of 0.5 mg. All studies used a matching placebo as the control intervention.

Outcomes

All studies explicitly stated a primary endpoint in the publication; five studies also stated secondary endpoints (Anton 2008; Iqbal 2009; Kleefstra 2006; Volpe 2001; Yazaki 2010).

Reporting of endpoints

BMI was measured in four studies (Iqbal 2009; Joseph 1999; Kleefstra 2006; Yazaki 2010), weight was measured in six studies (Anton 2008; Campbell 1999; Joseph 1999; Kaats 1996; Kaats 1998; Volpe 2001). Body fat (as a percentage) was measured in six studies (Campbell 1999; Joseph 1999; Kaats 1996; Kaats 1998; Volpe 2001; Yazaki 2010). Waist circumference was measured in three studies (Iqbal 2009; Joseph 1999; Volpe 2001). Lipids were measured in four studies (Iqbal 2009; Kleefstra 2006; Volpe 2001; Yazaki 2010). Fasting glucose was measured in four studies (Anton 2008; Iqbal 2009; Volpe 2001; Yazaki 2010). Three studies reported adverse events (Anton 2008; Kleefstra 2006; Yazaki 2010). Two studies assessed food intake (Anton 2008; Volpe 2001), and two studies assessed muscle size, and strength or power development during the trial (Campbell 1999; Volpe 2001).

No studies investigated death from any cause, health-related quality of life or the socioeconomic effects of treatment. For a summary of all outcomes assessed in each study, see Appendix 5.

Excluded studies

Sixteen publications were excluded after careful evaluation of the full-text article (Albarracin 2008; Bunting 1994; Diaz 2008; Docherty 2005; Earle 1989; Geohas 2007; Hoeger 1998; Joyal 2004; Pasman 1997; Pittler 2004; Rabinowitz 1983; Stupar 1999; Trent 1995; Wang 2010; Wilson 1995; Zenk 2007) - see Figure 1.

The reasons for exclusion were: intervention and control not comparable (Albarracin 2008; Diaz 2008; Geohas 2007; Hoeger 1998; Zenk 2007), study design (Bunting 1994; Joyal 2004; Pasman 1997; Pittler 2004; Stupar 1999; Wang 2010) and participants not being obese or overweight (Docherty 2005; Earle 1989; Rabinowitz 1983; Trent 1995; Wilson 1995). For further details, see 'Characteristics of excluded studies'.

Risk of bias in included studies

For details on the risk of bias of included studies see 'Characteristics of included studies'. For an overview of review authors' judgements about each 'Risk of bias' item for individual studies and across all studies, see Figure 2 and Figure 3. We investigated performance bias, detection bias and attrition bias separately for objective and subjective outcome measures. We defined weight loss (e.g. BMI, waist circumference, percentage body fat); blood pressure; lipids (e.g. total cholesterol, HDL-C and LDL-C; triglycerides); and fasting blood glucose as objective outcomes. We defined adverse events (e.g. gastrointestinal, nervous system, metabolism) and health-related quality of life as subjective outcomes.

Figure 2. Risk of bias graph: review authors' judgements about each risk of bias item presented as percentages across all included studies.

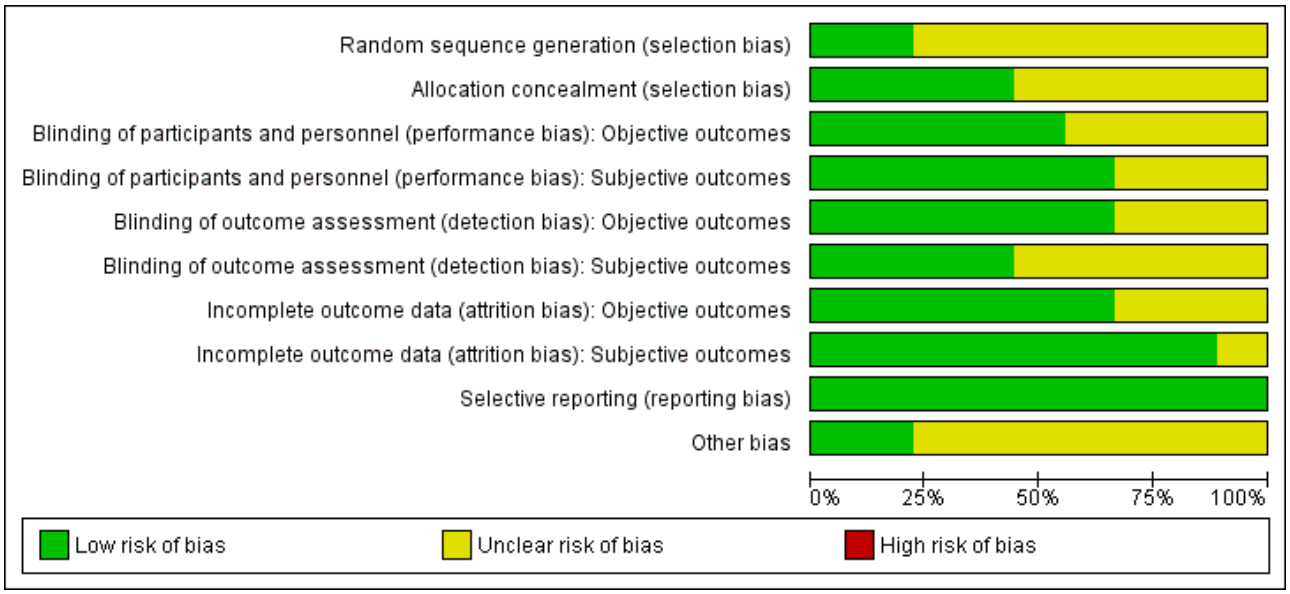
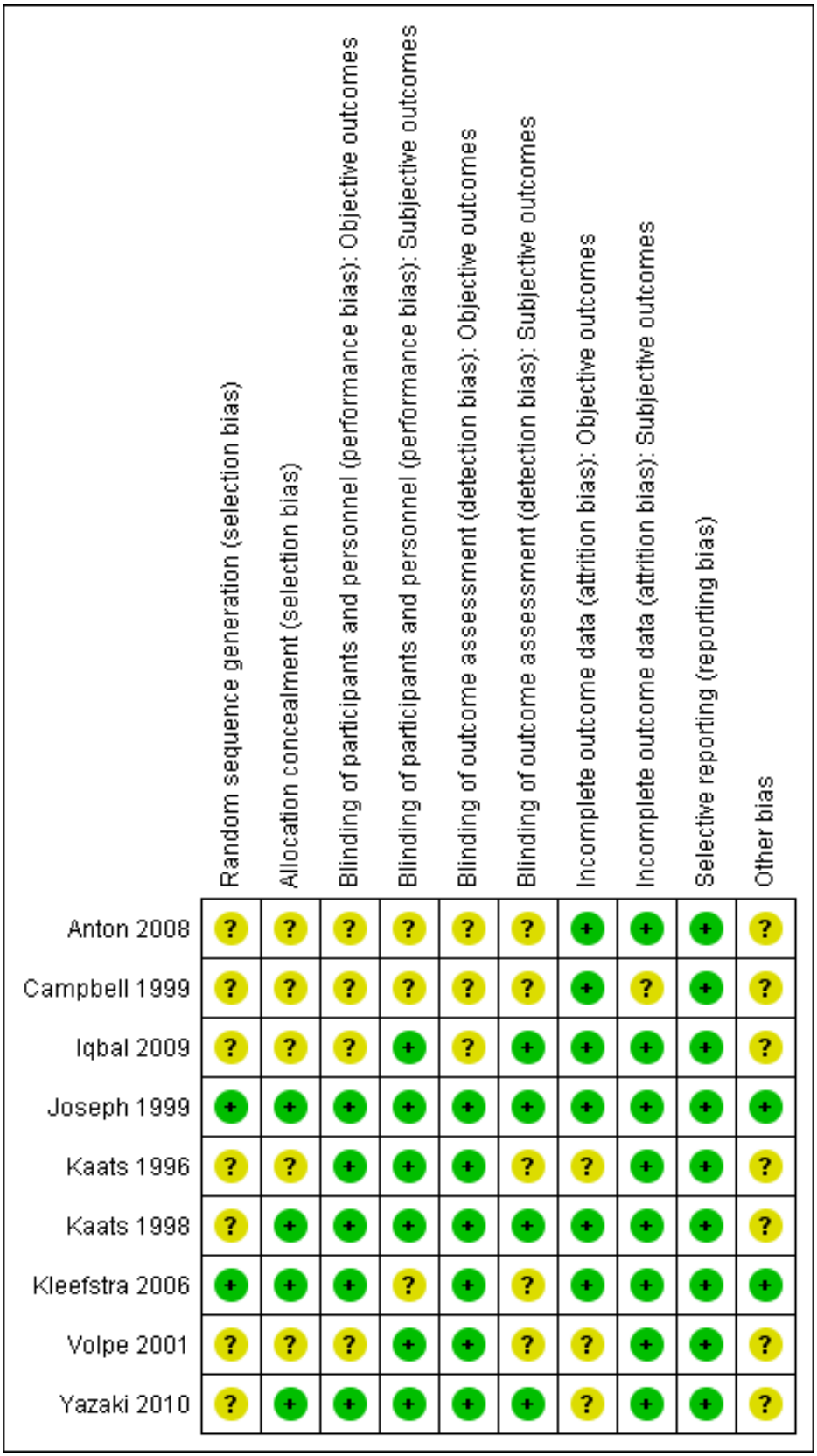


Figure 3. Risk of bias summary: review authors' judgements about each risk of bias item for each included study.



Allocation

Four trials reported that allocation to groups was concealed (Joseph 1999; Kaats 1998; Kleefstra 2006; Yazaki 2010); the remainder did not explain how concealment was carried out, and were thus graded 'unclear' for the domain based on this criterion. Two trials provided details on random sequence generation (Joseph 1999; Kleefstra 2006).

Blinding

Five studies explicitly stated that blinding of participants and personnel was undertaken (Joseph 1999; Kaats 1996; Kaats 1998; Kleefstra 2006; Yazaki 2010). Four studies did not provide sufficient information about blinding procedures (Anton 2008; Campbell 1999; Iqbal 2009; Volpe 2001).

Incomplete outcome data

Numbers of study withdrawals were described in six studies that had losses to follow up (Anton 2008; Campbell 1999; Iqbal 2009; Kleefstra 2006; Volpe 2001; Yazaki 2010). Analysis was reported as ITT in one study (Iqbal 2009). No ITT analysis was undertaken in six trials (Anton 2008; Campbell 1999; Kaats 1996; Kleefstra 2006; Volpe 2001; Yazaki 2010). One study used PP analyses (Kleefstra 2006). Two studies did not report losses to follow up (Joseph 1999; Kaats 1998). Detailed descriptions of participants' withdrawals and reasons underpinning them were not provided in the study by Kaats 1996.

Selective reporting

All trials met a low 'Risk of bias' criteria for selective reporting, as they reported the prespecified primary outcomes and all expected outcomes.

Other potential sources of bias

Seven trials had a commercial source of funding possibly creating a risk of bias (Anton 2008; Campbell 1999; Iqbal 2009; Kaats 1996; Kaats 1998; Volpe 2001; Yazaki 2010).

Effects of interventions

See: **Summary of findings for the main comparison**

Baseline characteristics

For details of baseline characteristics, see Appendix 3 and Appendix 4.

Chromium picolinate (pooled doses versus placebo)

We focused this review on investigating which dose of CrP versus placebo would prove most effective and therefore specified the comparisons ranked according to CrP dose.

However, in order to find out whether CrP works in general, we also analysed the effect on body weight of the pooled CrP doses versus placebo. The MD in weight between CrP and placebo groups after 12 to 16 weeks of treatment was in favour of CrP (MD -1.1 kg (95% CI -1.7 to -0.4); P = 0.001; 392 participants; 6 trials; I^2 = 0%; Analysis 1.1).

Chromium picolinate 200 µg versus placebo

Primary outcomes

Weight change outcomes

After 10 weeks of treatment, the one trial assessing weight loss (Kaats 1996) found no statistically significant differences in weight loss between the CrP 200 µg and placebo groups (MD -0.9 kg (95% CI -2.3 to 0.4); P = 0.18; 88 participants; Analysis 2.1). However, participants in the CrP groups lost a greater percentage of body fat (MD -1.1 kg (95% CI -2.0 to -0.2); P = 0.02; 88 participants; Analysis 2.2) and fat mass (MD -1.4 kg (95% CI -2.7 to -0.2); P = 0. 02; 88 participants; Analysis 2.3) than participants in the control groups.

Health-related quality of life

Not investigated.

Adverse events

Not reported.

Secondary outcomes

Death from any cause

Not reported.

Socioeconomic effects

Not investigated.

Chromium picolinate 400 µg versus placebo

Primary outcomes

Weight change outcomes

Change in body mass index

There was no statistically significant difference between the two groups at six weeks (MD 0.2 kg/m^2 (95% CI -2.4 to 2.8); P = 0.88; 42 participants; 1 trial; Analysis 3.1.1) and 12 weeks (MD 1 kg/m^2 (95% CI -1.3 to 3.3); P = 0.39; 42 participants; 1 trial; Analysis 3.1.2).

Change in weight loss

In a short-term, six-week trial there were no statistically significant differences between the two groups (MD -0.7 kg (95% CI -7.5 to 6.1); P = 0.84; 42 participants; 1 trial; Analysis 3.2.1). Three trials presented weight loss outcomes at around 12 weeks (Kaats 1996; Kaats 1998; Volpe 2001): participants in the CrP groups lost more weight than participants in the control intervention (MD -1.1 kg (95% CI -1.9 to -0.4); P = 0.003; 280 participants; 3 trials; I^2 = 0%; Analysis 3.2.2).

Change in percentage body fat

No statistically significant differences were apparent at six weeks (MD -0.9% (95% CI -2 to 0.2); P = 0.12; 122 participants; 1 trial; Analysis 3.3.1) or at 12 weeks (MD -0.9% (95% CI -2 to 0.2); P = 0.10; 280 participants; 3 trials; I^2 = 56%; Analysis 3.3.2).

Change in fat mass

No statistically significant differences were detected at six weeks (MD -0.4 kg (95% CI -4.6 to 3.8); P = 0.84; 42 participants; one trial; Analysis 3.4.1). At 12 weeks a decrease was observed in favour of CrP (MD -1.6 kg (95% CI -2.3 to -0.9); P < 0.0001; 280 participants; 3 trials; I^2 = 0%; Analysis 3.4.2).

Change in waist circumference

The change in waist circumference was not statistically significantly different between the two groups at six weeks (MD 0.2 cm (95% CI -5.8 to 6.2); P = 0.95; 42 participants; 1 trial; Analysis 3.5.1) or 12 weeks (MD -1.4 cm (95% CI -7.7 to 4.9); P = 0.66; 37 participants; 1 trial; Analysis 3.5.2).

Health-related quality of life outcomes

Not investigated.

Adverse events

One participant receiving CrP and one participant receiving placebo experienced a serious adverse event (see Appendix 8). Two participants receiving placebo left the study due to adverse events (see Appendix 9).

Secondary outcomes

Change in fasting glucose

Fasting glucose was examined in a single study (Volpe 2001). There were no statistically significant differences between the CrP and placebo groups at 12 weeks (MD -2 mg/dL (95% CI -12 to 8); P = 0.70; 37 participants; 1 trial; Analysis 3.6).

Change in total cholesterol

There was no statistically significant difference between the CrP group and placebo group after 12 weeks of treatment (MD -0.5 mg/dL (95% CI -23 to 24); P = 0.97; 37 participants; 1 trial; Analysis 3.7) (Volpe 2001).

Change in triacylglycerol

Change in triacylglycerol levels was not statistically significantly different between the two groups at 12 weeks (MD 2 mg/dL (95% CI -39 to 43); P = 0.92; 37 participants; 1 trial; Analysis 3.8) (Volpe 2001).

Death from any cause

Not reported.

Socioeconomic effects

Not investigated.

Chromium picolinate 500 µg versus placebo

Two studies (Iqbal 2009; Kleefstra 2006) with a combined total of 91 participants included data on the effect of CrP 500 µg versus placebo.

Primary outcomes

Weight change outcomes

Change in body mass index

One study (Kleefstra 2006) found no statically significant differences between the CrP and placebo groups at six months (MD 0.2 kg/m^2 (95% CI -0.45 to 0.9); P = 0.56; 31 participants; Analysis 4.1). Results were similar at 16 weeks (MD -0.8 kg/m^2 (95% CI -2.2 to 0.5); P = 0.23; 62 participants; Analysis 4.2).

Change in waist circumference

The change in waist circumference at 16 weeks was not statistically significantly different between the two groups (MD 0.6 cm (95% CI -1 to 2.3); P = 0.45; 60 participants; 1 trial; Analysis 4.3).

Health-related quality of life outcomes

Not investigated.

Adverse events

Not reported.

Secondary outcomes

Change in fasting glucose

No statistically significant differences were detected at 16 weeks between groups (MD 0.4 mg/dL (95% CI -0.2 to 0.9); P = 0.17; 60 participants; 1 trial; Analysis 4.4).

Change in blood pressure

Change in blood pressure at 16 weeks was not statistically significantly different between the two groups, for either systolic blood pressure (MD 0 mm Hg (95% CI -12 to 12); P = 1.00; 31 participants; 1 trial; Analysis 4.5) or diastolic blood pressure (MD 2 mm Hg (95% CI -5 to 9); P = 0.56; 31 participants; 1 trial; Analysis 4.6).

Change in total cholesterol

Change in total cholesterol was reported in two studies (Iqbal 2009; Kleefstra 2006).There was no statistically significant difference between the intervention and placebo groups (MD -0.1 mg/dL (95% CI -0.5 to 0.4); P = 0.88; 91 participants; 1 trial; I^2 = 0%; Analysis 4.7).

Change in triacylglycerol

There was no statistically significant difference between the CrP and placebo groups (MD -0.3 (95% CI -0.8 to 0.2); P = 0.26; 93 participants; 2 trials; I^2 = 0%; Analysis 4.8).

Death from any cause

Not reported.

Socioeconomic effects

Not investigated.

Chromium picolinate 1000 µg versus placebo

Five studies (Anton 2008; Campbell 1999; Joseph 1999; Kleefstra 2006; Yazaki 2010) with a combined total of 207 participants included data on the effects of CrP 1000 µg versus placebo.

Primary outcomes

Weight change outcomes

Change in weight loss

After 12 weeks of treatment, two trials(Campbell 1999; Joseph 1999) found that there was no statistically significant difference in weight loss between groups (MD -0.7 kg (95% CI -7.3 to 5.9); P = 0.85; 50 participants; 2 trials; I^2 = 0%; Analysis 5.1.1). Also, there was no statistically significant difference in BMI change at 24 weeks (MD 0.11 kg/m^2 (95% CI -0.1 to 0.3); P = 0.25; 90 participants; 2 trials; Analysis 5.2.1) or 12 weeks (MD 0.3 kg/m^2 (95% CI -0.01 to 0.6); P = 0.06; 99 participants; I^2 = 0%; 2 trials; Analysis 5.2.2).

Change in percentage body fat

There was no statistically significant difference with regard to percentage body fat change between intervention and comparator groups at 24 weeks (MD 1% (95% CI -0.4 to 2.6); P = 0.14; 58

participants; 1 trial; Analysis 5.3.1) or 12 weeks (MD 0.9% (95% CI -0.4 to 2.2); P = 0.16; 117 participants; 3 trials; Analysis 5.3.2).

Change in waist circumference

The change in waist circumference at 12 weeks did not differ statistically significantly between the two groups (MD -1.6 cm (95% CI -6.5 to 3.3); P = 0.52; 32 participants; 1 trial; Analysis 5.4).

Health-related quality of life outcomes

Not investigated.

Adverse events

Two studies reported adverse events at six months and found no statistically significant differences between groups (RR 4.03 (95% CI 0.46 to 35.11); P = 0.21; 94 participants; I^2 = 0%; Analysis 5.9.1); one study also found no statistically significant difference at 12 weeks (RR 0.30 (95% CI 0.01 to 7.02); P = 0.46; 40 participants; Analysis 5.9.2).

Two participants receiving CrP reported a serious adverse event (see Appendix 8) and left the study due to an adverse event (see Appendix 9).

Secondary outcomes

Change in fasting glucose

Fasting glucose was examined in two studies (Joseph 1999; Yazaki 2010) that found no statistically significant differences between groups at 12 weeks (MD 0.3 mg/dL (95% CI -1 to 1); P = 0.64; 99 participants; 2 trials; I^2 = 43%; Analysis 5.5.1) or 6 months (MD 0 mg/dL (95% CI -2 to 2); P = 1.0; 58 participants; Analysis 5.5.2).

Change in total cholesterol

There was no statistically significant difference in total cholesterol between the two groups at 24 weeks (MD 0.1 mg/dL (95% CI -0.7 to 0.5); P = 0.81; 90 participants; 2 trials; I^2 = 0%; Analysis 5.6.1) or 12 weeks (MD -0.1 mg/dL (95% CI -0.6 to 0.3); P = 0.57; 67 participants; 1 trial; Analysis 5.6.2).

Change in triacylglycerol

Change in triacylglycerol levels did not differ statistically significantly between the two groups at 6 months (MD -1 mg/dL (95% CI -3 to 1); P = 0.26; 90 participants; 2 trials; Analysis 5.7.1) or 12 weeks (MD -4 mg/dL (95% CI 95% CI -13 to 6); P = 0.45; 67 participants; 1 trial; Analysis 5.7.2).

Change in basal metabolic rate

Change in basal metabolic rate was not statistically significant between groups at 12 weeks (MD -0.4 MJ/day (95% CI 95% CI -1.4 to 0.6); P = 0.44; 18 participants; 1 trial; Analysis 5.8.1).

Change in blood pressure

Change in blood pressure did not differ statistically significantly between the two groups at 12 weeks (systolic blood pressure: MD 2 mm Hg (95% CI -1 to 5); P = 0.18; 67 participants; 1 trial; Analysis 5.10.1; diastolic blood pressure: MD 1 mm Hg (95% CI -2 to 4); P = 0.54; 67 participants; 1 trial; Analysis 5.11.1) or at 24 weeks (systolic blood pressure: MD 3 mm Hg (95% CI 95% -0.4 to 6); P = 0.08; 90 participants; 2 trials; I^2 = 0%; Analysis 5.10.2; diastolic blood pressure: MD 3 mm Hg (95% CI -1 to 7); P = 0.13; 90 participants; 2 trials; I^2 = 29%; Analysis 5.11.2).

Death from any cause

Not reported.

Socioeconomic effects

Not investigated.

Chromium picolinate 200 µg versus chromium picolinate 400 µg

One three-arm study (Kaats 1996) with a combined total of 99 participants investigated the effects of 200 µg CrP versus 400 µg CrP.

Primary outcomes

Weight change outcomes

Change in weight loss

After 10 weeks of treatment, there was no statistically significant difference between the two groups (MD 0.3 kg (95% CI -1 to 1.7); P = 0.65; 99 participants; Analysis 6.1).

Health-related quality of life outcomes

Not investigated.

Adverse events

Not reported.

Change in percentage body fat

No statistically significant difference between groups was apparent at 10 weeks (MD 0.5% (95% CI -0.5 to 1.5); P = 0.32; 99 participants; Analysis 6.2).

Change in fat mass

No statistically significant difference between groups was observed at 10 weeks (MD 0.5 kg (95% CI -0.7 to 1.6); P = 0.46; 99 participants; one trial; Analysis 6.3).

Secondary outcomes

Death from any cause

Not reported.

Socioeconomic effects

Not investigated

Chromium picolinate 500 µg versus chromium picolinate 1000 µg

One three-arm study (Kleefstra 2006) with 60 participants investigated the effects of 500 µg CrP versus 1000 µg CrP.

Primary outcomes

Weight change outcomes

After 24 weeks of treatment, one study found no statistically significant difference in change in BMI between groups (MD 0 kg/m^2 (95% CI -0.8 to 0.8); P = 1.00; 29 participants; Analysis 7.1).

Health-related quality of life outcomes

Not investigated.

Adverse events

Adverse events did not differ significantly between groups at six months (RR 5.00 (95% CI 0.26 to 97); P = 0.29; 34 participants; Analysis 7.6).

Secondary outcomes

Change in total cholesterol

Total cholesterol change at 24 weeks showed no statistically significant difference between groups (MD -0.3 mg/dL (95% CI -0.8 to 0.2); P = 0.21; 29 participants; Analysis 7.2).

Change in triacylglycerol

Triacylglycerol levels showed no statistically significant difference between groups at 24 weeks (MD 0.1 mg/dL (95% CI -0.4 to 0.6); P = 0.71; 29 participants; Analysis 7.3).

Change in blood pressure

There was no statistically significant change in systolic blood pressure (MD -6 mm Hg (95% CI -19 to 7); P = 0.37; 29 participants; one trial; Analysis 7.4) or diastolic blood pressure (MD -4 mm Hg (95% CI -12 to 4); P = 0.33; 29 participants; Analysis 7.5) between groups at 24 weeks.

Death from any cause

Not reported.

Socioeconomic effects

Not investigated.

Subgroup analyses

As there was no statistical heterogeneity across the study results with regard to body weight, we did not analyse the data by subgroups.

Sensitivity analyses

We did not perform sensitivity analyses due to the low number of studies included.

Assessment of reporting bias

Not performed due to the low number of included trials.

DISCUSSION

Summary of main results

Relatively few trials were identified that met the inclusion criteria for this review and most were relatively recent (published in the past 10 years). The trials were heterogeneous in nature, particularly in terms of interventions and outcomes, and sample sizes were small to medium, with 622 participants evaluated in total. The studies were conducted in the community setting, with interventions mainly delivered by health professionals, and provided outcome data at 12 to 16 weeks for weight and at 8 to 24 weeks for adverse events.

The findings of this review demonstrate that CrP supplements across all doses have some effect on weight loss after 12 to 16 weeks of treatment, but firm evidence for a specific dose could not be established.

Furthermore, there was no conclusive evidence for other outcomes of weight loss (e.g. BMI, waist circumference, percentage body fat), adverse events (e.g. gastrointestinal, nervous system, metabolism), blood pressure, lipids (e.g. total cholesterol, HDL-C, LDL-C, triglycerides) or fasting blood glucose.

Overall completeness and applicability of evidence

The duration of follow up of the included studies was a maximum of six months. Long-term efficacy was not evaluated, and only three trials (Anton 2008; Kleefstra 2006; Yazaki 2010) reported data on adverse events in each group. Therefore, the efficacy and safety of CrP could not firmly be established. Whether CrP supplementation should be used in clinical practice for overweight or obese people depends on the evaluation of its effects established by large double-blind RCTs investigating patient-important outcome measures.

Quality of the evidence

There was an unclear risk of selection bias for the majority of the included trials. Five studies explicitly stated that blinding of the participants and personnel was undertaken. Four studies did not provide sufficient information about blinding procedures. Numbers of study withdrawals were described in seven studies that had losses to follow-up. Analysis was reported as ITT in only one study. Two studies did not report losses to follow-up. No study could be clearly associated with selective reporting. Five trials had a commercial source of funding which may create a potential source of bias.

Potential biases in the review process

We used well-defined inclusion and exclusion criteria, independent data extraction by two assessors and the 'Risk of bias' assessment tool (Higgins 2009) in order to minimise potential biases in the review process. We conducted extensive electronic and manual searches to search for relevant articles. As we included only published data in our review, the possibility of publication bias cannot be ruled out. The major limitations of our review were that only a small number of studies met our inclusion criteria and a majority of these were of short-to-medium duration.

Agreements and disagreements with other studies or reviews

To date, one systematic review of 10 studies has been published that examined the effects of CrP in overweight or obese people (Pittler 2004). For body weight, a significant differential effect was found in favour of CrP (MD -1.1 kg (95% CI -1.8 to -0.4 kg); n = 489). This result is comparable to our pooled analysis of all CrP doses versus placebo. However, the clinical relevance of the effect is debatable. A definitive difference between our and Pittler's review is the fact that we included only participants who were overweight or obese at baseline.

AUTHORS' CONCLUSIONS

Implications for practice

We identified nine studies that met our inclusion criteria and most were relatively recent (published in the past 10 years).

The trials were heterogeneous in nature, particularly in terms of interventions and outcomes, and sample sizes were small to medium, with 622 participants evaluated in total. The studies were conducted in the community setting, with interventions mainly delivered by health professionals, and were of short-to-medium follow up (six months or less). We found no current reliable evidence to inform firm decisions about the efficacy or safety of CrP supplements in overweight or obese adults.

Implications for research

An insufficient number of studies were included to enable us to examine the longer-term impact of CrP supplements in overweight or obese people. Only one study had a follow-up of six months. Further double-blind RCTs of CrP are required to provide more conclusive evidence. Trials evaluating patient-important outcomes, such as health-related quality of life and morbidity endpoints, should be large and of reasonable duration. In addition, future prospective studies that carefully investigate the underlying mechanisms of the potential effects of CrP in preventing people from becoming overweight or obese are encouraged.

ACKNOWLEDGEMENTS

The review authors would like to thank the following people for commenting on the review: Lun Li and Jinhui Tian who gave good advice for this review.

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CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Anton 2008

Methods	**Parallel randomised controlled clinical trial**
Participants	**Inclusion criteria:** (1) be a healthy female without any chronic disease, (2) be a carbohydrate craver, determined by self-reported carbohydrate cravings on 2 or more days of the week, (3) be >18 and <50 years of age, (4) have a BMI between 25 and 39.9 kg/m^2 and (5) be a non-smoker. **Exclusion criteria:** participants were excluded if they had a diagnosable eating disorder or were taking any medications or dietary supplements (including CrP) that could influence appetite, hunger or satiety. **Diagnostic criteria:** BMI
Interventions	**Number of study centres:** 1

Anton 2008 *(Continued)*

	Treatment before study: not stated **Titration period:** not stated
Outcomes	**Outcomes reported in abstract of publication:** food intake at breakfast, lunch and dinner was directly measured; hunger levels, fat cravings and body weight
Study details	**Run-in period:** 8 weeks **Study terminated before regular end:** not stated
Publication details	**Language of publication:** English **Non-commercial funding:** this research was supported by the Health and Performance Enhancement Division of the Pennington Biomedical Research Center **Publication status:** peer review journal
Stated aim for study	Quote: "To assess the effect of CrPic in modulating food intake in healthy, overweight, adult women who reported craving carbohydrates"
Notes	Abbreviations: BMI: body mas index; CrP: chromium picolinate

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Participants were randomly assigned to receive either 1000 µg of chromium as CrP or placebo Comment: no detail is given on the methodology
Allocation concealment (selection bias)	Unclear risk	Comment: no detail is given
Blinding of participants and personnel (performance bias) Objective outcomes	Unclear risk	Comment: just mentions ''double-blind"; detailed information not provided
Blinding of participants and personnel (performance bias) Subjective outcomes	Unclear risk	Comment: just mentions ''double-blind"; detailed information not provided
Blinding of outcome assessment (detection bias) Objective outcomes	Unclear risk	Comment: just mentions ''double-blind"; detailed information not provided
Blinding of outcome assessment (detection bias) Subjective outcomes	Unclear risk	Comment: just mentions ''double-blind"; detailed information not provided
Incomplete outcome data (attrition bias) Objective outcomes	Low risk	Quote: "One participant in the placebo group dropped out of the study because of an adverse emotional reaction reportedly due to the study medication." No other adverse events were reported. Comment: nothing was detected

Anton 2008 *(Continued)*

Incomplete outcome data (attrition bias) Subjective outcomes	Low risk	Quote: "One participant in the placebo group dropped out of the study because of an adverse emotional reaction reportedly due to the study medication." No other adverse events were reported. Comment: nothing was detected
Selective reporting (reporting bias)	Low risk	Comment: the study protocol is not available
Other bias	Unclear risk	Comment. the trial had a commercial source of funding possibly creating a risk of bias

Campbell 1999

Methods	**Parallel randomised controlled clinical trial**
Participants	**Inclusion criteria:** men, age range 50 to 75 years; BMI range 27 to 34 kg/m^2; non-diabetic; physically able to safely engage in all aspects of the study protocol; clinically normal cardiac function, blood pressure, liver function and kidney function **Exclusion criteria:** not stated **Diagnostic criteria:** not stated
Interventions	**Number of study centres:** 1 **Treatment before study:** not stated **Titration period:** not stated
Outcomes	**Outcomes reported in abstract of publication:** body weight, each man's baseline maximal strength for each exercise was set as the greater of two one-repetition-maximum values obtained during the first two resistance exercise sessions; urinary creatinine excretion ($P < 0.001$), muscle strength ($P < 0.001$), arm-pull muscle power, knee-extension muscle power, fat-free mass ($P < 0.001$), whole body muscle mass ($P < 0.001$) and vastus lateralis type II fibre area ($P < 0.05$)
Study details	**Run-in period:** 13 weeks **Study terminated before regular end:** no
Publication details	**Language of publication:** English **Commercial / non-commercial / other funding:** supported by National Institute on Aging Grants T32 AG-0048, 1-R29-AG-13409 and RO1-AG-11811, by General Clinical Research Center Grant MO1-RR-10732, and by an independent monetary gift from Nutrition 21 **Publication status:** peer review journal
Stated aim for study	Quote: "To assess the effect of high-dose chromium picolinate supplementation on body composition, including body density, whole body muscle mass and muscle"
Notes	Abbreviations: BMI: body mass index; Cr: creatinine

Risk of bias

Bias	Authors' judgement	Support for judgement

Campbell 1999 *(Continued)*

Random sequence generation (selection bias)	Unclear risk	"Each man was randomly assigned in a double-blind fashion to either a chromium picolinate group or a placebo group" Comment: no detail is given on the methodology
Allocation concealment (selection bias)	Unclear risk	Comment: no details provided
Blinding of participants and personnel (performance bias) Objective outcomes	Unclear risk	Comment: no details provided
Blinding of participants and personnel (performance bias) Subjective outcomes	Unclear risk	Comment: no details provided
Blinding of outcome assessment (detection bias) Objective outcomes	Unclear risk	Comment: no details provided
Blinding of outcome assessment (detection bias) Subjective outcomes	Unclear risk	Comment: no details provided
Incomplete outcome data (attrition bias) Objective outcomes	Low risk	Eighteen of 23 men successfully completed the study protocol. The reasons for the five men withdrawing included the following: 1) a request by a participant's personal physician to avoid aggravation of a chronic hip injury; 2) an irritation of chronic elbow tendonitis, unrelated to resistance exercise; 3) a personal family commitment; 4) a resistance exercise-induced aggravation of an existing knee condition; and 5) a shoulder injury caused by slipping on ice. Comment: The primary outcome data were all reported
Incomplete outcome data (attrition bias) Subjective outcomes	Unclear risk	Comment: no details provided
Selective reporting (reporting bias)	Low risk	Comment: the study protocol is not available Comment: nothing was detected
Other bias	Unclear risk	Comment: the trial had a commercial source of funding possibly creating a risk of bias

Iqbal 2009

Methods	**Parallel randomised controlled clinical trial**
Participants	**Inclusion criteria:** non-diabetic population aged 18 to 75 years with metabolic syndrome and abdominal adiposity; participants' eligibility required waist circumference ≥ 102 cm for men and ≥ 89 cm for women and at least two of the following: systolic blood pressure ≥ 130 mm Hg or diastolic blood pressure ≥ 85 mm Hg or taking ≥ 1 antihypertensive agent; fasting blood glucose ≥ 6.1 mmol/L, but < 7 mmol/L; fasting triglycerides ≥ 1.68, but ≤ 8.96 mmol/L; or HDL-C ≤ 1 mmol/L for males and ≤ 1.29 mmol/L for females

Iqbal 2009 *(Continued)*

	Exclusion criteria: 2-hour plasma glucose value of ≥ 11.1 mmol/L, ASCVD, LDL-C > 4.9 mmol/L, liver transaminases three times the upper limit of normal, renal insufficiency, fibrates or dietary supplements (excluding a multivitamin with < 100 µg chromium) **Diagnostic criteria:** waist circumference, BMI, according to the criteria of the National Cholesterol Education Program Adult Treatment Panel III
Interventions	**Number of study centres:** 1 **Treatment before study:** not reported **Titration period:** not reported
Outcomes	**Outcomes reported in abstract of publication:** insulin sensitivity index derived from a frequently sampled intravenous glucose tolerance test. Prespecified secondary endpoints included changes in other measurements of glucose metabolism, oxidative stress, fasting serum lipids and high sensitivity C-reactive protein
Study details	**Run-in period:** 16 weeks **Study terminated before regular end:** no
Publication details	**Language of publication:** English **Commercial and non-commercial funding:** this work was supported by the following grants: R21D-K067241, K-23 AT-00058, and M01-RR00040 (Translational Research Center [TRC]). Nutrition 21 provided active drug and placebo. Dr Boston is the principal author of the modelling software MinMod Millenium **Publication status:** peer review journal
Stated aim for study	Quote: "To determine the effects of chromium picolinate (CrP) on glucose metabolism in patients with metabolic syndrome"
Notes	Abbreviations: BMI: body mass index

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "conducted a randomised, double-blind, placebo-controlled study of the safety and efficacy of 16 weeks of CrPic therapy and randomised in a 1:1 double-blind fashion to receive either CrPic or matching placebo." Comment: No other details given
Allocation concealment (selection bias)	Unclear risk	Comment: method of concealment is not described
Blinding of participants and personnel (performance bias) Objective outcomes	Unclear risk	Comment: method of blinding is not described
Blinding of participants and personnel (performance bias) Subjective outcomes	Low risk	Comment: no subjective outcomes
Blinding of outcome assessment (detection bias)	Unclear risk	Comment: no details provided

Iqbal 2009 *(Continued)*

Objective outcomes		
Blinding of outcome assessment (detection bias) Subjective outcomes	Low risk	Comment: no subjective outcomes
Incomplete outcome data (attrition bias) Objective outcomes	Low risk	Comment: three participants withdrew for personal reasons
Incomplete outcome data (attrition bias) Subjective outcomes	Low risk	Comment. no subjective outcomes
Selective reporting (reporting bias)	Low risk	Comment: the study protocol is available and there was no selective reporting
Other bias	Unclear risk	Comment: the trial had a commercial source of funding possibly creating a risk of bias

Joseph 1999

Methods	**Parallel randomised controlled clinical trial**
Participants	**Inclusion criteria:** moderately overweight older men and women (aged 54 to 71 years; BMI 26 to 36 kg/m^2) who were not actively involved in any physical training volunteered to participate in this 13-week study **Exclusion criteria:** included populations with any metabolic or cardiac abnormalities. When this study was performed, the 1979 recommendations of the National Diabetes Data Group (NDDG) 21 were used to exclude diabetics at screening. Populations with fasting plasma glucose greater than 7.77 mmol/L or 2-hour OGTT plasma glucose > 11.1 mmol/L and one additional 0 to 120-minute plasma glucose sample > 11.1 mmol/L were deemed diabetic and were excluded from the study **Diagnostic criteria:** according to the criteria of The National Diabetes Data Group (NDDG)
Interventions	**Number of study centres:** 1 **Treatment before study:** not stated **Titration period:** not stated RT consisted of 12 weeks of progressive RT twice weekly with a minimum of days, rest between training sessions
Outcomes	**Outcomes reported in abstract of publication:** weight, body fat, fat mass, fat free mass, basal plasma glucose or insulin levels, glycosylated haemoglobin, triglycerides, total cholesterol, LDL-C, HDL-C
Study details	**Run-in period:** 13 weeks **Study terminated before regular end:** no
Publication details	**Language of publication:** English **Non-commercial funding:** Supported by National Institutes of Health Grants No. 1-R29-AG13409 and RO1-AG11811, National Institute on Aging Grant No. T32-AG00048, an independent monetary gift from Nutrition 21, San Diego, CA, and General Clinical Research Center Grant No. MO1-RR10732.

Joseph 1999 *(Continued)*

	Publication status: peer review journal
Stated aim for study	Quote: "To assess the effect of 12 weeks of resistance training (RT) with or without chromium picolinate (CrP) supplementation on glucose tolerance in moderately overweight older men and women"
Notes	-

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Comment: randomised; computer-generated randomisation list
Allocation concealment (selection bias)	Low risk	Comment: hospital pharmacy
Blinding of participants and personnel (performance bias) Objective outcomes	Low risk	Quote: "... a double-blind fashion, all capsules, including placebo, were furnished by our hospital pharmacy and were indistinguishable from each other. Neither the researchers nor the patients knew into which group they had been randomised"
Blinding of participants and personnel (performance bias) Subjective outcomes	Low risk	Comment: no subjective outcomes
Blinding of outcome assessment (detection bias) Objective outcomes	Low risk	Quote: "All capsules, including placebo, were furnished by our hospital pharmacy and were indistinguishable from each other. Neither the researchers nor the patients knew into which group they had been randomized. Independent pharmacists dispensed either chromium capsules or placebo in numbered containers according to a computer-generated randomization list. No restrictions were used"
Blinding of outcome assessment (detection bias) Subjective outcomes	Low risk	Comment: no subjective outcomes
Incomplete outcome data (attrition bias) Objective outcomes	Low risk	Comment: no data missing
Incomplete outcome data (attrition bias) Subjective outcomes	Low risk	Comment: no subjective outcomes
Selective reporting (reporting bias)	Low risk	Comment: all of the outcomes listed in the methods section were reported as results
Other bias	Low risk	Comment: no other details given to assess whether an important risk of bias exists

Kaats 1996

Methods	**Parallel randomised controlled clinical trial**

Kaats 1996 *(Continued)*

Participants	**Inclusion criteria:** adults consulting their personal physician **Exclusion criteria:** not stated **Diagnostic criteria:** not stated
Interventions	**Number of study centres:** 1 **Treatment before study:** not stated **Titration period:** not stated
Outcomes	**Outcomes reported in abstract of publication:** body composition, body weight, percentage body fat, non-fat mass and body composition improvement
Study details	**Run-in period:** 72 days **Study terminated before regular end:** not stated
Publication details	**Language of publication:** English **Commercial funding:** "Funding for the study was provided by the Living at Goal Weight Center, San Antonio, Texas; Optimal Health Products, San Antonio, Texas; and Nutrition 21, Inc., San Diego, California." **Publication status:** peer review journal
Stated aim for study	Quote: "To examine the effect of chromium picolinate (CrP) on body composition"
Notes	-

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Comment: randomised, but method not stated
Allocation concealment (selection bias)	Unclear risk	Comment: not reported
Blinding of participants and personnel (performance bias) Objective outcomes	Low risk	Comment: none of the investigators, research technicians dispensing the product or populations knew which code corresponded to the amount of CrP in the canister
Blinding of participants and personnel (performance bias) Subjective outcomes	Low risk	Comment: no subjective outcomes
Blinding of outcome assessment (detection bias) Objective outcomes	Low risk	Comment: not details provided
Blinding of outcome assessment (detection bias) Subjective outcomes	Unclear risk	Comment: no subjective outcomes

Kaats 1996 *(Continued)*

Incomplete outcome data (attrition bias) Objective outcomes	Unclear risk	Quote: "Some concerns may be raised about the relatively high dropout rate in our study - 69 of 219 (31.5%). A comparison of their initial body composition scores revealed no significant difference between the three groups nor between any of the three groups of patients who completed or failed to complete the protocol" Comment: unclear influence of attrition rate
Incomplete outcome data (attrition bias) Subjective outcomes	Low risk	Comment. no subjective outcome
Selective reporting (reporting bias)	Low risk	Comment: all of the outcomes listed in the methods section were reported as results
Other bias	Unclear risk	Comment: the trial had a commercial source of funding possibly creating a risk of bias

Kaats 1998

Methods	**Parallel randomised controlled clinical trial**
Participants	**Inclusion criteria:** adults consulting their personal physician **Exclusion criteria:** not stated **Diagnostic criteria:** not stated
Interventions	**Number of study centres:** 1 **Treatment before study:** not stated **Titration period:** not stated
Outcomes	**Outcomes reported in abstract of publication:** body weight, percentage body fat, fat mass and fat-free mass
Study details	**Run-in period:** 90 days **Study terminated before regular end:** no
Publication details	**Language of publication:** English **Commercial funding:** this study has been supported financially by Nutrition 21, Inc., San Diego, California **Publication status:** peer review journal
Stated aim for study	Quote: "To determining whether the body composition changes observed in the initial study could be replicated in this study"
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement

Kaats 1998 *(Continued)*

Random sequence generation (selection bias)	Unclear risk	Comment: randomised, but method not stated
Allocation concealment (selection bias)	Low risk	Comment: independent local pharmacist
Blinding of participants and personnel (performance bias) Objective outcomes	Low risk	Quote: "None of the investigators, research technicians dispensing the product, or participants knew which participant's number corresponded to the placebo or active product. An independent local pharmacist acted as trustee for the study and randomly assigned participant's numbers to bottles that had been prelabeled with either an “X” or “Y” to correspond with either active product or placebo"
Blinding of participants and personnel (performance bias) Subjective outcomes	Low risk	Comment: no subjective outcomes
Blinding of outcome assessment (detection bias) Objective outcomes	Low risk	Comment: not details provided
Blinding of outcome assessment (detection bias) Subjective outcomes	Low risk	Comment: no subjective outcomes
Incomplete outcome data (attrition bias) Objective outcomes	Low risk	Comment: no dropouts
Incomplete outcome data (attrition bias) Subjective outcomes	Low risk	Comment: no subjective outcomes
Selective reporting (reporting bias)	Low risk	Comment: all of the outcomes listed in the methods section were reported as results
Other bias	Unclear risk	Comment: the trial had a commercial source of funding possibly creating a risk of bias

Kleefstra 2006

Methods	**Parallel randomised controlled clinical trial**
Participants	**Inclusion criteria:** Individuals with type 2 diabetes, glycosylated haemoglobin (A1c) ≥ 8%, daily use of insulin ≥ 50 units, creatinine ≤ 150 µmol/L for men and ≤ 120 µmol/L for women, creatinine clearance ≥ 50 ml/min, alanine aminotransferase ≤ 90 units/L and age < 75 years **Exclusion criteria:** included pregnancy, or intention to become pregnant during the study, and a history of liver or renal disease **Diagnostic criteria:** BMI, A1c
Interventions	**Number of study centres:** 1 **Treatment before study:** not stated

Kleefstra 2006 *(Continued)*

	Titration period: not stated
Outcomes	**Outcomes reported in abstract of publication:** A1c, BMI, blood pressure, lipid profile and insulin requirement.
Study details	**Run-in period:** 6 months **Study terminated before regular end:** no
Publication details	**Language of publication:** English **Commercial / non-commercial / other funding:** not stated **Publication status:** peer review journal
Stated aim for study	Quote: "To determine the effect of chromium treatment on glycemic control in a western population of insulin-dependent patients with type 2 diabetes".
Notes	Abbreviations: BMI: body mass index

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Comment: computer-generated randomisation list
Allocation concealment (selection bias)	Low risk	Comment: independent pharmacists dispensed either chromium capsules or placebo in numbered containers according to a computer-generated randomisation list.
Blinding of participants and personnel (performance bias) Objective outcomes	Low risk	Quote: "All capsules, including placebo, were furnished by our hospital pharmacy and were indistinguishable from each other. Neither the researchers nor the patients knew into which group they had been randomised"
Blinding of participants and personnel (performance bias) Subjective outcomes	Unclear risk	Quote: "All capsules, including placebo, were furnished by our hospital pharmacy and were indistinguishable from each other. Neither the researchers nor the patients knew into which group they had been randomised"
Blinding of outcome assessment (detection bias) Objective outcomes	Low risk	Comment: no details provided
Blinding of outcome assessment (detection bias) Subjective outcomes	Unclear risk	Comment: no details provided
Incomplete outcome data (attrition bias) Objective outcomes	Low risk	Comment: no attrition bias was detected
Incomplete outcome data (attrition bias) Subjective outcomes	Low risk	Quote: "Of 53 patients randomised, 1 patient was lost to follow-up, and all attempts to locate this participant were in vain (telephone contact, letters, and visits). Six other individuals, one in the placebo group, three in the 500 µg group, and two in the 1,000 µg group, discontinued the study for the following reasons: one patient required a blood transfusion and was hospitalised, and three other patients were hospitalised due to percutaneous transluminal

Kleefstra 2006 *(Continued)*

		coronary angioplasty, chronic obstructive pulmonary disease, and glycemic dysregulation.Two patients discontinued the study due to possible adverse effects. Unfortunately, intention-to-treat analyses were not possible because for five of six excluded patients follow-up data were lacking. However, the main conclusions of the per-protocol analyses would likely not have been different in an intention-to-treat analyses"
Selective reporting (reporting bias)	Low risk	Comment: all of the outcomes listed in the methods section were reported as results
Other bias	Low risk	Comment: no other details given to assess whether an important risk of bias exists

Volpe 2001

Methods	**Parallel randomised controlled clinical trial**
Participants	**Inclusion criteria:** 44 female participants, with a BMI between 27 and 41 kg/m^2, between 27 and 51 years of age, premenopausal, sedentary, not taking any dietary supplements, not taking any vitamin or mineral supplements containing chromium, not on a weight-loss programme, not taking any weight loss supplements, non-smoking and with no history of chronic diseases or recent acute illness. Participants were asked not to alter their dietary habits during the course of the study **Exclusion criteria:** not stated **Diagnostic criteria:** BMI
Interventions	**Number of study centres:** 1 **Treatment before study:** not stated **Titration period:** not stated
Outcomes	**Outcomes reported in abstract of publication:** body composition, resting metabolic rate, fasting plasma glucose, serum insulin, plasma glucagon, serum C-peptide and serum lipid concentrations or iron and zinc indices, serum total cholesterol concentration, exercise training
Study details	**Run-in period:** 12 weeks **Study terminated before regular end:** no
Publication details	**Language of publication:** English **Commercial and non-commercial funding:** "the authors would like to thank Nutrition 21 (San Diego, CA) for funding this project. This research is based upon work partially supported by the Cooperative State Research Extension, Education Service, U.S. Department of Agriculture Experiment Station, under Project No. MAS00757 Manuscript No. 3280" **Publication status:** peer review journal
Stated aim for study	Quote: "To investigate the effect of chromium picolinate (CP) supplementation on body composition, resting metabolic rate (RMR), selected biochemical parameters and iron and zinc status in moderately obese women participating in a 12-week exercise program"
Notes	Abbreviations: BMI: body mass index
Risk of bias	

Volpe 2001 *(Continued)*

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Forty-four free-living females were assigned, in a stratified randomised manner based on their BMI, to one of two groups" Comment: no other details given
Allocation concealment (selection bias)	Unclear risk	Comment: not reported
Blinding of participants and personnel (performance bias) Objective outcomes	Unclear risk	Quote from publication: "double-blind" Comment: no other details given
Blinding of participants and personnel (performance bias) Subjective outcomes	Low risk	Comment: no subjective outcomes
Blinding of outcome assessment (detection bias) Objective outcomes	Low risk	Comment: no details provided
Blinding of outcome assessment (detection bias) Subjective outcomes	Unclear risk	Comment: no details provided
Incomplete outcome data (attrition bias) Objective outcomes	Unclear risk	Quote: "Thirty-seven of the initial 44 people (84%) completed this study. Sixteen people reported forgetting to take their capsules and 13 people missed exercise training; however, no people reported forgetting to take the capsules more than five days (average 3 days) during the study period. Furthermore, none of these people missed exercise training more than four times (average 3) during the entire study. Two people did have minor problems with their knees or ankles, so they were unable to perform all of the specified weight training exercises (e.g. leg extension and calf raises)"
Incomplete outcome data (attrition bias) Subjective outcomes	Low risk	Comment: no subjective outcome
Selective reporting (reporting bias)	Low risk	Comment: all of the outcomes listed in the methods section were reported as results
Other bias	Unclear risk	Comment: the trial had a commercial source of funding possibly creating a risk of bias

Yazaki 2010

Methods	**Parallel randomised controlled clinical trial**
Participants	**Inclusion criteria:** overweight (BMI > 25 kg/m^2) non-smoking adults aged 25 to 75 years with abdominal adiposity (waist circumference > 80 cm in females and > 100 cm in males) **Exclusion criteria:** contraindication to abdominal computed tomography scans (weight > 375 pounds, claustrophobia, unstable vital signs, or radiation procedure in past six months), diagnosed diabetes, di-

Yazaki 2010 *(Continued)*

	agnosed eating disorder, uncontrolled hypertension, emphysema, intestinal or stomach disease, kidney disease, substance abuse, pregnancy or intention to become pregnant during the study **Diagnostic criteria:** BMI, waist circumference measures
Interventions	**Number of study centres:** 1 **Treatment before study:** not stated **Titration period:** not stated
Outcomes	**Outcomes reported in abstract of publication:** weight, height, blood pressure, percentage body fat, serum and urinary biomarkers
Study details	**Run-in period:** 24 weeks **Study terminated before regular end:** no
Publication details	**Language of publication:** English **Commercial funding:** supported by Nutrition 21, Inc **Publication status:** peer review journal
Stated aim for study	Quote: "Assess the effects of chromium picolinate supplementation, alone and combined with nutritional education, on weight loss in healthy overweight adults"
Notes	Abbreviations: BMI: body mass index

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "People were enrolled and randomized using balanced allocation within gender" Comment: no details provided
Allocation concealment (selection bias)	Low risk	Quote: "People and study personnel were blinded to the intervention. Chromium and placebo were prepackaged and shipped from the manufacturer to the study site. Bottles were labelled and coded by an unblinded individual unaffiliated with the study. Investigators thus only knew the treatment assignment (group A or B) of the people without knowledge of whether these contained chromium or placebo"
Blinding of participants and personnel (performance bias) Objective outcomes	Low risk	Quote: "People and study personnel were blinded to the intervention. Chromium and placebo were prepackaged and shipped from the manufacturer to the study site. Bottles were labelled and coded by an unblinded individual unaffiliated with the study. Investigators thus only knew the treatment assignment (group A or B) of the people without knowledge of whether these contained chromium or placebo"
Blinding of participants and personnel (performance bias) Subjective outcomes	Low risk	Comment: no subjective outcomes
Blinding of outcome assessment (detection bias) Objective outcomes	Low risk	Comment: no details provided

Yazaki 2010 *(Continued)*

Blinding of outcome assessment (detection bias) Subjective outcomes	Low risk	Comment: no subjective outcomes
Incomplete outcome data (attrition bias) Objective outcomes	Unclear risk	Comment: insufficient reporting of attrition/exclusions to permit judgement
Incomplete outcome data (attrition bias) Subjective outcomes	Low risk	Comment: no subjective outcomes
Selective reporting (reporting bias)	Low risk	Comment: the study protocol is not available
Other bias	Unclear risk	Comment: the trial had a commercial source of funding possibly creating a risk of bias

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
Albarracin 2008	Combination therapy of chromium picolinate and biotin versus placebo
Bunting 1994	Animal study
Diaz 2008	Combination therapy of chromium picolinate and conjugated linoleic acid in tonalin oil versus placebo and canola oil
Docherty 2005	Participants not obese or overweight
Earle 1989	Participants not obese or overweight
Geohas 2007	Combination therapy of chromium picolinate and biotin versus placebo
Hoeger 1998	Combination therapy of chromium picolinate, inulin, capsicum, L-phenylalanine and other lipotropic nutrients versus placebo
Joyal 2004	Not a randomised trial
Pasman 1997	Not a randomised trial
Pittler 2004	Not a randomised trial
Rabinowitz 1983	Participants not obese or overweight
Stupar 1999	Not a randomised trial
Trent 1995	Participants not obese or overweight
Wang 2010	Not a randomised trial
Wilson 1995	Participants not obese or overweight

Study	Reason for exclusion
Zenk 2007	Combination therapy investigating 3-acetyl-7-oxo-dehydroepiandrosterone alone (7-Keto) and in combination with calcium citrate, green tea extract, ascorbic acid, chromium nicotinate and cholecalciferol (HUM5007) versus placebo

DATA AND ANALYSES

Comparison 1. Chromium (all dosages) versus placebo

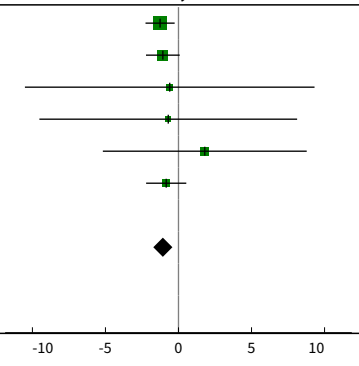
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Change in weight at 12-16 weeks	6	392	Mean Difference (IV, Random, 95% CI)	-1.07 [-1.73, -0.42]

Analysis 1.1. Comparison 1 Chromium (all dosages) versus placebo, Outcome 1 Change in weight at 12-16 weeks.

Study or subgroup	Chromium N	Chromium Mean(SD)	Placebo N	Placebo Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
Kaats 1996	66	-1.4 (2.9)	55	-0.1 (2.7)		43.18%	-1.26[-2.26,-0.26]
Kaats 1998	62	-2.9 (3.5)	60	-1.8 (3)		32.24%	-1.07[-2.22,0.08]
Campbell 1999	9	-0.2 (12.5)	9	0.4 (8.6)		0.44%	-0.6[-10.51,9.31]
Joseph 1999	17	0 (15.2)	15	0.7 (10)		0.55%	-0.7[-9.52,8.12]
Volpe 2001	20	0 (10.9)	17	-1.8 (10.7)		0.88%	1.8[-5.18,8.78]
Iqbal 2009	31	-0.1 (2.5)	31	0.7 (3)		22.71%	-0.84[-2.21,0.53]
Total * **	**205**		**187**			**100%**	**-1.07[-1.73,-0.42]**

Heterogeneity: Tau^2=0; Chi^2=0.91, df=5(P=0.97); I^2=0%

Test for overall effect: Z=3.2(P=0)

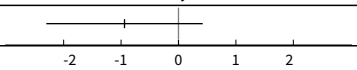


Comparison 2. Chromium (200 µg) versus placebo

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Change in weight at 10 weeks	1		Mean Difference (IV, Random, 95% CI)	Subtotals only
2 Change in percent body fat at 10 weeks [kg]	1		Mean Difference (IV, Random, 95% CI)	Subtotals only
3 Change in fat mass at 10 weeks [kg]	1		Mean Difference (IV, Random, 95% CI)	Subtotals only

Analysis 2.1. Comparison 2 Chromium (200 µg) versus placebo, Outcome 1 Change in weight at 10 weeks.

Study or subgroup	Chromium N	Chromium Mean(SD)	Placebo N	Placebo Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
Kaats 1996	33	-1.1 (3.4)	55	-0.1 (2.7)		0%	-0.94[-2.3,0.42]



Analysis 2.2. Comparison 2 Chromium (200 µg) versus placebo, Outcome 2 Change in percent body fat at 10 weeks [kg].

Study or subgroup	Chromium N	Chromium Mean(SD)	Placebo N	Placebo Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
Kaats 1996	33	-1.4 (2.2)	55	-0.3 (2.1)		0%	-1.1[-2.03,-0.17]

Analysis 2.3. Comparison 2 Chromium (200 µg) versus placebo, Outcome 3 Change in fat mass at 10 weeks [kg].

Study or subgroup	Chromium N	Chromium Mean(SD)	Placebo N	Placebo Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
Kaats 1996	33	-1.6 (2.9)	55	-0.2 (2.6)		0%	-1.44[-2.65,-0.23]

Comparison 3. Chromium (400 µg) versus placebo

Outcome or sub-group title	No. of studies	No. of partici-pants	Statistical method	Effect size
1 Change in body mass index	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
1.1 6 weeks	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
1.2 12 weeks	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
2 Change in weight	3		Mean Difference (IV, Random, 95% CI)	Subtotals only
2.1 6 weeks	1	42	Mean Difference (IV, Random, 95% CI)	-0.7 [-7.51, 6.11]
2.2 12 weeks	3	280	Mean Difference (IV, Random, 95% CI)	-1.14 [-1.89, -0.39]
3 Percent body fat change	3		Mean Difference (IV, Random, 95% CI)	Subtotals only
3.1 Short-term	1	122	Mean Difference (IV, Random, 95% CI)	-0.87 [-1.95, 0.21]
3.2 Medium-term	3	280	Mean Difference (IV, Random, 95% CI)	-0.90 [-1.98, 0.18]
4 Change in fat mass	3		Mean Difference (IV, Random, 95% CI)	Subtotals only

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
4.1 6 weeks	1	42	Mean Difference (IV, Random, 95% CI)	-0.43 [-4.61, 3.75]
4.2 12 weeks	3	280	Mean Difference (IV, Random, 95% CI)	-1.57 [-2.27, -0.87]
5 Change in waist circumference	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
5.1 6 weeks	1	42	Mean Difference (IV, Fixed, 95% CI)	0.20 [-5.81, 6.21]
5.2 12 weeks	1	37	Mean Difference (IV, Fixed, 95% CI)	-1.40 [-7.72, 4.92]
6 Change in fasting glucose	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
6.1 12 weeks	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
7 Change in total cholesterol	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
7.1 12 weeks	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
8 Change in triacylglycerol	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
8.1 12 weeks	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]

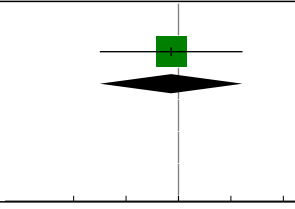
Analysis 3.1. Comparison 3 Chromium (400 µg) versus placebo, Outcome 1 Change in body mass index.

Study or subgroup	Chromium N	Chromium Mean(SD)	Placebo N	Placebo Mean(SD)	Mean Difference Fixed, 95% CI	Mean Difference Fixed, 95% CI
3.1.1 6 weeks						
Volpe 2001	21	0.1 (4.5)	21	-0.1 (4.2)		0.2[-2.43,2.83]
3.1.2 12 weeks						
Volpe 2001	21	0.2 (3.6)	21	-0.8 (4)		1[-1.3,3.3]

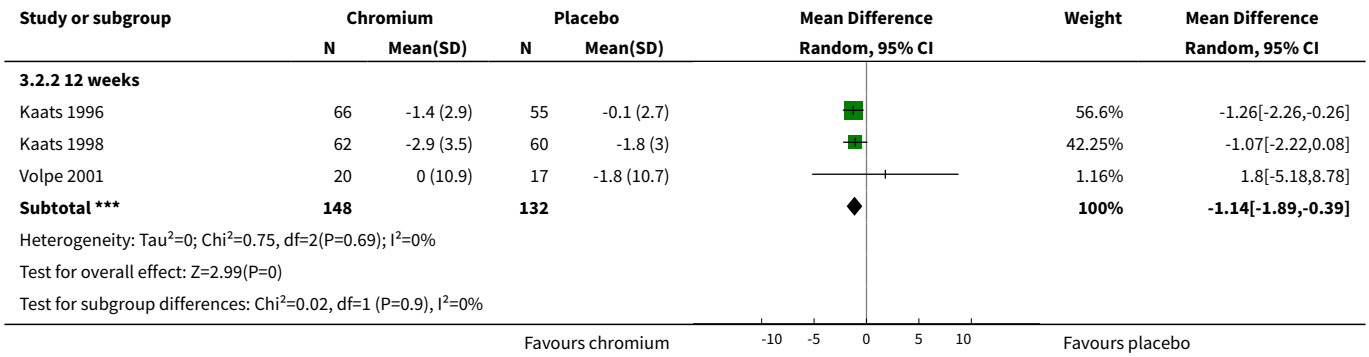
Favours chromium — Favours placebo

Analysis 3.2. Comparison 3 Chromium (400 µg) versus placebo, Outcome 2 Change in weight.

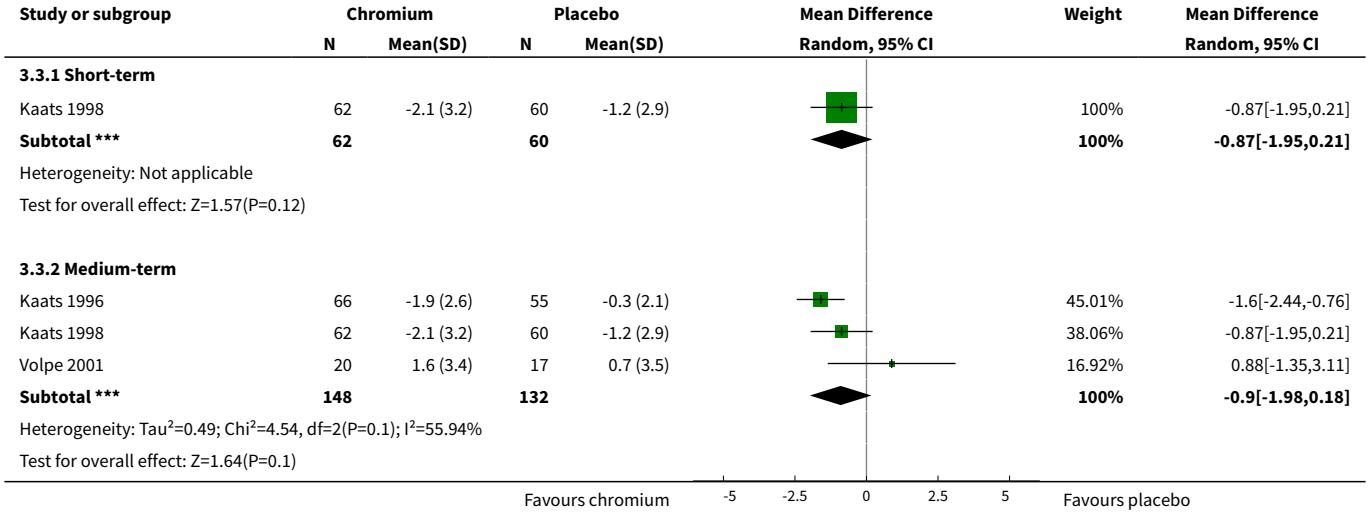
Study or subgroup	Chromium N	Chromium Mean(SD)	Placebo N	Placebo Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
3.2.1 6 weeks							
Volpe 2001	21	-0.1 (11)	21	0.6 (11.5)		100%	-0.7[-7.51,6.11]
Subtotal ***	**21**		**21**			**100%**	**-0.7[-7.51,6.11]**
Heterogeneity: Not applicable							
Test for overall effect: Z=0.2(P=0.84)							



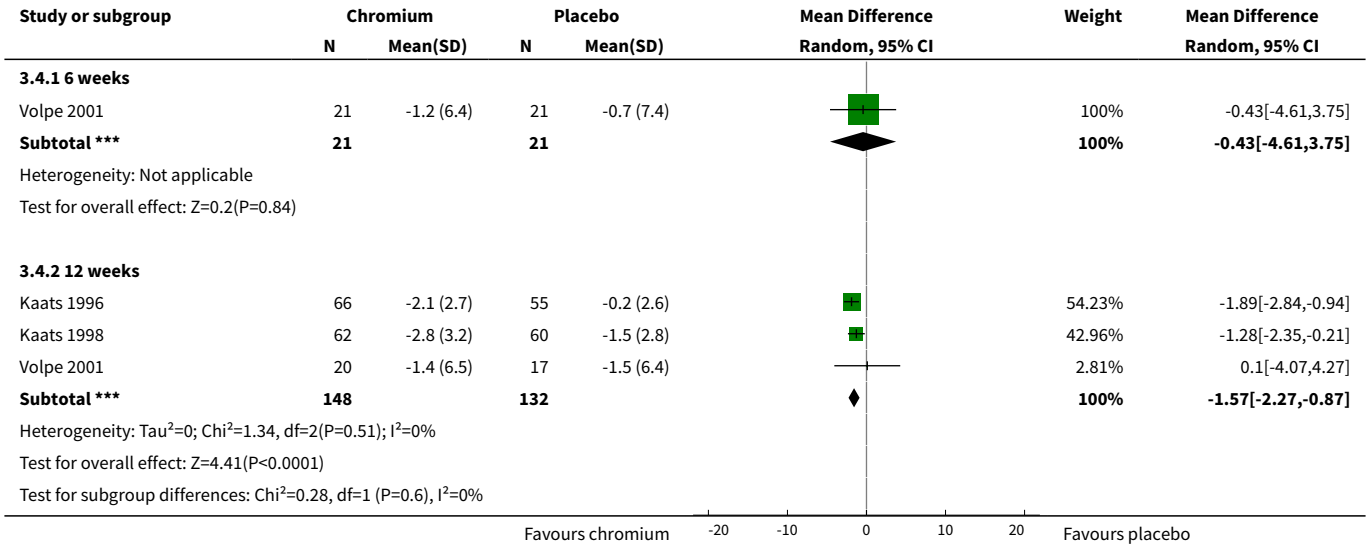
Favours chromium — Favours placebo



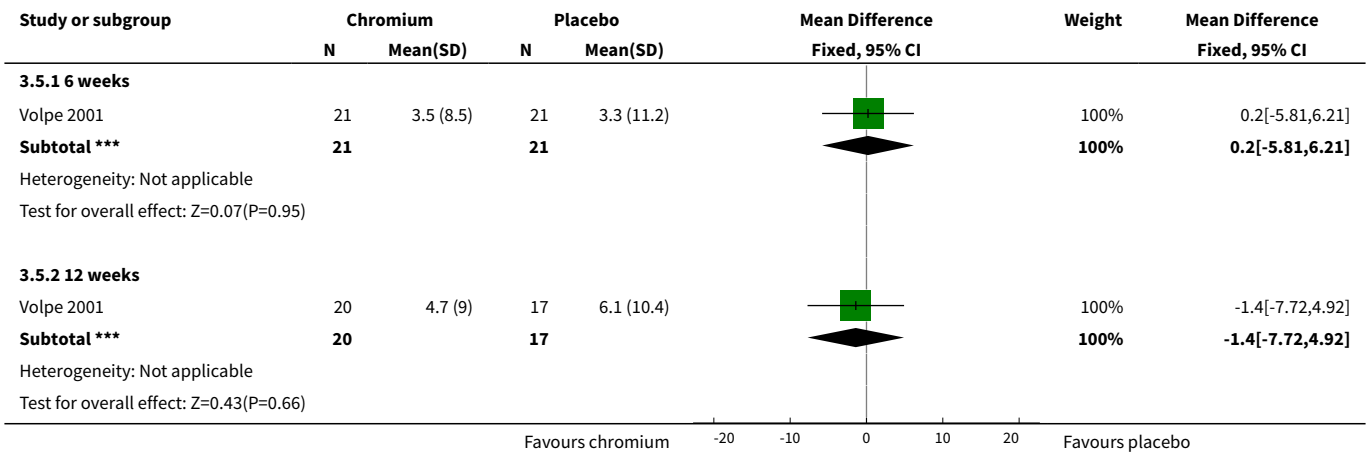
Analysis 3.3. Comparison 3 Chromium (400 µg) versus placebo, Outcome 3 Percent body fat change.



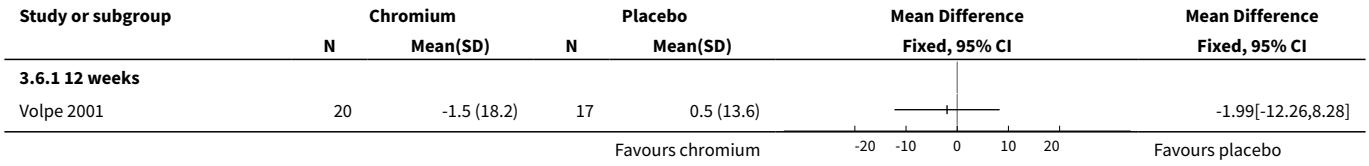
Analysis 3.4. Comparison 3 Chromium (400 µg) versus placebo, Outcome 4 Change in fat mass.



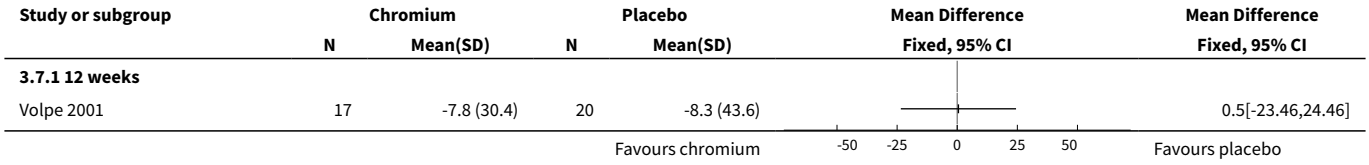
Analysis 3.5. Comparison 3 Chromium (400 µg) versus placebo, Outcome 5 Change in waist circumference.



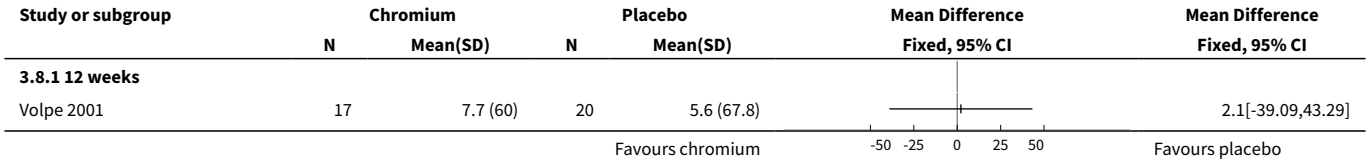
Analysis 3.6. Comparison 3 Chromium (400 µg) versus placebo, Outcome 6 Change in fasting glucose.



Analysis 3.7. Comparison 3 Chromium (400 µg) versus placebo, Outcome 7 Change in total cholesterol.



Analysis 3.8. Comparison 3 Chromium (400 µg) versus placebo, Outcome 8 Change in triacylglycerol.

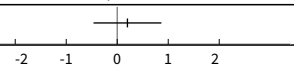


Comparison 4. Chromium (500 µg) versus placebo

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Change in body mass index at 6 months	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
2 Change in weight at 16 weeks	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
3 Change in waist circumference at 16 weeks	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
4 Change in fasting glucose at 16 weeks	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
5 Change in systolic blood pressure at 6 months	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
6 Change in diastolic blood pressure at 6 months	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
7 Change in total cholesterol	2	91	Mean Difference (IV, Random, 95% CI)	-0.05 [-0.46, 0.37]
8 Change in triacylglycerol	2	93	Mean Difference (IV, Random, 95% CI)	-0.28 [-0.76, 0.21]

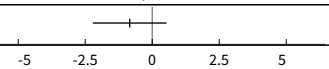
Analysis 4.1. Comparison 4 Chromium (500 µg) versus placebo, Outcome 1 Change in body mass index at 6 months.

Study or subgroup	Chromium		Placebo		Mean Difference	Mean Difference
	N	Mean(SD)	N	Mean(SD)	Fixed, 95% CI	Fixed, 95% CI
Kleefstra 2006	14	0.2 (1.1)	17	0 (0.7)		0.2[-0.47,0.87]



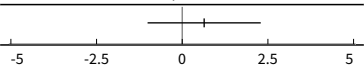
Analysis 4.2. Comparison 4 Chromium (500 µg) versus placebo, Outcome 2 Change in weight at 16 weeks.

Study or subgroup	Chromium		Placebo		Mean Difference	Mean Difference
	N	Mean(SD)	N	Mean(SD)	Fixed, 95% CI	Fixed, 95% CI
Iqbal 2009	31	-0.1 (2.5)	31	0.7 (3)		-0.84[-2.21,0.53]



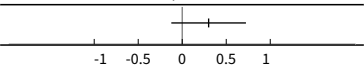
Analysis 4.3. Comparison 4 Chromium (500 µg) versus placebo, Outcome 3 Change in waist circumference at 16 weeks.

Study or subgroup	Chromium		Placebo		Mean Difference	Mean Difference
	N	Mean(SD)	N	Mean(SD)	Fixed, 95% CI	Fixed, 95% CI
Iqbal 2009	30	0.4 (2.3)	30	-0.3 (4)		0.64[-1.01,2.29]



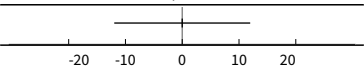
Analysis 4.4. Comparison 4 Chromium (500 µg) versus placebo, Outcome 4 Change in fasting glucose at 16 weeks.

Study or subgroup	Chromium		Placebo		Mean Difference	Mean Difference
	N	Mean(SD)	N	Mean(SD)	Fixed, 95% CI	Fixed, 95% CI
Iqbal 2009	31	0.3 (0.9)	31	-0 (0.8)		0.3[-0.12,0.72]



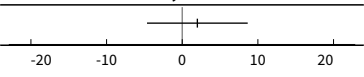
Analysis 4.5. Comparison 4 Chromium (500 µg) versus placebo, Outcome 5 Change in systolic blood pressure at 6 months.

Study or subgroup	Chromium		Placebo		Mean Difference	Mean Difference
	N	Mean(SD)	N	Mean(SD)	Fixed, 95% CI	Fixed, 95% CI
Kleefstra 2006	14	-7 (15)	17	-7 (19)		0[-11.97,11.97]



Analysis 4.6. Comparison 4 Chromium (500 µg) versus placebo, Outcome 6 Change in diastolic blood pressure at 6 months.

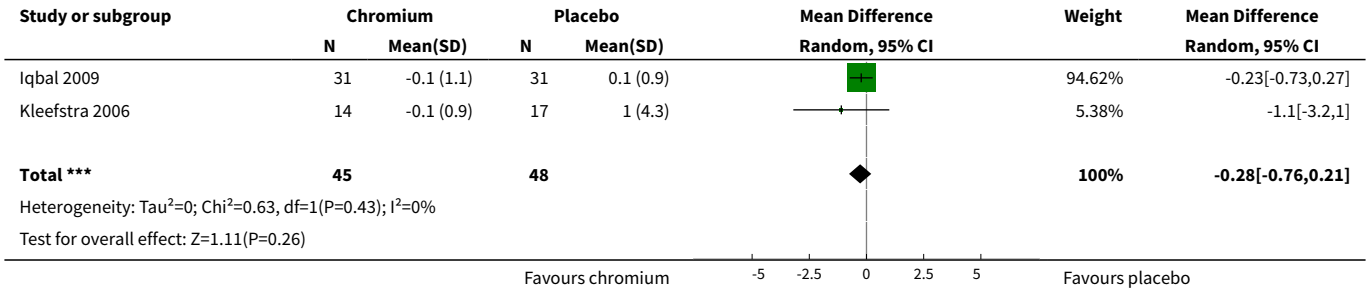
Study or subgroup	Chromium		Placebo		Mean Difference	Mean Difference
	N	Mean(SD)	N	Mean(SD)	Fixed, 95% CI	Fixed, 95% CI
Kleefstra 2006	14	-4 (11)	17	-6 (7)		2[-4.65,8.65]



Analysis 4.7. Comparison 4 Chromium (500 µg) versus placebo, Outcome 7 Change in total cholesterol.

Study or subgroup	Chromium		Placebo		Mean Difference	Weight	Mean Difference
	N	Mean(SD)	N	Mean(SD)	Random, 95% CI		Random, 95% CI
Iqbal 2009	30	-0.1 (1.1)	30	-0.1 (0.9)		65.95%	-0.07[-0.58,0.44]
Kleefstra 2006	14	0.2 (0.8)	17	0.2 (1.2)		34.05%	0[-0.71,0.71]
Total ***	**44**		**47**			**100%**	**-0.05[-0.46,0.37]**
Heterogeneity: Tau^2=0; Chi^2=0.02, df=1(P=0.87); I^2=0%							
Test for overall effect: Z=0.22(P=0.83)							

Analysis 4.8. Comparison 4 Chromium (500 µg) versus placebo, Outcome 8 Change in triacylglycerol.



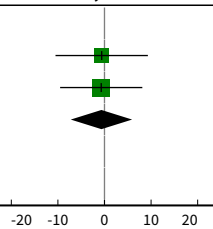
Comparison 5. Chromium (1000 µg) versus placebo

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Change in weight	2		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
1.1 12 weeks	2	50	Mean Difference (IV, Fixed, 95% CI)	-0.66 [-7.25, 5.93]
2 Change in body mass index	3		Mean Difference (IV, Random, 95% CI)	Subtotals only
2.1 6 months	2	90	Mean Difference (IV, Random, 95% CI)	0.11 [-0.08, 0.30]
2.2 12 weeks	2	99	Mean Difference (IV, Random, 95% CI)	0.28 [-0.01, 0.58]
3 Change in percent body fat	3		Mean Difference (IV, Random, 95% CI)	Subtotals only
3.1 6 months	1	58	Mean Difference (IV, Random, 95% CI)	1.1 [-0.35, 2.55]
3.2 12 weeks	3	117	Mean Difference (IV, Random, 95% CI)	0.93 [-0.35, 2.21]
4 Change in waist circumference	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
4.1 12 weeks	1		Mean Difference (IV, Fixed, 95% CI)	-1.60 [-6.53, 3.33]
5 Change in fasting glucose	2		Mean Difference (IV, Random, 95% CI)	Subtotals only
5.1 12 weeks	2	99	Mean Difference (IV, Random, 95% CI)	-0.25 [-1.29, 0.80]
5.2 6 months	1	58	Mean Difference (IV, Random, 95% CI)	0.0 [-2.14, 2.14]
6 Change in total cholesterol	2		Mean Difference (IV, Random, 95% CI)	Subtotals only
6.1 6 months	2	90	Mean Difference (IV, Random, 95% CI)	-0.07 [-0.68, 0.53]
6.2 12 weeks	1	67	Mean Difference (IV, Random, 95% CI)	-1.80 [-8.03, 4.43]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
7 Change in triacylglycerol	2		Mean Difference (IV, Random, 95% CI)	Subtotals only
7.1 6 months	2	90	Mean Difference (IV, Random, 95% CI)	-1.16 [-3.19, 0.87]
7.2 12 weeks	1	67	Mean Difference (IV, Random, 95% CI)	-3.7 [-13.38, 5.98]
8 Change in basal metabolic rate	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
8.1 12 weeks	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
9 Adverse events	3	134	Risk Ratio (M-H, Random, 95% CI)	1.75 [0.30, 10.43]
9.1 6 months	2	94	Risk Ratio (M-H, Random, 95% CI)	4.03 [0.46, 35.11]
9.2 12 weeks	1	40	Risk Ratio (M-H, Random, 95% CI)	0.30 [0.01, 7.02]
10 Change in systolic blood pressure	2		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
10.1 12 weeks	1	67	Mean Difference (IV, Fixed, 95% CI)	2.1 [-0.95, 5.15]
10.2 6 months	2	90	Mean Difference (IV, Fixed, 95% CI)	2.88 [-0.36, 6.12]
11 Change in diastolic blood pressure	2		Mean Difference (IV, Random, 95% CI)	Subtotals only
11.1 12 weeks	1	67	Mean Difference (IV, Random, 95% CI)	0.9 [-2.01, 3.81]
11.2 6 months	2	90	Mean Difference (IV, Random, 95% CI)	2.83 [-0.88, 6.55]

Analysis 5.1. Comparison 5 Chromium (1000 µg) versus placebo, Outcome 1 Change in weight.

Study or subgroup	Chromium N	Chromium Mean(SD)	Placebo N	Placebo Mean(SD)	Mean Difference Fixed, 95% CI	Weight	Mean Difference Fixed, 95% CI
5.1.1 12 weeks							
Campbell 1999	9	-0.2 (12.5)	9	0.4 (8.6)		44.19%	-0.6[-10.51,9.31]
Joseph 1999	17	0 (15.2)	15	0.7 (10)		55.81%	-0.7[-9.52,8.12]
Subtotal ***	**26**		**24**			**100%**	**-0.66[-7.25,5.93]**
Heterogeneity: Tau^2=0; Chi^2=0, df=1(P=0.99); I^2=0%							
Test for overall effect: Z=0.2(P=0.85)							

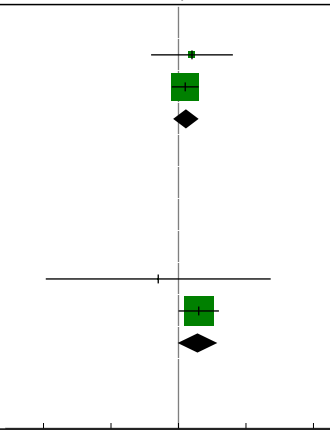


Favours chromium

Favours placebo

Analysis 5.2. Comparison 5 Chromium (1000 µg) versus placebo, Outcome 2 Change in body mass index.

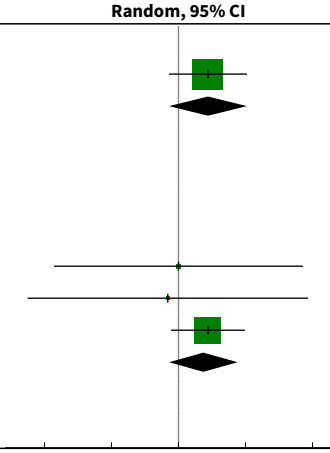
Study or subgroup	Chromium N	Chromium Mean(SD)	Placebo N	Placebo Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
5.2.1 6 months							
Kleefstra 2006	15	0.2 (1)	17	0 (0.7)		9.7%	0.2[-0.41,0.81]
Yazaki 2010	30	0.1 (0.2)	28	0 (0.5)		90.3%	0.1[-0.1,0.3]
Subtotal ***	**45**		**45**			**100%**	**0.11[-0.08,0.3]**
Heterogeneity: Tau^2=0; Chi^2=0.09, df=1(P=0.76); I^2=0%							
Test for overall effect: Z=1.14(P=0.25)							
5.2.2 12 weeks							
Joseph 1999	17	0 (2.4)	15	0.3 (2.4)		3.12%	-0.3[-1.97,1.37]
Yazaki 2010	35	0.3 (0.8)	32	0 (0.4)		96.88%	0.3[0,0.6]
Subtotal ***	**52**		**47**			**100%**	**0.28[-0.01,0.58]**
Heterogeneity: Tau^2=0; Chi^2=0.48, df=1(P=0.49); I^2=0%							
Test for overall effect: Z=1.87(P=0.06)							



Favours chromium — Favours placebo

Analysis 5.3. Comparison 5 Chromium (1000 µg) versus placebo, Outcome 3 Change in percent body fat.

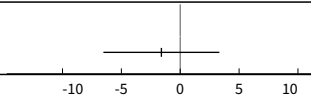
Study or subgroup	Chromium N	Chromium Mean(SD)	Placebo N	Placebo Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
5.3.1 6 months							
Yazaki 2010	30	0.2 (1)	28	-0.9 (3.8)		100%	1.1[-0.35,2.55]
Subtotal ***	**30**		**28**			**100%**	**1.1[-0.35,2.55]**
Heterogeneity: Not applicable							
Test for overall effect: Z=1.48(P=0.14)							
5.3.2 12 weeks							
Campbell 1999	9	1.6 (6)	9	1.6 (3.8)		7.59%	0[-4.64,4.64]
Joseph 1999	17	-1 (6.7)	15	-0.6 (8.2)		5.97%	-0.4[-5.63,4.83]
Yazaki 2010	35	0.3 (1.2)	32	-0.8 (3.8)		86.43%	1.1[-0.28,2.48]
Subtotal ***	**61**		**56**			**100%**	**0.93[-0.35,2.21]**
Heterogeneity: Tau^2=0; Chi^2=0.46, df=2(P=0.79); I^2=0%							
Test for overall effect: Z=1.42(P=0.16)							



Favours chromium — Favours placebo

Analysis 5.4. Comparison 5 Chromium (1000 µg) versus placebo, Outcome 4 Change in waist circumference.

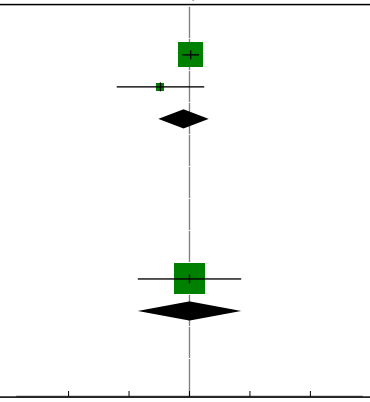
Study or subgroup	Chromium N	Chromium Mean(SD)	Placebo N	Placebo Mean(SD)	Mean Difference Fixed, 95% CI	Mean Difference Fixed, 95% CI
5.4.1 12 weeks						
Joseph 1999	17	0.1 (6.2)	15	1.7 (7.8)		-1.6[-6.53,3.33]



Favours chromium — Favours placebo

Analysis 5.5. Comparison 5 Chromium (1000 µg) versus placebo, Outcome 5 Change in fasting glucose.

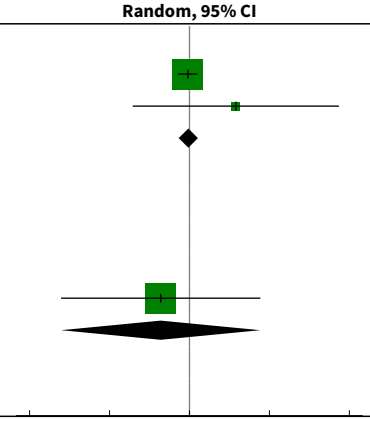
Study or subgroup	Chromium N	Chromium Mean(SD)	Placebo N	Placebo Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
5.5.1 12 weeks							
Joseph 1999	17	-0.3 (0.5)	15	-0.3 (0.5)		76.27%	0.05[-0.3,0.4]
Yazaki 2010	35	0 (3.1)	32	1.2 (4.3)		23.73%	-1.2[-3.01,0.61]
Subtotal ***	**52**		**47**			**100%**	**-0.25[-1.29,0.8]**
Heterogeneity: Tau^2=0.34; Chi^2=1.77, df=1(P=0.18); I^2=43.44%							
Test for overall effect: Z=0.46(P=0.64)							
5.5.2 6 months							
Yazaki 2010	30	1 (4.5)	28	1 (3.8)		100%	0[-2.14,2.14]
Subtotal ***	**30**		**28**			**100%**	**0[-2.14,2.14]**
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							



Favours chromium — Favours placebo

Analysis 5.6. Comparison 5 Chromium (1000 µg) versus placebo, Outcome 6 Change in total cholesterol.

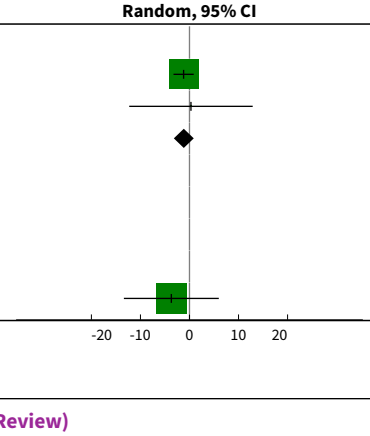
Study or subgroup	Chromium N	Chromium Mean(SD)	Placebo N	Placebo Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
5.6.1 6 months							
Kleefstra 2006	15	0.1 (0.4)	17	0.2 (1.2)		99.13%	-0.1[-0.71,0.51]
Yazaki 2010	30	5.6 (10.7)	28	2.7 (14)		0.87%	2.9[-3.55,9.35]
Subtotal ***	**45**		**45**			**100%**	**-0.07[-0.68,0.53]**
Heterogeneity: Tau^2=0; Chi^2=0.82, df=1(P=0.36); I^2=0%							
Test for overall effect: Z=0.24(P=0.81)							
5.6.2 12 weeks							
Yazaki 2010	35	1.6 (10.7)	32	3.4 (14.8)		100%	-1.8[-8.03,4.43]
Subtotal ***	**35**		**32**			**100%**	**-1.8[-8.03,4.43]**
Heterogeneity: Not applicable							
Test for overall effect: Z=0.57(P=0.57)							



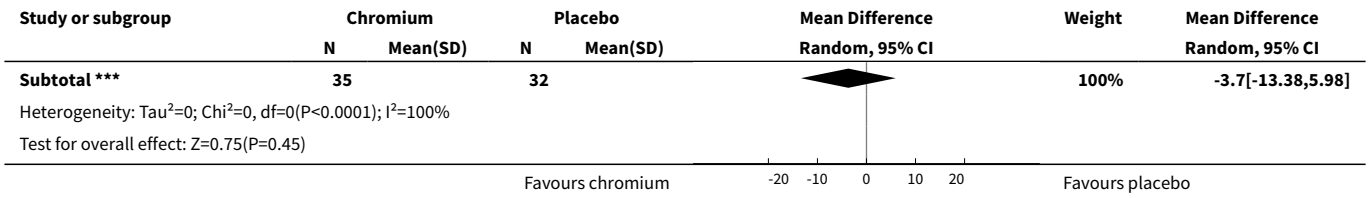
Favours chromium — Favours placebo

Analysis 5.7. Comparison 5 Chromium (1000 µg) versus placebo, Outcome 7 Change in triacylglycerol.

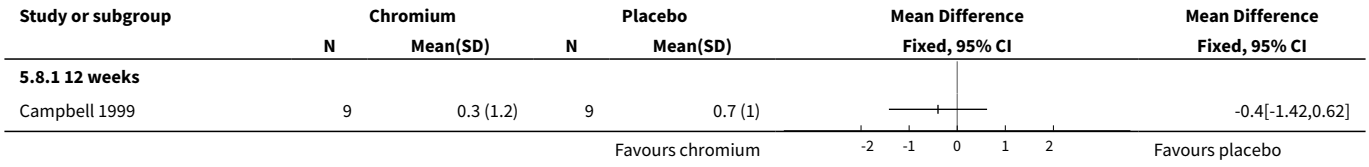
Study or subgroup	Chromium N	Chromium Mean(SD)	Placebo N	Placebo Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
5.7.1 6 months							
Kleefstra 2006	15	-0.2 (0.5)	17	1 (4.3)		97.39%	-1.2[-3.26,0.86]
Yazaki 2010	30	5.3 (25.2)	28	5 (23.7)		2.61%	0.3[-12.28,12.88]
Subtotal ***	**45**		**45**			**100%**	**-1.16[-3.19,0.87]**
Heterogeneity: Tau^2=0; Chi^2=0.05, df=1(P=0.82); I^2=0%							
Test for overall effect: Z=1.12(P=0.26)							
5.7.2 12 weeks							
Yazaki 2010	35	-0.4 (21.5)	32	3.3 (18.9)		100%	-3.7[-13.38,5.98]



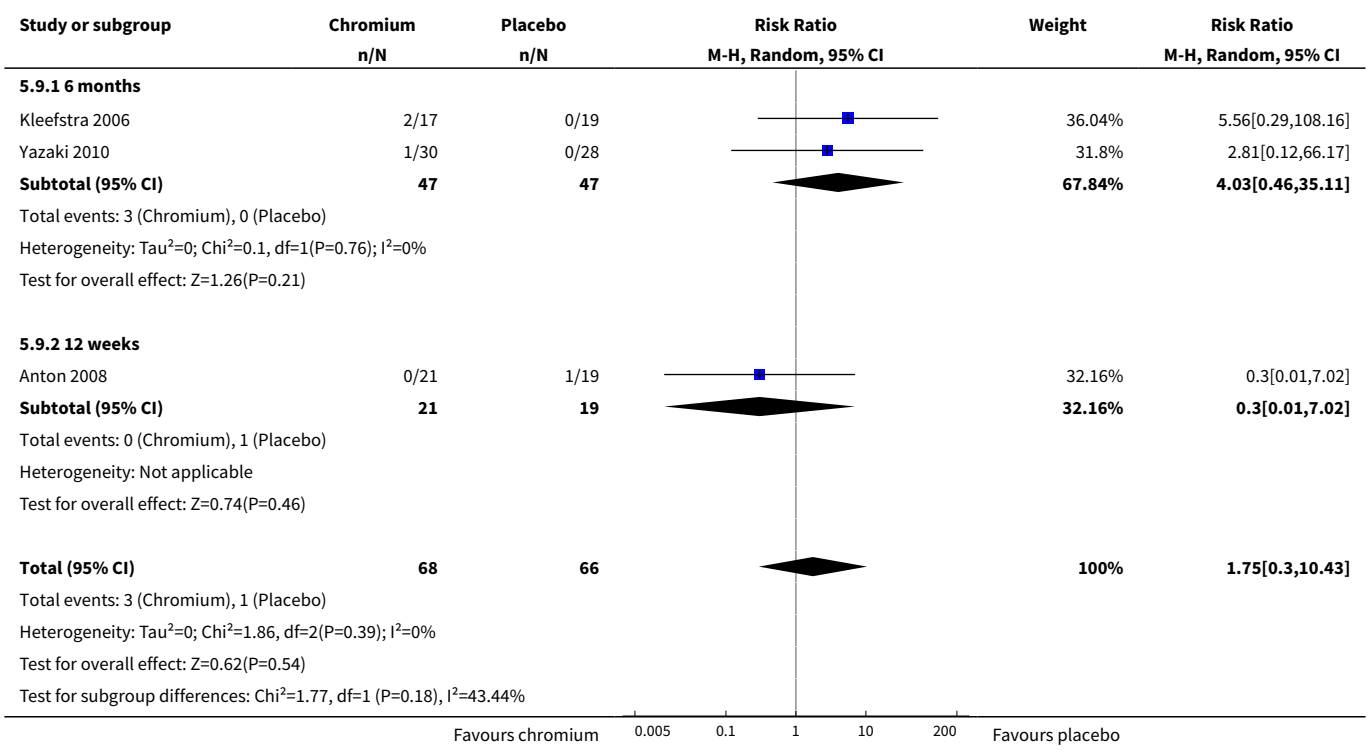
Favours chromium — Favours placebo



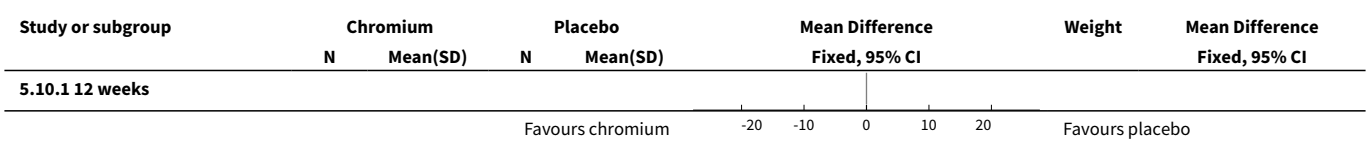
Analysis 5.8. Comparison 5 Chromium (1000 µg) versus placebo, Outcome 8 Change in basal metabolic rate.

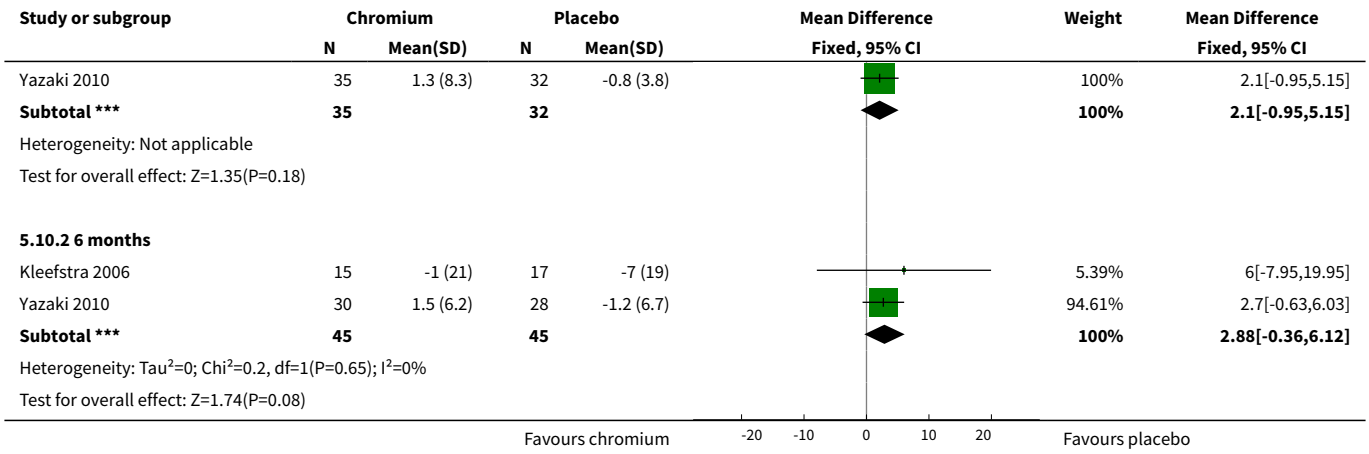


Analysis 5.9. Comparison 5 Chromium (1000 µg) versus placebo, Outcome 9 Adverse events.

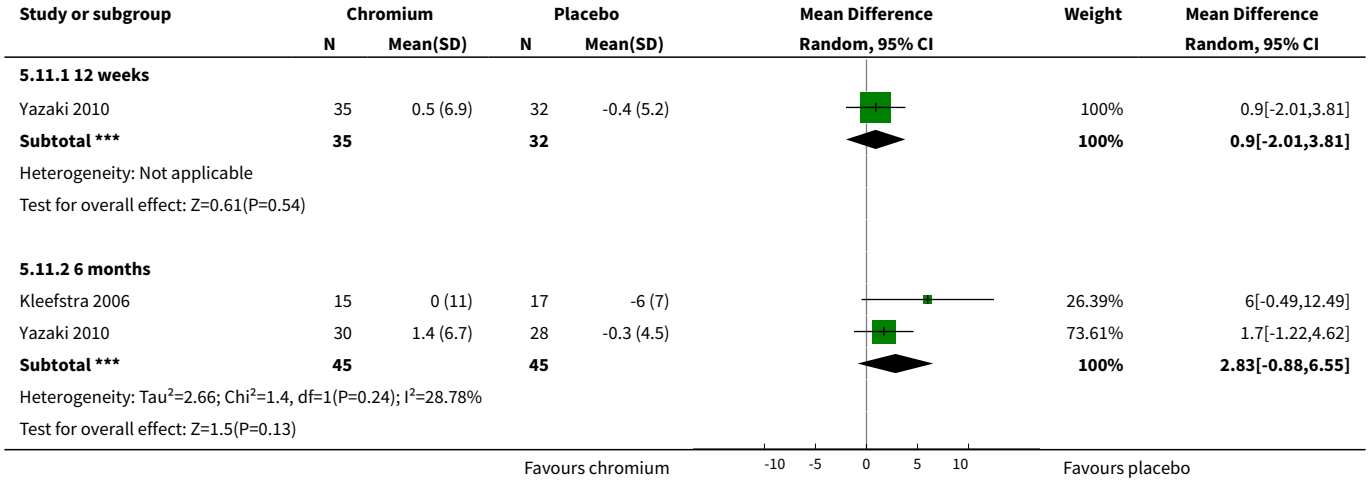


Analysis 5.10. Comparison 5 Chromium (1000 µg) versus placebo, Outcome 10 Change in systolic blood pressure.





Analysis 5.11. Comparison 5 Chromium (1000 µg) versus placebo, Outcome 11 Change in diastolic blood pressure.

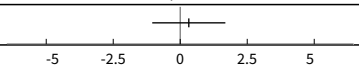


Comparison 6. Chromium (200 µg) versus chromium (400 µg)

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Change in weight 10 weeks	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
2 Change in percent body fat 10 weeks	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
3 Change in fat mass 10 weeks	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected

Analysis 6.1. Comparison 6 Chromium (200 µg) versus chromium (400 µg), Outcome 1 Change in weight 10 weeks.

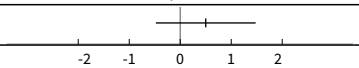
Study or subgroup	Chromium (200 ug) N	Chromium (200 ug) Mean(SD)	Chromium (400 ug) N	Chromium (400 ug) Mean(SD)	Mean Difference Fixed, 95% CI	Mean Difference Fixed, 95% CI
Kaats 1996	33	-1.1 (3.4)	66	-1.4 (2.9)		0.32[-1.04,1.68]



Favours chromium (200 ug) — Favours chromium (400 ug)

Analysis 6.2. Comparison 6 Chromium (200 µg) versus chromium (400 µg), Outcome 2 Change in percent body fat 10 weeks.

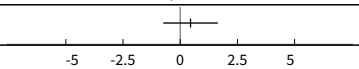
Study or subgroup	Chromium (200 ug) N	Chromium (200 ug) Mean(SD)	Chromium (400 ug) N	Chromium (400 ug) Mean(SD)	Mean Difference Fixed, 95% CI	Mean Difference Fixed, 95% CI
Kaats 1996	33	-1.4 (2.2)	66	-1.9 (2.6)		0.5[-0.48,1.48]



Favours chromium (200 ug) — Favours chromium (400 ug)

Analysis 6.3. Comparison 6 Chromium (200 µg) versus chromium (400 µg), Outcome 3 Change in fat mass 10 weeks.

Study or subgroup	Chromium (200 ug) N	Chromium (200 ug) Mean(SD)	Chromium (400 ug) N	Chromium (400 ug) Mean(SD)	Mean Difference Fixed, 95% CI	Mean Difference Fixed, 95% CI
Kaats 1996	33	-1.6 (2.9)	66	-2.1 (2.7)		0.45[-0.74,1.64]



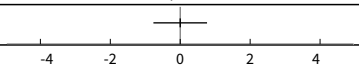
Favours chromium (200 ug) — Favours chromium (400 ug)

Comparison 7. Chromium (500 µg) versus chromium (1000 µg) at 6 months

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Change in body mass index	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
2 Change in total cholesterol	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
3 Change in triacylglycerol	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
4 Change in systolic blood pressure	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
5 Change in diastolic blood pressure	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
6 Adverse effects	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected

Analysis 7.1. Comparison 7 Chromium (500 µg) versus chromium (1000 µg) at 6 months, Outcome 1 Change in body mass index.

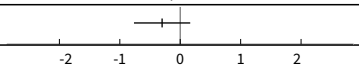
Study or subgroup	Chromium (500 ug) N	Chromium (500 ug) Mean(SD)	Chromium (1000 ug) N	Chromium (1000 ug) Mean(SD)	Mean Difference Fixed, 95% CI	Mean Difference Fixed, 95% CI
Kleefstra 2006	14	0.2 (1.1)	15	0.2 (1)		0[-0.77,0.77]



Favours chromium (500 ug) — Favours chromium (1000ug)

Analysis 7.2. Comparison 7 Chromium (500 µg) versus chromium (1000 µg) at 6 months, Outcome 2 Change in total cholesterol.

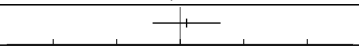
Study or subgroup	Chromium (500 ug) N	Chromium (500 ug) Mean(SD)	Chromium (1000 ug) N	Chromium (1000 ug) Mean(SD)	Mean Difference Fixed, 95% CI	Mean Difference Fixed, 95% CI
Kleefstra 2006	14	-0.2 (0.8)	15	0.1 (0.4)		-0.3[-0.77,0.17]



Favours chromium (500 ug) — Favours chromium (1000ug)

Analysis 7.3. Comparison 7 Chromium (500 µg) versus chromium (1000 µg) at 6 months, Outcome 3 Change in triacylglycerol.

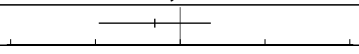
Study or subgroup	Chromium (500 ug) N	Chromium (500 ug) Mean(SD)	Chromium (1000 ug) N	Chromium (1000 ug) Mean(SD)	Mean Difference Fixed, 95% CI	Mean Difference Fixed, 95% CI
Kleefstra 2006	14	-0.1 (0.9)	15	-0.2 (0.5)		0.1[-0.44,0.64]



Favours chromium (500 ug) — Favours chromium (1000ug)

Analysis 7.4. Comparison 7 Chromium (500 µg) versus chromium (1000 µg) at 6 months, Outcome 4 Change in systolic blood pressure.

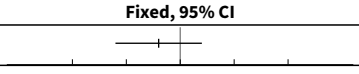
Study or subgroup	Chromium (500 ug) N	Chromium (500 ug) Mean(SD)	Chromium (1000 ug) N	Chromium (1000 ug) Mean(SD)	Mean Difference Fixed, 95% CI	Mean Difference Fixed, 95% CI
Kleefstra 2006	14	-7 (15)	15	-1 (21)		-6[-19.22,7.22]



Favours chromium (500 ug) — Favours chromium (1000ug)

Analysis 7.5. Comparison 7 Chromium (500 µg) versus chromium (1000 µg) at 6 months, Outcome 5 Change in diastolic blood pressure.

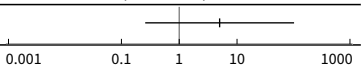
Study or subgroup	Chromium (500 ug) N	Chromium (500 ug) Mean(SD)	Chromium (1000 ug) N	Chromium (1000 ug) Mean(SD)	Mean Difference Fixed, 95% CI	Mean Difference Fixed, 95% CI
Kleefstra 2006	14	-4 (11)	15	0 (11)		-4[-12.01,4.01]



Favours chromium (500 ug) — Favours chromium (1000ug)

Analysis 7.6. Comparison 7 Chromium (500 µg) versus chromium (1000 µg) at 6 months, Outcome 6 Adverse effects.

Study or subgroup	Chromium (500 ug) n/N	Chromium (1000 ug) n/N	Risk Ratio M-H, Random, 95% CI	Risk Ratio M-H, Random, 95% CI
Kleefstra 2006	2/17	0/17		5[0.26,97]



ADDITIONAL TABLES

Table 1. Overview of study populations

Characteristic Study ID	Intervention(s) and control(s)	[N] Screened / eligible	[N] Ran-domised	[N] Safety	[N] ITT	[N] Finishing study	[%] Ran-domised finishing study	Follow-up[a]
1. Kaats 1996	I1: CrP 200 µg/day	233	33	33	-	33	100	72 days
	I2: CrP 400 µg/day		66	66	-	66	100	
	C: placebo		55	55	-	55	100	
total:			154	154	-	154	100	
2. Kaats 1998	I: CrP 400 µg/day	130	62	62	-	62	100	90 days
	C: placebo		60	60	-	60	100	
total:			122	122	-	122	100	
3. Joseph 1999	I: CrP 1000 µg/day + RT	35	17	17	-	17	100	12 weeks
	C: placebo + RT		15	15	-	15	100	
total:			32	32	-	32	100	
4. Kleefstra 2006	I1: CrP 500 µg/day	60	19	19	-	17	89	6 months
	I2: CrP 1000 µg/day		17	17	-	14	82	
	C: placebo		17	17	-	15	88	
total:			53	53	-	46	87	
5. Iqbal 2009	I: CrP 500 µg/day	153	33	33	28	28	84	16 weeks
	C: placebo		30	30	29	29	96	
total:			63	63	57	57	90	
6. Volpe 2001	I: CrP 400 µg/day + weight training	44	22	22	-	20	91	12 weeks

Table 1. Overview of study populations *(Continued)*

	C: placebo + weight training		22	22	-	17	77	
total:			44	44	-	37	84	
7. Anton 2008	I: CrP 400 µg/day	99	28	28	-	19	68	8 weeks
	C: placebo		28	28	-	21	75	
total:			56	56	-	40	71	
8. Campbell 1999	I: CrP 1000 µg/day + RT	23	9	9	-	9	100	13 weeks
	C: placebo + RT		9	9	-	9	100	
total:			18	18	-	18	100	
9. Yazaki 2010	I: CrP 400 µg/day	156	40	40	-	30	75	24 weeks
	C: placebo		40	40	-	28	70	
total:			80	80	-	58	72	
Grand total	***All interventions***		***346***			***320***	***93***	
	All controls		***276***			***256***	***93***	
	All interventions and controls		***622***			***576***	***93***	

[a]Duration of intervention and/or follow-up under randomised conditions until end of study
"-" denotes not reported
C: control; CrP: chromium picolinate; I: intervention; ITT: intention-to-treat; RT: resistance training

APPENDICES

Appendix 1. Search strategies

Search terms and databases
Unless otherwise stated, search terms are free text terms. Abbreviations: '$': stands for any character; '?': substitutes one or no character; adj: adjacent (i.e. number of words within range of search term); exp: exploded MeSH; MeSH: medical subject heading (MEDLINE medical index term); pt: publication type; sh: MeSH; tw: text word.
The Cochrane Library
#1 MeSH descriptor Obesity explode all trees #2 MeSH descriptor Weight Gain explode all trees #3 MeSH descriptor Weight Loss explode all trees #4 MeSH descriptor Body Mass Index explode all trees #5 (overweight in All Text or (over in All Text and weight in All Text)) #6 (adipos* in All Text or (fat in All Text and overload in All Text and syndrom* in All Text)) #7 (overeat* in All Text or (over in All Text and eat* in All Text)) #8 (overfeed* in All Text or (over in All Text and feed* in All Text)) #9 (weight in All Text and (gain in All Text or chang* in All Text)) #10 (body in All Text and mass in All Text and ind* in All Text) #11 MeSH descriptor Waist circumference explode all trees #12 MeSH descriptor Waist-Hip Ratio explode all trees #13 MeSH descriptor Abdominal fat explode all trees #14 MeSH descriptor Body fat distribution explode all trees #15 MeSH descriptor Skinfold thickness explode all trees #16 MeSH descriptor Overweight explode all trees #17 ((weight in All Text near/6 cyc* in All Text) or (weight in All Text near/6 reduc* in All Text) or (weight in All Text near/6 los* in All Text) or (weight in All Text near/6 maint* in All Text) or (weight in All Text near/6 decreas* in All Text)) #18 ((weight in All Text near/6 watch* in All Text) or (weight in All Text near/6 control* in All Text) or (weight in All Text near/6 chang* in All Text) or (weight in All Text near/6 gain* in All Text)) #19 BMI in All Text #20 (waist-hip in All Text and ratio* in All Text) #21 (waist in All Text and circumferenc* in All Text) #22 (body in All Text and (fat in All Text near/6 distribution* in All Text)) #23 ((abominal in All Text and fat in All Text) or (skinfold in All Text and thickness in All Text)) #24 (obes* in All Text or adipos* in All Text) #25 (#1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10 or #11 or #12) #26 (#13 or #14 or #15 or #16 or #17 or #18 or #19 or #20 or #21 or #22 or #23 or #24) #27 (#25 or #26) #28 MeSH descriptor chromium picolinate explode all trees #29 chromium picolinate in All Text #30 (#28 or #29) #31(#27 and #30)
MEDLINE
1 exp Obesity/ or exp Obesity hypoventilation syndrome/ or exp Obesity, abdominal/ or exp Obesity, morbid/ or exp Prader-Willi Syndrome/ 2 exp Overweight/ 3 exp Adipose tissue/ 4 exp Weight gain/ or exp Weight loss/

(Continued)

5 exp body fat distribution/ or exp body mass index/ or exp waist circumference/ or exp skinfold thickness/ or exp waist-hip ratio/

6 exp Body Composition/

7 (overweight$ or over weight$).tw,ot.

8 fat overload syndrom$.tw,ot.

9 (overeat$ or over eat$).tw,ot.

10 (overfeed$ or over feed$).tw,ot.

11 (adipos$ or obes$).tw,ot.

12 (weight adj3 (cyc$ or reduc$ or los$ or maint$ or decreas$ or watch$ or control$ or gain$ or chang$)).tw,ot.

13 (body mass ind$ or waist-hip ratio$).tw,ot.

14 skinfold thickness$.tw,ot.

15 abdominal fat$.tw,ot.

16 ((abdominal or subcutaneous or intra-abdominal or visceral or retroperitoneal or retro peritoneal) adj3 fat*).tw,ot.

17 or/1-16

18 exp chromium picolinate/

19 chromium picolinate.tw,ot.

20 18 or 19

21 17 and 20

22 randomized controlled trial.pt.

23 controlled clinical trial.pt.

24 randomi?ed.ab.

25 placebo.ab.

26 drug therapy.fs.

27 randomly.ab.

28 trial.ab.

29 groups.ab.

30 or/22-29

31 Meta-analysis.pt.

32 exp Technology Assessment, Biomedical/

33 exp Meta-analysis/

34 exp Meta-analysis as topic/

35 hta.tw,ot.

36 (health technology adj6 assessment$).tw,ot.

37 (meta analy$ or metaanaly$ or meta?analy$).tw,ot.

38 (search* adj10 (medical databas*or medline or pubmed or embase or cochrane or cinahl or psycinfo or psyclit or healthstar or biosis or current content* or systemat*)).tw,ot.

(Continued)

39 or/31-38

40 30 or 39

41 (comment or editorial or historical-article).pt.

42 40 not 41

43 21 and 42

44 (animals not (animals and humans)).sh.

45 43 not 44

EMBASE

1 exp Obesity/

2 exp weight change/ or exp weight control/ or exp weight gain/ or exp weight reduction/

3 exp body mass/ or exp waist circumference/ or exp waist hip ratio/

4 exp abdominal fat/ or exp body fat distribution/

5 exp skinfold thickness/

6 (obes$ or adipos* or overweight or over weight).tw,ot.

7 (overeat or over eat or overfeed or over feed or fat overload syndrom$).tw,ot.

8 (weight adj6 (cyc$ or reduc$ or los$ or maint$ or decreas$ or watch$ or control or chang$ or gain)).tw,ot.

9 (body mass ind$ or waist hip ratio or waist circumferenc$).tw,ot.

10 (body fat adj3 distribution*).tw,ot.

11 (abdominal fat or skinfold thickness).tw,ot.

12 or/1-11

13 exp chromium picolinate/

14 chromium picolinate.tw,ot.

15 13 or 14

16 12 and 15

17 exp Randomized Controlled Trial/

18 exp Controlled Clinical Trial/

19 exp Clinical Trial/

20 exp Comparative Study/

21 exp Drug comparison/

22 exp Randomization/

23 exp Crossover procedure/

24 exp Double blind procedure/

25 exp Single blind procedure/

26 exp Placebo/

(Continued)

27 exp Prospective Study/

28 ((clinical or control$ or comparativ$ or placebo$ or prospectiv$ or randomi?ed) adj3 (trial$ or stud$)).ab,ti.

29 (random$ adj6 (allocat$ or assign$ or basis or order$)).ab,ti.

30 ((singl$ or doubl$ or trebl$ or tripl$) adj6 (blind$ or mask$)).ab,ti.

31 (cross over or crossover).ab,ti.

32 or/17-31

33 exp meta analysis/

34 (metaanaly$ or meta analy$ or meta?analy$).ab,ti,ot.

35 (search$ adj10 (medical database$ or medline or pubmed or embase or cochrane or cinahl or psycinfo or psyclit or healthstar or-biosis or current content$ or systematic$)).ab,ti,ot.

36 exp Literature/

37 exp Biomedical Technology Assessment/

38 hta.tw,ot.

39 (health technology adj6 assessment$).tw,ot.

40 or/33-39

41 32 or 40

42 (comment or editorial or historical-article).pt.

43 41 not 42

44 16 and 43

45 limit 44 to human

46 44 not 45

ISI Web of Knowledge

#1 Topic= (Obesity) OR Topic= (Overweight) OR Topic= (Weight Gain) OR Topic= (Weight Loss) OR Topic= (Body Mass Index) OR-Topic= (Waist circumference) OR Topic= (Waist-Hip Ratio) OR Topic= (Abdominal fat) OR Topic= (Body fat distribution) OR Topic= (Sk-infold thickness) OR Topic= (BMI)

#2 Topic= (chromium picolinate)

#3 #1 AND #2 (201 citations)

Chinese Biomedical Database (CBM)

#1 "Obesity"[Mesh]

#2 Obesity [ti/ab]

#3 "Overweight"[Mesh]

#4 "Overweight"[ti/ab]

#5 Weight Gain [ti/ab]

#6 "Weight Gain"[Mesh]

#7 Weight Loss [ti/ab]

(Continued)

#8 "Weight Loss"[Mesh]
#9 Body Mass Index [ti/ab]

#10 "Body Mass Index"[Mesh]

#11 Waist circumference [ti/ab]

#12"Waist circumference"[Mesh]

#13 Waist-Hip Ratio [ti/ab]

#14"Waist-Hip Ratio"[Mesh]

#15 "Abdominal fat"[ti/ab]

#16"Abdominal fat"[Mesh]

#17 Body fat distribution [ti/ab]

#18 "Body fat distribution"[Mesh]

#19 Skinfold thickness [ti/ab]

#20 Skinfold thickness [Mesh]

#21 "BMI"[Mesh]

#22 BMI [ti/ab]

#23 #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #2

#24 chromium picolinate[ti/ab]

#25 "chromium picolinate"[Mesh]

#26 #24 OR #25

#27 #23 AND #26

#28 limit 27 to human

China Journal Full-text Database

#1 Obesity OR Overweight OR Weight Gain OR Weight Loss OR Body Mass Index OR Waist circumference OR Waist-Hip Ratio OR Abdominal fat OR Body fat distribution OR Skinfold thickness OR BMI

#2 chromium picolinate

#3 #1 AND #2

Chinese Scientific Journals Full-text Database

#1 Obesity OR Overweight OR Weight Gain OR Weight Loss OR Body Mass Index OR Waist circumference OR Waist-Hip Ratio OR Abdominal fat OR Body fat distribution OR Skinfold thickness OR BMI

#2 chromium picolinate

#3 #1 AND #2

'My NCBI' alert service

("picolinic acid" [Supplementary Concept] OR "picolinic acid" [All Fields] OR "chromium picolinate" [All Fields]) AND Randomized Controlled Trial [ptyp]

Appendix 2. Description of interventions

Characteristic	Intervention(s) [route, frequency, total dose/day]	Comparator(s) [route, frequency, total dose/day]
Kaats 1996	I1: chromium picolinate once a day, 200 µg/day	Placebo once a day
	I2: chromium picolinate once a day, 400 µg/day	
Kaats 1998	Chromium picolinate once a day, 400 µg/day	Placebo once day
Joseph 1999	Chromium picolinate twice daily, 1000 µg/day + RT (twice weekly for 12 weeks)	Placebo + RT (twice weekly for 12 weeks)
Kleefstra 2006	I1: Chromium picolinate twice daily, 500 µg/day	Placebo capsule twice daily
	I2: Chromium picolinate twice daily, 1000 µg/day	
Iqbal 2009	Chromium picolinate capsule twice daily, 500 µg/day	Placebo capsule twice daily
Volpe 2001	Chromium picolinate once a day, 400 µg/day + a supervised weight-training and walking program (twice weekly for 12 weeks)	Placebo once a day + a supervised weight-training and walking program (twice weekly for 12 weeks)
Anton 2008	Chromium picolinate 1000 µg/day	Placebo
Campbell 1999	Chromium picolinate twice daily, 924 µg/day + RT (twice weekly for 12 weeks)	Placebo twice daily + RT (twice weekly for 12 weeks)
Yazaki 2010	Chromium picolinate capsule twice daily, 500 µg	Placebo capsule twice daily, 815 mg

Footnotes

I: intervention; RT: resistance training

Appendix 3. Baseline characteristics (I)

Characteristic	Intervention(s) and comparator(s)	Duration of intervention	Participating population	Study period [year(s)]	Country	Setting	Duration of disease [mean/range years (SD), or as reported]
Kaats 1996	I1: CrP 200 µg/day I2: CrP 400 µg/day C: placebo	72 days	Participants were recruited from the first 233 volunteers who responded to a news story about the study run on the local central broad-casting system	1996	USA	Community volunteer	-
Kaats 1998	I: CrP 400 µg/day C: placebo	90 days	Participants were recruited from a variety of fitness and athletic clubs in San Antonio and Houston, Texas	1998	USA	Community volunteer	-
Joseph 1999	I: CrP 1000 µg/day + resistance training C: placebo + resistance training	12 weeks	Moderately overweight older men and women	1999	USA	Community volunteer	-
Kleefstra 2006	I1: CrP 500 µg/day I2: CrP 1000 µg/day C: placebo	6 months	Participants with type 2 diabetes mellitus	2006	USA	Outpatients	-
Iqbal 2009	I: CrP 500 µg/day C: placebo	16 weeks	Nondiabetic participants aged 18 to 75 years with metabolic syndrome and abdominal adiposity	2009	USA	Outpatients	-
Volpe 2001	I: CrP 400 µg/day + weight training C: placebo + weight training	12 weeks	Pre-menopausal women with a BMI between 27 and 41 kg/m^2	2001	USA	Community volunteer	-
Anton 2008	I: CrP 400 µg/day	8 weeks	Healthy, overweight adult women who reported craving for carbohydrates	2008	USA	Community volunteer	-

(Continued)

	C: placebo						
Campbell 1999	I: CrP 1000 µg/day + resistance training	13 weeks	Older men	1999	USA	Community volunteer	-
	C: placebo + resistance training						
Yazaki 2010	I: CrP 400 µg/day	24 weeks	Healthy overweight adults	2010	USA	Community volunteer	-
	C: placebo						

Footnotes

"-" denotes not reported

BMI: body mass index; C: comparator: CrP: chromium picolinate; I: intervention; SD: standard deviation

Appendix 4. Baseline characteristics (II)

Characteristic	Intervention(s) and comparator(s)	Sex [female %]	Age [mean/range years (SD), or as reported]	FBG [mg/dl]	BP systolic/diastolic [mm Hg]	BMI [mean kg/m^2]	Co-medications / Co-interventions	Co-morbidities
Kaats 1996	I1: CrP 200 µg/day	-	45.9 ± 11.9	-	-	30.3 ± 5.5	-	-
	I2: CrP 400 µg/day	-	45.7 ± 11.8	-	-	30.6 ± 5.1	-	-
	C: placebo	-	44.3 ± 11.2	-	-	30.6 ± 5.5	-	-
Kaats 1998	I: CrP 400 µg/day	-	41.1 ± 10.5	-	-	30.2 ± 7.1	-	-
	C: placebo	-	43.5 ± 7.6	-	-	28.4 ± 5.4	-	-
Joseph 1999	I: CrP 1000 µg/day + resistance training	47.1	63 ± 4	5.73 ± 0.43 mmol/L	-	28.9 ± 2.5	Control diet + resistance training	-
	C: placebo + resistance training	46.7	60 ± 4	5.73 ± 0.43 mmol/L	-	29.3 ± 2.4	Control diet + resistance training	-
Kleefstra 2006	I1: CrP 500 µg/day	86.2	60 ± 8.8	-	147 ± 24 / 85 ± 10	35 ± 7.2	Insulin	-
	I2: CrP 1000 µg/day	84.9	59 ± 6.4	-	156 ± 25 / 84 ± 14	33 ± 4.2	Insulin	-
	C: placebo	83.1	62 ± 7.5	-	159 ± 20 / 83 ± 10	34 ± 4.3	Insulin	-
Iqbal 2009	I: CrP 500 µg/day	60.6	47.7 ± 10	4.74 ± 0.8 mmol/L	130 ± 12 / 81 ± 10	37.8 ± 9	Insulin	-
	C: placebo	30.0	51.1 ± 13	4.54 ± 0.6 mmol/L	129 ± 15 / 79 ± 10	35.2 ± 6	Insulin	-
Volpe 2001	I: CrP 400 µg/day + weight training	100	42.6 ± 6.5	42.6 ± 6.5	91 ± 13	27-41	Weight training	-

(Continued)

	C: placebo + weight training	100	42.5 ± 4.2	42.5 ± 4.2	91 ± 6	27-41	Weight training	-
Anton 2008	I: CrP 400 µg/day	0	32 ± 10.2	87.1 ± 1.4	115 ± 13 / 74 ± 10	30.7 ± 4.2	Control diet	-
	C: placebo	0	34.5 ± 9.7	87.9 ± 6.8	114 ± 11 / 74 ± 10	31.9 ± 4.7	Control diet	-
Campbell 1999	I: CrP 1000 µg/day + resistance training	0	50-75	-	-	27-34	Resistance training	-
	C: placebo + resistance training	0	50-75	-	-	27-34	Resistance training	-
Yazaki 2010	I: CrP 400 µg/day	50	25-75	-	133 ± 17 / 80 ± 10	36.0 ± 6.7	-	-
	C: placebo	50	25-75	-	137 ± 18 / 81 ± 11	36.1 ± 7.6	-	-

Footnotes

"-" denotes not reported

"±" denotes single standard deviation

BP: blood pressure; BMI: body mass index; C: control; CrP: chromium picolinate; FBG: fasting blood glucose; I: intervention

Appendix 5. Matrix of study endpoints (publications)

Characteristic Study ID	Endpoint	Time of measurement[a]	Outcome reporting[b] [analysed & reported as not significant (e.g. P > 0.05)]	Outcome reporting[b] [analysed but not reported]	Outcome reporting[b] [measured & not analysed or analysed but not reported because of non-significant results]	Outcome reporting[b] [not mentioned but likely to have been measured & analysed but not reported because of non-significant results]
Kaats 1996	**Body composition improvement** (P)	0, 72 days	N/A	N/A	N/A	N/A
	Body weight (P)	0, 72 days	x	N/A	N/A	N/A
	Fat weight (P)	0, 72 days	N/A	N/A	N/A	N/A
	Percentage body fat (S)	0, 72 days	N/A	N/A	N/A	N/A
	Non-fat mass (S)	0, 72 days	x	N/A	N/A	N/A
Kaats 1998	**Body weight** (P)	0, 90 days	N/A	N/A	N/A	N/A
	Fat weight (P)	0, 90 days	N/A	N/A	N/A	N/A
	Percentage body fat (S)	0, 90 days	N/A	N/A	N/A	N/A
	Fat-free mass (S)	0, 90 days	x	N/A	N/A	N/A
Joseph 1999	Fasting glucose (P)	1, 13 weeks	N/A	N/A	N/A	N/A
	Fasting insulin (P)	1, 13 weeks	x	N/A	N/A	N/A
	Fasting C-peptide (S)	1, 13 weeks	x	N/A	N/A	N/A
	Weight loss (S)	1, 13 weeks	N/A	N/A	N/A	N/A
	BMI (S)	1, 13 weeks	x	N/A	N/A	N/A
	Waist circumference (S)	1, 13 weeks	x	N/A	N/A	N/A
	Waist to hip ratio (O)	1, 13 weeks	x	N/A	N/A	N/A
Kleefstra 2006	A1c (P)	0, 1, 3, 6 months	x	N/A	N/A	N/A
	Lipid profile (S)	0, 1, 3, 6 months	x	N/A	N/A	N/A
	BMI (S)	0, 1, 3, 6 months	x	N/A	N/A	N/A

(Continued)

	Blood pressure (S)	0, 1, 3, 6 months	x	N/A	N/A	N/A
	Plasma chromium concentration (S)	0, 1, 3, 6 months	x	N/A	N/A	N/A
Iqbal 2009	Insulin sensitivity index (P)	0, 16 weeks	x	N/A	N/A	N/A
	Glucose metabolism (S)	0, 16 weeks	N/A	N/A	N/A	N/A
	Oxidative stress (S)	0, 16 weeks	x	N/A	N/A	N/A
	Fasting serum lipids (S)	0, 16 weeks	x	N/A	N/A	N/A
	C-reactive protein (S)	0, 16 weeks	x	N/A	N/A	N/A
	Weight (O)	0, 16 weeks	x	N/A	N/A	N/A
	Waist circumference (O)	0, 16 weeks	x	N/A	N/A	N/A
Volpe 2001	**Percentage body fat** (P)	0, 6, 12 weeks	N/A	N/A	N/A	N/A
	Fat mass (P)	0, 6, 12 weeks	N/A	N/A	N/A	N/A
	BMI (P)	0, 6, 12 weeks	x	N/A	N/A	N/A
	Body weight (P)	0, 6, 12 weeks	x	N/A	N/A	N/A
	Resting metabolic rate (P)	0, 6, 12 weeks	x	N/A	N/A	N/A
	Biochemical parameters (S)	0, 6, 12 weeks	x	N/A	N/A	N/A
Anton 2008	Food intake (P)	0, 1, 8 weeks	N/A	N/A	N/A	N/A
	Hunger levels (P)	0, 1, 8 weeks	N/A	N/A	N/A	N/A
	Adverse events (P)	0, 1, 8 weeks	N/A	N/A	N/A	N/A
	Body weight (S)	0, 1, 8 weeks	N/A	N/A	N/A	N/A
	Fat cravings (S)	0, 1, 8 weeks	N/A	N/A	N/A	N/A
	Glucose and insulin (O)	0, 1, 8 weeks	x	N/A	N/A	N/A
Campbell 1999	**Fat-free mass** (P)	0, 6, 12 weeks	N/A	N/A	N/A	N/A
	Body weight (P)	0, 6, 12 weeks	x	N/A	N/A	N/A
	Urinary creatinine excretion (P)	0, 6, 12 weeks	N/A	N/A	N/A	N/A
	Total body water (P)	0, 6, 12 weeks	N/A	N/A	N/A	N/A
	Body muscle mass (P)	0, 6, 12 weeks	N/A	N/A	N/A	N/A
	Vastus lateralis type II fibre area (S)	0, 6, 12 weeks	N/A	N/A	N/A	N/A

(Continued)

	Skinfold thickness (S)	0, 6, 12 weeks	N/A	N/A	N/A	N/A
	Resting metabolic rate (S)	0, 6, 12 weeks	x	N/A	N/A	N/A
	Percentage body fat (S)	0, 6, 12 weeks	N/A	N/A	N/A	N/A
	Fat mass (S)	0, 6, 12 weeks	N/A	N/A	N/A	N/A
Yazaki 2010	**BMI** (P)	0, 12, 24 weeks	x	N/A	N/A	N/A
	Waist to hip ratio (P)	0, 12, 24 weeks	x	N/A	N/A	N/A
	Percentage body fat (S)	0, 12, 24 weeks	x	N/A	N/A	N/A
	Blood pressure (S)	0, 12, 24 weeks	x	N/A	N/A	N/A
	Basic metabolic (S)	0, 12, 24 weeks	x	N/A	N/A	N/A
	Urinalysis (O)	0, 12, 24 weeks	x	N/A	N/A	N/A

Footnotes:

"-" denotes not reported

"x" denotes "yes"

[a]Underlined times of measurement denote data as reported in the results section of the publication (other times represent planned but not reported points in time)

[b]Constitutes 'high risk of bias' according to the Outcome Reporting Bias In Trials (ORBIT) study classification system for missing or incomplete outcome reporting in reports of randomised trials (Kirkham 2010)

(P) primary or (S) secondary endpoint(s) refer to verbatim statements in the publication, (O) other endpoints relate to outcomes which were not specified as 'primary' or 'secondary' outcomes in the publication

Endpoint in bold = review primary outcome

A1c: HbA1c (glycosylated haemoglobin A1c); BMI: body mass index; N/A: not applicable

Appendix 6. Matrix of study endpoints (protocol/trial documents)

Characteristic Study ID (trial identifier)	Endpoint	Time of measurement
Kaats 1996	-	-
Kaats 1998	-	-
Joseph 1999	-	-
Kleefstra 2006	-	-
Iqbal 2009	Insulin sensitivity index, glucose metabolism, oxidative stress,	0, 16 weeks

(Continued)

	fasting serum lipids, C-reactive protein, weight, waist circumference	
Volpe 2001	-	-
Anton 2008	-	-
Campbell 1999	-	-
Yazaki 2010	-	-

Footnotes

"-" denotes no protocol was detected

Appendix 7. Definition of endpoint measurement

Characteristic Study ID	Overweight and obesity	Cardiovascular mortality	Morbidity	Health-related quality of life
Kaats 1996	WHO guidelines	-	-	-
Kaats 1998	WHO guidelines	-	-	-
Joseph 1999	WHO guidelines	-	-	-
Kleefstra 2006	WHO guidelines	-	-	-
Iqbal 2009	WHO guidelines	-	-	-
Volpe 2001	WHO guidelines	-	-	-
Anton 2008	WHO guidelines	-	-	-
Campbell 1999	WHO guidelines	-	-	-
Yazaki 2010	WHO guidelines	-	-	-

Footnotes

"-" denotes not reported

WHO: World Health Organization

Appendix 8. Adverse events (I)

Characteristic Study ID	Intervention(s) and comparator(s)	Randomised / Safety [N]	Deaths [N]	All adverse events [N]	All adverse events [%]	Severe/serious adverse events [N]	Severe/serious adverse events [%]
Kaats 1996	I1: CrP 200 µg/day	33	No participant died	-	-	-	-
	I2: CrP 400 µg/day	66	No participant died	-	-	-	-
	C: placebo	55	No participant died	-	-	-	-
Kaats 1998	I: CrP 400 µg/day	62	No participant died	-	-	-	-
	C: placebo	60	No participant died	-	-	-	-
Joseph 1999	I: CrP 1000 µg/day + resistance training	17	No participant died	-	-	-	-
	C: placebo + resistance training	15	No participant died	-	-	-	-
Kleefstra 2006	I1: CrP 500 µg/day	17	No participant died	0	0	0	0
	I2: CrP 1000 µg/day	17/15	No participant died	2	13	2	13
	C: placebo	19	No participant died	0	0	0	0
Iqbal 2009	I: CrP 500 µg/day	33	No participant died	-	-	-	-
	C: placebo	30	No participant died	-	-	-	-
Volpe 2001	I: CrP 400 µg/day + weight training	22	No participant died	-	-	-	-
	C: placebo + weight training	20	No participant died	-	-	-	-
Anton 2008	I: CrP 400 µg/day	21	No participant died	0	0	0	0
	C: placebo	19/18	No participant died	1	6	1	6

(Continued)

Campbell 1999	I: CrP 1000 µg/day + resistance training	9	No participant died	-	-	-	-
	C: placebo + resistance training	9	No participant died	-	-	-	-
Yazaki 2010	I: CrP 400 µg/day	40/39	No participant died	1	3	1	3
	C: placebo	40	No participant died	0	0	0	0

Footnotes

"-" denotes not reported

C: control; CrP: chromium picolinate; I: intervention

Appendix 9. Adverse events (II)

Characteristic	Intervention(s) and comparator(s)	Randomised / Safety [N]	Left study due to adverse events [N]	Left study due to adverse events [%]	Hospitalisation [N]	Hospitalisation [%]	Outpatient treatment [N]	Outpatient treatment [%]	Symptoms [N]	Symptoms [%]
Kaats 1996	I1: CrP 200 µg/day	33	-	-	-	-	-	-	-	-
	I2: CrP 400 µg/day	66	-	-	-	-	-	-	-	-
	C: placebo	55	-	-	-	-	-	-	-	-
Kaats 1998	I: CrP 400 µg/day	62	-	-	-	-	-	-	-	-
	C: placebo	60	-	-	-	-	-	-	-	-
Joseph 1999	I: CrP 1000 µg/day + resistance training	17	-	-	-	-	-	-	-	-
	C: placebo + resistance training	15	-	-	-	-	-	-	-	-
Kleefstra 2006	I1: CrP 500 µg/day	17	0	0	-	-	-	-	-	-
	I2: CrP 1000 µg/day	17/15	2	13	-	-	-	-	-	-
	C: placebo	19	0	0	-	-	-	-	-	-
Iqbal 2009	I: CrP 500 µg/day	33	-	-	-	-	-	-	-	-
	C: placebo	30	-	-	-	-	-	-	-	-
Volpe 2001	I: CrP 400 µg/day + weight training	22	-	-	-	-	-	-	-	-
	C: placebo + weight training	20	-	-	-	-	-	-	-	-
Anton 2008	I: CrP 400 µg/day	21	0	0	0	0	0	0	0	0
	C: placebo	19/18	1	6	-	-	-	-	-	-

(Continued)

Campbell 1999	I: CrP 1000 µg/day + resistance training	9	-	-	-	-	-	-	-	-
	C: placebo + resistance training	9	-	-	-	-	-	-	-	-
Yazaki 2010	I: CrP 400 µg/day	40/39	0	0	0	0	0	0	0	0
	C: placebo	40	1	6	-	-	-	-	-	-

Footnotes

"-" denotes not reported

C: control; CrP: chromium picolinate; I: intervention

Appendix 10. Survey of authors' providing information on trials

We tried our best to obtain relevant missing data from all authors of included studies but received no reply.

CONTRIBUTIONS OF AUTHORS

Hongliang Tian (TH): protocol drafting, search strategy development, trial selection, data interpretation and review drafting.

Xiaohu Guo (GX): protocol drafting, trial selection, data extraction, data analysis, data interpretation and review drafting.

Xiyu Wang (WX): protocol drafting, search strategy development, acquiring trial reports and review drafting.

Zhiyun He (HZ): acquiring trial reports, trial selection, data extraction, data analysis, data interpretation and review drafting.

Rao Sun (SR): protocol drafting, search strategy development, acquiring trial reports, trial selection and review drafting.

Sai GE (GS): protocol drafting, search strategy development, data extraction, data analysis, data interpretation and review drafting.

Zongjiu Zhang (ZZ): protocol drafting, search strategy development, acquiring trial reports, trial selection, data extraction, data analysis, data interpretation and review drafting.

DECLARATIONS OF INTEREST

None known

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

Timing of outcome measurement: changed from "Short-term: 1 to 4 weeks, medium-term: more than 4 weeks to 12 weeks" to "Short-term: 1 to 6 weeks, medium-term: more than 6 weeks to 12 weeks".

INDEX TERMS

Medical Subject Headings (MeSH)

*Dietary Supplements; Obesity [*drug therapy]; Overweight [drug therapy]; Picolinic Acids [*administration & dosage]; Randomized Controlled Trials as Topic; Resistance Training; Weight Lifting; Weight Loss

MeSH check words

Adult; Humans