J Appl Physiol 140: 76–87, 2026.
First published December 9, 2025; doi:10.1152/japplphysiol.00861.2025

american physiological society | JOURNAL OF APPLIED PHYSIOLOGY

SYSTEMATIC REVIEW

Carbohydrate ingestion during prolonged exercise and net skeletal muscle glycogen utilization: a meta-analysis

Jeffrey A. Rothschild,[1,2] Harrison Dudley-Rode,[2,3] Harriet Carpenter,[2] Abbie S. M. Smith,[2] Daniel J. Plews,[2] and Ed Maunder[2,3]

[1]*High Performance Sport New Zealand, Auckland, New Zealand;* [2]*Sports Performance Research Institute New Zealand, Auckland University of Technology, Auckland, New Zealand; and* [3]*School of Sport, Exercise, and Health, Faculty of Health and Environmental Sciences, Auckland University of Technology, Auckland, New Zealand*

Abstract

Although some studies report attenuated net muscle glycogenolysis with carbohydrate ingestion, others show no effect, possibly due to small sample sizes or methodological differences. Objective of this study is to determine whether carbohydrate ingestion during endurance exercise reduces net skeletal muscle glycogen use and to identify potential moderating factors. A meta-analysis was conducted using data from 31 studies, which included 48 unique effect sizes derived from crossover trials comparing carbohydrate versus placebo ingestion during prolonged endurance exercise. Standardized mean differences (SMDs) in net muscle glycogen use were calculated. A multilevel random-effects model accounted for repeated estimates within studies. Subgroup and meta-regression analyses tested potential moderators. Sensitivity analyses were conducted using a range of plausible pre-/postcorrelation values. Carbohydrate ingestion was associated with a small but statistically significant muscle glycogen-sparing effect [SMD = −0.16, 95% confidence interval (CI): −0.30 to −0.02, $P = 0.021$]. Subgroup and moderator analyses revealed no significant effects of exercise mode, carbohydrate type, ingestion rate, or preexercise glycogen on the observed effect. Translating the standardized effect into absolute units, carbohydrate ingestion was estimated to spare ∼24 mmol·kg^{-1} dry wt (95% CI: 4–45 mmol·kg^{-1}) of muscle glycogen, relative to placebo, during ∼100 min of exercise. Carbohydrate ingestion during endurance exercise leads to a small but statistically significant reduction in net skeletal muscle glycogen utilization. Although no consistent moderating variables were identified, the direction of effect was consistent across studies, and the absolute magnitude of sparing may be physiologically meaningful during prolonged or repeated efforts.

exercise; glycogenolysis; metabolism; nutrition; skeletal muscle

INTRODUCTION

Carbohydrate ingestion during endurance exercise is a well-established strategy for enhancing performance (1–3). The mechanisms through which carbohydrate ingestion during endurance exercise improves performance are not completely understood. Skeletal muscle glycogen stores are limited and can be depleted to very low concentrations during prolonged, vigorous exercise (4–6), and this depletion has been mechanistically linked to fatigue (7–11). Similarly, the decline in blood glucose concentrations that can occur during prolonged exercise may also contribute to fatigue (12–15).

Alongside preservation of blood glucose concentrations, a plausible explanation for the performance benefit of carbohydrate ingestion is the ability to attenuate net skeletal muscle glycogenolysis by displacing endogenous carbohydrate use with oxidation of ingested carbohydrates. This is supported by evidence showing substantial reductions in endogenous carbohydrate oxidation when carbohydrates are ingested during exercise (16–20). However, although some studies have demonstrated a reduction in net skeletal muscle glycogen utilization with carbohydrate ingestion (21, 22), the majority have not (23–28). Various mechanisms have been posited for the discrepancies in the literature, including moderating effects of exercise modality and/or the specific muscle sampled, exercise intensity, the amount, type, and timing of carbohydrate ingestion, as well as preexercise nutritional and training status of study participants (29). However, many of these studies had relatively small sample sizes, potentially limiting their power to detect small-to-moderate effects. Thus, a meta-analytic approach may be better suited to evaluate whether carbohydrate ingestion during endurance exercise has a muscle glycogen-sparing effect.

Accordingly, the aim of this meta-analysis was to determine whether carbohydrate ingestion during endurance exercise reduces net skeletal muscle utilization, thus preserving muscle glycogen stores. We hypothesized that the existing literature would demonstrate a small magnitude

Correspondence: E. Maunder (ed.maunder@aut.ac.nz).
Submitted 10 September 2025 / Revised 14 October 2025 / Accepted 3 December 2025

skeletal muscle glycogen-sparing effect of carbohydrate ingestion during endurance exercise.

METHODS

This systematic review with meta-analysis was conducted following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (30). The study protocol was preregistered at the International Prospective Register of Systematic Reviews (PROSPERO; Identification Code: 627850). The protocol registration occurred after pilot searches, but before any formal systematic searches were conducted.

Search Strategy

The following Boolean search terms were used: "carbohydrate*" AND "muscle glycogen*" AND "run*" OR "cycl*" OR "bicycl*". The intervention term "carbohydrate*" was used to capture studies that involved carbohydrate ingestion. The outcome term "muscle glycogen*" was used to capture studies that quantified net muscle glycogen utilization, or provided data that could be used to quantify net muscle glycogen utilization. The population terms "run*", "cycl*", and "bicycle*" were used to capture studies that used running or cycling models. The search string was developed through an optimization process. Searches were performed in MEDLINE/EBSCO, PubMed, and Scopus.

Inclusion and Exclusion Criteria

Studies were included if they met the following inclusion criteria: *1*) the study was published in English in a peer-reviewed journal, *2*) the study was performed in healthy, nondiabetic, nonobese humans, *3*) the study used a crossover design where exercise was performed with and without carbohydrate ingestion, *4*) the exercise protocol was >20 min, *5*) the exercise performed was either cycling or running, *6*) the external work rate and exercise duration were controlled and fixed between the placebo and carbohydrate trials, *7*) net muscle glycogen utilization was quantified using either muscle biopsy or magnetic resonance spectroscopy [studies measuring muscle glycogen oxidation using stable isotopes were excluded as glycogen synthesis is possible during exercise (31, 32), and stable isotope methods cannot accurately quantify oxidation in the first hour of exercise due to the slow turnover of the bicarbonate pool (33)], *8*) muscle glycogen use was quantified from the start of the exercise protocol, *9*) muscle glycogen use was quantified in the vastus lateralis/quadriceps femoris or gastrocnemius, and *10*) end-exercise muscle biopsy samples were obtained within 5 min of exercise cessation. Studies not meeting these criteria were excluded.

Text Screening

Article titles and abstracts were independently screened by two researchers (H.C. and C.S.) using (Covidence systematic review software, Veritas Health Innovation, Melbourne, Australia). The full text of each paper was then assessed against the a priori inclusion and exclusion criteria by two researchers. Discrepancies were resolved by consensus with a third researcher (E.M.).

Quality of Evidence Assessment

Study quality was independently assessed by two researchers (H.D.R. and J.A.R.) and verified by a third researcher (E.M.). Specifically, methodological quality was assessed using the Cochrane Risk of Bias tool 2 for randomized clinical studies (34), with context-specific considerations for preintervention dietary control, adequacy of washout, clarity of carbohydrate drink composition, and internal consistency of reported glycogen outcomes (Supplemental Files).

Data Extraction

The following data from studies satisfying the inclusion and exclusion criteria were extracted: sample size and participant age, sex, body mass, maximal oxygen consumption ($\dot{V}O_{2max}$), exercise duration, exercise intensity (as continuous or interval, due to the homogeneity in protocols), preexercise carbohydrate ingestion (<4 h), carbohydrate ingestion rate during exercise, composition of ingested carbohydrates (as percent of total carbohydrate intake derived from glucose or glucose-containing compounds, e.g., glucose polymers, maltodextrin, sucrose), carbohydrate ingestion frequency, and mean and standard deviation of pre- and postexercise glycogen content. Where numerical values were not provided in the text and only presented in figures, software (DigitizeIt, Brunswick, Germany) was used for obtaining mean and standard deviation values.

Statistical Analysis

Descriptive data are presented as means ± standard deviation. All analyses were performed in RStudio (R version 4.3.1) using the esc and metafor packages. For each study, the between-condition standardized mean difference (SMD) in muscle glycogen utilization was calculated using group-level means, standard deviations, sample sizes, and the within-subject correlation between pre- and postexercise measurements. Where this correlation was not available, a 0.5 correlation was assumed, based on the median of the 16 values calculated from the available raw data. Sensitivity analyses using a range of plausible correlation values (0.2–0.9) were conducted to evaluate the robustness of the results (35). No other imputation methods were used. The SMDs were calculated using the unbiased estimation method (vtype = "UB"), appropriate for paired-sample designs. Model parameters were estimated using restricted maximum likelihood (REML), with effect sizes weighted by the inverse of their sampling variance.

A multilevel random-effects meta-analysis was conducted with a random intercept for study to account for the nonindependence of multiple effect sizes within studies. Subgroup analyses were performed by exercise modality (run or cycle) and glycogen measurement unit (dry weight or wet weight). Moderator analyses (i.e., meta-regressions) were used to assess whether study-level variables influenced the effect of carbohydrate ingestion on muscle glycogen utilization. The following variables were considered, with the number of effect sizes included for each: exercise intensity (continuous vs. interval exercise, $n = 48$); exercise duration ($n = 48$); participant maximal oxygen consumption ($\dot{V}O_{2max}$) ($n = 48$); preexercise glycogen value (for studies reporting mmol·kg^{-1} wet or dry wt, $n = 45$); glycogen measurement units ($n = 48$);

carbohydrate ingestion type ($n = 46$), rate ($n = 48$), and frequency during exercise ($n = 47$); and carbohydrate ingestion within 4 h before exercise ($n = 48$). For preexercise glycogen values, wet weight measures were converted to dry weight using a conversion factor of 4.35 (36), and the mean of the carbohydrate and placebo groups was calculated. Between-study heterogeneity was quantified using the estimated between-study variance (τ^2) (37), I^2 (proportion of total variability due to heterogeneity), and H^2 (ratio of total to sampling variability), with Cochran's Q statistic and its associated P value reported as a test for excess dispersion. The τ^2 estimate was obtained using restricted maximum likelihood (REML), with additional sensitivity estimates from alternative estimators (DerSimonian–Laird, Sidik–Jonkman). Although no universal benchmarks exist for interpreting τ^2, larger values reflect greater between-study heterogeneity and may indicate the presence of important moderators, methodological differences, or outliers. Standardized mean differences were interpreted as follows: small (0.20–0.49), moderate (0.50–0.79), and large (>0.80) (38). Publication bias was assessed both visually, using funnel plots, and statistically, using a multilevel Egger-type regression test, in which the standard error of the effect size was included as a predictor in a mixed-effects model (39). Statistical significance was defined as $P \leq 0.05$.

RESULTS

A summary of the search process is shown in Fig. 1.

Study Characteristics

The 31 studies included 48 unique effect sizes (due to different study arms or measures at multiple time points, e.g., muscle glycogen measurements after 120 and 180 min of exercise) and 279 participants (273 male, 6 female; age 26.8 ± 6.0 yr) (21–26, 28, 40–62). The number of effect sizes in cycling and running were 40 and 8, respectively. Exercise duration was 117.4 ± 51.6 min. Muscle glycogen was measured per unit dry weight ($n = 22$), wet weight ($n = 23$), protein ($n = 1$), and mmol/L ($n = 2$). All but one study extracted the muscle biopsy from the vastus lateralis, the remaining study reported sampling from the quadriceps femoris, but did not report the specific muscle (60). A summary of studies is shown in Fig. 2.

Methodological Quality of the Studies

Risk of bias was assessed using the ROB2 tool for crossover trials (34). Most studies were judged to have either low risk of bias (10 studies) or some concerns (19 studies), with only two studies rated as having an overall high risk of bias (Fig. 3). The primary sources of bias are related to randomization and blinding, which would not be expected to meaningfully influence the primary analysis, and lack of clarity regarding the carbohydrate composition of the test beverages.

Net Muscle Glycogen Utilization

A total of 48 effect sizes from crossover studies were included in the meta-analysis, comparing net muscle

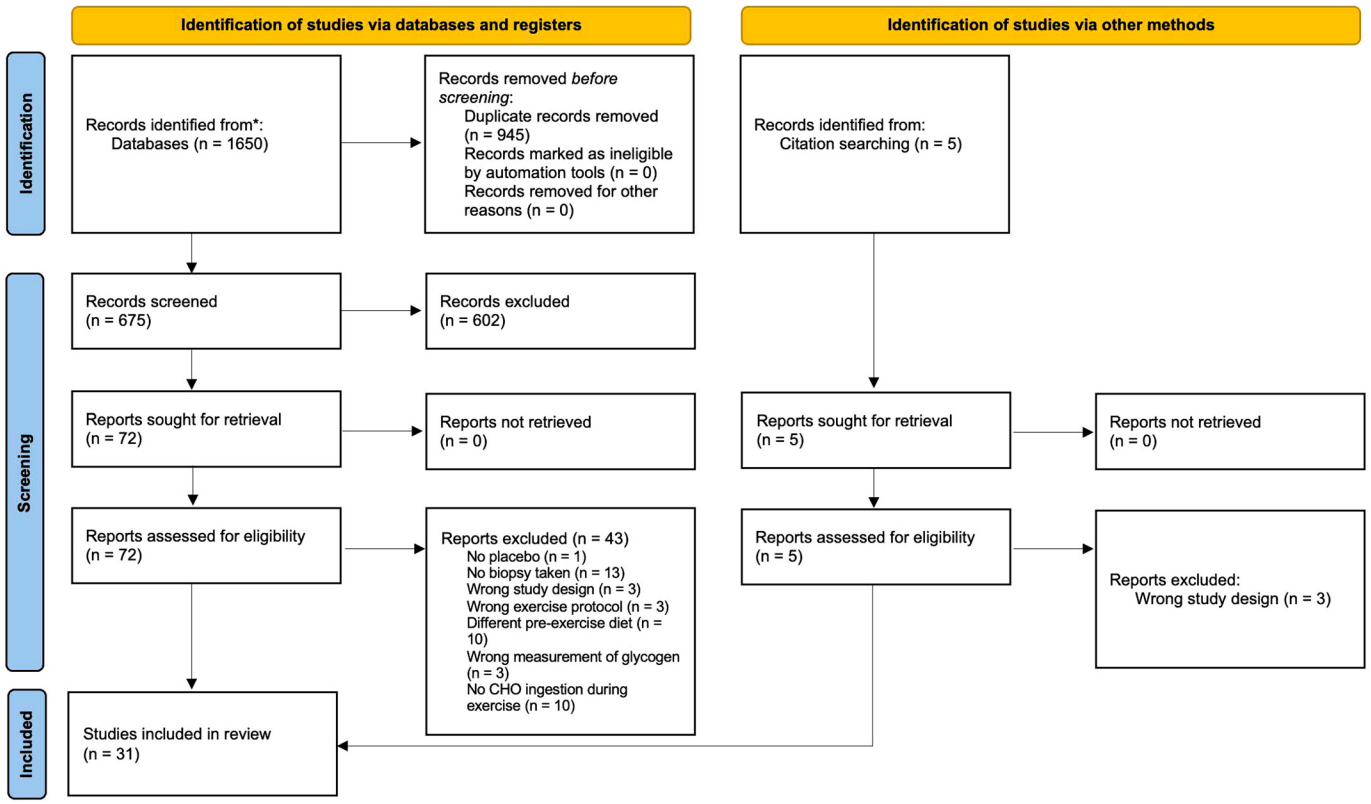


Figure 1. Literature search flow chart. n = number of studies.

Study	Protocol					VO_2max (ml·kg^{-1}·min^{-1})	Exercise Duration (min)	Moderators		
	N	CHO (g·h^{-1})	Glu (%)	Freq (h^{-1})	Intensity			Exercise mode	Type	Glycogen units
Arkinstall et al., 2001 Cycle	7	64	100	3	69	52	60	Cycling	Continuous	dry wt
Arkinstall et al., 2001 Run	7	64	100	3	78	54	60	Running	Continuous	dry wt
Blomstrand et al., 1995	5	40		4	75	69	60	Cycling	Continuous	wet wt
Chryssanthopoulos et al., 2002	8	46	100	3	70	59	60	Running	Continuous	dry wt
Clark et al., 2019	16	60	56	4	65	52	120	Cycling	Continuous	dry wt
Cluberton et al., 2005	6	20	100	1	74	46	60	Cycling	Continuous	dry wt
Coyle et al., 1986 part 1	5	148	100	3	71	65	105	Cycling	Continuous	wet wt
Coyle et al., 1986 part 2	7	108	100	3	72	70	180	Cycling	Continuous	wet wt
de Oliveira et al., 2024	13	60	100	3		57	120	Cycling	Interval	dry wt
Dumke et al., 2013	8	37	100	2		53	60	Cycling	Interval	wet wt
Erickson et al., 1987	5	48	100	2.7	68	65	90	Cycling	Continuous	wet wt
Fell et al., 2021	8	45	88	2	64	60	180	Cycling	Continuous	dry wt
Fielding et al., 1985	9	22	50	2		50	240	Cycling	Interval	wet wt
Flynn et al., 1987	8	22	100	3		64	120	Cycling	Interval	wet wt
Foskett et al., 2008	6	90	100	4		60	90	Running	Interval	dry wt
Gonzalez et al., 2015	9	102	100	4		60	180	Cycling	Continuous	mmol/L
Hargreaves & Briggs 1988	5	60	100	2	70	68	120	Cycling	Continuous	wet wt
Hargreaves et al., 1984	10	43	50	1		62	240	Cycling	Interval	wet wt
Lee-Young et al., 2006	8	64	100	4	65	48	120	Cycling	Continuous	dry wt
McConell et al., 2000	6	81	100	4	83	66	73	Cycling	Continuous	dry wt
Menzies et al., 2020	6	60	50	12	77	61	75	Running	Continuous	dry wt
Mitchell et al., 1989	10	74	71	4	70	63	105	Cycling	Continuous	wet wt
Nicholas et al., 1999	6	44	73	4		56	105	Running	Interval	dry wt
Nieman et al., 2003	16	60	54	4	70	45	180	Running	Continuous	dry wt
Nieman et al., 2005	15	74	54	4	74	54	150	Cycling	Continuous	wet wt
Slivka et al., 2008	9	60		2		60	120	Cycling	Continuous	wet wt
Tsintzas et al., 1995	7	49	80	3	70	54	60	Running	Continuous	dry wt
Tsintzas et al., 1996	8	33	80	3	70	62	104	Running	Continuous	dry wt
Vigh-Larsen et al., 2024	11	55	67			57	130	Cycling	Interval	dry wt
Yan et al., 1993	9	80	64	4	70	64	135	Cycling	Continuous	dry wt
Yaspelkis III & Ivy, 1991	12	74	68	4	49	66	120	Cycling	Continuous	µmols/g protein
Yaspelkis III et al., 1993	7	54	75	3		71	190	Cycling	Interval	wet wt
Zachwieja et al., 1993	8	87	38	4	68	55	120	Cycling	Continuous	wet wt

Figure 2. Study characteristics included in the meta-analysis. Protocol characteristics include carbohydrate intake rate (CHO, g·h^{-1}), percent CHO from glucose or glucose-containing compounds including glucose polymers, maltodextrin, sucrose (Glu %), ingestion frequency (Freq, bolus·h^{-1}), exercise mode (run or cycle), type of exercise (continuous vs. Interval), and the units used for reporting muscle glycogen concentration. Exercise intensity is shown as %$\dot{V}O_{2max}$, for studies prescribing intensity as percentage of $\dot{V}O_{2max}$. Missing values for glucose percentage indicate unclear reporting, missing values for ingestion frequency indicates continuous sipping. The analysis includes 31 studies with 48 unique effect sizes. Exercise modality included cycling ($n = 23$ studies), running ($n = 7$ studies), and both cycling and running ($n = 1$ study).

glycogen utilization between carbohydrate and placebo conditions during endurance exercise. The pooled SMD was −0.16 [95% confidence interval (CI): −0.30 to −0.02], $P = 0.021$, indicating a small but statistically significant muscle glycogen-sparing effect of carbohydrate ingestion (Fig. 4). The direction of effect predominantly favored carbohydrate ingestion, with most studies reporting numerically lower glycogen depletion compared with placebo. However, individual effect sizes varied substantially, ranging from negative effects (e.g., −1.09) to positive effects (e.g., + 0.93). Between-study heterogeneity was minimal across all model types, suggesting that the true effect size was relatively consistent across studies despite differences in protocols, measurement methods, and participant characteristics. In the multilevel model, the estimated between-study variance was $\tau^2 = 1.20 \times 10^{-10}$. A univariate fixed-effects model (assuming independence) produced a Cochran's $Q(47) = 31.93$, $P = 0.95$, with $I^2 = 0\%$ and $H^2 = 0.68$, indicating no excess dispersion beyond sampling variability. In the corresponding random-effects model (REML), the estimated τ^2 was 0, with a 95% confidence interval of 0 to 0.018, and $H^2 = 1.00$, reflecting no between-study heterogeneity. Alternative τ^2 estimators (e.g., Sidik–Jonkman) yielded slightly higher values ($\tau^2 = 0.079$), but all consistently indicated low heterogeneity. No evidence of small-study effects was detected (Egger test $P = 0.989$).

Subgroup analyses revealed a statistically significant glycogen-sparing effect of carbohydrate ingestion during running trials (SMD = −0.38 [−0.74, −0.02], $P = 0.036$), with no observed between-study heterogeneity ($\tau^2 = 0$; $I^2 = 0\%$; $Q(7) = 5.85$, $P = 0.557$). In cycling trials, no significant effect was observed (SMD = −0.12 [−0.28, 0.03], $P = 0.107$), and heterogeneity remained low ($\tau^2 = 0$; $I^2 = 0\%$; $Q(39) = 24.4$, $P = 0.967$). When stratified by glycogen measurement unit, there were now significant effects for dry weight measures (SMD = −0.20 [−0.41, −0.009], $P = 0.060$), with very low heterogeneity ($\tau^2 = 0.000007$; $I^2 = 0\%$; $Q(21) = 18.4$, $P = 0.626$), or wet weight measures (SMD = −0.10 [−0.30, 0.11], $P = 0.347$), with no between-study heterogeneity ($\tau^2 = 0$; $I^2 = 0\%$; $Q(22) = 9.56$, $P = 0.990$). Forest plots for subgroup analyses are shown in Supplemental Figs. 1–4. These findings suggest that the glycogen-sparing effect of carbohydrate ingestion may be more detectable in running protocols; however, these null findings likely reflect limited statistical power within subgroups, increasing the risk of type II errors, rather than confirming a true absence of moderation.

Small-study effects were evaluated using a multilevel meta-regression with standard error (SE) as a predictor, an approach analogous to Egger's test adapted for multilevel models (39). The coefficient for SE was not statistically significant ($\beta = 0.012$, $P = 0.989$), indicating no evidence of small-study effects or funnel plot asymmetry (Fig. 5).

Moderation

None of the tested moderators (carbohydrate dose, ingestion frequency, exercise duration, exercise mode, starting

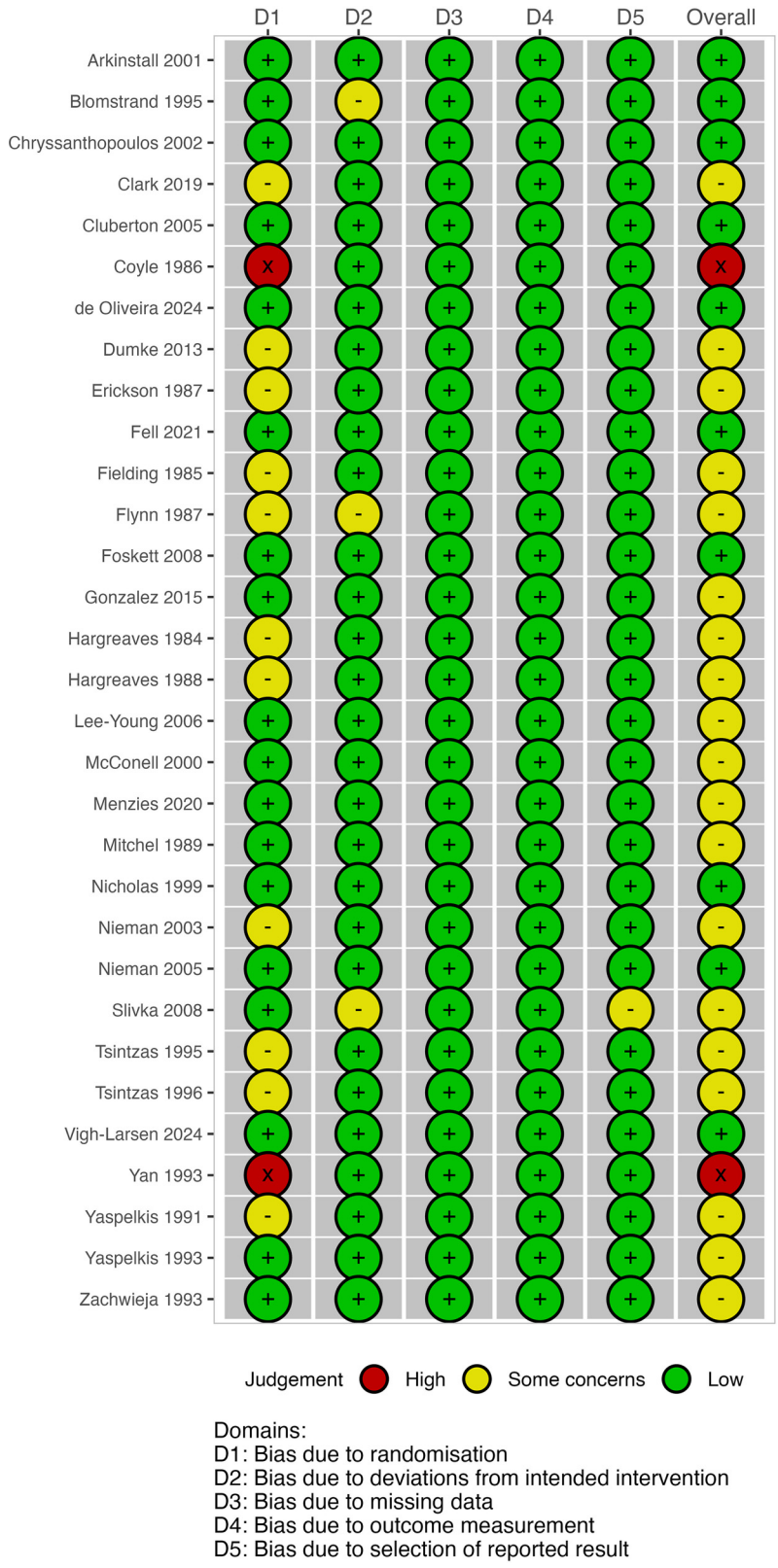


Figure 3. Risk of bias assessment for all included studies.

glycogen value, or preexercise carbohydrate) were significantly associated with the effect size in univariable models (all $P > 0.05$). Therefore, a multivariable model was not pursued. To illustrate the range of study characteristics, distributions of key moderator variables are shown in Fig. 6.

Sensitivity Analysis

Sensitivity to imputed correlation coefficients was checked using values between 0.2 and 0.9. A significant effect was found for all correlation values, indicating an

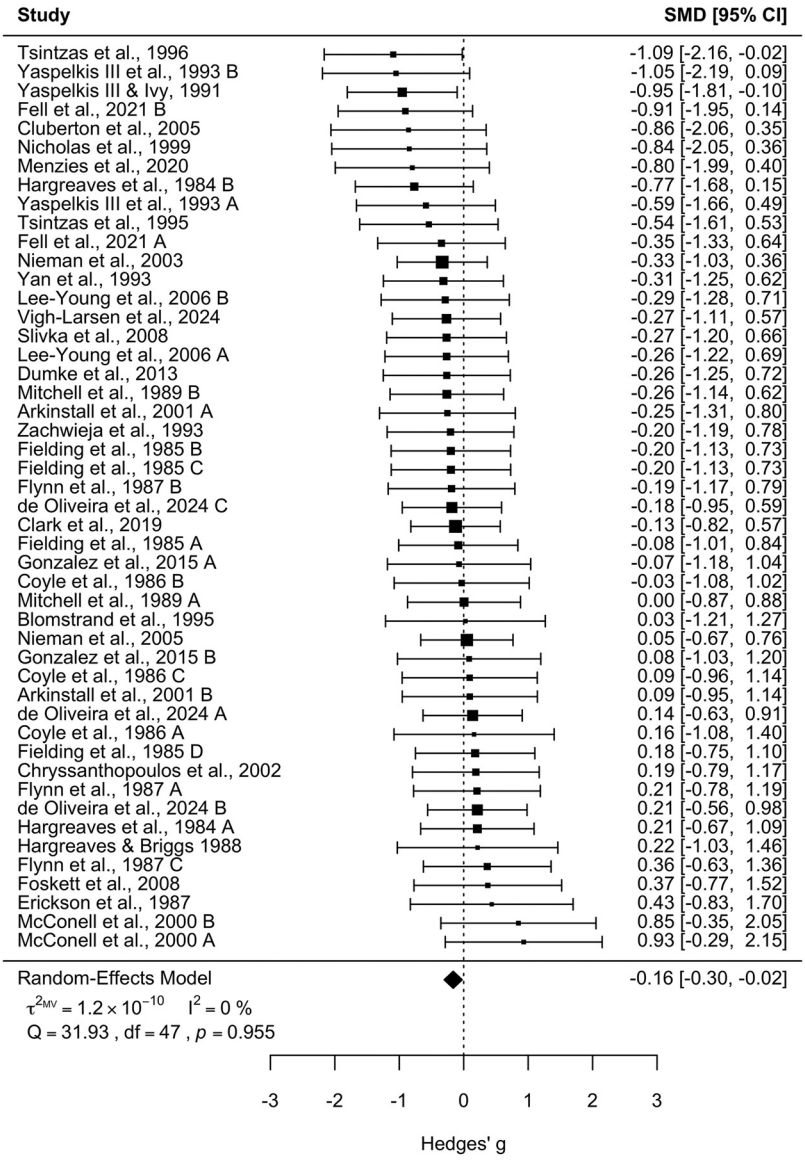


Figure 4. Forest plot from multilevel meta-analysis showing standardized mean differences (SMD) in muscle glycogen utilization between carbohydrate ingestion and placebo conditions during endurance exercise. Each line represents an individual study arm or time point, with squares sized by inverse variance weighting and horizontal lines indicating 95% confidence intervals. Letters following study name correspond to studies with multiple comparison arms or time points, defined in supplemental file. Negative values reflect reduced glycogen utilization (i.e., glycogen sparing) with carbohydrate ingestion. The diamond at the bottom shows the overall random effects estimate from the multilevel model. Between-study heterogeneity was negligible ($\tau^2 = 0$).

overall robustness to imputed within-subject correlations (Fig. 7).

DISCUSSION

The primary finding from this meta-analysis is that carbohydrate ingestion during exercise induces a small but statistically significant reduction in net skeletal muscle glycogen utilization. Subgroup and moderation analyses were conducted to explore whether study-level characteristics influenced this effect. Among subgroups, running-based studies showed a significant effect of carbohydrate ingestion, whereas cycling studies did not reach statistical significance. However, moderation testing indicated that these differences were not statistically different. In line with this, none of the categorical or continuous moderators including exercise type or duration, carbohydrate intake rate, composition or timing, or starting glycogen concentration were statistically significant in meta-regression models. These findings suggest that although a muscle glycogen-sparing effect is observed on average, no individual study-level factor consistently explains the variability in effect sizes across the included trials.

A meta-analysis by Areta and Hopkins (36) examined a broad range of studies reporting muscle glycogen at rest and during endurance exercise, regardless of whether carbohydrate was ingested. Among their subgroup analyses, they reported the effect of carbohydrate ingestion compared with no intake, finding a mean difference of −7 mmol/kg dry wt (90% CI: −23 to +9), which they classified as a trivial effect (36). Although their analysis included a limited subset of studies with carbohydrate supplementation and yielded a wide confidence interval, the direction of effect is consistent with this analysis. Furthermore, they included a wider range of study protocols including noncrossover studies, studies using glucose infusion, and nonplacebo-controlled interventions. Our findings, derived from a focused multilevel meta-analysis of placebo-controlled crossover studies, show a small but statistically significant reduction in net muscle glycogen utilization with carbohydrate ingestion during exercise (Fig. 4).

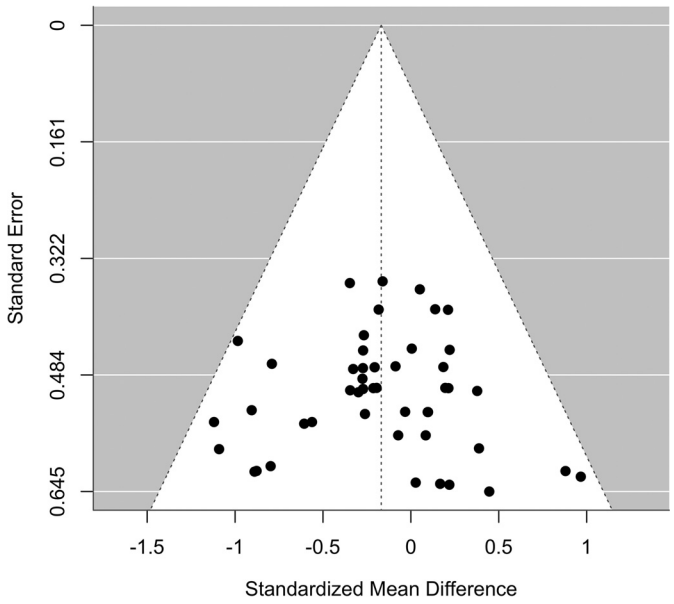


Figure 5. Funnel plot of standardized mean differences and standard errors. The plot shows no clear asymmetry, and a multilevel meta-regression (Egger-type test) confirmed the absence of small-study effects ($\beta = 0.012$, $P = 0.989$). Note: Because multiple effect sizes per study were modeled using a multilevel approach, interpretation of the funnel plot should be made with caution.

Several physiological processes may help explain the observed muscle glycogen-sparing effect of carbohydrate ingestion during endurance exercise. Carbohydrate ingestion increases plasma glucose concentrations (13, 63, 64) and stimulates glucose transporter type 4 translocation to the plasma membrane in skeletal muscle (65). This increases skeletal muscle glucose uptake and therefore plasma glucose oxidation rates (66). The data from our meta-analysis suggest that some of the additional plasma glucose oxidation that occurs when carbohydrate is ingested reduces the reliance on intramuscular glycogen to meet energy demands (Fig. 4). The small size of the muscle glycogen-sparing effect that we report when carbohydrate is ingested during exercise reflects the simultaneous suppression of fatty acid oxidation (16–20, 67). Accordingly, assuming movement economy is unchanged with carbohydrate ingestion, the reduction in net muscle glycogen utilization must be smaller than the net increase in plasma glucose oxidation. In addition, it is possible that increased muscle glycogen synthesis contributes to the small reduction in net muscle glycogen utilization during exercise with carbohydrate ingestion, as net increases in muscle glycogen content have been observed following low-intensity exercise with carbohydrate ingestion (31, 32). Together, these adaptations provide a mechanistic basis for how carbohydrate ingestion may preserve muscle glycogen stores.

The reasons for the performance-enhancing effects of carbohydrate ingestion are not fully understood, but are believed to involve stimulation of the central nervous system through oral carbohydrate sensing, the provision of an additional fuel source for ATP production during exercise, improved TCA cycle flux, and its ability to reduce liver glycogen breakdown and maintain blood glucose concentrations (1, 15, 49, 68). Our analysis suggests that a small reduction in net muscle glycogen utilization should also be considered a plausible contributor to the commonly observed beneficial effects of carbohydrate ingestion during exercise on performance (2). Nearly all effect sizes (46 out of 48) included in our analysis were reported as nonsignificant (Fig. 4). However, the average sample size across all effect sizes was $n = 8.8$, which provides insufficient statistical power to detect small effects of carbohydrate ingestion on skeletal muscle glycogenolysis. Indeed, with a crossover design, a sample size of nine has 80% power to detect an effect size of 1.07, well above the effect sizes typically observed in this context. Furthermore, 309 participants would be needed to detect a significant difference between groups for our effect size of 0.16. This issue has recently been highlighted in the context of muscle metabolism research (69).

If the magnitude of the reduction in net muscle glycogen utilization with carbohydrate ingestion varies between subcellular compartments, the effect on performance could be larger or smaller than the overall effect on overall net muscle glycogen utilization observed here suggests (8). For example, intramyofibrillar glycogen appears to be associated with tetanic Ca^{2+} handling (9, 10) and is preferentially depleted during exercise (70, 71). Accordingly, if carbohydrate ingestion during exercise disproportionately preserves intramyofibrillar glycogen, it is possible that a meaningful effect on endurance performance would result. Investigation into the effect of carbohydrate ingestion during exercise on net utilization of specific subcellular muscle glycogen depots is therefore warranted.

To contextualize our overall effect size, we simulated an example scenario using studies that measured glycogen in mmol·kg^{-1} dry wt. Assuming a starting concentration of 550 mmol·kg^{-1} and exercise duration of 110 min (average of the included studies), the average decline in the placebo condition was 270 mmol·kg^{-1}, resulting in an end value of 280 mmol·kg^{-1}. In contrast, with carbohydrate ingestion, the average decline was 247 mmol·kg^{-1}, leading to an end value of 303 mmol·kg^{-1}. This reflects a muscle glycogen-sparing effect of ~24 mmol·kg^{-1} (95% CI: 4–45 mmol·kg^{-1}). Although this difference is small, it could plausibly offer a meaningful advantage during prolonged or repeated efforts, particularly in light of suggestions that high-intensity performance may be impaired when muscle glycogen drops below ~250–300 mmol·kg^{-1} dry wt (72). However, the data presented here do not allow us to determine the practical significance of this effect.

We also investigated potential moderating variables, including the type, amount, and frequency of carbohydrate ingestion; exercise type (i.e., interval vs. continuous); starting muscle glycogen concentration; and the unit of glycogen measurement, but none were statistically significant. In response to observations of professional cyclists routinely consuming carbohydrate at levels well above previous recommendations, recent studies have investigated the potential benefits of ingesting carbohydrate at rates as high as 120 g·h^{-1} (73, 74). Increased oxidation of exogenous carbohydrate has been reported with 120 g·h^{-1} compared with 90 g·h^{-1}, but endogenous carbohydrate oxidation rates were not different (73). In fact, glucose ingestion at rates that exceed intestinal transport capacity (90 vs. 60 g·h^{-1}) has also been reported to accelerate muscle glycogen oxidation (18). Likewise, no difference in glycogen use was observed when

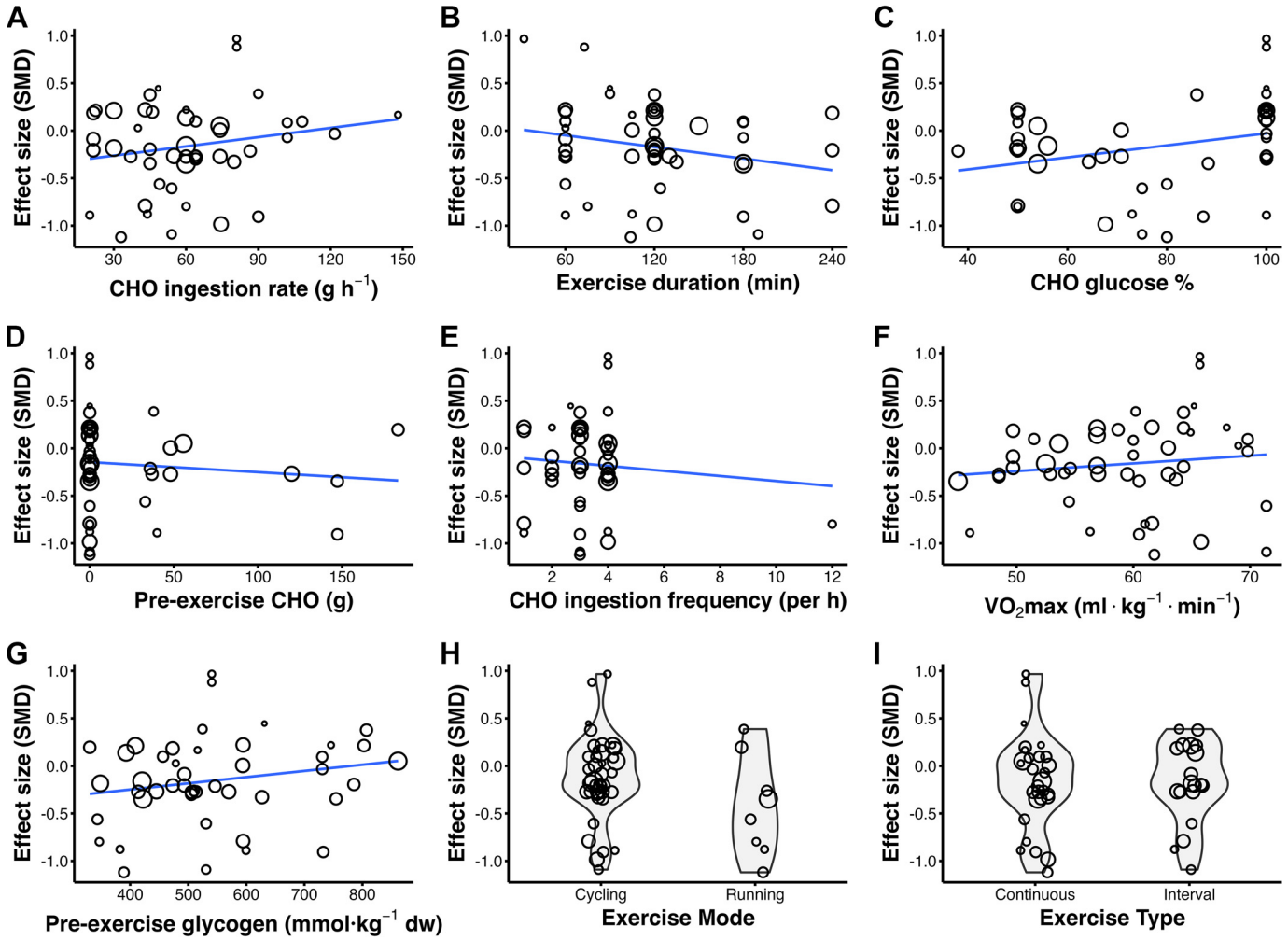
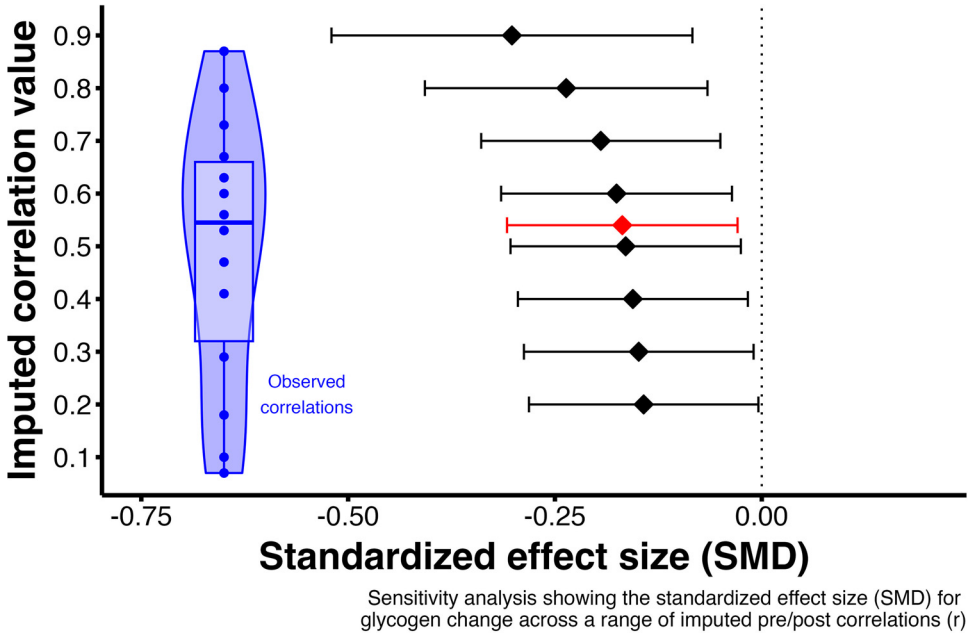


Figure 6. Meta-regression plots examining the relationship between study-level variables and standardized mean difference (SMD) in muscle glycogen utilization between carbohydrate and placebo conditions: (*A*) carbohydrate ingestion rate, (*B*) exercise duration, (*C*) proportion of the ingested carbohydrate from glucose, (*D*) pre-exercise carbohydrate intake, (*E*) carbohydrate ingestion frequency, (*F*) mean maximum oxygen uptake of the study participants, (*G*) pre-exercise muscle glycogen concentration, (*H*) exercise modality, and (*I*) continuous or interval exercise. Negative SMD relates to a glycogen sparing effect. Each point represents an effect size from an individual study arm, with point size scaled by the inverse of its sampling variance (i.e., precision). For *G*, values reflect the mean of the preexercise carbohydrate and placebo groups. Blue lines represent simple linear regressions for visualization only; moderator effects were formally tested using multilevel metaregression models accounting for study-level clustering and inverse-variance weighting. No significant moderators were identified (all $P > 0.05$).

cyclists consumed either 45 or 90 g·h^{-1} carbohydrate (47). Thus, any potential benefits of high-dose carbohydrate ingestion are unlikely related to further attenuations in net muscle glycogenolysis. However, it is important to note that very high carbohydrate intakes, such as those commonly consumed by professional cyclists (e.g., ≥100 g·h^{-1}), were not typically assessed in the included studies (Fig. 6*A*). Therefore, investigation of contemporary, optimized strategies such as individualized dosing on net muscle glycogen utilization, including in specific subcellular depots (8), are warranted (75). If these strategies do confer a performance advantage, it is possible that mechanisms beyond glycogen sparing are involved.

Our finding of no effect of carbohydrate type aligns with previous studies, showing no difference in glycogen breakdown between glucose and sucrose (49) or between various combinations of maltodextrin, glucose, and fructose (25). The lack of moderating effect of exercise type is also consistent with multiple studies comparing continuous versus variable intensity cycling, which found no differences in total glycogen use, although fiber-type-specific depletion patterns do occur (54, 76). It is well established that glycogen use during exercise is greater when starting from higher glycogen concentrations (77). Mechanistically, low initial muscle glycogen reduces substrate availability by limiting glycogen phosphorylase activity and indirectly downregulates carbohydrate oxidation via reduced activation of pyruvate dehydrogenase (78). Consequently, exercise performed with higher starting muscle glycogen concentrates elicits higher rates of net muscle glycogenolysis (79). Therefore, one could hypothesise that carbohydrate ingestion-induced reductions in net muscle glycogen utilization are likely to be greater with higher starting glycogen levels, as this would result in greater rates of net muscle glycogen utilization in the control



Sensitivity analysis showing the standardized effect size (SMD) for glycogen change across a range of imputed pre/post correlations (r)

Figure 7. Sensitivity of standardized effect size to imputed pre-/postcorrelation values. Standardized mean differences (SMDs) in glycogen change between carbohydrate and placebo conditions are shown across a range of imputed within-condition pre-/postcorrelations ($r = 0.2$ to 0.9). Diamonds represent the estimated effect sizes from a multilevel random-effects meta-analysis, with horizontal bars indicating 95% confidence intervals. The vertical dotted line at 0 represents the null effect. A violin plot on the left displays the distribution of observed pre-/postcorrelation values calculated from raw data (where available), with individual values shown as points. The red diamond highlights the effect estimate derived using the median of the observed correlations, which was used in the primary analysis.

condition. However, preexercise glycogen concentration was not a significant moderator in our analysis. Taken together, these results suggest that the glycogen-sparing effect of carbohydrate ingestion during exercise appears consistent across a range of protocols and conditions, without clear influence from specific study-level characteristics.

Effect size calculations for within-subject designs require estimates of the prepost correlation. We were able to obtain participant-level data for the recent studies through author correspondence; however, many included studies that were published 30–40 years ago, making data retrieval unfeasible. In such cases, a conservative correlation value of 0.5 is commonly used (80). We instead chose to use the median of the observed correlations from available datasets, which was also 0.50. Our results were robust across a range of imputed correlation values, but it is noteworthy that the observed prepost correlations varied widely (Fig. 7). This variation may reflect small differences in biopsy site, tissue handling and weighing, muscle fiber-type composition, and/or individual differences in substrate utilization (81–83).

Among subgroups, running-based studies showed a significant effect of carbohydrate ingestion, whereas cycling studies did not reach statistical significance. A key consideration is that all studies included in our analysis used muscle samples taken from the quadriceps and not the gastrocnemius. The gastrocnemius sees greater net muscle glycogen utilization during level-gradient running than the quadriceps (84). Therefore, it is possible that our exercise modality subgroup analysis was influenced by net glycogen utilization being assessed in primary versus secondary muscle groups. Nevertheless, moderation testing indicated these differences were not statistically different ($P = 0.195$), which is likely to mean sampling variability and lower statistical power in the smaller subgroups account for differences in the subgroup analysis, rather than true physiological differences. This is supported by a small ($n = 7$) individual study reporting no difference in the effect of carbohydrate ingestion on net muscle glycogen utilization between running and cycling (24). Muscle-specific investigation of the effects of carbohydrate ingestion during exercise on net muscle glycogen utilization is warranted.

Nearly all included studies involved young males. Consequently, the effect of carbohydrate ingestion during exercise on net muscle glycogen utilization in females cannot be ascertained. Consideration of biological sex in this context is important, given that sex differences in substrate metabolism are well-documented. For instance, Tarnopolsky et al. (85) found that males had ~25% greater muscle glycogen utilization than females during prolonged treadmill running, which they attributed to higher carbohydrate and protein oxidation rates. However, other studies have reported similar glycogen utilization between sexes (17, 86, 87), highlighting the complexity of sex-related responses. These findings underscore the need for research specific to females and, more specifically, investigation into the effect of carbohydrate ingestion during exercise on net muscle glycogen utilization in females.

CONCLUSIONS

In summary, this meta-analysis provides evidence that carbohydrate ingestion during exercise induces a small but statistically significant reduction in net skeletal muscle glycogen utilization. Although subgroup and moderator analyses did not identify any consistent study-level characteristics that significantly influenced the magnitude of this effect, the direction of results was generally consistent across protocols. Importantly, the estimated glycogen-sparing effect, although small, may offer a meaningful physiological advantage during prolonged or repeated efforts, particularly when muscle glycogen stores approach critically low levels. These findings reinforce current carbohydrate intake guidelines for endurance performance and underscore the importance of contextualizing carbohydrate strategies within the demands of

specific exercise tasks. Future research should prioritize diverse populations and investigate the effects of high-dose carbohydrate feeding protocols that more closely reflect contemporary elite athlete practices.

DATA AVAILABILITY

Raw data and code use in this analysis is posted at https://osf.io/vjwsu/.

SUPPLEMENTAL MATERIAL

Supplemental Figs. S1–S4 and Supplemental Tables S1 and S2: https://doi.org/10.6084/m9.figshare.30483119.

DISCLOSURES

No conflicts of interest, financial or otherwise, are declared by the authors.

AUTHOR CONTRIBUTIONS

J.A.R. prepared figures; J.A.R. and E.M. drafted manuscript; J.A.R., H.D.-R., H.C., A.S.M.S., D.J.P., and E.M. edited and revised manuscript; J.A.R., H.D.-R., H.C., A.S.M.S., D.J.P., and E.M. approved final version of manuscript.

REFERENCES

1. **Podlogar T**, **Wallis GA.** New horizons in carbohydrate research and application for endurance athletes. *Sports Med* 52: 5–23, 2022. doi:10.1007/s40279-022-01757-1.
2. **Stellingwerff T**, **Cox GR.** Systematic review: carbohydrate supplementation on exercise performance or capacity of varying durations. *Appl Physiol Nutr Metab* 39: 998–1011, 2014. doi:10.1139/apnm-2014-0027.
3. **Burke LM**, **Hawley JA**, **Wong SHS**, **Jeukendrup AE.** Carbohydrates for training and competition. *J Sports Sci* 29, *Suppl* 1: S17–S27, 2011. doi:10.1080/02640414.2011.585473.
4. **Bergström J**, **Hermansen L**, **Hultman E**, **Saltin B.** Diet, muscle glycogen and physical performance. *Acta Physiol Scand* 71: 140–150, 1967. doi:10.1111/j.1748-1716.1967.tb03720.x.
5. **Hermansen L**, **Hultman E**, **Saltin B.** Muscle glycogen during prolonged severe exercise. *Acta Physiol Scand* 71: 129–139, 1967. doi:10.1111/j.1748-1716.1967.tb03719.x.
6. **Bergström J**, **Hultman E.** A study of the glycogen metabolism during exercise in man. *Scand J Clin Lab Invest* 19: 218–228, 1967. doi:10.3109/00365516709090629.
7. **Nielsen J**, **Jensen R**, **Ørtenblad N.** Assessments of individual fiber glycogen and mitochondrial volume percentages reveal a graded reduction in muscle oxidative power during prolonged exhaustive exercise. *Scand J Med Sci Sports* 34: e14571, 2024. doi:10.1111/sms.14571.
8. **Ørtenblad N**, **Westerblad H**, **Nielsen J.** Muscle glycogen stores and fatigue. *J Physiol* 591: 4405–4413, 2013. doi:10.1113/jphysiol.2013.251629.
9. **Ørtenblad N**, **Nielsen J**, **Saltin B**, **Holmberg HC.** Role of glycogen availability in sarcoplasmic reticulum Ca^{2+} kinetics in human skeletal muscle. *J Physiol* 589: 711–725, 2011. doi:10.1113/jphysiol.2010.195982.
10. **Nielsen J**, **Cheng AJ**, **Ørtenblad N**, **Westerblad H.** Subcellular distribution of glycogen and decreased tetanic Ca^{2+} in fatigued single intact mouse muscle fibres. *J Physiol* 592: 2003–2012, 2014. doi:10.1113/jphysiol.2014.271528.
11. **Nielsen J**, **Dubillot P**, **Stausholm MLH**, **Ørtenblad N.** Specific ATPases drive compartmentalized glycogen utilization in rat skeletal muscle. *J Gen Physiol* 154: e202113071, 2022. doi:10.1085/jgp.202113071.
12. **Coyle EF**, **Hagberg JM**, **Hurley BF**, **Martin WH**, **Ehsani AA**, **Holloszy JO.** Carbohydrate feeding during prolonged strenuous exercise can delay fatigue. *J Appl Physiol Respir Environ Exerc Physiol* 55: 230–235, 1983. doi:10.1152/jappl.1983.55.1.230.
13. **Dudley-Rode H**, **Zinn C**, **Plews DJ**, **Charoensap T**, **Maunder E.** Carbohydrate ingestion during prolonged exercise blunts the reduction in power output at the moderate-to-heavy intensity transition. *Eur J Appl Physiol* 125: 1349–1359, 2025. doi:10.1007/s00421-024-05687-w.
14. **Coyle EF**, **Coggan AR**, **Hemmert K**, **Lowe RC**, **Walters TJ.** Substrate usage during prolonged exercise following a preexercise meal. *J Appl Physiol (1985)* 59: 429–433, 1985. doi:10.1152/jappl.1985.59.2.429.
15. **Coggan AR**, **Coyle EF.** Reversal of fatigue during prolonged exercise by carbohydrate infusion or ingestion. *J Appl Physiol (1985)* 63: 2388–2395, 1987. doi:10.1152/jappl.1987.63.6.2388.
16. **Wallis GA**, **Rowlands DS**, **Shaw C**, **Jentjens RLPG**, **Jeukendrup AE.** Oxidation of combined ingestion of maltodextrins and fructose during exercise. *Med Sci Sports Exerc* 37: 426–432, 2005. doi:10.1249/01.MSS.0000155399.23358.82.
17. **Wallis GA**, **Dawson R**, **Achten J**, **Webber J**, **Jeukendrup AE.** Metabolic response to carbohydrate ingestion during exercise in males and females. *Am J Physiol Endocrinol Physiol* 290: E708–E715, 2006. doi:10.1152/ajpendo.00357.2005.
18. **Wallis GA**, **Yeo SE**, **Blannin AK**, **Jeukendrup AE.** Dose-response effects of ingested carbohydrate on exercise metabolism in women. *Med Sci Sports Exerc* 39: 131–138, 2007. doi:10.1249/01.mss.0000241645.28467.d3.
19. **Jentjens RLPG**, **Achten J**, **Jeukendrup AE.** High oxidation rates from combined carbohydrates ingested during exercise. *Med Sci Sports Exerc* 36: 1551–1558, 2004. doi:10.1249/01.MSS.0000139796.07843.1D.
20. **Jentjens RLPG**, **Venables MC**, **Jeukendrup AE.** Oxidation of exogenous glucose, sucrose, and maltose during prolonged cycling exercise. *J Appl Physiol (1985)* 96: 1285–1291, 2004. doi:10.1152/japplphysiol.01023.2003.
21. **Tsintzas O-K**, **Williams C**, **Boobis L**, **Greenhaff P.** Carbohydrate ingestion and single muscle fiber glycogen metabolism during prolonged running in men. *J Appl Physiol (1985)* 81: 801–809, 1996. doi:10.1152/jappl.1996.81.2.801.
22. **Yaspelkis BB 3rd**, **Patterson JG**, **Anderla PA**, **Ding Z**, **Ivy JL.** Carbohydrate supplementation spares muscle glycogen during variable-intensity exercise. *J Appl Physiol (1985)* 75: 1477–1485, 1993. doi:10.1152/jappl.1993.75.4.1477.
23. **Coyle EF**, **Coggan AR**, **Hemmert K**, **Ivy JL.** Muscle glycogen utilization during prolonged strenuous exercise when fed carbohydrate. *J Appl Physiol (1985)* 61: 165–172, 1986. doi:10.1152/jappl.1986.61.1.165.
24. **Arkinstall MJ**, **Bruce CR**, **Nikolopoulos V**, **Garnham AP**, **Hawley JA.** Effect of carbohydrate ingestion on metabolism during running and cycling. *J Appl Physiol (1985)* 91: 2125–2134, 2001. doi:10.1152/jappl.2001.91.5.2125.
25. **Flynn MG**, **Costill DL**, **Hawley JA**, **Fink WJ**, **Neufer PD**, **Fielding RA**, **Sleeper MD.** Influence of selected carbohydrate drinks on cycling performance and glycogen use. *Med Sci Sports Exerc* 19: 37–40, 1987.
26. **Foskett A**, **Williams C**, **Boobis L**, **Tsintzas K.** Carbohydrate availability and muscle energy metabolism during intermittent running. *Med Sci Sports Exerc* 40: 96–103, 2008. doi:10.1249/mss.0b013e3181586b2c.
27. **Vigh-Larsen JF**, **Ørtenblad N**, **Nielsen J**, **Emil Andersen OLE**, **Overgaard K**, **Mohr M.** The role of muscle glycogen content and localization in high-intensity exercise performance: a placebo-controlled trial. *Med Sci Sports Exerc* 54: 2073–2086, 2022. doi:10.1249/MSS.0000000000003002.
28. **McConell GK**, **Canny BJ**, **Daddo MC**, **Nance MJ**, **Snow RJ.** Effect of carbohydrate ingestion on glucose kinetics and muscle metabolism during intense endurance exercise. *J Appl Physiol (1985)* 89: 1690–1698, 2000. doi:10.1152/jappl.2000.89.5.1690.
29. **Tsintzas K**, **Williams C.** Human muscle glycogen metabolism during exercise. Effect of carbohydrate supplementation. *Sports Med* 25: 7–23, 1998. doi:10.2165/00007256-199825010-00002.
30. **Page MJ**, **McKenzie JE**, **Bossuyt PM**, **Boutron I**, **Hoffmann TC**, **Mulrow CD**, **Shamseer L**, **Tetzlaff JM**, **Akl EA**, **Brennan SE**, **Chou R**, **Glanville J**, **Grimshaw JM**, **Hróbjartsson A**, **Lalu MM**, **Li T**, **Loder EW**, **Mayo-Wilson E**, **McDonald S**, **McGuinness LA**, **Stewart LA**, **Thomas J**, **Tricco AC**, **Welch VA**, **Whiting P**, **Moher D.** The PRISMA

2020 statement: an updated guideline for reporting systematic reviews. *BMJ* 372: n71, 2021. doi:10.1136/bmj.n71.
31. **Price TB**, **Taylor R**, **Mason GF**, **Rothman DL**, **Shulman GI**, **Shulman RG.** Turnover of human muscle glycogen with low-intensity exercise. *Med Sci Sports Exerc* 26: 983–991, 1994.
32. **Kuipers H**, **Keizer HA**, **Brouns F**, **Saris WHM.** Carbohydrate feeding and glycogen synthesis during exercise in man. *Pflugers Arch* 410: 652–656, 1987. doi:10.1007/BF00581327.
33. **Barstow TJ**, **Cooper DM**, **Sobel EM**, **Landaw EM**, **Epstein S.** Influence of increased metabolic rate on [13C]bicarbonate washout kinetics. *Am J Physiol Regul Integr Comp Physiol* 259: R163–R171, 1990. doi:10.1152/ajpregu.1990.259.1.R163.
34. **Sterne JAC**, **Savović J**, **Page MJ**, **Elbers RG**, **Blencowe NS**, **Boutron I**, **Cates CJ**, **Cheng H-Y**, **Corbett MS**, **Eldridge SM**, **Emberson JR**, **Hernán MA**, **Hopewell S**, **Hróbjartsson A**, **Junqueira DR**, **Jüni P**, **Kirkham JJ**, **Lasserson T**, **Li T**, **McAleenan A**, **Reeves BC**, **Shepperd S**, **Shrier I**, **Stewart LA**, **Tilling K**, **White IR**, **Whiting PF**, **Higgins JPT.** RoB 2: a revised tool for assessing risk of bias in randomised trials. *BMJ* 366: l4898, 2019. doi:10.1136/bmj.l4898.
35. **Higgins JP**, **Thomas J**, **Chandler J**, **Cumpston M**, **Li T**, **Page MJ**, **Welch VA.** *Cochrane Handbook For Systematic Reviews of Interventions*. John Wiley & Sons, 2019.
36. **Areta JL**, **Hopkins WG.** Skeletal muscle glycogen content at rest and during endurance exercise in humans: a meta-analysis. *Sports Med* 48: 2091–2102, 2018. doi:10.1007/s40279-018-0941-1.
37. **Higgins JPT**, **Thompson SG**, **Deeks JJ**, **Altman DG.** Measuring inconsistency in meta-analyses. *BMJ* 327: 557–560, 2003. doi:10.1136/bmj.327.7414.557.
38. **Cohen J.** *Statistical Power for the Behavioral Sciences* (2nd ed.). Academic Press, 1988.
39. **Rodgers MA**, **Pustejovsky JE.** Evaluating meta-analytic methods to detect selective reporting in the presence of dependent effect sizes. *Psychol Methods* 26: 141–160, 2021. doi:10.1037/met0000300.
40. **Blomstrand E**, **Andersson S**, **Hassmén P**, **Ekblom B**, **Newsholme EA.** Effect of branched-chain amino acid and carbohydrate supplementation on the exercise-induced change in plasma and muscle concentration of amino acids in human subjects. *Acta Physiol Scand* 153: 87–96, 1995. doi:10.1111/j.1748-1716.1995.tb09839.x.
41. **Chryssanthopoulos C**, **Williams C**, **Nowitz A.** Influence of a carbohydrate-electrolyte solution ingested during running on muscle glycogen utilisation in fed humans. *Int J Sports Med* 23: 279–284, 2002. doi:10.1055/s-2002-29078.
42. **Clark IE**, **Vanhatalo A**, **Thompson C**, **Wylie LJ**, **Bailey SJ**, **Kirby BS**, **Wilkins BW**, **Jones AM.** Changes in the power-duration relationship following prolonged exercise: estimation using conventional and all-out protocols and relationship with muscle glycogen. *Am J Physiol Regul Integr Comp Physiol* 317: R59–R67, 2019. doi:10.1152/ajpregu.00031.2019.
43. **Cluberton LJ**, **Mcgee SL**, **Murphy RM**, **Hargreaves M.** Effect of carbohydrate ingestion on exercise-induced alterations in metabolic gene expression. *J Appl Physiol (1985)* 99: 1359–1363, 2005. doi:10.1152/japplphysiol.00197.2005.
44. **de Oliveira NG**, **de Oliveira LF**, **da Silva RP**, **Oliveira TN**, **Möller GB**, **Murasaki J**, **Ramires MA**, **de Almeida Azevedo R**, **Artioli GG**, **Roschel H**, **Gualano B**, **Saunders B.** Trehalose improved 20-min cycling time-trial performance after 100-min cycling in amateur cyclists. *Int J Sport Nutr Exerc Metab* 34: 199–206, 2024. doi:10.1123/ijsnem.2023-0241.
45. **Dumke CL**, **Slivka DR**, **Cuddy JS**, **Hailes WS**, **Ruby BC.** Skeletal muscle metabolic gene response to carbohydrate feeding during exercise in the heat. *J Int Soc Sports Nutr* 10: 40, 2013. doi:10.1186/1550-2783-10-40.
46. **Erickson MA**, **Schwarzkopf RJ**, **McKenzie RD.** Effects of caffeine, fructose, and glucose ingestion on muscle glycogen utilization during exercise. *Med Sci Sports Exerc* 19: 579–583, 1987.
47. **Fell JM**, **Hearris MA**, **Ellis DG**, **Moran JEP**, **Jevons EFP**, **Owens DJ**, **Strauss JA**, **Cocks M**, **Louis JB**, **Shepherd SO**, **Morton JP.** Carbohydrate improves exercise capacity but does not affect subcellular lipid droplet morphology, AMPK and p53 signalling in human skeletal muscle. *J Physiol* 599: 2823–2849, 2021 [Erratum in *J Physiol* 2025]. doi:10.1113/JP281127.
48. **Fielding RA**, **Costill DL**, **Fink WJ**, **King DS**, **Hargreaves M**, **Kovaleski JE.** Effect of carbohydrate feeding frequencies on muscle glycogen use during exercise. *Med Sci Sports Exerc* 17: 472–476, 1985. doi:10.1249/00005768-198508000-00012.
49. **Gonzalez JT**, **Fuchs CJ**, **Smith FE**, **Thelwall PE**, **Taylor R**, **Stevenson EJ**, **Trenell MI**, **Cermak NM**, **van Loon LJC.** Ingestion of glucose or sucrose prevents liver but not muscle glycogen depletion during prolonged endurance-type exercise in trained cyclists. *Am J Physiol Endocrinol Physiol* 309: E1032–E1039, 2015. doi:10.1152/ajpendo.00376.2015.
50. **Hargreaves M**, **Briggs CA.** Effect of carbohydrate ingestion on exercise metabolism. *J Appl Physiol (1985)* 65: 1553–1555, 1988. doi:10.1152/jappl.1988.65.4.1553.
51. **Hargreaves M**, **Costill DL**, **Coggan A**, **Fink WJ**, **Nishibata J.** Effect of carbohydrate feedings on muscle glycogen utilization and exercise performance. *Med Sci Sports Exerc* 16: 219–222, 1984.
52. **Lee-Young RS**, **Palmer MJ**, **Linden KC**, **LePlastrier K**, **Canny BJ**, **Hargreaves M**, **Wadley GD**, **Kemp BE**, **McConell GK.** Carbohydrate ingestion does not alter skeletal muscle AMPK signaling during exercise in humans. *Am J Physiol Endocrinol Physiol* 291: E566–E573, 2006. doi:10.1152/ajpendo.00023.2006.
53. **Menzies C**, **Wood M**, **Thomas J**, **Hengist A**, **Walhin JP**, **Jones R**, **Tsintzas K**, **Gonzalez JT**, **Betts JA.** Frequent carbohydrate ingestion reduces muscle glycogen depletion and postpones fatigue relative to a single bolus. *Int J Sport Nutr Exerc Metab* 30: 203–209, 2020. doi:10.1123/ijsnem.2019-0291.
54. **Mitchell JB**, **Costill DL**, **Houmard JA**, **Fink WJ**, **Pascoe DD**, **Pearson DR.** Influence of carbohydrate dosage on exercise performance and glycogen metabolism. *J Appl Physiol (1985)* 67: 1843–1849, 1989. doi:10.1152/jappl.1989.67.5.1843.
55. **Nicholas CW**, **Tsintzas K**, **Boobis L**, **Williams C.** Carbohydrate-electrolyte ingestion during intermittent high-intensity running. *Med Sci Sports Exerc* 31: 1280–1286, 1999. doi:10.1097/00005768-199909000-00008.
56. **Nieman DC**, **Davis JM**, **Henson DA**, **Gross SJ**, **Dumke CL**, **Utter AC**, **Vinci DM**, **Carson JA**, **Brown A**, **McAnulty SR**, **McAnulty LS**, **Triplett NT.** Muscle cytokine mRNA changes after 2.5 h of cycling: influence of carbohydrate. *Med Sci Sports Exerc* 37: 1283–1290, 2005. doi:10.1249/01.mss.0000175054.99588.b1.
57. **Slivka D**, **Hailes W**, **Cuddy J**, **Ruby B.** Caffeine and carbohydrate supplementation during exercise when in negative energy balance: effects on performance, metabolism, and salivary cortisol. *Appl Physiol Nutr Metab* 33: 1079–1085, 2008. doi:10.1139/H08-093.
58. **Tsintzas OK**, **Williams C**, **Boobis L**, **Greenhaff P.** Carbohydrate ingestion and glycogen utilization in different muscle fibre types in man. *J Physiol* 489: 243–250, 1995. doi:10.1113/jphysiol.1995.sp021046.
59. **Vigh-Larsen JF**, **Kruse DZ**, **Moseholt MB**, **Hansen LGB**, **Christensen AL**, **Bæk A**, **Andersen OE**, **Mohr M**, **Overgaard K.** No effects of carbohydrate ingestion on muscle metabolism or performance during short-duration high-intensity intermittent exercise. *Scandinavian Med Sci Sports* 34: e14731, 2024. doi:10.1111/sms.14731.
60. **Yan Z**, **Spencer MK**, **Katz A.** No effect of carbohydrate feeding on glycogen synthase in human muscle during exercise. *Clin Physiol* 13: 265–270, 1993. doi:10.1111/j.1475-097x.1993.tb00326.x.
61. **Yaspelkis BB 3rd**, **Ivy JL.** Effect of carbohydrate supplements and water con exercise metabolism in the heat. *J Appl Physiol (1985)* 71: 680–687, 1991. doi:10.1152/jappl.1991.71.2.680.
62. **Zachwieja JJ**, **Costill DL**, **Fink WJ.** Carbohydrate ingestion during exercise: effects on muscle glycogen resynthesis after exercise. *Int J Sport Nutr* 3: 418–430, 1993. doi:10.1123/ijsn.3.4.418.
63. **Clark IE**, **Vanhatalo A**, **Thompson C**, **Joseph C**, **Black MI**, **Blackwell JR**, **Wylie LJ**, **Tan R**, **Bailey SJ**, **Wilkins BW**, **Kirby BS**, **Jones AM.** Dynamics of the power-duration relationship during prolonged endurance exercise and influence of carbohydrate ingestion. *J Appl Physiol (1985)* 127: 726–736, 2019. doi:10.1152/japplphysiol.00207.2019.
64. **Coggan AR**, **Coyle EF.** Effect of carbohydrate feedings during high-intensity exercise. *J Appl Physiol (1985)* 65: 1703–1709, 1988. doi:10.1152/jappl.1988.65.4.1703.
65. **Goodyear LJ**, **Hirshman MF**, **Napoli R**, **Calles J**, **Markuns JF**, **Ljungqvist O**, **Horton ES.** Glucose ingestion causes GLUT4 translocation in human skeletal muscle. *Diabetes* 45: 1051–1056, 1996. doi:10.2337/diab.45.8.1051.
66. **Bosch AN**, **Dennis SC**, **Noakes TD.** Influence of carbohydrate ingestion on fuel substrate turnover and oxidation during prolonged exercise. *J Appl Physiol (1985)* 76: 2364–2372, 1994. doi:10.1152/jappl.1994.76.6.2364.

67. **Jentjens RLPG**, **Moseley L**, **Waring RH**, **Harding LK**, **Jeukendrup AE.** Oxidation of combined ingestion of glucose and fructose during exercise. *J Appl Physiol (1985)* 96: 1277–1284, 2004. doi:10.1152/japplphysiol.00974.2003.
68. **Spencer MK**, **Yan Z**, **Katz A.** Carbohydrate supplementation attenuates IMP accumulation in human muscle during prolonged exercise. *Am J Physiol Cell Physiol* 261: C71–C76, 1991. doi:10.1152/ajpcell.1991.261.1.C71.
69. **Houtvast DCJ**, **Betz MW**, **Van Hooren B**, **Vanbelle S**, **Verdijk LB**, **van Loon LJC**, **Trommelen J.** Underpowered studies in muscle metabolism research: determinants and considerations. *Clin Nutr ESPEN* 64: 334–343, 2024. doi:10.1016/j.clnesp.2024.10.152.
70. **Marchand I**, **Tarnopolsky MA**, **Adamo KB**, **Bourgeois JM**, **Chorneyko K**, **Graham TE.** Quantitative assessment of human muscle glycogen granules size and number in subcellular locations during recovery from prolonged exercise. *J Physiol* 580: 617–628, 2007. doi:10.1113/jphysiol.2006.122457.
71. **Nielsen J**, **Holmberg HC**, **Schrøder HD**, **Saltin B**, **Ørtenblad N.** Human skeletal muscle glycogen utilization in exhaustive exercise: role of subcellular localization and fibre type. *J Physiol* 589: 2871–2885, 2011. doi:10.1113/jphysiol.2010.204487.
72. **Vigh-Larsen JF**, **Ørtenblad N**, **Spriet LL**, **Overgaard K**, **Mohr M.** Muscle glycogen metabolism and high-intensity exercise performance: a narrative review. *Sports Med* 51: 1855–1874, 2021. doi:10.1007/s40279-021-01475-0.
73. **Podlogar T**, **Bokal Š**, **Cirnski S**, **Wallis GA.** Increased exogenous but unaltered endogenous carbohydrate oxidation with combined fructose-maltodextrin ingested at 120 g h−1 versus 90 g h−1 at different ratios. *Eur J Appl Physiol* 122: 2393–2401, 2022. doi:10.1007/s00421-022-05019-w.
74. **Hearris MA**, **Pugh JN**, **Langan-Evans C**, **Mann SJ**, **Burke L**, **Stellingwerff T**, **Gonzalez JT**, **Morton JP.** 13C-glucose-fructose labelling reveals comparable exogenous CHO oxidation during exercise when consuming 120 g/h in fluid, gel, jelly chew or co-ingestion. *J Appl Physiol (1985)* 132: 1394–1406, 2022. doi:10.1152/japplphysiol.00091.2022.
75. **Podlogar T**, **Cooper-Smith N**, **Gonzalez JT**, **Wallis GA.** Personalised carbohydrate feeding during exercise based on exogenous glucose oxidation: a proof-of-concept study. *Perform Nutr* 1: 2, 2025. doi:10.1186/s44410-025-00003-9.
76. **Palmer GS**, **Borghouts LB**, **Noakes TD**, **Hawley JA.** Metabolic and performance responses to constant-load vs. variable-intensity exercise in trained cyclists. *J Appl Physiol (1985)* 87: 1186–1196, 1999. doi:10.1152/jappl.1999.87.3.1186.
77. **Roepstorff C**, **Vistisen B**, **Donsmark M**, **Nielsen JN**, **Galbo H**, **Green KA**, **Hardie DG**, **Wojtaszewski JFP**, **Richter EA**, **Kiens B.** Regulation of hormone-sensitive lipase activity and Ser563 and Ser565 phosphorylation in human skeletal muscle during exercise. *J Physiol* 560: 551–562, 2004. doi:10.1113/jphysiol.2004.066480.
78. **Hearris MA**, **Hammond KM**, **Fell JM**, **Morton JP.** Regulation of muscle glycogen metabolism during exercise: implications for endurance performance and training adaptations. *Nutrients* 10: 298, 2018. doi:10.3390/nu10030298.
79. **Hargreaves M**, **McConell G**, **Proietto J.** Influence of muscle glycogen on glycogenolysis and glucose uptake during exercise in humans. *J Appl Physiol (1985)* 78: 288–292, 1995. doi:10.1152/jappl.1995.78.1.288.
80. **Elbourne DR**, **Altman DG**, **Higgins JP**, **Curtin F**, **Worthington HV**, **Vail A.** Meta-analyses involving cross-over trials: methodological issues. *Int J Epidemiol* 31: 140–149, 2002. doi:10.1093/ije/31.1.140.
81. **Horwarth O**, **Envall H**, **Röja J**, **Emanuelsson EB**, **Sanz G**, **Ekblom B**, **Apró W**, **Moberg M.** Variability in vastus lateralis fiber type distribution, fiber size, and myonuclear content along and between the legs. *J Appl Physiol (1985)* 131: 158–173, 2021. doi:10.1152/japplphysiol.00053.2021.
82. **Rothschild JA**, **Kilding AE**, **Stewart T**, **Plews DJ.** Factors influencing substrate oxidation during submaximal cycling: a modelling analysis. *Sports Med* 52: 2775–2795, 2022. doi:10.1007/s40279-022-01727-7.
83. **Nederveen JP**, **Ibrahim G**, **Fortino SA**, **Snijders T**, **Kumbhare D**, **Parise G.** Variability in skeletal muscle fibre characteristics during repeated muscle biopsy sampling in human vastus lateralis. *Appl Physiol Nutr Metab* 45: 368–375, 2020. doi:10.1139/apnm-2019-0263.
84. **Costill DL**, **Jansson E**, **Gollnick PD**, **Saltin B.** Glycogen utilization in leg muscles of men during level and uphill running. *Acta Physiol Scand* 91: 475–481, 1974. doi:10.1111/j.1748-1716.1974.tb05703.x.
85. **Tarnopolsky LJ**, **MacDougall JD**, **Atkinson SA**, **Tarnopolsky MA**, **Sutton JR.** Gender differences in substrate for endurance exercise. *J Appl Physiol (1985)* 68: 302–308, 1990. doi:10.1152/jappl.1990.68.1.302.
86. **Roepstorff C**, **Steffensen CH**, **Madsen M**, **Stallknecht B**, **Kanstrup I-L**, **Richter EA**, **Kiens B.** Gender differences in substrate utilization during submaximal exercise in endurance-trained subjects. *Am J Physiol Endocrinol Physiol* 282: E435–E447, 2002. doi:10.1152/ajpendo.00266.2001.
87. **Riddell MC**, **Partington SL**, **Stupka N**, **Armstrong D**, **Rennie C**, **Tarnopolsky MA.** Substrate utilization during exercise performed with and without glucose ingestion in female and male endurance trained athletes. *Int J Sport Nutr Exerc Physiol* 13: 407–421, 2003. doi:10.1123/ijsnem.13.4.407.