



Effects of Carbohydrate Mouth Rinse on Cycling Time Trial Performance: A Systematic Review and Meta-Analysis

Cayque Brietzke¹ · Paulo Estevão Franco-Alvarenga¹ · Hélio José Coelho-Júnior² · Rodrigo Silveira¹ · Ricardo Yukio Asano¹ · Flávio Oliveira Pires¹

© Springer Nature Switzerland AG 2018

Abstract

Background Despite the growing number of studies reporting carbohydrate mouth rinse effects on endurance performance, no systematic and meta-analysis review has been conducted to elucidate the level of evidence of carbohydrate mouth rinse effects on cycling trial performance such as time-, work-, and distance-based trials.

Objectives The objective of this study were to establish the effect of a carbohydrate mouth rinse on cycling performance outcomes such as mean power output and time to complete a trial, together with the risk of bias in the cycling-carbohydrate mouth rinse literature.

Methods We systematically reviewed randomized placebo-controlled trials that assessed carbohydrate mouth rinse effects on mean power output and time to complete the trial. A random-effects meta-analysis assessed the standardized mean difference between carbohydrate and placebo mouth rinses.

Results Thirteen studies (16 trials) were qualitatively (systematic review) and quantitatively (meta-analysis) analyzed with regard to mean power output ($n = 175$) and time to complete the trial ($n = 151$). Overall, the reviewed studies showed a low risk of bias and homogeneous results for mean power output ($I^2 = 0\%$) and time to complete the trial ($I^2 = 0\%$). When compared with placebo, the carbohydrate mouth rinse improved mean power output (standardized mean difference = 0.25; 95% confidence interval 0.04–0.46; $p = 0.02$), but not the time to complete the trial (standardized mean difference = -0.13; 95% confidence interval -0.36 to 0.10; $p = 0.25$).

Conclusion The present systematic and meta-analytic review supports the notion that a carbohydrate mouth rinse has the potential to increase mean power output in cycling trials, despite showing no superiority over placebo in improving time to complete the trials.

Electronic supplementary material The online version of this article (<https://doi.org/10.1007/s40279-018-1029-7>) contains supplementary material, which is available to authorized users.

✉ Flávio Oliveira Pires
piresfo@usp.br

¹ Exercise Psychophysiology Research Group, School of Arts, Sciences and Humanities, University of São Paulo, 1000 Arlindo Bétio Avenue, Ermelino Matarazzo, São Paulo, SP 03828-000, Brazil

² Applied Kinesiology Laboratory, University of Campinas, 701 Érico Veríssimo Avenue, Barão Geraldo, Campinas, SP 13.083-851, Brazil

Key Points

A carbohydrate (CHO) mouth rinse improves mean power output, but not the time to complete a cycling time trial.

There is a high level of evidence with a low risk of bias in the cycling-CHO mouth rinse literature.

Further systematic studies are required to assess the level of evidence of CHO mouth rinse effects on different exercise modes.

Future CHO mouth rinse studies should take the blinding of outcome assessment into account.

1 Introduction

The use of a carbohydrate (CHO) mouth rinse to potentiate endurance exercise performance has been proposed since the seminal article by Carter et al. [1]. Recently, the Academy of Nutrition and Dietetics, Dietitians of Canada, and the American College of Sports Medicine stated that CHO mouth rinse may improve endurance performance in long-lasting exercises from 45 to 75 min [2]. It has been suggested that rinsing the mouth with a CHO solution with concentrations no less than 6% for 5–10 s may potentiate endurance exercise performance as a result of an enhanced cerebral activation [3–5]. Therefore, in contrast to peripheral mechanisms suggested when ingesting a CHO solution (i.e., decreased glucose oxidation rate and improved muscle glycogen sparing) [6–8], rinsing the mouth with a CHO solution may improve exercise performance because of the enhanced activation of cerebral structures involved in the reward system, cognitive control, emotional behavior, and interoceptive responses [3, 9, 10].

A number of studies have confirmed that a CHO mouth rinse may potentiate endurance performance in different exercise modes [11–15], although some have reported negligible effects [16–19]. The study by Carter et al. [1] was possibly the first to report an improved 1-h cycling time trial performance with a CHO mouth rinse, as indicated by a reduced time and increased mean power output (W_{MEAN}) when compared with a placebo (PLA) condition. Accordingly, other studies verified improvements in endurance performance when participants rinsed their mouth with a CHO solution [12, 20, 21]. For example, Lane et al. [14] expanded the notion that a CHO mouth rinse may potentiate endurance performance in a 1-h cycling time trial, regardless of the fasting state. In addition, a recent study demonstrated that participants improved their time to exhaustion when they rinsed their mouth with a CHO solution during constant cycling at 80% of the respiratory compensation point [12]. Hence, even though some have failed to find improvements in endurance performance with a CHO mouth rinse [16–18, 22], the consensus suggests that this is effective to improve endurance exercise performance.

The growing number of CHO mouth rinse studies during the last decade has enabled the publication of narrative [23–26] and systematic reviews [27, 28] designed to elucidate the actual CHO mouth rinse contribution to endurance performance. In this regard, systematic reviews may be required to better establish the quality of evidence from studies exploring this topic, given that their methodology is more straightforward than that of narrative reviews [29]. To the best of our knowledge, two systematic reviews have attempted to elucidate the actual CHO mouth rinse effects

on endurance performance [27, 28]. However, one quantified the CHO mouth rinse effect size on endurance performance by using pooled data derived from studies different in nature such as cycling and running [28], while the other reported the overall mean difference in power output during cycling exercises [27]. Most importantly, neither systematically searched and selected studies or analyzed metadata (i.e., meta-analysis) according to straightforward criteria [29], thus possibly introducing bias that may have lowered the level of evidence reviewed. It is advisable to review evidence from the literature regarding endurance performance and a CHO mouth rinse, assessing the risk of bias of studies before quantifying the magnitude of the effect.

Considering the relevance and applicability of ergogenic supplementations in cycling modalities, athletes, trainers, and coaches may be interested to know the actual CHO mouth rinse effects on cycling performance. In fact, there is a widespread use of supplements proposed to improve performance in cycling modalities, as cyclists are frequently exposed to self-imposed pressure and peer pressure to improve performance [30]. Therefore, this audience may benefit from a systematic review conducted according to straightforward criteria. Accordingly, the present analysis systematically reviewed randomized placebo-controlled trials that assessed the effectiveness of a CHO mouth rinse to improve time and W_{MEAN} during cycling trials. We reviewed the CHO mouth rinse effects on cycling trial performance assuming that time-, work-, and distance-based trials are a motivational and more realistic scenario that resembles practical situations met in cycling competitions and training sessions [1, 3, 31, 32].

2 Methods

The systematic review and meta-analysis were fully conducted according to the *Cochrane Handbook for Systematic Reviews of Interventions* [29] and the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) statement [33].

2.1 Eligibility Criteria

We included randomized crossover trials that investigated the effects of a CHO mouth rinse on cycling trial performance based on time, physical work, or distance, having W_{MEAN} and time as performance outcomes. A CHO mouth rinse protocol was eligible if the solution included no less than 6% of CHO, being rinsed from 5 to 10 s. Studies were included if they met the following eligibility criteria: (1) type of literature: original articles (excluding gray literature indexed by non-scientific databases as well as abstracts of

scientific events); (2) subjects: participants between 18 and 35-year-old; (3) intervention: a CHO mouth rinse during cycling trial based on time, work, or distance; (4) control group: PLA condition; and (5) outcomes: W_{MEAN} and time to complete the trial. Studies that investigated CHO mouth rinse effects on endurance performance in hypoxic or hot environments, after a depleted-muscle glycogen state or in addition to substances others than CHO mouth rinse, were excluded from the analysis.

2.2 Data Sources and Search

After an initial search, we identified a small number of studies in other databases and decided to systematically search publications in PubMed and Web of Science databases covering all available evidence. The search was initially performed in August 2017, and updated in October 2018. We further included a study if a potential article was quoted in these initially reviewed articles. PubMed and Web of Science article alert systems were also used to inform us of articles related to our search terms that were published after our initial search. The following terms were used in the search: CHO mouth rinse OR carbohydrate mouth rinse OR CHO mouthwash OR carbohydrate mouth rinse AND performance OR CHO mouth rinse AND performance. Original and complete articles published in any language were eligible. The numbers of studies retrieved from PubMed and Web of Science in the updated search are shown in Table S1 of the Electronic Supplementary Material (ESM). Complete lists of the search term queries for each database are provided in Appendix S1 of the ESM.

2.3 Study Selection and Data Collection

The titles, abstracts, and full texts of the selected articles were independently reviewed by two researchers to check for eligibility criteria. The data extraction process focused on the following information: (1) title, type of publication (original, review, commentaries, letters), information on publication (year, country, research center or department), funding statement, and disclosure of potential conflicts of interest; and (2) design and methods of the study, participants selected (sample size, age, male or female participants), control group (randomization, type of PLA), intervention (duration of CHO mouth rinse, type and concentration of CHO solution), and outcomes reported (W_{MEAN} and time to complete the trial). Corresponding authors were contacted if some data were unavailable. Importantly, the data extraction from selected articles was independently processed by two researchers (C.B. and P.E.F.A.), and eventual disagreements with regard to the inclusion of a given article were decided by a supervisor (R.Y.A.).

2.4 Risk of Bias Assessment

The studies included in this meta-analysis were assessed for risk of bias according to the Cochrane Collaboration's recommendation for systematic reviews [29]: (a) random sequence generation (selection bias); (b) blinding of participants and personnel (performance bias); (c) blinding of outcome assessment (detection bias); (d) incomplete outcome data (attrition bias); and (e) selective reporting (reporting bias). These aspects were categorized as unclear risk of bias, low risk of bias, and high risk of bias. Two researchers (C.B. and P.E.F.A.), blinded to information that could be used to identify the articles' authorship (authors, affiliations, journals), independently assessed the articles' risk of bias. A researcher experienced in systematic reviews and meta-analysis (H.J.C.J) resolved eventual disagreements.

2.5 Statistical Analyses

Carbohydrate mouth rinse effects were analyzed in terms of absolute final values after a CHO or PLA mouth rinse (i.e., mean and standard deviation). Thus, the standardized mean difference (SMDs) in W_{MEAN} (expressed as W) and time to complete the cycling trials (expressed as minutes) between CHO and PLA mouth rinse conditions were calculated. A random-effects model was used to calculate the pooled effect size by computing the SMD from each study. Furthermore, we assumed that eligible studies were similar in clinical and methodological aspects and therefore characterized by a low degree of heterogeneity. The heterogeneity of the treatment effect between CHO and PLA manipulations was evaluated through I^2 statistics and the Chi-square test, and classified according to Higgins et al. [34]. Importantly, previous studies have reported that an I^2 from 0 to 50% represents a low heterogeneity, from 50 to 74% a moderate heterogeneity, and from 75% onwards a high heterogeneity [34, 35]. The SMD was interpreted as: 0.2–0.4 = small effect size, 0.5–0.7 = moderate effect size, and > 0.8 = large effect size [29]. Additionally, funnel plots and Egger's regression analysis were used to assess publication bias. These analyses were performed through the Review Manager software, Version 5.3 (Cochrane Collaboration Copenhagen, The Nordic Cochrane Centre, Copenhagen, Denmark), with a significance level set at 5% ($p < 0.05$).

3 Results

3.1 Search Results and Study Characteristics

The flow diagram illustrates the process of a systematic and meta-analytic review including identification, screening, eligibility, and inclusion and exclusion of articles (Fig. 1).

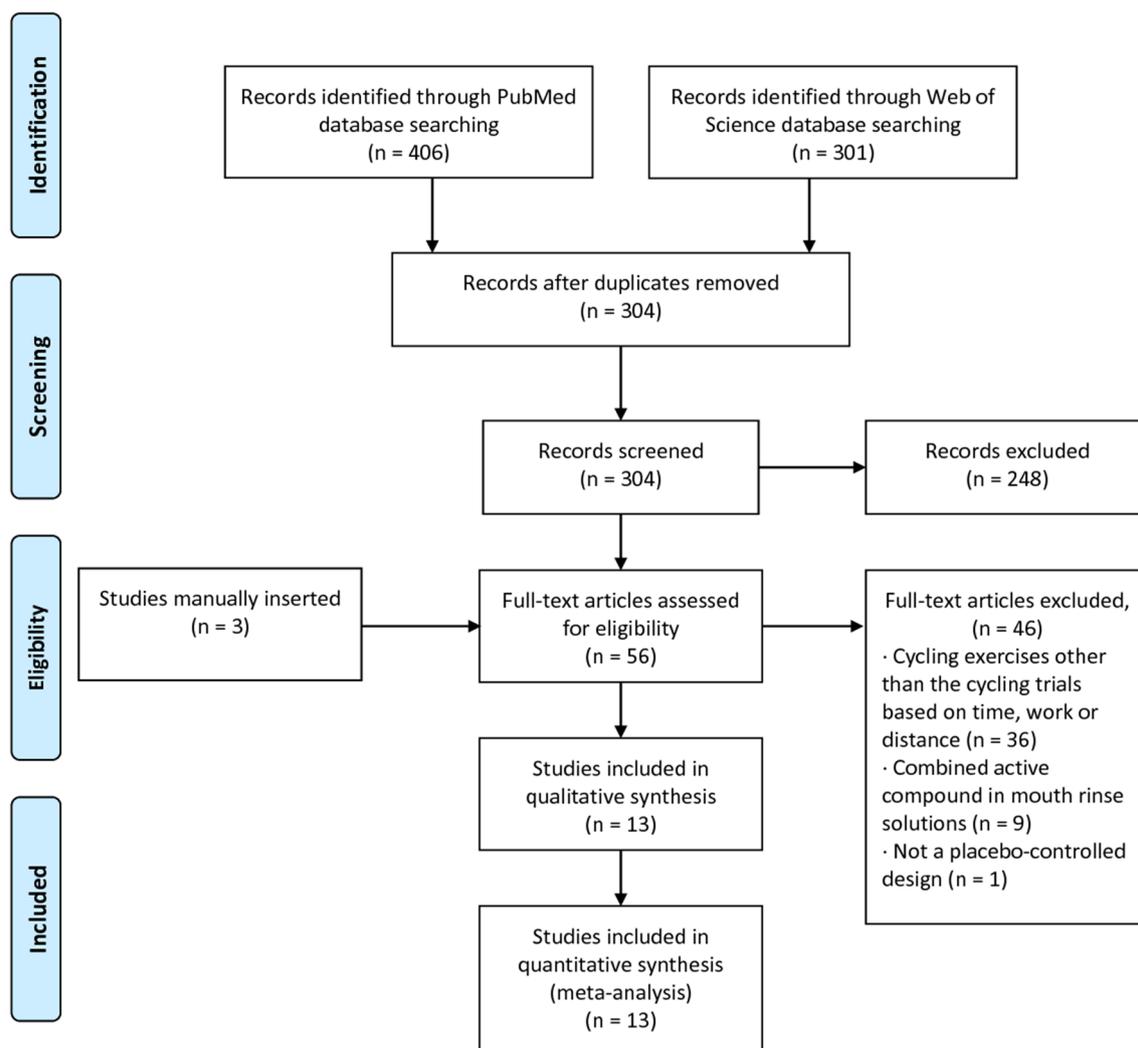


Fig. 1 Flow diagram of the systematic and meta-analysis process

Initially, 707 references were screened and checked for duplication, thus 304 references remained after exclusion of duplicated records. The abstracts of the remaining references were then screened according to inclusion criteria and 248 references were considered ineligible. The remaining studies ($n=56$) were checked in full. As shown in Appendix S2 of the ESM, some studies were ineligible because they investigated cycling exercises other than cycling trials based on time, work, or distance ($n=36$). Additionally, studies ($n=9$) that either did not investigate isolated CHO mouth rinse effects on performance (i.e., studies that either combined active compounds with CHO or changed the experimental environment when investigating CHO mouth rinse effects) or did not include a placebo-controlled trial ($n=1$) were not eligible. Consequently, ten studies fulfilled all inclusion criteria and were eligible for meta-analysis. Furthermore, three studies were manually inserted because they were published

after the initial search [19, 36, 37]; therefore, 13 studies were included in the present meta-analysis.

As the studies by Chambers et al. [3], Lane et al. [14] and Trommelen et al. [17] used a double-designed protocol, that is one study with two cycling trial experiments, the number of trials reviewed was 16. Moreover, a double-design study used a time-based cycling trial [14]; thus, the power output measured during a fixed 1-h cycling trial, rather than the time to complete the trial, was the single performance parameter available in this protocol. Hence, we could not consider the time to complete the trial as a performance outcome because these data were unavailable. As a result, the meta-analysis was performed with 16 trials (number of volunteers = 175) and 14 trials (number of volunteers = 151) reporting W_{MEAN} and time as performance outcomes, respectively. Importantly, eligible studies used a 2- to 7-day washout period between trials.

Table 1 summarizes the selected studies. All the studies included in this review used a randomized crossover design with a PLA-controlled condition, reporting W_{MEAN} as the performance outcome. With the exception of one study, all studies also reported the time to complete the trial. Regarding the CHO mouth rinse protocols, 56.25% of the studies used a 5-s CHO mouth rinse while 43.75% of the studies used a 10-s CHO mouth rinse. Most studies manipulated CHO solution as maltodextrin (56.25%), some studies used glucose (18.75%), and other studies used either sucrose (12.5%) or a commercial CHO-electrolyte solution (12.5%).

3.2 Meta-Analysis Results

A low heterogeneity ($Tau^2 = 0.00$; $Chi^2 = 14.48$, $df = 15$, $p = 0.49$; $I^2 = 0\%$) was observed in 100% of the studies ($n = 175$) that reported W_{MEAN} as the performance outcome. Similarly, a low heterogeneity ($Tau^2 = 0.00$; $Chi^2 = 13.03$, $df = 13$, $p = 0.45$; $I^2 = 0\%$) was further observed in studies ($n = 151$) reporting the time to complete the trial as the performance outcome. Meta-analysis results showed that the CHO mouth rinse improved W_{MEAN} when compared with the PLA mouth rinse ($Z = 2.29$, $p = 0.02$, $SMD = 0.25$, 95% CI 0.04–0.46; Fig. 2). However, no significant effect was observed in the time to

Table 1 Studies included in the systematic review and meta-analysis

Study	Study design	<i>N</i>	Age of participants, years (mean ± SD)	CHO mouth rinse protocol	Control	Cycling trial	Outcomes
Carter et al. [1]	CS	9	24.0 ± 3.8	5 s of a 6.4% maltodextrin mouth rinse	PLA (water)	Work-based	W_{MEAN} and T
Beelen et al. [16]	CS	14	24.0 ± 1.0	5 s of a 6.4% maltodextrin mouth rinse	PLA (water)	Work-based	W_{MEAN} and T
Chambers et al. a [3]	CS	8	29.0 ± 9.0	10 s of a 6.4% glucose mouth rinse	PLA (commercial sweetener)	Work-based	W_{MEAN} and T
Chambers et al. b [3]	CS	8	22.0 ± 3.0	10 s of a 6.4% maltodextrin mouth rinse	PLA (commercial sweetener)	Work-based	W_{MEAN} and T
Pottier et al. [15]	CS	12	30.2 ± 5.3	5 s of a 100-mL isotonic CES mouth rinse	PLA (aspartame)	Work-based	W_{MEAN} and T
Lane et al. a [14]	CS	12	28.0 ± 5.0	10 s of a 10% maltodextrin mouth rinse	PLA (commercial sweetener)	Time-based	W_{MEAN}
Lane et al. b [14]	CS	12	28.0 ± 5.0	10 s of a 10% maltodextrin mouth rinse	PLA (commercial sweetener)	Time-based	W_{MEAN}
Ispoglou et al. [25]	CS	9	30.0 ± 6.7	5 s of a 6% CES mouth rinse	PLA (aspartame)	Work-based	W_{MEAN} and T
Trommelen et al. a [17]	CS	14	27.0 ± 6.0	5 s of a 6.4% sucrose mouth rinse	PLA (aspartame)	Work-based	W_{MEAN} and T
Trommelen et al. b [17]	CS	14	27.0 ± 6.0	5 s of a 6.4% sucrose mouth rinse	PLA (aspartame)	Work-based	W_{MEAN} and T
Devenney et al. [4]	CS	12	22.0 ± 7.0	5 s of a 6% maltodextrin mouth rinse	PLA (not reported)	Work-based	W_{MEAN} and T
Kulaksiz et al. [18]	CS	9	24.0 ± 2.0	5 s of a 6% maltodextrin mouth rinse	PLA (not reported)	Distance-based	W_{MEAN} and T
James et al. [5]	CS	12	40.0 ± 8.0	5 s of a 7% maltodextrin mouth rinse	PLA (fruit juice)	Work-based	W_{MEAN} and T
Murray et al. [36]	CS	8	24.0 ± 2.0	10 s of a 6.4% glucose mouth rinse	PLA (not reported)	Distance-based	W_{MEAN} and T
Pires et al. [19]	CS	9	36.9 ± 6.4	10 s of a 6.4% glucose mouth rinse	PLA (saccharin)	Distance-based	W_{MEAN} and T
Ferreira et al. [37]	CS	14	30.4 ± 6.2	10 s of a 6.4% of maltodextrin mouth rinse	PLA (water)	Distance-based	W_{MEAN} and T

CES carbohydrate-electrolyte solution, CHO carbohydrate, CS crossover study, SD standard deviation, PLA placebo, T total time, W_{MEAN} mean power output

'a' and 'b' denote different experiments within the same study

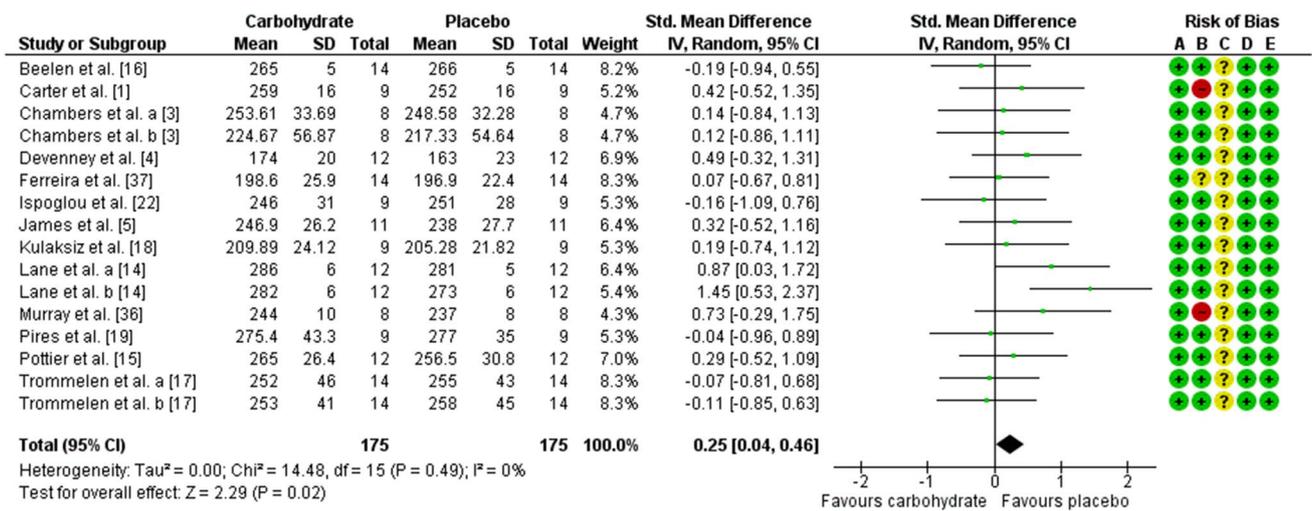


Fig. 2 Forest plot comparing the mean power output between carbohydrate and placebo mouth rinses; ‘a’ and ‘b’ denote different experiments within the same study. *CI* confidence interval, *IV* inverse variance, *SD* standard deviation, *Std* standardized

complete the trial between CHO and PLA mouth rinses ($Z = 1.14, p = 0.25; SMD = -0.13, 95\% CI -0.36$ to 0.10 ; Fig. 3). Figures 2 and 3 depict the changes in W_{MEAN} and time to complete cycling trials between CHO and PLA mouth rinses.

3.3 Risk of Bias

Overall, studies included in the present review reported a high level of evidence, as 100% of the studies showed a low risk of bias when considering random sequential generation, incomplete outcome data, and selective report criteria.

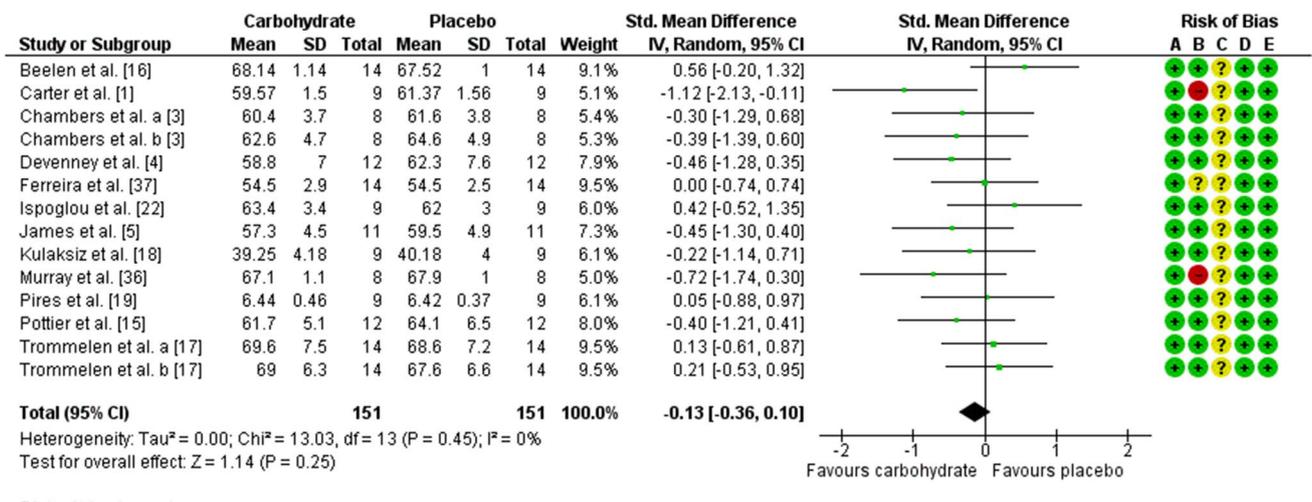


Fig. 3 Forest plot comparing time of exercise (minutes) between carbohydrate and placebo mouth rinses; ‘a’ and ‘b’ denote different experiments within the same study. *CI* confidence interval, *IV* inverse variance, *SD* standard deviation, *Std* standardized

Furthermore, 81.25% of the studies adequately blinded participants to procedures. In contrast, owing to a single-blinded design, two studies [1, 36] showed a high risk while another showed an unclear risk [37] of bias. With respect to detection bias (i.e., blinding outcome assessment), 100% of the studies showed an unclear risk of bias. Figures 4 and 5 depict these results.

Egger’s linear regression indicated no potential publication biases for either W_{MEAN} ($p=0.13$) or time to complete the trial ($p=0.13$). The funnel plots (Figure S1 of the ESM) depict the distribution of these data.

4 Discussion

The present analysis systematically reviewed the level of evidence for CHO mouth rinse effects on W_{MEAN} and time to complete the trial during cycling trials measured by time, work, or distance. The straightforward methodology used to select well-designed CHO mouth rinse studies confirmed that there is a high level of scientific evidence suggesting that a CHO mouth rinse improves cycling W_{MEAN} , but not the time to complete the trial.

4.1 Level of Evidence Reviewed and Publication Bias

Overall, the analysis indicated a low risk of bias as the studies included in this review were conducted within a controlled random sequence generation (i.e., low risk of selection bias), with low incomplete outcome data (i.e., low risk of attrition bias) and low selective reporting (i.e., low risk of outcome bias). Furthermore, most studies (81.25%) demonstrated a low risk of bias with regard to blinding of participants to procedures, as they adequately blinded participants and personnel from the substance manipulated. Indeed, only the studies by Carter et al. [1] and Murray et al. [36] used a single-blind design such that researchers involved in experimental procedures and analysis were aware of the participants’ allocation and the substance rinsed in each trial. However, the results of the meta-analysis remained similar

when these studies [1, 36] were removed from the analysis (Figures S2 and S3 of the ESM).

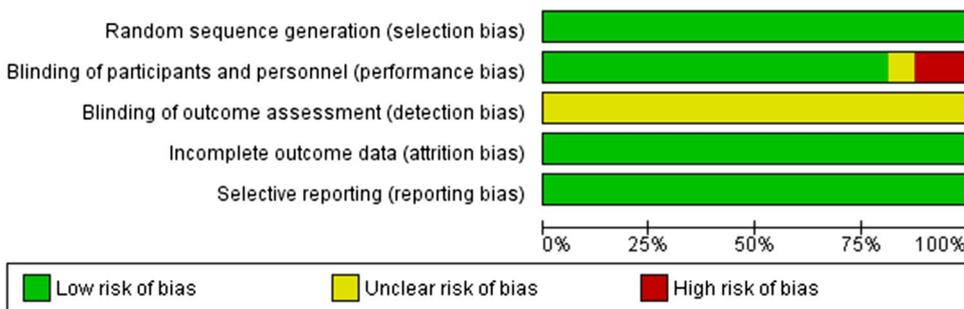
Importantly, it must be highlighted that no CHO mouth rinse study has disclosed if researchers involved in data analysis were further blinded to manipulation, and the risk of detection bias (blinding of outcome assessment) is therefore unclear in the literature. Accordingly, and given that the absence of disclosures concerning blinding of outcome assessments is frequent in the sports science and nutrition literature, future CHO mouth rinse studies should take this methodological aspect into account because it may negatively affect detection bias and influence the assessment of outcomes [29].

Furthermore, analysis of Egger’s linear regression indicated no potential publication biases that may have significantly influenced the W_{MEAN} or time of exercise results in the current meta-analysis. Additionally, the funnel plots highlighted a symmetrical data distribution, thereby reinforcing no potential publication biases.

4.2 Carbohydrate Mouth Rinse Effects on Cycling Trial Performance

The current meta-analysis showed that CHO mouth rinse improves cycling W_{MEAN} , despite not improving the time to complete a trial ended by work or distance. Two recent reviews reported equivocal conclusions regarding the CHO mouth rinse effects on endurance performance, as Ataide-Silva et al. [27] suggested a 5.05 W increase in W_{MEAN} (0.90–9.20) with a CHO mouth rinse in relation to PLA, while Peart [28] observed only a 0.19 W increase in W_{MEAN} . The current review agrees with the increase in W_{MEAN} (SMD=0.51) reported by Ataide-Silva et al. [27] as we also observed a relevant increase in cycling W_{MEAN} (SMD=0.25) with a CHO mouth rinse. The difference between the magnitude of the effects reported by Ataide-Silva et al. [27] and Peart [28] may have been due to a methodologic bias, as the earlier analysis estimated the mean difference in W_{MEAN} during cycling exercises, whilst the latter estimated the mean effect size in power output to quantify the CHO mouth rinse effects on endurance performance. Importantly, neither analysis systematically searched for

Fig. 4 Summary of the risk of bias of the reviewed studies



	Random sequence generation (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)
Beelen et al. [16]	+	+	?	+	+
Carter et al. [1]	+	-	?	+	+
Chambers et al. a [3]	+	+	?	+	+
Chambers et al. b [3]	+	+	?	+	+
Devenney et al. [4]	+	+	?	+	+
Ferreira et al. [37]	+	?	?	+	+
Ispoglou et al. [22]	+	+	?	+	+
James et al. [5]	+	+	?	+	+
Kulaksiz et al. [18]	+	+	?	+	+
Lane et al. a [14]	+	+	?	+	+
Lane et al. b [14]	+	+	?	+	+
Murray et al. [36]	+	-	?	+	+
Pires et al. [19]	+	+	?	+	+
Pottier et al. [15]	+	+	?	+	+
Trommelen et al. a [17]	+	+	?	+	+
Trommelen et al. b [17]	+	+	?	+	+

Fig. 5 Risk of bias of each selected study; ‘a’ and ‘b’ denote different experiments within the same study

selected studies or analyzed metadata (i.e., meta-analysis) according to straightforward criteria. Moreover, Peart [28] included different exercise modes (i.e., cycling and running) in his review, thus potentially affecting the conclusions. In

contrast, the fact that Ataide-Silva et al. [27] failed to use a straightforward methodology to search for and select studies did not appear to drive their conclusions in a different direction from those obtained in the current review. Therefore, the overall suggestion is that a CHO mouth rinse may improve cycling performance by $\sim 1.69\%$ when expressed as W_{MEAN} .

Interestingly, our findings demonstrated that a CHO mouth rinse may improve cycling W_{MEAN} without changing the time to complete a cycling trial. One may expect that an improved cycling W_{MEAN} should be reflected in an improved time to complete the trial, given the direct link between these two parameters. Perhaps this mismatch between W_{MEAN} and time to complete the trial may be owing to the different total number of volunteers used to calculate the beneficial CHO effects in these two outcomes. In this regard, as reported in the results session (see Sect. 3.1), one eligible study was designed with a time-based cycling trial [14] so that the time to complete the trial was not a performance outcome in this study. Consequently, as the single performance outcome derived from this study was W_{MEAN} , the present meta-analysis was performed with a different number of volunteers for W_{MEAN} ($n = 175$) and time to complete the trial ($n = 151$). To provide some information about this mismatch between W_{MEAN} and time to complete the trial, we reanalyzed the results after removing the study by Lane et al. [14] from the W_{MEAN} data, thus using the same number of volunteers in both performance variables. This reanalysis indicated that the W_{MEAN} also did not improve with CHO mouth rinsing, thereby suggesting that the CHO mouth rinse may also have no superiority over PLA for improving W_{MEAN} . However, this suggestion has to be interpreted with caution, as we could not rule out a likely beneficial CHO mouth rinse effect on both W_{MEAN} and time to complete the trial if both performance parameters had been reported by Lane et al. [14].

Furthermore, analysis of Figs. 2 and 3 showed that five studies showed no superiority of the CHO mouth rinse to the PLA mouth rinse in W_{MEAN} and time to complete the trial, respectively. We analyzed these studies separately to identify methodological features that may potentially explain these results. All studies reporting no beneficial CHO mouth rinse effects on cycling performance-tested participants in a fed state. According to Lane et al. [14] there may be greater activation of cerebral structures involved in the reward system in the presence of hunger and low satiety, such that a CHO mouth rinse would potentially increase the activation of cerebral structures involved in exercise performance in a fasted state. Interestingly, Trommelen et al. [17] observed that a CHO mouth rinse did not improve exercise performance in either a fed or a fasted state. The reason for the ineffectiveness of CHO mouth rinses in a fasted state in this study remains unclear, but the use of a $2 \times 2 \times 8$ repeated-measures design conducted with only 14 subjects may have reduced the CHO effect.

Of interest is whether a CHO mouth rinse is a supplementation strategy as effective as CHO ingestion for improving cycling performance. In this regard, the current review found a SMD of 0.25 and -0.13 for W_{MEAN} and time to complete the trial, respectively, which represents a small effect size on these performance outcomes. Similarly, a recent systematic review and meta-analysis of the benefits of CHO ingestion reported a SMD of 0.45 and -0.34 on W_{MEAN} and time to complete the trial, respectively, thereby also finding small effect sizes [38]. From a practical perspective, therefore, based on these two systematic reviews and meta-analyses, one may conclude that a CHO mouth rinse leads to a cycling performance improvement seemingly comparable to that seen with CHO ingestion.

4.3 Methodological Aspects

Some aspects of the current review should be highlighted. First, we decided to include only original studies that measured endurance performance in cycling trials measured by time, physical work, or distance. Although this ensured the homogeneity of the studies analyzed in this review, it limited inferences concerning other exercise modes such as running. We decided to review the cycling literature given the relevance and applicability of ergogenic supplementations in cycling modalities. In fact, a qualitative cycling study reported that the more committed cyclists were to the sport, the greater the pressure to use supplements to improve performance [30]. The aforementioned findings are unique and indicate a low risk of bias in the CHO-cycling literature, although there is an unclear risk of bias associated with the blinding of the outcome assessment. Future studies may be designed to review the CHO mouth rinse literature involving other exercise modes.

Furthermore, another methodological feature of the current review is that we analyzed data from crossover studies. In this sense, crossover designs may be considered as a threat to the meta-analysis, as the washout period between multiple trials may possibly influence the beneficial CHO mouth rinse effects. We carefully checked the revised studies for the presence of a washout period, and e-mailed the authors if this information was missing. In this regard, only one study [4] neither reported the washout period nor replied to our e-mail. Assuming that CHO mouth rinse effects on cycling performance are immediate and timely [39], we considered a 2- to 7-day washout period as adequate for participants to recover from previous exercise session-derived residual fatigue. Therefore, the 2- to 7-day washout period reported by the studies included in the present review likely did not affect the main outcomes of the meta-analysis.

Given the level of methodological rigor applied in this review, we consider it is important to disclose that one of the reviewed studies described different numbers of participants

in the methods ($n = 14$) section and the abstract ($n = 11$) [37]. In this regard, we assumed the number of participants reported in the methods section as the accurate data. However, we performed the metadata analysis considering both numbers of participants (i.e., $n = 11$ vs. $n = 14$) to confirm that this did not affect the results.

5 Conclusions

In summary, using a straightforward methodology to review randomized placebo-controlled studies in the endurance performance-CHO mouth rinse literature, our analysis provided evidence that the CHO mouth rinse has the potential to increase cycling W_{MEAN} , despite being unable to improve the time to complete cycling trials.

Acknowledgements Flávio Oliveira Pires is grateful to the National Council for Scientific and Technological Development (CNPq-Brazil) for his researcher scholarship (#307072/2016-9). The authors thank ES Chambers, TN Kulaksız, and RM James for providing the requested data.

Compliance with Ethical Standards

Funding This analysis is part of a carbohydrate mouth rinse project supported by the São Paulo Research Foundation (FAPESP-Brazil) (#2016/16496-3). This study was financed in part by the Coordination of Improvement of Higher Education Personnel (CAPES-Brazil), Finance Code 001 (Cayque Brietzke, Hélio José Coelho-Júnior, Paulo Estevão Franco-Alvarenga and Rodrigo Silveira).

Conflict of interest Cayque Brietzke, Paulo Estevão Franco-Alvarenga, Hélio José Coelho-Júnior, Rodrigo Silveira Silva, Ricardo Yukio Asano, and Flávio Oliveira Pires have no conflicts of interest that are directly relevant to the contents of this review.

References

1. Carter JM, Jeukendrup AE, Jones DA. The effect of carbohydrate mouth rinse on 1-h cycle time trial performance. *Med Sci Sports Exerc.* 2004;36:2107–11.
2. Thomas DT, Erdman KA, Burke LM. Position of the Academy of Nutrition and Dietetics, Dietitians of Canada, and the American College of Sports Medicine: nutrition and athletic performance. *J Acad Nutr Diet.* 2016;116:501–28.
3. Chambers ES, Bridge MW, Jones DA. Carbohydrate sensing in the human mouth: effects on exercise performance and brain activity. *J Physiol.* 2009;587:1779–94.
4. Devenney S, Collins K, Shortall M. Effects of various concentrations of carbohydrate mouth rinse on cycling performance in a fed state. *Eur J Sport Sci.* 2016;16:1073–8.
5. James RM, Ritchie S, Rollo I, James LJ. No dose response effect of carbohydrate mouth rinse on cycling time-trial performance. *Int J Sport Nutr Exerc Metab.* 2017;27:25–31.
6. Tsintzas OK, Williams C, Boobis L, Greenhaff P. Carbohydrate ingestion and glycogen utilization in different muscle fibre types in man. *J Physiol.* 1995;489:243–50.

7. Coyle EF, Coggan AR, Hemmert MK, Ivy JL. Muscle glycogen utilization during prolonged strenuous exercise when fed carbohydrate. *J Appl Physiol.* 1986;61:165–72.
8. Hargreaves M, Costill DL, Coggan A, Fink WJ, Nishibata I. Effect of carbohydrate feedings on muscle glycogen utilization and exercise performance. *Med Sci Sport Exerc.* 1984;16:219–22.
9. Robertson CV, Marino FE. A role for the prefrontal cortex in exercise tolerance and termination. *J Appl Physiol.* 2016;120:464–6.
10. Turner CE, Byblow WD, Gant N. Creatine supplementation enhances corticomotor excitability and cognitive performance during oxygen deprivation. *J Neurosci.* 2015;35:1773–80.
11. Ataíde-Silva T, Ghiarone T, Bertuzzi R, Stathis CG, Leandro CG, Lima-Silva AE. CHO mouth rinse ameliorates neuromuscular response with lower endogenous CHO stores. *Med Sci Sports Exerc.* 2016;48:1810–20.
12. Bastos-Silva VJ, Melo Ade A, Lima-Silva AE, Moura FA, Bertuzzi R, de Araujo GG. Carbohydrate mouth rinse maintains muscle electromyographic activity and increases time to exhaustion during moderate but not high-intensity cycling exercise. *Nutrients.* 2016;8:49.
13. Rollo IAN, Williams C, Nevill M. Influence of ingesting versus mouth rinsing a carbohydrate solution during a 1-h run. *Med Sci Sport Exerc.* 2011;43:468–75.
14. Lane SC, Bird SR, Burke LM, Hawley JA. Effect of a carbohydrate mouth rinse on simulated cycling time-trial performance commenced in a fed or fasted state. *Appl Physiol Nutr Metab.* 2013;38:134–9.
15. Pottier A, Bouckaert J, Gilis W, Roels T, Derave W. Mouth rinse but not ingestion of a carbohydrate solution improves 1-h cycle time trial performance. *Scand J Med Sci Sport.* 2010;20:105–11.
16. Beelen M, Berghuis J, Bonaparte B, Ballak SB, Jeukendrup AE, van Loon LJC. Carbohydrate mouth rinsing in the fed state: lack of enhancement of time-trial performance. *Int J Sport Nutr Exerc Metab.* 2009;19:400–9.
17. Trommelen J, Beelen M, Mullers M, Gibala MJ, van Loon LJC, Cermak NM. A sucrose mouth rinse does not improve 1-hr cycle time trial performance when performed in the fasted or fed state. *Int J Sport Nutr Exerc Metab.* 2015;25:576–83.
18. Kulaksız TN, Koşar ŞN, Bulut S, Güzel Y, Willems MET, Hazir T, et al. Mouth rinsing with maltodextrin solutions fails to improve time trial endurance cycling performance in recreational athletes. *Nutrients.* 2016;8:2–15.
19. Pires FO, Brietzke C, Pinheiro FA, Veras K, de Mattos ECT, Rodacki ALF, et al. Carbohydrate mouth rinse fails to improve four-kilometer cycling time trial performance. *Nutrients.* 2018;10:342.
20. Fraga C, Velasques B, Koch AJ, Machado M, Paulucio D, Ribeiro P, et al. Carbohydrate mouth rinse enhances time to exhaustion during treadmill exercise. *Clin Physiol Funct Imaging.* 2017;37:17–22.
21. Bavaresco BG, Gomes YDSBL, Dos Pinheiro Anjos ER, Antonelli BA, Gomes DGESC, de Pires Mélo MIH, et al. Carbohydrate mouth rinse improves cycling performance carried out until the volitional exhaustion. *J Sports Med Phys Fit.* 2017. <https://doi.org/10.23736/S0022-4707.17.07980-4> (Epub ahead of print).
22. Ispoglou T, O’Kelly D, Angelopoulou A, Bargh M, O’Hara JP, Duckworth LC. Mouth rinsing with carbohydrate solutions at the postprandial state fail to improve performance during simulated cycling time trials. *J Strength Cond Res.* 2015;29:2316–25.
23. Rollo I, Williams C. Effect of mouth-rinsing carbohydrate solutions on endurance performance. *Sports Med.* 2011;41:449–61.
24. Jeukendrup AE. Oral carbohydrate rinse: placebo or beneficial? *Curr Sports Med Rep.* 2013;12:222–7.
25. Jeukendrup AE, Chambers ES. Oral carbohydrate sensing and exercise performance. *Curr Opin Clin Nutr Metab Care.* 2010;13:447–51.
26. Jeukendrup AE, Rollo I, Carter JM. Carbohydrate mouth rinse: performance effects and mechanisms. *Sport Sci Exch.* 2013;26:1–8.
27. de Ataíde e Silva TA, Di Calvalcanti Alves de Souza ME, de Amorim JF, Stathis CG, Leandro CGG, Lima-Silva AE. Can carbohydrate mouth rinse improve performance during exercise? A systematic review. *Nutrients.* 2013;6:1–10.
28. Peart DJ. Quantifying the effect of carbohydrate mouth rinsing on exercise performance. *J Strength Cond Res.* 2017;31:1737–43.
29. Higgins JP, Altman DG, Gøtzsche PC, Jüni P, Moher D, Oxman AD, et al. The Cochrane Collaboration’s tool for assessing risk of bias in randomised trials. *BMJ.* 2011;343:d5928.
30. Stewart B, Outram S, Smith ACT. Doing supplements to improve performance in club cycling: a life-course analysis. *Scand J Med Sci Sports.* 2013;23:e361–72.
31. Pires FO, Dos Anjos CA, Covolan RJ, Pinheiro FA, St Clair Gibson A, Noakes TD, et al. Cerebral regulation in different maximal aerobic exercise modes. *Front Physiol.* 2016;7:253.
32. Silva RAS, Silva-Júnior FL, Pinheiro FA, Souza PFM, Boullosa DA, Pires FO. Acute prior heavy strength exercise bouts improve the 20-km cycling time trial performance. *J Strength Cond Res.* 2014;28:2513–20.
33. Liberati A, Altman DG, Tetzlaff J, Mulrow C, Gøtzsche PC, Ioannidis JP, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration. *Ann Intern Med.* 2009;151:W65–94.
34. Higgins JPT, Thompson SG, Deeks JJ, Altman DG. Measuring inconsistency in meta-analyses. *BMJ.* 2003;327:557–60.
35. Sedgwick P. Meta-analyses: what is heterogeneity? *BMJ.* 2015;350:h1435.
36. Murray KO, Paris HL, Fly AD, Chapman RF, Mickleborough TD. Carbohydrate mouth rinse improves cycling time-trial performance without altering plasma insulin concentration. *J Sports Sci Med.* 2018;17:145–52.
37. Ferreira AMJ, Farias-Junior LF, Mota TAA, Elsangedy HM, Marcadenti A, Lemos TMAM, et al. Carbohydrate mouth rinse and hydration strategies on cycling performance in 30 km time trial: a randomized, crossover, controlled trial. *J Sport Sci Med.* 2018;17:181–7.
38. Pöschmüller M, Schwingshackl L, Colombani PC, Hoffmann G. A systematic review and meta-analysis of carbohydrate benefits associated with randomized controlled competition-based performance trials. *J Int Soc Sports Nutr.* 2016;13:27.
39. Gant N, Stinear CM, Byblow WD. Carbohydrate in the mouth immediately facilitates motor output. *Brain Res.* 2010;1350:151–8.