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Effects of Medium-Chain Triglyceride and Medium-Chain Fatty Acid Supplementation on Skeletal Muscle Morphology, Metabolism, and Function in Adult Humans and Animals: A Protocol for a Systematic Review and Meta-Analysis

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Abstract

Background. Medium-chain triglycerides (MCT) and medium-chain fatty acids (MCFA) have distinct metabolic properties and may influence skeletal muscle metabolism and function; however, evidence is fragmented and inconsistent.

Aim. The aim of this systematic review and meta-analysis is to evaluate the clinically relevant and mechanistic effects of MCFA/MCT supplementation on skeletal muscle morphology, metabolism, and function in adult humans and adult animal models.

Data Sources. Peer-reviewed studies will be identified through systematic searches of major electronic databases, and reference lists of included studies will be screened to identify additional relevant publications.

Participants and Interventions. Eligible studies will include randomised controlled trials conducted in adult human and adult animal models, comparing the effects of oral MCFA/MCT supplementation with placebo oils, usual diet, or calorie-matched controls.

Study Appraisal and Synthesis Methods. Risk of bias will be assessed using RoB 2 for human studies and the SYRCLE tool for animal studies. Where appropriate, random-effects meta-analyses will be conducted; otherwise, findings will be synthesised narratively. The certainty of evidence will be evaluated using the GRADE framework. Human and animal studies will be synthesised and analysed separately to distinguish clinically relevant outcomes from mechanistic evidence and to avoid inappropriate cross-species inference.

Conclusions. This protocol outlines a transparent and rigorous approach to synthesising current evidence on MCFA/MCT supplementation and skeletal muscle-related outcomes. The findings are expected to clarify existing evidence gaps and inform future research in nutrition and muscle health.

Keywords: Medium-chain fatty acids; skeletal muscle; muscle metabolism; muscle function; randomised controlled trials

1. INTRODUCTION

Medium-chain fatty acids (MCFA) and medium-chain triglycerides (MCT) exhibit distinct metabolic characteristics compared with long-chain fatty acids, including rapid intestinal absorption, preferential hepatic uptake, accelerated oxidation, and carnitine-independent mitochondrial transport (Mumme et al., 2015; Papamandjaris et al., 1998; Takeuchi et al., 2008). Because of these properties, MCFA/MCT supplementation has been associated with alterations in energy expenditure, β-oxidation, and ketone body availability – processes in which skeletal muscle plays a central regulatory role (Chapman-Lopez et al., 2022; Takada et al., 2022; Yakupova et al., 2022). These metabolic processes are associated with enhanced mitochondrial function, increased diet-induced thermogenesis, reduced adipose tissue deposition and improved insulin sensitivity (Bach et al., 1982; Nosaka et al., 2020; St-Onge et al., 2003; Watanabe et al., 2022), suggesting a potential role of MCFA/MCT in modulating substrate availability, functional outcomes, and metabolic regulation in skeletal muscle.

Human experimental studies suggest that MCFA intake may influence skeletal muscle-related outcomes through several of key pathways relevant to this review. Specifically, MCFA consumption has been shown to increase circulating active (acylated) ghrelin, potentially stimulating anabolic signalling via growth hormone and IGF-1 pathways (Nishi et al., 2005). In parallel, experimental evidence indicates that MCFA/MCT supplementation may induce mitochondrial adaptations in skeletal muscle, including enhanced mitochondrial biogenesis and fatty acid oxidation capacity, with chain length-specific effects observed for octanoic (C8:0) and decanoic (C10:0) acids (Abe et al., 2016; Charlot et al., 2022; Ishizawa et al., 2015). These adaptations are directly relevant to muscle oxidative metabolism and fatigue resistance. Recent human imaging evidence further supports these mechanisms, demonstrating that 3-month MCT supplementation reduces glucose uptake and increases muscle density in gait-related skeletal muscles, with changes inversely associated with circulating β-hydroxybutyrate levels (Mutoh et al., 2025). Consistent with these mechanisms, observations from athletic and free-living populations suggest that MCT supplementation may influence substrate utilisation during exercise and perceived fatigue, aligning with the functional outcomes assessed in this review (Kojima et al., 2023; Nosaka et al., 2018; Nosaka et al., 2020). Despite this mechanistic rationale, evidence linking MCFA/MCT supplementation to skeletal muscle-related outcomes remains limited and inconsistent.

Skeletal muscle health is a critical determinant of functional capacity, metabolic health, and quality of life, particularly in ageing populations and individuals undergoing rehabilitation. Conditions such as sarcopenia, frailty, and age-related declines in physical performance are characterised by reductions in muscle size and strength (Mastavičiūtė et al., 2021). Given the central role of skeletal muscle in energy metabolism and functional performance, nutritional interventions that influence substrate utilisation and mitochondrial function, such as MCFA/MCT supplementation, may have potential relevance for supporting muscle function in these populations. However, the clinical implications of these mechanistic effects remain unclear due to inconsistent findings across studies.

Variability in findings across populations and studies has been attributed to differences in intervention duration, background diet, study design, industry involvement, and the predominance of short-term trials in the existing literature. To date, no systematic review has comprehensively synthesised evidence from randomised controlled trials (RCTs) examining the effects of MCFA/MCT supplementation on skeletal muscle morphology, metabolism, and functional performance across adult populations; a structured synthesis of human and animal randomised studies is therefore warranted to clarify the consistency of observed effects, distinguish clinical outcomes from mechanistic evidence, and identify key sources of heterogeneity. Clarifying the relationship between mechanistic and clinically relevant

outcomes may improve interpretation of the potential role of MCFA/MCT supplementation in exercise rehabilitation, healthy ageing, and muscle function support.

Accordingly, this systematic review aims to evaluate the effects of MCFA/MCT supplementation on clinically relevant skeletal muscle outcomes and mechanistic muscle-related metabolic adaptations in adult humans and adult animal models. Specifically, this review will address the following research questions: 1) Whether MCFA/MCT supplementation influences skeletal muscle mass, structure, or fibre-related characteristics; 2) Whether MCFA/MCT supplementation affects muscle-related metabolic outcomes, including fat oxidation and insulin sensitivity; 3) Whether MCFA/MCT supplementation improves muscle strength, physical performance, or fatigue resistance; 4) How intervention characteristics and methodological factors contribute to heterogeneity in the observed effects. Human evidence will primarily inform clinically relevant implications for skeletal muscle health and functional performance, whereas animal evidence will be interpreted as mechanistic support to contextualise potential biological pathways and sources of heterogeneity.

2. METHODS

2.1. Type of review. This protocol was developed in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses for Protocols (PRISMA-P) 2015 statement and its accompanying explanation and elaboration documents (Moher et al., 2015; Shamseer et al., 2015). The conduct and reporting of the completed systematic review will follow the PRISMA 2020 statement (Page et al., 2021). This systematic review protocol was prospectively registered in the International Prospective Register of Systematic Reviews (PROSPERO, registration number CRD420251236337) to enhance transparency and minimise the risk of selective reporting. The registration details the review rationale, research questions, and predefined objectives, as well as the eligibility criteria, search strategy, study selection process, data extraction procedures, and planned methods for risk-of-bias assessment and data synthesis.

2.2. Search strategy. Only peer-reviewed studies will be considered eligible for inclusion. Electronic searches will be conducted in major bibliographic databases, including PubMed, Embase, the Cochrane Central Register of Controlled Trials (CENTRAL), Web of Science, and Scopus. Supplementary searches will be performed using additional platforms (e.g. EBSCOhost, ScienceDirect, SpringerLink, Sage Journals, and Taylor & Francis Online) to identify potentially relevant records not captured by primary database searches. No restrictions on region or publication date will be applied. Studies published in English, Lithuanian, or Chinese will be considered eligible based on the language proficiency of the review team, which enables accurate screening, extraction, and interpretation of study findings without external translation resources. Where potentially relevant studies are identified in other languages, English abstracts and, where feasible, automated translation tools will be used during preliminary screening to assess eligibility. The potential for language bias associated with these restrictions will be acknowledged as a limitation of the review. In addition to database searches, reference lists of all included studies and relevant reviews will be manually screened to identify additional eligible publications through backward and forward citation tracking. Where necessary, corresponding authors may be contacted to clarify study details or outcome reporting.

Search strategies were developed using a combination of controlled vocabulary terms and free-text keywords to capture the target intervention, population, and outcomes. Boolean operators were used to structure and refine the searches, with synonymous terms and spelling variations combined using "OR" and key concepts combined using "AND". Key concepts related to MCT and MCFA supplementation, skeletal muscle morphology, metabolism and function, and randomised intervention study designs

were incorporated into the search strategy. To improve search precision while maintaining sensitivity, a limited number of exclusion terms ("NOT") were applied cautiously during pilot testing to remove clearly irrelevant records (e.g. engineering, microbiological, or non-interventional publications). Exclusion filters were intentionally restricted to avoid inadvertent removal of potentially eligible studies. The final search strategy was validated against known relevant publications to ensure appropriate sensitivity and reproducibility. Search strategies will prioritise sensitivity over specificity during initial retrieval.

Medical Subject Headings (MeSH) and equivalent controlled vocabulary terms were identified through a two-stage process. First, indexing terms assigned to relevant records retrieved from PubMed were examined. Second, the MeSH database was searched directly to identify additional related terms and hierarchical mappings. Controlled vocabulary terms were combined with free-text keywords to maximise search sensitivity and ensure consistency across databases, with strategies adapted to the syntax and indexing of each database. The strategy was developed through pilot testing and validation against known eligible studies to ensure an appropriate balance between sensitivity and specificity. To ensure comprehensiveness of the review, an updated literature search will be conducted prior to final data synthesis and manuscript submission. Any newly identified records will undergo the same predefined screening, eligibility assessment, and data extraction procedures as studies identified in the original search.

The full electronic search strategies for all databases are provided in the Supplementary Table 1 to enhance transparency and reproducibility.

2.3. Inclusion and exclusion criteria

1) Study designs. We will include RCTs, including both parallel-group and crossover designs, conducted in adult human participants and, for animal studies, randomised or controlled intervention studies will be included. Observational studies, including cohort, case-control, and cross-sectional studies, as well as uncontrolled pre–post studies, case series, case reports, narrative reviews, systematic reviews, meta-analyses, conference abstracts without full data, and other non-interventional publications will be excluded. Human and animal studies will be treated as two distinct evidence streams throughout eligibility assessment, synthesis, and certainty grading, and will not be pooled.

2) Participants. We will include studies conducted in adult populations. For human studies, eligible participants will be adults aged 18 years or older, including healthy individuals without clinically diagnosed diseases (e.g. cancer). For animal studies, only adult animal models that have reached species-specific physiological maturity will be included, while studies involving immature, juvenile, or actively growing animals will be excluded. Definitions of adulthood will be determined according to commonly accepted developmental stages and age ranges for each species, based on study reporting and relevant laboratory animal standards where appropriate.

3) Intervention. Eligible interventions include supplementation with caproic (C6:0), caprylic (C8:0), capric (C10:0), and lauric (C12:0) fatty acids; MCT; or medium- and long-chain triglyceride blends (MLCTs), administered orally in any form. Interventions will encompass purified MCT or MCFA preparations as well as dietary replacement strategies, enriched oils, or food-based vehicles, provided that the MCFA/MCT component is clearly defined and quantifiable. Studies combining MCFA/MCT supplementation with co-interventions, such as exercise training or additional dietary modifications, will be included only when these co-interventions are applied identically across intervention and comparator groups.

4) Comparator. Eligible comparators will include placebo oils (e.g. long-chain triglycerides or fatty acids), usual diet, no-supplement control conditions, or other calorie-matched control interventions. Studies lacking an appropriate control group will be excluded.

5) Outcomes. Primary outcomes will be categorised into: 1) clinically relevant skeletal muscle outcomes, including muscle mass or lean body mass, muscle strength (maximal or dynamic), physical performance (e.g. endurance), fatigue resistance, and insulin sensitivity; and 2) mechanistic or metabolic outcomes, including muscle structure (e.g. fibre size, cross-sectional area), metabolic function (e.g. substrate utilisation, oxidative metabolism, mitochondrial biogenesis, and related metabolic markers).

Outcomes will be assessed at post-intervention time points using validated imaging, biochemical, physiological, or performance-based methods, as reported in the included studies. Secondary outcomes will include adverse events and tolerability related to MCFA/MCT supplementation, such as gastrointestinal symptoms or withdrawal due to side effects.

6) Intervention duration and timing. Eligibility thresholds for intervention duration were selected based on the expected temporal characteristics of skeletal muscle adaptations. Muscle morphology and muscle mass outcomes generally require longer intervention periods to induce measurable structural adaptations, such as changes in lean mass, fibre characteristics, or muscle cross-sectional area; therefore, a minimum duration of four weeks was required for these outcomes. In contrast, metabolic and functional responses, including substrate utilisation, mitochondrial adaptations, exercise metabolism, fatigue resistance, and related performance outcomes, may occur over shorter timeframes and were therefore eligible following interventions of at least two weeks. As lifespan differs in animal studies, suitable intervention durations will be identified on a species-by-species basis to closely reflect the chosen durations for human studies. Adverse events will be collected irrespective of intervention duration.

All records retrieved from the literature searches will be imported into Rayyan (Qatar Computing Research Institute). Screening questions and eligibility criteria for title/abstract screening (level 1) and full-text screening (level 2) will be developed a priori based on the predefined inclusion and exclusion criteria.

Prior to formal screening, a calibration exercise will be conducted to pilot and refine the screening questions and to ensure consistency between reviewers. Titles and abstracts, followed by full-text articles, will be independently screened by two reviewers (N.X. and M.S.) using Rayyan. Any disagreements will be resolved through discussion, with involvement of a third reviewer (S.R.G.) as needed.

Where necessary, corresponding authors will be contacted to obtain additional information to clarify study eligibility. Reasons for exclusion at the full-text screening stage will be documented. Reviewers will not be blinded to journal titles, study authors, or institutional affiliations.

2.4. Data extraction. Data extraction will be performed independently and in duplicate by two reviewers (N.X. and A.F.) using standardised data extraction forms developed a priori. Prior to formal data extraction, calibration exercises will be conducted to pilot the extraction forms and ensure consistency between reviewers. Disagreements between reviewers will be resolved by discussion, with unresolved conflicts adjudicated by a third reviewer, consistent with the screening process. For all included studies, extracted information will comprise author and year of publication, country of study, study design, comparator conditions, outcome measures and assessment tools, results for all primary and secondary outcomes, and information relevant to study quality and risk of bias. For all studies, intervention characteristics will be extracted, including the type of MCT/MCFA, fatty acid composition, dose, duration, and any co-interventions applied. Where available, data on adherence, adverse events, dropout rates, and reasons for withdrawal will also be extracted.

For human studies, additional extracted data will include participant characteristics such as age, sex, baseline health status, body composition, and physical activity or training status, as well as formulation-specific aspects of supplementation relevant to human administration.

For animal studies, additional extracted data will include species, strain, sex, age or developmental stage, baseline and post-intervention body weight, housing and experimental conditions, background diet, and route of administration, e.g. oral gavage, ad libitum, etc.

For studies with multiple intervention arms, relevant groups will be combined where appropriate to prevent double counting of comparator groups. Where required data are missing or unclear, corresponding authors will be contacted, and no post hoc data assumptions will be made.

When multiple outcome measures or assessment tools are reported for the same outcome domain within a study, validated and commonly used measures will be prioritised. Where outcomes are reported as composite measures, both composite and individual components will be extracted. Outcomes will be collected in all reported data forms (e.g. continuous or dichotomous). Due to potential variation in outcome definitions across studies, definitions used by individual studies will be extracted and documented.

For analytical purposes, outcomes will be categorised according to intervention duration. In human studies, interventions lasting 2–4 weeks will be classified as short-term, those lasting >4 to <12 weeks as mid-term, and those lasting ≥12 weeks as long-term interventions. Similar timeframes will be developed for animal studies on a species-by-species basis, where appropriate. Outcomes reported at multiple post-intervention time points will be extracted rather than selecting a single time point a priori and assigned to the corresponding duration category based on the timing of outcome assessment. This duration-based categorisation is prespecified and will be used to explore time-dependent effects of MCFA/MCT supplementation.

For continuous outcomes, change-from-baseline data will be preferred over endpoint values where available, as they partially account for baseline imbalances; however, change and endpoint data will not be pooled together and will be analysed separately when necessary. Dichotomous outcomes will be analysed as reported. No post hoc outcome redefinition or data-driven time point selection will be undertaken.

For crossover trials, data from the first treatment period will be extracted, where available, to avoid potential carry-over effects. If first-period data are unavailable, appropriately adjusted paired analyses will be used where reported; otherwise, the study will be included in narrative synthesis only. As only individually randomised trials will be included, no unit-of-analysis adjustments for cluster designs will be required.

2.5. Data synthesis and analysis. Human and animal studies will be analysed and synthesised separately throughout all stages of the review. Quantitative meta-analyses will be conducted independently for human trials and for animal studies when at least two studies within the same evidence category report sufficiently comparable outcomes. Where quantitative synthesis is not feasible due to limited study numbers, methodological heterogeneity, or incompatible outcome measures, findings will be summarised using structured narrative synthesis within the respective evidence category. Evidence derived from adult animal models will be interpreted as mechanistic support and will not be used to infer direct clinical effects in humans. Clinical and mechanistic outcomes will be synthesised and interpreted separately where appropriate to improve conceptual clarity and avoid overinterpretation of mechanistic findings.

Where appropriate, quantitative synthesis will be performed using random-effects meta-analysis, given the anticipated clinical and methodological heterogeneity across studies. Continuous outcomes will be pooled using mean differences (MD) when outcomes are measured on the same scale, or standardised mean differences (SMD) when different measurement scales are used. Dichotomous outcomes will be collected throughout the intervention period and synthesised using risk ratios (RR) or risk differences (RD), where applicable. Skewed data and outcomes unsuitable for quantitative synthesis will be summarised descriptively. Meta-analyses will be conducted using R (RStudio) and RevMan software. Effect sizes from human and animal studies will not be pooled. Statistical heterogeneity will be assessed

using the I^2 statistic, with values of <40% indicating low heterogeneity, 40–75% moderate heterogeneity, and >75% substantial heterogeneity. Substantial heterogeneity will prompt cautious interpretation and, where appropriate, subgroup or sensitivity analyses.

Pre-specified subgroup analyses will be considered exploratory and hypothesis-generating. It will only be conducted when enough studies (>2) with adequate methodological comparability are available. Planned subgroup analyses include intervention characteristics (e.g. MCFA/MCT type, dosage, and intervention duration) and population characteristics (e.g. sex and age). Depending on the volume and quality of available evidence, subgroup analyses may be prioritised to minimise overinterpretation of sparse or highly heterogeneous data. Sensitivity analyses will be conducted where appropriate, including exclusion of studies judged to be at high risk of bias or with substantial missing data, and leave-one-out analyses when feasible.

2.6. Quality assessment. Risk of bias will be independently assessed by two reviewers. Randomised controlled trials will be evaluated using the Cochrane Risk of Bias 2 (RoB 2) tool, while animal studies will be assessed using the SYRCLE risk-of-bias tool. Judgements will be made independently for each domain in accordance with the guidance of the respective tools and rated as low, some concerns, or high risk of bias. Where insufficient information is reported, study authors will be contacted for clarification. No overall numerical risk-of-bias score will be calculated.

Meta-bias will be assessed at the outcome level. Publication bias and small-study effects will be evaluated when at least ten studies are available using visual inspection of funnel plots and Egger's Regression Test. Evidence of asymmetry will be interpreted cautiously, considering between-study heterogeneity and study size. Potential selective outcome reporting will be considered in conjunction with risk-of-bias assessments at the study level.

The certainty of evidence for each outcome will be evaluated using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach for outcomes derived from human randomised controlled trials only, considering risk of bias, inconsistency, indirectness, imprecision, and publication bias. Evidence from animal studies will not be graded using GRADE and will be considered separately as mechanistic or supportive evidence rather than indicators of clinical certainty. Overall certainty will be rated as high, moderate, low, or very low.

Risk-of-bias assessments and certainty-of-evidence evaluations will inform interpretation of the review findings and strength of conclusions. Overall GRADE ratings for key human outcomes will be presented in the final review and incorporated into the discussion of clinical relevance, consistency, and confidence in the available evidence. Findings supported primarily by studies at high risk of bias or by low-certainty evidence will be interpreted cautiously.

3. DISCUSSION

Before initiating the systematic review, it is important to consider the key strengths of the planned methodology as well as the potential limitations that may arise during the review process.

3.1. Strength of the systematic review. A primary strength of this review is its focused examination of the effects of MCT/MCFA supplementation on skeletal muscle-related outcomes. Although MCFA/MCT have been widely investigated in relation to metabolic health and body composition, evidence specifically addressing skeletal muscle morphology, metabolism, and functional performance remains fragmented. By targeting muscle-specific endpoints, this review addresses a clearly defined and underexplored evidence gap.

A further methodological strength is the inclusion of randomised/controlled studies conducted in adult human participants and adult animal models, with human and animal evidence treated as distinct

but complementary streams. This parallel evidence framework may strengthen translational interpretation by enabling comparison between clinically relevant outcomes observed in humans and mechanistic adaptations identified in adult animal models, while maintaining appropriate separation between biological and clinical inference.

The protocol was prospectively registered and developed in accordance with PRISMA-P guidelines, enhancing transparency and reducing the risk of selective reporting. Use of established risk-of-bias tools (RoB 2 for human trials and SYRCLE for animal studies), together with outcome-level GRADE assessment for human evidence, further strengthens the methodological rigor and interpretability of the planned review.

3.2. Limitation of the systematic review. Firstly, restriction to studies published in languages accessible to the review team may introduce language bias and potentially limit identification of relevant evidence published in other languages.

Secondly, substantial clinical and methodological heterogeneity across studies is expected, arising from variation in MCFA/MCT composition, dosage, intervention duration, outcome assessment methods, and participant characteristics. Although subgroup and exploratory analyses are prespecified, the number of eligible studies may be insufficient to fully explain these sources of heterogeneity.

The certainty of evidence may also be constrained by limitations within individual studies, including small sample sizes, short intervention durations, incomplete reporting of adherence, and limited transparency in randomisation or allocation procedures. These factors may increase risk of bias and limit the strength of causal inference despite rigorous methodological assessment. An additional consideration is the potential influence of commercial bias within the MCFA/MCT literature (Mumme & Stonehouse, 2015). While industry funding does not invalidate study findings, it may increase the likelihood of selective reporting or overestimation of effects.

Furthermore, although inclusion of animal studies provides valuable mechanistic insight, differences in experimental conditions and outcome measures limit direct translational inference, and animal findings should therefore be interpreted as supportive rather than confirmatory for human skeletal muscle outcomes.

4. CONCLUSIONS AND PERSPECTIVES

In conclusion, this protocol describes a systematic review and meta-analysis designed to evaluate the effects of MCT/MCFA supplementation on skeletal muscle morphology, metabolism, and function. The review will apply predefined eligibility criteria and a comprehensive, reproducible search strategy to identify relevant randomised studies.

Data extraction and synthesis will be conducted using structured and transparent methods, with quantitative meta-analysis performed where appropriate and narrative synthesis applied when statistical pooling is not feasible. Risk of bias will be assessed using established tools, and the certainty of evidence will be evaluated using the GRADE framework for human studies.

Through this approach, the planned review aims to provide a rigorous synthesis of existing evidence and to identify key gaps to inform future research on MCFA/MCT supplementation and skeletal muscle health.

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Supplementary Table 1. **Full electronic search strategies for all databases**

Bibliographic Database	**Search Terms**
PubMed	#1 (“Fatty Acids, Medium-Chain”[Mesh] OR “medium-chain fatty acid”[tw] OR MCFA[tw] OR MCT[tw] OR “MCT oil”[tw] OR “medium chain triglyceride*”[tw] OR “medium-chain triglycerides”[tw] OR “medium-chain saturated fatty acids”[tw] OR “medium-chain SFA”[tw] OR “medium-chain diacylglycerol”[tw] OR “medium- and long-chain triglycerides”[tw] OR MLCT[tw] OR “caproic acid”[tw] OR “hexanoic acid”[tw] OR “C6”[tw] OR “C6:0”[tw] OR “caprylic acid”[tw] OR “octanoic acid”[tw] OR “C8”[tw] OR “C8:0”[tw] OR “capric acid”[tw] OR “decanoic acid”[tw] OR “C10”[tw] OR “C10:0”[tw] OR “lauric acid”[tw] OR “dodecanoic acid”[tw] OR “C12”[tw] OR “C12:0”[tw]) NOT (“Spinal Nerves”[Mesh] OR “Cervical Vertebrae”[Mesh] OR “Cervical Plexus”[Mesh] OR “C6 nerve”[tw] OR “C7 nerve”[tw] OR “C8 nerve”[tw] OR “cervical nerve”[tw] OR “cervical nerves”[tw] OR radiculopathy[tw] OR neuropathy[tw] OR “cervical radiculopathy”[tw] OR “brachial plexus”[tw]) NOT (“moderate continuous training”[tw] OR “moderate-intensity continuous training”[tw]) NOT (“metronomic chemotherapy”[tw] OR “metronomic chemotherap*”[tw] OR “MCT regimen”[tw] OR “MCT protocol”[tw] OR “metronomic treatment”[tw]) NOT (“multicomponent training”[tw] OR “multi-component training”[tw] OR “multicomponent exercise”[tw] OR “multicomponent exercise training”[tw] OR “metacognitive training”[tw]) #2 (“Muscle, Skeletal”[Mesh] OR “Muscle Strength”[Mesh] OR “Muscle Fatigue”[Mesh] OR “Physical Endurance”[Mesh] OR “Exercise Test”[Mesh] OR “Physical Fitness”[Mesh] OR “Quality of Life”[Mesh] OR muscle mass[tw] OR lean mass[tw] OR lean body mass[tw] OR fat free mass[tw] OR appendicular lean mass[tw] OR appendicular muscle mass[tw] OR “cross-sectional area”[tw] OR muscle fibre*[tw] OR muscle fiber*[tw] OR “muscle morphology”[tw] OR “muscle structure”[tw] OR biopsy[tw] OR muscle strength[tw] OR muscular strength[tw] OR “maximal voluntary contraction”[tw] OR MVC[tw] OR dynamometry[tw] OR grip strength[tw] OR “knee extension strength”[tw] OR “one repetition maximum”[tw] OR 1RM[tw] OR muscle endurance[tw] OR fatigability[tw] OR “fatigue resistance”[tw] OR muscle fatigue[tw] OR physical performance[tw] OR functional performance[tw] OR functional capacity[tw] OR “walking speed”[tw] OR gait speed[tw] OR TUG[tw] OR “time to exhaustion”[tw] OR endurance performance[tw] OR aerobic performance[tw] OR “VO2peak”[tw] OR VO2max[tw] OR “oxygen consumption”[tw] OR metabolism[tw] OR metabolic[tw] OR mitochondrial[tw] OR oxidative[tw] OR “fat oxidation”[tw] OR “substrate utilization”[tw] OR “energy expenditure”[tw] OR “insulin resistance”[tw] OR HOMA-IR[tw] OR OGTT[tw] OR insulin[tw] OR glucose[tw] OR adverse events[tw] OR side effects[tw] OR tolerability[tw]) #3 (“Randomized Controlled Trial”[Publication Type] OR “Controlled Clinical Trial”[Publication Type] OR randomized[tiab] OR randomised[tiab] OR randomly[tiab] OR “random allocation”[tw] OR “randomly assigned”[tw] OR placebo[tw] OR “double blind”[tw] OR “single blind”[tw] OR “clinical trial”[pt]) #4 humans[mh] OR animals[mh] #1 and #2 and #3 and #4

Bibliographic Database	Search Terms
Embase	Title: (‘medium chain fatty acid’ OR mcfa OR mct OR ‘mct oil’ OR ‘medium chain triglyceride*’ OR ‘medium chain triglycerides’ OR ‘medium chain saturated fatty acid*’ OR ‘medium chain sfa’ OR ‘medium chain diacylglycerol’ OR ‘medium and long chain triglyceride*’ OR mlct OR ‘caproic acid’ OR ‘hexanoic acid’ OR c6 OR ‘c6:0’ OR ‘caprylic acid’ OR ‘octanoic acid’ OR c8 OR ‘c8:0’ OR ‘capric acid’ OR ‘decanoic acid’ OR c10 OR ‘c10:0’ OR ‘lauric acid’ OR ‘dodecanoic acid’ OR c12 OR ‘c12:0’) NOT (‘spinal nerve’ OR ‘cervical vertebra’ OR ‘cervical plexus’ OR ‘c6 nerve’ OR ‘c7 nerve’ OR ‘c8 nerve’ OR ‘cervical nerve’ OR ‘cervical nerves’ OR radiculopathy OR neuropathy OR ‘cervical radiculopathy’ OR ‘brachial plexus’) NOT (‘moderate continuous training’ OR ‘moderate intensity continuous training’) NOT (‘metronomic chemotherapy’ OR ‘metronomic chemotherap*’ OR ‘mct regimen’ OR ‘mct protocol’ OR ‘metronomic treatment’) NOT (‘multicomponent training’ OR ‘multi component training’ OR ‘multicomponent exercise’ OR ‘multicomponent exercise training’ OR ‘metacognitive training’) Abstract: (muscle OR skeletal muscle OR muscle strength OR muscle fatigue OR physical endurance OR exercise test OR physical fitness OR quality of life OR muscle mass OR lean mass OR lean body mass OR fat free mass OR appendicular lean mass OR appendicular muscle mass OR cross sectional area OR muscle fibre* OR muscle fiber* OR muscle morphology OR muscle structure OR biopsy OR muscular strength OR maximal voluntary contraction OR MVC OR dynamometry OR grip strength OR knee extension strength OR one repetition maximum OR 1RM OR muscle endurance OR fatigability OR fatigue resistance OR physical performance OR functional performance OR functional capacity OR walking speed OR gait speed OR TUG OR time to exhaustion OR endurance performance OR aerobic performance OR VO2peak OR VO2max OR oxygen consumption OR metabolism OR metabolic OR mitochondrial OR oxidative OR fat oxidation OR substrate utilization OR energy expenditure OR insulin resistance OR HOMA-IR OR OGTT OR insulin OR glucose OR adverse events OR side effects OR tolerability) AND (muscle OR skeletal muscle OR physiology OR biological OR “in vivo” OR exercise OR training OR physical activity OR rehabilitation OR metabolism OR metabolic)
Cochrane Library	Title: ((medium NEXT chain NEXT fatty NEXT acid*) OR MCFA OR MCT OR (MCT NEXT oil) OR (medium NEXT chain NEXT triglyceride*) OR (medium NEXT chain NEXT saturated NEXT fatty NEXT acid*) OR (medium NEXT chain NEXT SFA) OR (medium NEXT chain NEXT diacylglycerol) OR MLCT OR (medium NEXT long NEXT chain NEXT triglyceride*) OR (caproic NEXT acid) OR (hexanoic NEXT acid) OR C6 OR (caprylic NEXT acid) OR (octanoic NEXT acid) OR C8 OR (capric NEXT acid) OR (decanoic NEXT acid) OR C10 OR (lauric NEXT acid) OR (dodecanoic NEXT acid) OR C12) NOT (juvenile OR “young rat” OR weanling OR postnatal OR infant OR infants) Full text: ((muscle NEXT mass) OR (lean NEXT mass) OR (lean NEXT body NEXT mass) OR (fat NEXT free NEXT mass) OR (appendicular NEXT lean NEXT mass) OR (appendicular NEXT muscle NEXT mass) OR (cross NEXT sectional NEXT area) OR muscle fibre* OR muscle fiber* OR (muscle NEXT morphology) OR (muscle NEXT structure) OR biopsy OR (muscle NEXT strength) OR (maximal NEXT voluntary NEXT contraction) OR MVC OR dynamometry OR (grip NEXT strength) OR (knee NEXT extension NEXT strength) OR 1RM OR (muscle NEXT endurance) OR fatigability OR (fatigue NEXT resistance) OR (physical NEXT performance) OR (functional NEXT performance) OR (walking NEXT speed) OR (gait NEXT speed) OR TUG OR (time NEXT to NEXT exhaustion) OR (endurance NEXT performance) OR (aerobic NEXT performance) OR VO2peak OR VO2max OR (oxygen NEXT consumption) OR (fat NEXT oxidation) OR (substrate NEXT utilization) OR (energy NEXT expenditure) OR (insulin NEXT resistance) OR HOMA-IR OR OGTT OR glucose OR (adverse NEXT events) OR (side NEXT effects) OR tolerability)

Bibliographic Database	Search Terms
EBSCOhost	#1 Title: (“medium-chain fatty acid” OR MCFA OR MCT OR “MCT oil” OR “medium chain triglyceride*” OR “medium-chain triglyceride*” OR “medium-chain saturated fatty acid*” OR “medium-chain SFA” OR “medium-chain diacylglycerol” OR MLCT OR “medium and long chain triglyceride*” OR “caproic acid” OR “hexanoic acid” OR “C6” OR “C6:0” OR “caprylic acid” OR “octanoic acid” OR “C8” OR “C8:0” OR “capric acid” OR “decanoic acid” OR “C10” OR “C10:0” OR “lauric acid” OR “dodecanoic acid” OR “C12” OR “C12:0”) #2 (TX “muscle mass” OR TX “lean mass” OR TX “lean body mass” OR TX “fat free mass” OR TX “appendicular lean mass” OR TX “appendicular muscle mass” OR TX “cross-sectional area” OR TX muscle fibre* OR TX muscle fiber* OR TX “muscle morphology” OR TX “muscle structure” OR TX biopsy OR TX “muscle strength” OR TX “muscular strength” OR TX “maximal voluntary contraction” OR TX MVC OR TX dynamometry OR TX “grip strength” OR TX “knee extension strength” OR TX “one repetition maximum” OR TX 1RM OR TX “muscle endurance” OR TX fatigability OR TX “fatigue resistance” OR TX “muscle fatigue” OR TX “physical performance” OR TX “functional performance” OR TX “functional capacity” OR TX “walking speed” OR TX gait speed OR TX TUG OR TX “time to exhaustion” OR TX “endurance performance” OR TX “aerobic performance” OR TX VO2peak OR TX VO2max OR TX “oxygen consumption” OR TX metabolism OR TX metabolic OR TX mitochondrial OR TX oxidative OR TX “fat oxidation” OR TX “substrate utilization” OR TX “energy expenditure” OR TX “insulin resistance” OR TX HOMA-IR OR TX OGTT OR TX insulin OR TX glucose OR TX “adverse events” OR TX “side effects” OR TX tolerability) #3 (TX randomized OR TX randomised OR TX randomly OR TX “random allocation” OR TX “randomly assigned” OR TX placebo OR TX “double blind” OR TX “single blind” OR TX “clinical trial”) #1 and #2 and #3
Scopus	(TITLE-ABS-KEY(“medium-chain fatty acid” OR MCFA OR MCT OR “MCT oil” OR “medium chain triglyceride*” OR “medium-chain triglyceride*” OR “medium-chain saturated fatty acid*” OR “medium-chain SFA” OR “medium-chain diacylglycerol” OR MLCT OR “medium and long chain triglyceride*” OR “caproic acid” OR “hexanoic acid” OR “C6” OR “C6:0” OR “caprylic acid” OR “octanoic acid” OR “C8” OR “C8:0” OR “capric acid” OR “decanoic acid” OR “C10” OR “C10:0” OR “lauric acid” OR “dodecanoic acid” OR “C12” OR “C12:0”)) AND TITLE-ABS-KEY(“muscle mass” OR “lean mass” OR “lean body mass” OR “fat free mass” OR “appendicular lean mass” OR “appendicular muscle mass” OR “cross-sectional area” OR muscle fibre* OR muscle fiber* OR “muscle morphology” OR “muscle structure” OR biopsy OR “muscle strength” OR “muscular strength” OR “maximal voluntary contraction” OR MVC OR dynamometry OR “grip strength” OR “knee extension strength” OR “one repetition maximum” OR “1RM” OR “muscle endurance” OR fatigability OR “fatigue resistance” OR “muscle fatigue” OR “physical performance” OR “functional performance” OR “functional capacity” OR “walking speed” OR gait speed OR TUG OR “time to exhaustion” OR “endurance performance” OR “aerobic performance” OR VO2peak OR VO2max OR “oxygen consumption” OR metabolism OR metabolic OR mitochondrial OR oxidative OR “fat oxidation” OR “substrate utilization” OR “energy expenditure” OR “insulin resistance” OR HOMA-IR OR OGTT OR insulin OR glucose OR “adverse events” OR “side effects” OR tolerability) AND TITLE-ABS-KEY(randomized OR randomised OR randomly OR “random allocation” OR “randomly assigned” OR placebo OR “double blind” OR “single blind” OR “clinical trial”) AND (TITLE-ABS-KEY(human OR humans OR animal OR animals) AND NOT TITLE-ABS-KEY(juvenile OR “young rat” OR weanling OR postnatal OR infant))

Bibliographic Database	Search Terms
Web of Science	#1 TS=("medium-chain fatty acid" OR MCFA OR MCT OR "MCT oil" OR "medium chain triglyceride*" OR "medium-chain triglyceride*" OR "medium-chain saturated fatty acid*" OR "medium-chain SFA" OR "medium-chain diacylglycerol" OR MLCT OR "medium and long chain triglyceride*" OR "caproic acid" OR "hexanoic acid" OR C6 OR "C6:0" OR "caprylic acid" OR "octanoic acid" OR C8 OR "C8:0" OR "capric acid" OR "decanoic acid" OR C10 OR "C10:0" OR "lauric acid" OR "dodecanoic acid" OR C12 OR "C12:0") NOT TS=("cervical nerve" OR "c6 nerve" OR "c7 nerve" OR "c8 nerve" OR radiculopathy OR neuropathy OR "cervical radiculopathy" OR "brachial plexus") #2 TS=("muscle mass" OR "lean mass" OR "lean body mass" OR "fat free mass" OR "appendicular lean mass" OR "appendicular muscle mass" OR "cross-sectional area" OR muscle fibre* OR muscle fiber* OR "muscle morphology" OR "muscle structure" OR biopsy OR "muscle strength" OR "muscular strength" OR "maximal voluntary contraction" OR MVC OR dynamometry OR "grip strength" OR "knee extension strength" OR "one repetition maximum" OR 1RM OR "muscle endurance" OR fatigability OR "fatigue resistance" OR "muscle fatigue" OR "physical performance" OR "functional performance" OR "functional capacity" OR "walking speed" OR gait speed OR TUG OR "time to exhaustion" OR "endurance performance" OR "aerobic performance" OR VO2peak OR VO2max OR "oxygen consumption" OR metabolism OR metabolic OR mitochondrial OR oxidative OR "fat oxidation" OR "substrate utilization" OR "energy expenditure" OR "insulin resistance" OR HOMA-IR OR OGTT OR insulin OR glucose OR "adverse events" OR "side effects" OR tolerability) #3 TS=(human OR humans OR animal OR animals) #4 AND (TS=("randomized controlled trial") OR TS=("controlled clinical trial") OR TS=(randomized) OR TS=(randomised) OR TS=(randomly) OR TS=("random allocation") OR TS=("randomly assigned") OR TS=(placebo) OR TS=("double blind") OR TS=("single blind") OR TS=("clinical trial")) #1 and #2 and #3 and #4

Bibliographic Database	Search Terms
Sage	Abstract: (“medium-chain fatty acid” OR MCFA OR MCT OR “MCT oil” OR “medium chain triglyceride” OR “medium-chain triglyceride” OR “medium-chain saturated fatty acid” OR “medium-chain SFA” OR “medium-chain diacylglycerol” OR MLCT OR “medium and long chain triglyceride” OR caproic OR hexanoic OR caprylic OR octanoic OR capric OR decanoic OR lauric OR dodecanoic) AND NOT (“cervical nerve” OR “c6 nerve” OR “c7 nerve” OR “c8 nerve” OR radiculopathy OR neuropathy OR “cervical radiculopathy” OR “brachial plexus” OR “moderate continuous training” OR “metronomic chemotherapy” OR “multicomponent training” OR “metacognitive training” OR “minimal clinically important difference” OR MCID OR “MCT score”) AND (human OR humans OR adult* OR “older adult” OR elderly OR animal OR animals OR mouse OR mice OR rat OR rats) Full text: (“muscle mass” OR “lean mass” OR “lean body mass” OR “fat free mass” OR “appendicular lean mass” OR “appendicular muscle mass” OR “cross-sectional area” OR “muscle fibre” OR “muscle fiber” OR “muscle morphology” OR “muscle structure” OR biopsy OR “muscle strength” OR “muscular strength” OR MVC OR “grip strength” OR “knee extension strength” OR “one repetition maximum” OR 1RM OR “muscle endurance” OR fatigability OR “fatigue resistance” OR “muscle fatigue” OR “physical performance” OR “functional performance” OR “functional capacity” OR “walking speed” OR “gait speed” OR TUG OR “time to exhaustion” OR “endurance performance” OR “aerobic performance” OR VO2peak OR VO2max OR “oxygen consumption” OR metabolism OR metabolic OR mitochondrial OR oxidative OR “fat oxidation” OR “substrate utilization” OR “energy expenditure” OR “insulin resistance” OR HOMA-IR OR OGTT OR insulin OR glucose OR “adverse events” OR “side effects” OR tolerability) AND (randomized OR randomised OR randomly OR “random allocation” OR “randomly assigned” OR placebo OR “double blind” OR “single blind” OR “clinical trial”)
ScienceDirect	Find articles with these terms: (“medium-chain fatty acid” OR “medium chain triglyceride” OR “medium-chain saturated fatty acid” OR “medium-chain SFA” OR “medium-chain diacylglycerol” OR “dodecanoic acid” OR “C6:0” OR “C8:0” OR “C10:0”) Abstracts: (“medium- and long-chain triglycerides” OR “caproic acid” OR “hexanoic acid” OR “caprylic acid” OR “octanoic acid” OR “capric acid” OR “decanoic acid” OR “lauric acid” OR “C12:0”)

Bibliographic Database	Search Terms
Springer	Key words: (“medium-chain fatty acid” OR “medium chain triglyceride” OR “medium-chain saturated fatty acid” OR “medium-chain SFA” OR “medium-chain diacylglycerol” OR “dodecanoic acid” OR “C6:0” OR “C8:0” OR “C10:0” OR “medium- and long-chain triglycerides” OR “caproic acid” OR “hexanoic acid” OR “caprylic acid” OR “octanoic acid” OR “capric acid” OR “decanoic acid” OR “lauric acid” OR “C12:0”) AND (“muscle mass” OR “lean mass” OR “lean body mass” OR “fat free mass” OR “appendicular lean mass” OR “appendicular muscle mass” OR “cross-sectional area” OR “muscle fibre” OR “muscle fiber” OR “muscle morphology” OR “muscle structure” OR biopsy OR “muscle strength” OR “muscular strength” OR MVC OR “grip strength” OR “knee extension strength” OR “one repetition maximum” OR 1RM OR “muscle endurance” OR fatigability OR “fatigue resistance” OR “muscle fatigue” OR “physical performance” OR “functional performance” OR “functional capacity” OR “walking speed” OR “gait speed” OR TUG OR “time to exhaustion” OR “endurance performance” OR “aerobic performance” OR VO2peak OR VO2max OR “oxygen consumption” OR metabolism OR metabolic OR mitochondrial OR oxidative OR “fat oxidation” OR “substrate utilization” OR “energy expenditure” OR “insulin resistance” OR HOMA-IR OR OGTT OR insulin OR glucose OR “quality of life” OR “SF-36” OR satisfaction OR “self-efficacy” OR “adverse events” OR “side effects” OR tolerability) Title: (“medium-chain fatty acid” OR “medium chain triglyceride” OR “medium-chain saturated fatty acid” OR “medium-chain SFA” OR “medium-chain diacylglycerol” OR “dodecanoic acid” OR “C6:0” OR “C8:0” OR “C10:0” OR “medium- and long-chain triglycerides” OR “caproic acid” OR “hexanoic acid” OR “caprylic acid” OR “octanoic acid” OR “capric acid” OR “decanoic acid” OR “lauric acid” OR “C12:0”)
Taylor & Francis	Title: (“medium-chain fatty acid” OR “medium chain triglyceride” OR “medium-chain triglyceride” OR MCFA OR MCT OR “MCT oil” OR “medium-chain saturated fatty acid” OR “medium-chain SFA” OR “medium-chain diacylglycerol” OR MLCT OR “medium and long chain triglyceride” OR caproic acid OR hexanoic acid OR caprylic acid OR octanoic acid OR capric acid OR decanoic acid OR lauric acid OR dodecanoic acid OR C6 OR C8 OR C10 OR C12) NOT (“cervical nerve” OR “cervical nerves” OR radiculopathy OR neuropathy OR “cervical radiculopathy” OR “brachial plexus” OR “moderate continuous training” OR “moderate-intensity continuous training” OR “metronomic chemotherapy” OR “multicomponent training” OR “metacognitive training” OR “minimal clinically important difference” OR MCID OR “MCT score”)