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CORRECTION

Correction to: The Effect of Acute Caffeine Ingestion on Endurance Performance: A Systematic Review and Meta-Analysis

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Abstract

Introduction Caffeine is a widely used ergogenic aid with most research suggesting it confers the greatest effects during endurance activities. Despite the growing body of literature around the use of caffeine as an ergogenic aid, there are few recent meta-analyses which quantitatively assess the effect of caffeine on endurance exercise.

Objectives To summarise studies which have investigated the ergogenic effects of caffeine on endurance time-trial performance and to quantitatively analyse the results of these studies to gain a better understanding of the magnitude of caffeine's ergogenic effect on endurance time-trial performance.

Methods A systematic review was carried out on randomised placebo-controlled studies investigating the effects of caffeine on endurance performance and a meta-analysis was conducted to determine the ergogenic effect of caffeine on endurance time-trial performance.

Results 44 studies met the inclusion criteria and were included in the meta-analysis. Caffeine has a small but evident effect on endurance performance when taken in moderate doses (3–6 $mg \cdot kg^{-1}$) as well as an overall improvement following caffeine compared to placebo in mean power output ($2.92 \pm 2.18\%$; Effect Size $= 0.22 \pm 0.15$) and time-trial completion time ($2.26 \pm 2.60\%$; Effect Size $= 0.28 \pm 0.12$). However, differences in responses to caffeine ingestion have been shown, with two studies reporting slower time-trial performance while five studies reported lower mean power output during the time-trial. Caffeine can be used effectively as an ergogenic aid when taken in moderate doses, such as during sports when a small increase in endurance performance can lead to significant differences in placements as athletes are often separated by small margins.

1 Introduction

The desire to win their sporting event often drives competitive athletes to utilise training methods and supplements to gain an advantage over their opponents. In the 2012 and 2016 Olympic games, in many sports, changes in performance of only 1% were sufficient to result in the difference between winning a gold or silver medal [1]. Therefore, if a particular supplement or training method can lead to small but definite improvements, it could mean the difference between first or second place, particularly in elite level sports.

Caffeine is a widely used supplement by athletes at various levels of competition as well as a wide range of sporting disciplines [2]. It has been reported that 74% of elite athletes may use caffeine as an ergogenic aid prior to or during an event or sport, with endurance sports showing the highest prevalence rate for caffeine use [2]. This is likely due to caffeine's high accessibility and few

Following the online publication of this article, an error was identified by one of the cited authors. This led to the identification of a number of other numerical errors affecting the results, tables & figures, as well as some numerical data reported in the discussion and conclusions. These errors were minor and did not affect the overall narrative of the discussion or conclusions. The full article, with all corrections made, is republished below.

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negative side effects as well as evidence suggesting that it is ergogenic at low-to-moderate doses (1–6 mg·kg^{-1}) [3, 4]. Possible mechanisms of action for the ergogenic effects of caffeine include increased mobilisation of intracellular calcium and free fatty acid mobilisation, but adenosine receptor antagonism has been proposed to be the major contributing factor to the ergogenic effects of caffeine for endurance performance [3, 4]. Thus caffeine supplementation is most prevalent in endurance sports as there is more consistent improvements in performance following caffeine ingestion, whereas in short-term high-intensity activities, inconsistent results have been observed [2, 5]. However, while the consensus view is that caffeine has an ergogenic effect for endurance performance [4, 6], there is a large variability in effect size between studies [6].

Studies investigating the effects of caffeine ingestion on endurance performance have primarily used two different protocols, time to exhaustion (TTE) or time trials (TT). Those using TTE protocols have found larger coefficients of variation [7] but are less applicable to a real-world environment as no mainstream sports use time to exhaustion measures of performance. It has also been found that a small change in power output can result in very large changes in TTE duration, whereas a change in power output during a TT reflects a similar change in time to complete the TT distance [7]. However, it should also be noted that a change in mean power output will result in a non-proportional change in overall completion time dependant on the length of exercise. Smaller changes in mean power output would be expected in longer duration exercise. Therefore, TT offer a more real-world testing environment which is applicable to coaches and athletes as the results can be easily translated to a sport setting. This does not mean TTE trials do not add significant evidence to the body of literature, however, only TT studies will be examined in the present review.

Numerous narrative reviews on caffeine's effects on endurance performance have been published [3, 4, 8–12], however, the available meta-analyses' are either old or do not accurately assess the effects of caffeine on endurance performance [1, 5, 13, 14]. A meta-analysis by Doherty and Smith [5] was published in 2004, the same year that caffeine was removed from the WADA banned list and a large number of studies have since investigated the effects of caffeine as an ergogenic aid. A meta-analysis by Christensen et al. [1] analysed the effects of multiple, popular ergogenic substances on intense endurance exercise. However, the authors only included studies which had closed-end performance tests which lasted 45 s–8 min. The meta-analysis by Souza et al. [13] only included studies that used energy drinks, many of which contain other potentially ergogenic substances such as taurine which might influence the outcome. This means that the effects of caffeine could not be isolated and the effect of the energy drinks on performance could not be directly attributed to caffeine. A systematic review by Ganio et al. [14] reported the effects of caffeine on endurance performance from 1985 to 2007. While this was not a meta-analysis the authors reported percentage change in performance outcomes following caffeine ingestion compared to placebo which gives some estimate of the overall effect of caffeine on endurance performance.

The reason for the lack of meta-analyses on the effects of caffeine on endurance performance may be due to the large range of performance outcomes reported by studies, as well as the use of different testing protocols making it difficult to find sufficient studies to include in the analysis while still maintaining focused inclusion criteria. As a result, there is currently a need to objectively quantify the ergogenic effect of caffeine on endurance time-trial performance, particularly from more recent studies.

The aim of this meta-analysis is to summarise the most recent studies which have investigated the ergogenic effects of caffeine on endurance time-trial performance and to quantitatively analyse the results of these studies to gain a better understanding of the magnitude of caffeine's ergogenic effect on endurance time-trial performance.

2 Methods

This systematic review and meta-analysis is presented using the Preferred Method Items for Systematic Reviews and Meta-Analysis statement format as suggested by PRISMA [15]. For clarity, a study will refer to a whole published article which may include multiple trials.

2.1 Literature Search

In August 2017 a literature search was carried out in accordance with PRISMA guidelines for systematic reviews (Fig. 1) [15]. A search of Web of Science, PUBMED, Scopus, and ProQuest was carried out using a combination of the keywords: *caffeine, caffeinated, coffee, exercise, endurance, performance, time trial*. The PUBMED search is shown below. After the initial search was completed, duplicates were removed and title and abstracts of remaining studies were screened for eligibility. The remaining studies were read in full and assessed for eligibility and included in the final review and analysis. Attempts were made to contact authors for missing information.

PUBMED search: ((caffeine[Title/Abstract] OR caffeinated[Title/Abstract] OR tea[Title/Abstract] OR coffee[Title/Abstract] OR 1,3,7-Trimethylxanthine[Title/Abstract] OR theine[Title/Abstract] OR energy drinks[Title/Abstract])

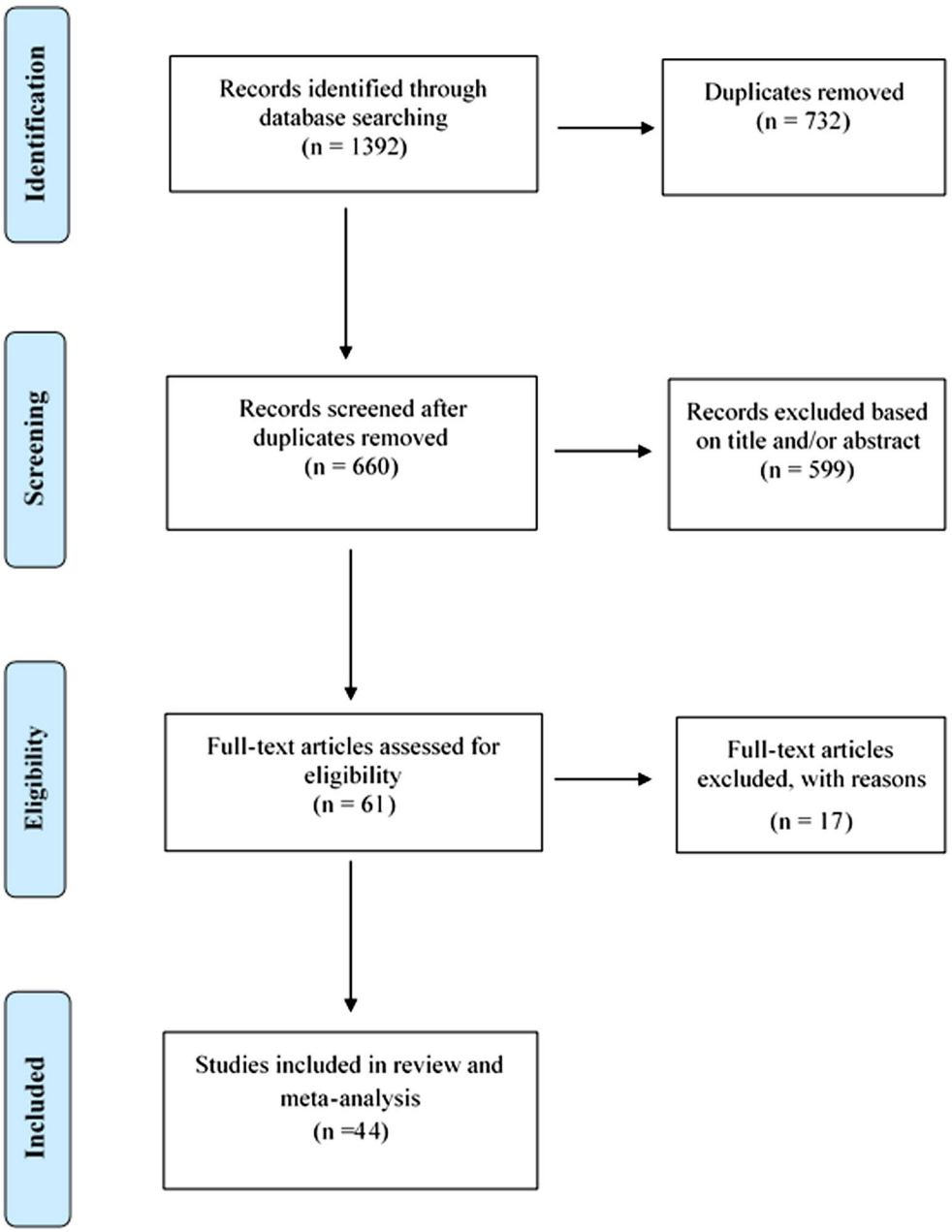

Fig. 1 Process of elimination and inclusion of studies for review based on PRISMA guidelines

AND (Endurance[All Fields] OR (endurance[All Fields] AND ("exercise"[MeSH Terms] OR "exercise"[All Fields])) OR (endurance[All Fields] AND performance[All Fields]) OR performance[All Fields] OR ("athletic performance"[MeSH Terms] OR ("athletic"[All Fields] AND "performance"[All Fields]) OR "athletic performance"[All Fields]) OR (("exercise"[MeSH Terms] OR "exercise"[All Fields]) AND performance[All Fields]) OR ("exercise"[MeSH Terms] OR "exercise"[All Fields]) OR ("running"[MeSH Terms] OR "running"[All Fields]) OR cycling[All Fields]))

AND ("time-trial"[All Fields] OR "time trial"[All Fields] OR (("time"[MeSH Terms] OR "time"[All Fields]) AND ("clinical trials as topic"[MeSH Terms] OR ("clinical"[All Fields] AND "trials"[All Fields] AND "topic"[All Fields]) OR "clinical trials as topic"[All Fields] OR "trial"[All Fields])))

2.2 Selection Criteria/Study Eligibility

Studies in adult (> 18 years) men and women reporting the effects of caffeine on a measure of endurance performance were considered for inclusion in this review. As many studies often combined caffeine with carbohydrate ingestion, studies that had co-ingestives taken with caffeine were included only if the effect of caffeine could be isolated such that identical solutions were given to participants, one with caffeine and one without. This led to any studies that used energy drinks being excluded from the review as caffeine was not isolated in these studies. Studies using caffeinated gum were also excluded from this review as the rate of absorption and bioavailability of caffeine from gum differs from that of capsules and tablets [16]. Caffeine also had to be ingested as an acute dose of larger than 3 $mg \cdot kg^{-1}$ prior to the start of exercise (pre-load or time trial), and not consumed during the exercise protocol. Only studies written in English were included in this review.

Included studies were also required to utilise a time trial (TT) component as a measure of performance and the total duration of the exercise (pre-load and time trial combined) must have been > 5 min. TT performance had to have been reported in either time or a measure of power output (total work done, mean power output, relative power output) to be included in the meta-analysis. Studies taking place in extreme environments (high altitude, high or low temperatures) were included only if both placebo and caffeine conditions took place in the same extreme environment.

2.3 Quality Assessment

Study quality was assessed using the Physiotherapy Evidence Database Scale (PEDro) [17]. The PEDro scale has been shown to be an acceptable method of reliably assessing the internal validity of randomised control trials [17]. The PEDro scale scores studies using an 11-point scale with a maximum of 10 points being awarded to a single study. The first point is awarded for stating eligibility criteria and is not included in the final score. Items 2-11 assess randomisation, blinding, attrition, selective reporting and statistical analysis and a point is awarded if the criteria are sufficiently met. Any studies which scored < 6 were not included in the final review and meta-analysis. All studies' quality assessment was carried out by K.S and moderated by A.A.

2.4 Data Extraction

Data were extracted and placed into spreadsheets and later summarised (Tables 1 and 2). Information collected from each study included age, $VO_{2max/peak}$, caffeine dose and time of caffeine dose ingestion, mode of exercise, exercise protocol, time performance outcomes for placebo and caffeine trials, and power output performance outcomes for placebo and caffeine trials. Studies were grouped by the method of reporting performance outcomes. Those studies which measured endurance performance using time were grouped together (Table 1), and those which reported endurance performance outcomes as a measure of power (total work done, mean power output, relative power output) were grouped together (Table 2). This standardised outcome variables across the studies in each table. Some studies reported both time and power output variables as endurance performance outcomes and were thus included in both tables (Tables 1 and 2).

2.5 Data Analysis

Data analysis of the spreadsheets was completed using Excel (Microsoft Excel, 2010).

Total exercise duration was calculated by adding pre-load exercise duration to mean placebo TT duration. Placebo and caffeine TT durations were different for time to completion trials but were the same in trials which recorded work completed in a set amount of time. Performance outcomes of power output (total work done, relative power output) were converted to mean power output (MPO) using the equation for work and power (where P = power, W = work, and T = time):

$$P = \frac{W}{T}$$

Total work done during TT was converted to MPO by dividing mean total work done during TT by mean placebo TT duration. Relative PO was converted to MPO by multiplying mean relative PO by the mean body mass of the sample.

Mean percentage change was calculated between treatment and placebo groups for both time to complete TT and MPO during TT. Effect sizes (ES) were calculated using random effect meta-analysis with Hedges' g correction. Effect size and meta-regression analysis was carried out using STATA meta-analysis (metan) and meta-regression (metareg) software packages (StataCorp. 2017. *Stata Statistical Software: Release 15*. College Station, TX: StataCorp LLC). Hedges' g is calculated as the difference in mean over the weighted pooled standard deviation:

$$Hedges'g = \frac{M_1 - M_2}{SD_{pooled}}$$

Effect size thresholds were categorized as; < 0.19 = trivial, 0.2–0.59 = small, 0.6–1.19 = moderate, 1.2–1.99 = large, 2.0–3.99 = very large, > 4.0 = extremely large [18]. Confidence intervals of the effect size were

Table 1 Summary of studies measuring the effect of caffeine ingestion on time trial time as a measure of endurance performance

Study	Sample	Age	VO_{2max}	Caffeine dose; timing	Mode of exercise	Exercise protocol	Total exercise duration (min)	Time trial improvement over placebo (%)	Effect size	Upper and lower 95% CI
Roelands et al. [37]	8M	23 ± 5		6 mg·kg^{-1}; 60	Cycling	60 min 55%W_{max}; 0.75*W_{max}*1800	36.6	− 3.0	− 0.24	− 1.22; 0.75
Cohen et al. [38]	5M; 2F	33.3 ± 9.2		9 mg·kg^{-1}; 60	Running	21 Km TT	86.5	− 0.1	− 0.01	− 1.06; 1.03
Jacobson et al. [39]	8M	21.2 ± 3.7	65.2 ± 3.2	6 mg·kg^{-1}; 60	Cycling	120 min 63% W_{max}; 7KJ·Kg^{-1} TT	153	0.7	0.03	− 0.95; 1.01
Skinner et al. [40]	10M	20.6 ± 1.4	58.2 ± 6.8	6 mg·kg^{-1}; 60	Rowing	2 Km TT	6.73	0.3	0.05	− 0.82; 0.93
Bortolotti et al. [41]	13M	26 ± 10		6 mg·kg^{-1}; 60	Cycling	20 Km TT	37	0.5	0.06	− 0.71; 0.82
Astorino et al. [42]	8M	26.7 ± 5.9	46.5 ± 6.3	5 mg·kg^{-1}; 60	Cycling	10 Km TT	19	0.3	0.08	− 0.90; 1.06
Potgieter et al. [43]	14M; 12F	37.8 ± 10.8		6 mg·kg^{-1}; 60	Triathlon	1.5 Km swim; 40 Km cycle; 10 Km run	151	1.3	0.10	− 0.45; 0.64
Stadheim et al. [44]	13M	21.9 ± 2.7	72.6 ± 5.7	4.5 mg·kg^{-1}; 45	Double poling	26 min 40–70% VO_{2peak}; 8 Km TT	59	0.9	0.10	− 0.67; 0.87
Skinner et al. [40]	10M	20.6 ± 1.4	58.2 ± 6.8	4 mg·kg^{-1}; 60	Rowing	2 Km TT	6.73	0.6	0.11	− 0.76; 0.99
Cohen et al. [38]	5M; 2F	33.3 ± 9.2		5 mg·kg^{-1}; 60	Running	21 Km TT	86.5	0.8	0.12	− 0.93; 1.17
Acker-Hewitt et al. [45]	10M	28 ± 9	66 ± 9	6 mg·kg^{-1}; 60	Cycling	20 min 60% VO_{2max}; 20 Km TT (last 5 Km graded)	64.2	1.4	0.12	− 0.76; 1.00
Carr et al. [46]	6M; 2F			6 mg·kg^{-1}; 30	Rowing	2 Km TT	6.7	0.7	0.12	− 0.86; 1.10
Church et al. [47]	10M; 10F	24.1 ± 2.9	45 ± 3.7	3 mg·kg^{-1}; 60	Running	5 Km TT	29	1.9	0.13	− 0.49; 0.75
O'Rourke et al. [48]	15M	32.2 ± 8.8		5 mg·kg^{-1}; 60	Running	5 Km TT	18	1.0	0.15	− 0.56; 0.87
O'Rourke et al. [48]	15M	29 ± 5.7		5 mg·kg^{-1}; 60	Running	5 Km TT	22	1.1	0.16	− 0.56; 0.88
Desbrow et al. [49]	9M	29.4 ± 4.5	61.7 ± 4.8	3 mg·kg^{-1}; 60	Cycling	120 min 65% W_{max}; 7 KJ·Kg^{-1} TT	150	1.9	0.16	− 0.77; 1.09
MacIntosh and Wright [50]	7M; 4F	22.4 ± 0.9		6 mg·kg^{-1}; 150	Swimming	20 min self-paced warm up; 10 min rest; 1.5 km TT	41.35	1.8	0.17	− 0.60; 0.94
Kilding et al. [51]	10M	24.2 ± 5.4		3 mg·kg^{-1}; 60	Cycling	20 min 60–65% MPO; 5 min high intensity efforts; 3 Km TT	29	0.8	0.17	− 0.71; 1.05
Jacobson et al. [39]	8M	21.2 ± 3.7	65.2 ± 3.2	6 mg·kg^{-1}; 60	Cycling	120 min 63% W_{max}; 7 KJ/Kg TT	150	4.1	0.18	− 0.8; 1.16
Dean et al. [52]	8M	36.4 ± 6.1	52.5 ± 6.1	3 mg·kg^{-1}; 60	Cycling	60 min 60% $VO_{2max;}$ 40 Km TT	120	1.4	0.22	− 0.77; 1.20
Guest et al. [53]	101M	25 ± 4	47.7 ± 11	4 mg·kg^{-1}; 75	Cycling	Vertical jump, handgrip, wingate; 10 km TT	18.1	2.8	0.22	− 0.05; 0.50
Bell et al. [54]	10M; 2F	33 ± 8	57.5 ± 3.4	4 mg·kg^{-1}; 90	Running	10 Km TT with additional 11 kg load	46.8	1.7	0.26	− 0.55; 1.06
Astorino et al. [42]	8M	26.7 ± 5.9	46.5 ± 6.3	5 mg·kg^{-1}; 60	Cycling	10 Km TT	19	1.0	0.26	− 0.72; 1.25

Table 1 (continued)

Study	Sample	Age	VO_{2max}	Caffeine dose; timing	Mode of exercise	Exercise protocol	Total exercise duration (min)	Time trial improvement over placebo (%)	Effect size	Upper and lower 95% CI
Astorino et al. [55]	8M; 1F	27.4 ± 5.9	57.5 ± 3.9	5 mg·kg^{-1}; 60	Cycling	10 Km TT	17	1.6	0.27	− 0.66; 1.20
Astorino et al. [42]	8M	28 ± 6	56.9 ± 3.8	5 mg·kg^{-1}; 60	Cycling	10 Km TT	17	1.6	0.27	− 0.72; 1.25
Skinner et al. [56]	14M	31 ± 5.2	69.5 ± 6.1	6 mg·kg^{-1}; 135	Cycling	40 Km TT	59	1.1	0.27	− 0.48; 1.01
Womack et al. [57]	19M	26.1 ± 7.8	59.6 ± 10.3	6 mg·kg^{-1}; 60	Cycling	40 Km TT	72	1.8	0.30	− 0.34; 0.94
Stadheim et al. [58]	10M	20 ± 3.16	69.3 ± 7.27	6 mg·kg^{-1}; 45	Double poling	26 min 40–70% VO_{2peak}; 8 Km TT	60	4.1	0.30	− 0.58; 1.19
Astorino et al. [43]	8M	28 ± 6	56.9 ± 3.8	5 mg·kg^{-1}; 60	Cycling	10 Km TT	17	2.0	0.32	− 0.66; 1.31
Astorino et al. [55]	8M; 1F	27.4 ± 5.9	57.5 ± 3.9	5 mg·kg^{-1}; 60	Cycling	10 Km TT	17	1.9	0.33	− 0.61; 1.26
Desbrow et al. [59]	16M	32.6 ± 8.3	60.4 ± 4.1	6 mg·kg^{-1}; 90	Cycling	0.75*W_{max}*3600 KJ TT	65	2.8	0.35	− 0.35; 1.05
de Souza Goncalves et al. [60]	40M	36 ± 8	50.7 ± 7.5	6 mg·kg^{-1}; 60	Cycling	0.85*W_{max}*1800 KJ TT	31	2.9	0.36	− 0.08; 0.80
Irwin et al. [61]	12M	28.3 ± 5.8	63.7 ± 7.4	3 mg·kg^{-1}; 90	Cycling	0.75* W_{max} *3600 KJ TT	60	3.0	0.38	− 0.43; 1.19
Felippe et al. [62]	11M	34 ± 13	55 ± 13	5 mg·kg^{-1}; 60	Cycling	4 Km TT	6.7	1.8	0.38	− 0.46; 1.23
Graham-Paulson et al. [63]	11M	24 ± 4	42.9 ± 7.3	4 mg·kg^{-1}; 55	Cycling	30 min 65% VO_{2peak}; 10 Km TT	47	2.1	0.39	− 0.46; 1.23
Cox et al. [64]	12M	27.1 ± 4.5	66.4 ± 4.5	6 mg·kg^{-1}; 60	Cycling	120 min 70% VO_{2peak}; 7 KJ·Kg^{-1} TT	29.3	3.4	0.40	− 0.41; 1.21
Quinlivan et al. [65]	11M	31.6 ± 6.1	60.7 ± 8.1	3 mg·kg^{-1}; 90	Cycling	0.75*W_{max}*3600 KJ TT	64.6	3.1	0.43	− 0.42; 1.28
Glaister et al. [66]	14F	31 ± 7	52.3 ± 4.9	5 mg·kg^{-1}; 60	Cycling	20 Km TT	35	2.1	0.49	− 0.27; 1.24
Desbrow et al. [59]	16M	32.6 ± 8.3	60.4 ± 4.1	3 mg·kg^{-1}; 90	Cycling	0.75* W_{max} *3600 KJ TT	65	4.2	0.51	− 0.20; 1.21
Conway et al. [67]	8M	25.5 ± 14.1	72 ± 11	6 mg·kg^{-1}; 60	Cycling	90 min 70% VO_{2max}; 0.8*W_{max}*1800	118	15.9	0.51	− 0.49; 1.51
Walker et al. [68]	9M	23 ± 3	71.2 ± 6.8	6 mg·kg^{-1}; 60	Cycling	90 min 70% VO_{2max}; 0.7*W_{max}*1800 TT	118	3.9	0.58	− 0.37; 1.53
Skinner et al. [56]	14M	31 ± 5.2	69.5 ± 6.1	6 mg·kg^{-1}; 60	Cycling	40 Km TT	59	2.0	0.63	− 0.13; 1.39
Womack et al. [57]	16M	24 ± 6.9	59 ± 9.3	6 mg·kg^{-1}; 60	Cycling	40 Km TT	74	4.9	0.71	0.01; 1.43
Pitchford et al. [69]	9M	22–42	64.4 ± 6.8	3 mg·kg^{-1}; 90	Cycling	0.75*W_{max}*2880 KJ TT	64	6.8	0.76	− 0.21; 1.72
de Santos et al. [70]	8M	32.6 ± 5.4	57.5 ± 5.8	5 mg·kg^{-1}; 60	Cycling	4 km TT	7	2.9	0.92	− 0.12; 1.97
Hodgson et al. [71]	8M	41 ± 7	58 ± 3	5 mg·kg^{-1}; 60	Cycling	30 min 55% VO_{2max}; 0.7*W_{max}*2700 KJ TT	70	4.3	1.31	0.20; 2.42

W_{max} work rate max, *TT* time trial, *KJ* kilojoules, *M* males, *F* females, *CI* confidence interval, $VO_{2max/peak}$ maximal oxygen uptake (ml/kg/min)

also calculated using $\alpha = 0.05$. Data is presented as mean ± standard deviation or mean ± 95% CI where appropriate. Studies were ordered based on their mean effects size from smallest to largest. Meta-regression analysis was carried out to examine the impact of the variables of VO_2, exercise mode, exercise duration and caffeine dose on the effect of caffeine on endurance performance compared to placebo. Publication bias was assessed using the Begg and Egger test [19] by plotting effect size against the standard error with 95% CI using a funnel plot.

3 Results

The literature searches of the databases returned a total of 1392 potentially eligible studies (Fig. 1). The results from the searches of each database were collated and 732 duplicates were removed leaving 660 remaining records. The titles and abstracts of the remaining studies were then screened for an isolated effect of caffeine, a measure of endurance performance, and an acceptable exercise protocol containing a TT component. Following screening, 61 studies remained and were read in full to ensure studies met inclusion and exclusion criteria. Of the studies that were read in full two were removed as they were additional publications from previous studies [20, 21], six studies did not provide sufficient data to be included in the meta-analysis [22–27]. Two studies were excluded as the exercise durations were less than 5 min [28, 29]. A further two studies were excluded for administering a caffeine dose < 3 $mg \cdot kg^{-1}$ [30, 31], and four studies were removed for administering caffeine during the exercise protocol [32–35]. A study was also excluded based on the fact that participants were assigned groups based on genotype which is related to caffeine sensitivity [36]. A summary of the studies which reported time and power output are presented in Tables 1 and 2, respectively.

A total of 57 trials from 44 studies were identified and included in the final analysis (Tables 1 and 2). The number of participants across all trials totalled 1001, with 639 participants included in the studies which reported time, and 350 participants included in studies which reported power output. Of the total participants across all trials 82 were female and one study did not specify the gender of the participants and so were assumed to be male [48]. The mean age of participants and their VO_{2max} were 27.7 ± 5.1 years and 58.3 ± 8.0 $ml \cdot kg^{-1} \cdot min^{-1}$ respectively across all studies. One study did not report the age of participants [46], and 10 studies did not report VO_{2max} or VO_{2peak} values of participants [38, 41, 43, 46, 48, 50, 51, 73, 77, 80].

Of the different protocols used to measure time trial performance 23 studies used time to complete a set distance [38, 40–48, 50–58, 62, 63, 66, 70], 13 used time to complete a set amount of work [37, 39, 49, 59–61, 64, 65, 67–69, 71, 76], and 9 studies used amount of work done in a set amount of time [72–75, 77–80]. Forty-one trials administered caffeine 60 min prior to exercise with the remainder of studies administering caffeine at 30 min [46], 45 min [44, 58, 73], 55 min [63], 75 min [53] 90 min [54, 59, 61, 65, 69], and 120–150 min [56] prior to exercise.

The mean caffeine dose administered was 5.0 ± 1.3 $mg \cdot kg^{-1}$, with 20 studies (23 trials) using 6 $mg \cdot kg^{-1}$ [37, 39–41, 43, 45, 46, 50, 56–60, 64, 67, 68, 76–78, 80], 9 studies (14 trials) using 5 $mg \cdot kg^{-1}$ [36, 38, 42, 48, 55, 62, 66, 70, 71, 74], 4 studies (4 trials) using 4 $mg \cdot kg^{-1}$ [40, 53, 54, 63], 11 studies (11 trials) used 3 $mg \cdot kg^{-1}$ [47, 49, 51, 52, 59, 61, 65, 69, 73, 75, 79], 1 study each used 4.5 [44], 200 mg [31], 250 mg [72], and 9 $mg \cdot kg^{-1}$ [38].

Cycling was the most common form of exercise used by 33 of the 44 studies (41 trials), while 4 studies (6 trials) used running [38, 47, 48, 54], and 2 studies used double poling (Nordic skiing) [44, 58], 3 studies (4 trials) used rowing [40, 46, 73], 1 study used triathlon [43] and one study used swimming [50]. Twenty studies (21 trials) used a pre-load exercise protocol which requires exercise of a fixed duration being completed immediately before the time trial portion [39, 44, 45, 50–52, 58, 59, 63, 64, 67, 68, 71, 72, 74, 75, 77–79]. The mean total exercise duration was 56.0 ± 43.3 min, with a mean pre-load duration of 55.8 ± 40.6 min and a mean time trial duration of 34.7 ± 27.3 min. Overall, caffeine time-trials were faster compared to placebo by 2.26 ± 2.60% (Fig. 2) with a mean effect size of 0.28 (95% CI; ± 0.12; $P < 0.0001$; $I^2 = 0.0\%$; Fig. 3). Similarly, power output in caffeine trials were greater compared to placebo trials by 2.92 ± 2.18% (Fig. 4) with a mean effect size of 0.22 (95% CI; ± 0.15; $P = 0.004$; $I^2 = 0\%$; Fig. 5). Only two trials [37, 38] showed a slower time trial time following caffeine ingestion compared to placebo. However, 4 trials (3 studies) [41, 42, 56] had lower MPO during caffeine trials compared to placebo. Meta-regression analysis showed no significant relationship between the effect size of both power output and time, and the independent variables; VO_2 ($P_{PO} = 0.96$; $P_{time} = 0.83$), caffeine dose ($P_{PO} = 0.607$; $P_{time} = 0.819$); exercise mode ($P_{PO} = 0.54$; $P_{time} = 0.1$), and exercise duration ($P_{PO} = 0.971$; $P_{time} = 0.932$).

The mean PEDro score across all studies was 9.7; 37 studies scored 10, 2 studies scored 9 [38, 45] and 6 studies scored 8 [42, 55, 63, 68, 71, 80]. "Blinding of assessors" and "blinding of therapists" were the two items most commonly failed with 5 studies failing to have double blinding [38, 42, 55, 68, 71]. Three studies failed "Subjects were randomly allocated to groups" [45, 63, 80] and 2 studies failed "concealment of allocation" [63, 80]. According to the funnel plots (Figs. 6 and 7) only one study [62] produced an estimate of effect size outside the calculated confidence

Table 2 Summary of studies measuring the effect of caffeine ingestion on time trial power output as a measure of endurance performance

Study	Sample	Age	VO_{2max}	Caffeine dose and timing	Mode of exercise	Exercise protocol	Total exercise duration (min)	Time trial improvement over placebo (%)	Effect size	Upper and lower 95% CI
Astorino et al. [42]	8M	26.7 ± 5.9	46.5 ± 6.3	5 mg/kg^{-1}; 60	Cycling	10 Km TT	19	− 1.5	− 0.13	− 1.12; 0.85
Skinner et al. [56]	14M	31 ± 5	69.5 ± 6.1	6 mg/kg^{-1}; 60	Cycling	40 Km TT	59	− 0.8	− 0.07	− 0.81; 0.67
Skinner et al. [56]	14M	31 ± 5	69.5 ± 6.1	6 mg/kg^{-1}; 135	Cycling	40 Km TT	59	− 0.7	− 0.06	− 0.80; 0.68
Bortolotti et al. [41]	13M	26 ± 10		6 mg/kg^{-1}; 60	Cycling	20 Km TT	37	− 1.1	− 0.06	− 0.83; 0.71
Skinner et al. [40]	10M	20.6 ± 1.4	58.2 ± 6.8	6 mg/kg^{-1}; 60	Rowing	2 Km TT	6.73	0.9	0.06	− 0.82; 0.93
Astorino et al. [42]	8M	26.7 ± 5.9	46.5 ± 6.3	5 mg/kg^{-1}; 60	Cycling	10 Km TT	19	0.9	0.08	− 0.91; 1.06
Collomp et al. [72]	8M	26 ± 5.9	54.4 ± 6.2	3.56 mg/kg^{-1}; 60	Cycling	10 min 90% VO_{2max}; 10 min rest; 10 min TT	20	2.2	0.11	− 0.87; 1.09
Christensen et al. [73]	11M; 1F	25.3 ± 2.3		3 mg/kg^{-1}; 45	Rowing	6 min TT	6	1.8	0.11	− 0.69; 0.91
Skinner et al. [40]	10M	20.6 ± 1.4	58.2 ± 6.8	4 mg/kg^{-1}; 60	Rowing	2 Km TT	6.73	1.7	0.11	− 0.76; 0.99
Carr et al. [46]	6M; 2F			6 mg/kg^{-1}; 30	Rowing	2 Km TT	6.7	2.3	0.12	− 0.86; 1.10
Astorino et al. [42]	8M	28 ± 6	56.9 ± 3.8	5 mg/kg^{-1}; 60	Cycling	10 Km TT	17	1.5	0.12	− 0.86; 1.10
Black et al. [74]	5M; 9F	21.5 ± 1.9	40.9 ± 6.7	5 mg/kg^{-1}; 60	Cycling	30 min 60% VO_{2peak}; 10 min TT	90	4.2	0.13	− 0.61; 0.87
Astorino et al. [55]	8M; 1F	27.4 ± 5.9	57.5 ± 3.9	5 mg/kg^{-1}; 60	Cycling	10 Km TT	17	1.8	0.14	− 0.78; 1.07
Jenkins et al. [75]	13M	26.3 ± 6.8	55.2 ± 7.2	3 mg/kg^{-1}; 60	Cycling	15 min 80% VO_{2peak}; 15 min TT	30	3.0	0.15	− 0.62; 0.92
Saunders et al. [76]	42M	37 ± 8	50 ± 6.8	6 mg/kg^{-1}; 60	Cycling	0.85*W_{max}*1500	25	2.7	0.17	− 0.26; 0.59
Wallman et al. [77]	10F	22 ± 2		6 mg/kg^{-1}; 60	Cycling	15 min 65% HR_{max}; 10 min TT	25	5.9	0.19	− 0.69; 1.07
Acker-Hewitt et al. [45]	10M	28 ± 9	66 ± 9	6 mg/kg^{-1}; 60	Cycling	20 min 60% VO_{2max}; 20 Km TT (last 5 Km graded)	64.2	3.8	0.19	− 0.69; 1.07
Kilding et al. [51]	10M	24.2 ± 5.4		3 mg/kg^{-1}; 60	Cycling	20 min 60–65% MPO; 5 min high intensity efforts; 3 Km TT	29	2.1	0.20	− 0.68; 1.08
Beaumont and James [78]	8M	22 ± 1	55.9 ± 5.8	6 mg/kg^{-1}; 60	Cycling	60 min 55% W_{max}; 30 min work TT	90	3.1	0.21	− 0.77; 1.20
Ganio et al. [79]	11M	25 ± 6	58.7 ± 2.9	3 mg/kg^{-1}; 60	Cycling	90 min 60–70% VO_{2max}; 15 min KJ TT	105	4.8	0.22	− 0.62; 1.06
Laurence et al. [80]	12M	25.5 ± 2.2		6 mg/kg^{-1}; 60	Cycling	30 min TT	30	5.2	0.23	− 0.57; 1.03
Irwin et al. [61]	12M	28.3 ± 5.8	63.7 ± 7.4	3 mg/kg^{-1}; 90	Cycling	0.75*W_{max}*3600 KJ TT	60	3.4	0.25	− 0.56; 1.05
Quinlivan et al. [65]	11M	31.6 ± 6.1	60.7 ± 8.1	3 mg/kg^{-1}; 90	Cycling	0.75*W_{max}*3600 KJ	64.6	2.8	0.25	− 0.59; 1.09
Walker et al. [68]	9M	23 ± 3	71.2 ± 6.8	6 mg/kg^{-1}; 60	Cycling	90 min 70% VO_{2max}; 0.7*W_{max}*1800 TT	118	4.1	0.26	− 0.67; 1.19

Table 2 (continued)

Study	Sample	Age	VO_{2max}	Caffeine dose and timing	Mode of exercise	Exercise protocol	Total exercise duration (min)	Time trial improvement over placebo (%)	Effect size	Upper and lower 95% CI
Astorino et al. [42]	8M	28 ± 6	56.9 ± 3.8	5 mg/kg^{-1}; 60	Cycling	10 Km TT	17	4.2	0.32	− 0.67; 1.31
Astorino et al. [55]	8M; 1F	27.4 ± 5.9	57.5 ± 3.9	5 mg/kg^{-1}; 60	Cycling	10 Km TT	17	4.0	0.32	− 0.61; 1.25
Glaister et al. [66]	14F	31 ± 7	52.3 ± 4.9	5 mg/kg^{-1}; 60	Cycling	20 Km TT	35	5.2	0.41	− 0.34; 1.16
Dean et al. [52]	8M	36.4 ± 6.1	52.5 ± 6.1	3 mg/kg^{-1}; 60	Cycling	60 min 60% VO_{2max}; 40 Km TT	120	4.7	0.58	− 0.43; 1.58
de Santos et al. [70]	8M	32.6 ± 5.4	57.5 ± 5.8	5 mg/kg^{-1}; 60	Cycling	4 km TT	7	6.3	0.65	− 0.37; 1.66
Hodgson et al. [71]	8M	41 ± 7	58 ± 3	5 mg/kg^{-1}; 60	Cycling	30 min 55% VO_{2max}; 0.7*W_{max}*2700	70	6.1	1.11	0.04; 2.19
Felippe et al. [62]	11M	34 ± 13	55 ± 13	5 mg/kg^{-1}; 60	Cycling	4 Km TT	6.7	6.1	1.74	0.73; 2.75

W_{max} work rate max, *TT* time trial, *KJ* kilojoules, *M* males, *F* females, *CI* confidence interval, HR_{max} maximal heart rate, $VO_{2max/peak}$ maximal oxygen uptake (ml/kg/min)

intervals which suggests a low risk of publication bias across all studies.

4 Discussion

The purpose of this systematic review and meta-analysis was to critically evaluate the effect of acute caffeine ingestion on endurance time-trial performance. The main finding was that acute caffeine ingestion has a small but significant effect on endurance performance (MPO: ES = 0.22 ± 0.15, P = 0.004; Time: ES = 0.28 ± 0.12, P < 0.001), evident by an increase in mean power output (2.92 ± 2.18%) and faster time-trial times (2.26 ± 2.60%) compared to placebo trials. The similar improvement in power output and TT time supports the statement by Hopkins [81] that a 1% change in endurance power output measured on an ergometer is equivalent to a 1% change in running time-trial speed or time. These findings are similar to Ganio et al. [14] who reported a mean improvement in endurance performance following caffeine ingestion of 3.2 ± 4.3% across all exercise modalities. However, an earlier meta-analysis by Doherty et al. [5] reported much larger mean improvements following caffeine ingestion. They found an increase in endurance performance during cycling tests of 22.3 ± 13.3% and 19.0 ± 13.6% during running tests. However, the analysis by Doherty et al. [5] included trials which used time to exhaustion protocols which may have affected the results. Hopkins [81] reported that a 1% change in power output can lead to a 15% change in time to exhaustion, which may explain why they found large increases in endurance performance.

Meta-regression analysis showed no association between caffeine dose, VO_2, exercise duration, and exercise mode and mean performance improvement between caffeine and placebo. This suggests that caffeine doses of between 3–6 mg·kg^{-1} have a similar ergogenic effect on endurance performance. Therefore, individuals who may feel more sensitive to caffeine, or who want to minimise potential negative side effects, can potentially use a low dose (3 mg·kg^{-1}) of caffeine and still maintain similar ergogenic effects to a moderate dose (6 mg·kg^{-1}).

As seen in Figs. 3 and 5 intra-study variation is large, as many studies reported individuals who performed worse following caffeine ingestion compared to placebo, despite a mean improvement in performance across all participants in the studies following caffeine ingestion. A number of factors can influence individual responses and metabolism of caffeine including smoking [82], age [83], and gender [84]. Smoking increases enzyme activity which causes caffeine to be metabolised faster [82]. Likewise, the older an individual is, the slower the rate of caffeine metabolism in the body [83]. Gender can also play a large role on the rate of caffeine metabolism such that women

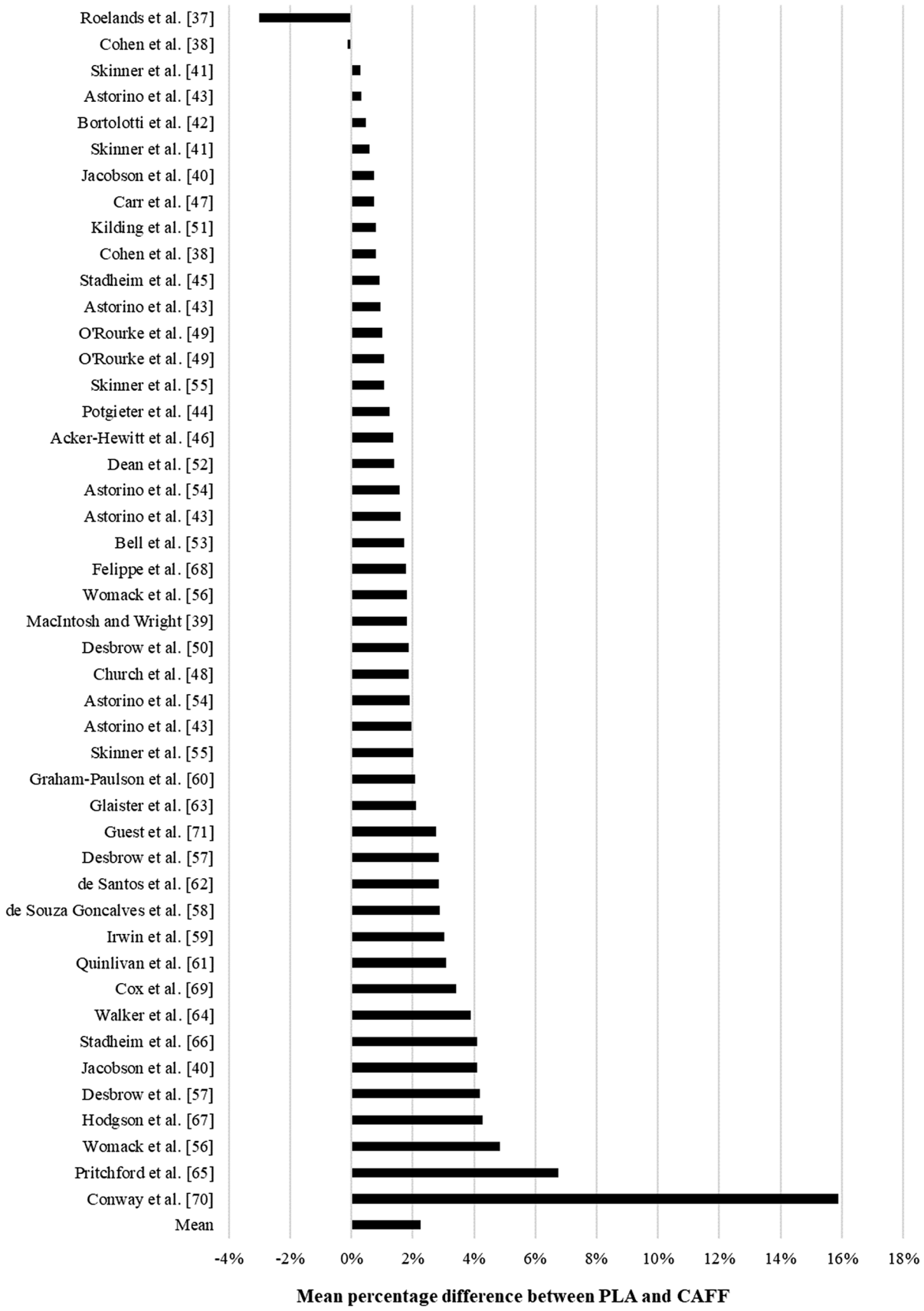

Fig. 2 Mean percent improvement in time trial performance (time) following caffeine ingestion compared to placebo trial. *PLA* placebo trials; *CAFF* caffeine trials

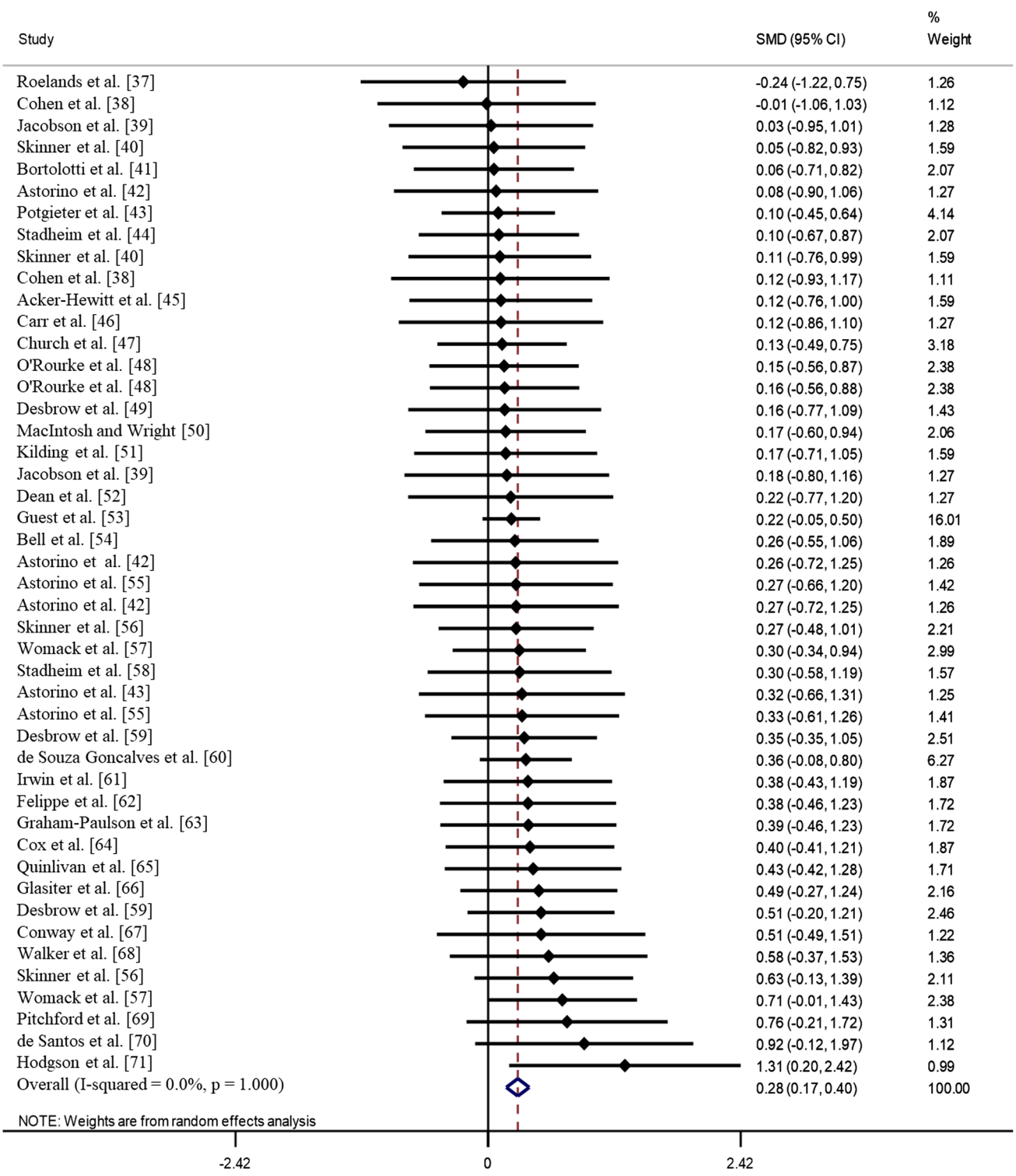

Fig. 3 Effect size of caffeine ingestion on time trial performance (time) compared to placebo with 95% confidence intervals. Overall mean effect and 95% CI is presented with I^2 and Chi squared p values in parentheses. *SMD* standard mean difference; *CI* confidence interval

metabolise caffeine at different rates which is dependent on the stage of the menstrual cycle, as well as the use of oral-contraceptives, which can prolong the half-life of caffeine in the body [84]. Thus, when conducting caffeine supplementation studies, factors such as sex, age and

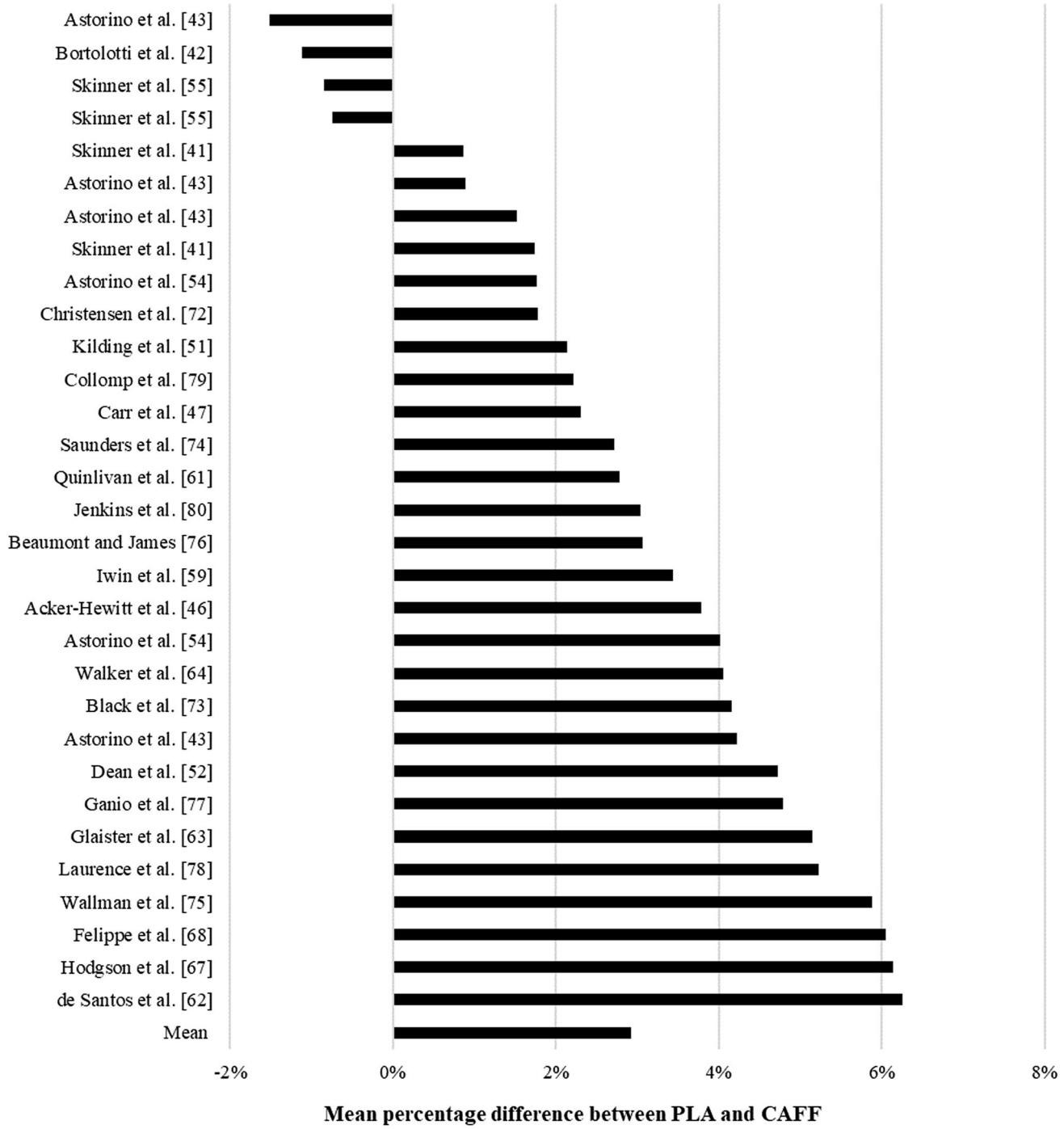

Fig. 4 Mean percent improvement in time trial performance (MPO) following caffeine ingestion compared to placebo trial. *PLA* placebo trials; *CAFF* caffeine trials

smoking status should be taken into consideration when designing the study and comparisons that will be made.

Genetics has also been shown to contribute to the variability in responses to caffeine ingestion [85]. Specifically the CYP1A2 and ADORA2A genes have been identified as large contributors to caffeine metabolism and caffeine sensitivity, respectively [85]. CYP1A2 is part of the cytochrome P450 enzyme family which is responsible for approximately 75% of the metabolism of drugs and is responsible for the metabolising caffeine into paraxanthine, theobromine and theophylline [86]. An A → C polymorphism of the CYP1A2 has been associated with

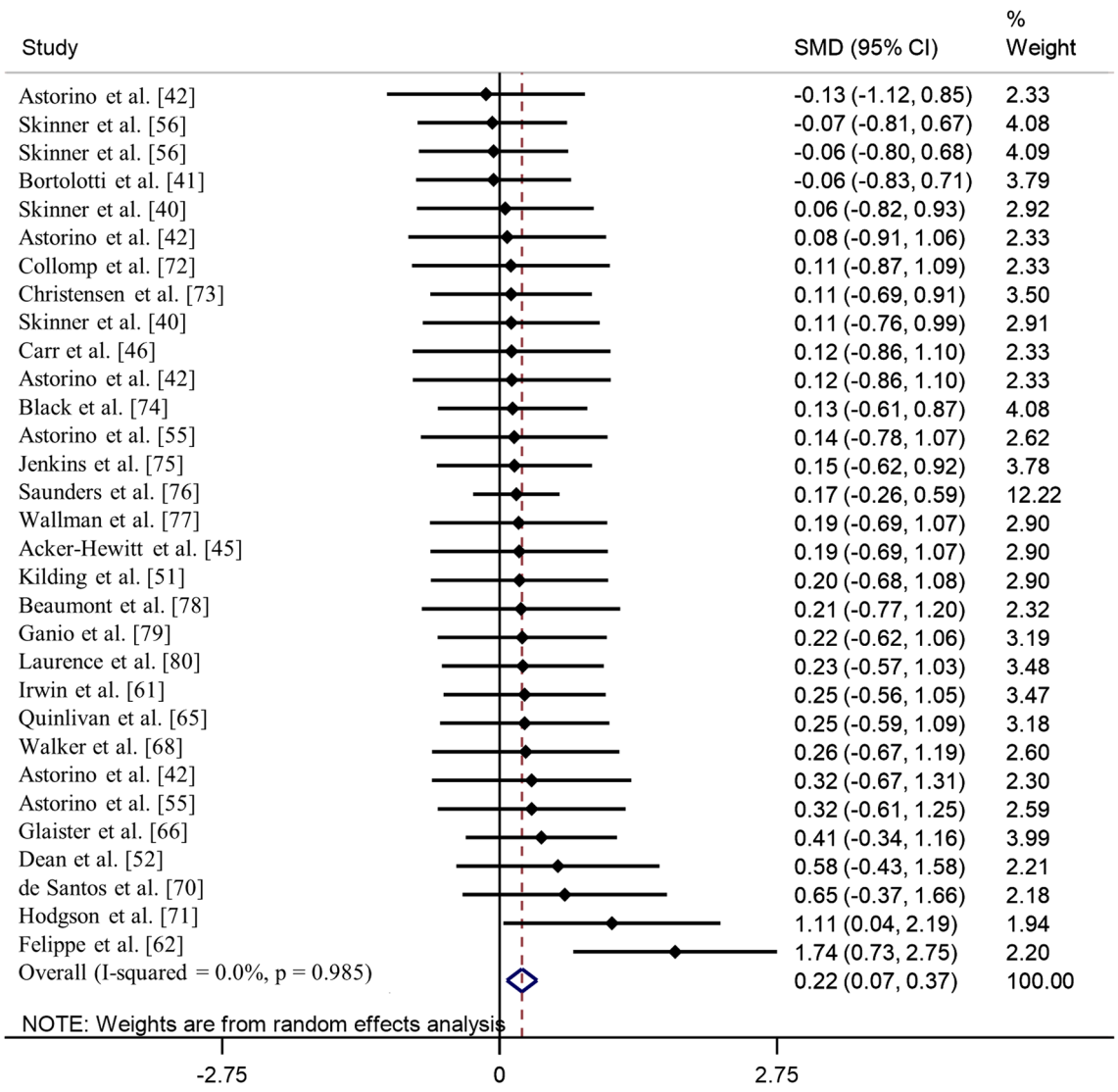

Fig. 5 Effect size of caffeine ingestion on mean power output compared to placebo with 95% confidence intervals. Overall mean effect and 95% CI is presented with I^2 and Chi squared p value in parentheses. *SMD* standard mean difference; *CI* confidence interval

changes in the rate of caffeine metabolism [87, 88]. Those with the homozygous A/A allele have been found to metabolise caffeine faster than C allele carriers (A/C and C/C); homozygous C/C individuals have the slowest caffeine metabolism [88–90]. A slower caffeine metabolism such as that found in A/C and C/C allele carriers could result in a longer half-life thus prolonging the ergogenic effect of caffeine whereas faster metabolism would result in a faster breakdown of caffeine, reducing the half-life of caffeine in the body. Caffeine typically has a half-life of 3–5 h in healthy adults, therefore those with a faster metabolism may not experience the ergogenic effects of caffeine for the duration of an event if it is metabolised prior to the end of the exercise in long duration activities such as, marathons, triathlons and ultra-endurance events. Only one study included in the present review conducted genetic analysis pertaining to caffeine metabolism [57]. Womack et al. [57] tested participants' CYP1A2 genotype and reported that fast metabolisers of caffeine (A/A) performed better in a 40 km cycle time-trial following caffeine ingestion compared to slow metabolisers of caffeine (A/C and C/C). However, more research is needed to determine the effects of CYP1A2 genotype on the ergogenicity of caffeine as well as controlling for confounding variables such as other genetic factors (ADORA2A) and epigenetic factors such as, age, smoking, gender and ethnicity.

The ADORA2A gene encodes for certain adenosine receptors found predominantly in the brain. As caffeine is an adenosine receptor antagonist it is likely that variations in the ADORA2A gene will affect the actions of

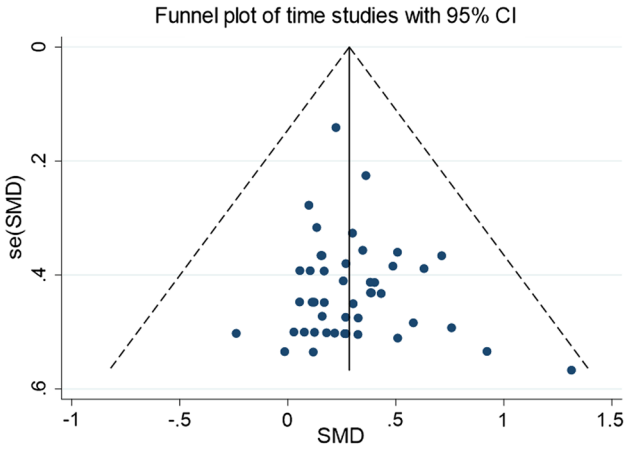

Fig. 6 Funnel plot of standard mean difference against standard error for time-trial completion time. *se*(*SMD*) standard error of the mean difference; *SMD* standard mean difference; *CI* confidence interval

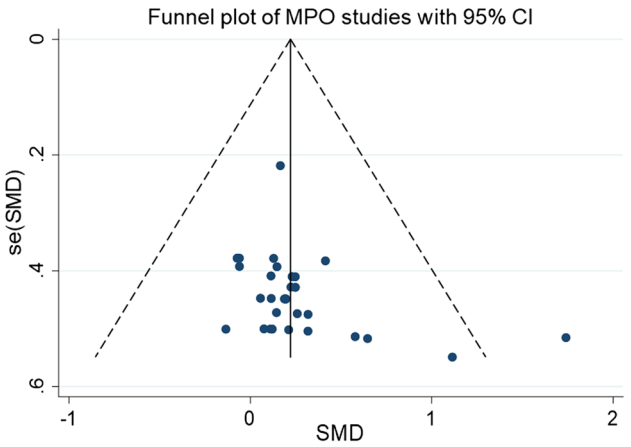

Fig. 7 Funnel plot of standard mean difference against standard error for MPO. *se*(*SMD*) standard error of the mean difference; *SMD* standard mean difference; *CI* confidence interval

caffeine on the adenosine receptor. Little research exists on ADORA2A and the effects it could have on caffeine and exercise. However, it has been reported that individuals with the T/T allele experienced increased anxiety following acute caffeine ingestion, which may suggest a higher caffeine sensitivity compared to the C/T and C/C alleles. To the authors' knowledge only one study has investigated the potential effects of ADORA2A genotype on caffeine ergogenicity during endurance exercise [36]. Loy et al. [36] grouped participants based on their ADORA2A genotype. As seen in Fig. 4 Loy et al. [36] reported the highest and lowest changes in endurance performance following caffeine ingestion compared to placebo. Carriers of the C allele variant showed a decreased endurance performance (− 4.08%) following caffeine ingestion compared to placebo, while the homozygous T allele carriers showed increased endurance performance following caffeine ingestion compared to placebo (13.4%). However, each group only consisted of 6 participants which limits the impact of the finding, but still suggests that ADORA2A genotype may have a large effect on the effectiveness of caffeine supplementation for endurance exercise. Significantly more work needs to be conducted to determine the role genetics could potentially play on the ergogenicity of caffeine (as well as other popular supplements) in order to fully maximise its effects.

5 Applications

With the prevalence of caffeine use before and during elite endurance events [2, 91] being as high as 89% it is unlikely that caffeine will give athletes an essential edge over their competitors, but rather it may prevent them from being disadvantaged compared to other competitors who are also likely to be consuming caffeinated supplements. The fastest official half-marathon time is 58 min 23 s. With the average performance increase found across the studies presented here being 2.52%, over a 58 min event this equates to a 1.46 min improvement, this is the difference between 1st (58:23) and 97th place (59:45) in the list of current fastest half-marathon times [92]. Therefore, whether or not an athlete consumes caffeine prior or during an endurance event may have a large impact on the overall results. However, many of the studies included in this review were conducted on recreationally trained athletes and not of the elite level, thus it is possible that the proposed effect of caffeine is not generalisable to elite level athletes. While meta-regression analysis showed no relationship between VO_2 and effect of caffeine, further investigation using a meta-analytical approach on the effects of caffeine at an elite sports players' level is warranted.

Athletes may also want to familiarise themselves with caffeine consumption during training and find the consumption protocol which provides the best possible effects for their own individual needs. To date, not enough research exists for individualised recommendations, thus it is up to the athlete and training staff to determine the best timing, dosage and method to consume caffeine for the athletes training and competition needs.

6 Limitations and Future Considerations

The present meta-analysis does not include time-to-exhaustion studies as they have greater variability and less reliability than time-trial studies [7]. Furthermore, cycling is the main exercise modality used in these studies,

most likely due to the ease of measurement when using a cycle ergometer. However, results may vary when other exercise modalities are employed in the testing protocols, but a larger variety of exercise modalities would provide stronger evidence for the ergogenic effects of caffeine on endurance performance in multiple sports. Additionally, many of the participants used in the included studies were recreationally trained athletes, and further studies comparing the differences in the ergogenicity of caffeine between recreational and elite athletes is warranted.

Many athletes consume a range of supplements such as vitamins, bicarbonate, caffeine, nitrates and beta-alanine during training and competition, and it has been reported that 19% of athletes co-ingest caffeine with other substances [1, 2, 51]. As a result, there are many studies that have begun investigating the effects of caffeine in combination with other popular supplements, however, more work is still required in this area.

7 Conclusions

The results of the present meta-analysis indicate caffeine has a small positive effect (2.52%; ES = 0.26) on endurance performance. However, large inter-individual responses to caffeine ingestion still exist and reasons for this variance between individuals should be further explored and taken into consideration when prescribing caffeine supplementation for athletes.

Compliance with Ethical Standards

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Conflict of interests The authors Kyle Southward, Ajmol Ali and Kay Rutherfurd-Markwick declare that they have no conflicts of interest declare that they have no competing interests to declare in relation to this manuscript.

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