Effects of quercetin supplementation on cardiometabolic outcomes: a double-blind, placebo-randomized controlled trial.

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Abstract

Quercetin has demonstrated potential cardiovascular and metabolic effects, but its efficacy in healthy adults before the onset of cardiometabolic disease remains unclear. This randomized, double-blind, placebo-controlled parallel-group trial examined whether 20 days of once-daily 400 mg quercetin supplementation improved systolic blood pressure and other cardiometabolic and health-related outcomes compared with placebo. Forty individuals were randomly assigned to receive either Pure quercetin (DoNotAge.org) or placebo. Outcomes were assessed at baseline and after 20 days, and available follow-up data were analysed according to participants' original randomised allocation. Post-intervention values were compared using linear regression models adjusted for the corresponding baseline measurement, with systolic blood pressure designated as the primary outcome; *b* denotes the adjusted between-group mean difference and *d* the corresponding effect size. Thirty-eight participants completed the trial, with one participant lost to follow up in each arm, no adverse events were recorded and mean compliance exceeded 98% in both groups. Adjusted systolic blood pressure was significantly lower following quercetin supplementation than placebo (b = −6.92 mmHg, d = −0.93). Quercetin also

significantly reduced triglyceride concentrations (b = −0.35 mmol/L d = −0.74) and Epworth Sleepiness Scale scores (b = −1.88 points, d = −0.73). These findings indicate that quercetin supplementation may improve systolic blood pressure, triglycerides and sleep efficacy in healthy adults. Larger and longer trials are now required to establish the reproducibility and mechanistic basis of these findings, particularly in populations exhibiting early hypertensive or metabolic abnormalities.

Introduction

Cardiometabolic disease comprises interrelated abnormalities in blood pressure, glucose regulation, lipid metabolism and adiposity, including hypertension, insulin resistance, dyslipidaemia and adverse anthropometric indices (Ahmed et al., 2018; Montes et al., 2021). These abnormalities often develop progressively, contributing to endothelial dysfunction, atherosclerosis and increased risk of cardiovascular disease, type 2 diabetes mellitus and chronic kidney disease. Cardiometabolic conditions impose a substantial global mortality and economic burden (Danaei et al., 2014); cardiovascular disease alone accounted for an estimated 19.8 million deaths in 2022, approximately 32% of all global deaths (World Health Organization, 2025). Interventions that improve cardiometabolic health before overt disease develops are therefore of considerable preventive importance (Arnett et al., 2019).

Pharmacological management of established cardiometabolic disease includes antihypertensive, lipid-lowering, antiplatelet and glucose-lowering treatments (Arnett et al., 2019). Although effective, these therapies may be associated with contraindications, adverse reactions, treatment burden and incomplete adherence (Fuchs & Fuchs, 2025; Tedla et al., 2016). They also do not eliminate residual cardiometabolic risk or directly address all behavioural and nutritional determinants of disease (Burnier and Egan, 2019). These considerations support investigation of dietary bioactive compounds such as quercetin, which has demonstrated favourable short-term tolerability in human supplementation studies (Han et al., 2020), as potentially accessible strategies for modifying cardiometabolic risk factors before pharmacological treatment becomes necessary. Such approaches may therefore have particular relevance to primary prevention in otherwise healthy individuals.

Diet is a major modifiable determinant of cardiometabolic health (Ruskovska et al., 2020). Dietary patterns rich in fruits, vegetables, whole grains, legumes, nuts and unsaturated fats are associated with lower cardiovascular risk and mortality (Aune et al., 2017; Lichtenstein et al., 2021), potentially through effects on blood pressure, lipids, glucose regulation and inflammation (Lichtenstein et al., 2021). However, sustained dietary change can be challenging (Lichtenstein et al., 2021). Supplementation enables a defined quantity of an individual bioactive compound to be administered consistently, thereby permitting its specific physiological effects to be investigated.

Quercetin is a naturally occurring polyphenolic compound belonging to the flavonol subclass of flavonoids (Boots et al., 2008; Larson et al., 2012). Chemically, it is identified as 3,3′,4′,5,7-pentahydroxyflavone, with a molecular formula of $C_{15}H_{10}O_7$. Its structure comprises the characteristic three-ring flavonoid backbone and five hydroxyl groups, which contribute to its redox activity and capacity to interact with enzymes and cellular signalling pathways (Boots et al., 2008). Quercetin occurs naturally in capers, onions, apples, berries, grapes, broccoli and tea, as well as in smaller quantities in red wine and other plant-derived foods (Larson et al., 2012). However, its concentration varies considerably according to plant species, cultivar, growing conditions, storage and food preparation. Habitual dietary intake in Western populations has generally been estimated at approximately 10–40 mg/day, substantially below the supra-nutritional quantities commonly administered in supplementation studies (Larson et al., 2012). For example, raw red onions contain approximately 39 mg of quercetin per 100 g, meaning that approximately 1 kg would be required to provide the 400 mg daily dose administered in the present study (USDA, 2018). Furthermore, whereas whole foods contain quercetin alongside other nutrients and bioactive constituents, supplementation enables the administration of a standardised quantity of the isolated compound. Within foods, quercetin occurs predominantly in glycosylated forms, including quercetin-3-O-glucoside, quercetin-4′-O-glucoside and quercetin-3-O-rutinoside, commonly known as rutin (Larson et al., 2012). In contrast, sugar-free quercetin aglycone is frequently used in commercially available supplements. Following absorption, quercetin undergoes extensive metabolism through glucuronidation, sulfation and methylation, meaning that circulating exposure consists principally of conjugated metabolites rather than free

quercetin aglycone (Graefe et al., 2001; Manach et al., 2005). These metabolites are therefore likely to mediate the physiological effects of supplementation through redox regulation, modulation of enzyme activity and intracellular signalling pathways (Boots et al., 2008).

Evidence for the proposed cardiovascular and cardiometabolic mechanisms of quercetin derives predominantly from in vitro investigations involving cultured cells and isolated vascular preparations, alongside in vivo experiments in animal models, with comparatively limited mechanistic confirmation in humans (Boots et al., 2008; Larson et al., 2012; Li et al., 2016). These experimental investigations suggest that quercetin may attenuate oxidative stress and inflammatory signalling, inhibit angiotensin-converting enzyme activity, modulate the renin–angiotensin–aldosterone system, increase endothelial nitric oxide bioavailability, reduce endothelin-1 activity and promote vascular smooth-muscle relaxation (Larson et al., 2012; Li et al., 2016). Additional experimental evidence suggests potential effects on lipid oxidation, glucose metabolism, platelet activity and the expression of genes involved in inflammatory and vascular regulation (Boots et al., 2008; Larson et al., 2012; Li et al., 2016). Supporting these proposed vascular mechanisms, Sánchez et al. (2006) demonstrated reduced vascular NADPH oxidase activity and increased endothelial nitric oxide synthase activity in spontaneously hypertensive rats following quercetin administration. Similarly, Duarte et al. (2001) reported reductions in systolic, diastolic and mean arterial blood pressure of approximately 18%, 23% and 21%, respectively, alongside improved endothelium-dependent relaxation and reductions in indices of oxidative stress, cardiac hypertrophy and renal hypertrophy in spontaneously hypertensive rats following five weeks of quercetin administration.

Human intervention studies have yielded less consistent findings, with favourable blood-pressure responses often confined to particular subgroups. Edwards et al. (2007) administered 730 mg/day for 28 days to adults with prehypertension or stage 1 hypertension in a placebo-controlled crossover trial. Although systolic and diastolic blood pressure fell by approximately 7 and 5 mmHg, respectively, from baseline among participants with stage 1 hypertension, significant between-treatment differences were not reported; no effect was observed in prehypertension, and metabolic biomarkers were unchanged. Egert et al. (2009) investigated 150 mg/day for six weeks in 93 overweight or obese adults with metabolic syndrome traits. Systolic

blood pressure decreased by 2.6 mmHg overall, but the reduction relative to placebo was significant only in participants aged 25–50 years. Oxidised LDL cholesterol also decreased, whereas most metabolic outcomes were unchanged and HDL cholesterol declined.

Brüll et al. (2015) reported a placebo-adjusted reduction of 3.9 mmHg in 24-hour systolic blood pressure among participants with stage 1 hypertension following six weeks of 162 mg/day quercetin from onion-skin extract, but not among those with prehypertension; other vascular and metabolic indices were unchanged. Conversely, Dower et al. (2015) found no improvement in blood pressure, endothelial function or insulin resistance following four weeks of quercetin-3-glucoside in adults with elevated systolic blood pressure. In pre-hyperuricaemic men, 500 mg/day for four weeks reduced plasma uric acid without affecting blood pressure or fasting glucose (Shi and Williamson, 2016). Lee et al. (2011) observed favourable changes in lipids, blood pressure and glucose among male smokers receiving quercetin-rich onion-peel extract, although between-group effects were not reported for most outcomes. Finally, single doses of 200 or 400 mg quercetin increased brachial artery diameter without altering blood pressure over five hours in normotensive, normocholesterolaemic adults (Pérez et al., 2014). Collectively, these trials suggest potential vascular benefits but inconsistent cardiometabolic effects, with substantial variation in participant characteristics, supplement formulation and exposure duration.

Meta-analytic findings also suggest modest blood-pressure effects against a background of clinical heterogeneity. Serban et al. (2016) pooled seven trials involving healthy adults and populations with cardiometabolic risk or established conditions, including women with rheumatoid arthritis or type 2 diabetes, and reported reductions of 3.04 mmHg in systolic and 2.63 mmHg in diastolic blood pressure. However, both estimates became non-significant after removal of an influential trial, and randomisation and allocation concealment were often insufficiently reported. Huang et al. (2020) similarly found a 3.09-mmHg reduction in systolic blood pressure across studies differing in dose, duration and population. Popiolek-Kalisz and Fornal (2022) reported reductions of 2.38 mmHg overall and 1.82 mmHg in normotensive participants, whereas effects on diastolic blood pressure were restricted to those with prehypertension or hypertension. Neither of these latter blood-pressure meta-analyses provided an outcome-specific GRADE certainty assessment. An umbrella

review found modest reductions in systolic blood pressure and fasting insulin, although heterogeneity was substantial (I^2 = 88.3% and 75.0%, respectively); no significant effects were identified for other major cardiometabolic outcomes, and certainty ranged from very low to moderate (Arabi et al., 2023). Although the contributing trials included both men and women, including some studies restricted to one sex, the available pooled evidence does not establish whether the cardiometabolic effects of quercetin differ between sexes (Serban et al., 2016; Huang et al., 2020; Popiolek-Kalisz and Fornal, 2022).

Taken together, the evidence is most consistent for a modest reduction in systolic blood pressure, making this a pertinent primary outcome, whereas effects on lipid, glycaemic and anthropometric indices remain uncertain. Moreover, findings from studies combining healthy and at-risk populations and employing different quercetin preparations, including onion-derived extracts (Brüll et al., 2015; Lee et al., 2011), cannot establish the effects of isolated quercetin specifically in otherwise healthy adults. Cardiometabolic abnormalities may arise before diagnostic thresholds are reached (Harding et al., 2016; Arnett et al., 2019), providing a rationale for investigating supplementation in a primary-prevention context without the additional influences of established disease or pharmacological treatment. To our knowledge, no placebo-controlled, parallel-group trial has evaluated systolic blood pressure as a prespecified primary outcome alongside a broad range of cardiometabolic and health-related outcomes in otherwise healthy adults. The present trial therefore examined the effects of 400 mg of isolated quercetin administered once daily for 20 days.

Rationale

A placebo-controlled investigation incorporating systolic blood pressure alongside anthropometric, lipid, glycaemic and resting cardiovascular outcomes may establish whether the proposed physiological effects of quercetin translate into measurable short-term changes in healthy adults. Resting heart rate was included as a complementary measure of cardiovascular function, given its established association with cardiovascular risk and the opportunity to examine whether any blood-pressure response was accompanied by a change in cardiac rate (Zhang et al., 2016). Sleep-related outcomes were also examined because sleep disturbances are associated with adverse cardiometabolic health (Matricciani et al., 2021), allowing the study to

evaluate sleep quality, daytime sleepiness and insomnia symptoms alongside traditional cardiometabolic indices.

Aim

The aim of the current study was to investigate the effects of 20 days of once-daily 400 mg quercetin supplementation on cardiometabolic and other health-related outcomes in healthy adults compared with placebo. The primary objective was to determine the effect on systolic blood pressure; secondary objectives were to examine anthropometric measures, cardiometabolic biomarkers, diastolic blood pressure, resting heart rate, psychological wellbeing and sleep-related outcomes.

Hypotheses

It was hypothesised that quercetin supplementation would reduce systolic blood pressure relative to placebo and favourably influence anthropometric, cardiometabolic, resting cardiovascular, psychological wellbeing and sleep-related measures.

Materials and methods

Study design and setting

This parallel-group randomized controlled trial was reported in accordance with CONSORT guidance (Hopewell et al., 2025). The trial was conducted at the University of Lancashire in Preston, Lancashire, north-west England. Consistent with our previous supplementation trial, the study employed a 20-day, randomized, placebo-controlled, parallel-group design (Sinclair et al., 2023) (Figure 1). Following eligibility screening and enrolment, participants were individually randomized using Random Allocation Software to receive either quercetin or placebo. Screening involved a structured review of participants' health histories to confirm the inclusion and exclusion criteria, including assessment of major comorbidities that could influence study outcomes or participant safety.

Study outcomes were assessed at baseline and following 20 days of supplementation. Consistent with previous trials involving cardiometabolic indices, the primary outcome was the between-group difference in systolic blood pressure at 20 days after adjustment for baseline values (Sinclair et al., 2021; Kimble et al., 2021). Secondary

outcomes comprised between-group differences in anthropometric measurements, dietary intake, cardiometabolic biomarkers, diastolic blood pressure, resting heart rate, psychological wellbeing and sleep-related indices. All experimental visits were conducted in the morning following an overnight fast of at least 10 h. Participants were instructed to arrive adequately hydrated and to avoid strenuous exercise, alcohol and nutritional supplements for 24 h, and caffeine for 12 h, before each visit.

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Inclusion criteria

Participants were eligible for inclusion if they were aged 18–64 years, were generally healthy, had a body mass index (BMI) < 30 kg/m² and were able to provide informed consent.

Exclusion criteria

Participants were excluded if they were pregnant; had diagnosed diabetes mellitus, another metabolic condition or uncontrolled hypertension; had a known allergy or intolerance to quercetin or any ingredient contained in the study supplements; habitually used quercetin-containing supplements; or regularly used prescribed medication or antioxidant supplements.

Sample size

Existing quercetin trials have employed either crossover designs or recruited participants with established cardiometabolic risk, and therefore did not provide a transferable standardized between-group effect estimate for the present trial (Edwards et al., 2007; Egert et al., 2009; Brüll et al., 2015). In the absence of a suitably comparable parallel-group trial examining the effects of quercetin supplementation on systolic blood pressure in healthy adults; a pragmatic a priori sample-size calculation was based on the standardized systolic blood-pressure effect observed in our previous 20-day supplementation trial conducted in the same target population (Sinclair et al., 2023). Assuming an expected effect size of d = 0.94, a two-sided α of 0.05 and 80% statistical power, 18 participants were required in each trial arm. Taking into account an expected attrition of 10%, that was conservatively selected taking into account the loss to follow rates observed in our previous trials (Sinclair et al., 2022; Sinclair et al.,

2023; Sinclair et al., 2026), this revealed that 20 participants would be necessary in each trial arm, with a total N of 40.

Participants and recruitment

Recruitment commenced on 5th January 2025 and continued until 4th June 2026, with data collection concluding on 13th August 2026. Men and women from a range of racial and ethnic backgrounds residing in Preston and the surrounding areas were recruited through advertisements placed on public noticeboards and distributed via social media. Individuals interested in participating were invited to contact the research team to obtain further information, discuss the study procedures and ask any questions before enrolment. Written informed consent was obtained from all participants before their involvement in any study procedures.

Ethical approval and trial registration

This study was granted ethical approval by the University of Lancashire HEALTH Ethics Committee (HEALTH 0016), and all participants submitted written informed consent before participating, adhering to the principles stated in the Declaration of Helsinki. The trial was preregistered on clinicaltrials.gov (NCT06230861).

Dietary intervention

Following completion of the baseline data-collection session, participants were provided with either Quercetin or placebo capsules for 20 days. Participants allocated to the Quercetin arm were instructed to consume one capsule containing 400 mg of Pure Quercetin (DoNotAge.org) each morning with 250 mL of water. The active supplement consisted of Quercetin powder enclosed within a vegetable-cellulose capsule, with no additional fillers reported by the manufacturer. Participants allocated to the placebo arm followed the same supplementation schedule but received an identical vegetable-cellulose capsule containing cornstarch and no Quercetin. The trial was double-blind: participants and researchers responsible for supplement distribution, data collection and outcome assessment were unaware of treatment allocation throughout the intervention. An independent researcher prepared and coded the supplement containers, and the allocation code was not released until data collection, and the primary analysis had been completed. The active and placebo

capsules were identical in appearance and were supplied in identical coded containers.

The 400 mg/day dose represented a commercially available single-capsule regimen and was lower than doses employed in previous human trials. These included 500 mg/day for four weeks in healthy adults (Shi and Williamson, 2016) and 730 mg/day for 28 days in adults with prehypertension or stage 1 hypertension (Edwards et al., 2007). Furthermore, a dose-escalation safety trial found that Quercetin was tolerated at doses of up to 2,000 mg/day for one week, with no severe study-drug-related adverse events (Han et al., 2020). Collectively, this evidence supported the tolerability of the comparatively conservative dose of 400 mg/day administered during the present 20-day intervention.

Throughout the study, participants were instructed to maintain their habitual dietary intake and exercise routines and to refrain from consuming any additional Quercetin-containing supplements. Participants completed a 4-day dietary diary covering the four consecutive days immediately preceding both the baseline and 20-day assessments, consistent with our previous supplementation studies (Sinclair et al., 2022; Sinclair et al., 2025; Sinclair et al., 2026). All four recorded days were included in the nutritional analysis, with mean daily dietary intakes calculated using WinDiets Nutritional Analysis Software Suite Version 1.0 (Robert Gordon University, Aberdeen, UK). This enabled daily energy, total fat, saturated fatty acid, protein, carbohydrate, sugar, fibre, alcohol, vitamin A, thiamine, riboflavin, niacin, vitamin B6, vitamin B12, folate, vitamin C, vitamin D, vitamin E, calcium, magnesium, salt, iron and zinc intakes to be examined and potential dietary changes during the intervention to be monitored.

At the post-intervention data-collection session, participants returned all unused capsules to the laboratory to enable percentage compliance to be calculated. Blinding efficacy was assessed by asking participants which trial arm they believed they had been allocated to. Loss to follow-up and adverse events were monitored and recorded in both trial arms throughout the intervention.

Data collection

Blood pressure and resting heart rate

Blood pressure and resting heart rate were measured with participants seated in an upright position. Systolic blood pressure, diastolic blood pressure and resting heart rate were recorded using a non-invasive automated blood pressure monitor (OMRON M2, Kyoto, Japan), in accordance with the recommendations of the European Society of Hypertension (Stergiou et al., 2021). Three measurements were obtained at 1-min intervals (Pickering et al., 2005), with the mean of the final two readings used for analysis.

Anthropometric measurements

Body mass (kg) and stature (m) were measured without footwear and used to calculate BMI (kg/m²). Stature was measured using a stadiometer (Seca, Hamburg, Germany), and body mass was recorded using calibrated weighing scales (Seca 875, Hamburg, Germany). Body composition was assessed using a phase-sensitive multifrequency bioelectrical impedance analyser (Seca mBCA 515, Hamburg, Germany), from which body fat percentage (%) and fat mass (kg) were quantified (Bosy-Westphal et al., 2017). Waist circumference was measured at the midpoint between the inferior margin of the final rib and the iliac crest. Hip circumference was measured around the pelvis at the point of maximum protrusion of the buttocks, without compression of the underlying soft tissues (Czernichow et al., 2011). These measurements were subsequently used to calculate the waist-to-hip ratio.

Haematological testing

Capillary blood samples were collected by finger-prick using a disposable lancet after the sampling site had been cleaned with a 70% ethanol wipe. Capillary triglyceride, total cholesterol and glucose concentrations (mmol/L) were measured immediately using three handheld analysers (MultiCareIn, MultiCare Medical, USA). LDL cholesterol (mmol/L) was estimated from total cholesterol and triglyceride concentrations using the formula described by Anandaraja et al. (2005). HDL cholesterol (mmol/L) was subsequently calculated by rearranging the equation developed by Chen et al. (2010) to make HDL cholesterol the subject of the formula. These estimation approaches have demonstrated strong correlations with corresponding lipoprotein concentrations determined using immunoassay techniques ($r = 0.948–0.970$) (Anandaraja et al., 2005; Chen et al., 2010). Total cholesterol-to-HDL cholesterol and LDL cholesterol-to-HDL cholesterol ratios were calculated in

accordance with Millán et al. (2009). Finally, the triglyceride-glucose index was calculated as the natural logarithm of fasting triglyceride concentrations multiplied by fasting glucose concentrations and divided by two: ln [triglycerides (mg/dL) × glucose (mg/dL)/2] (Guerrero-Romero et al., 2010). Concentrations recorded in mmol/L were converted to mg/dL before calculation of the triglyceride-glucose index.

Questionnaires

Sleep disruption has been associated with adverse cardiometabolic health (Matricciani et al., 2021). Overall sleep quality was therefore assessed using the Pittsburgh Sleep Quality Index (Buysse et al., 1989), daytime sleepiness using the Epworth Sleepiness Scale (Smith et al., 2008), and insomnia symptoms using the Insomnia Severity Index (Morin et al., 2011). Collectively, these questionnaires provided complementary assessments of sleep quality, daytime sleepiness and insomnia symptom severity. The Pittsburgh Sleep Quality Index contains 19 individual items that generate seven component scores: subjective sleep quality, sleep latency, sleep duration, sleep efficiency, sleep disturbance, use of sleep medication and daytime dysfunction. These components produce a global score ranging from 0 to 21, with lower scores indicating better sleep quality. The Epworth Sleepiness Scale presents eight everyday situations in which the likelihood of falling asleep is rated from 0 to 3. Responses are summed to produce a total score ranging from 0 to 24, with higher scores indicating greater daytime sleepiness. The Insomnia Severity Index contains seven items in which sleep-related difficulties are rated from 0 to 4. The responses are summed to provide a total score ranging from 0 to 28, with higher scores representing greater insomnia severity.

As psychological wellbeing may be impaired in individuals with cardiometabolic disease (Gheshlagh et al., 2016), functional health and general wellbeing were assessed using the COOP/WONCA questionnaire (Bentsen et al., 1999), depressive symptoms using the Beck Depression Inventory (Wang and Gorenstein, 2013), and state and trait anxiety using the State-Trait Anxiety Inventory (Spielberger et al., 1983). Together, these instruments provided a multidimensional assessment of psychological wellbeing. The COOP/WONCA questionnaire comprises six scales assessing physical fitness, feelings, daily activities, social activities, change in health and overall health. Each scale is scored from 1 to 5, and the final score represents the mean of the six scales, with higher scores indicating poorer functional health. The Beck Depression

Inventory contains 21 items in which depressive symptoms are rated from 0 to 3. Item scores are summed to produce a total score ranging from 0 to 63, with higher scores indicating more severe depressive symptoms. The State-Trait Anxiety Inventory contains 20 items assessing state anxiety and a further 20 items assessing trait anxiety. Each item is rated from 1 to 4, producing separate state- and trait-anxiety scores ranging from 20 to 80, with higher scores indicating greater anxiety.

Statistical analysis

Baseline demographic and clinical characteristics were summarised descriptively for each trial arm. In accordance with CONSORT guidance, formal hypothesis testing of baseline differences was not undertaken (Hopewell et al., 2025). Continuous variables are reported as means with their corresponding standard deviations, whereas categorical variables are presented as percentages (%) or frequencies (N). Between-arm differences in compliance (%) were examined using linear regression models with trial arm entered as a fixed factor.

Intervention outcomes were analysed according to participants' original randomised allocation using an available-case approach, whereby participants without corresponding follow-up measurements were excluded from the relevant baseline-adjusted analyses. Missing follow-up values were not imputed, as carrying forward baseline observations would require an unverified assumption of no change and would not account for the uncertainty associated with the missing outcomes. Consistent with our previously published supplementation trial (Sinclair et al., 2026), treatment effects for continuous outcomes were estimated as between-arm differences at 20 days after adjustment for the corresponding baseline value of the same outcome. Post-intervention measurements were therefore analysed using linear regression models with trial arm entered as a fixed factor and the relevant baseline measurement included as a covariate. This approach is recommended for randomised controlled trials in which continuous outcomes are assessed at baseline and follow-up (Vickers & Altman, 2001; Twisk et al., 2018). For each analysis, the adjusted mean difference between trial arms at 20 days (*b*), corresponding 95% confidence interval and associated P-value are presented. Effect sizes were calculated as semi-standardised adjusted mean differences (*d*) by dividing b by the residual standard deviation from

the fitted regression model (Shieh, 2023). Effect sizes were interpreted as 0.2 = small, 0.5 = medium and 0.8 = large (Cohen, 1988).

Participant blinding was assessed using a one-way chi-square (χ^2) goodness-of-fit test. Two-way Pearson chi-square tests of independence were applied, where estimable, to bivariate cross-tabulations comparing trial arms. These analyses examined between-arm differences in loss to follow-up and adverse-event incidence. Monte Carlo simulation was used to obtain probability values for chi-square analyses. All statistical analyses were performed using SPSS version 31 (IBM Inc., SPSS, Chicago, IL, USA), with statistical significance accepted at $P \leq 0.05$ for all hypothesis tests conducted throughout the analysis.

Results

Baseline demographic, anthropometric, and health information

Baseline characteristics of participants are presented in Table 1.

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Compliance, loss to follow up, and adverse events

Total trial completion numbers were Quercetin N = 19 and placebo N = 19, with one participant lost to follow-up from each trial arm (Figure 1). The Pearson chi-square test was non-significant, indicating no difference between trial arms in loss to follow-up ($\chi^2_{(1)} = 0.000$, P = 1.000). No adverse events were reported in either group. Therefore, a between-group chi-square analysis of adverse events could not be performed. Mean compliance was 98.68 ± 3.27% in the Quercetin arm and 99.74 ± 1.15% in the placebo arm, with no statistically significant difference between groups (P = 0.198).

Blinding efficacy

Of the 38 participants that completed the trial 52.6% (N = 20) correctly identified their designated trial arm. The Chi-squared test was non-significant (P = 0.746) indicating that an effective blinding strategy was adopted.

Anthropometric measurements

Adjusted post-intervention anthropometric measurements at 20 days did not differ significantly between the placebo and Quercetin trial arms after controlling for baseline values (P = 0.254–0.948) (Table 2).

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Blood pressure and resting heart rate

Adjusted post-intervention systolic blood pressure at 20 days was significantly lower in the Quercetin arm than in the placebo arm (*b* = −6.92 mmHg, 95% CI = −11.84 to −2.00, P = 0.007, *d* = −0.93). No other statistically significant differences were observed (P = 0.159–0.340) (Table 3).

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Haematological testing

Adjusted post-intervention triglyceride concentrations (*b* = −0.35 mmol/L, 95% CI = −0.65 to −0.04, P = 0.029, *d* = −0.74) at 20 days were significantly lower in the Quercetin arm than in the placebo arm. No other statistically significant differences were observed (P = 0.084–0.742) (Table 4).

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Questionnaires

Adjusted post-intervention Epworth Sleepiness Scale scores at 20 days were significantly lower in the Quercetin arm than in the placebo arm (*b* = −1.88, 95% CI = −3.58 to −0.18, P = 0.031, *d* = −0.73). No other statistically significant differences were observed (P = 0.087–0.911) (Table 5).

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Diet diaries

Across all dietary intake measures, adjusted post-intervention values at 20 days were similar between the placebo and Quercetin trial arms after controlling for baseline values, with no statistically significant between-group differences observed (P = 0.078–0.957) (Table 6).

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Discussion

The current randomized, double-blind, placebo-controlled parallel-group trial aimed to examine the effects of 20 days of once-daily 400 mg quercetin supplementation on cardiometabolic and other health-related outcomes in healthy adults. The primary objective was to determine whether quercetin supplementation reduced systolic blood pressure compared with placebo, while the secondary objectives were to examine its influence on additional cardiovascular, anthropometric, haematological, psychological-wellbeing and sleep-related indices. To our knowledge, this represents the first parallel-group placebo-controlled trial to examine systolic blood pressure as the prespecified primary outcome while concurrently evaluating a broader profile of cardiometabolic and health-related outcomes in this population. The findings supported the primary hypothesis and partially supported the secondary hypothesis, as quercetin significantly reduced systolic blood pressure, triglyceride concentrations and daytime sleepiness compared with placebo. No significant between-group differences were observed for the remaining outcomes.

In relation to the primary outcome, adjusted systolic blood pressure at 20 days was significantly (6.92 mmHg) lower in the quercetin arm than in the placebo arm, representing a large effect (d = −0.93). This finding agrees closely with Edwards et al. (2007), who observed an approximately 7-mmHg reduction following 28 days of 730 mg/day quercetin supplementation in participants with stage 1 hypertension, although no corresponding effect was evident in their prehypertensive subgroup. The magnitude of the present effect was greater than the 2.6-mmHg reduction reported by Egert et al. (2009) after six weeks of 150 mg/day quercetin in overweight adults with a high-cardiovascular-risk phenotype and the 3.9-mmHg treatment difference in 24-h systolic blood pressure observed by Brüll et al. (2015) among their hypertensive subgroup. The present findings contrast with Dower et al. (2015), who found no reduction in blood pressure after four weeks of 160 mg/day quercetin-3-glucoside in adults with systolic blood pressure between 125 and 160 mmHg. The current treatment effect was larger than the significant meta-analytic reductions in systolic blood pressure reported by Serban et al. (2016; −3.04 mmHg), Huang et al. (2020; −3.09 mmHg), Popiolek-Kalisz and Fornal (2022; −2.38 mmHg) and Arabi et al. (2023; −1.90 mmHg).

Several mechanisms may explain the quercetin-mediated reduction in systolic blood pressure, including attenuation of vascular oxidative stress through reduced NADPH-oxidase activity, preservation of endothelial nitric oxide synthase activity and nitric oxide bioavailability, and direct relaxation of vascular smooth muscle (Sánchez et al., 2006; Larson et al., 2012). Modulation of angiotensin-converting enzyme activity and endothelin-1 signalling has also been proposed. However, human findings remain inconclusive: Edwards et al. (2007) found no accompanying reduction in systemic oxidative-stress markers, while Brüll et al. (2015) observed no changes in endothelial function, angiotensin-converting enzyme activity, endothelin-1 or indices of oxidation and inflammation. Importantly, the observed reduction in systolic blood pressure may be clinically meaningful if sustained longitudinally. A meta-analysis of pharmacological trials demonstrated that each sustained 5-mmHg reduction in systolic blood pressure was associated with an approximately 10% lower risk of major cardiovascular events, irrespective of baseline blood pressure or previous cardiovascular disease (Blood Pressure Lowering Treatment Trialists' Collaboration, 2021). Although these findings cannot be directly extrapolated to the present short-term supplementation trial, the magnitude of the observed 6.92-mmHg reduction suggests that quercetin may have clinically relevant cardiovascular benefits if such effects are maintained over longer periods. Given that elevated blood pressure represents a leading modifiable contributor to cardiovascular morbidity and mortality (Oparil et al., 2018; Forouzanfar et al., 2017), longer-duration trials are warranted to establish the persistence and clinical significance of these findings.

In support of our secondary hypothesis, triglyceride concentrations were significantly (0.35 mmol/L) lower in the quercetin arm than in the placebo arm at 20 days, with a moderate effect size (d = −0.74). Importantly, dietary intake was also monitored throughout the intervention, and no statistically significant between-group differences were observed across the measured dietary variables at 20 days after adjustment for baseline values (P = 0.078–0.957; Table 6). These findings suggest that differences in recorded dietary intake are unlikely to account for the observed reductions in triglyceride concentrations and systolic blood pressure, although dietary influences cannot be definitively excluded. This finding is notable because several previous trials (Edwards et al., 2007; Egert et al., 2009; Brüll et al., 2015), did not identify significant changes in triglyceride concentrations. The present reduction was similar to meta-

analysis (0.28 mmol/L) reported by Sahebkar (2017) in higher-dose, longer-duration trials and that (0.38 mmol/L) identified by Huang et al. (2020) after ≥8 weeks, despite the lower dose and shorter duration used here. However, neither found a significant overall effect, consistent with Tabrizi et al. (2020). Potential mechanisms have principally been identified in preclinical models. Notably quercetin has been shown to increase hepatic lipid ω-oxidation and reduce circulating lipid concentrations in mice (Hoek-van den Hil et al., 2013), whilst diabetic-rat models suggest that it may suppress hepatic lipogenic signalling, restore peroxisome proliferator-activated receptor-α activity and attenuate thioredoxin-interacting protein/NLRP3-mediated inflammation and lipid accumulation (Wang et al., 2013). Importantly, elevated triglycerides are associated with atherosclerotic cardiovascular risk (Yuan et al., 2007), and reductions in triglycerides have been associated with fewer major vascular events across lipid-lowering trials (Nordestgaard and Varbo, 2014; Marston et al., 2019). As such, the findings from this trial lend support to the concept that quercetin supplementation may be important in the preventative management of hypertriglyceridemia.

In further support of our secondary hypothesis, quercetin supplementation also significantly reduced Epworth Sleepiness Scale scores compared with placebo with a moderate effect size (d = −0.73). Human evidence concerning quercetin and sleep remains limited. Consistent with our findings, eight weeks of lecithin-based quercetin (500 mg/day) improved sleep quality in individuals with chronic fatigue (Rondanelli et al., 2023), while the same dose increased self-reported night-time sleep in an open-label randomized trial of adults with type 2 diabetes (Mantadaki et al., 2024). Preclinical evidence indicates that quercetin can alter sleep architecture, with administration in rats increasing non-rapid-eye-movement sleep and modifying rapid-eye-movement sleep partly through γ-aminobutyric acid type A receptor signalling (Kambe et al., 2010). However, the dose and route employed in that animal study preclude direct translation to oral human supplementation, and neither neurological signalling nor sleep architecture was examined in this study. Regardless, poor sleep quality is associated with adverse cardiometabolic health (Matricciani et al., 2021) and carries substantial health and societal costs (Grandner, 2018); therefore, quercetin may represent a useful supplementary approach for supporting sleep-related health.

Overall, the current randomized, double-blind, placebo-controlled trial demonstrated effective blinding, excellent compliance and high and balanced retention. No adverse

events were reported in either trial arm, consistent with previous human supplementation investigations demonstrating favourable short-term tolerability of quercetin (Han et al., 2020). Nevertheless, adverse-event monitoring should remain an integral component of future investigations, particularly those involving larger samples and longer supplementation periods. These findings indicate that 400 mg/day quercetin was well-tolerated and low cost (approximately £26 for 60 capsules) intervention and can be easily incorporated into habitual dietary patterns. Notably, this trial noted adjusted systolic blood pressure and triglyceride concentrations were significantly lower in the quercetin arm, indicating that supplementation may represent a practical approach for supporting cardiometabolic health. Importantly, whilst other supplementary modalities such as Montmorency tart cherry and blueberry juice have also demonstrated beneficial effects on blood pressure and other cardiometabolic outcomes (Sinclair et al., 2022; Chai et al., 2018), these products contribute additional sugar (≈15 g per serving) and dietary energy (≈80 kcal per serving). In contrast, the quercetin capsules administered in the present study contained no added sugars and provided a negligible estimated energy contribution (approximately 1.6 kcal per capsule, based on 400 mg of quercetin and an assumed energy value of 4 kcal/g). Quercetin supplementation may therefore offer a practical alternative for supporting blood-pressure and lipid control while minimising additional dietary sugar and energy intake, thereby facilitating the maintenance of a healthy body weight.

As with any randomized controlled trial, this investigation is not without limitations. Participants were generally healthy and exhibited predominantly normal cardiometabolic values at baseline, potentially creating floor effects and limiting generalizability to populations with established cardiometabolic abnormalities. Furthermore, blood pressure was assessed using clinic-based measurements, which cannot characterise variations throughout the day. Future trials may therefore benefit from 24-h ambulatory monitoring, which provides a more comprehensive representation of systemic blood pressure and reduces the influence of white-coat hypertension (Pena-Hernandez et al., 2020). Although several pathways have been postulated to explain the cardiometabolic effects of quercetin; plasma quercetin metabolites, endothelial function, nitric oxide availability, oxidative stress and hepatic lipid-metabolism markers were not assessed. Consequently, supplementation exposure could not be biochemically confirmed and the mechanisms underlying the

observed improvements remain unclear. Future investigations should characterise these pathways more directly and determine whether they can be harnessed to optimise the health-related effects of quercetin. Objective monitoring also represents an important priority, as physical activity was not controlled for and could influence blood pressure, triglycerides, resting heart rate and sleep-related outcomes, whilst all sleep-related measurements were based on self-report. Subsequent trials should incorporate continuous actigraphy to quantify both physical activity and sleep, alongside polysomnography where feasible, to establish whether the reduction in self-reported daytime sleepiness corresponds to objective improvements in sleep duration, efficiency or architecture. Finally, owing to the observed reductions in systolic blood pressure and triglycerides, particular attention should be directed towards individuals with elevated blood pressure or stage 1 hypertension, those exhibiting two emerging metabolic-syndrome components consistent with a pre-metabolic-syndrome phenotype, and those with established metabolic syndrome. As elevated blood pressure and triglycerides represent two defining components of metabolic syndrome (Alberti et al., 2009), such studies would determine whether quercetin can improve or delay progression towards metabolic syndrome or support its management once established.

Conclusion

The current randomized, double-blind, placebo-controlled trial demonstrated that 20 days of once-daily 400 mg Pure quercetin supplementation from DoNotAge.org significantly reduced systolic blood pressure compared with placebo, supporting the primary hypothesis. The secondary hypothesis was also supported in relation to triglyceride concentrations and sleep efficacy, although no significant effects were observed for the remaining cardiometabolic and health-related outcomes. The intervention was associated with excellent compliance, effective blinding, high retention and no reported adverse events. The adjusted between-group differences of −6.92 mmHg for systolic blood pressure, −0.35 mmol/L for triglyceride concentrations and −1.88 points for Epworth Sleepiness Scale scores indicate that quercetin supplementation may have short-term cardiometabolic and health-related benefits. Larger and longer trials are now required to establish the reproducibility and mechanistic basis of these findings, particularly in populations exhibiting early hypertensive or metabolic abnormalities.

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Author Contributions

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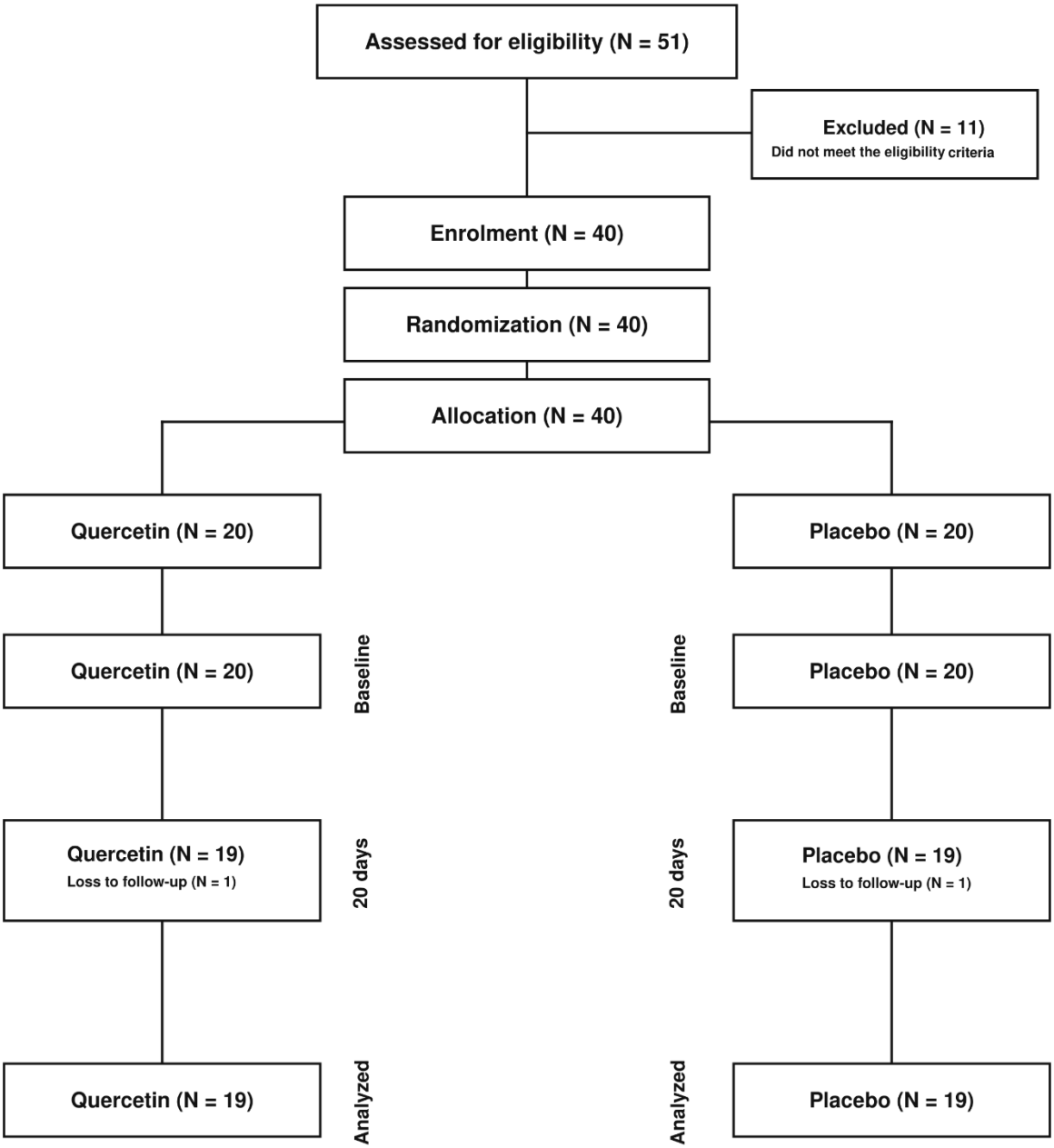
Figure labels



Note: Forty participants were randomised (20 per trial arm). One participant in each arm was lost to follow-up and did not provide 20-day outcome data. Consequently, the baseline-adjusted outcome analyses included 38 participants (19 per arm), analysed according to their original randomised allocation.

Figure 1: CONSORT flow diagram.

988 Table 1. Baseline demographic and participant characteristics

	Total		Placebo		Quercetin	
	Mean	*SD*	**Mean**	*SD*	**Mean**	*SD*
Sex	Male = 35%		Male = 35%		Male = 35%	
	Female = 65%		Female = 65%		Female = 65%	
Age (years)	32.98	12.21	33.50	13.28	32.45	11.35
Mass (kg)	72.38	13.31	74.48	15.25	70.27	11.04
Stature (cm)	173.60	10.60	175.66	12.32	171.53	8.36
BMI (kg/m²)	23.89	2.92	23.94	2.94	23.84	2.98
Smoking status	Yes = 5%		Yes = 5%		Yes = 5%	
	No = 87.5%		No = 85%		No = 90%	
	Previous = 7.5%		Previous = 10%		Previous = 5%	
Ethnicity	Caucasian = 85% Asian = 10% Black = 5%		Caucasian = 90% Asian = 0% Black = 10%		Caucasian = 80% Asian = 20% Black = 0%	
Alcohol (units/week)	2.71	5.34	2.64	6.55	2.77	3.96
Education	College = 27.5% A-level = 17.5% Bachelor's = 15% Postgraduate = 15% Doctoral = 10% High school = 5% Vocational = 10%		College = 35% A-level = 15% Bachelor's = 10% Postgraduate = 20% Doctoral = 5% High school = 5% Vocational = 10%		College = 20% A-level = 20% Bachelor's = 20% Postgraduate = 10% Doctoral = 15% High school = 5% Vocational = 10%	
Employment status	Full time = 57.5% Part time = 5% Student = 27.5%		Full time = 50% Part time = 10% Student = 40%		Full time = 65% Part time = 0% Student = 15%	

	Total		Placebo		Quercetin	
	Mean	*SD*	**Mean**	*SD*	**Mean**	*SD*
	Part-time work / full-time student = 10%		Part-time work / full-time student = 0%		Part-time work / full-time student = 20%	
Marital status	Married = 32.5% Single = 35% Civil partnership = 30% Divorced = 2.5%		Married = 35% Single = 35% Civil partnership = 25% Divorced = 5%		Married = 30% Single = 35% Civil partnership = 35% Divorced = 0%	
Children	0 = 60% 1 = 10% 2 = 22.5% 3 = 7.5%		0 = 50% 1 = 15% 2 = 30% 3 = 5%		0 = 70% 1 = 5% 2 = 15% 3 = 10%	

Notes: *Continuous variables are presented as means and standard deviations (SD), and categorical variables as percentages. Baseline characteristics are presented for all 40 randomised participants (20 per trial arm).* ***Abbreviations:*** *BMI = body mass index; SD = standard deviation.*

Table 2: Anthropometric outcomes at baseline and Day 20.

	Placebo				**Quercetin**				***b***	**95% CI**		**P-value**	***d***
	Baseline		**20-days**		**Baseline**		**20-days**						
	Mean	**SD**	**Mean**	**SD**	**Mean**	**SD**	**Mean**	**SD**		**Lower**	**Upper**		
Mass (kg)	74.48	15.25	74.61	15.51	70.27	11.04	70.56	10.38	-0.05	-0.84	0.73	0.891	-0.05
Body mass index (kg/m²)	23.94	2.94	23.85	2.94	23.84	2.98	23.79	2.84	0.01	-0.24	0.26	0.948	0.02
Body fat (%)	23.80	6.53	23.20	6.29	23.89	8.57	24.88	8.81	0.83	-0.97	2.62	0.355	0.30
Fat mass (kg)	17.29	4.94	16.99	4.87	16.71	6.33	17.37	6.04	0.40	-0.82	1.63	0.511	0.22
Waist circumference (cm)	79.24	8.09	79.60	8.80	77.31	7.71	78.75	7.04	0.94	-1.40	3.28	0.422	0.27
Waist-to-hip ratio	0.80	0.06	0.80	0.06	0.77	0.05	0.80	0.06	0.02	-0.01	0.04	0.254	0.39

Notes: *Values are presented as means and standard deviations (SD). b = adjusted mean difference at 20 days between the quercetin and placebo trial arms, controlling for the corresponding baseline value; CI = 95% confidence interval for b; P-value = probability value for the adjusted between-group difference at 20 days; d = semi-standardised adjusted effect size, calculated by dividing b by the residual standard deviation. Negative b values indicate lower adjusted values in the quercetin arm compared with placebo. Bold text indicates a statistically significant adjusted between-group difference (P ≤ 0.05).* ***Abbreviations:*** *BMI = body mass index; SD = standard deviation.*

Table 3: Blood pressure and resting heart-rate outcomes at baseline and Day 20.

	Placebo				Quercetin				*b*	95% CI		P-value	*d*
	Baseline		20-days		Baseline		20-days						
	Mean	SD	Mean	SD	Mean	SD	Mean	SD		Lower	Upper		
Systolic blood pressure (mmHg)	120.20	8.68	120.58	10.65	120.10	8.79	113.79	7.62	-6.92	-11.84	-2.00	**0.007**	-0.93
Diastolic blood pressure (mmHg)	78.10	9.93	76.68	7.78	79.45	5.30	73.79	7.80	-3.36	-8.10	1.38	0.159	-0.47
Resting heart rate (Beats/min)	63.75	16.26	67.32	18.70	69.65	11.85	68.58	8.80	-2.76	-8.55	3.03	0.340	-0.32

Notes: *Values are presented as means and standard deviations (SD). b = adjusted mean difference at 20 days between the quercetin and placebo trial arms, controlling for the corresponding baseline value; CI = 95% confidence interval for b; P-value = probability value for the adjusted between-group difference at 20 days; d = semi-standardised adjusted effect size, calculated by dividing b by the residual standard deviation. Negative b values indicate lower adjusted values in the quercetin arm compared with placebo. Bold text indicates a statistically significant adjusted between-group difference (P ≤ 0.05).* ***Abbreviation:*** *SD = standard deviation.*

Table 4: Haematological outcomes at baseline and Day 20.

	Placebo				Quercetin				*b*	95% CI		P-value	*d*
	Baseline		20-days		Baseline		20-days						
	Mean	SD	Mean	SD	Mean	SD	Mean	SD		Lower	Upper		
Total cholesterol (mmol/L)	4.15	0.78	4.37	0.86	4.42	0.81	4.29	0.74	-0.29	-0.72	0.13	0.172	-0.46
LDL cholesterol (mmol/L)	2.52	0.62	2.68	0.72	2.74	0.80	2.72	0.67	-0.10	-0.49	0.29	0.610	-0.17
Glucose (mmol/L)	4.85	1.30	5.05	1.26	6.38	1.39	5.85	1.01	0.52	-0.33	1.38	0.220	0.46
Triglycerides (mmol/L)	1.19	0.52	1.29	0.66	1.26	0.68	1.02	0.48	-0.35	-0.65	-0.04	**0.029**	-0.74
Triglyceride-glucose index	8.32	0.55	8.32	0.59	8.63	0.54	8.36	0.54	-0.06	-0.44	0.31	0.742	-0.11
HDL cholesterol (mmol/L)	1.08	0.07	1.11	0.08	1.11	0.09	1.11	0.07	−0.01	−0.06	0.03	0.569	−0.19
Total:HDL cholesterol ratio	3.75	0.48	4.00	0.56	3.95	0.46	3.92	0.53	−0.24	−0.52	0.03	0.084	−0.59
LDL:HDL cholesterol ratio	2.26	0.42	2.44	0.54	2.41	0.56	2.47	0.53	−0.06	−0.36	0.23	0.668	−0.14

Notes: *Values are presented as means and standard deviations (SD). b = adjusted mean difference at 20 days between the quercetin and placebo trial arms, controlling for the corresponding baseline value; CI = 95% confidence interval for b; P-value = probability value for the adjusted between-group difference at 20 days; d = semi-standardised adjusted effect size, calculated by dividing b by the residual standard deviation. Negative b values indicate lower adjusted values in the quercetin arm compared with placebo. Bold text indicates a statistically significant adjusted between-group difference (P ≤ 0.05). LDL and HDL cholesterol concentrations were estimated using the equations described in the Methods.* ***Abbreviations:*** *LDL = low-density lipoprotein; HDL = high-density lipoprotein; SD = standard deviation.*

Table 5: Questionnaire outcomes at baseline and Day 20.

	Placebo				Quercetin				*b*	95% CI		P-value	*d*
	Baseline		20-days		Baseline		20-days						
	Mean	SD	Mean	SD	Mean	SD	Mean	SD		Lower	Upper		
STAI state anxiety	31.70	8.30	30.74	8.67	35.25	11.72	30.58	10.52	-2.91	-6.85	1.03	0.142	-0.50
STAI trait anxiety	36.30	10.15	35.16	11.44	38.60	13.99	33.68	11.25	-2.68	-6.65	1.29	0.179	-0.45
COOP/WONCA	2.09	0.47	2.07	0.54	2.18	0.61	2.02	0.72	-0.13	-0.38	0.12	0.313	-0.33
Beck Depression Inventory	5.60	4.54	5.63	4.86	9.05	8.65	7.32	8.21	-1.30	-3.25	0.65	0.183	-0.46
Pittsburgh Sleep Quality Index	4.80	1.51	4.53	2.06	5.40	2.52	5.00	2.96	-0.07	-1.27	1.14	0.911	-0.04
Epworth Sleepiness Scale	5.30	3.33	5.68	4.49	5.10	3.52	4.16	3.48	-1.88	-3.58	-0.18	**0.031**	-0.73
Insomnia Severity Index	6.05	3.39	5.84	3.67	7.80	4.99	5.89	4.46	-1.52	-3.28	0.23	0.087	-0.59

Notes: *Values are presented as means and standard deviations (SD). b = adjusted mean difference at 20 days between the quercetin and placebo trial arms, controlling for the corresponding baseline value; CI = 95% confidence interval for b; P-value = probability value for the adjusted between-group difference at 20 days; d = semi-standardised adjusted effect size, calculated by dividing b by the residual standard deviation. Negative b values indicate lower adjusted scores in the quercetin arm compared with placebo. Bold text indicates a statistically significant adjusted between-group difference (P ≤ 0.05).* ***Abbreviations:*** *STAI = State-Trait Anxiety Inventory; SD = standard deviation.*

Table 6. Dietary intake outcomes at baseline and Day 20.

	Placebo				Quercetin				*b*	95% CI		P-value	*d*
	Baseline		20-days		Baseline		20-days						
	Mean	SD	Mean	SD	Mean	SD	Mean	SD		Lower	Upper		
Energy intake (Kcal)	1849.46	657.24	1907.77	617.69	1981.57	547.49	2156.33	424.43	157.37	−105.66	420.39	0.229	0.48
Total fat (g)	71.72	39.43	85.77	45.05	72.93	29.46	88.50	22.85	2.04	−21.63	25.71	0.860	0.07
Saturated fatty acids (g)	22.89	14.47	27.09	13.15	24.51	11.74	27.78	11.16	0.25	−9.20	9.71	0.957	0.02
Protein (g)	76.52	37.68	84.65	32.62	78.91	31.17	91.23	26.45	5.26	−13.13	23.64	0.561	0.23
Carbohydrate (g)	234.27	79.54	208.44	72.42	254.61	72.84	255.98	70.76	32.57	−3.89	69.03	0.078	0.72
Sugars (g)	104.51	49.68	72.14	36.74	100.11	57.41	87.07	36.76	16.39	−9.67	42.45	0.207	0.50
Fibre (g)	18.58	9.46	16.61	5.08	14.19	7.16	15.71	7.61	0.69	−4.17	5.55	0.771	0.12
Alcohol (g)	2.53	6.35	2.18	7.10	8.94	24.89	6.54	16.78	0.27	−4.33	4.87	0.904	0.05
Vitamin A (µg)	403.77	439.72	676.77	345.18	589.07	581.23	764.91	854.47	72.45	−471.76	616.66	0.786	0.11
Thiamin (mg)	1.73	0.89	1.44	0.50	1.65	0.92	1.83	0.98	0.43	−0.16	1.01	0.144	0.58
Riboflavin (mg)	1.60	0.71	1.48	0.83	1.81	0.91	1.67	0.91	0.04	−0.46	0.54	0.873	0.06
Niacin (mg)	35.43	18.65	36.97	11.94	36.09	14.12	42.87	14.49	5.64	−3.80	15.07	0.230	0.47
Vitamin B6 (mg)	1.53	0.76	1.54	0.55	1.59	0.66	1.77	0.70	0.20	−0.21	0.61	0.327	0.39
Vitamin B12 (µg)	4.67	4.20	5.76	6.68	4.92	2.62	4.42	2.92	−1.58	−4.82	1.67	0.326	−0.39
Folate (µg)	249.08	99.81	221.62	87.60	219.29	147.84	249.04	116.29	45.39	−11.51	102.28	0.113	0.64
Vitamin C (mg)	80.02	60.59	72.05	59.44	129.09	219.97	73.55	77.75	−6.77	−59.19	45.65	0.792	−0.10
Vitamin D (µg)	2.78	4.24	4.87	5.76	4.63	4.11	5.40	6.23	−0.83	−5.13	3.47	0.693	−0.16
Vitamin E (mg)	9.10	5.42	9.96	7.73	9.74	6.25	11.65	5.58	1.32	−3.36	5.99	0.567	0.22
Calcium (mg)	891.15	386.48	881.31	438.59	855.07	415.11	972.36	393.73	106.85	−199.28	412.97	0.478	0.28
Magnesium (mg)	284.46	115.36	312.15	137.50	269.36	94.11	320.82	106.35	22.43	−39.72	84.57	0.464	0.29
Salt (g)	5.53	3.19	4.93	1.79	5.52	2.17	5.82	2.51	0.89	−0.77	2.55	0.280	0.43
Iron (mg)	10.93	4.33	10.85	3.70	11.31	4.94	12.66	5.32	1.58	−1.45	4.62	0.292	0.42
Zinc (mg)	8.80	4.38	8.86	2.02	8.11	3.65	9.44	2.93	0.62	−1.44	2.67	0.542	0.24

Notes: *Values are presented as means and standard deviations (SD). Dietary intake was assessed using four-day dietary diaries immediately preceding each assessment, with mean daily intakes calculated across all four recorded days. b = adjusted mean difference at 20 days between the quercetin and placebo trial arms, controlling for the corresponding baseline value; CI = 95% confidence interval for b; P-value = probability value for the adjusted between-group difference at 20 days; d = semi-standardised adjusted effect size, calculated by dividing b by the residual standard deviation. Negative b values indicate lower adjusted dietary intake in the quercetin arm compared with placebo. Bold text indicates a statistically significant adjusted between-group difference (P ≤ 0.05).* ***Abbreviation:*** *SD = standard deviation.*