Impacts of carbohydrate-restricted diets on micronutrient intakes and status: a systematic review

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ABSTRACT

A systematic review of published evidence on micronutrient intake/status with carbohydrate-restricted diets (CRD) was conducted in Web of Science, Medline, Embase, Scopus, CENTRAL, and ClinicalTrials.gov up to October 2018. We identified ten studies: seven RCTs (‘Atkins’-style, n=5; ’paleolithic’ diets, n=2), two Atkins-style non-controlled trials and one cross-sectional study. Prescribed carbohydrate varied 4%-34% of energy intake. Only one non-controlled trial prescribed multivitamin supplements. Dietary intakes/status were reported over 2-104 weeks, with weight losses 2-9 kg. No diagnoses of deficiency were reported. Intakes of thiamine, folate, magnesium, calcium, iron, and iodine all decreased significantly (-10 to -70% from baseline) with any CRD types. Atkins diet trials (n=6; 4-34%E carbohydrate) showed inconsistent changes in vitamin A, E and β-carotene intakes, while a single ‘paleolithic’ diet trial (28%E carbohydrate) reported increases in these micronutrients. One other ‘paleolithic’ diet (30%E carbohydrate) reported a rise in moderate iodine deficiency from 15% to 73% after 6 months. In conclusion, few studies have assessed the impacts of CRD on micronutrients. Studies with different designs point towards reductions in several vitamins and minerals, with potential risk of micronutrient inadequacies. Trial reporting standards are expected to include analysis of micronutrient intake/status. Micronutrients in foods and/or supplements should be considered when designing, prescribing or following CRDs.

Abbreviations

RCT, randomised controlled trial

CHO, carbohydrate

PRISMA, Preferred Reporting Items of Systematic reviews and Meta-analyses

CENTRAL, Cochrane Central Register of Controlled Trials

RNI, Reference Nutrient Intake

EAR, estimated average requirement

RBC, red blood cell

DRV, dietary reference values

INTRODUCTION

Carbohydrate-restricted diets have been promoted and used globally for weight management, and for treatment of diabetes, under either medical supervision or self-guidance. The Health Information National Trends Survey (USA) of 5,586 participants reported high awareness of carbohydrate-restricted diet (86.6%) with 17% of responders having tried this diet (1). In the UK, media reporting suggests that 7% of men and 10% of women are trying carbohydrate-restricted diets (2), similar to data from Finland (3).

The Active ‘Low-Carber’ Forums online survey (n=3134) reported that only 50% of respondents had support from their doctors, while 6% reported that their doctors did not encourage them, despite achieving weight loss. Online support forums were the most important source of information for 60% of the respondents, while 75% reported that government websites/publications were not important to them (4).

Although a topic of scientific and public debates, extensive and rigorous evidence review finds no clear evidence from systematic reviews and meta-analyses of randomised controlled trials (RCT) for superiority from either high- or low-carbohydrate diets for weight control or for diabetes care (5-8). Most clinical guidelines allow flexibility over carbohydrate (CHO) content, to suit personal preference, but the role of high CHO foods as sources of micronutrients appears rather neglected in this debate (9, 10). Very limited previous evidence has suggested that micronutrient content and adequacy may be compromised (11). Restricting consumptions of CHO-rich foods such as wholegrains, cereals and fruits might reduce consumptions of B-vitamins, minerals and antioxidant nutrients, potentially risking deficiencies. The present systematic review has evaluated up-to-date published literature to assess the reported impacts of carbohydrate-restricted diet on micronutrient intake and micronutrient status.

METHODS

This systematic review was conducted following a protocol registered in PROSPERO, registration number CRD42018085483 and it has been reported in accordance to the Preferred Reporting Items of Systematic Reviews and Meta-analyses (PRISMA) guideline (12).

Search and information source

A systematic literature search was conducted in electronic databases as following Web of Science Core Collection, Medline (OVID), EMBASE (OVID), Scopus, and Cochrane Central Register of Controlled Trials (CENTRAL); and ClinicalTrials.gov for trial registry record until October 2017, for initial searching. Having established the methodological approach, we updated search for Web of Science Core Collection, Medline (OVID), EMBASE (OVID), and Scopus databases in October 2018. We also searched for additional articles from reference lists of included full-texts and consulted experts in the field for relevant articles.

Search limit of English language and human studies were applied. Search terms as free texts and MeSH terms related to carbohydrate-restricted diet and micronutrient intakes or statuses were used, including the following micronutrients found in CHO rich foods: thiamine, riboflavin, niacin, folate, cobalamin, zinc, magnesium, selenium and iron. Full search strategy for Medline is available online (Supplemental Table S1).

Eligibility criteria

Papers were included if they reported micronutrient intakes and/or status in adult participants (≥ 18 years) who have followed carbohydrate-restricted diet as either being assigned to carbohydrate-restricted diet intervention or being identified in observational studies. The study designs allowed any intervention studies (either randomised or non-randomised controlled trials), cohort, cross-sectional or case-control studies. Carbohydrate-restricted diets included the Atkins diet, the Zone diet, the 'paleolithic' diet, ketogenic diets, or a prescribed carbohydrate-restricted diet as stated by the authors of the published studies. Papers were excluded if the study included a co-intervention (such as drug, or exercise administered alongside carbohydrate-restricted diet); subjects <18 years old; did not report micronutrient intakes and/or status in each diet arm (for intervention studies).

Study selection and data extraction

All records retrieved from each database were exported to EndNote (EndNote X8, Thomson Reuters, New York, USA). After duplicates removal, two reviewers, CC and DG, independently screened titles, abstracts and full-texts against eligibility criteria. A third reviewer (EC) was consulted when there was disagreement between the two reviewers. Data extraction was performed in the template created using Microsoft Excel by CC and DG independently, and disagreements were solved by consensus and consultation with the third reviewer (EC). The extracted data included: authors, year, study design, participant characteristics, sample size, details of intervention, dietary intakes, duration of study, micronutrient intakes/status, and supplement use.

Risk of bias assessment

Two reviewers independently assessed the risk of bias among included studies using the Cochrane Risk of Bias Tool, for RCTs, which comprises of six categories: random sequence generation; allocation concealment; blinding of participants and personnel; blinding of outcome assessment; incomplete outcome data; and selective reporting. The nature of the trials required open intervention with no blinding of the trial participants or the investigators. For observational studies and non-controlled trials, the quality assessment tools for observational cohort and cross-sectional studies, and for before-after (pre-post) studies with no control group (National Institute of Health) were used respectively. Risk of bias assessments were conducted for micronutrient intake outcome and micronutrient status outcome separately.

Data Synthesis

A narrative synthesis was implemented for the present systematic review, as there were limited numbers and high heterogeneities of studies included. Actual intakes of micronutrients were translated into percentages of recommended intakes according to the guideline of the country where the study was conducted, including UK, USA, Australia, Sweden, and Iceland. Changes from baseline intake of each micronutrient were calculated as percentage for each time-point of follow-up. Among weight loss trials, correlation analyses between changes in body weight and reduced intakes of each micronutrient were performed using Spearman's rank correlation.

RESULTS

A total of 595 records was retrieved from literature searching and 62 records from additional sources. After duplicates removal, 533 records were screened on the basis of title and abstract by two researchers independently, resulting in 52 full-texts to be assessed against the inclusion and exclusion criteria. A total of ten studies met the eligibility including seven RCTs, two non-controlled clinical trials and one cross-sectional study (Figure 1). Excluded full-texts with reasons are shown in Supplemental Table S2.

Risk of bias and quality assessment

The risk of bias of included RCTs is shown in Table 1 (including Supplemental Table S3-4 for detailed assessment) for micronutrient intakes and status; all studies were of low risk of bias. The blinding of the outcome assessors was judged as low risk of bias for all RCTs, as the outcomes are objective (both dietary intakes and plasma/urine biomarkers of micronutrients). Two RCTs were judged as at high risk of attrition bias due to substantial dropout rate (i.e. ≥20%). Two non-controlled trials of Atkins and Atkins-style diets met 9/10 items of the quality assessment tool for pre-post studies; and a cross-sectional study met 6/8 items of the quality assessment tools for observational cohort and cross-sectional studies. These three studies were also judged as low risk of bias (Supplemental Table S5-6).

Study characteristics

Among clinical trials, the Atkins and Atkins-style diets were used in five RCTs and two non-controlled trials; and the 'paleolithic' diet in two RCTs. Durations of intervention ranged from 2 weeks to 24 months (104 weeks). All trials with Atkins-style diet (n=7) were conducted in adults with overweight and obesity, but neither established cardiovascular diseases nor diabetes mellitus. One Atkins-style diet trial included patients with high liver fat content. Two studies with the 'paleolithic' diets were conducted in self-reported healthy women and postmenopausal women. Sample sizes ranged from 10 to 293 participants (Table 1).

Eight clinical trials aimed primarily to assess the effects of carbohydrate-restricted diet for weight loss and body composition, either with or without comparison to other weight loss diets (6 Atkins-style diets, 2 'paleolithic' diets). Of these, one crossover RCT additionally assessed effects of Atkins diet on antioxidant vitamin status. One other non-controlled trial assessed the effect of 'isocaloric' carbohydrate-restricted diet on liver fat content and gut microbiota without body weight loss in patients with high liver fat content. There was no report of clinically diagnosed micronutrient deficiency among the included trials. Only one trial prescribed multivitamins supplement to the participants, with one other trial reporting the number of participants who started taking supplements after the carbohydrate-restricted diet. The rest of the included studies did not report on supplement use (Table 1).

Four clinical trials provided diet books for participants to follow without any further instructions, while three clinical trials conducted counselling sessions, two short-term trials (2-4 weeks) provided all foods and drinks to their participants. A cross-sectional study of people voluntarily following carbohydrate-restricted diet did not report on the sources of their carbohydrate-restricted diet information. Amount of CHO contributing to total energy intake varied among studies ranging from 4% to 34%. However, mean CHO intakes met pre-specified CHO contents (adherence) in only 4/6 trials during 4 weeks to 3 months treatment time (Table 2).

Changes in body weight and energy intake in the included studies

Of eight weight loss trials, reported energy intakes per day decreased by approximately -300 to -1000 kcal (median -656 kcal), [-1255 kJ to -4184 kJ; median -2745 kJ], and body weight changes ranged from -3.2 to -8.5 kg over 2 weeks to 24 months. In contrast, a study of 'isocaloric' carbohydrate-restricted diet that aimed to maintain body weight reported an increase in reported energy intake of +880 kcal but demonstrated mean weight loss of -1.9 kg (Table 3-4).

Micronutrient intakes

Micronutrient intakes among the studies included were assessed by self-reported dietary records (n=6), and 24-hr dietary recalls (n=2), while two of the studies provided all foods and drinks to their participants (Table 1). Table 3 and 4 show amounts of micronutrient intakes per day, percentage of recommended intake in the country where the study was conducted, and the changes from baseline of each micronutrient in included studies. Numbers of studies that reported micronutrients are as following: thiamine (n=6), folate (n=8), vitamin B12 (n=4), vitamin C (n=9), vitamin A (n=7), beta-carotene (n=4), vitamin E (n=6), calcium (n=7), magnesium (n=6), iron (n=6), iodine (n=2), zinc (n=5), and selenium (n=4).

Among all weight loss trials (reduced energy intake; assessed by dietary records and/or 24-hr recalls), there were reductions (from baseline) in thiamine intake (-35 to -68%, n=5), folate (-15 to -71%, n=6), calcium (-13 to -63%, n=5), magnesium (-9 to -54%, n=4), iron (-13 to -57%, n=4), and iodine (-47%, n=1). All these micronutrients were also lower than the country-specific recommended intakes and accounted for 35 to 80% of recommended intake. One single-arm trial with 'isocaloric' intake (all food provided) in patients with high liver fat showed a significant increase in thiamine, but reductions in magnesium and iodine intakes, while no significant changes for folate, calcium or iron (Table 3 and 4). When comparing to control diets, most of the RCTs showed that participants in carbohydrate-restricted diet group had lower intakes of thiamine, folate, calcium, magnesium, iron and iodine (Table 5).

Approximately 30% increase in vitamin B12 intake was reported in clinical trials of 4 to 8-week Atkins diet compared to baseline, two- to six-fold higher than the recommended intake. Atkins diet trials reported reduced vitamin C intake, by -3 to -71% from baseline, but the 'paleolithic diet' showed a significant increase in vitamin C intake by 57%. Similarly, Atkins diet trials (n=6) showed inconsistent findings regarding vitamin A, E, and beta-carotene intakes, while a single 'paleolithic diet' trial showed increases in these micronutrients (vitamin A, E, and beta-carotene intakes) by +100%, +46%, and +167% respectively (Table 3). Intakes of zinc and selenium did not change markedly; the intakes at baseline and at the end of trials were both above recommended intakes (Table 4). Dietary data for vitamin B12, A, C, E, beta-carotene, zinc and selenium among the included studies were assessed by either self-reported dietary records, 24-hr recalls, or analysis of all foods provided by researchers.

Correlations between changes in body weight and micronutrient intakes

There were strong correlations between amount of weight loss (kg) and actual intakes of thiamine (rho=0.83, p=0.167), magnesium (rho=0.95, p=0.051) and iron (rho=0.95, p=0.051). As percentage of Reference Nutrient Intake (%RNI), there were only strong correlations between weight loss and %RNI of magnesium (rho=0.92, p=0.026) and iron (rho=0.82, p=0.089).

Micronutrient adequacy

No case of clinical micronutrient deficiency was reported. Only one RCT by Gardner et al. reported micronutrient adequacy by showing the proportion of participants whose intakes were below estimated average requirement (EAR) after 8 weeks on an Atkins diet for weight loss. Three non-consecutive 24-hr dietary recalls were used in this study. Intakes of thiamine, folate and vitamin C all fell below EAR in approximately 50% of participants, 70% for magnesium and 30% for iron. Importantly, there was a three-fold increase in the proportion of participants who had iron intakes below EAR at the end of the Atkins diet trial (from 3% to 32% of participants).

Micronutrient status

Measure of micronutrient status were reported only in four studies, including Atkins diet (n=1), paleolithic diet (n=2), and 'isocaloric' carbohydrate-restricted diet (n=1) for folate, vitamin A, carotenoids, vitamin E and iodine (Table 6). Serum and red blood cell (RBC) folate increased after 2 weeks of 'isocaloric' carbohydrate-restricted diet (+9 nmol/L) and 4 weeks of a 'paleolithic' diet (+90 nmol/L) respectively, which are in disagreement with reported folate intakes (Table 3). The Atkins diet resulted in an increase in plasma vitamin C concentration, but reductions (-2 to -40% from baseline) in plasma retinol, carotenoids, and α-tocopherol. In contrast, the 'paleolithic' diet reported increases in plasma lycopene, α- and β-carotenes (Table 6).

Iodine status was reported in only one RCT showing a significant reduction in median 24-hour urine iodine concentration after a 'paleolithic' diet at both 6 months (36 μg/L) and 2 years (57 μg/L), compared to baseline (68 μg/L); one to two-fold lower than the control diet (no change through the study, 70 μg/L) (Table 6). Importantly, there was a rise in proportion of women with urine iodine concentration <50 μg/L, which is the internationally agreed cut-off for moderate iodine deficiency, from 15% at baseline to 73% at 6 months on the 'paleolithic' diet (Table 6).

DISCUSSION

Most carbohydrate-restricted diets are used for weight control. Losing weight requires an energy restricted (i.e. macronutrient-restricted) diet for a significant period of time. However, the body still requires adequate micronutrient intake to maintain normal metabolic function. If the weight loss diet is not well designed nutritionally, micronutrient insufficiencies can develop. The present paper is a systematic review of published evidence, up to October 2018, on the impact of carbohydrate-restricted diets on micronutrient intakes and status. Although rather few published studies on carbohydrate-restricted diets have reported their effects on micronutrients, we have identified some consistent patterns of reduced micronutrient intakes, and to levels lower than control-diets, when people follow diets which limit CHO-rich foods. A variety of carbohydrate-restricted diets were examined, mostly primarily aiming for weight control. Given the lack of consistent difference in weight loss, compared to higher CHO diets (6, 13, 14), these findings might provide grounds to prefer weight-control diets which do not excessively restrict CHO more than other macronutrients.

Intakes of thiamine, folate, magnesium, calcium, iron and iodine all decreased after following any types of carbohydrate-restricted diet (Figure 2). This probably reflects the fact that CHO-rich staple foods are a good source of vitamins and minerals, either naturally presented or being fortified, and for some they usually form the main sources to reach dietary reference values (DRVs). For example, the DRV (UK) of thiamine for a healthy adult man is 1 mg/day. This would be met by about 100g of commercial breakfast cereal, 400g of wholemeal breads. Not all CHO-rich foods are such rich source of thiamine, thus to reach the DRV would require about 500g of baked potato, but this compares with 1000g of beef, or 1250 g of boiled eggs, or 5000g of cheese (15). Although iodine is not a nutrient acquired from CHO-rich foods, both Atkins and 'paleolithic' diets exclude milk/dairy from the diets leading to lower iodine intake. Our systematic review showed that both iodine intake and iodine status (urinary biomarker) were reduced after following a 'paleolithic' diet (23, 31). In the UK, bread and fortified breakfast cereals, milk and milk products, and vegetable including potatoes are the top three food-groups as sources of the vitamins and minerals (16), which are reported to be reduced on carbohydrate-restricted diets.

The reduced intakes with carbohydrate-restricted diets in studies reviewed here could have important clinical consequences. There have been case reports of severe, potentially life-threatening, thiamine deficiency from following extreme or prolonged carbohydrate-restricted diets. Bilateral optic neuropathy was reported in two patients who followed a prolonged CHO-restricted diet (17) and Wernike's encephalopathy with cardiac beriberi was reported in a young man with obesity who cut out all breads, cereal and pasta for several months (18). Given that weight loss may promote reproductive function in women with overweight/obesity, inadequate intake of folate and iodine in women of child-bearing age both increase risk of foetal maldevelopment, and iron deficiency is already frequent in young women (19, 20). Increased risk by 17-22% of type 2 diabetes has been reported with low magnesium consumption (21, 22).

For other vitamins, different advice between specific carbohydrate-restricted diets regarding fruits and vegetables intake probably explains the variable effects on some micronutrients. Reductions in carotenoid intakes and plasma concentrations were reported after an Atkins diet (24), while there were increases in carotenoid intakes and plasma concentrations after a 'paleolithic' diet (23). The 'paleolithic' diet (23) also showed an increase in vitamin C intake, reflecting advice to consume more fruits than typical Atkins diets, which mostly showed reductions in vitamin C intakes (25, 26) (Figure 2). However, one trial with a modified Atkins diet showed an increase in plasma vitamin C concentration, probably because fruit juice was included in the meals provided (24).

Despite reduced intake of folate, serum and RBC folate increased following an 'isocaloric' carbohydrate-restricted diet and one 'paleolithic' diet. This is proposed to be due to a carbohydrate-restricted diet induced increment in folate-producing gut bacteria as demonstrated in the study by Mardinoglu et al.(27) or it may reflect a limitation in the food composition database used (23). The intakes of some micronutrients (status not reported), specifically B12, zinc and selenium, did consistently increase after carbohydrate-restricted diet – however, intakes were adequate at baseline.

Limitations and strength

It was disappointing, but perhaps interesting given the amount of media interest, that so few of the many studies on carbohydrate-restricted diets have reported micronutrient intakes or status. The lack of reporting of measured micronutrient status is concerning, given the potential for serious deficiencies, and because there are always questions about the reliability of dietary assessment methods to report intakes. Two out of 10 included studies used the memory-based 24-hour dietary recall, while the rest used a prospective approach (dietary record) and/or supplied all foods and drinks to participants. Only four out of 10 studies employed an objective biomarker measurement for at least one micronutrient.

There is a wide variety of what people consider to be a 'low-carbohydrate diet', as low as 20-50 g of carbohydrate per day or up to 40-45% of total energy intake as seen in many low-carbohydrate diet papers (6, 7, 23, 25). For people who are not wishing to lose weight, under 50 g of carbohydrate per day leaves a large (somewhat less practical) amount of calories to be derived from non-CHO sources. The compositions of control diets in RCTs also varied in macronutrient contents.

Only one trial reported proportion of participants below EAR, but this could be more clinically meaningful if all studies could have reported on proportion below lower reference nutrient intakes. Another important point relates to the between-country variation in terms of recommended intake, which would lead to different apparent dietary adequacy for some micronutrients. For example, the UK RNI for folate and vitamin C are 200 mcg and 40 mg per day while these are 400 mcg and 90 mg for USA. If the USA recommended intakes were used for all studies, the numbers of inadequate intakes reported could be greater in some other countries.

Despite the Atkins diet book recommending dietary supplements, most of the included studies did not report on supplement use causing difficulties in estimating of how significant the problem of inadequacy is. There is no guideline on the use of micronutrient supplementation while on energy restricted diets. The present systematic review has found frequent and consistent reductions in intake or status, such that micronutrient supplementation might be recommended routinely with carbohydrate-restricted diets.

Conclusion

This study has used rigorous systematic review methodology to establish a rather consistent finding of multiple micronutrient inadequacy in free-living participants following carbohydrate-restricted diet. All included studies seem to be at low risk of bias. Future research should report on micronutrient status as well as dietary intakes, to inform not only the benefits of the intervention, but also the risk of micronutrient inadequacies, which could help readers/practitioners' decision-making. There is a case for recommending routine use of micronutrient supplementation with carbohydrate-restricted diets.

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Table Legends:

Table 1. Characteristics of included studies (n=10)

Values are presented as mean ± SD unless otherwise indicated.

RCT, randomised controlled trial; CRD, carbohydrate-restricted diet; BMI, bod mass index; CVD, cardiovascular disease; MCD, moderate carbohydrate diet; N/A, not applicable

Table 2. Mode of diet delivery, prescribed carbohydrate-restricted diets, and macronutrient intakes in the studies included.

Values are presented as mean ± SD unless otherwise indicated.

SFA, saturated fatty acids; MUFA, monounsaturated fatty acids; CRD, carbohydrate-restricted diet; CHO, carbohydrate; Pro, protein; E, energy; SFA, saturated fatty acids; OWL, ongoing weight loss; LFD, low fat diet; LEARN, Lifestyle, Exercise, Attitudes, Relationships, Nutrition; AGHE, Australian Guideline to Healthy Eating; NNR, Nordic Nutrition Recommendations; MTV/MTM, multivitamins/multimineral; N/A, not applicable

[a] no SD was reported.

Table 3. Actual intakes of vitamins, percentage of recommended intakes and changes from baseline.

Values are expressed as mean (SD) unless otherwise indicated.

M, men; W, women; wk, week; mo, month; BW, body weight; EI, energy intake; RI, recommended intake.

[a] cross-sectional study, [b] values are median (Interquartile range).

Table 4. Mineral intakes, percentage of recommended intakes and changes from baseline.

Values are expressed as mean (SD) unless otherwise indicated.

M, men; W, women; wk, week; mo, month; BW, body weight; EI, energy intake; RI, recommended intake.

[a] cross-sectional study, [b] values are median (Interquartile range).

Table 5 Micronutrient intakes following carbohydrate-restricted diets compared to control diets.

Values are mean (SD) unless otherwise indicated.

CRD, carbohydrate-restricted diet; LFD, low-fat diet; RNI, reference nutrient intake; AGHE, Australian Guideline Healthy Eating.

* $p<0.05$, ** $p<0.01$, *** $p<0.001$ compared between groups.

[a] no SD reported.

[b] no statistical comparison between groups

[c] P-values obtained from ANOVA, pairwise comparisons were significantly different (Tukey's Studentised range test)

[d] P-values for mean difference of change (end - baseline) between groups

Table 6. Plasma and urine biomarkers of micronutrients

Values are mean ± SD unless otherwise indicated.

CRD, carbohydrate-restricted diet; UIC, urine iodine concentration; UIE, urine iodine excretion; IQR, interquartile range; ns, not significant

[a] no SD reported

[b] p-value compared to baseline

[c] p-value from the longitudinal analysis compared to baseline

Legends for Figures

Figure 1. Study selection flow diagram.

WoS, Web of Sciences; CENTRAL, Cochrane Central Register of Controlled Trials; CRD, carbohydrate-restricted diet.

Figure 2. Percentage of changes from baseline intakes at the end of each study by micronutrients

Table 1. Characteristics of included studies (n=10)

Author/ country	Study design	Study population	Age, BMI	Primary outcome of studies	Duration of interventions	Dietary assessment methods	Supplement use	Overall risk of bias
Miller 2003 USA (28)	Single arm clinical trial	9 men and 9 women, overweight & obesity, without clinical cardiovascular disease and diabetes.	Age 39.8 ± 8 y BMI 36.4 ± 6.5 kg/m^2	Weight loss and dietary intake	4 weeks	3-day dietary record	Multivitamin daily provided by a research team	Low
Brehm 2003 USA (29)	Parallel RCT	53 women with obesity, without clinical cardiovascular disease and diabetes. (completers=42)	Age 44.2 ± 7 y BMI 33.2 ± 1.8 kg/m^2	Weight loss	6 months	3-day weighed food record	Not reported	Low
Truby 2008 UK (26)	Parallel RCT	293 men and women, overweight & obesity, without clinical cardiovascular disease and diabetes. (completers=240)	Age 40 ± 10 y BMI 32 ± 3 kg/m^2	Weight loss	6-month trial but dietary intake reported only over the first 2 months.	7-day estimated dietary record	Not reported	Low
Gardner 2010 USA (25)	Parallel RCT	311 women, overweight & obesity, without clinical cardiovascular disease and diabetes. (completers=291)	Age 42 ± 5 y BMI 32 ± 4 kg/m^2	Weight loss	12-month trial but dietary intake reported only over the first 8 weeks.	3 separate, non-consecutive, 24-hr dietary recalls	Voluntarily taking MTV/MTM, n=3; Calcium, n=3.	Low
Johnston 2011 UK (24)	Cross-over RCT	16 men, overweight & obesity without clinical cardiovascular disease and diabetes.	Age 55 ± 14 y BMI 36 ± 6 kg/m^2	Weight loss and antioxidant micronutrient status	4 weeks of CRD crossover with 4 weeks of MCD.	Research staff supplied all foods and drinks.	Not reported	Low
Bazzano 2014 (30)	Parallel RCT	148 men and women without clinical cardiovascular disease and diabetes. (completers=119)	Age 45.8 + 9.9 y BMI 35.2 + 3.8 kg/m^2	Weight loss	12 months	2 days 24-hr dietary recalls	Not reported	Low
Genoni 2016 Australia (23)	Parallel RCT	42 healthy women (completers=39)	Age 47 ± 13 y BMI 27 ± 4 kg/m^2	Body weight change, CVD risk factors	4 weeks	3-day weighed food record	Not reported	Low

Manousou 2018 Sweden (31)	Parallel RCT	70 women, postmenopausal, overweight & obesity without clinical cardiovascular disease and diabetes. (completers=49)	Age 60 ± 6.3 y BMI 32.6 ± 3.4 kg/m^2	Weight loss and body composition	24 months	4-day estimated dietary record	Not reported	Low
Mardinoglu 2018 (27)	Single arm clinical trial	10 adults (8 men) with high liver fat content	Age 53.7±3.65 y BMI 34.1±1.2 kg/m^2	Liver fat loss	2 weeks	All food provided	Not reported	Low
Elidottir 2016 Iceland (32)	Cross-sectional study	54 adults voluntarily following CRD	Age 43 ± 11 y BMI 30 ± 4 kg/m^2	To assess dietary intakes and CVD risk factors	N/A	3-day weighed food record	Not reported	Low

Values are presented as mean ± SD unless otherwise indicated.
RCT, randomised controlled trial; CRD, carbohydrate-restricted diet; BMI, bod mass index; CVD, cardiovascular disease; MCD, moderate carbohydrate diet; N/A, not applicable

Table 2. Mode of diet delivery, prescribed carbohydrate-restricted diets, and macronutrient intakes in the studies included.

Author/ country	Mode of diet delivery	Pre-specified CRD	Baseline	CRD (Intermediate)	CRD (Last time-point)	Comparator (Last time-point)
Miller 2003 USA (28)	A copy of Dr Atkins' New Diet Revolution book was provided.	<20 g CHO/day, ad libitum for fat. Add 5 g CHO/day up to 30 g/day during ongoing weight loss weeks.	***Baseline*** E 2481 ± 723 kcal (10.4 ± 3 MJ) CHO 43%, Pro 16% Fat 41%	***Induction 2 weeks*** E1400 ± 472 kcal (5.9 ± 2 MJ) CHO 21 g (6%) Pro 29%, Fat 64%	***OWL: 2 weeks*** E 1558 ± 490 kcal (6.5 ± 2 MJ) CHO 24 g (6%) Pro 29%, Fat 64%	N/A
Brehm 2003 USA (29)	Dietitians led group sessions for participants to follow the Atkins diet.	<20 g CHO/day, ad libitum for fat. After 2 weeks, increase CHO to 40-60 g/day.	***Baseline*** [a] E 1608 kcal (6.7 MJ) CHO 47%, Pro 16% Fat 37% (SFA 12.4%)	***3 months*** [a] E1156 kcal (4.8 MJ) CHO 41 g (15%) Pro 28% Fat 57% (SFA 21%)	***6 months*** [a] E 1302 kcal (5.5 MJ) CHO 97 g (30%) Pro 23% Fat 46% (SFA 17%)	***LFD 6 months*** [a] E 1247 kcal (5.2 MJ) CHO 53%, Pro 18% Fat 29% (SFA 11%)
Truby 2008 UK (26)	A copy of Dr Atkins' New Diet Revolution book was provided.	Participants were asked to follow the book. Ad libitum	***Baseline*** E 2283 ± 643 kcal (9.6 ± 2.7 MJ) CHO 42%, Pro 16% Fat 37%	***2 months*** E 1627 ± 551 kcal (6.8 ± 2.3 MJ) CHO 12%, Pro 28% Fat 57%, Alcohol 3%	Not reported	***Control 2 months*** E 1899 ± 624 kcal (8 ± 2.6 MJ) CHO 42%, Pro 16% Fat 37%, Alcohol 5%
Gardner 2010 USA (25)	A copy of Dr Atkins' New Diet Revolution book was provided.	Induction phase <20 g CHO/day, duration depended on participants. Ongoing phase CHO <50 g/day.	***Baseline*** E 1929 ± 509 kcal (8.1 ± 2.1 MJ) CHO 46%, Pro 17% Fat 36% (SFA 12%)	***8 weeks*** E 1373 ± 340 kcal (5.7 ± 1.4 MJ) CHO 58 g (17%) Pro 28% Fat 55% (SFA 20%)	Not reported	***LEARN 8 weeks*** E 1478 ± 444 kcal (6.2 ± 1.9 MJ) CHO 49%, Pro 20% Fat 30% (SFA 10%)
Johnston 2011 UK (24)	Research staff supplied all foods and drinks for a very low carbohydrate diet.	Low-carb, hi-protein: 4% CHO, 30% Protein, 66% Fat. 70% of energy requirement.	***Baseline*** [a] E 2744 kcal (11.5 MJ) CHO 52%, Pro 12% Fat 38% (SFA 13%)	N/A	***4 weeks*** [a] E 1906 kcal (8 MJ) CHO 22 g (4%) Pro 29% Fat 67% (SFA 21%)	N/A
Bazzano 2014 (30)	Dietitian led counselling sessions. A handbook of diet recipes, menu, food & shopping lists, meal planner was provided. 1 meal replacement per day was provided.	<40 g CHO/day, no specific energy goal. Participants also received education on SFA, MUFA, and trans fats, with emphasis on the benefits of MUFA and to limit trans fats.	***Baseline*** E 1998 ± 740 kcal (8.4 ± 3.1 MJ) CHO 48%, Pro 17% Fat 33% (SFA 11%)	***3 months*** E 1258 ± 409 kcal (5.3 ± 1.7 MJ) CHO 97 g (29%) Pro 26% Fat 43% (SFA 14%) ***6 months*** E 1324 ± 537 kcal (5.5 ± 2.2 MJ) CHO 93 g (28%) Pro 26% Fat 44% (SFA 13%)	***12 months*** E 1448 ± 610 kcal (6.1 ± 2.6 MJ) CHO 127 g (34%) Pro 24% Fat 41% (SFA 13%)	***LFD 12 months*** E 1527 ± 522 kcal (6.4 ± 2.2 MJ) CHO 54%, Pro 19% Fat 30% (SFA 9%)

Genoni 2016 Australia (23)	A copy of the Paleo Diet book was provided.	Advise for lean meats, fish, egg, nuts, fruits and vegetables, almond milk. No corn, white potatoes, and legumes. No grains, cereals and dairy products. Ad libitum	***Baseline*** E 1864 ± 461 kcal (7.8 ± 1.9 MJ) CHO 39%, Pro 21% Fat 34% (SFA 12%)	N/A	***4 weeks*** E 1414 ± 347 kcal (5.9 ± 1.5 MJ) CHO 103 g (28%) Pro 27% Fat 40% (SFA 12%)	***AGHE 4 weeks*** E 1591 ± 412 kcal (6.7 ± 1.7 MJ) CHO 41%, Pro 22% Fat 33% (SFA 12%)
Manousou 2018 Sweden (31)	Participants attended group session with diet and cooking practice for a Paleolithic diet.	30% CHO, 30% Pro, 40% Fat. Advise for lean meats, fish, egg, nuts, fruits and vegetables. No cereals, beans, refined fat & sugar, salt, soft drinks and bakery products. Ad libitum	***Baseline*** E 1993 ± 412 kcal (8.3 ± 1.7 MJ) CHO 44%, Pro 17% Fat 34%	***6 months*** E 1590 ± 327 kcal (6.7 ± 1.4 MJ) CHO 29%, Pro 24% Fat 44%	***24 months*** E 1531 ± 436 kcal (6.4 ± 1.8 MJ) CHO 31%, Pro 23% Fat 42%	***NNR 24 months*** E 1716 ± 279 kcal (7.2 ± 1.2 MJ) CHO 43%, Pro 17% Fat 35%
Mardinoglu 2018 (27)	Research staffs supplied all foods and drinks	'Isocaloric' CRD, did not aim for weight loss.	***Baseline*** E 2235 ± 221 kcal (9.4 ± 0.9 MJ) CHO 40%, Pro 20% Fat 40% (SFA 14%)	N/A	***2 weeks*** E 3115 ± 410 kcal (13 ± 1.7 MJ) CHO 4%, Pro 24% Fat 72% (SFA 10%)	N/A
Elidottir 2016 Iceland (32)	Voluntary adherence to CRD.	N/A, cross-sectional study	N/A	N/A	E 1928 ± 534 kcal (8.1 ± 2.2 MJ) CHO 10%, Pro 23% Fat 66% (SFA 26%)	N/A

Values are presented as mean ± SD unless otherwise indicated.
SFA, saturated fatty acids; MUFA, monounsaturated fatty acids; CRD, carbohydrate-restricted diet; CHO, carbohydrate; Pro, protein; E, energy; SFA, saturated fatty acids; OWL, ongoing weight loss; LFD, low fat diet; LEARN, Lifestyle, Exercise, Attitudes, Relationships, Nutrition; AGHE, Australian Guideline to Healthy Eating; NNR, Nordic Nutrition Recommendations; MTV/MTM, multivitamins/multimineral; N/A, not applicable
[a] no SD was reported.

Table 3. Actual intakes of vitamins, percentage of recommended intakes and changes from baseline.

	Time points	BW loss (kg)	EI change (kcal)	EI change (MJ)	Thiamine			Folate			B12			Vitamin C		
					Intake (mg)	%RI	Baseline change (%)	Intake (µg)	%RI	Baseline change (%)	Intake (µg)	%RI	Baseline change (%)	Intake (mg)	%RI	Baseline change (%)
Miller (M)	baseline				2.8 (2.1)	233		496 (446)	124		8 (6.3)	333		90 (77)	100	
2003 US	2 wk	-3.8	-1081	-4.5	3.9 (8.7)	325	+39	142 (62)	36	-71	7.6 (6.4)	317	-5	31 (27)	34	-66
	4 wk	-5.3	-923	-3.9	0.9 (0.3)	75	-68	191 (56)	48	-62	9 (3.3)	375	+13	26 (22)	29	-71
Miller (W)	baseline				1.5 (0.3)	136		209 (65)	52		4.3 (1.3)	179		84 (46)	112	
2003 US	2 wk	-3.8	-1081	-4.5	0.9 (1.1)	82	-40	236 (279)	59	+13	7 (4.7)	292	+63	48 (48)	64	-43
	4 wk	-5.3	-923	-3.9	0.8 (0.4)	73	-47	177 (105)	44	-15	5.6 (2.8)	233	+30	41 (33)	55	-51
Brehm	baseline				-	-	-	155.1	39		-	-	-	70.3	94	
2003 US	3 mo	-7.6	-452	-1.9	-	-	-	139.7	35	-10	-	-	-	35.7	48	-49
	6 mo	-8.5	-306	-1.3	-	-	-	195.9	49	+26	-	-	-	58.5	78	-17
Truby	baseline				-	223 (186)			139 (49)		-	-	-		224 (126)	
2008 UK	2 mo	-5.2	-656	-2.7	-	146 (49)	-35		93 (44)	-33	-	-	-		132 (104)	-41
Gardner	baseline				1.6 (0.5)	146		535 (207)	134		4.9 (4.3)	204		94 (59)	125	
2010 US	2 mo	-4.3	-556	-2.3	0.9 (0.4)	82	-44	329 (141)	82	-39	6.6 (7.9)	275	+35	66 (39)	88	-30
Johnston	baseline				-	-	-	-	-	-	-	-	-	153	383	
2011 UK	4 wk	-6.8	-838	-3.5	-	-	-	-	-	-	-	-	-	148	370	-3
Bazzano	baseline				-	-	-	410 (190)	103		-	-	-	87 (60)	118	
2014 US	3 mo	-5.7	-740	-3.1	-	-	-	290 (130)	73	-29	-	-	-	68 (45)	90	-24
	6 mo	-5.6	-674	-2.8	-	-	-	320 (170)	80	-22	-	-	-	81 (55)	108	-9
	12 mo	-5.3	-550	-2.3	-	-	-	310 (150)	78	-24	-	-	-	73 (68)	97	-18
Genoni	baseline				1.55 (0.6)	141		396 (136)	99		-	-	-	107 (50)	238	
2016 Aus	4 wk	-3.2	-450	-1.9	0.96 (0.5)	87	-38	317 (85)	79	-20	-	-	-	168 (84)	373	+57
Mardinoglu	baseline				1.64 (0.4)	126		365 (168)	122		11 (12)	567		142 (83)	190	
2018 Sweden	2 wk	-1.9	+880	+3.7	2.9 (0.5)	223	+77	345 (16)	115	-5	12 (0.7)	607	+7	154 (6)	206	+8
Elidottir [a, b]	Men	-	-	-	1.6 (1.4)	123	-	319 (295)	106	-	7 (5)	350	-	53 (77)	71	-
2016 Iceland	Women	-	-	-	1.0 (1.3)	91	-	275 (335)	92	-	7 (4)	350	-	76 (92)	101	-

Values are expressed as mean (SD) unless otherwise indicated. M, men; W, women; wk, week; mo, month; BW, body weight; EI, energy intake; RI, recommended intake.
[a] cross-sectional study, [b] values are median (Interquartile range).

Table 3. Actual intakes of vitamins, percentage of recommended intakes and changes from baseline (continued).

					Vitamin A			**Beta-Carotene**			**Vitamin E**		
	Time points	**BW loss (kg)**	**EI change (kcal)**	**EI change (MJ)**	**Intake (µg)**	**%RI**	**Baseline change (%)**	**Intake (µg)**	**%RI**	**Baseline change (%)**	**Intake (mg)**	**%RI**	**Baseline change (%)**
Miller (M)	baseline				1553 (1733)	173		-	-	-	15 (16)	100	
2003	2 wk	-3.8	-1081	-4.5	513 (238	57	-67	-	-	-	29 (69)	193	+93
	4 wk	-5.3	-923	-3.9	622 (355	69	-60	-	-	-	7.1 (2.5)	47	-53
Miller (W)	baseline				779 (387)	111		-	-	-	9.4 (3.8)	63	
2003	2 wk	-3.8	-1081	-4.5	1023 (1094)	146	+31	-	-	-	11 (15)	71	+14
	4 wk	-5.3	-923	-3.9	703 (385)	100	-10	-	-	-	7 (5)	47	-26
Brehm	baseline				-	-	-	-	-	-	-	-	-
2003	3 mo	-7.6	-452	-1.9	-	-	-	-	-	-	-	-	-
	6 mo	-8.5	-306	-1.3	-	-	-	-	-	-	-	-	-
Truby	baseline				-	182 (192)		-	-	-	-	-	-
2008	2 mo	-5.2	-656	-2.7	-	175 (257)	-4	-	-	-	-	-	-
Gardner	baseline				681 (289)	97		-	-	-	8.4 (4.1)	56	
2010	2 mo	-4.3	-556	-2.3	743 (323)	106	+9	-	-	-	8.7 (4.8)	58	+4
Johnston	baseline				533	76		3705	-		7.2	n/a	
2011	4 wk	-6.8	-838	-3.5	625	89	+17	3778	-	+2	11.9	n/a	+65
Bazzano [b]	baseline				-	-	-	490 (1310)	-		-	-	-
2014	3 mo	-5.7	-740	-3.1	-	-	-	890 (1990)	-	+82	-	-	-
	6 mo	-5.6	-674	-2.8	-	-	-	600 (1500)	-	+22	-	-	-
	12 mo	-5.3	-550	-2.3	-	-	-	420 (1420)	-	-14	-	-	-
Genoni	baseline				1015 (448)	145		4258 (2508)	-		9.8 (2.5)	140	
2016	4 wk	-3.2	-450	-1.9	2032 (1359)	290	+100	11379 (7966)	-	+167	14.3 (7.3)	204	+46
Mardinoglu	baseline				1517 (2243)	169		4116 (2503)	-		13.8 (4.5)	138	
2018	2 wk	-1.9	+880	+3.7	724 (35)	80	-52	3011 (134)	-	-27	30.9 (1.5)	309	+125
Elidottir [a,b]	Men	-	-	-	956 (773)	106	-	-	-	-	16 (13)	160	-
2016	Women	-	-	-	880 (472)	126	-	-	-	-	17 (8)	213	-

Values are expressed as mean (SD) unless otherwise indicated. M, men; W, women; wk, week; mo, month; BW, body weight; EI, energy intake; RI, recommended intake.
[a] cross-sectional study, [b] values are median (Interquartile range).

Table 4. Mineral intakes, percentage of recommended intakes and changes from baseline.

					Calcium			Magnesium			Iron		
	Time points	BW loss (kg)	EI change (kcal)	EI change (MJ)	Intake (mg)	%RI	Baseline change (%)	Intake (mg)	%RI	Baseline change (%)	Intake (mg)	%RI	Baseline change (%)
Miller (M)	baseline				1139 (458)	114		350 (149)	83		21 (12)	263	
2003 US	2 wk	-3.8	-1081	-4.5	420 (180)	42	-63	163 (61)	39	-53	9 (4)	113	-57
	4 wk	-5.3	-923	-3.9	503 (153)	50	-56	180 (41)	43	-49	12 (3)	150	-43
Miller (W)	baseline				801 (309)	80		280 (72)	88		13 (3)	72	
2003 US	2 wk	-3.8	-1081	-4.5	513 (223)	51	-36	129 (42)	40	-54	8 (2)	44	-39
	4 wk	-5.3	-923	-3.9	517 (268)	52	-36	182 (163)	57	-35	8 (4)	44	-39
Brehm	baseline				591	59		-	-	-	-	-	-
2003 US	3 mo	-7.6	-452	-1.9	444	44	-25	-	-	-	-	-	-
	6 mo	-8.5	-306	-1.3	739	74	+25	-	-	-	-	-	-
Truby	baseline					125 (44)		-	106 (33)		-	136 (60)	
2008 UK	2 mo	-5.2	-656	-2.7		92 (38)	-26	-	75 (38)	-29	-	91 (49)	-33
Gardner	baseline				851 (314)	85		291 (88)	91		14.8 (4.8)	82	
2010 US	2 mo	-4.3	-556	-2.3	742 (273)	74	-13	231(86)	72	-21	10.5 (4.1)	58	-29
Genoni	baseline				771 (204)	77		359 (85)	112		12.7 (2.6)	71	
2016 Aus	4 wk	-3.2	-450	-1.9	355 (91)	36	-54	328 (97)	103	-9	11.1 (2.7)	62	-13
Mardinoglu	baseline				1187 (342)	148		414 (74)	118		15.7 (3.3)	175	
2018 Sweden	2 wk	-1.9	+880	+3.7	1160 (472)	145	-2	338 (49)	97	-18	15.7 (1.6)	171	-2
Elidottir [a,b]	Men	-	-	-	770 (564)	96	-	245 (148)	70	-	11 (7)	122	-
2016 Iceland	Women	-	-	-	774 (566)	97	-	254 (114)	91	-	9 (6)	60	-

Values are expressed as mean (SD) unless otherwise indicated. M, men; W, women; wk, week; mo, month; BW, body weight; EI, energy intake; RI, recommended intake.
[a] cross-sectional study, [b] values are median (Interquartile range).

Table 4. Mineral intakes, percentage of recommended intakes and changes from baseline (continued).

					Iodine			Zinc			Selenium		
	Time points	**BW loss (kg)**	**EI change (kcal)**	**EI change (MJ)**	**Intake (µg)**	**%RI**	**Baseline change (%)**	**Intake (µg)**	**%RI**	**Baseline change (%)**	**Intake (µg)**	**%RI**	**Baseline change (%)**
Miller (M)	baseline				-	-	-	16 (7)	146		167 (68)	304	
2003 US	2 wk	-3.8	-1081	-4.5	-	-	-	14 (5)	127	-13	142 (107)	258	-15
	4 wk	-5.3	-923	-3.9	-	-	-	17 (4)	155	+6	146 (54)	266	-13
Miller (W)	baseline				-	-	-	10 (2)	125		128 (21)	233	
2003 US	2 wk	-3.8	-1081	-4.5	-	-	-	11 (4)	138	+10	108 (34)	196	-16
	4 wk	-5.3	-923	-3.9	-	-	-	12 (6)	150	+20	112 (40)	204	-13
Brehm	baseline				-	-	-	-	-	-	-	-	-
2003 US	3 mo	-7.6	-452	-1.9	-	-	-	-	-	-	-	-	-
	6 mo	-8.5	-306	-1.3	-	-	-	-	-	-	-	-	-
Truby	baseline				-	-	-	-	119 (33)		-	100 (33)	
2008 UK	2 mo	-5.2	-656	-2.7	-	-	-	-	139 (49)	+17	-	149 (225)	+49
Gardner	baseline				-	-	-	10.7 (3.7)	134		107 (36)	195	
2010 US	2 mo	-4.3	-556	-2.3	-	-	-	11 (3.5)	138	+3	114 (44)	207	+6.5
Genoni	baseline				120 (39)	80		11.5 (2.4)	144		-	-	-
2016 Aus	4 wk	-3.2	-450	-1.9	64 (23)	43	-47	11.8 (3.4)	148	+3	-	-	-
Mardinoglu	baseline				281 (133)	187		13.8 (2.3)	153		89.7 (34.4)	149	
2018 Sweden	2 wk	-1.9	+880	+3.7	177 (10)	118	-37	15.3 (1)	170	+11	146.5 (8.8)	244	+63
Elidottir [a,b]	Men	-	-	-	-	-	-	-	-	-	-	-	-
2016 Iceland	Women	-	-	-	-	-	-	-	-	-	-	-	-

Values are expressed as mean (SD) unless otherwise indicated. M, men; W, women; wk, week; mo, month; BW, body weight; EI, energy intake; RI, recommended intake.
[a] cross-sectional study, [b] values are median (Interquartile range).

Table 5 Micronutrient intakes following carbohydrate-restricted diets compared to control diets.

Micronutrients	Brehm (2003)				Truby (2008)		Gardner (2010)	
	3 months [a]		6 months [a]		2 months [b] %RNI		2 months [c]	
	Atkins (n=22)	LFD (n=20)	Atkins (n=22)	LFD (n=20)	Atkins (n=30)	Control (n=26)	Atkins (n=73)	LEARN (n=73)
Thiamine (mg)	-	-	-	-	146 (49)	178 (76)	0.9 (0.4)	1.4 (0.4) *
Folate (µg)	139.7	221.7	195.9	193.9	93 (44)	114 (36)	329 (141)	470 (190) ***
Vitamin B12 (µg)	-	-	-	-	-	-	6.6 (7.9)	5.7 (10.2)
Vitamin C (mg)	35.7	94.2 **	58.5	53.1	132 (104)	205 (214)	66 (39)	100 (62) ***
Vitamin A (µg)	-	-	-	-	175 (257)	118 (66)	743 (323)	689 (327)
Carotene (µg)	-	-	-	-	-	-	-	-
Vitamin E (mg)	-	-	-	-	-	-	8.7 (4.8)	7.2 (4.2)
Magnesium (mg)	-	-	-	-	75 (38)	95 (31)	231 (86)	286 (89) **
Calcium (mg)	444.2	567.2	739.0	662.6	92 (38)	111 (41)	742 (273)	801 (339)
Iron (mg)	-	-	-	-	91 (49)	104 (46)	10.5 (4.1)	13.7 (5.2) ***
Zinc (µg)	-	-	-	-	139 (49)	103 (31)	11 (3.5)	8.9 (3.1) ***
Selenium (µg)	-	-	-	-	149 (225)	87 (61)	114 (44)	97 (34) ***
Iodine (µg)	-	-	-	-	-	-	-	-

Values are mean (SD) unless otherwise indicated. CRD, carbohydrate-restricted diet; LFD, low-fat diet; RNI, reference nutrient intake; AGHE, Australian Guideline Healthy Eating.
* $p<0.05$, ** $p<0.01$, *** $p<0.001$ compared between groups.
[a] no SD reported.
[b] no statistical comparison between groups
[c] P-values obtained from ANOVA, pairwise comparisons were significantly different (Tukey's Studentised range test)
[d] P-values for mean difference of change (end - baseline) between groups

Table 5 Micronutrient intakes following carbohydrate-restricted diets compared to control diets (continued).

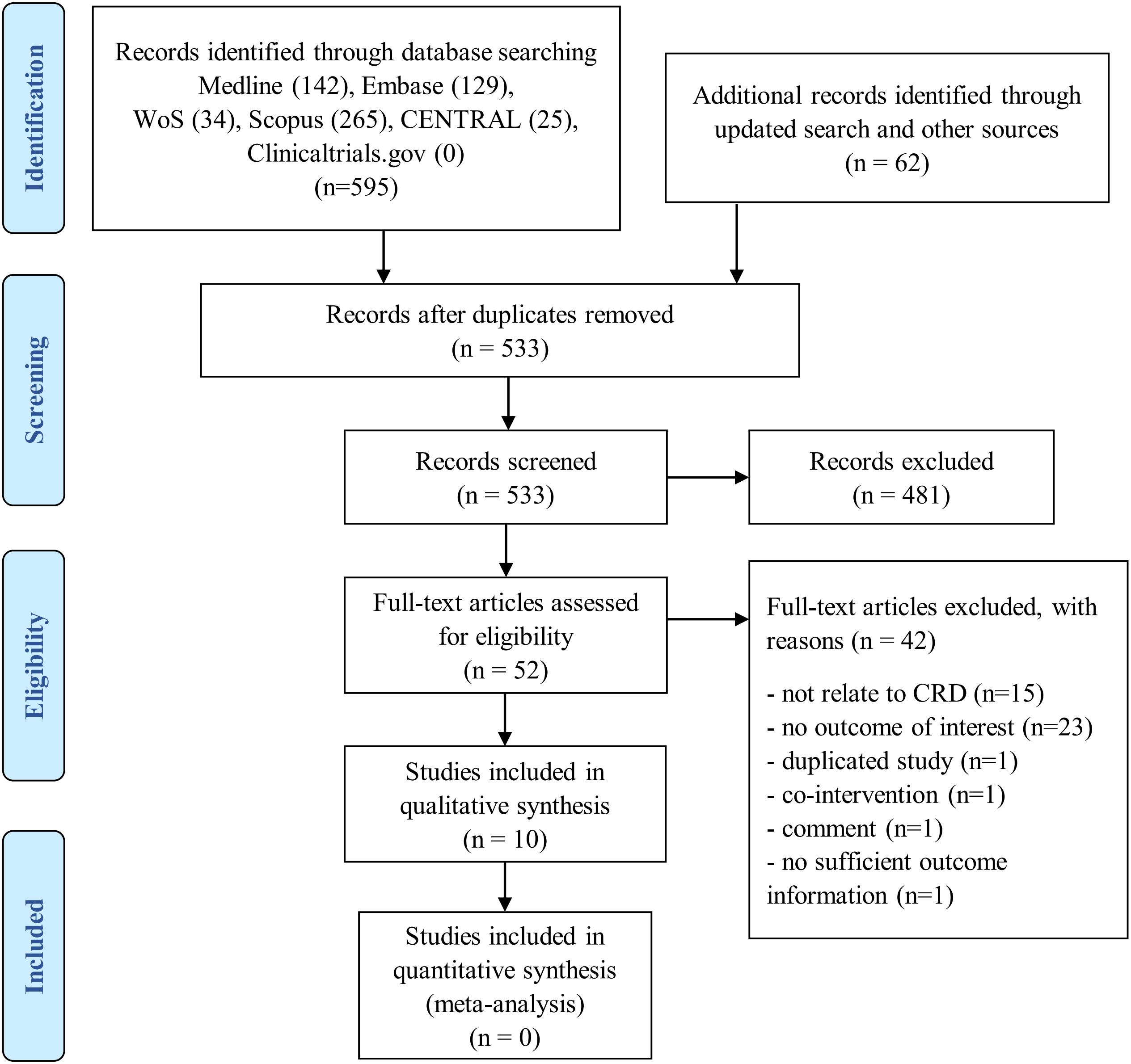
Micronutrients	Bazzano (2014)						Genoni (2016)	
	3 months [b]		6 months [b]		12 months [b]		4 weeks [d]	
	CRD	LFD	CRD	LFD	CRD	LFD	Paleolithic diet	AGHE
	n=62	n=61	n=54	n=50	n=54	n=49	(n=22)	(n=17)
Thiamine (mg)	-	-	-	-	-	-	0.96 (0.5)	1.49 (11)*
Folate (µg)	290 (130)	360 (230)	320 (170)	380 (220)	310 (150)	350 (200)	317(85)	350 (132)
Vitamin B12 (µg)	-	-	-	-	-	-	-	-
Vitamin C (mg)	68 (45)	83 (68)	81 (55)	85 (66)	73 (68)	83 (61)	168 (84)	95.6 (51)*
Vitamin A (µg)	-	-	-	-	-	-	2032 (1359)	984 (679)*
Carotene (µg)	890 (1990)	990 (2030)	600 (1500)	740 (2440)	420 (1420)	1000 (2350)	11379 (7966)	4386 (3642)**
Vitamin E (mg)	-	-	-	-	-	-	14.3 (7.3)	9 (5)**
Magnesium (mg)	-	-	-	-	-	-	328 (97)	366 (106)
Calcium (mg)	-	-	-	-	-	-	355 (91)	759 (247)**
Iron (mg)	-	-	-	-	-	-	11.1 (2.7)	10.6 (3.2)
Zinc (µg)	-	-	-	-	-	-	11.8 (3.4)	10.3 (3.1)
Selenium (µg)	-	-	-	-	-	-	-	-
Iodine (µg)	-	-	-	-	-	-	64 (23)	145 (40)**

Values are mean (SD) unless otherwise indicated. CRD, carbohydrate-restricted diet; LFD, low-fat diet; RNI, reference nutrient intake; AGHE, Australian Guideline Healthy Eating.
* p<0.05, ** p<0.01, *** p<0.001 compared between groups.
[a] no SD reported.
[b] no statistical comparison between groups
[c] P-values obtained from ANOVA, pairwise comparisons were significantly different (Tukey's Studentised range test)
[d] P-values for mean difference of change (end - baseline) between groups

Table 6. Plasma and urine biomarkers of micronutrients

Biochemical measures	Baseline [a]	End	p-value
Atkins Diet (Johnstone 2011)		**4 weeks [a]**	
Retinol (μg/ml)	0.623	0.456	<0.001
α-Tocopherol (μg/ml)	11.46	9.30	<0.001
β-Cryptoxanthin (μg/ml)	0.065	0.039	<0.001
Lycopene (μg/ml)	0.392	0.244	<0.001
α-Carotene (μg/ml)	0.039	0.035	0.002
β-Carotene (μg/ml)	0.135	0.132	0.004
Xanthophyll (μg/ml)	0.186	0.207	<0.001
Vitamin C (μmol/L)	46.5	51.7	<0.001
Paleolithic diet (Genoni 2016)		**4 weeks**	
Lycopene (μmol/L)	0.61 ± 0.3	0.52 ± 0.2	ns
α-Carotene (μmol/L)	0.39 ± 0.4	0.46 ± 0.2	ns
β-Carotene (μmol/L)	1.54 ± 1.3	2.41 ± 1.8	<0.05
Red cell folate (nmol/L)	894 ± 214	981 ± 300	<0.01
'Isocaloric' CRD (Mardinoglu 2018)		**2 weeks**	
Serum folate (nmol/L)	25.6±4.1	34.5±5.5	<0.001
Paleolithic diet (Manousou 2018)		**6 months [b]**	**End (2 years) [b]**
24-h UIC (μg/L)	68 (IQR 37)	36 (IQR 36), p=0.001	57 (IQR 32), p=0.033
24-h UIE (μg/L)	124.5 (IQR 88)	77 (IQR 65), p=0.001	113.5 (IQR 79), ns
Proportion of subjects according to 24-h UIC, n (%)	**Baseline (n=34)**	**6 months (n=30)**	**p-value [c]**
<50 μg/L	5 (15)	22 (73)	0.001
51-100 μg/L	23 (68)	5 (17)	0.001
101-200 μg/L	6 (18)	3 (10)	ns
>200 μg/L	0	0	

Values are mean ± SD unless otherwise indicated.
CRD, carbohydrate-restricted diet; UIC, urine iodine concentration; UIE, urine iodine excretion; IQR, interquartile range; ns, not significant
[a] no SD reported
[b] p-value compared to baseline
[c] p-value from the longitudinal analysis compared to baseline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for eligibility
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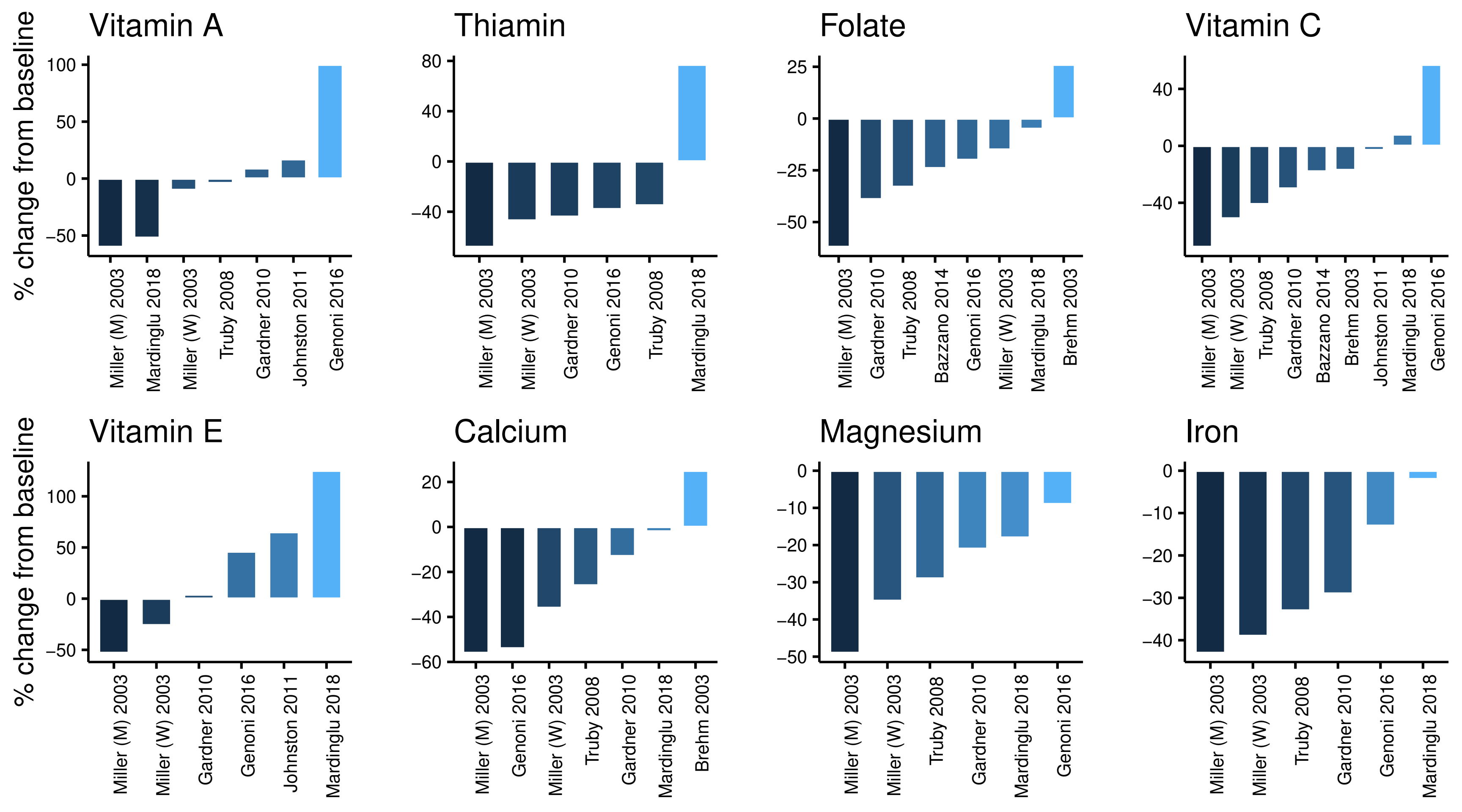
- not relate to CRD (n=15)
- no outcome of interest (n=23)
- duplicated study (n=1)
- co-intervention (n=1)
- comment (n=1)
- no sufficient outcome
information (n=1)
Studies included in
qualitative synthesis
(n = 10)
Included
Studies included in
quantitative synthesis
(meta-analysis)
(n = 0)


Vitamin A
Thiamin
Folate
Vitamin C
Vitamin E
Calcium
Magnesium
Iron
% change from baseline
Miller (M) 2003
Mardinglu 2018
Miller (W) 2003
Truby 2008
Gardner 2010
Johnston 2011
Genoni 2016
Bazzano 2014
Brehm 2003