

# **Polyphenols and Performance: A Systematic Review and Meta-Analysis**

Vaughan Somerville<sup>1</sup> · Cameron Bringans<sup>2</sup> · Andrea Braakhuis<sup>1</sup>

© Springer International Publishing Switzerland 2017

#### Abstract

*Background* Polyphenols exert physiological effects that may impact athletic performance. Polyphenols are antioxidants that have been noted to hinder training adaptations, yet conversely they stimulate stress-related cell signalling pathways that trigger mitochondrial biogenesis and influence vascular function.

*Objective* To determine the overall effect of polyphenols on human athletic performance.

*Methods* A search strategy was completed using MED-LINE, EMBASE, CINAHL, AMED and SPORTDiscus in April 2016. The studies were screened and independently reviewed by two researchers against predetermined criteria for eligibility. As a result of this screening, 14 studies were included for meta-analysis. Of these, the studied populations were predominately-trained males with an average intervention dose of  $688 \pm 478 \text{ mg} \cdot \text{day}^{-1}$ .

*Results* The pooled results demonstrate polyphenol supplementation for at least 7 days increases performance by 1.90% (95% CI 0.40–3.39). Sub-analysis of seven studies using quercetin identified a performance increase of 2.82% (95% CI 2.05–3.58). There were no adverse effects reported in the studies in relation to the intervention.

*Conclusion* Overall the pooled results show that polyphenols, and of note quercetin, are viable supplements to improve performance in healthy individuals.

## **Key Points**

Polyphenol supplementation for at least 7 days has a clear moderate benefit on performance in healthy individuals.

The performance benefits of quercetin are superior to those of other polyphenol supplements.

More research is needed on optimal dose; however, greater intakes could improve the performance response.

#### **1** Introduction

The popularity of perceived naturally occurring plant extracts and phytochemicals to enhance physical performance, exercise recovery and maintain health has increased dramatically in recent years at both collegiate and Olympic levels, with vitamins or multi-vitamins being the most common choice [1-3]. Sporting supplements are becoming more widespread with winning and losing coming down to a matter of millimetres and milliseconds as athletes verge on the edge of what is physically attainable. Part of the attraction of phytochemicals is the perception of food as medicine to improve health, the fact that they are generally less expensive, and the proposed fewer

Vaughan Somerville vsom721@aucklanduni.ac.nz

<sup>&</sup>lt;sup>1</sup> Department of Nutrition and Dietetics, Faculty of Medical and Health Science, The University of Auckland, Auckland, New Zealand

<sup>&</sup>lt;sup>2</sup> Department of Surgery, Faculty of Medical and Health Science, School of Medicine, The University of Auckland, Auckland, New Zealand

side effects than manufactured drugs [2, 4]. One important plant-derived substance that has shown great promise of late is polyphenols.

Polyphenols are micronutrients found in plants and their products, including berries, wine, green tea and chocolate, and are therefore incorporated into the everyday human diet [5]. Polyphenols are a growing area of research because of their novel pleiotropic effect on different human conditions such as chronic diseases, ageing and immunity [5–9]. Currently there are over 8000 polyphenols identified that are distinguished into four main groups: flavonoids, stilbenes, lignans and phenolic acids, all with a range and variation of in vivo effects.

Polyphenol supplementation is currently controversial, as although polyphenols demonstrate antioxidant activity that may dampen training adaptations [10-12], they also influence other mechanisms which tend toward a performance benefit [10-12]. Polyphenols have been purported to improve performance by increasing mitochondrial biogenesis in two ways. Firstly, they stimulate stress-related cell signalling pathways that increase expression of genes encoding cytoprotective proteins such as nuclear respiratory factor 2 (NRF2) [13, 14]. NRF2, a member of the Cap-N-Collar family of transcription factors, plays an important role in mitochondrial biogenesis, and variants of the NRF2 gene have been associated with endurance performance [15]. Secondly, select polyphenols such as quercetin, resveratrol and curcumin have been reported to modulate muscle function and mitochondrial biogenesis by activating sirtuins (SIRT1) and increasing peroxisome proliferator-activated receptor  $\gamma$  coactivator (PGC-1 $\alpha$ ) activity [16]. In addition, evidence shows that various polyphenols improve flow-mediated dilatation and endothelial function in humans by increasing endothelial nitric oxide synthesis [17–21]. In sports where the rate of blood flow and maximum cardiac output are important determinants of cardiovascular performance, by acting on endothelial function, polyphenols could aid overall athletic performance [22, 23]. Further to these mechanisms, quercetin also binds and antagonises the adenosine receptor, which may improve performance in a caffeine-like manner [24].

Recently both narrative and systematic reviews have been published supporting a role for polyphenol supplementation on athletic performance [25–28]. However, despite these reviews, the overall effect polyphenols have on performance is inconclusive as the majority of studies involve a small sample size. With respect to sample sizes, the reality is that experimentally impractical large samples are required for a clear within-study conclusion; the advantage of meta-analysis is the pooling of smaller samples to provide a large sample estimate. To date, there have been meta-analyses of quercetin, a specific polyphenol, reporting a performance increase ranging from 0.74–3.0% [27, 28]. Results from the meta-analyses suggest quercetin supports performance in endurance events; however, the data collected and type of statistical analysis used means conclusions from such meta-analyses are difficult to make. The advantage of the current analysis is the effort to adjust each performance test to a common metric, thus improving the pooled sample and confidence in the conclusions generated.

The objectives of this systematic review were to critically examine the studies involving polyphenols and performance, and determine the overall effect of dietary polyphenols on performance.

## 2 Methods

#### 2.1 Search Strategy

All literature that investigated the effect of polyphenols and performance was searched and obtained using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement guidelines with a predetermined search strategy [29]. The search was conducted using Medical Subject Headings and Boolean operators where appropriate. There was no limit on date, status or language of publication. The search strategy was run using MED-LINE, EMBASE, CINAHL, AMED and SPORTDiscus. The strategy itself consisted of two main concepts: polyphenols (dietary and individual) and exercise. The metaRegister of controlled trials (mRCT), http://www. clinicaltrials.gov, the World Health Organization (WHO) International Clinical Trials Registry Platform (ICTRP), and Google Scholar were also searched using the terms "Polyphenol" and "Exercise" to obtain articles that may have been omitted.

#### 2.2 Study Selection

Once all the articles were identified, two reviewers screened the titles and abstracts for inclusion and any duplicates were deleted. As a result of this screening, 124 full-text articles remained. The reference lists of these remaining articles, including reviews, were assessed for additional papers and ten more were selected. The same two reviewers then independently assessed the 134 articles against the predetermined criteria.

To be included, studies must: (i) be primary intervention studies designed as randomized controlled trials (RCTs); (ii) be either single or double blind; (iii) include healthy participants (trained or untrained) aged between 18 and 70 years; and (iv) contain a polyphenol intervention (either dietary or individual)  $\geq$ 7 days. The primary outcomes collected were measures of performance that could be

converted to a power output for meta-analysis. These included percentage difference in performance between control and intervention group, exercise time to fatigue, distance covered in a pre-selected time period, time to complete a certain distance, maximum power output and anaerobic threshold. Studies including maximal oxygen uptake  $(VO_{2max})$  were excluded with the large inherent error during measurement [30].

Studies were also excluded if they: (i) had participants with a history of, or current, cardiovascular, pulmonary or endocrinological disease, malignancy, obesity and/or immune defects or allergies, e.g. allergic rhinitis; (ii) used red wine as the intervention due to an alcohol effect on performance; or (iii) used spirulina or beetroot juice as the intervention due to the confounding compounds in these products. Based on this, two authors (VS, CB) determined the included studies with any inconsistencies settled by a third author (AB). Overall, 14 studies were included for meta-analysis. The process and reasons are illustrated in Fig. 1.

#### 2.3 Data Collection and Quality Assessment

Data were extracted independently by two authors (VS, CB) and entered into a created form. Collected data included: (i) characteristics of the participants (age, sex and location); (ii) study design (setting, duration and characteristics); (iii) intervention protocol (dose and duration of polyphenol); (iv) performance outcomes; and (v) bias. Attempts were made to contact one investigator for additional data [31].

Two authors (VS, CB) then independently completed a bias assessment for the study based on the following six categories as per the Cochrane Handbook: (i) sequence generation; (ii) allocation concealment; (iii) blinding; (iv) missing outcome data; (v) risk of reporting bias; and (vi) other sources of bias [31]. Publication bias was also accounted for by plotting the effect size as a percentage against the standard error (SE) for each study.

#### 2.4 Statistical Analysis

For meta-analysis, all performance data were converted to a common metric, representing the percentage effect on mean power in an equivalent time trial. Initially raw performance data were transformed into a percentage of intervention versus control outcomes. Data were converted to power by multiplying the percentage effect by the following: running or cycling on a Monark ergometer, 1; cycling on a Velotron ergometer, 2.5; rowing, 3 [32, 33]. Inversely, if the performance measure was time to exhaustion at a constant power/speed, then the percentage effect was divided by 15 [32, 34]. Converted performance effects for incremental tests to fatigue or tests with a preload were calculated as an assumed fraction at which the test started.

Flat ground distance = speed + 
$$(0.045 \times \text{ incline } \times \text{ speed})$$
(1)

Askari et al. [35] and Kuo et al. [36] used the Bruce protocol starting at a slow walk [37]. We reduced the overall distance reported by 260 m, which was the calculated ground distance achieved before the speed was at such a point to initiate the trial based on the protocol and using Eq. 1, and time by 180 s, respectively. If studies provided exact p values, SE of the calculated percentage effect was calculated dividing the effect by the inverse of the *p* value multiplied by the degrees of freedom. If there was no exact p value, the SE was estimated using the Sportscience Web-based Excel sheet (and assuming a within-subject variation of 2.0) [38]. Data from crossover trials were adjusted to the sample size equivalent to that of a parallel design study to correctly calculate inferential information (SE) [32]. For those crossover studies with sufficient data to calculate accurate inferential information, the sample size remained as reported. Crossover studies were excluded if treatment allocation was not random and there was no pre-study performance test, which minimizes the risk of unit of analysis errors. The magnitudes of the effects were assessed based on the thresholds of 0.5, 1.5, 2.7, 4.2 and 6.7% for small, moderate, large, very large and extremely large, respectively [39].

## **3** Results

#### 3.1 Study Selection

After the search strategy was run, a total of 4794 articles were screened by abstract and title. As a result of screening, 124 full-text articles remained. The reference lists of all remaining articles, including reviews, were assessed for additional papers and ten more were added. Two authors (VS, CB) then independently assessed the 134 articles against the predetermined search criteria. Of these 134 articles, 120 were excluded based on numerous reasons (see Fig. 1). As a result, 14 studies were included in the final meta-analysis.

#### 3.2 Study Characteristics

The characteristics of the 14 studies are summarized in Table 1. The studies included a total of 348 participants of whom 300 and 282 were male and trained, respectively. Ten of the studies were parallel design randomized



Fig. 1 Schematic representation of process and reason for selection for the 14 studies included in the meta-analysis

controlled trials (RCTs) and in total the studies averaged  $688 \pm 478 \text{ mg} \cdot \text{day}^{-1}$  polyphenol for an intervention period of 31 days, excluding Toscano et al. [40] as they based their polyphenol consumption on each participant's weight. Of these papers, seven used quercetin as their intervention while the remaining used individual polyphenols (resveratrol, catechins and anthocyanins), a polyphenol mix, or food-based polyphenol combinations.

#### 3.3 Polyphenols and Performance

#### 3.3.1 Overall Meta-Analysis

The meta-analysis of performance with its associated risk of bias analysis is displayed in Fig. 2. Overall there was a moderate clear improvement in performance.

# 3.3.2 Quercetin Subgroup Analysis

With seven studies using quercetin alone as supplementation, sub-analysis was performed and are displayed in Fig. 3, again with risk of bias summary. The studies included a total of 187 male participants with an average daily intake of 764.3 mg·day<sup>-1</sup>. Once separated, there was again a clear moderate improvement in performance.

# 3.4 Adverse Effects

Of the 14 included studies, only three reported on the incidence of adverse effects [36, 45, 46]. The three studies all reported no adverse effects as a result of the intervention or placebo.

References					
	Participants	Study design	Intervention	Outcomes measured (min)	Original conclusion
Askari et al. [35]	56 male students of Isfahan University having an athletic history of $\leq 3$ years	Double-blind parallel RCT	500 mg·day <sup><math>-1</math></sup> quercetin for 56 days	Distance covered in $VO_{2max}$ test based on Bruce protocol (10) <sup>a</sup>	Author does not state
Bigelman et al. [41]	58 moderately trained males and females recruited from Army and Air Force Reserve Officers' Training Corps (ROTC)	Double-blind parallel RCT	1000 mg·day <sup>-1</sup> quercetin, 400 mg·day <sup>-1</sup> isoquercetin and 120 mg·day <sup>-1</sup> EGCG for 42 days <sup>b</sup>	Time to complete a 36.6-m sprint (0.1) <sup>c</sup>	No change
Braakhuis et al. [42]	23 trained female runners	Double-blind crossover RCT <sup>d</sup>	300 mg·d <sup>-1</sup> anthocyanins for 23 days	A 5-km running time trial on outside track (23) <sup>c</sup>	No change
Cureton et al. [43]	30 young and recreationally active, but not endurance-trained men	Double-blind parallel RCT	1000 mg·d <sup>-1</sup> quercetin for 9–16 days <sup>b</sup>	Work done in 10-min maximal effort cycling trial following the 1 h of cycling at 50% VO <sub>2peak</sub> (10) <sup>c</sup>	No change
Davis et al. [44]	12 regularly active/fit men and woman who were not highly trained	Double-blind crossover RCT <sup>d</sup>	1000 mg·d <sup><math>-1</math></sup> quercetin for 7 days	Time to fatigue at a constant power output of 75% VO <sub>2max</sub> (90) <sup>c</sup>	Increase in performance
Kang et al. [45]	38 active males	Double-blind parallel RCT	66 mg·day <sup>-1</sup> polyphenol for 30 days	Submaximal running time to exhaustion at 80% of the maximal heart rate after a preload (28) <sup>e</sup>	No change
Kuo et al. [36]	40 males with no regular exercise or participation in sports for at least 3 months	Double-blind parallel RCT	36.75 mg·day <sup>-1</sup> EGC; 120.5 mg·day <sup>-1</sup> EGCG; 17.25 mg·day <sup>-1</sup> EC; and 32.5 mg·day <sup>-1</sup> ECG (=207 mg·day <sup>-1</sup> catechins) for 28 days	Run time to exhaustion using a Bruce protocol (13) <sup>a</sup>	No change
MacRae et al. [46]	<ol> <li>elite male cyclists who regularly compete and have had at least</li> <li>months' continuous training</li> </ol>	Double-blind crossover RCT <sup>d</sup>	600 mg·day <sup>-1</sup> quercetin for 42 days <sup>b</sup>	Time to complete 29.82 km using a Velotron ergometer (52) <sup>e</sup>	Increase in performance
Nieman et al. [47]	30 males who have been sedentary for previous 6 months	Double-blind crossover RCT <sup>d</sup>	$1000 \text{ mg} \cdot \text{day}^{-1}$ quercetin for 14 days	Distance covered in 12-min time trial on a treadmill (12) <sup>e</sup>	Increase in performance
Roberts et al. [48]	14 recreationally active males	Double-blind parallel RCT	400 mg·d <sup>-1</sup> EGCG for 28 days	Distance covered during 40-min trial on a Monark ergometer (40) <sup>c</sup>	Increase in performance
Scholten et al. [49]	35 physically active males	Double-blind parallel RCT	$1000 \text{ mg} \cdot \text{day}^{-1}$ quercetin for 56 days	5-km running time trial (27) <sup>c</sup>	No change
Scribbans et al. [50]	16 males who engaged in less than 3 h of structured aerobic exercise per week	Double-blind parallel RCT	$150 \text{ mg}\cdot\text{day}^{-1}$ 99% <i>trans</i> -resveratrol for 28 days	Wingate test (0.5) <sup>c</sup>	Decrease in performance
Skarpańska- Stejnborn et al. [51]	22 males of the Polish rowing team attending the 2006 Youth World Championship	Double-blind parallel RCT	1.2 g·day <sup><math>-1</math></sup> artichoke-leaf extract for 35 days	2-km rowing time trial (6) <sup>c</sup>	Author does not state

nec
ontii
ğ
le ]
Tab

References	Participants	Study design	Intervention	Outcomes measured (min)	Original conclusion
Toscano et al. [40]	28 male and female recreational runners	Double-blind parallel RCT	10 ml/kg·day <sup><math>-1</math></sup> of juice containing 1.82 g/L of total phenols for 28 days	Run time to exhaustion at constant speed (90) <sup>c</sup>	Increase in performance
RCT randomized con uptake	trolled trial, EGCG epigallocatechin gallate	, EGC epigallocatechin,	EC epicatechin, ECG epicatechin gallate, VO2	<i>nax</i> maximal oxygen uptake, <i>VO2pee</i>	ak peak oxygen
<sup>a</sup> Indicates Stage 1 o.	f Bruce protocol removed from calculation	of percentage effect			
<sup>b</sup> Intervention and pl	acebo also include other vitamins				
<sup>c</sup> Indicates the percer	ntage effect was unchanged or modified usi	ng explained protocol			
<sup>d</sup> Sample size was m	ultiplied by 4 when insufficient inferential	data, as the study utilize	d a crossover protocol		
e Performance test w.	as completed after a preload exercise sessic	it was assumed that t	his would approximately double the performanc	ce effect, and the effect was according	gly adjusted by

halving

## 3.5 Bias

The full bias summary can be seen alongside the metaanalysis (Figs. 2, 3). Overall the studies had a predominantly low risk of bias in blinding, incomplete outcome data and other bias categories. The remaining categories were essentially unclear, with only two studies having a high risk in any category [43, 46]. Both these studies received funding from a source with a potential interest in a positive result, but no 'Conflict of Interest' statement was present.

## 3.5.1 Publication Bias

Figure 4 shows that the publication bias analysis was symmetrical in its plots but tended towards positive results (effect size >1) and had one obvious outlier [35].

# 4 Discussion

To the authors' knowledge this is the first meta-analysis of polyphenols and their effect on human athletic performance. The results of this meta-analysis suggest that polyphenol supplementation is associated with a clear moderate improvement of performance with no reported adverse effects. Furthermore, this effect is marginally increased when quercetin is the polyphenol supplement. Because the data were adjusted for different exercise protocols, this is an important real-world result for sport team management, such as managers and strength and conditioning coaches, and dieticians, as polyphenol supplementation can improve performance in any sport code irrespective of duration.

This meta-analysis is in line with previous literature that has generally reported that polyphenols tend to improve performance [25, 27, 28]. There are two previous metaanalyses on quercetin; however, they contain certain limitations: not adjusting for exercise protocols, comparing merely post-intervention performance differences rather than pre- and post-performance increase/decrease, and using  $VO_{2max}$  as an accepted performance measure, which has the possibility of influencing the data given the large inherent error during measurement [30]. Despite these limitations, our findings concerning the effects of polyphenol supplementation on performance fall within the range reported in the previous literature [27, 28]. This does not validate the results of the previous meta-analyses but does show that when the data are adjusted correctly, there is still a positive effect on performance.

There are ranges of mechanisms by which polyphenols may exert the reported beneficial performance effect. Although a detailed mechanistic review is beyond the

				Mean Difference	Mean Differen	ce Risk of Bias
Study or Subgroup	Mean Difference	SE	Weight	IV, Random, 95% Cl	IV, Random, 95	%CI ABCDEF
Askari et al. [35]	-15	11.33	0.4%	-15.00 [-37.21, 7.21]		<b>+ ? + ? ? +</b>
Bigelman et al. [41]	1.2	1.68	6.5%	1.20 [-2.09, 4.49]	+	
Braakhuis et al. [42]	0	0.87	8.4%	0.00 [-1.71, 1.71]	- +	?? 🕈 🖶 ? 🖶
Cureton et al. [43]	2.5	1.04	8.0%	2.50 [0.46, 4.54]	-	? 🔁 🔁 ? 🔵
Davis et al. [44]	0.9	0.81	8.5%	0.90 [-0.69, 2.49]	+	?? 🔁 🖶 ???
Kang et al. [45]	2.9	1.43	7.1%	2.90 [0.10, 5.70]	-	•••••?•
Kuo et al. (36)	2.2	1.27	7.5%	2.20 [-0.29, 4.69]	-	???•?•
MacRae and Mefferd (46)	7.4	0.84	8.4%	7.40 [5.75, 9.05]	+	? 🔁 🔁 ? ? 🔵
Nieman et al. [47]	1.5	0.72	8.7%	1.50 [0.09, 2.91]	-	?? 🔁 🖶 ???
Roberts et al. [48]	2.8	1.52	6.9%	2.80 [-0.18, 5.78]	•	?? 🕈 🖶 ???
Scholten et al. [49]	2.7	1.42	7.1%	2.70 [-0.08, 5.48]	-	🛨 ? 🛨 ? ? 🔁
Scribbans et al. [50]	-4.4	1.42	7.1%	-4.40 [-7.18, -1.62]		?? 🕈 🖶 ? 🖶
Skarpanska-Stejnborn et al. [51]	4.4	1.22	7.6%	4.40 [2.01, 6.79]	-	?? 🔁 🔁 ? 🔁
Toscano et al. [40]	1	1.07	7.9%	1.00 [-1.10, 3.10]	+	🔁 ? ? 🖶 ? 🖶
Total (95% CI)			100.0%	1.90 [0.40, 3.39]	•	
Heterogeneity: Tau <sup>2</sup> = 6.20; Chi <sup>2</sup> =	77.51, df = 13 (P < 0					
Test for overall effect: Z = 2.49 (P =	0.01)				-50 -25 0	25 50
······					Favours control Favo	urs polyphenol

**Fig. 2** Forest plot of the effect of polyphenol supplementation for at least 7 days on performance in healthy individuals presented as percentage effect on mean power in an equivalent time trial. *a* Random sequence generation (selection bias); *b* Allocation concealment bias (selection bias); *c* Blinding of participants and

personnel (performance bias); *d* Incomplete outcome data (attrition bias); *e* Selective reporting (reporting bias); *f* Other bias. *CI* confidence interval, *IV* inverse variance, *SE* standard error, + high risk, - low risk, ? unclear risk



Fig. 3 Sub-analysis forest plot of the effect of quercetin supplementation for at least 7 days on performance in healthy individuals presented as percentage effect on mean power in an equivalent time trial. a Random sequence generation (selection bias); b Allocation concealment bias (selection bias); c Blinding of participants and

scope of this review, the following points can be noted. Firstly, select polyphenols included in this study, namely quercetin, resveratrol and catechins have been reported to activate SIRT1 [16]. SIRT1 deacetylates PGC-1 $\alpha$ , consequently increasing PGC-1 $\alpha$  activity and up-regulating mitochondrial biogenesis [7, 52]. By altering mitochondrial activity and/or numbers, it is plausible that a positive exercise adaption will occur, similar to training. As such, the authors hypothesise from the results that this could be a potential mechanism for the performance benefit. All the evidence surrounding mitochondrial biogenesis mechanism, however, has not been substantiated in human trials, so the authors can only speculate on this mechanism. Secondly, improvements in vascular function and blood flow have been reported with human interventions, and

personnel (performance bias); *d* Incomplete outcome data (attrition bias); *e* Selective reporting (reporting bias); *f* Other bias. *CI* confidence interval, *IV* inverse variance, *SE* standard error, + high risk, - low risk, ? unclear risk

may induce improved athletic performance. Both epigallocatechin gallate and resveratrol have been reported to have vasodilatory effects by increasing endothelial nitric oxide synthesis [19–21]. Increasing nitric oxide synthesis may help match tissue perfusion of both oxygen and other substrates to the working muscles during exercise, improving performance endurance [53–55]. Thirdly, and less likely, there have been recent publications reporting catechins/green tea extract increases fat oxidation at rest and/or during exercise, although more research is needed to substantiate the claim [56–59]. If confirmed, this provides another potential mechanism supporting a performance improvement by increasing fatty acid utilisation, subsequently decreasing the carbohydrate oxidisation rate and improving exercise capacity. Of the studies included in this



Fig. 4 Scatter plot to investigate publication bias. The effect size (%) was plotted against the standard error (%) of each study. The *dotted line* represents the value of the standard error that divides the graph into a symmetrical plot

review, three used green tea products or extracts and of these. Kuo et al. [36] and Roberts et al. [48] utilised performance tests of longer duration.

The average intake of polyphenols in studies included in the meta-analysis was  $688 \text{ mg} \cdot \text{day}^{-1}$ , which equates to a dietary intake of approximately 200 g of dark chocolate, 250 ml of green tea and 300 mg of mixed berries (blackcurrant, strawberry and blackberry) [60]. This suggests that, although supplementation may be easier for some, this intake can be achieved naturally by everyday foods. Of the studies included, only two studies [40, 51] had food-based interventions, while the remaining used individual or combinations of specific polyphenols. Further research is needed on the complex question of the relative effects of food versus supplements on athletic performance.

It is of note that guercetin alone shows an increased performance improvement compared with the full array of polyphenols in Fig. 2 (2.82 vs. 1.90%). In the quercetin sub-analysis, six of the seven studies had an intervention dose of quercetin around or greater than the average intake of 688 mg  $day^{-1}$ . Interestingly, achieving this intake of quercetin from the diet, would involve consuming either 2.4 kg of dark chocolate or 72 L of red wine daily, both unrealistic for an athlete, supporting the notion of specific quercetin supplementation [60]. This increased performance benefit leads the authors to propose two theories: firstly that quercetin may have a greater performance increase compared with other polyphenols, and/or secondly that a greater performance improvement may be associated daily polyphenol with increased supplementation. Accordingly, further research needs to be conducted around varying doses of quercetin and other polyphenols to determine if this is a specific polyphenol effect or a dosealone effect.

Some studies included substances other than polyphenols, notably vitamin C and caffeine, in their intervention and placebo arms. For example, both MacRae et al. [46] and Kang et al. [45] included 300 and 400 mg  $day^{-1}$  of vitamin C, respectively, in their intervention and placebo supplements. Vitamin C has been reported to impair mitochondrial biogenesis and subsequent training adaptations [61, 62]. The daily levels in both these studies, however, are at a level purported not to have a significant detrimental effect on adaptation, which is supported by the observed effects in these studies [61, 62]. As vitamin C was in both the placebo and the intervention, its effect on the performance of each group should have been identical; however, we could not account for a synergistic effect with the other polyphenols that may have masked or increased the overall effect. Kang et al. [45] also used caffeine in their supplement, which is reported to improve performance with a daily intake of 2–6 mg/kg·day<sup>-1</sup>; however, this dose was not reached by Kang et al. [45] in either group based on the dose range for a 70-kg male [63, 64]. The authors decided studies with other naturally consumed components in both the intervention and placebo were allowed in this review as the authors acknowledge that this is part of everyday nutrition, and therefore mimics the real world more closely.

With regard to the study populations, of note was also the effect of women included in the study population. Of the four studies that included women, all of them reported a mean percentage effect less than the overall result (1.9%)[40–42, 44]. This leads researchers to propose that the performance effect may be influenced by the differences in overall biology in males and females; however, none of these studies differentiated the sexes in their statistical analysis. Consequently, further research assessing the effects of the same polyphenol dose in men and women should be completed to confirm this. Similarly, of the three studies that included non-trained participants, two reported a mean effect that was less than that of the meta-analysed results [47, 50]. Again, further research is needed to determine if exercise/training in conjunction with polyphenol supplementation may have a synergistic effect, resulting in an increased performance benefit.

Further to this, three of the included studies had a performance outcome that was short (<10 min) while the remainder had a longer period of performance [41, 50, 51]. The three short studies reported unchanged, decreased and increased performance, respectively, which was similar to the array of results in the long studies. As such, more research is required investigating at the same polyphenol intervention with different performance measures, to determine if there is a difference in performance improvement based on duration of the exercise modality.

The overall assessment of bias amongst the included studies was deemed low; however, it would be remiss not to mention the key aspects of concern, including a lack of detail around study blinding, incomplete data reported and sponsored funding. Whilst the authors recognise that sponsored funding does not imply data adaption to appease sponsor interests, most studies did not outline to what degree the sponsor influenced the reporting and publication of findings.

Publication bias is also a potential issue in this or any other meta-analysis. As illustrated in Fig. 4, there were only two studies found in the search that reported a negative effect of polyphenol supplementation on performance. This could either be due to polyphenols consistently having a performance benefit effect, or conversely that those papers with negative results were not published. The potential for the latter is a distinct possibility given the difficulties in publishing studies with negative or trivial results. Consequently, although based on the papers identified in the comprehensive search there is an overall positive effect, the authors acknowledge there is a potential that select papers may not have been published that could alter the overall improvement effect and/or size.

For future research conducted on the performance effects of dietary polyphenols, we would recommend including the following research design: (i) provide adequate detail on the method of blinding and participant follow-up to ascertain whether the study was in fact blinded; (ii) report performance data in raw values, including basic variance data (SD); and (iii) if commercially sponsored, provide sufficient detail as to the nature and extent of that support. Further to this, the authors would advise crossover studies with varying doses of the same polyphenol to analyse the dose effect, and similarly crossover studies with the same dose of different individual polyphenols. These two designs would enable researchers to optimise both type and dose of polyphenol supplementation to achieve performance benefit. In addition to the general notes on research reporting, very few studies outlined comprehensive dietary control measures. We would recommend that along with a placebo-controlled design, researchers should attempt to quantify the participants' dietary intake of polyphenols, as those with low intakes are likely to respond more favourably to dietary intervention. Some effort to quantify dietary intake would support the interpretation of outcomes.

## **5** Conclusion

In conclusion, to the authors' knowledge this is the first meta-analysis analysing the effect of polyphenols on performance, while converting all exercise data to a common metric. Overall the meta-analysis reports that polyphenol supplementation, of note quercetin, for at least 7 days has a clear moderate benefit on athletic performance.

**Author contributions** VS and AB conceived and designed the study; VS and CB performed the literature search and were responsible for decisions on inclusion/exclusion of articles (with AB as the decider if there was disagreement); VS analysed the data; VS and AB wrote the article.

#### **Compliance with Ethical Standards**

**Funding** No sources of funding were used to assist in the preparation of this article.

**Conflict of interest** Vaughan Somerville, Cameron Bringans and Andrea Braakhuis declare that they have no conflicts of interest relevant to the content of this review.

#### References

- 1. Darvishi L, Askari G, Hariri M, et al. The use of nutritional supplements among male collegiate athletes. Int J Prev Med. 2013;4(Suppl 1):S68–72.
- Kim J, Kang S, Jung H, et al. Dietary supplementation patterns of Korean Olympic athletes participating in the Beijing 2008 Summer Olympic Games. Int J Sport Nutr Exerc Metab. 2011;21(2):166–74.
- Knapik JJ, Steelman RA, Hoedebecke SS, et al. Prevalence of dietary supplement use by athletes: systematic review and metaanalysis. Sports Med. 2016;46(1):103–23.
- 4. Petróczi A, Naughton DP, Mazanov J, et al. Limited agreement exists between rationale and practice in athletes' supplement use for maintenance of health: a retrospective study. Nutr J. 2007;6(1):34–41.
- Manach C, Scalbert A, Morand C, et al. Polyphenols: food sources and bioavailability. Am J Clin Nutr. 2004;79(5):727–47.
- Mandel S, Youdim MB. Catechin polyphenols: neurodegeneration and neuroprotection in neurodegenerative diseases. Free Radic Biol Med. 2004;37(3):304–17.
- Lagouge M, Argmann C, Gerhart-Hines Z, et al. Resveratrol improves mitochondrial function and protects against metabolic disease by activating SIRT1 and PGC-1α. Cell. 2006;127(6):1109–22.
- Somerville VS, Braakhuis AJ, Hopkins WG. Effect of flavonoids on upper respiratory tract infections and immune function: a systematic review and meta-analysis. Adv Nutr. 2016;7(3):488–97.
- 9. Ristow M. Unraveling the truth about antioxidants: mitohormesis explains ROS-induced health benefits. Nat Med. 2014;20(7):709–11.
- Draeger CL, Naves A, Marques N, et al. Controversies of antioxidant vitamins supplementation in exercise: ergogenic or ergolytic effects in humans? J Int Soc Sports Nutr. 2014;11(1):4–7.
- Gomez-Cabrera MC, Ristow M, Vina J. Antioxidant supplements in exercise: worse than useless? Am J Physiol Endocrinol Metab. 2012;302(4):E476,7 (author reply E478–9).
- Gomez-Cabrera MC, Salvador-Pascual A, Cabo H, et al. Redox modulation of mitochondriogenesis in exercise. Does antioxidant supplementation blunt the benefits of exercise training? Free Radic Biol Med. 2015;86:37–46.
- Eynon N, Alves AJ, Sagiv M, et al. Interaction between SNPs in the NRF2 gene and elite endurance performance. Physiol Genomics. 2010;41(1):78–81.

- Visioli F. Polyphenols in sport: facts or fads? In: Lamprecht M, editor. Boca Raton: Taylor & Francis Group, LLC; 2015.
- Stevenson DE. Polyphenols as adaptogens-the real mechanism of the antioxidant effect? In: Anonymous. Croatia: InTech Rijeka; 2012. p. 143–62.
- Malaguti M, Angeloni C, Hrelia S. Polyphenols in exercise performance and prevention of exercise-induced muscle damage. Oxid Med Cell Longev. 2013;2013:825928. doi:10.1155/2013/ 825928 (Epub 2013 Jul 24).
- Labonté K, Couillard C, Motard-Bélanger A, et al. Acute effects of polyphenols from cranberries and grape seeds on endothelial function and performance in elite athletes. Sports. 2013;1(3):55–68.
- Ghosh D, Scheepens A. Vascular action of polyphenols. Mol Nutr Food Res. 2009;53(3):322–31.
- Kim JA, Formoso G, Li Y, et al. Epigallocatechin gallate, a green tea polyphenol, mediates NO-dependent vasodilation using signaling pathways in vascular endothelium requiring reactive oxygen species and Fyn. J Biol Chem. 2007;282(18):13736–45.
- 20. Nicholson SK, Tucker GA, Brameld JM. Effects of dietary polyphenols on gene expression in human vascular endothelial cells. Proc Nutr Soc. 2008;67(01):42–7.
- Fisher ND, Hughes M, Gerhard-Herman M, et al. Flavanol-rich cocoa induces nitric-oxide-dependent vasodilation in healthy humans. J Hypertens. 2003;21(12):2281–6.
- 22. Bassett DR, Howley ET. Limiting factors for maximum oxygen uptake and determinants of endurance performance. Med Sci Sports Exerc. 2000;32(1):70–84.
- Noakes T. Physiological models to understand exercise fatigue and the adaptations that predict or enhance athletic performance. Scand J Med Sci Sports. 2000;10(3):123–45.
- 24. Alexander SP. Flavonoids as antagonists at A1 adenosine receptors. Phytother Res. 2006;20(11):1009–12.
- Braakhuis AJ, Hopkins WG. Impact of dietary antioxidants on sport performance: a review. Sports Med. 2015;45(7):939–55.
- Myburgh KH. Polyphenol supplementation: benefits for exercise performance or oxidative stress? Sports Med. 2014;44(1):57–70.
- 27. Pelletier DM, Lacerte G, Goulet ED. Effects of quercetin supplementation on endurance performance and maximal oxygen consumption: a meta-analysis. Int J Sport Nutr Exerc Metab. 2013;23(1):73–82.
- Kressler J, Millard-Stafford M, Warren GL. Quercetin and endurance exercise capacity: a systematic review and metaanalysis. Med Sci Sports Exerc. 2011;43(12):2396–404.
- 29. Moher D, Liberati A, Tetzlaff J, et al. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. Ann Intern Med. 2009;151(4):264–9.
- McArdle WD, Katch FI, Katch VL. Essentials of exercise physiology. Philadelphia: Lippincott Williams & Wilkins; 2006.
- Wilborn CD, Taylor LW, Campbell BI, et al. Effects of methoxyisoflavone, ecdysterone, and sulfo-polysaccharide supplementation on training adaptations in resistance-trained males. J Int Soc Sports Nutr. 2006;3(2):19–27.
- Hopkins W, Marshall S, Batterham A, et al. Progressive statistics for studies in sports medicine and exercise science. Med Sci Sports Exerc. 2009;41(1):3–13.
- Saunders MJ, Moore RW, Kies AK, et al. Carbohydrate and protein hydrolysate coingestions improvement of late-exercise time-trial performance. Int J Sport Nutr Exerc Metab. 2009;19(2):136–49.
- Hinckson EA, Hopkins WG. Reliability of time to exhaustion analyzed with critical-power and log-log modeling. Med Sci Sports Exerc. 2005;37(4):696–701.
- 35. Askari G, Ghiasvand R, Paknahad Z, et al. The effects of quercetin supplementation on body composition, exercise

performance and muscle damage indices in athletes. Int J Prev Med. 2013;4(1):21-6.

- 36. Kuo Y, Lin J, Bernard JR, et al. Green tea extract supplementation does not hamper endurance-training adaptation but improves antioxidant capacity in sedentary men. Appl Physiol Nutr Metab. 2015;40(10):990–6.
- Hill J, Timmis A. Exercise tolerance testing. BMJ. 2002;324(7345):1084–7.
- Hopkins WG. A spreadsheet for deriving a confidence interval, mechanistic inference and clinical inference from a P value. Sportscience. 2007;11:16–21.
- 39. Carr AJ, Hopkins WG, Gore CJ. Effects of acute alkalosis and acidosis on performance. Sports Med. 2011;41(10):801–14.
- Toscano LT, Tavares RL, Toscano LT, et al. Potential ergogenic activity of grape juice in runners. Appl Physiol Nutr Metab. 2015;40(9):899–906.
- 41. Bigelman KA, Fan EH, Chapman DP, et al. Effects of six weeks of quercetin supplementation on physical performance in ROTC cadets. Mil Med. 2010;175(10):791–8.
- 42. Braakhuis AJ, Hopkins WG, Lowe TE. Effects of dietary antioxidants on training and performance in female runners. Eur J Sport Science. 2014;14(2):160–8.
- 43. Cureton KJ, Tomporowski PD, Singhal A, et al. Dietary quercetin supplementation is not ergogenic in untrained men. J Appl Physiol (1985). 2009;107(4):1095–104.
- 44. Davis JM, Carlstedt CJ, Chen S, et al. The dietary flavonoid quercetin increases  $VO_{2max}$  and endurance capacity. Int J Sport Nutr. 2010;20(1):56–62.
- 45. Kang SW, Hahn S, Kim J, et al. Oligomerized lychee fruit extract (OLFE) and a mixture of vitamin C and vitamin E for endurance capacity in a double blind randomized controlled trial. J Clin Biochem Nutr. 2012;50(2):106–13.
- 46. MacRae H, Mefferd KM. Dietary antioxidant supplementation combined with quercetin improves cycling time trial performance. Int J Sport Nutr Exerc Metab. 2006;16(4):405–19.
- 47. Nieman DC, Williams AS, Shanely RA, et al. Quercetin's influence on exercise performance and muscle mitochondrial biogenesis. Med Sci Sports Exerc. 2010;42(2):338–45.
- Roberts JD, Roberts MG, Tarpey MD, et al. The effect of a decaffeinated green tea extract formula on fat oxidation, body composition and exercise performance. J Int Soc Sports Nutr. 2015;12(1):1–9.
- 49. Scholten SD, Sergeev IN, Song Q, et al. Effects of vitamin D and quercetin, alone and in combination, on cardiorespiratory fitness and muscle function in physically active male adults. Open Access J Sports Med. 2015;6:229.
- Scribbans TD, Ma JK, Edgett BA, et al. Resveratrol supplementation does not augment performance adaptations or fibretype-specific responses to high-intensity interval training in humans. Appl Physiol Nutr Metab. 2014;39(11):1305–13.
- Skarpanska-Stejnborn A, Pilaczynska-Szczesniak L, Basta P, et al. The influence of supplementation with artichoke (*Cynara* scolymus L.) extract on selected redox parameters in rowers. Int J Sport Nutr Exerc Metab. 2008;18(3):313–27.
- Rohas LM, St-Pierre J, Uldry M, et al. A fundamental system of cellular energy homeostasis regulated by PGC-1alpha. Proc Natl Acad Sci. 2007;104(19):7933–8.
- Kingwell BA. Nitric oxide-mediated metabolic regulation during exercise: effects of training in health and cardiovascular disease. FASEB J. 2000;14(12):1685–96.
- Green DJ, Maiorana A, O'Driscoll G, et al. Effect of exercise training on endothelium-derived nitric oxide function in humans. J Physiol. 2004;561(1):1–25.
- Roberts CK, Barnard RJ, Jasman A, et al. Acute exercise increases nitric oxide synthase activity in skeletal muscle. Am J Physiol. 1999;277(2 Pt 1):E390–4.

- 56. Dulloo AG, Duret C, Rohrer D, et al. Efficacy of a green tea extract rich in catechin polyphenols and caffeine in increasing 24-h energy expenditure and fat oxidation in humans. Am J Clin Nutr. 1999;70(6):1040–5.
- Hodgson AB, Randell RK, Jeukendrup AE. The effect of green tea extract on fat oxidation at rest and during exercise: evidence of efficacy and proposed mechanisms. Adv Nutr. 2013;4(2):129–40.
- Kim H, Quon MJ, Kim J. New insights into the mechanisms of polyphenols beyond antioxidant properties; lessons from the green tea polyphenol, epigallocatechin 3-gallate. Redox Biol. 2014;2:187–95.
- Randell RK, Hodgson AB, Lotito SB, et al. No effect of 1 or 7 d of green tea extract ingestion on fat oxidation during exercise. Med Sci Sports Exerc. 2013;45(5):883–91.

- 60. Rothwell JA, Perez-Jimenez J, Neveu V, et al. Phenol-Explorer 3.0: a major update of the Phenol-Explorer database to incorporate data on the effects of food processing on polyphenol content. Database (Oxford). 2013;2013:bat070.
- 61. Braakhuis AJ. Effect of vitamin C supplements on physical performance. Curr Sports Med Rep. 2012;11(4):180–4.
- 62. Gomez-Cabrera MC, Domenech E, Romagnoli M, et al. Oral administration of vitamin C decreases muscle mitochondrial biogenesis and hampers training-induced adaptations in endurance performance. Am J Clin Nutr. 2008;87(1):142–9.
- 63. Burke LM. Caffeine and sports performance. Appl Physiol Nutr Metab. 2008;33(6):1319–34.
- Goldstein ER, Ziegenfuss T, Kalman D, et al. International society of sports nutrition position stand: caffeine and performance. J Int Soc Sports Nutr. 2010;7(1):1–5.