# MONASH University

**Clinical Evidence on Efficacy and Safety of Whey Protein Supplements on Performance and Recovery among Athletes: A Systematic Review and Meta-analysis**

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# Abstract

**Introduction**

Athletes train physically to reach beyond their potential maximum aerobic threshold. However, due to declines in muscle performance, sports injuries and fatigue, athletes seek ergogenic aids/supplements. Whey protein supplements (WPS) are often used in conjunction with physiotherapy and psychotherapy to regain muscle performance and enhance the recovery process. However, some clinical evidence suggests that other protein supplements are better than WPS. This study provides conclusive evidence the efficacy and safety of WPS as compared to other protein supplements on performance and recovery among athletes.

**Aim**

This systematic review and meta-analysis aims to explore the clinical evidence on the efficacy and safety of WPS in sports performance and recovery among athletes.

**Methodology**

A comprehensive literature search was performed to identify relevant randomised control trials (RCTs) and non-RCT that investigated the efficacy and safety of WPS on sports performance and recovery among athletes. The Cochrane Risk of Bias Assessment and Risk of Bias in Non-Randomised Studies of Interventions tools were used to assess the quality of the studies. Meta-analysis was conducted using the random-effects model with STATA version 14.2.

**Results**

A total of 333,257 research articles were identified. Of these 50 studies (45 RCTs and 5 non-RCTs) were included for qualitative synthesis and 38 studies for meta-analysis with a total of 835 participants. For risk of bias (RoB) assessment, 8 RCTs had high RoB and a non-RCT has serious RoB. Meta-analysis showed that WPS increases **heart rate** by 0.52 bpm (CI= -1.07,2.11; $I^2$=62.3%; p=0.002), **respiratory exchange ratio** by 0.004 (CI=-0.003,0.01; $I^2$=14.5%; p=0.32), **maximum volume of oxygen** by 1.33 ml/kg/min (CI=4.71,7.36; $I^2$=98.8%; p=0.00), **muscle glycogen** level by 9.08 mmol/L (CI=-23.19,41.36; $I^2$=97.8%; p=0.00), **essential amino acids** level by 624.03 nmol/L (CI=169.27,1078.8; $I^2$=100%; p=0.00), **branched-chain amino acids** level by 458.57 nmol/L (CI=179.96,737.18; $I^2$=100%; p=0.00) and **insulin** concentration by 7.13 µU/ml (CI=5.00,9.25; $I^2$=99.8%; p=0.00) compared to the control group (without WPS).

Additionally, WPS was shown to decrease **rate of perceived exertion** by 0.258 (CI= -1.09,0.57; $I^2$=95.1%; p=0.00), **myoglobin** level by 11.74 ng/ml (CI=-30.24,6.76; $I^2$=79.6%; p=0.007), **maximum power** by 3.14 watt (CI=-129.47,123.2; $I^2$=97.4%; p=0.00), **average power** by 2.57 watt (CI=-1.07,2.11; $I^2$=62.3%; p=0.002), **body mass** by 4.1 kg (CI=-5.84,-2.36; $I^2$=47.9%; p=0.04), **creatine kinase** level by 47.05 U/L (CI=-129.47,35.37; $I^2$=98.4%; p=0.000), **glucose** level by 0.17 mmol/L (CI=-0.33,-0.01; $I^2$=99.1%; p=0.000), **cortiso**l level by 5.40 nmol/L (CI=-10.14,-0.66; $I^2$=75.9%; p=0.000) and **testosterone** level by 0.37 nmol/L (CI=-0.86,0.12; $I^2$=90.8%; p=0.000) compared to the control group.

**Conclusion**

The findings revealed that the clinical evidence supports the efficacy and safety of WPS as an ergogenic aid on athletes' sports performance and recovery. Firstly, from the comprehensive search strategy and RoB assessment, the overall quality of clinical evidence was found to be valid and reliable.
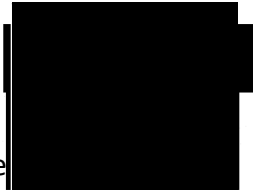
Subsequently, the ergogenic benefits of WPS maintains cardiorespiratory fitness by allowing athletes to inhale more oxygen while greatly increasing physical performance. Furthermore, the ample supply of amino acid from WPS is known to enhance recovery and supply of energy for re-establishment of strength. Moreover, the positive impact of WPS on the essential biomarkers (myoglobin, creatine kinase and cortisol) aids athletes by delaying or attenuating fatigue and reducing the risk of sports injuries while athletes are reaching beyond their potential aerobic threshold.

## Declaration

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This thesis includes (0) original papers published in peer reviewed journals and 1 submitted publications. The core theme of the thesis is clinical evidence and safety of whey protein supplements on performance and recovery among athletes: a systematic review and meta-analysis. The ideas, development and writing up of all the papers in the thesis were the principal responsibility of myself, the student, working within the Jeffrey Cheah School of Medicine & Health Sciences under the supervision of Tahir Mehmood Khan.

The inclusion of co-authors reflects the fact that the work came from active collaboration between researchers and acknowledges input into team-based research.
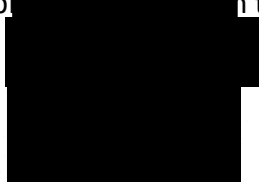
In the case of my contribution to the work involved the following:

| Thesis Chapter | Publication Title | Status *(published, in press, accepted or returned for revision, submitted)* | Nature and % of student contribution | Co-author name(s) Nature and % of Co-author's contribution* | Co-author(s), Monash student Y/N* |
|---|---|---|---|---|---|
| Chapter 1,2,3 4,5,6 and 7 | Effectiveness of whey protein on the serum levels of amino acid, creatinine kinase and myoglobin of athletes: a systematic review and meta-analysis | Submitted | 50%. Conceived and conducted the study, drafted and wrote the entire manuscript, had full access to all of the data in the study and takes responsibility for integrity of the data and accuracy of the data analysis, data acquisition, data interpretation and references | Tahir Mehmood Khan as second reviewer for non-RCT RoB assessment, contributed to the study concept and design, and revise the manuscript; 40%<br><br>Hani Faidah: revise on the manuscripts; 10% | N |

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The undersigned hereby certify that the above declaration correctly reflects the nature and extent of the student's and co-authors' contributions to this work. In instances where I am not the responsible author I have consulted with the responsible author to agree on the respective contributions of the authors.

**Main Supervisor signature:** ▮▮▮▮▮▮▮                    **Date:** 31 January 2018

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**List of common abbreviations**

| | |
|---|---|
| Branched-chain amino acids | BCAA |
| Confidence intervals | CI |
| Essential amino acids | EAA |
| I-squared | $I^2$ |
| Maximum volume of oxygen | $VO_{2max}$ |
| Percentage | % |
| Preferred Reporting Items for Systematic Reviews and Meta-Analyses | PRISMA |
| Randomised controlled trials | RCTs |
| Rate of perceived exertion | RPE |
| Reference daily intake | RDI |
| Respiratory exchange ratio | RER |
| Risk of bias | RoB |
| Risk of Bias in Non-Randomized Studies of Interventions | ROBINS-I |
| Weighted mean difference | WMD |
| Whey protein | WP |
| Whey protein supplements | WPS |
| World Anti-doping Agency | WADA |

# CHAPTER 1: INTRODUCTION

**Title:** Clinical evidence on efficacy and safety of whey protein supplements on performance and recovery among athletes:  A systematic review and meta-analysis

## 1   Chapter 1: Introduction

Athletes train to be skilful and physically fit to compete and ensure success against their opponents. The effect of athletes' stamina, body structure and skill development are essential to able to do so, while an effective nutrition and diet plan to ensure good health and well-being of athletes. However, many athletes in this competitive process face fatigue and tiredness that often led to injuries. It is observed that often athletes take support from ergogenic aids to maintain their performance and to gain a competitive edge. Unfortunately, various athletes develop a strong will to win at all cost, and this intention led them to use supplements that might have illegal substances which are known to have harmful and life-threatening effects on the athlete health such as alcohol, steroid and caffeine (Silver, 2001). Another important factor about their choice of supplements is a recommendation from their coaches and inspiration from their professional sports heroes who admit to consuming supplements containing substances banned by World Anti-doping Agency (WADA) (Frank, Patel, Lopez, & Willis, 2017). For an instant, Mark McGwire, American professional baseball player, admitted the use of a brand name "Andro" supplement that contains androstenedione for a year has led sales of Andro spike high and out of stock (Rovell, 2010). Hence, options for supplements are limited for athletes to compete ethically. One of the popular and easy to purchase protein supplement in sports is whey protein supplements (WPS) as it has shown ergogenic aids which absorbed rapidly, includes all the essential amino acids, and has a high proportion of branched-chain amino acids (Frank et al., 2017; MacKenzie-Shalders, Byrne, Slater, & King, 2015).

## 1.1 Statement of the problem

Athletes often use a variety of substances to prevent from sports fatigue and sports injuries to maximum their aerobic threshold and physical strength (Thomas Jr & Motley, 1984). There are various systematic review and meta-analysis published that summaries the effect of whey protein (WP) as a dietary supplement (Miller, Alexander, & Perez, 2014; Nissen & Sharp, 2003; Schoenfeld, Aragon, & Krieger, 2013). However, there is a lack of consensus over the use of WP, yet, some clinical studies concluded consuming other protein sources or supplements are better than WP (Taylor, Wilborn, Roberts, White, & Dugan, 2016), which is in contrast with some other studies (Hansen et al., 2016; Kraemer et al., 2015) that support WP in comparison to others. Moreover, quality of studies and risk of bias is another issue that is often neglected while scrutinising the evidence of other supplements in comparison to WP. The current systematic review and meta-analysis aim to explore the clinical efficacy and safety of WPS on athletes' performance and recovery.

## 1.2    Research questions

The primary question of this systematic review and meta-analysis is to determine if WPS is effectively and safely enhancing sports performance and recovery among athletes. The review compares WPS with other comparators such as carbohydrate supplement, protein-containing foods include animal sources and vegetarian sources, vitamins, minerals and placebos. This has led to specific questions guiding this review which are: -

1) How are the efficacy and safe of WPS on enhancing sports performance and recovery among athletes?

2) How are the effects of WPS as compare to the comparators for athletes, and

3) What are the effects of WPS on the vital signs, serum protein, strength and body composition, blood profile and hormones of muscle performance and recovery?

### 1.3 Purpose of the study

The aim of this study is to presents a systematic review and meta-analysis evaluating clinical evidence and safety of whey protein supplements on sports performance and recovery among athletes.

Objectives were accomplished as follow: -

1. To conduct a systematic review of the studies reporting the efficacy and safety of WPS.

2. To evaluate the risk of bias and quality of included studies.

3. To assess the clinical evidence efficacy and safety of WP on the outcomes against comparators by performing a meta-analysis on: -

   a. Vital signs of heart rate, respiratory exchange ratio (RER), rate perceived exertion (RPE) and maximum volume of oxygen ($VO_{2max}$);

   b. Serum protein which was myoglobin and muscle glycogen;

   c. Strength and body composition which were maximum power, average power and body mass;

   d. Blood profile was essential amino acid (EAA), branched-chain amino acid (BCAA), creatine kinase and glucose;

   e. Hormones which were insulin, cortisol and testosterone.

# CHAPTER 2: LITERATURE REVIEW

## 2    Chapter 2: Literature review

## 2.1    What is whey protein?

Whey protein is one of the two proteins found in milk. It found in the water water-soluble part of milk which is separated when milk is coagulated or when pH of milk is reduced to 4.6 pH by adding acidic substances i.e. lemon juice or vinegar (Frank et al., 2017). Using different processing techniques, WP can be of following four types;


- Whey protein concentrate (WPC)

- Whey protein isolate (WPI)

- Whey protein hydrolysate (WPH)

- Denature whey proteins


The least processed of whey is WPC which has lowest concentrates of protein. When WPC further processed and purified into WPI. For WPH, WP considered pre-digested whereby WPH partial hydrolysis production. The process of hydrolysation will remove allergenic epitopes and give an excess of free BCAA and proline. Thus, WPH does not require as much digestion and generally higher cost compare another form of WP (Geiser, 2003). Lastly, WP can be denatured by heat as high as above 72°C associated with the pasteurization process. Some native remedies to denature WP by triggers hydrophobic interactions with other proteins (Lee, 1992).

## 2.2   Historical perspective of whey protein

Whey protein was discovered around 5,500 BC in Poland (Science in Poland, 2012). Around 400 BC, Hippocrates, the Father of Modern Medicine, one of the first to recognise WP benefits to human body and started prescribing to his patients. He called it "serum", for it is an immune system booster. During the times of the Roman Empire (around 130 AD), Galen, the great physician of Rome, picked up where Hippocrates left off about WP (Detour, 2017).

At mid-1700 in Gais, Switzerland, WP has cured and healed sickly people who could not be cured by traditional means. The stories of miraculous cures spread across the Europe and Italian became popular for separating liquid whey from milk (Detour, 2017). In 1940, many companies commercialised WP as a supplement and available in market alone or in combination with other substances (Detour, 2017; Latif, 2011). Hence, athletes have sought WPS as an ergogenic benefit for enhanced performances and recovery.

## 2.3 Reasons for athletes search for ergogenic aids

### 2.3.1 Sports performance and activities

Athletes will have high-intensive activities or camps before sports competition such as strength training, plyometric training, endurance exercise, resistance training etc. (Madigan, Stoeber, & Passfield, 2016). The main purpose of these activities is to enhance ability and strength of muscletendon unit to improve the fitness level of athletes (Saez de Villarreal, Requena, & Cronin, 2012). An instant, an elite volleyball player trained for approximately 200 vertical jumps daily, also, a basketball elite regularly perform about 50 vertical jumps and 105 sprints (Wahl et al., 2016). Energy is essential for athletes to do these activities and maximize in sports performance constantly. They may require energy about 60% to 70% especially for endurance athletes. Availability of energy, allows glycogen to realise and break down glucose. Yet, storage of glycogen are limited and need to be replenished daily. As short as a minute of anaerobic exercise burn off almost all energy supplied from glycogen (Maclaren, 1999). Therefore, Athletes need a larger amount of energy storage which fat can supply. However, fat does not provide energy meant for high-intensive exercise in short duration. Fat only supplies energy to low or moderate-intensity exercise that lasting 4 to 6 hours. Thus, the longer period of time exercising, the greater supply of energy from fat (Brukner & Khan, 2009).

Many athletes are required to achieve ideal weight for sports performance. A large amount of muscle mass is needed in certain sports such as throwing, sprinting, powerlifting, weightlifting and soccer/football. Some sports require groups of athletes to have particular weight to compete such as lightweight rowers, boxers, jockey and martial art exponents. Some groups of athletes require extremely low body fat level such as ballet, gymnastics and

distance running. Therefore, it is really important to select the supplements carefully according to athletes' desire body composition (Brukner & Khan, 2009).

### 2.3.2   Sports Injuries and fatigue

The sum of these strenuous training and consistent high muscle activity definitely cause discomfort over the time (Raeder et al., 2016). Subsequently, oxidative stress causes fatigue and lead to muscle damage (Brown, DiSilvestro, Babaknia, & Devor, 2004). In some situations, athletes are motivated to carry on their routine exercise, regardless of fatigue (Ferreira et al., 2016). This will lead them to muscle soreness which also known as delayed onset muscle soreness (DOMS). The DOMS will take place within 24 hours after the long and high-intensive training (Eston, Finney, Baker, & Baltzopoulos, 1996). Other complications that come along with the DOMS are muscle shortening, swelling, painful and inflexibility on active movement, and loss of strength.

Inadequate rest and lack of care towards the DOMS, the muscle will be more tender or sore. This can further lead to loss of skeletal muscle mass, induce muscle damages and fracture injuries known as sports injuries (Cleak & Eston, 1992; McInnis & Ramey, 2016). One of the most common injuries is musculoskeletal injuries that trigger from vigorous muscle motion such as the tension of two-joint muscles, characterised by the muscles contracting eccentrically and fast-twitch muscle (Page, 1995).

### 2.3.3   Enhancing performance and recovery

To enhance performance, athletes drive for optimizing performance, they may fail to balance training, diets and rest which is essential for recovery from minor injuries (Kraemer et al., 2015). Especially during competitions, the best performances are seen during semi-finals rather than finals, may due to lack of energy and inability to recover (Al-Nawaiseh, Pritchett, & Bishop, 2016). Adequate recovery from fatigue in competition is important to enhance performance (Al-Nawaiseh et al., 2016). Furthermore, athletes who need to alter their body composition, may not necessarily have a healthy body composition (Brukner & Khan, 2009). In long-term, athletes could suffer decrement of performance capacity and health problems (Hansen et al., 2016). Hence, enhancing performance and recovery from fatigue and injuries go hand in hand.

For sports injuries, on average, 6 to 10 days are considered as an ideal timeframe for muscle tissue to regenerate and allow athletes to regain their mobility (Cleak & Eston, 1992). Although athletes can recover from injuries from a medical perspective in this time, the stamina required to participate and perform in competitions may require additional time, depending on the severity of injury, re-establishment of strength, speed and physique (Kraemer, Denegar, & Flanagan, 2009).

While athletes are recovering from the sports injuries, they encounter psychology difficulties as well. For example, anxiety due to an injury which happens to be near to an upcoming competition which frustrates athlete due to fear of failure to achieve recovery in time (Wiese-Bjornstal, 2010). In addition to physiotherapy sessions, athletes consume medications and supplements to boost the recovery process and performance. Often it

happened that some supplements do not disclose the presence of some illegal substances

which prohibited by doping agencies — for example, anabolic androgenic steroids, diuretics

and epinephrine—which can jeopardize athletes' careers as they may face penalties or be

removed from competitions if caught (Wiese-Bjornstal, 2010). In some cases, these

substances lead to additional complications that prolong the recovery process and

opportunities to participate in competitions are lost (McInnis & Ramey, 2016).


## 2.4    Ergogenic advantages of whey protein

Whey protein has biologically active components provide ample advantages to enhance

human function than other protein sources. The net protein utilization rate for WP is 92%

compared to rates of non-fat milk solids at 86%, casein at 78%, and soy at 72% (Phillips,

Tang, & Moore, 2009). A higher utilization rate gives an ergogenic advantage to athletes by

decreasing fatigue and enhancing stamina because of the higher levels of EAA and BCAA

when WP is used (Chang et al., 2015; Kingsbury, Kay, & Hjelm, 1998). Whey protein contains

nearly 50% of all EAA and about 26% of BCAA (Miller et al., 2014). Branched-chain amino

acids induction by WP can reduce fatigue level and may decline in plasma glutamine levels

(Cribb, Williams, Carey, & Hayes, 2006). In addition, BCAA stimulates muscle protein

synthesis after physical exercise and suppress muscle protein breakdown to promote

muscle regeneration (Devries & Phillips, 2015; Kraemer et al., 2015). Moreover, WP aids

with fat loss thus assisting athletes with weight maintenance and improve body composition

parameters (Frank et al., 2017).

Whey protein has the potential to lower the levels of myoglobin, cortisol and creatine kinase that acts as a blood marker for muscle damage, marker of exercise recovery, marker of indirect muscle damage respectively (Gunnarsson et al., 2013; Hansen et al., 2016; Lollo et al., 2014). It is noticed that the group of athletes consuming WP had lower levels of these biomarkers, which give the potential to athletes to go beyond their maximum aerobic threshold and driving their maximum physical strength while delaying muscle damage (Thomas Jr & Motley, 1984).

## 2.5    Side effects of whey protein

Whey protein is likely safe supplement; however, when consumed in higher doses can cause some side effect such as increased bowel movements, thirst, bloating, cramps and headache. Then again consistent high doses may cause acne (Nordqvist, 2017; WedMD.com, 2017). For some who are allergic to milk proteins, may be specifically allergic to whey, thus, possibly to avoid using WP (WedMD.com, 2017).

## 2.6    World Anti-Doping Agency

Doping means athletes use drugs or illegal substances to enhance their performances. Doping in sport is probably one of the major problems faced by sports authorities (Willick, Miller, & Eichner, 2016). The first report drug-related death was in 1896 when Arthur Vincent Linton, British cyclist, found dead from an overdose of 'trimethyl'. At the 1960 Summer Olympic in Rome, Kurt Jensen, Danish cyclist, died due to the use of amphetamines and nicotinic acid contributed to his death. A tragedy of Tom Simpson, British cyclist, died in front of huge television audience in the 1967 Tour de France, and autopsy confirms the use of amphetamines by him. In the late 1960 and 1970, western athletes, especially by power athletes, began to use anabolic steroids. At the 1964 Tokyo Olympics, many athletes found dead because of consumed performance-enhancing drugs the (Brukner & Khan, 2009).

These deaths and usage of drugs have led the International Olympic Committee (IOC) to establish a Medical Commission in 1967 and prohibited the use of pharmaceutical agents to enhance performance. Drug testing by IOC was done for the first time in 1968 Olympics in Mexico, and full scale testing was launched in the 1972 Olympics in Munich. In 1974, a reliable test has developed and anabolic was listed as prohibited substances in 1975 by the IOC. In late 1970, many athletes were disqualified due to consumption of drugs that enhances athletes' strength — such as throwing events and weightlifting. Later in 1983-85, Many substances were included in the prohibited list such as caffeine, testosterone, beta-blockers, diuretics and glucocorticosteriods (Brukner & Khan, 2009).

While drugs testing techniques were developing, blood doping was used. Both blood and urine sampling techniques were developed to identify the use the of illegal substance by athletes during competition (Brukner & Khan, 2009). In 1998, increase number of organization involved in developing sports policies and in February 1999, the IOC held the World Conference of Doping in Sport in Lausanne, Switzerland. As a result, WADA was established in November 1999. Furthermore, WADA was established to promote, coordinate and monitor illicit drugs use in sports internationally. For that, athletes are able to look after their health along with WADA vision whereby "A World where all the athletes can compete in a doping-free sporting environment" (World Anti-Doping Agency [WADA], 2017c).

After WADA established, availability and consumption of supplements, along with physiotherapy and psychotherapy, have been recognised as ergogenic advantages in sports performance and recovery (Chan, Hagger, & Spray, 2011; Wiese-Bjornstal, 2010). However, dietary and nutritional supplements have become distressing matters. For many countries and manufacturers of supplements have lack of quality control, some supplements contain substances that were prohibited such as caffeine and alcohol (Willick et al., 2016). Furthermore, the supplements can purchase legally at any health store (Calfee & Fadale, 2006).

Although WADA does not involve in the testing and of certification process dietary and nutritional supplements, WADA is extremely cautious in supplementation consumption for athletes. During doping hearing, misuse of supplements and poorly labelled dietary supplement are inadequate defences (WADA, 2017a). WADA-accredited laboratory once did examine, approximately 15 percent (%) of 600 nutritional supplements were tested and contained anabolic steroids that were not disclosed on the bottle label, packaging or leaflets (Willick et al., 2016).

## 2.7    Recent research reports

Whey protein has had a large impact on nutritional supplements for community especially athletes. This may because abovementioned, and according to Reference Daily Intake (RDI), athletes who undertaking strenuous training and strength-training programs require approximately 1.2-1.7 g/kg per day. For an instant, an 80 kg endurance athlete requires about 96-136 g of protein per day (Bolster et al., 2005; Tipton et al., 2004). A variety of individual studies have been conducted and examined upon the effect and safety of WPS to improve athletes' performance and recovery. One of the recent studies findings suggests that WP powder has anti-fatigue effects and improve exercise capacity by increasing the production of haemoglobin, and haematocrit meanwhile mean corpuscular volume essentially stay the same (Ronghui, 2015). Furthermore, WP able to reduces markers of muscle damage and enhanced athletic performance with the addition of calcium beta-hydroxy-betamethylbutyrate and a slow-release carbohydrate (Kraemer et al., 2015). Similarly, a study shows that WP consumption before and after each exercise session improves elite orienteers recovery and their ability to cope with a strenuous training load (Hansen et al., 2015). A study further indicates WP improves female athletes' body

composition with select training adaptations during 8 weeks intervention (Taylor et al., 2016). Conversely, a finding shows that carbohydrate-casein hydrolysate could reduce time effect for diastolic suppression following 2.5 hours of moderate-hard cycling while maintaining all measures of systolic function following prolonged strenuous endurance exercise compared to WP supplements ingestion tended (Oosthuyse & Millen, 2016).

There is a limited number of systematic reviews and meta-analyses on the effect of nutrient or dietary supplements which included WP located. Nissen 2013 present meta-analysis has determined the effect of dietary supplements augment lean mass gains and strength gains with resistance exercise in healthy adults (Nissen & Sharp, 2003). Also, Schoenfeld 2013 conducted a meta-analysis has determined about protein timing is a viable strategy for muscle strength and hypertrophy (Schoenfeld et al., 2013). Lastly, a recent meta-analysis article supports the effect of WP has improved body composition parameters and overall healthy diet among participants at least 18 years old and above (Miller et al., 2014).

Although the available systematic reviews and meta-analyses report on the effect of protein or dietary supplements as ergogenic aids and had compared with the comparison, these review studies only focus on physical performance (lean mass, muscle strength and hypertrophy). Yet, the effect of protein on recovery from sports injuries and fatigue have not explored. Most importantly, these studies did not review and analyse based on athletes' perspective. This is because, according to RDI, athletes require protein 2 or 3 times more than an average person (0.8 g/kg per day) (Brukner & Khan, 2009).  As WADA is in concern, the safety of available nutrient or dietary supplements especially WP has yet to investigate. As of this writing, no systematic reviews or meta-analyses were located that

comprehensively examine the safety and effect of WP on sports performance and recovery among athletes. Therefore, in this study, the safety and effect of WP on sports performance and recovery among athletes had identified, selected, appraised, discussed and summarized. Moreover, this study will begin to bridge the gap in the literature by systematically reviewing and conducting meta-analysis on all available studies on WP on sports performance and recovery among athletes.

## 2.8    Overview of methodology

### 2.8.1    Systematic review and meta-analysis

A systematic review and meta-analysis summarise existing clinical evidence on a topic. In this study, it describes the usage of the clinical evidence for the care and decision-making of intervention known as a systematic review of intervention (Green et al., 2011). The process of systematic review uses explicit methods to identify, select, appraise, and synthesize results from similar but separate studies. Generally, steps involve in the systematic review are Step 1 framing the question; Step 2: identifying relevant work; Step 3: assessing the quality of the studies; Step 4: summarizing the clinical evidence and Step 5: interpreting the findings (Khan, Kunz, Kleijnen, & Antes, 2003). At Step 4, meta-analysis can be implemented as it is the statistical analysis that collects, integrate and analyse a large of results from the individual studies. Additionally, meta-analysis is an optional component of a systematic review (Glass, 1976). Implementation of meta-analysis in this study as there is a number of eligible articles that gives valuable records of numerical data (Khan et al., 2003).

The main purpose of systematic review and meta-analysis in this study is because of the era of information and technology, there is massive medical, nursing and allied healthcare professional research published internationally (Hemingway & Brereton, 2009). Furthermore, the expectation of sports performance, sports fatigue and sports injuries are common in athletes' lifestyle and livelihood. It is imperative that effectiveness of interventions be examined for safety and positive effect. It is impossible for practitioners and decision-makers; in this study is sportspeople and their support staff, to keep abreast of the latest and newest supplements available. Moreover, conflicts of conclusions and biases may arise from the individual studies. Therefore, there is not always a single robust conclusion (Green et al., 2011). With a systematic review and meta-analysis has made it possible for them as the review integrates and analyse the clinical evidence on topic of interest.

However, this methodology has its limitations. One of the main limitations is a systematic review and meta-analysis did not overcome problems that were inherent in the primary studies. Also, the review did not correct the biases of the primary studies (Garg, Hackam, & Tonelli, 2008). Besides, there would have imprecision related to the impossibility of generalizing diverse characteristics from study to study such as age, gender or geographic factors (Higgins & Green, 2011). Therefore, researchers and readers should keep in mind on these limitations when interpreting the results of this systematic review and meta-analysis.

## 2.8.2 Risk of bias

When an article seems to deviation away from the truth, results or inferences, the article is at risk of bias (RoB). Risk of Bias appears in the article methodological segment whereby, biases can be varying in magnitude, direction or both which mislead the true intervention effect. Hence, it is important to assess all the inclusive articles for the RoB as articles results may be consistent but they may be in preconception (Higgins & Altman, 2008).

Many tools have been suggested to assess RoB. The tools can be in a form of scales or checklists (Juni, Altman, & Egger, 2001). However, these tools are not recommended as they are impossible to distinguish or validating whereabouts is RoB given in a study. Likewise, there are studies that involve subjective matters such as the patients or subjects have cancers that blinding allocation is unethical. For scoring in scales, it has discouraged to practice as the sum number of the scoring does not justify the weights assigned (Higgins & Altman, 2008).

The tools that the Cochrane has recommended is the Cochrane Risk of Bias Assessment tool to assess the RoB for randomized controlled trials (RCTs) (Higgins, Altman, et al., 2011). On the other hand, assessing the RoB for non-RCTs studies by using Risk of Bias in Non-Randomized Studies of Interventions (ROBINS-I) tool (Sterne et al., 2016). The ROBINS-I tool is the upgrade version of Cochrane Risk of Bias Assessment Tool: for Non-Randomized Studies of Interventions (ACROBAT-NRSI) that able to assess interventions of non-RCTs that compare two or more interventions. The ROBINS-I tool is created in a manner that allows reviewer authors to present their judgement that is comparable to the Cochrane risk of bias tool (Sterne et al., 2016).

# CHAPTER 3: METHODS

## 3    Chapter 3: Methods

### 3.1    Overview

A systematic review and meta-analysis were conducted as the search terms were identified, references were compiled, and eligible literature was comprehensively selected. For the inclusive eligible literature, data extraction was retrieved individually. The processes were according to Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) (Moher, Liberati, Tetzlaff, & Altman, 2009). The description of all the processes is given in this chapter. Moreover, the protocol of this study was registered in PROSPERO 2016 and the register identification is CRD42016041842 (Lam, Khan, & Quek, 2016).

### 3.2    Problem formulation

The problem being investigated by the systematic review and meta-analysis is to determine the effect and safety of WPS as compare to other protein supplements on sports performance and recovery among athletes. The data extraction associated with the five categories of outcomes which are vital signs, serum protein, strength and body composition, blood profile and hormones. In addition, this study has investigated the effect and safety of WPS on the outcomes against comparators

### 3.3 Search strategy for identification of relevant studies

The following strategy was used to identify and determine the eligibility for a study.

### 3.3.1 Databases selected

There was a comprehensive literature search on databases as well as specific journals:

PubMed, EMBASE via Ovid, Scopus, Cochrane, Cumulative Index to Nursing and Allied

Health Literature (CINAHL) via EBSCOhost, SPORTDiscus, Health & Medicine Database via

ProQuest, Wiley Online Library, Web of Science, ScienceDirect, Taylor & Francis and SAGE.

### 3.3.2 Search terms and search strings

The search strategy used the keyword of 'whey*' combined individually with 'athlete*',

'injur*', 'muscle*', 'perform*' and 'recover*' to find relevant articles from the databases

(Lemez & Baker, 2015). Thesaurus terms were applied to medical databases such as

PubMed and EMBASE, which were Medical Subject Headings (MeSH) and Embase Subject

Headings (EMTREE) (Centre for Reviews Dissemination, 2009).

A proper care was taken to remove the error by resetting filters. For instance, the PubMed

database has a filtering function for selected species of human or animal. When filtered on

animal species' studies, studies examined on humans were found, as the WP could originate

from cow's milk. Therefore, when filtered on human species only, studies categorised under

the animal species that examined humans may have been omitted. Hence, the databases'

filtering or customising functions were not used as the function would eliminate relevant

articles.

### 3.3.3   Searching other resources

Manual searches in bibliographies of relevant review articles were also performed to identify any other paper that was not indexed in the selected databases.

### 3.3.4   Inclusion criteria

All experimental and observational studies were considered for potential inclusion in this systematic review. No restriction was placed on language. The searched timeframe was from the inception of the databases until June 2016. However, the studies design on expert opinions, case reports/series, surveys, review articles, editorials, commercial advertisements, magazine articles, unpublished articles and these were excluded.

### 3.3.5   Population of interest

The participants included in this study were active athletes who experienced fatigue and had recovered and/or had been hindered in their performance. Also, the studies that observed on participations who are resistance-trained, trained and physically active were deem be athletes as these participants undertook overpowering physical activities during the intervention that were equivalent to athletes. Regardless of athletes' age and gender. However, the studies that observed on retired athletes, mixed athletes with non-athletes, animals, cells, and gels were excluded.

### 3.3.6 Interventions

The intervention was WP or supplements containing WP. The intervention was found in the form of isolate, concentrate, hydrolysate, denature and protein bars.

### 3.3.7 Comparators

Comparators were carbohydrate supplements, protein-containing foods from animal sources (e.g., meat, fish, dairy products, and eggs), protein-containing vegetarian sources (e.g., tofu, legumes, and soy protein), vitamins (e.g., multivitamin, vitamin B, beta-carotene, and folic acid), minerals (e.g., calcium, iron and zinc) and placebos (include no treatment and treatment as usual).

### 3.3.8 Outcomes measure

Collection of information on all outcomes measure in this systematic review and meta-analysis are pre-specified according to the interest. The outcomes measure has five outcomes which associated with objectives given in Chapter 1.2: -

a. Vital signs of athletes which were heart rate, RER, RPE and $VO_{2max}$,

b. Serum protein which was myoglobin and muscle glycogen,

c. Strength and body composition which was maximum power, average power and body mass,

d. Blood profile which was EAA, BCAA, creatine kinase and glucose,

e. Hormones which were insulin, cortisol and testosterone.

### 3.3.9 Literature search and selection process

The relevant articles were compiled, and duplicate articles were removed by using EndNote X7. Then a screening was done on titles and abstracts of the relevant articles based on the inclusion and the exclusion criteria. After that, full-text articles of the screened articles were retrieved.

A detailed on the data collection procedures and storage of the studies was records and keep track including 1) search engine searched; 2) number of the studies; 3) number of duplicates; 4) key words used; and 5) professionals contacts. Studies were located primarily through Monash University library system and were saved in an electronic folder.

Standalone abstracts or conference proceedings have received assistance from the Monash University Malaysia Library for document delivery service and contacted the first or corresponding author to acquire for the full text of the articles. When electronic versions were not available, hard copies were made and kept in a designated file. Also, when full-text English language articles were not available, the original language will be sent for English language translations.

### 3.4   Data extraction

The extracted data were entered into Microsoft Excel 2016, namely (Boutron, Moher, Altman, Schulz, & Ravaud, 2008): -

1.  General information (first author surname, title, year of publication, journal name).

2.  The article study methods and characteristic (study design).

3.  Participants (age, gender, weight, heights and sporting activity)

4.  Intervention (dose of WP and number times consumed).

5.  Comparators (type, dose and number times consumed).

6.  Outcomes: -

    a.  Outcomes that contributed to sports performance and recovery.

    b.  The data obtained after the participants consumed the intervention or control.

    c.  Most of the data located within the text of the articles and presented in tabular form or graphs

    d.  When data was in standard error or standard error mean, it was transformed into a standard deviation (Higgins, Thompson, Deeks, & Altman, 2011b).

### 3.5 Assessment of risk of bias for included studies

The inclusive studies were assessed for RoB by two reviewers independently. Both assessment results were compared and verified for accuracy. A Cochrane Risk of Bias Assessment tool criteria were used to assess the quality of the RCTs (Higgins, Altman, et al., 2011) (Table 1 and Appendix 3). The ROBINS-I tool was used to assess interventions of non-RCTs, comparing two or more interventions and presenting a judgement. As such, it is comparable to the Cochrane Risk of Bias Assessment tool (Sterne et al., 2016). The domains were: bias due to confounding, bias in selection of participants into the study, bias in classification of interventions, bias due to deviations from intended intervention, bias due to missing data, bias in measurement of outcomes, and bias in selection of the reported result (Appendix 3 and Appendix 4). The judgement about the domains was: low risk of bias, moderate risk of bias, serious risk of bias, critical risk of bias, and no information (Sterne et al., 2016).

Table 1. **The Cochrane Risk of Bias tool for RCTs**. Source from (Higgins & Altman, 2008).

| Domains | Assessment |
|---|---|
| Sequence generation: Was the allocation sequence adequately generated? | Yes, No, or Unclear |
| Allocation Concealment: Was the sequence generation adequately concealed before group assignments? | |
| Blinding of participants and personnel: Was knowledge of the allocated interventions adequately hidden from the participants and personnel after participants were assigned to respective groups? | |
| Blinding of outcome assessors: Was knowledge of the allocated interventions adequately hidden from the outcome assessors after participants were assigned to respective groups? | |
| Incomplete outcome data: Were incomplete outcome data adequately addressed? | |
| Selective outcome reporting: Are reports of the study free of suggestion of selective outcome reporting? | |
| Other sources of bias: Was the study apparently free of other problems that could put it at a risk of bias? | |
| Study Quality† | |

† "Yes" in all Domains would place a study at "Low Risk of Bias";
  "No" in any of the Domains would place a study at "High Risk of Bias";
  "Unclear" in any of the domains would place the study at "Unclear Risk of Bias"


Table 2**. Summarized domains of the ROBINS-I tool**. Source from (Sterne et al., 2016)

| Domains | Assessment |
|---|---|
| Bias due to confounding | Low risk of bias, Moderate risk of bias, Serious risk of bias, Critical risk of bias, or No information |
| Bias in Selection of Participants into the study | |
| Bias in classification of interventions | |
| Bias due to deviations from intended intervention | |
| Bias due to missing data | |
| Bias in measurement of outcomes | |
| Bias in section of the reported result | |
| Overall RoB judgement | |

### 3.6    Data synthesis

Meta-analysis is statistical measurement and procedure for combining data from the multiple studies and developed a statistically single conclusion. The purposes of the meta-analysis are precise estimate effect magnitude, identify the reason for the variation and common effect and safety of data (Lipsey & Wilson, 2001). The following expressed the meta-analysis procedure.

### 3.6.1    Effect size

Rule of thumbs, an effect size is describing a number effect the magnitude of the relationship between two variables. In a meta-analysis, the core finding is effect size that is the overall effect estimated from the inclusive studies (Lipsey & Wilson, 2001).

The type of data for this analysis was continuous data, which contained mean, standard deviation and sample size (Saez de Villarreal et al., 2012). A random-effect model was selected since there were no identical studies throughout all the included studies and the participants were various categories of athletes, which could have had an impact on the intervention effect (Borenstein, Hedges, Higgins, & Rothstein, 2009). For the meta-analysis arm, WP or supplements containing WP were considered the experimental or intervention arm while comparators were control arm (alternative supplements or proteins with equivalent quantity and similar visuals such as carbohydrate, placebo, maltodextrin and bovine colostrum). The outcomes parameters were on the vital signs of athletes, serum protein, strength and body composition, blood profiles and hormones. The mean effect size is computed as a weighted mean difference (WMD) at 95% confidence interval (CI), whereby the weights are equivalent to each study effect size. Higher weight present studies with

larger sample sizes as well as studies with less random variations. The WMD was preferred as the outcome measurements in all studies were made on the same scale. For the studies reporting, at graph computed from the software, the diamond in the last row of the graph illustrates the overall effect size (Ried, 2006).

### 3.6.2   Assessing heterogeneity

Heterogeneity is the degree to which the effect sizes differ between the studies. For this study, clinical and methodological heterogeneity were discussed. The clinical heterogeneity usually referring to the studies differ in term of the participant, interventions (how the intervention is implemented; a dose of intervention), outcome definitions and study design (Fletcher, 2007). Whereas, the methodological heterogeneity implying to data analysis strategy, study design and risk of bias (Fletcher, 2007; Pigott & Shepperd, 2013). The appearance of l heterogeneity could be caused by clinical, methodological differences between the studies and unknown study characteristics (Fletcher, 2007). I-squared ($I^2$) carried out to determine appearance and measurement of the heterogeneity. $I^2$ has ranges between 0 and 100% (whereby 0% to 24% consider no heterogeneity; 25% to 49% consider low heterogeneity; 50% to 74% consider moderate heterogeneity; and 75% and above consider high heterogeneity (Higgins, Thompson, Deeks, & Altman, 2003).

### 3.6.3 Subgroup analysis

Subgroup analysis is formal statistical comparisons are made across the subgroups within an outcome. In this study, subgroup analyses were to investigate heterogeneous results. When the $I^2$ appeared to have 50% and above, subgroup meta-analyses were conducted by activities or exercises instructed during the study and intervention duration range (days) (Higgins, Thompson, Deeks, & Altman, 2011a). Since random-effects models were used for the subgroup analyses, the statistics relate to variation in the mean effects in the different subgroups (Higgins, Thompson, et al., 2011a).

### 3.6.4 Publication bias

A funnel plot and Egger test were conducted to examine for publication bias (Egger, Smith, Schneider, & Minder, 1997; Lipsey & Wilson, 2001). A funnel plot examines relationships between estimated intervention effects and a measure of study size for any presence of bias. When no publication bias exists, the funnel plot appears mostly symmetrical. Otherwise, the funnel plot appears asymmetrical when there is publication bias. Egger test was performed to add robustness to the funnel plot results by measuring the intervention effect in a linear regression on their standard errors (Egger et al., 1997). The reporting of publication bias performed when there were at least 10 studies included in the meta-analysis (Higgins & Green, 2011).

### 3.6.5 Sensitivity analysis

A systematic review and meta-analysis process involves a sequence of decisions for study design, attrition, missing data, type of treatment, source of research examined, sample size etc. Some decisions of these factors may be either clear or unclear (Higgins, Thompson, et al., 2011a). Therefore, a sensitivity analysis is a process to ensure robustness in data analysis. In this study, sensitivity analyses were pre-specified in the study protocol as abovementioned (Higgins, Thompson, et al., 2011a). Such as the search strategy, the eligibility criteria, type of data analysed (continuous data), analysis methods (such as random-effects methods and WMD). Additionally, sensitivity analyses are confused with subgroup analyses. Firstly, sensitivity analyses do not estimate the effect of removed the studies from the analysis, whereas estimates are produced for each subgroup at subgroup analyses. Informal comparisons are made in sensitivity analyses, while formal statistical comparisons are made across the subgroups in subgroup analyses (Higgins, Thompson, et al., 2011a).

### 3.6.6 Software

The meta-analysis was performed using a random-effects model with STATA version 14®. The command to performed the meta-analysis was installed in STATA – such as "metan" and "metafunnel" (Harris et al., 2008) (Appendix 2). Computed statistical information included WMD, 95% CI, weight percentage, heterogeneity chi-squared ($\chi^2$), $I^2$ for variation in WMD attributable to heterogeneity, Tau-squared to estimate between-study variance, and forest plot. Subgroup analyses, funnel plots and Egger tests were also compute using STATA.

# CHAPTER 4: RESULTS

**4    Chapter 4: Results**

This chapter presents findings on 835 athletes who were participants in 45 RCTs and 5 non-RCTs studies. This section mainly emphasises on the characteristics of included studies, quality assessment of the studies, RoB, results from the meta-analysis and publication bias. All additional analysis and detailed description of the results part are shown from Appendix 1 till Appendix 5.

**4.1    Included studies**

There were 333,257 research articles were identified from the databases and 1,773 studies were through manual search from relevant review articles (Figure 1). Upon removal of duplicate 221,064 studies were subjected to further screening, of those 220,895 were excluded. After screening the titles and abstracts, 169 studies selected for the full-text screening. Subsequently, 50 studies were eligible based on criteria mentioned in the Chapter 3.2.1-3.2.9. Hence, a total of 50 studies were included to determine qualitative synthesis and 38 studies were undergone the meta-analysis as part of the quantitative synthesis. Additionally, the PRISMA checklist shown in Appendix 1 describes further in details for accuracy and transparency in reporting.
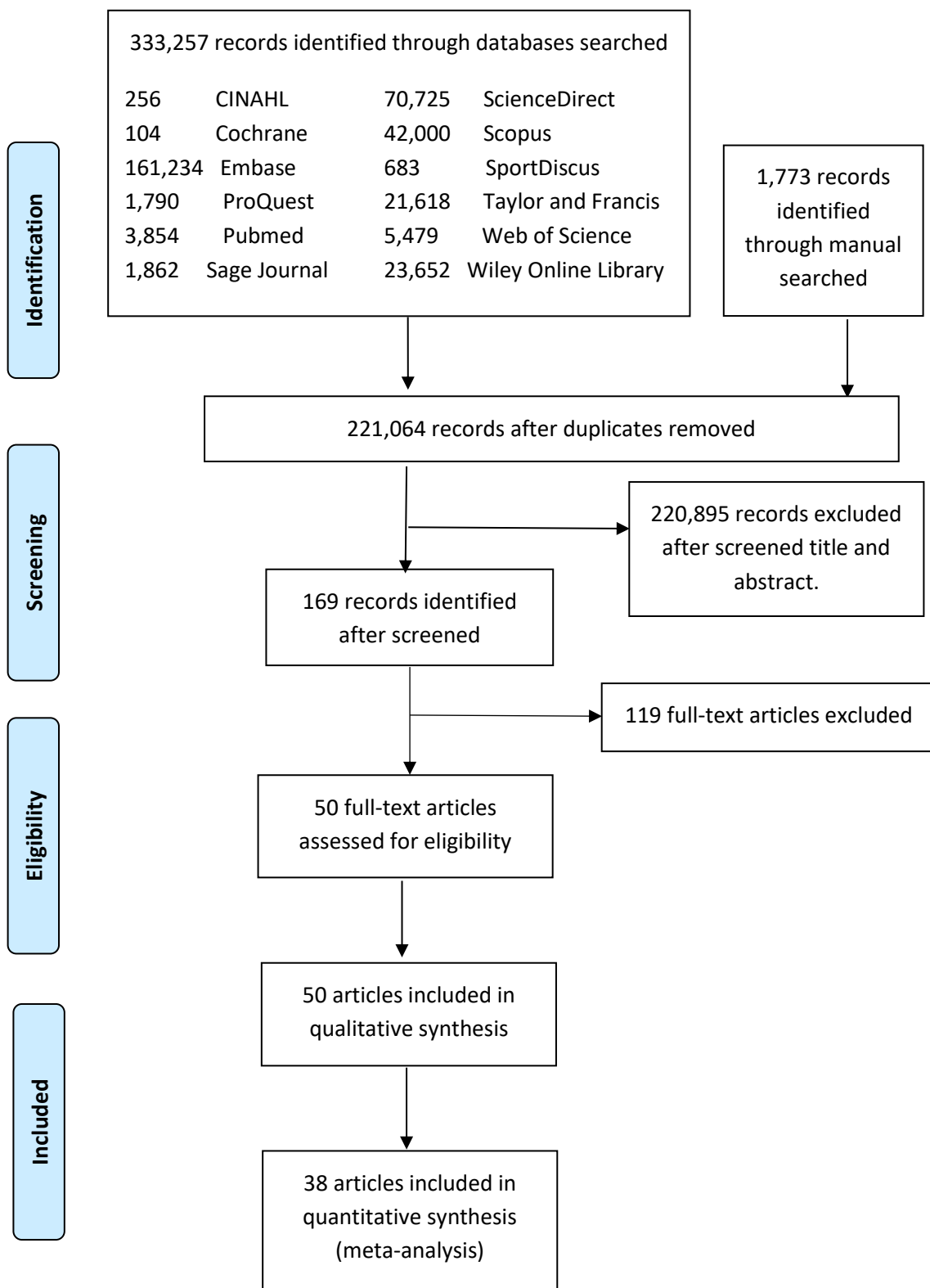
Figure 1. PRISMA flow diagram.

Box contents:

Identification

333,257 records identified through databases searched

| 256 | CINAHL | 70,725 | ScienceDirect |
| 104 | Cochrane | 42,000 | Scopus |
| 161,234 | Embase | 683 | SportDiscus |
| 1,790 | ProQuest | 21,618 | Taylor and Francis |
| 3,854 | Pubmed | 5,479 | Web of Science |
| 1,862 | Sage Journal | 23,652 | Wiley Online Library |

1,773 records identified through manual searched

221,064 records after duplicates removed

Screening

220,895 records excluded after screened title and abstract.

169 records identified after screened

Eligibility

119 full-text articles excluded

50 full-text articles assessed for eligibility

Included

50 articles included in qualitative synthesis

38 articles included in quantitative synthesis (meta-analysis)

**4.2 Study characteristic**

**4.2.1 Study designs**

The descriptive study characteristics are presented in Table 3. Of these studies, 45 studies were RCTs that has 37 studies were **blinding**, while 8 studies were **non-blinding** (Al-Nawaiseh et al., 2016; Areta et al., 2014; Gunnarsson et al., 2013; Hoffman et al., 2009; Impey et al., 2015; Parr et al., 2014; Ronghui, 2015; Yang, 2014). Nearly quarter of the inclusive studies (14) (Brown et al., 2004; Cribb et al., 2006; Gunnarsson et al., 2013; Hoffman et al., 2009; Jauhari, Sulaeman, Riyadi, & Ekayanti, 2014; Joy et al., 2013; S. C. Li & Zhao, 2007; Lollo, Amaya-Farfan, & de Carvalho-Silva, 2011; Lollo et al., 2014; Rankin, Shute, Heffron, & Saker, 2006; Ronghui, 2015; Taylor et al., 2016; Wilborn et al., 2013; Yang, 2014) **did not mention** any further about the study design. The most reported study design was **crossover** (8) (Cury-boaventura et al., 2008; Highton, Twist, Lamb, & Nicholas, 2012; Hill, Stathis, Grinfeld, Hayes, & McAinch, 2013; Mero et al., 1997; A. R. Nelson et al., 2013; Oosthuyse, Carstens, & Millen, 2015; Oosthuyse & Millen, 2016; Vegge, Rønnestad, & Ellefsen, 2012), followed by **placebo controlled** (5) (Coombes, Conacher, Austen, & Marshall, 2002; Hofman, Smeets, Verlaan, Lugt, & Verstappen, 2002; Shing, Jenkins, Stevenson, & Coombes, 2006; Shing et al., 2007; Shing, Peake, Suzuki, Jenkins, & Coombes, 2013). Only one study each were **parallel** (Detko et al., 2013) and **placebo controlled with crossover** (Fukuda, Smith, Kendall, & Stout, 2010).

On the other hand, 5 studies were non-RCTs with **crossover** (2) (Fahlström, Fahlström, Lorentzon, & Henriksson-Larsén, 2006; Morifuji et al., 2012) design and each for counterbalanced, longitudinal and parallel study design. Moreover, one of the five non-RCTs was **non-binding** (She, 2005).

### 4.2.2 Origins

Demographic (Table 3) has the most studies were from **Australia** (11) (Areta et al., 2014; Brinkworth, Buckley, Bourdon, Gulbin, & David, 2002; Buckley & Scammell, 2000; Burke et al., 2012; Coombes et al., 2002; Cribb et al., 2006; Hill et al., 2013; Parr et al., 2014; Shing et al., 2006; Shing et al., 2007; Shing et al., 2013) and **United State** (11) (Al-Nawaiseh et al., 2016; Brown et al., 2004; Fukuda et al., 2010; Hoffman et al., 2009; Joy et al., 2013; Kraemer et al., 2015; Rankin et al., 2006; Schroer et al., 2014; Smith et al., 2010; Taylor et al., 2016; Wilborn et al., 2013). One study each from **Canada** (Tang et al., 2007), **Indonesia** (Jauhari et al., 2014), **Japan** (Morifuji et al., 2012), **Netherlands** (A. R. Nelson et al., 2013), **Norway** (Vegge et al., 2012), **Spain** (Cepero et al., 2010) and **Sweden** (Fahlström et al., 2006). Additionally, the researchers who consistent in publishing the most regarding WPS for athletes were Shing and colleagues with three publication (Shing et al., 2006; Shing et al., 2007; Shing et al., 2013). Follow by two publication each from Hansen and colleagues (Hansen, Bangsbo, Jensen, Bibby, & Madsen, 2015; Hansen et al., 2016), Lollo and colleagues (Lollo et al., 2011; Lollo et al., 2014), Oosthuyse and colleagues (Oosthuyse et al., 2015; Oosthuyse & Millen, 2016).

### 4.2.3 Participants

The total number of participants was 835, with 681 males and 110 females and 44 participants were not taken account regarding their gender. Furthermore, the minimum participants were 6 participants (Hill et al., 2013) and the maximum was 51 participants (Buckley 2000). As the interested is at all age of athletes, the average age gap is between 15.5 and 39 years old, yet 2 studies did not have details on age (Buckley & Scammell, 2000; Ronghui, 2015). The average weight of participants are ranged 55.6 kg to 99.2 kg but 5 studies did not have details on weight (Buckley & Scammell, 2000; Ronghui, 2015; She, 2005; Tang et al., 2007; Vegge et al., 2012). Correspondingly, participants' average height is between 155.5 cm to 183 cm, yet 12 studies did not have details on heights. Additionally, the participants in the studies included in this meta-analysis were resistance-trained, physically active and athletes in these sporting events: soccer/football, badminton, basketball, rugby, hockey, bodybuilding, triathlon, orienteering, track and field, sprinting, jumping, hockey, rowing and weightlifting.

Participants consumed supplements, on average, between 1-15 times in a day. In extreme cases, one study has participants taking supplements every 15 minutes (Schroer, Saunders, Baur, Womack, & Luden, 2014) while another study has participants consume them once every two days (Ronghui, 2015). Participants took supplements either before, during and/or after physical activities. As physical activities during intervention duration, some studies had a normal routine and/or sports which athletes always usually do and some had a set of resistance activities.

Table 3. **Characteristics of 50 inclusive studies**

| First Author Surname and Year | Country of study | Study Design | Categories of athletes | Average age[1] | Average weight (kg)[1] | Average height (cm)[1] | Male | Female | Total | Intervention Group (WP) | Number of times to consume WP supplement in a day | Control Group | Number of times to consume supplement in a day | Intervention duration (day) | Physical activity during intervention duration | Consume the supplementation during intervention duration |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | | | | | | | |
| Al-Nawaiseh 2016 (Al-Nawaiseh et al., 2016) | United States | Random, crossover, counterbalanced | College athletes, college-club athletes | 21.5 | 76.5 | NA | 11 | 11 | 22 | 23 g with 10.6 g EAA, 7.3 g of conditionally EAA, and 5.6 g of non-EAA ON was mixed with 200 ml of skimmed milk to form a protein shake. 2 oral doses of 1,000 mg of vitamin C (ascorbic acid with citrus bioflavonoids) and 400 IU of vitamin E soft gel capsules (d-a-tocopherol) | 3 | Placebo (non-treatment) | 3 | 17 | Stretch and cycle | Before, during, after physical activity |

[1] Mean ± Standard Deviation
NA = not available

| Study | Country | Study design | Population | Age | Weight | Height | | | | Intervention | | Comparator | | | Exercise | Timing |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Areta 2014 (Areta et al., 2014) | Australia | Random, within-subject, counterbalanced | Young, healthy, resistance-trained | 27.5 | 76.5 | NA | 8 | 7 | 15 | 15 g with 86.8 g of protein, 1.5 g of fat, and 3.1 g/100 g of carbohydrates | 1 | Placebo | 1 | 60 | Leg press | During physical activity |
| | | | | | | | | | | 30 g with 86.8 g of protein, 1.5 g of fat, and 3.1 g/100 g of carbohydrates | 1 | | | | | |
| Breen 2011 (Breen et al., 2011) | Finland | Random, counterbalanced, single-blinding | Cyclists | 29.0 | 77.2 | NA | 10 | - | 10 | 1)10.2 g with 25.4 g carbohydrate dissolved in 250 ml of cold water; 2) 20.4 g with 50.8 g carbohydrate dissolved in 250 ml of cold water | 2 | 1) 25.2 g of carbohydrate dissolved in 250 ml of cold water, 2) 50.4 g CHO dissolved in 250 ml of cold water | 2 | 28 | Cycle | After physical activity |
| Brinkworth 2002 (Brinkworth et al., 2002) | Australia | Random, placebo-controlled, parallel, double-blinding | Rower | 20.6 | 69.7 | 175.4 | - | 13 | 13 | 60 g with mixed with 85 ml warm water and 40 ml of milk | 2 | 60 g bovine colostrum protein powder mixed with 85 ml warm water and 40 ml of milk | 2 | 63 | Row | Before and after physical activity |

| Study | Country | Design | Population | Age | Weight | Height | | | | Intervention | | Comparator | | | Exercises | Funding |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Brown 2004 (Brown et al., 2004) | United States | Random, double-blinding | Weight lifters | 20.8 | 79.7 | 179.0 | 9 | - | 9 | 11 g with assortment of micronutrients | 3 | 11 g of soy protein and an assortment of micronutrients | 3 | 63 | 1) chest press; 2) chest fly; 3) incline press; 4) lat pull-down; 5) seated row; 6) military press; 7) lateral raise; 8) preacher curl; 9) bicep curl; 10) supine tricep extension; 11) seated tricep extension; 12) leg press; 13) calf raise; and 14) abdominal crunches. | Unknown |
| | | | | | | | | | | | | Placebo (did not consume a protein product) | 3 | | | |
| Buckley 2000 (Buckley & Scammell, 2000) | Australia | Random, placebo controlled, parallel, double-blinding | Moderately trained recreational athletes | NA | NA | NA | 51 | - | 51 | 60 g | 1 | 60 g bovine colostrum protein powder | 1 | 56 | 1 study) vertical jump performance; 2 study) treadmill runs; 3 study) rower | Unknown |

| Study | Country | Design | Population | Age | Weight | Height | n | | n | Intervention | | Comparator | | Total n | Exercise | Timing |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Burke 2012 (Burke et al., 2012) | Australia | Random, placebo controlled, counterbalanced, double-blinding | Resistance-trained | 27.0 | 94.3 | NA | 12 | - | 12 | 25 g with 5 g of leucine and 500 ml | 1 | Placebo | 1 | 15 | Single-leg resistance exercise | Before physical activity |
| | | | | | | | | | | 25 g with 5 g of leucine and 33 ml | 15 | | | | | |
| Cepero 2010 (Cepero et al., 2010) | Spain | Random, counterbalanced, double-blinding | Cyclists | 39.0 | 74.4 | 176.0 | 15 | - | 15 | 0.02 with Energy 36 kcal/100 ml, 7% carbohydrates, vitamins B, E, C, D 25%/L DRI, Folic Acid 25%/L DRI | 1 | 9% Carbohydrate, Energy 36 kcal/100 ml, Vitamins B, E, C, D 25%/L DRI, Folic Acid 25%/L DRI | 1 | 16 | Cycle | During physical activity |
| | | | | | | | | | | | | 2% casein hydrolysate, Energy 36 kcal/100 ml, 7% Carbohydrates, Vitamins B, E, C, D 25%/L DRI, Folic Acid 25%/L DRI | 1 | | | |

| Study | Country | Design | Participants | Age | Weight | Height | N | | N | Intervention | | Control | | | Exercise | Timing |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Coombes 2002 (Coombes et al., 2002) | Australia | Random, placebo-controlled study, double-blinding | Cyclists | 30.0 | 74.0 | NA | 28 | - | 28 | 60 g (pure) / 40 g with 20 g/d oral bovine colostrum | 2 / 2 | 60 g bovine colostrum | 2 | 56 | Warm up, stretching exercises, cycle | Before and after physical activity |
| Cribb 2006 (Cribb et al., 2006) | Australia | Random, double-blinding | Bodybuilders | 26.5 | 81.9 | 178.5 | 13 | - | 13 | 90 g with 3 g carbohydrate, 1.5 g/100 g fat | 3 | 90 g protein, 3 g carbohydrate, 1.5 g/100 g fat | 3 | 70 | Barbell bench press, cable pull-down, and barbell squat | After physical activity |
| Cury-boaventura 2008 (Cury-boaventura et al., 2008) | Brazil | Random, crossover, double-blinding | Triathletes | 24.9 | 69.3 | 178.0 | 9 | - | 9 | 4 tablets of 700 mg with 175 mg of glutamine dipeptide | 1 | 50 g of maltodextrin in 250 ml of water | 1 | 9 | Two exhaustive exercise trials | Before physical activity |
| Detko 2013 (Detko et al., 2013) | United Kingdom | Random, parallel, double-blinding | Cyclists | 33.0 | 79.0 | 178.0 | 7 | - | 7 | 0.2 g/kg with MD (0·5 g/kg/h), 0.1 g/kg/h of L-leucine and 0.1 g/kg/h of L-phenylalanine | 7 | Maltodextrin (0.9 g/kg/h) and GAL (0.3 g/kg/h) beverage | 7 | 1 | Cycle | Before, during, after physical activity |

| Study | Country | Design | Population | Age | Weight | Height | | | | Intervention | n | Control | n | n | Exercise | Timing |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Fahlström 2006 (Fahlström et al., 2006) | Sweden | Non-random, crossover, double-blinding | Badminton player | 19.7 | 68.3 | 177.0 | 14 | 4 | 18 | 3.1-3.56% with fat 0.0014-0.017%, carbohydrate 9.3-10%m energy/100g 211-231 kj (51-56 kcal)/100g, energy/pack of 250 ml 525-575 kj (125-140 kcal) | 2 | 0.01% fat, 2.5-2.7 % carbohydrate, 0.01% protein, 4.3-46 kj (10-11 kcal)/100 g, 107-115 kj (25-27 kcal) | 2 | 241 | Badminton | During and after physical activity |
| Fukuda 2010 (Fukuda et al., 2010) | United States | Random, placebo-controlled crossover, single-blinding | Trained, recreationally active | 25.7 | 70.9 | 172.2 | 10 | | 10 | 8 g with Kilojoules, Cholesterol, Sodium, carbohydrates, Sugars, Vitamin A, Vitamin V, Calcium, Vitamin B6, Vitamin B12 | 1 | Kilojoules, Maltodextrin, Proprietary blend | 1 | 14 | Run | Before exercise |
| Gunnarsson 2013 (Gunnarsson et al., 2013) | Denmark | Random | Soccer players | 24.0 | 80.5 | 182.0 | 16 | - | 16 | HPC with carbohydrates | 1 | Placebo (normal diet) | 1 | 2 | Soccer game | After physical activity |
| Hansen 2015 (Hansen et al., 2015) | Denmark | Random, block, single-blinding | Elite orienteers | 21.7 | 64.3 | 175.8 | 8 | 10 | 18 | 0.3 g/kg with 1 g/kg carbohydrate, | 2 | 1.3 g/kg carbohydrate | 2 | 7 | Run | Before and after physical activity |

| Study | Country | Design | Population | Age | Weight | Height | n | | n | Intervention | n | Control | n | Duration | Exercise | Timing |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Hansen 2016 (Hansen et al., 2016) | Denmark | Random, block, single-blinding | Elite orienteers | 19.5 | 71.9 | 183.0 | 18 | - | 18 | 0.2 g/kg/h with 1 g/kg/h of carbohydrate | 4 | 1.2 g/kg/h of carbohydrate | 4 | 7 | Cycle, mix of distance training, interval training, mountain climb | After physical activity |
| Highton 2012 (Highton et al., 2012) | United Kingdom | Random, crossover, double-blinding | Soccer, rugby union | 23.4 | 75.3 | 177.5 | 9 | - | 9 | 2% with 6% carbohydrate | 5 | 8% carbohydrate | 5 | 14 | Walk and sprint | During physical activity |
| Hill 2013 (Hill et al., 2013) | Australia | Random, crossover, single-blinding | Cyclists and triathletes | 29.0 | 74.0 | 183.0 | 6 | - | 6 | 1.2 g/kg/day with carbohydrate, fat | 2 | Protein, carbohydrate and fat | 2 | 44 | Cycle | During and after physical activity |
| Hoffman 2009 (Hoffman et al., 2009) | United States | Random | Resistance-trained (30/33 were college's football) | 20.1 | 99.2 | 182.1 | 33 | - | 33 | 42 g of a proprietary blend of protein (enzymatically hydrolysed collagen protein isolate, WPI, and casein protein isolate) with 2 g of carbohydrate | 2 | Placebo (normal diet) | 2 | 70 | High pull, bench press, seated shoulder press, dumbbell shoulder press/behind-the-neck, triceps push-downs, partner neck exercise etc | Before and after physical activity |
| | | | | | | | | | | 42 g of a proprietary blend of protein (enzymatically hydrolysed collagen protein isolate, WPI, and casein protein isolate), 2 g of carbohydrate, 2 g of carbohydrate | 2 | | | | | |

| Study | Country | Design | Population | Age | Weight | Height | n | n | n total | Intervention | n | Comparison | n | Duration | Exercise/Test | Timing |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Hofman 2002 (Hofman et al., 2002) | Netherlands | Random, placebo-controlled, single-blinding | Hockey player | 22.7 | 71.4 | 176.3 | 18 | 17 | 35 | 20 g | 2 | 20 g | 2 (am/pm) | 56 | Hockey, sprint test, suicide test, shuttle run test, vertical jump | Before and after physical activity |
| Impey 2015 (Impey et al., 2015) | United Kingdom | Random, counterbalanced (Latin Squares approach) | Cyclists and triathletes | 29.0 | 79.4 | 179.7 | 9 | - | 9 | 22 g with 2.1 g leucine, 4.9 g BCAA, 9.3 EAA, 500 ml water | 1 | 5 g/kg carbohydrate 2 g/ kg protein, 1 g/kg fat | 1 | 7 | Cycle | Before physical activity |
| | | | | | | | | | | 22 g protein (4.8 g leucine, 7.5 g BCAA, 13.1 g EAA, 100mg Caffeine, 1 g HMB) | 1 | | | | | |
| Jauhari 2014 (Jauhari et al., 2014) | Indonesia | Random, double-blinding | Badminton player | 20.0 | 64.6 | 170.0 | 18 | - | 18 | 23 g with 437.99 kcal energy, 23 g carbohydrate | 1 | Tempeh (437.99 kcal energy, 48 g carbohydrate, 17.1 g fat and 23 g protein) | 1 | 4 | Resistance exercise was conducted using squat | After physical activity |
| | | | | | | | | | | | | Placebo | 1 | | | |
| Joy 2013 (Joy et al., 2013) | United States | Random, double-blinding | Resistance training experience | 21.3 | 76.1 | 177.8 | 24 | - | 24 | 48 g | 1 | 48 grams of rice | 1 | 56 | Resistance training, cycle test | Before physical activity |

| Study | Country | Design | Population | Age | Weight | Height | n | | n | Intervention | n | Comparison | n | Duration | Tests | Timing |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Kraemer 2015 (Kraemer et al., 2015) | United States | Non-random, counterbalanced within-group, double-blinding | Resistance training experience | 22.6 | 86.2 | 175.3 | 13 | - | 13 | 20 g with 100 kcal, 2.5 g carbohydrate, 1 g fat | 2 | RP supplement (260 kcal, 20 g protein, 1.5 g HMB, 41 g carbohydrate, 2 g fat) | 2 | 56 | Cycle, dynamic stretches, jump test | Before and during physical activity |
| Li 2007 (S. C. Li & Zhao, 2007) | China | Random, Blinding | Amateur football players | 21.0 | 64.8 | 172.4 | 16 | - | 16 | 25 g with 800 ml | 2 | 25 g carbohydrate 800 ml | 2 | 72 | Cycle, jump, push up, run | After physical activity |
| Lollo 2011 (Lollo et al., 2011) | Brazil | Random, double-blinding | Soccer players | 19.0 | 74.4 | 181.5 | 24 | - | 24 | 91.4% / 87% | 1 / 1 | 88.6% casein | 1 | 56 | Cycle, soccer | After physical activity |
| Lollo 2014 (Lollo et al., 2014) | Brazil | Random, double-blinding | Soccer players | 18.0 | 74.0 | 178.5 | 24 | - | 24 | 0.5 g/kg concentrate / 0.5 g/kg of hydrolysed | 2 / 2 | Maltodextrin | 2 | 180 | Soccer training | Before and after physical activity |

| Study | Country | Design | Population | Age | Weight | Height | | | | Intervention | | Comparison | | | Exercise | Timing |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Macdermid 2006 (Macdermid & Stannard, 2006) | New Zealand | Random, balanced order, blinding | Cyclists | 33.6 | 68.6 | 175.4 | 7 | - | 7 | 1.2–1.4 g/kg/d with carbohydrate intake of 7–10 g/kg | 1 | Protein intake of 3–4 g/kg/d and a carbohydrate intake of ≤ 5 g/kg | 1 | 16 | Cycle | During physical activity |
| Mero 1997 (Mero et al., 1997) | Finland | Random, crossover, double-blinding | Sprinters and jumpers | 25.0 | 76.1 | 181.0 | 9 | - | 9 | 125 ml with IGF-I and 0.057 g/l igg | 1 | 125 ml Bioenervi | 1 | 41 | Leg extensors, leg flexors, jump, run, squat, calf raises, breach press, skip | After physical activity |
| | | | | | | | | | | | | 25 ml Bioenervi | 1 | | | |
| Morifuji 2012 (Morifuji et al., 2012) | Japan | Non-random, crossover, double-blinding | Trained men | 22.0 | 61.1 | 171.3 | 8 | - | 8 | 3.0 g with 17.5 g carbohydrate | 4 | 17.5 g carbohydrate (Carbohydrates were provided as maltodextrin) | 4 | 9 | Cycle | After physical activity |
| | | | | | | | | | | 8.0 g with 17.5 g carbohydrate | 4 | | | | | |
| Naclerio 2015 (Naclerio, Larumbe-Zabala, Cooper, Allgrove, & Earnest, 2015) | United Kingdom | Random, counterbalanced, cross over, double-blinding | Amateur soccer players | 24.0 | 77.5 | 181.0 | 16 | - | 16 | 14.5 g with multi-ingredient (MTN; carbohydrate (53 g), L-glutamine (5 g), and L-carnitine L-tartrate (1.5 g), | 4 | 69.5 g carbohydrate | 4 | 13 | Run, jog, run | Before, during, after physical activity |
| | | | | | | | | | | | | Placebo | 4 | | | |

| Study | Country | Design | Population | Age | Weight | Height | n | - | n | Intervention | n | Comparison | n | | Exercise | Timing |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Nelson 2013 (A. R. Nelson et al., 2013) | New Zealand | Random, crossover, double-blinding | Cyclists or triathletes | 35.0 | 76.9 | 182.0 | 12 | - | 12 | 1.9 g/kg/day with leucine, carbohydrate–fat | 3 | Isocaloric carbohydrate–fat control | 3 | 26 | Cycle | After physical activity |
| Oosthuyse 2015 (Oosthuyse et al., 2015) | South Africa | Random, four way crossover, double-blinding | Cyclists | 38.9 | 78.5 | 179.8 | 8 | - | 8 | 15 g/h | 9 | Casein hydrolysate with 63 g/h fructose | 9 | 11 | Cycle | Before and during physical activity |
| | | | | | | | | | | | | Carbohydrate | 9 | | | |
| Oosthuyse 2016 (Oosthuyse & Millen, 2016) | South Africa | Random, four way crossover, double-blinding | Cyclists | 38.9 | 78.5 | 179.8 | 8 | - | 8 | Carbohydrate-whey hydrolysate | 3 | Carbohydrate | 3 | 30 | Cycle | Before and during physical activity |
| | | | | | | | | | | | | Carbohydrate-casein hydrolysate | 3 | | | |
| | | | | | | | | | | | | Placebo | 3 | | | |
| Parr 2014 (Parr et al., 2014) | Australia | Random, counterbalanced, crossover | Physically active | 21.4 | 79.3 | NA | 8 | - | 8 | 25 g | 2 | 25 g maltodextrin with alcohol | 2 | 16 | Plate-loaded leg extension | After physical activity |
| | | | | | | | | | | 25 g with alcohol | 6 | | | | | |
| Rankin 2006 (Rankin et al., 2006) | United States | Random, blinding | Well-trained | 22.6 | 72.5 | NA | 20 | - | 20 | 40 g with 0.92 cysteine | 2 | 40 g nonhydrolyzed casein, 0.12 cysteine | 2 | 21 | Cycle | Before and after physical activity |

| Study | Country | Design | Population | Age | Weight | Height | n | n | n | Intervention | Frequency | Comparison | Frequency | Duration | Exercise | Timing |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Ronghui 2015 (Ronghui, 2015) | China | Random | Basketball athletes | NA | NA | NA | | 10 | 10 | 20 g with 250 ml of whole milk | Once every two days | Oligosaccharides 40 g dissolved in 250 ml of whole milk | Once every two days | 30 | Cycle | After physical activity |
| Schroer 2014 (Schroer et al., 2014) | United States | Random, counterbalanced, placebo-controlled, double-blinding | Cyclists | 22.3 | 70.0 | 167.0 | 4 | 4 | 8 | 45 g/L | Every 15 minutes | 15 g/ of L-alanine<br><br>Placebo | Every 15 minutes | 16 | Cycle | Before and after physical activity |
| She 2005 (She, 2005) | China | Non-random, longitudinal | Track and field athletes | 15.5 | NA | NA | 8 | 8 | 16 | Whey with sugar, changbai jing xian ling hematopoietic fermin | 1 | Changbai jing xian ling (1)<br>Changbai jing xian ling, hematopoietic fermin (1)<br>Changbai jing xian ling, hematopoietic fermin, sugar (1) | 1 | 330 | Field and track training | Unknown |
| Shing 2006 (Shing et al., 2006) | Australia | Random, placebo controlled, double-blinding | Road cyclists | 28.0 | 76.4 | 179.9 | 29 | - | 29 | 10 g with 50 ml water and 100 ml skim milk | 1 | 10 g Intact bovine CPC, 50 ml water and 100 ml skim milk | 1 | 70 | Cycle | Unknown |

| Shing 2007 (Shing et al., 2007) | Austra lia | Random, placebo controlled, double-blinding | Road cyclists | 28.0 | 76.4 | 179.5 | 29 | - | 29 | 10 g with 50 ml water and 100 ml skim milk | 1 | 10 g Intact bovine CPC, 50 ml water and 100 ml skim milk | 1 | 63 | Cycle | Before physical activity |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Shing 2013 (Shing et al., 2013) | Austra lia | Random, placebo controlled, double-blinding | Road cyclists | 22.5 | 70.6 | 175.5 | 10 | - | 10 | 10 g with 50 ml water and 100 ml skim milk | 2 | 10 g Intact bovine CPC, 50 ml water and 100 ml skim milk | 2 | 56 | Cycle | Before and after physical activity |
| Smith 2010 (Smith, Fukuda, Kendall, & Stout, 2010) | United States | Random, placebo controlled parallel, single-blinding | Moder ately-trained | 21.1 | 66.2 | 173.4 | | 24 | 24 | 8 g with cholesterol, sodium carbohydrates, sugar, vitamin A, C B12, B6 | 1 | Maltodextrin: 17 g | 1 | 21 | Run | Before physical activity |
| Tang 2007 (Tang et al., 2007) | Canad a | Random, crossover, counterbalanced, double-blinding | Resista nce-trained | 21.0 | NA | NA | 8 | - | 8 | 10 g with 21 g of fructose (500 kj) in 227 ml of water | 1 | Carbohydrate in the form of 21 g of fructose and 10 g of maltodextrin (500 kj) in 227 ml of water | 1 | 16 | Resistance exercise, weight lifted | Before physical activity |

| Study | Country | Design | Population | Age | Weight | Height | | | | Intervention | | Control | | | Exercise | Timing |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Taylor 2016 (Taylor et al., 2016) | United States | Random, double-blinding | Basketball players | 20.5 | 67.1 | 169.5 | | 14 | 14 | 24 g with in water | 2 | 24 g of maltodextrin | 2 | 56 | Lower body resistance, "explosive" exercises such as squat jumps, push jerks, and hang cleans), training drills | Before and after physical activity |
| Vegge 2012 (Vegge et al., 2012) | Norway | Random, crossover, double-blinding | Cyclists | 22.0 | NA | NA | 12 | - | 12 | 15.3 g/h with maltodextrin (1); 12.4 g/h with 2.7 g/h nutripeptin, 60 g/h maltodextrin (1) | 1; 1 | 60 g/h maltodextrin | 1 | 60 | Cycle | During physical activity |
| Wilborn 2013 (Wilborn et al., 2013) | United States | Random, double-blinding | Basketball players | 20.5 | 67.0 | 155.5 | | 16 | 16 | 24 g with 120 calories, 1 g of total fat, 4 g of total carbohydrate | 2 | 24 g Casein protein g of total fat, 3 g of carbohydrates | 2 | 56 | Jump, run, side shuffle, bench press and leg press | Before and after physical activity |
| Witard 2014 (Witard et al., 2014) | United Kingdom | Non-random, parallel, single-blinding | Weight lifter | 21.0 | 82.3 | 180.7 | 48 | - | 48 | 10 g (1); 20 g (1); 40 g (1) | 1; 1; 1 | Placebo | 1 | 10 | Leg-press and -extension exercises, | After physical activity |
| Yang 2014 (Yang, 2014) | China | Random | Track and field athletes | 16.0 | 55.6 | 169.0 | 14 | 6 | 20 | 1) 900 ml, 2)2.5 ml | 3 | 1) purified water 900 ml, 2) 2.5 ml | 3 | 1 | Track and field | Before and after physical activity |

## 4.3 Risk of bias

### 4.3.1 Overview

A total of 45 RCTs were assessed using the Cochrane Risk of Bias Assessment tool (Appendix 3). The outcome of the assessment (Figure 2) is 18 studies (40%) have overall low RoB, 19 studies (42%) have overall unclear RoB and 8 studies (18%) have overall high RoB (Breen et al., 2011; Burke et al., 2012; Fukuda et al., 2010; Hansen et al., 2015; Hansen et al., 2016; Hill et al., 2013; Hofman et al., 2002; Smith et al., 2010).

For five non-RCTs were assessment based on the ROBINS-I (Appendix 4), only a study has overall serious RoB (She, 2005), while four studies have overall low RoB (Fahlström et al., 2006; Kraemer et al., 2015; Morifuji et al., 2012; Witard et al., 2014).

### 4.3.2 Risk of bias for RCTs

The summary of overall (Figure 2) and individual studies (Figure 3) show that the allocation concealment and the selective outcome reporting domain have high RoB. The allocation concealment has 27 studies (60%) low RoB and 7 studies (16%) high RoB (Breen et al., 2011; Fukuda et al., 2010; Hansen et al., 2015; Hansen et al., 2016; Hill et al., 2013; Hofman et al., 2002; Smith et al., 2010). The high RoB is because of the 7 studies conducted in single blinding, thus, either participants or investigators could possibly foresee assignments and impact on participants' behaviour and participation and outcome assessment.

For selective outcome reporting, it has 44 studies (98%) low RoB and one study (2%) high

RoB (Burke et al., 2012). This because Burke and colleagues reported using have more than

one primary outcomes that were for measurements. On the other hand, all RCTs have low

RoB on incomplete outcome data and other sources of bias domains.
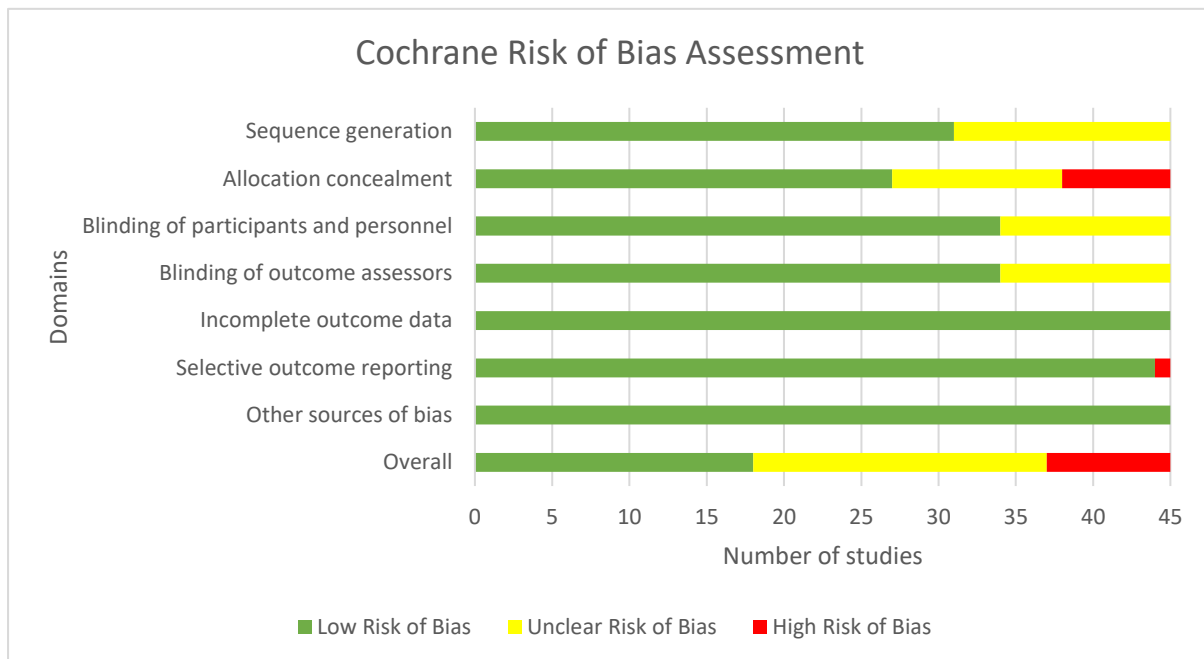


Figure 2. Summary of the Cochrane Risk of Bias Assessment for the RCTs

| First Author Surname and Year | Sequence generation | Allocation concealment | Blinding of participants, personnel | Blinding of outcome assessors | Incomplete outcome data | Selective outcome reporting | Other sources of bias | Overall |
|---|---|---|---|---|---|---|---|---|
| Al-Nawaiseh 2016 | + | ? | ? | ? | + | + | + | ? |
| Areta 2014 | + | ? | ? | ? | + | + | + | ? |
| Breen 2011 | + | - | + | + | + | + | + | - |
| Brinkworth 2002 | + | + | + | + | + | + | + | + |
| Brown 2004 | ? | + | + | + | + | + | + | ? |
| Buckley 2000 | + | + | + | + | + | + | + | + |
| Burke 2012 | + | + | + | + | + | - | + | - |
| Cepero 2010 | + | + | + | + | + | + | + | + |
| Coombes 2002 | + | + | + | + | + | + | + | + |
| Cribb 2006 | ? | + | + | + | + | + | + | ? |
| Cury-boaventura 2008 | + | + | + | + | + | + | + | + |
| Detko 2013 | + | + | + | + | + | + | + | + |
| Fukuda 2010 | + | - | + | + | + | + | + | - |
| Gunnarsson 2013 | ? | ? | ? | ? | + | + | + | ? |
| Hansen 2015 | + | - | + | + | + | + | + | - |
| Hansen 2016 | + | - | + | + | + | + | + | - |
| Highton 2012 | + | + | + | + | + | + | + | + |
| Hill 2013 | + | - | + | + | + | + | + | - |
| Hoffman 2009 | ? | ? | ? | ? | + | + | + | ? |
| Hofman 2002 | + | - | + | + | + | + | + | - |
| Impey 2015 | + | ? | ? | ? | + | + | + | ? |
| Jauhari 2014 | ? | + | + | + | + | + | + | ? |
| Joy 2013 | ? | + | + | + | + | + | + | ? |
| Li 2007 | ? | ? | ? | ? | + | + | + | ? |
| Lollo 2011 | ? | + | + | + | + | + | + | ? |
| Lollo 2014 | ? | + | + | + | + | + | + | ? |
| Macdermid 2006 | + | ? | ? | ? | + | + | + | ? |
| Mero 1997 | + | + | + | + | + | + | + | + |
| Naclerio 2015 | + | + | + | + | + | + | + | + |
| Nelson 2013 | + | + | + | + | + | + | + | + |
| Oosthuyse 2015 | + | + | + | + | + | + | + | + |
| Oosthuyse 2016 | + | + | + | + | + | + | + | + |
| Parr 2014 | + | ? | ? | ? | + | + | + | ? |
| Rankin 2006 | ? | ? | ? | ? | + | + | + | ? |
| Ronghui 2015 | ? | ? | ? | ? | + | + | + | ? |
| Schroer 2014 | + | + | + | + | + | + | + | + |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Shing 2006 | + | + | + | + | + | + | + | + |
| Shing 2007 | + | + | + | + | + | + | + | + |
| Shing 2013 | + | + | + | + | + | + | + | + |
| Smith 2010 | + | - | + | + | + | + | + | - |
| Tang 2007 | + | + | + | + | + | + | + | + |
| Taylor 2016 | ? | + | + | + | + | + | + | ? |
| Vegge 2012 | + | + | + | + | + | + | + | + |
| Wilborn 2013 | ? | + | + | + | + | + | + | ? |
| Yang 2014 | ? | ? | ? | ? | + | + | + | ? |

| + | Low Risk of Bias | ? | Unclear Risk of Bias | - | High Risk of Bias |
|---|---|---|---|---|---|

Figure 3. Summary of the Cochrane Risk of Bias Assessment for the individual RCTs.

### 4.3.3  Risk of bias for non-RCTs

Based on ROBINS-I, the summary of overall (Figure 4) illustrate that serious RoB lies on bias in bias in measurement of outcomes domains: one study (20%) serious RoB and 4 studies (80%) low RoB (Fahlström et al., 2006; Kraemer et al., 2015; Morifuji et al., 2012; Witard et al., 2014). Figure 5 shows that She (2005) is the study caused the serious RoB as it was not blinded study and the duration of given supplements was differ. On the other hand, three domains have low RoB: Bias in selection of participants into the study, bias due to deviations from intended intervention and bias due to missing data.
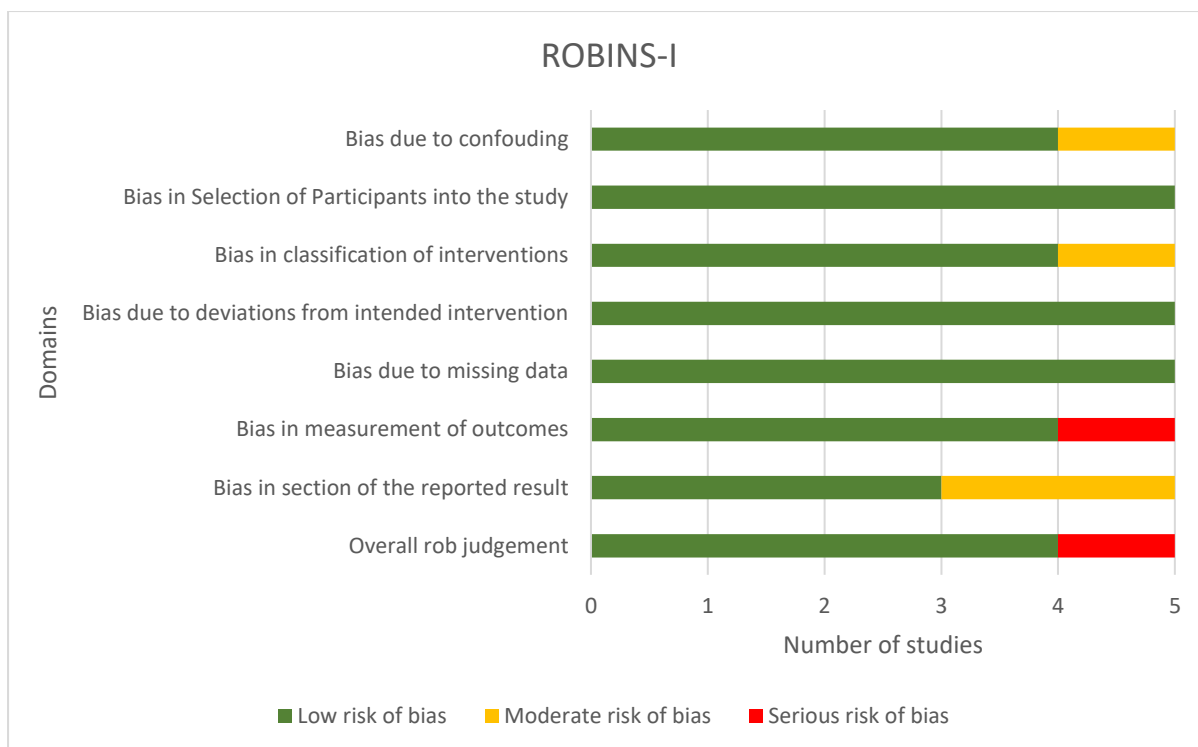
Figure 4. Summary of ROBINS-I for the non-RCTs

| First Author Surname and Year | Bias due to confouding | Bias in Selection of Participants into the study | Bias in classification of interventions | Bias due to deviations from intended intervention | Bias due to missing data | Bias in measurement of outcomes | Bias in section of the reported result | Overall RoB judgement |
|---|---|---|---|---|---|---|---|---|
| Fahlström 2006 | + | + | + | + | + | + | ? | + |
| Kraemer 2015 | + | + | + | + | + | + | + | + |
| Morifuji 2012 | + | + | + | + | + | + | + | + |
| She 2005 | ? | + | ? | + | + | – | + | – |
| Witard 2014 | + | + | + | + | + | + | ? | + |

| + | Low risk of bias | ? | Moderate risk of bias | – | Serious risk of bias |
|---|---|---|---|---|---|

Figure 5. Summary of ROBINS-I for the individual non-RCTs

**4.4    Meta-analysis**

The meta-analysis of 38 studies was conducted and outcomes analyzed were: -

   a. Vital signs of athletes which were heart rate, RER, RPE and $VO_{2max}$ ;

   b. Serum protein which was myoglobin and muscle glycogen;

   c. Strength and body composition which were maximum power, average power and body mass;

   d. Blood profile which was EAA, BCAA, creatine kinase and glucose;

   e. Hormones which were insulin, cortisol and testosterone.


The forest plots generated by STATA software divided into four columns. The first column is the lists of eligible individual study IDs. The study IDs displays as first author surname and year. In this study, most of the meta-analysis outputs and graphs appear to have repeated of same study IDs. This is because one publication was compared more than one interventions or comparators groups. Therefore, letters A, B and C were used to distinguish 2 or 3 groups separately reported within one publication (Fotino, Thompson-Paul, & Bazzano, 2013).


The second column visual display on the individual study results. The filled vertical line in the middle is called 'the line of no effect' or "line of null effect", which has the value of 0 in case of a continuous outcome variable (Ried, 2006). Moreover, the filled vertical line is a separation between the control arms or groups and the experimental arm or the intervention groups. The horizontal lines (whiskers) through the filled squares illustrate 95% CI for the individual study. The size of filled squares is the weight of the individual study in the meta-analysis. The open diamond in the last row indicates an overall result of the meta-

analysis the third column gives the numerical results of WMD and 95% CI on the individual study. Then, the fourth column gives the numerical results of percentage weighted influence (%) on the individual study. Lastly, at the scale of supplements effect, intervention described as WPS, while others as comparators or control.

### 4.4.1 Vital signs outcome

#### a) Heart rate

Twelve studies met the inclusion criteria for effect of WPS on heart rate. Figure 6 illustrates that heart rate slight increase by the overall of 0.52 bpm (CI = -1.07, 2.11; $I^2$ = 62.3%; p = 0.002) in the intervention group compared to the control groups (Appendix 5: 8.5.1. a). Nine studies were favourable to the intervention group: Gunnarsson (2013) study carried the highest (26.65%) weighted influences and Schroer -B (2014) study carried the lowest (1.47%) weighted influences. Oppositely, three studies reported favourable to the control group. Two of these three studies had large weighted influence: Impey (2015) study carried the highest (24.88%) weighted influences and Li (2007) study carried the lowest (1.74%) weighted influences. For the publication bias, the funnel plot (Figure 7) described that there was slight publication bias as the majority studies were within 95% confidence limits and asymmetrical, along with Egger test, where the bias was -0.63 (CI = -1.47, 1.35; p = 0.92) (Appendix 5: 8.5.1. a) iv).

| Study ID | WMD (95% CI) | N, mean (SD); Intervention Group | N, mean (SD); Control Group | % Weight |
|---|---|---|---|---|
| Breen (2011) | -1.00 (-2.39, 0.39) | 10, 171 (2) | 10, 172 (1) | 23.19 |
| Gunnarsson (2013) | 2.00 (1.29, 2.71) | 9, 166 (.67) | 7, 164 (.76) | 26.65 |
| Highton (2012) | 1.00 (-5.47, 7.47) | 9, 163 (7) | 9, 162 (7) | 4.96 |
| Impey (2015) | -1.00 (-2.09, 0.09) | 9, 163 (1) | 9, 164 (1.33) | 24.88 |
| Li (2007) | -1.00 (-12.67, 10.67) | 8, 138 (11.6) | 8, 139 (12.2) | 1.74 |
| Oosthuyse -A (2016) | 3.00 (-4.90, 10.90) | 8, 87 (7) | 8, 84 (9) | 3.53 |
| Oosthuyse -B (2016) | 2.00 (-5.37, 9.37) | 8, 87 (7) | 8, 85 (8) | 3.98 |
| Oosthuyse -C (2016) | 3.00 (-8.47, 14.47) | 8, 87 (7) | 8, 84 (15) | 1.79 |
| Schroer -A (2014) | 5.00 (-5.23, 15.23) | 8, 146 (13) | 8, 141 (7) | 2.22 |
| Schroer -B (2014) | 2.00 (-10.74, 14.74) | 8, 146 (13) | 8, 144 (13) | 1.47 |
| Vegge -A (2012) | 1.00 (-8.60, 10.60) | 12, 150 (12) | 12, 149 (12) | 2.49 |
| Vegge -B (2012) | 1.00 (-7.49, 9.49) | 12, 150 (9) | 12, 149 (12) | 3.11 |
| Overall  (I-squared = 62.3%, p = 0.002) | 0.52 (-1.07, 2.11) | 109 | 107 | 100.00 |

NOTE: Weights are from random effects analysis

Favor Control Group        Favor Intervention Group

Figure 6. Forest plot of the effect of WPS on heart rate (bpm).
Impey (2015) = WP vs carbohydrate
Oosthuyse -A (2016) = WP with carbohydrate vs carbohydrate,
Oosthuyse -B (2016) = WP with carbohydrate vs carbohydrate-casein,
Oosthuyse -C (2016) = WP with carbohydrate vs placebo,
Schroer -A (2014) = WP vs L-alanine,
Schroer -B (2014) = WP vs placebo,
Vegge -A (2012) = WP with maltodextrin vs maltodextrin,
Vegge -B (2012) = WP with nutripeptin and maltodextrin vs maltodextrin.
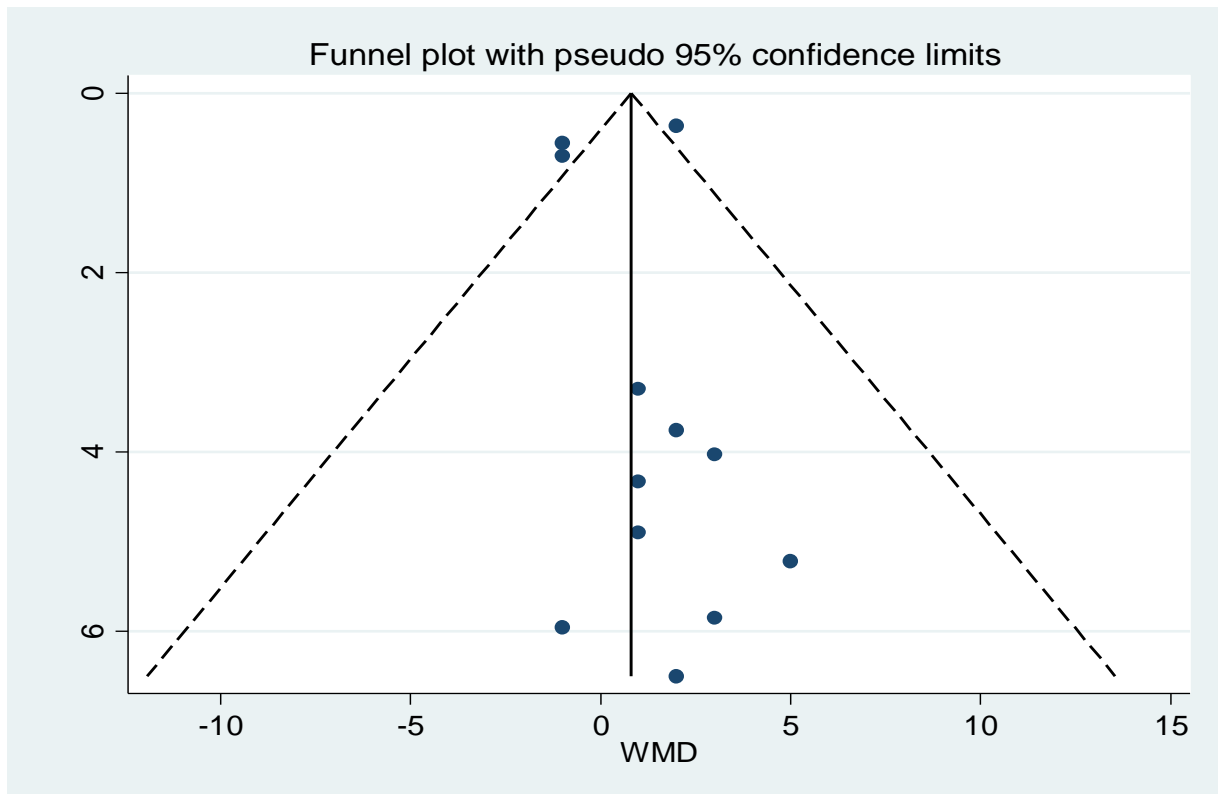
Figure 7. Funnel plot of the effect of WPS on heart rate (bpm) published studies.

Subgroup analyses conducted as there was moderate heterogeneity ($I^2$) of 62.3%. The subgroup analysis by the physical activities in Figure 8 demonstrations the cycle subgroup had no heterogeneity ($I^2$ = 0%; CI = -2.07, 0.6), while the other subgroups had standalone study. Figure 9 shows subgroup meta-analysis of intervention duration range has no heterogeneity at range period of 21-40 days ($I^2$ = 0%; CI = -2.07, 0.6) and 41-60 days ($I^2$ = 0%; CI = -5.36, 7.36). However, the other subgroups did not explain the heterogeneity as the $I^2$ value remained high and standalone study (Appendix 5: 8.5.1. a) v).
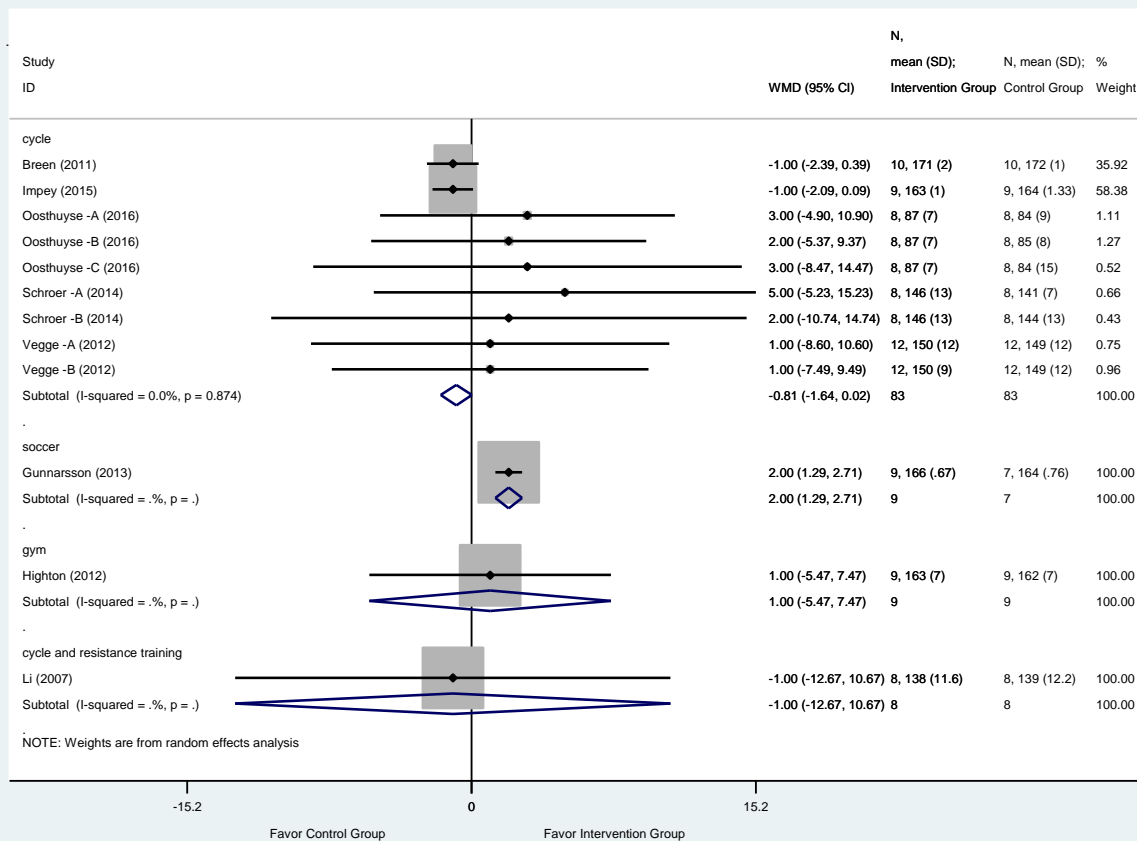
Figure 8. Funnel plot of subgroup by physical activities on the effect of WPS on heart rate (bpm).
Oosthuyse -A (2016) = WP with carbohydrate vs carbohydrate,
Oosthuyse -B (2016) = WP with carbohydrate vs carbohydrate-casein,
Oosthuyse -C (2016) = WP with carbohydrate vs placebo,
Schroer -A (2014) = WP vs L-alanine,
Schroer -B (2014) = WP vs placebo,
Vegge -A (2012) = WP with maltodextrin vs maltodextrin,
Vegge -B (2012) = WP with nutripeptin and maltodextrin vs maltodextrin.

| Study ID | WMD (95% CI) | N, mean (SD); Intervention Group | N, mean (SD); Control Group | % Weight |
|---|---|---|---|---|
| **21-40** | | | | |
| Breen (2011) | -1.00 (-2.39, 0.39) | 10, 171 (2) | 10, 172 (1) | 92.53 |
| Oosthuyse -A (2016) | 3.00 (-4.90, 10.90) | 8, 87 (7) | 8, 84 (9) | 2.85 |
| Oosthuyse -B (2016) | 2.00 (-5.37, 9.37) | 8, 87 (7) | 8, 85 (8) | 3.28 |
| Oosthuyse -C (2016) | 3.00 (-8.47, 14.47) | 8, 87 (7) | 8, 84 (15) | 1.35 |
| Subtotal (I-squared = 0.0%, p = 0.586) | -0.73 (-2.07, 0.60) | 34 | 34 | 100.00 |
| . | | | | |
| **1-20** | | | | |
| Gunnarsson (2013) | 2.00 (1.29, 2.71) | 9, 166 (.67) | 7, 164 (.76) | 41.48 |
| Highton (2012) | 1.00 (-5.47, 7.47) | 9, 163 (7) | 9, 162 (7) | 10.60 |
| Impey (2015) | -1.00 (-2.09, 0.09) | 9, 163 (1) | 9, 164 (1.33) | 39.60 |
| Schroer -A (2014) | 5.00 (-5.23, 15.23) | 8, 146 (13) | 8, 141 (7) | 4.97 |
| Schroer -B (2014) | 2.00 (-10.74, 14.74) | 8, 146 (13) | 8, 144 (13) | 3.34 |
| Subtotal (I-squared = 81.0%, p = 0.000) | 0.86 (-1.57, 3.28) | 43 | 41 | 100.00 |
| . | | | | |
| **61-80** | | | | |
| Li (2007) | -1.00 (-12.67, 10.67) | 8, 138 (11.6) | 8, 139 (12.2) | 100.00 |
| Subtotal (I-squared = .%, p = .) | -1.00 (-12.67, 10.67) | 8 | 8 | 100.00 |
| . | | | | |
| **41-60** | | | | |
| Vegge -A (2012) | 1.00 (-8.60, 10.60) | 12, 150 (12) | 12, 149 (12) | 43.86 |
| Vegge -B (2012) | 1.00 (-7.49, 9.49) | 12, 150 (9) | 12, 149 (12) | 56.14 |
| Subtotal (I-squared = 0.0%, p = 1.000) | 1.00 (-5.36, 7.36) | 24 | 24 | 100.00 |

NOTE: Weights are from random effects analysis

-15.2     0     15.2

Favor Control Group     Favor Intervention Group

Figure 9. Funnel plot of subgroup by intervention period range on the effect of WPS on heart rate (bpm).
Oosthuyse -A (2016) = WP with carbohydrate vs carbohydrate,
Oosthuyse -B (2016) = WP with carbohydrate vs carbohydrate-casein,
Oosthuyse -C (2016) = WP with carbohydrate vs placebo,
Schroer -A (2014) = WP vs L-alanine,
Schroer -B (2014) = WP vs placebo,
Vegge -A (2012) = WP with maltodextrin vs maltodextrin,
Vegge -B (2012) = WP with nutripeptin and maltodextrin vs maltodextrin.

## b) Respiratory exchange ratio

Of the collected studies, five studies were found that involved WPS with RER. Figure 10 indicating the overall is 0.004 (CI = -0.003, 0.01; $I^2$ = 14.5%; p = 0.32) of RER increase in the intervention group compared to the control group (Appendix 5: 8.5.1. b). There also was low heterogeneity between studies. The individual studies were either at the no effect line or favourable to the intervention group. Among the studies, Breen (2011) study had the highest (66.2%) weighted influences and Schroer -A (2014) study had the lowest (4.08%) weighted influences.
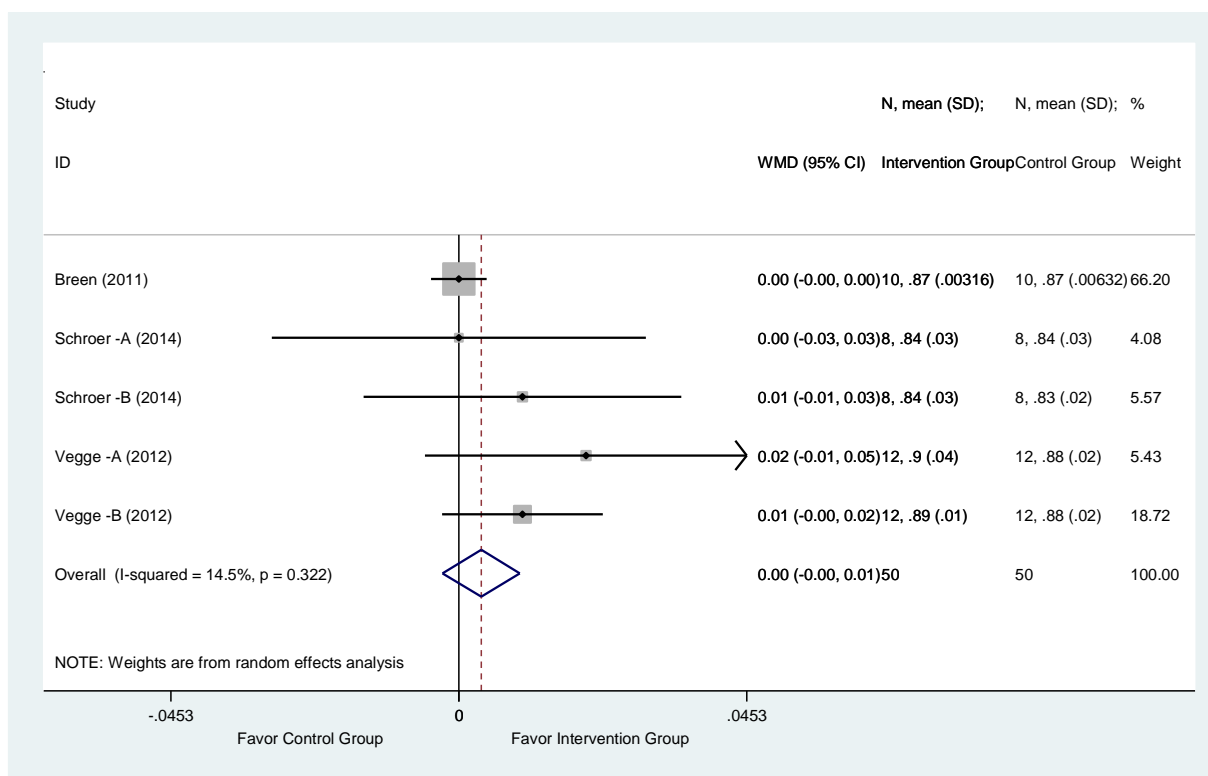


Figure 10. Forest plot of the effect of WPS on RER.
Schroer -A (2014) = WP vs L-alanine,
Schroer -B (2014) = WP vs placebo,
Vegge -A (2012) = WP with maltodextrin vs maltodextrin,
Vegge -B (2012) = WP with nutripeptin and maltodextrin vs maltodextrin.

## c) Rate perceived exertion

A total of eight studies that involved WPS and RPE (Figure 11). The analysis implying that the overall of RPE was 0.258 (CI = -1.09, 0.57; $I^2$ = 95.1%; p = 0.00) reduce in the intervention group than the control group (Appendix 5: 8.5.1. c). Two studies were favourable to the intervention group: Breen (2011) and Impey -A (2015) with weighted influence of 14.22% and 14.18% respectively. While, five studies were favourable to the control group: Impey -B (2015) study carried the highest (14.18%) weighted influences and Schroer -B (2014) study carried the lowest (11%) weighted influences. The subgroup analyses were conducted as there was high heterogeneity (95.1%), (Appendix 5: 8.5.1. c) iii). However, heterogeneity of both subgroup analyses remaining moderate-high between studies and a standalone study. Hence, the subgroup analyses did not explain the heterogeneity.
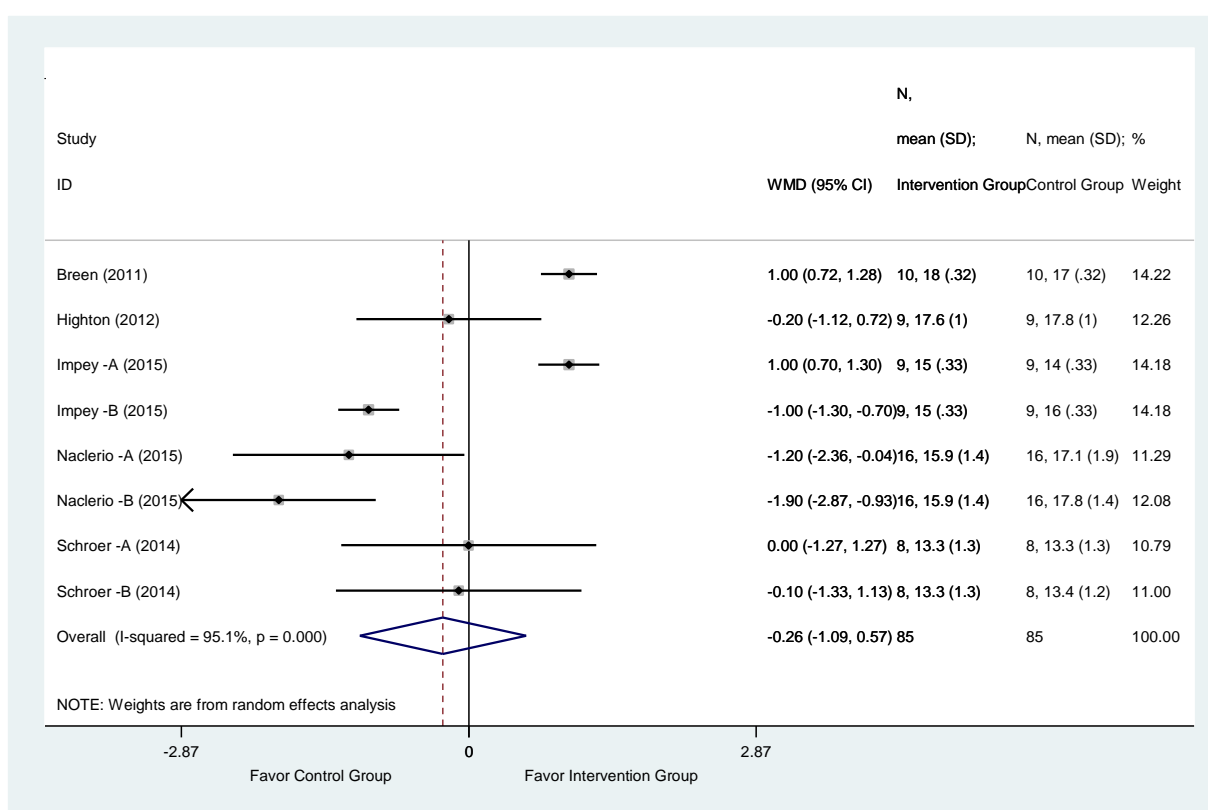


Figure 11. Forest plot of the effect of WPS on RPE.
Impey -A (2015) = WP protein vs carbohydrate,
Impey -B (2015) = WP with caffeine vs carbohydrate,
Naclerio -A (2015) = WP with multi-ingredient vs carbohydrate,
Naclerio -B (2015) = WP with multi-ingredient vs placebo,
Schroer -A (2014) = WP vs L-alanine,
Schroer -B (2014) = WP vs placebo.

### d) Maximum volume of oxygen

A total of nine studies met the inclusion criteria for effect of WP on $VO_{2max}$ , as shown in Figure 12. A slight rise of $VO_{2max}$ by 1.33 ml/kg/min (CI = 4.71, 7.36; $I^2$ = 98.8%; p = 0.00) in the intervention group compared to the control group (Appendix 5: 8.5.1. d). Five of nine studies carried were favourable to the intervention group: Vegge -A (2012) study carried the highest (16.96%) weighted influences and Schroer -A and -B (2014) studies carried the lowest (0.04%) weighted influence. Two studies favourable to the control group were Coombes -A and -B (2002) with weighted influence of 15%. Breen (2011) and Shing (2006) were studies that lies on the no effect line with 17.5% and 0.03% weighted influence respectively.



| Study ID | WMD (95% CI) | N, mean (SD); Intervention Group | N, mean (SD); Control Group | % Weight |
|---|---|---|---|---|
| Breen (2011) | 0.00 (-0.64, 0.64) | 10, 50.9 (.82) | 10, 50.9 (.63) | 17.50 |
| Coombes -A (2002) | -4.00 (-8.74, 0.74) | 10, 56 (2) | 9, 60 (7) | 15.82 |
| Coombes -B (2002) | -1.00 (-6.27, 4.27) | 9, 59 (4) | 9, 60 (7) | 15.47 |
| Schroer -A (2014) | 60.00 (-238.93, 358.93) | 8, 2740 (310) | 8, 2680 (300) | 0.04 |
| Schroer -B (2014) | 30.00 (-264.16, 324.16) | 8, 2740 (310) | 8, 2710 (290) | 0.04 |
| Shing (2006) | 0.00 (-378.74, 378.74) | 15, 4930 (520) | 14, 4930 (520) | 0.03 |
| Smith (2010) | 10.90 (10.32, 11.48) | 13, 56.2 (.75) | 11, 45.3 (.69) | 17.50 |
| Vegge -A (2012) | 0.40 (-2.24, 3.04) | 12, 41.3 (3.2) | 12, 40.9 (3.4) | 16.96 |
| Vegge -B (2012) | 0.60 (-2.73, 3.93) | 12, 41.5 (4.8) | 12, 40.9 (3.4) | 16.64 |
| Overall (I-squared = 98.8%, p = 0.000) | 1.32 (-4.71, 7.36) | 97 | 93 | 100.00 |

NOTE: Weights are from random effects analysis

-379   0   379
Favor Control Group   Favor Intervention Group

Figure 12. Forest plot of the effect of WPS on $VO_{2max}$ (ml/kg/min).
Coombes -A (2002) = WP alone vs bovine colostrum,
Coombes -B (2002) = WP with bovine colostrum vs bovine colostrum,
Schroer -A (2014) = WP vs L-alanine,
Schroer -B (2014) = WP vs placebo,
Vegge -A (2012) = WP with maltodextrin vs maltodextrin,
Vegge -B (2012) = WP with nutripeptin and maltodextrin vs maltodextrin.

The subgroup analyses were performed as high heterogeneity (98.8%) was detected. Figure 13 shows two subgroup analyses had no heterogeneity: cycle subgroup ($I^2$ = 0.0%; CI = -0.57, 0.65) and resistance and the cycle subgroup ($I^2$=0.0%; CI = -6.18, 0.86). Moreover, two subgroup analysis by intervention period range (Figure 14) had no evidence of heterogeneity: 1-20 days ($I^2$ = 0.0%; CI = -164.91, 254.43) and 41-60 days ($I^2$= 0.0%; CI = -2.11, 1.46). However, the other subgroups did not explain the heterogeneity as the $I^2$ value remained high and standalone study (Appendix 5: 8.5.1. d) iii).

| Study ID | WMD (95% CI) | N, mean (SD); Intervention Group | N, mean (SD); Control Group | % Weight |
|---|---|---|---|---|
| **cycle** | | | | |
| Breen (2011) | 0.00 (-0.64, 0.64) | 10, 50.9 (.82) | 10, 50.9 (.63) | 91.24 |
| Schroer -A (2014) | 60.00 (-238.93, 358.93) | 8, 2740 (310) | 8, 2680 (300) | 0.00 |
| Schroer -B (2014) | 30.00 (-264.16, 324.16) | 8, 2740 (310) | 8, 2710 (290) | 0.00 |
| Shing (2006) | 0.00 (-378.74, 378.74) | 15, 4930 (520) | 14, 4930 (520) | 0.00 |
| Vegge -A (2012) | 0.40 (-2.24, 3.04) | 12, 41.3 (3.2) | 12, 40.9 (3.4) | 5.37 |
| Vegge -B (2012) | 0.60 (-2.73, 3.93) | 12, 41.5 (4.8) | 12, 40.9 (3.4) | 3.38 |
| Subtotal (I-squared = 0.0%, p = 0.996) | 0.04 (-0.57, 0.65) | 65 | 64 | 100.00 |
| . | | | | |
| **cycle and resistance training** | | | | |
| Coombes -A (2002) | -4.00 (-8.74, 0.74) | 10, 56 (2) | 9, 60 (7) | 55.27 |
| Coombes -B (2002) | -1.00 (-6.27, 4.27) | 9, 59 (4) | 9, 60 (7) | 44.73 |
| Subtotal (I-squared = 0.0%, p = 0.407) | -2.66 (-6.18, 0.86) | 19 | 18 | 100.00 |
| . | | | | |
| **run** | | | | |
| Smith (2010) | 10.90 (10.32, 11.48) | 13, 56.2 (.75) | 11, 45.3 (.69) | 100.00 |
| Subtotal (I-squared = .%, p = .) | 10.90 (10.32, 11.48) | 13 | 11 | 100.00 |
| . | | | | |
| NOTE: Weights are from random effects analysis | | | | |

-379     0     379

Favor Control Group     Favor Intervention Group

Figure 13. Forest plot of subgroup by physical activities on the effect of WPS on $VO_{2max}$ (ml/kg/min).
Coombes -A (2002) = WP alone vs bovine colostrum,
Coombes -B (2002) = WP with bovine colostrum vs bovine colostrum,
Schroer -A (2014) = WP vs L-alanine,
Schroer -B (2014) = WP vs placebo,
Vegge -A (2012) = WP with maltodextrin vs maltodextrin,
Vegge -B (2012) = WP with nutripeptin and maltodextrin vs maltodextrin.
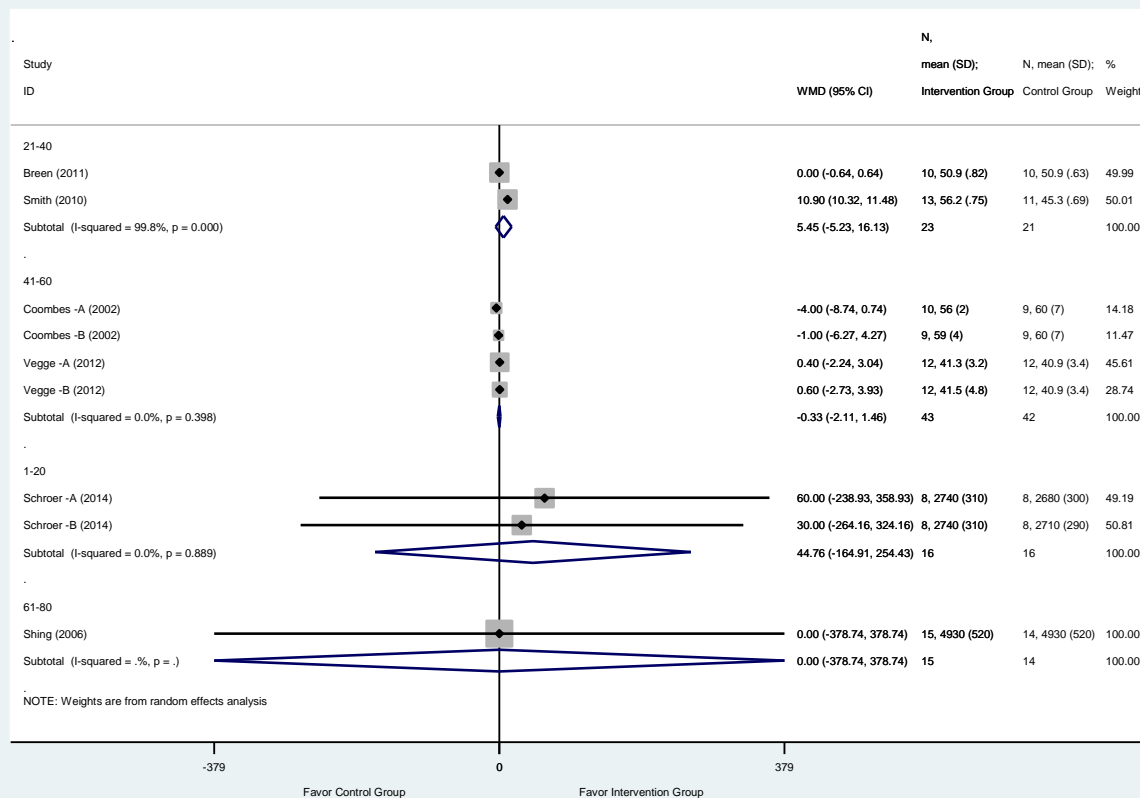
Figure 14. Forest plot of subgroup by intervention period range on the effect of WPS on $VO_{2max}$ (ml/kg/min).

Coombes -A (2002) = WP alone vs bovine colostrum,

Coombes -B (2002) = WP with bovine colostrum vs bovine colostrum,

Schroer -A (2014) = WP vs L-alanine,

Schroer -B (2014) = WP vs placebo,

Vegge -A (2012) = WP with maltodextrin vs maltodextrin,

Vegge -B (2012) = WP with nutripeptin and maltodextrin vs maltodextrin.

### 4.4.2 Serum protein outcome

#### a) Myoglobin

Three studies were found that involved WPS with myoglobin. Figure 15 illustrates that the

overall of myoglobin level reduces in the intervention group by 11.74 ng/ml (CI=-30.24, 6.76;

$I^2$ = 79.6%; p = 0.007) compared to the control group, yet has moderate-high heterogeneity

(Appendix 5: 8.5.2. a). Of two studies were favourable to the control group: Naclerio -A

(2015) (weighted = 44.02%) and Naclerio –B (2015) (weighted = 15.03%). While, Gunnarsson

(2013) study lie on the no effect line and had highest weighted influence amount of 40.95%.

However, the subgroup analyses did not explain the heterogeneity as the $I^2$ value remained

high and a standalone study (Appendix 5: 8.5.2. a) iii).



Figure 15. Forest plot of the effect of WPS on myoglobin (ng/ml).
Naclerio -A (2015) = WP with multi-ingredient vs carbohydrate,
Naclerio -B (2015) = WP with multi-ingredient vs placebo.

**b) Muscle glycogen**

Only three studies were found that involved WPS with muscle glycogen. Figure 16 indicating the overall of intervention group has enhanced muscle glycogen level compared to the control group by 9.08 mmol/L (CI =-23.19, 41.36: $I^2$ = 97.8%; p = 0.00) (Appendix 5: 8.5.2. b). Detko (2013) and Gunnarsson (2013) studies were favourable to the intervention group, while Hill (2013) study favourable to the control group. The weighted influence of the studies was fairly distributed among three studies: Detko (2013) study carried the highest (34.82%) weighted influences and Hill (2013) study carried the lowest (31.11%) weighted influences. Moreover, the heterogeneity was presented between studies with an $I^2$ of 97.8%. However, the subgroup analyses did not explain the heterogeneity as the $I^2$ value remained high and standalone study (Appendix 5: 8.5.2. b) iii).



Figure 16. Forest plot of the effect of WPS on muscle glycogen (mmol/L).

### 4.4.3 Strength and body composition outcome

#### a) Maximum power

Of the collected studies, eight studies met the inclusion criteria for maximum power. The

overall of maximum power shows in Figure 17 has slight decrease of 3.14 watt (CI = -129.47,

123.2; $I^2$ = 97.4%; p = 0.00) in the intervention group compared to the control group and

high heterogeneity (Appendix 5: 8.5.3. a). Six of eight studies were favorable to the

intervention group: Shing (2006) study carried the highest (13.38%) weighted influences and

Hoffman -B (2009) study carried the lowest (11.78%) weighted influences. Only two studies

were favorable to the control group with similar weighted influence: Hansen (2016) (weight

= 13.39%) and Macdermid (2006) (weight = 12.32%).
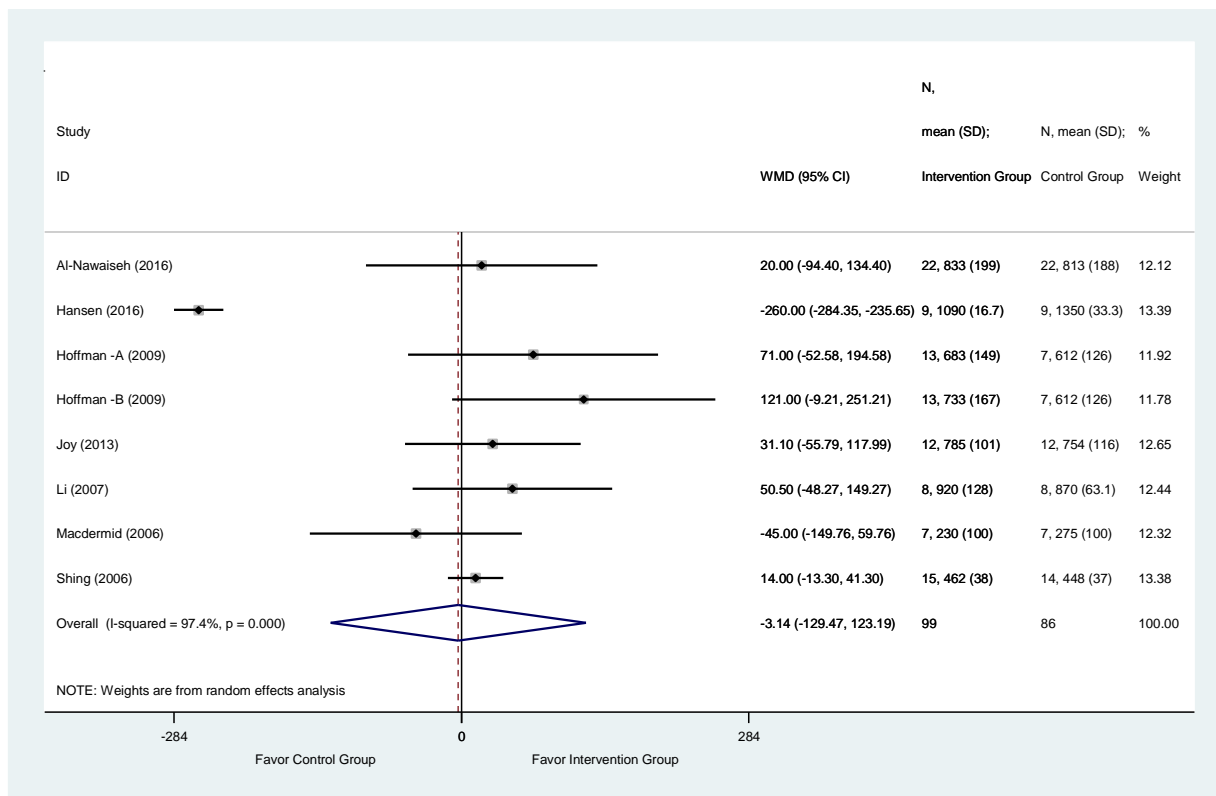


Figure 17. Forest plot of the effect of WPS on maximum power (watt).
Hoffman -A (2009) = WP with carbohydrate vs placebo,
Hoffman -B (2009) = WP with fat and carbohydrate vs placebo.

The physical active subgroup analysis in Figure 18 reports that the gym subgroup ($I^2$ = 0%;

CI = 5.06, 184.33) of has and no evidence of heterogeneity, while the cycle subgroup has low

($I^2$ = 12.3%; CI = -30.16, 44.30) heterogeneity. For the intervention duration range subgroup

analysis (Figure 19), range period of 61-80 days subgroup had low $I^2$ of 13.6% (CI = -5.57,

68.18). However, the other subgroups remained has high value of $I^2$ and a standalone

study, thus did not explain the heterogeneity (Appendix 5: 8.5.3. a) iii).



| Study ID | WMD (95% CI) | N, mean (SD); Intervention Group | N, mean (SD); Control Group | % Weight |
|---|---|---|---|---|
| cycle and resistance training | | | | |
| Al-Nawaiseh (2016) | 20.00 (-94.40, 134.40) | 22, 833 (199) | 22, 813 (188) | 24.17 |
| Hansen (2016) | -260.00 (-284.35, -235.65) | 9, 1090 (16.7) | 9, 1350 (33.3) | 26.15 |
| Joy (2013) | 31.10 (-55.79, 117.99) | 12, 785 (101) | 12, 754 (116) | 25.01 |
| Li (2007) | 50.50 (-48.27, 149.27) | 8, 920 (128) | 8, 870 (63.1) | 24.67 |
| Subtotal (I-squared = 96.6%, p = 0.000) | -42.91 (-242.89, 157.06) | 51 | 51 | 100.00 |
| gym | | | | |
| Hoffman -A (2009) | 71.00 (-52.58, 194.58) | 13, 683 (149) | 7, 612 (126) | 52.61 |
| Hoffman -B (2009) | 121.00 (-9.21, 251.21) | 13, 733 (167) | 7, 612 (126) | 47.39 |
| Subtotal (I-squared = 0.0%, p = 0.585) | 94.70 (5.06, 184.33) | 26 | 14 | 100.00 |
| cycle | | | | |
| Macdermid (2006) | -45.00 (-149.76, 59.76) | 7, 230 (100) | 7, 275 (100) | 11.75 |
| Shing (2006) | 14.00 (-13.30, 41.30) | 15, 462 (38) | 14, 448 (37) | 88.25 |
| Subtotal (I-squared = 12.3%, p = 0.285) | 7.07 (-30.17, 44.30) | 22 | 21 | 100.00 |

NOTE: Weights are from random effects analysis

-284          0          284

Favor Control Group          Favor Intervention Group

Figure 18. Forest plot of subgroup by physical activities on the effect of WPS on maximum power (watt).
Hoffman -A (2009) = WP with carbohydrate vs placebo,
Hoffman -B (2009) = WP with fat and carbohydrate vs placebo.
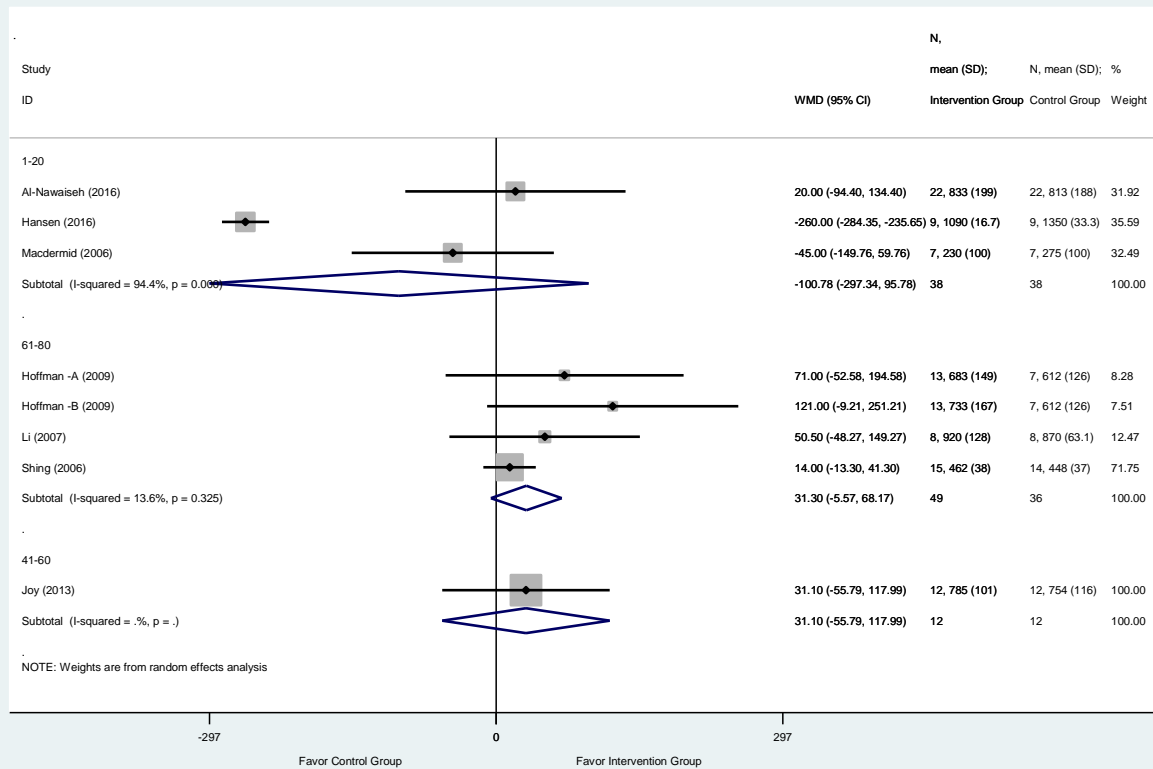
Figure 19. Forest plot of subgroup by intervention period range on the effect of WPS on maximum power (watt).
Hoffman -A (2009) = WP with carbohydrate vs placebo,
Hoffman -B (2009) = WP with fat and carbohydrate vs placebo.

## b) Average power

Nine studies met the inclusion criteria for average power. Figure 20 illustrates that slight decrease of average power by 2.57 watt (CI = -1.07, 2.11; $I^2$ = 62.3%; p = 0.002) in the intervention group compared to the control group, and moderate heterogeneity was detected (Appendix 5: 8.5.3. b). There were four studies favourable to the intervention group: Highton (2012) study carried the highest (51.46%) weighted influences and Li (2007) study carried the lowest (0.45%) weighted influences. Four studies favourable to the control group as well: Hansen (2016) study carried the highest (45.12%) weighted influences and Macdermid (2006) study carried the lowest (0.09%) weighted influences. For Hoffman -A (2009) study, the study had weighted influences of 0.52% that lied on the no effect line.
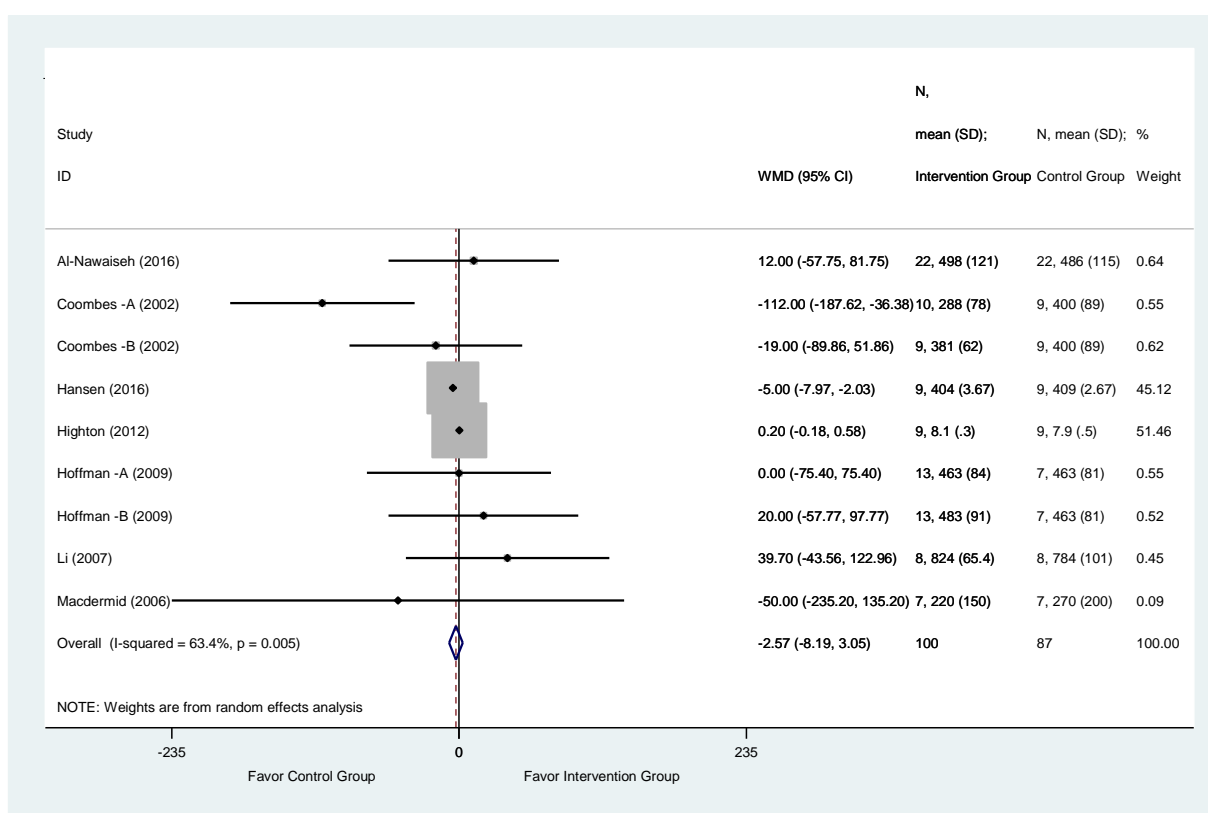


Figure 20. Forest plot of the effect of WPS on average power (watt).
Coombes -A (2002) = WP alone vs bovine colostrum,
Coombes -B (2002) = WP with bovine colostrum vs bovine colostrum,
Hoffman -A (2009) = WP with carbohydrate vs placebo,
Hoffman -B (2009) = WP with fat and carbohydrate vs placebo.

The physical activities subgroup analysis (Figure 21) had no heterogeneity ($I^2$ = 0%; CI = -0.18, 0.58) in the gym subgroup, and the cycle and resistance subgroup had low heterogeneity ($I^2$= 46.8%; CI = -49.85, 19.25). For the intervention duration range subgroup analysis (Figure 22), the period range of 61-80 days had no heterogeneity ($I^2$ = 0%; CI = -26.78, 63.1). However, the other period range did not explain about the heterogeneity as the $I^2$ value remained moderately high (Appendix 5: 8.5.3. b) iii).
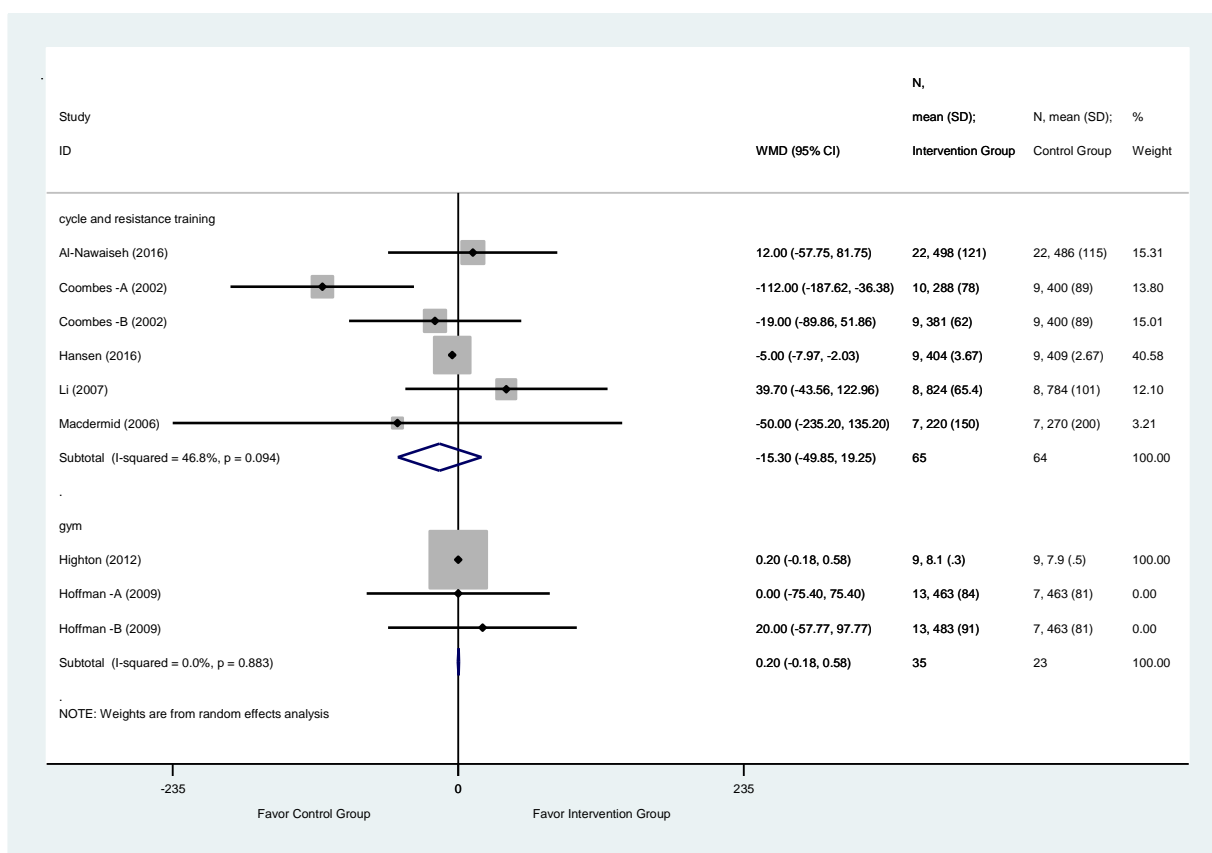


Figure 21. Forest plot of subgroup by physical activities on the effect of WPS on average power (watt).
Coombes -A (2002) = WP alone vs bovine colostrum,
Coombes -B (2002) = WP with bovine colostrum vs bovine colostrum,
Hoffman -A (2009) = WP with carbohydrate vs placebo,
Hoffman -B (2009) = WP with fat and carbohydrate vs placebo.
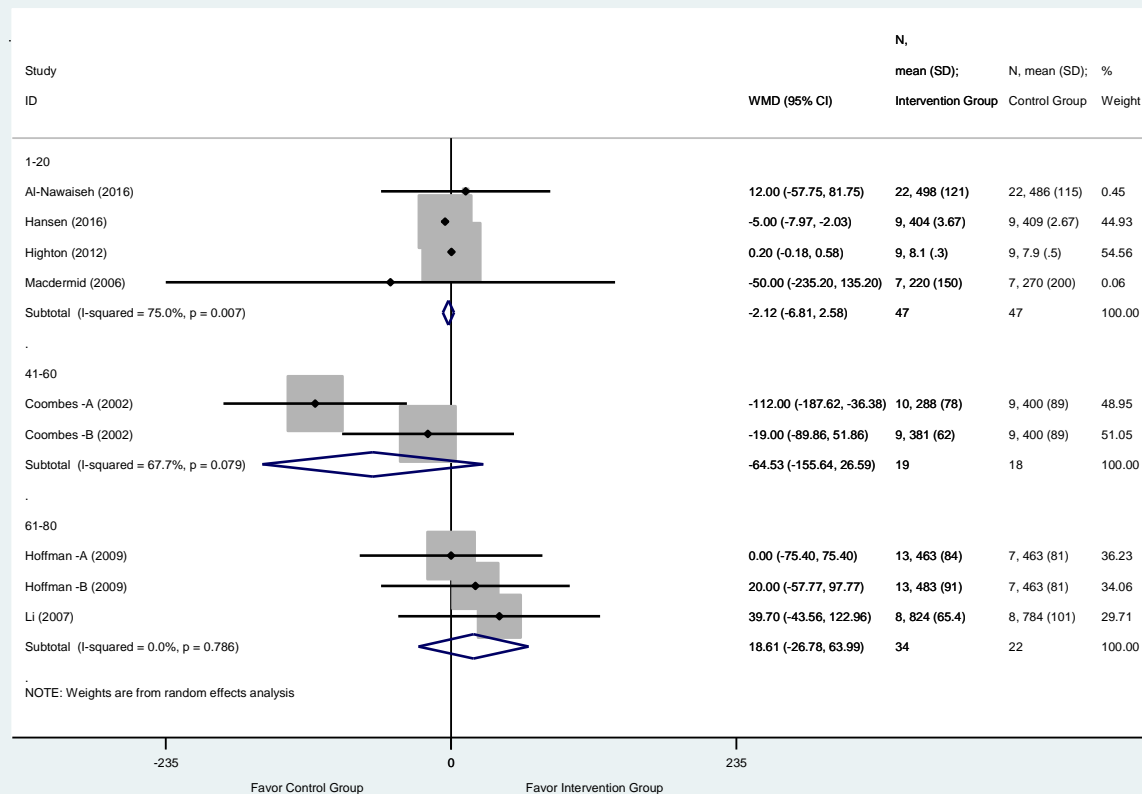
Figure 22. Forest plot of subgroup by intervention period range on the effect of WPS on average power (watt).

Coombes -A (2002) = WP alone vs bovine colostrum,

Coombes -B (2002) = WP with bovine colostrum vs bovine colostrum,

Hoffman -A (2009) = WP with carbohydrate vs placebo,

Hoffman -B (2009) = WP with fat and carbohydrate vs placebo.

**c) Body mass**

A total of ten studies assessed the effect of WPS on body mass. Figure 23 shows that body mass reduces the overall of 4.1 kg (CI = -5.84, -2.36; $I^2$ = 47.9%; p = 0.04) in the intervention group than the control group, with low evidence of heterogeneity (Appendix 5: 8.5.3. c). Four of ten studies were favourable to the intervention group: Taylor (2016) study carried the highest (4.14%) weighted influences and Macdermid (2006) study carried the lowest (0.43%) weighted. While, five studies reported favourable to the control group: Lollo -B (2011) study carried the highest (27.68%) weighted influences and Hoffman -B (2009) study carried the lowest (0.62%) weighted influences. The funnel plot (Figure 24) described that there slight publication bias as most of the studies were within 95% confidence limits and only one study were not within the confidence limits, along with Egger test, where the bias was 1.096 (CI = -0.12, 2.31, p = 0.071) (Appendix 5: 8.5.3. c) iv).

| Study ID | WMD (95% CI) | N, mean (SD); Intervention Group | N, mean (SD); Control Group | % Weight |
|---|---|---|---|---|
| Coombes -A (2002) | 2.00 (-10.40, 14.40) | 10, 75 (17) | 9, 73 (10) | 1.86 |
| Coombes -B (2002) | 0.00 (-7.97, 7.97) | 9, 73 (7) | 9, 73 (10) | 4.17 |
| Hoffman -A (2009) | 1.90 (-20.95, 24.75) | 13, 102 (18.5) | 7, 100 (27.7) | 0.57 |
| Hoffman -B (2009) | -3.80 (-25.70, 18.10) | 13, 96.3 (14.1) | 7, 100 (27.7) | 0.62 |
| Lollo -A (2011) | -6.89 (-8.24, -5.54) | 8, 71.1 (1.41) | 8, 78 (1.34) | 27.56 |
| Lollo -B (2011) | -4.30 (-5.63, -2.97) | 8, 73.7 (1.38) | 8, 78 (1.34) | 27.68 |
| Lollo -A (2014) | -2.40 (-5.39, 0.59) | 8, 73.6 (3) | 8, 76 (3.1) | 16.75 |
| Lollo -B (2014) | -4.20 (-7.29, -1.11) | 8, 71.8 (3.2) | 8, 76 (3.1) | 16.21 |
| Macdermid (2006) | 0.20 (-26.06, 26.46) | 7, 67.8 (35.1) | 7, 67.6 (5) | 0.43 |
| Taylor (2016) | 1.20 (-6.80, 9.20) | 8, 67 (10) | 6, 65.8 (5) | 4.14 |
| Overall (I-squared = 47.9%, p = 0.044) | -4.10 (-5.84, -2.36) | 92 | 77 | 100.00 |

NOTE: Weights are from random effects analysis

Figure 23. Forest plot of the effect of WPS on body mass (kg).
Coombes -A (2002) = WP alone vs bovine colostrum,
Coombes -B (2002) = WP with bovine colostrum vs bovine colostrum,
Hoffman -A (2009) = WP with carbohydrate vs placebo,
Hoffman -B (2009) = WP with fat and carbohydrate vs placebo,
Lollo -A (2011) = 91.4% of WP vs casein,
Lollo -B (2011) = 87 % of WP vs casein,
Lollo -A (2014) = WP concentrate vs maltodextrin,
Lollo -B (2014) = WP hydrolysed vs maltodextrin.
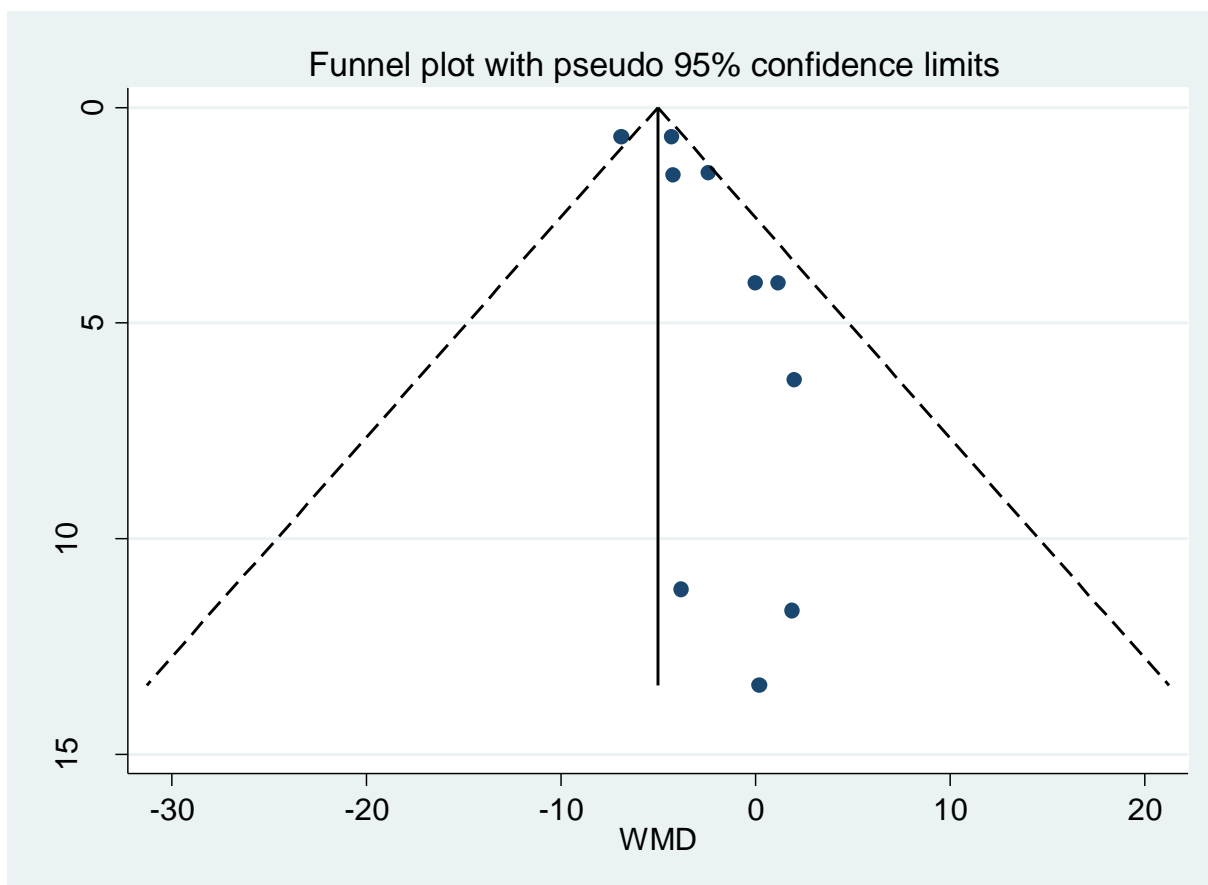
Figure 24. Funnel plot of the effect of WPS on body mass (kg) published studies.

### 4.4.4 Blood profile outcome

### a) Essential amino acid

Of the collected studies, six studies involved WPS with EAA outcome, as shown in Figure 25.

The overall WMA estimated for EAA induce in the intervention group by 624.03 nmol/L (CI =

169.27, 1078.8; $I^2$ = 100%; p = 0.00) compared to the control groups, although high

heterogeneity was detected (Appendix 5: 8.5.4. a). The individual studies were all

favourable to the intervention and their weighted influence of the individual studies was

similarly distributed For the subgroup analyses (Figure 26), the subgroup analysis on

intervention duration range shows that 41-60 days range subgroup had no heterogeneity

($I^2$= 0%; CI = 546.09, 1135.75). However, overall the subgroup analyses merely explained

about the heterogeneity as the $I^2$ value remained high and a standalone study (Appendix 5:

8.5.4. a) iii).

| Study ID | WMD (95% CI) | N, mean (SD); Intervention Group | N, mean (SD); Control Group | % Weight |
|---|---|---|---|---|
| Areta -A (2014) | 700.00 (295.12, 1104.88) | 15, 1500 (800) | 15, 800 (10) | 15.30 |
| Areta -B (2014) | 1000.00 (569.82, 1430.18) | 15, 1800 (850) | 16, 800 (10) | 15.06 |
| Impey -A (2015) | 50.00 (37.68, 62.32) | 9, 1700 (13.3) | 9, 1650 (13.3) | 17.41 |
| Impey -B (2015) | 1202.00 (1192.70, 1211.30) | 9, 1700 (13.3) | 9, 498 (5) | 17.41 |
| Parr -B (2014) | 402.00 (386.51, 417.49) | 8, 1200 (10) | 8, 798 (20) | 17.41 |
| Tang (2007) | 450.00 (437.75, 462.25) | 8, 1150 (14.1) | 8, 700 (10.6) | 17.41 |
| Overall (I-squared = 100.0%, p = 0.000) | 624.03 (169.27, 1078.80) | 64 | 65 | 100.00 |

NOTE: Weights are from random effects analysis

-1430    0    1430

Favor Control Group    Favor Intervention Group

Figure 25. Forest plot of the effect of WPS on EAA (nmol/L).
Areta -A (2014) = 15 g WP vs placebo,
Areta -B (2014) = 30 g WP vs placebo,
Impey -A (2015) = WP protein vs carbohydrate,
Impey -B (2015) = WP with caffeine vs carbohydrate.

| Study ID | WMD (95% CI) | N, mean (SD); Intervention Group | N, mean (SD); Control Group | % Weight |
|---|---|---|---|---|
| **41-60** | | | | |
| Areta -A (2014) | 700.00 (295.12, 1104.88) | 15, 1500 (800) | 15, 800 (10) | 53.03 |
| Areta -B (2014) | 1000.00 (569.82, 1430.18) | 15, 1800 (850) | 16, 800 (10) | 46.97 |
| Subtotal (I-squared = 0.0%, p = 0.320) | 840.92 (546.09, 1135.75) | 30 | 31 | 100.00 |
| . | | | | |
| **1-20** | | | | |
| Impey -A (2015) | 50.00 (37.68, 62.32) | 9, 1700 (13.3) | 9, 1650 (13.3) | 25.00 |
| Impey -B (2015) | 1202.00 (1192.70, 1211.30) | 9, 1700 (13.3) | 9, 498 (5) | 25.00 |
| Parr -B (2014) | 402.00 (386.51, 417.49) | 8, 1200 (10) | 8, 798 (20) | 25.00 |
| Tang (2007) | 450.00 (437.75, 462.25) | 8, 1150 (14.1) | 8, 700 (10.6) | 25.00 |
| Subtotal (I-squared = 100.0%, p = 0.000) | 526.01 (-19.14, 1071.17) | 34 | 34 | 100.00 |

NOTE: Weights are from random effects analysis

Figure 26. Forest plot of subgroup by intervention period range on the effect of WPS on EAA (nmol/L).
Areta -A (2014) = 15 g WP vs placebo,
Areta -B (2014) = 30 g WP vs placebo,
Impey -A (2015) = WP protein vs carbohydrate,
Impey -B (2015) = WP with caffeine vs carbohydrate.

### b) Branched-chain amino acid

Nine studies reported the outcome relevant to BCAA, as shown in Figure 27. The overall of

BCAA level was increased by 458.57 nmol/L (CI=179.96, 737.18; $I^2$ =100%; p = 0.00) and all

studies were favourable to the intervention group (Appendix 5: 8.5.4. b). The weighted

influence of all the individual studies was equally distributed of 11%. Moreover, the

subgroups analyse unable to explained about the heterogeneity as the $I^2$ value remained

high and a standalone study (Appendix 5: 8.5.4. b) iii).
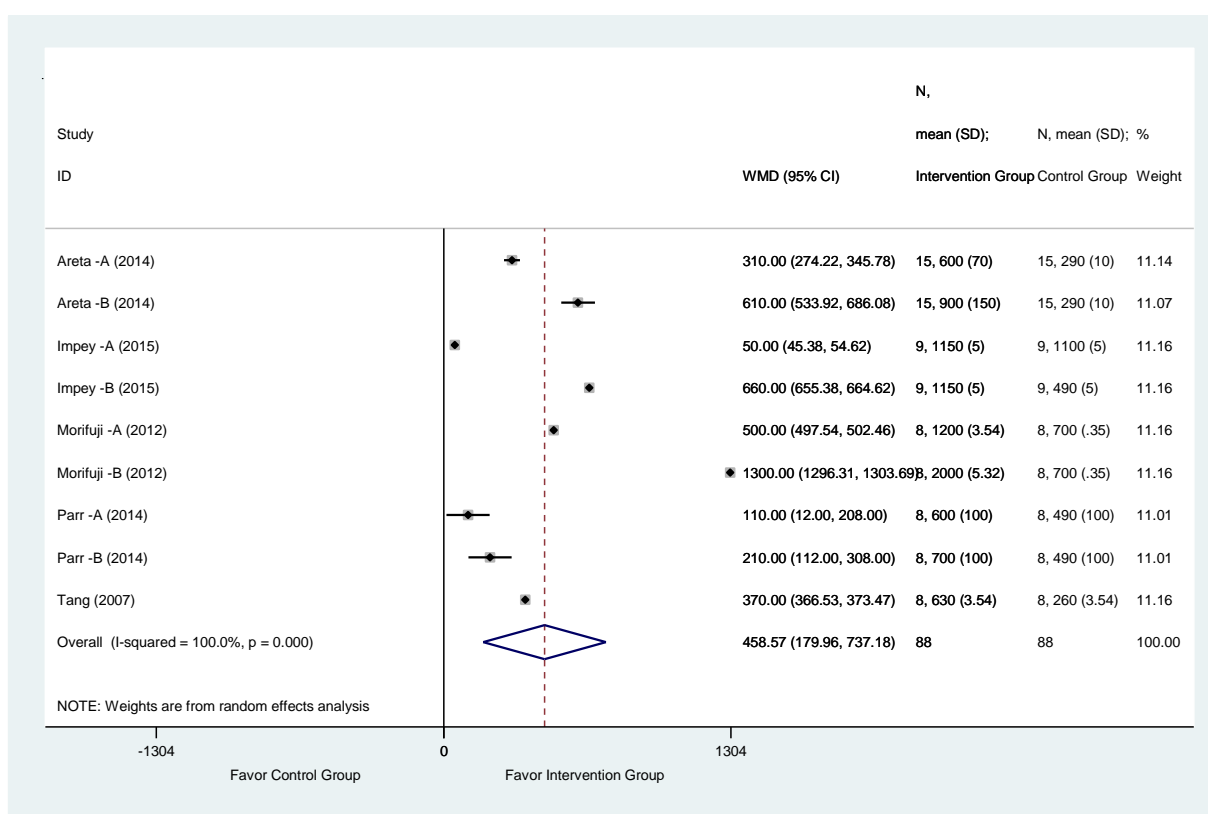


Figure 27. Forest plot of the effect of WPS on BCAA (nmol/L).
Areta -A (2014) = 15 g WP vs placebo,
Areta -B (2014) = 30 g WP vs placebo,
Impey -A (2015) = WP protein vs carbohydrate,
Impey -B (2015) = WP with caffeine vs carbohydrate,
Morifuji -A (2012) = 3.0 g WP vs carbohydrate,
Morifuji -B (2012) = 8.0 g WP vs carbohydrate,
Parr -A (2014) = 25 g WP vs maltodextrin with alcohol,
Parr -B (2014) = 25 g WP with alcohol vs maltodextrin with alcohol.

**c) Creatine kinase**

A total of thirteen studies involved WPS with creatine kinase. Figure 28 illustrates that the overall of creatine kinase level was 47.05 U/L (CI=-129.47, 35.37; $I^2$ =98.4%; p = 0.000) lower in the intervention group than in the control group, although high heterogeneity (Appendix 5: 8.5.4. c). Six studies were also favourable to the intervention group: Gunnarsson (2013) study carried the highest (8.30%) weighted influences and Naclerio -A (2015) study carried the lowest (6.13%) weighted influences. Also, six studies were favourable to the control group: Hansen (2015) study carried the highest (8.28%) weighted influences and Naclerio -B (2015) study carried the lowest (5.24%) weighted influences. Hansen (2016) only study that lie on the no effect line with weighed influence of 8.38%. For the publication bias, the funnel plot (Figure 29) depict there was publication bias as the majority of studies were away from average and outside of the 95% confidence limits, along with Egger test (Appendix 5: 8.5.4. c) iv), where the bias was -2.1 (CI = -9.96, 5.75; p = 0.567).
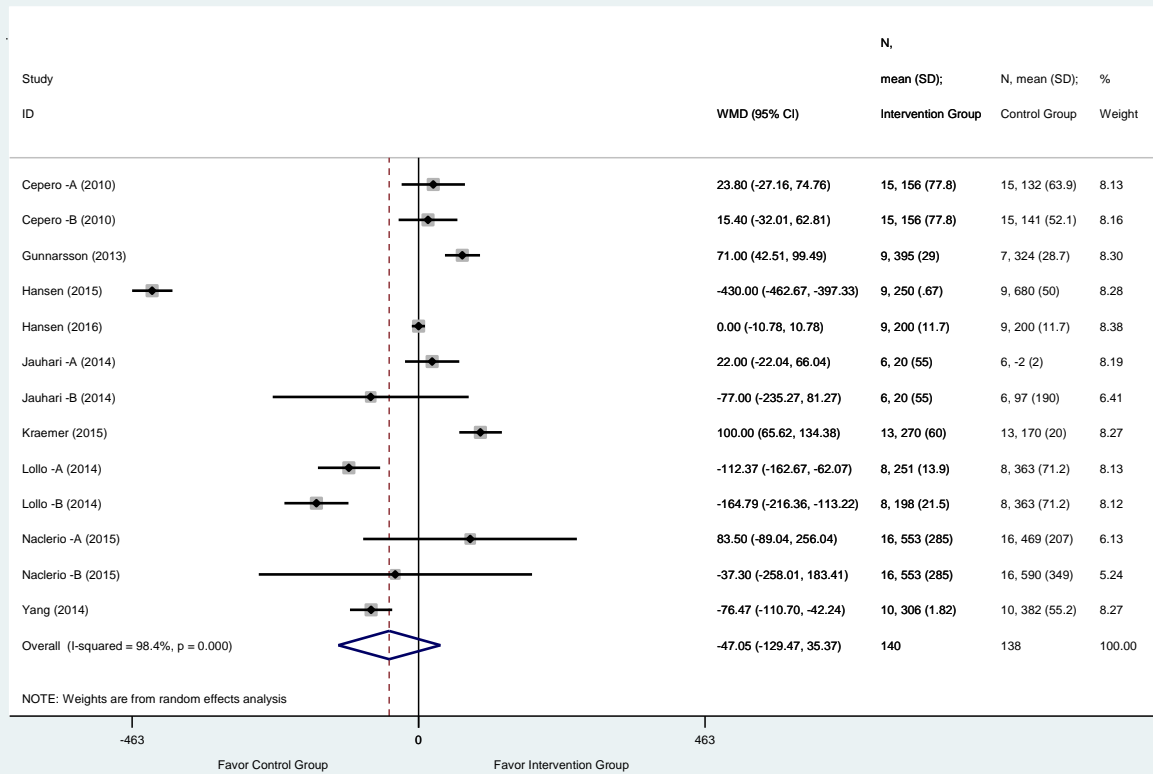
Figure 28. Forest plot of the effect of WPS on creatine kinase (U/L).
Cepero -A (2010) = WP vs carbohydrate,
Cepero -B (2010) = WP vs casein,
Jauhari -A (2014) = WP vs tempeh,
Jauhari -B (2014) = WP vs placebo,
Lollo -A (2014) = WP concentrate vs maltodextrin,
Lollo -B (2014) = WP hydrolysed vs maltodextrin,
Naclerio -A (2015) = WP with multi-ingredient vs carbohydrate,
Naclerio -B (2015) = WP with multi-ingredient vs placebo.
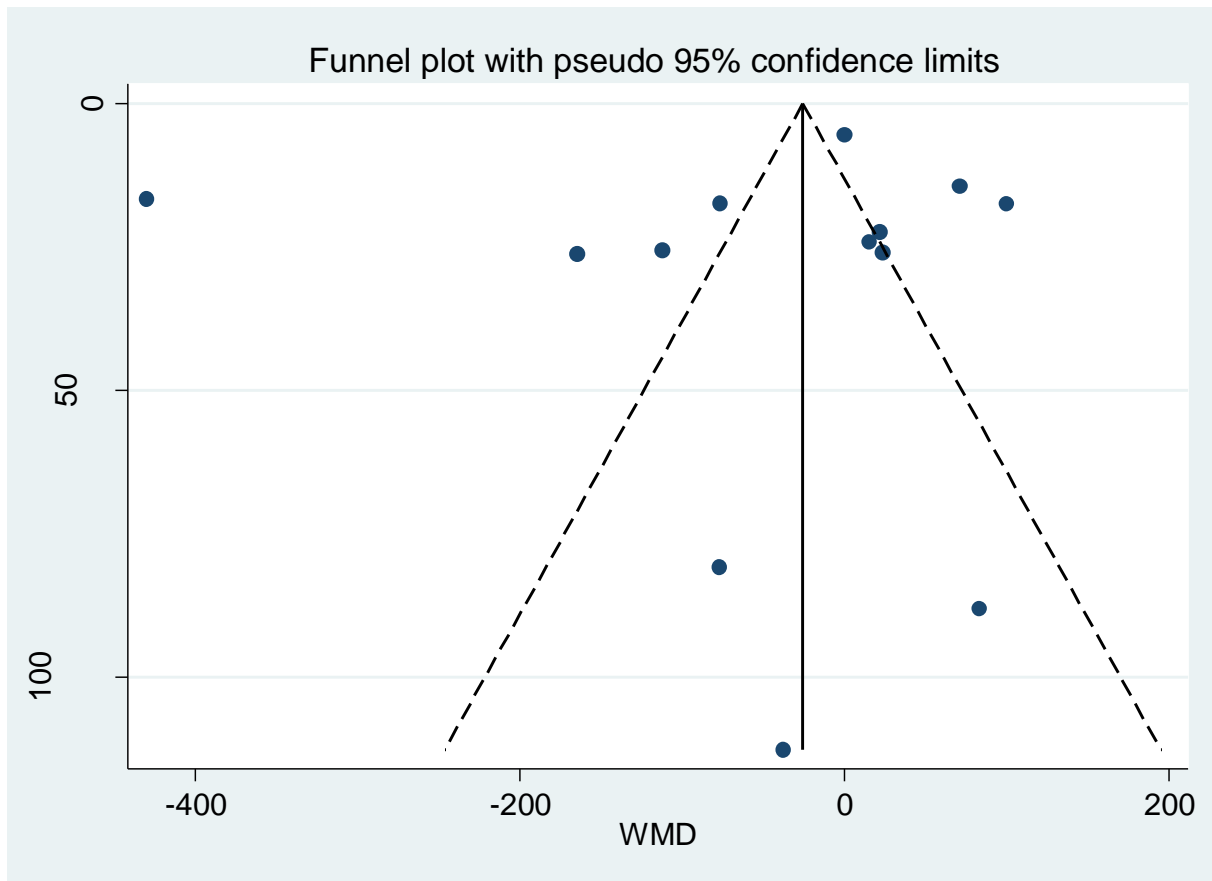
Figure 29. Funnel plot of the effect of WPS on creatine kinase (U/L) published studies.

For the subgroup analyses, the physical activities analysis (Figure 30) shows that the cycle group was no heterogeneity ($I^2$= 0%; CI = -15.42, 54.01) and the resistance exercise subgroup had low evidence and of heterogeneity ($I^2$= 28.3%; CI = -73.71, 79.47). However, the other subgroup did not explain the high heterogeneity as the $I^2$ value remained high and a standalone study (Appendix 5: 8.5.4. c) v).
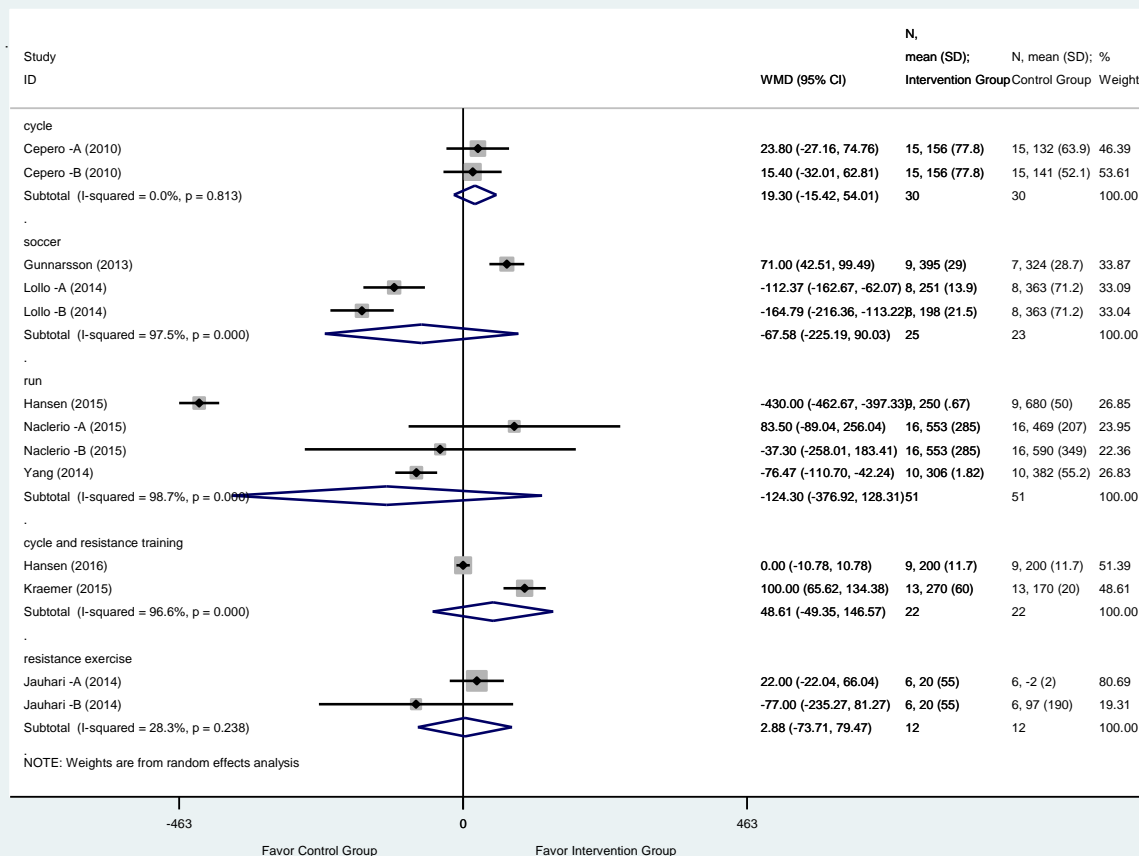
Figure 30. Forest plot of subgroup by physical activities the effect of WPS on creatine kinase (U/L).
Cepero -A (2010) = WP vs carbohydrate,
Cepero -B (2010) = WP vs casein,
Jauhari -A (2014) = WP vs tempeh,
Jauhari -B (2014) = WP vs placebo,
Lollo -A (2014) = WP concentrate vs maltodextrin,
Lollo -B (2014) = WP hydrolysed vs maltodextrin,
Naclerio -A (2015) = WP with multi-ingredient vs carbohydrate,
Naclerio -B (2015) = WP with multi-ingredient vs placebo.

**d) Glucose**

Seventeen studies met the inclusion criteria for glucose, as shown in Figure 31. The overall of blood glucose level was slightly lower 0.17 mmol/L (CI=-0.33, -0.01; $I^2$ = 99.1%; p = 0.000) in the intervention group than in the control group, high heterogeneity was presented (Appendix 5: 8.5.4. d). Five studies were favourable to the intervention group: Lollo -B (2011) study carried the highest (7.51%) weighted influences and Macdermid (2006) study carried the lowest (3.05%) weighted influences. While, eleven of the seventeen studies were favourable to the control group: Impey -B (2015) and Lollo -A (2011) studies carried the highest (7.51%) weighted influence and Cepero -B (2010) study carried the lowest (0.93%) weighted influences. Impey -A (2015) study lies on the no effect line with 7.51% weighted influences. There was publication bias as the funnel plot (Figure 32) show the majority of studies away from 95% confidence limits and asymmetrical, along with Egger test (Appendix 5: 8.5.4. d) iv), where the bias was -0.75 (CI = -8.36, 6.85; p = 0.837).
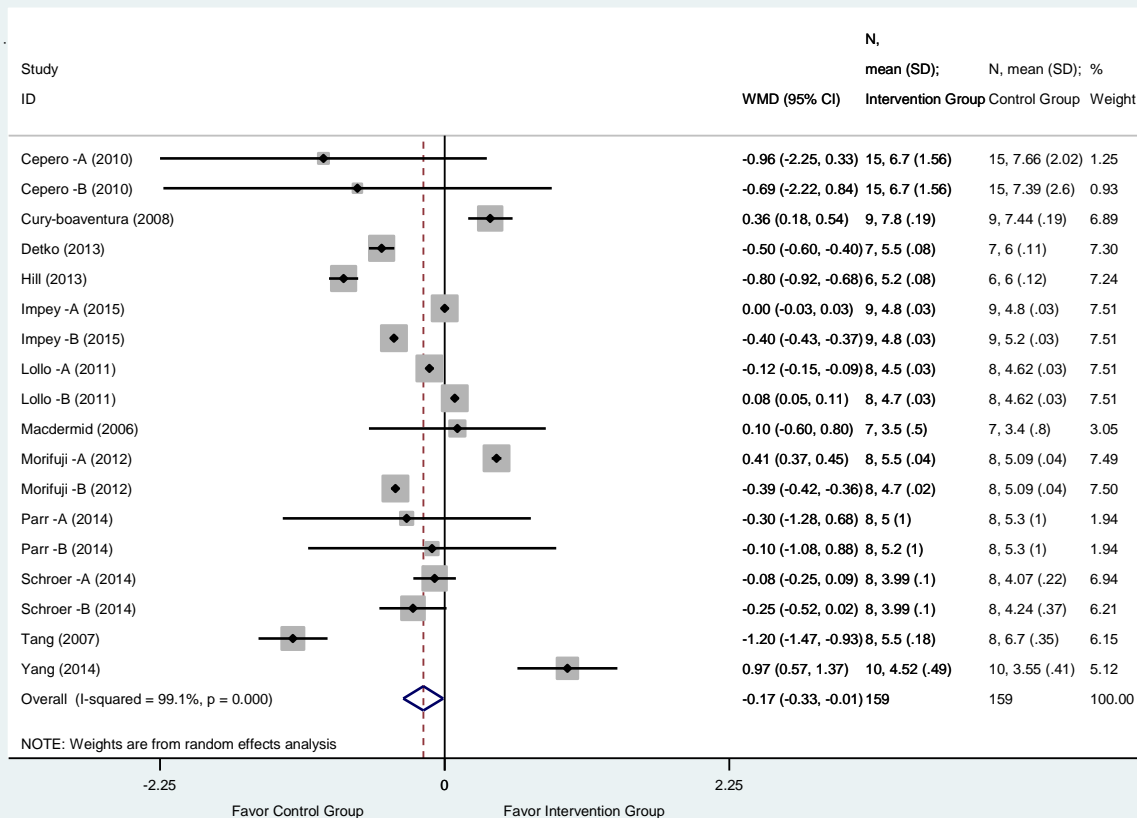
Figure 31. Forest plot of the effect of WPS on glucose (mmol/L).
Cepero -A (2010) = WP vs carbohydrate,
Cepero -B (2010) = WP vs casein,
Impey -A (2015) = WP protein vs carbohydrate,
Impey -B (2015) = WP with caffeine vs carbohydrate,
Lollo -A (2011) = 91.4% WP vs casein,
Lollo -B (2011) = 87 % WP vs casein,
Morifuji -A (2012) = 3.0 g WP vs carbohydrate,
Morifuji -B (2012) = 8.0 g WP vs carbohydrate,
Parr -A (2014) = 25 g WP vs maltodextrin with alcohol,
Parr -B (2014) = 25 g WP with alcohol vs maltodextrin with alcohol,
Schroer -A (2014) = WP vs L-alanine,
Schroer -B (2014) = WP vs placebo.
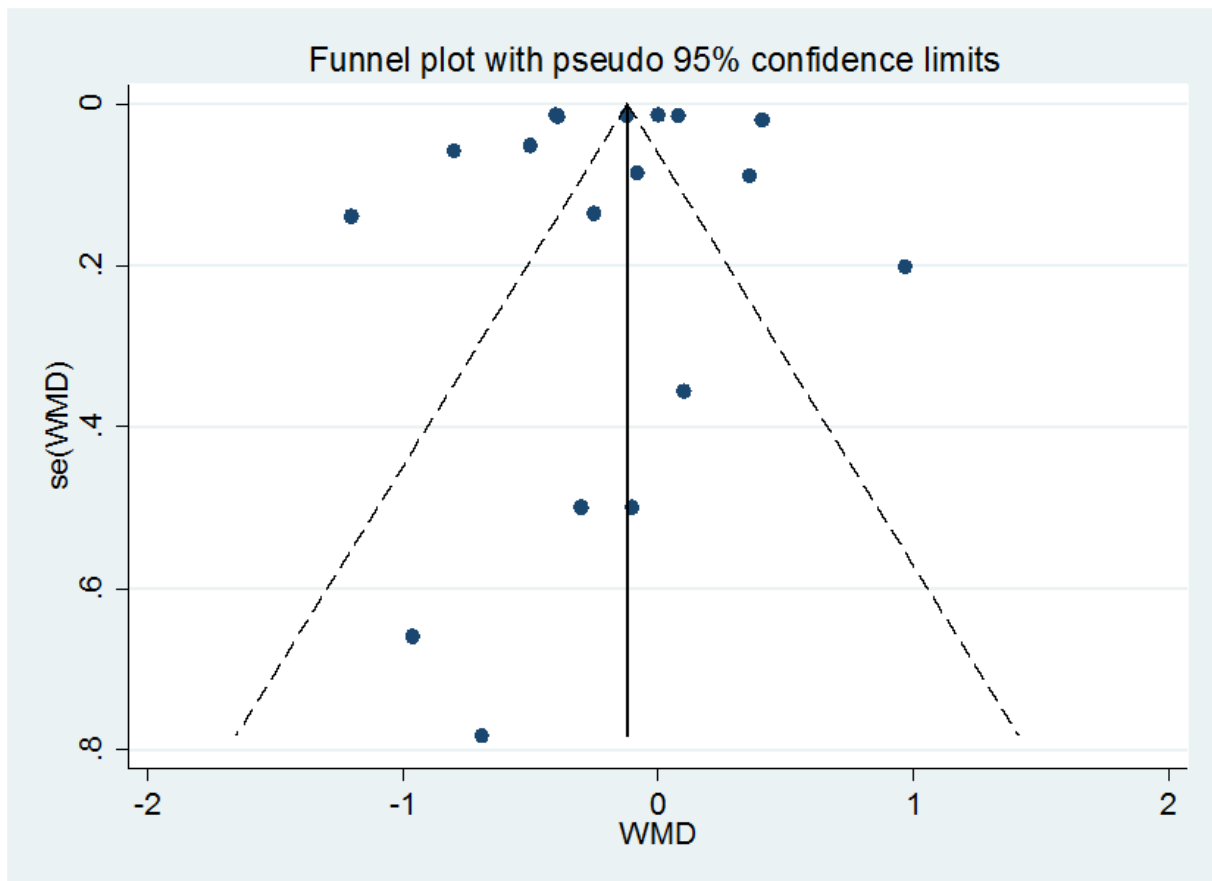
Figure 32. Funnel plot of the effect of WPS on glucose (mmol/L) published studies.

The subgroup analyses reported that the leg subgroup had no heterogeneity ($I^2$ = 0%; CI = -0.89, 0.49) (Figure 33). While, the other subgroup (Appendix 5: 8.5.4. d) v) did not explain the heterogeneity as the $I^2$ value remained high and a standalone study.
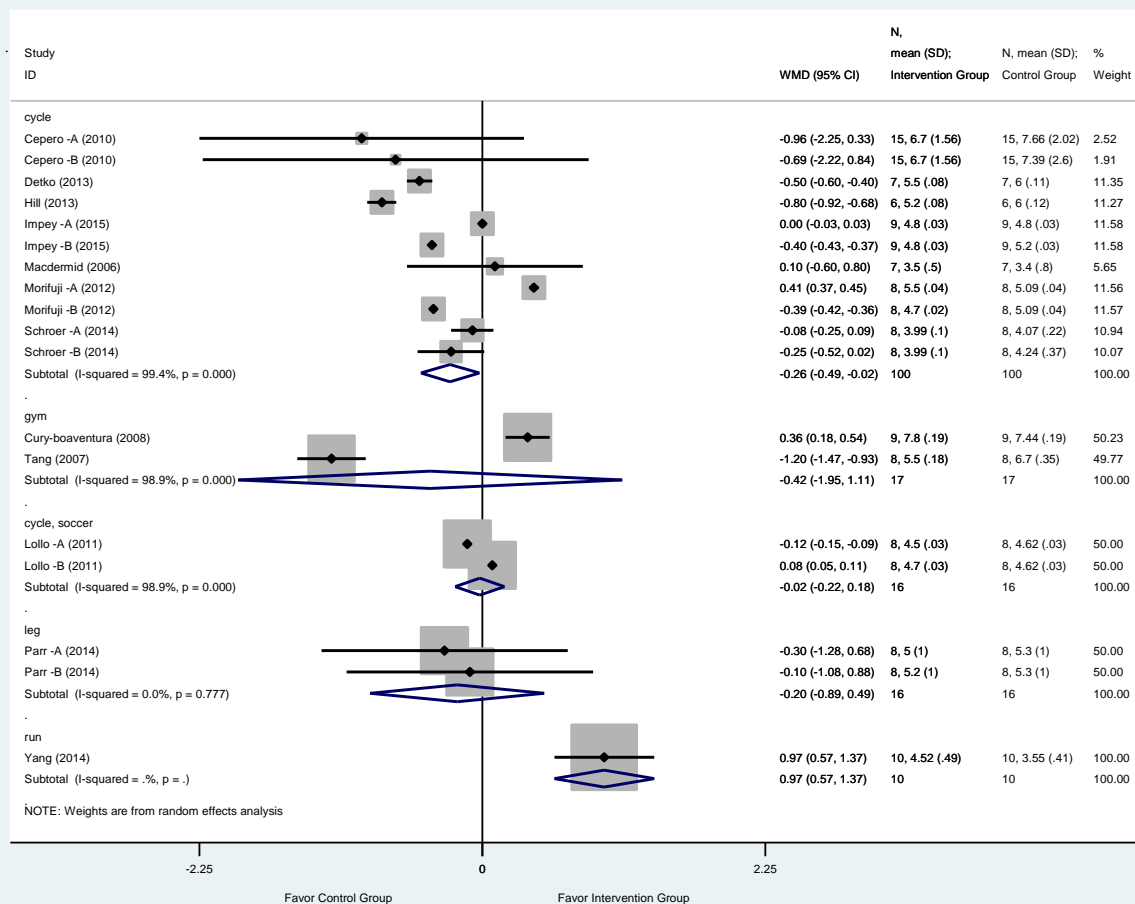
Figure 33. Forest plot of subgroup by physical activities on the effect of WPS on glucose (mmol/L).

Cepero -A (2010) = WP vs carbohydrate,
Cepero -B (2010) = WP vs casein,
Impey -A (2015) = WP protein vs carbohydrate,
Impey -B (2015) = WP with caffeine vs carbohydrate,
Lollo -A (2011) = 91.4% WP vs casein,
Lollo -B (2011) = 87 % WP vs casein,
Morifuji -A (2012) = 3.0 g WP vs carbohydrate,
Morifuji -B (2012) = 8.0 g WP vs carbohydrate,
Parr -A (2014) = 25 g WP vs maltodextrin with alcohol,
Parr -B (2014) = 25 g WP with alcohol vs maltodextrin with alcohol,
Schroer -A (2014) = WP vs L-alanine,
Schroer -B (2014) = WP vs placebo.

### 4.4.5  Hormones outcome

#### a) Insulin

Nineteen of the collected studies met the inclusion criteria for insulin level. Figure 34 showing strong evidence that the overall of insulin level was 7.13 µU/ml (CI = 5.00, 9.25; $I^2$ = 99.8%; p = 0.00) higher in the intervention group than the control group, with high heterogeneity (Appendix 5: 8.5.5. a). Thirteen studies were favourable to the intervention group: Impey -A (2015), Impey -B (2015) and Morifuji -A (2012) studies carried the highest (6.77%) weighted influence and Oosthuyse -A (2015) study carried the highest (1.44%) weighted influences. On the other hand, six studies were favourable to the control group: Burke -A (2012) and Mero -A (1997) studies carried the highest (6.77%) weighted influences and Oosthuyse -B (2015) study carried the lowest (1.32%) weighted influences. There is publication bias as the funnel plot (Figure 35) shows most of the studies away from 95% confidence limits and asymmetrical , along with Egger test (Appendix 5: 8.5.5. a) iv), where bias was -0.0628 (CI = -1.47, 1.35; p = 0.92). However, the subgroup analyses did not explain the high heterogeneity as the $I^2$ value remained high and standalone study (Appendix 5: 8.5.5. a) v).
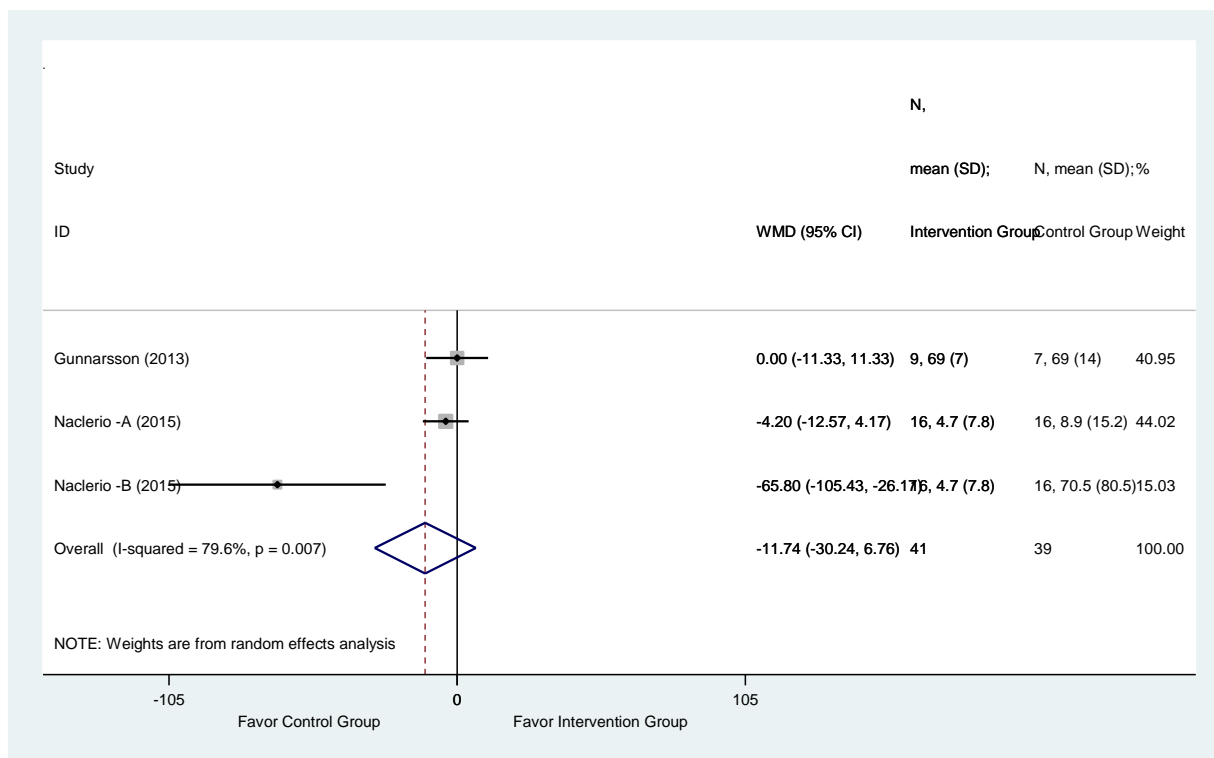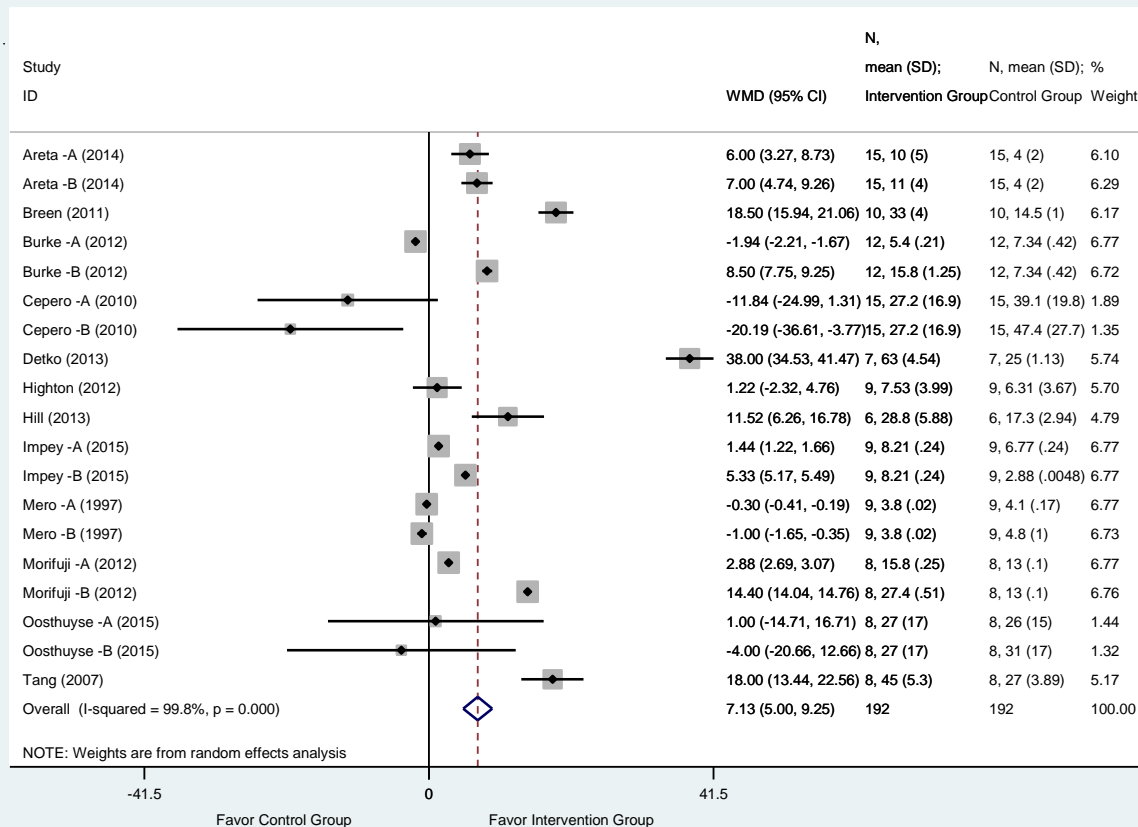
Figure 34. Forest plot of the effect of WPS on insulin (μU/ml).
Areta -A (2014) = 15 g WP vs placebo,
Areta -B (2014) = 30 g WP vs placebo,
Burke -A (2012) = 500 ml WP vs placebo,
Burke -B (2012) = 33 ml WP vs placebo,
Cepero -A (2010) = WP vs carbohydrate,
Cepero -B (2010) = WP vs casein,
Impey -A (2015) = WP protein vs carbohydrate,
Impey -B (2015) = WP with caffeine vs carbohydrate,
Morifuji -A (2012) = 3.0 g WP vs carbohydrate,
Morifuji -B (2012) = 8.0 g WP vs carbohydrate,
Mero -A (1997) = WP vs 125-ml Bioenervi,
Mero -B (1997) = WP vs 25-ml Bioenervi,
Oosthuyse -A (2015) = WP vs casein,
Oosthuyse -B (2015) = WP vs carbohydrate.
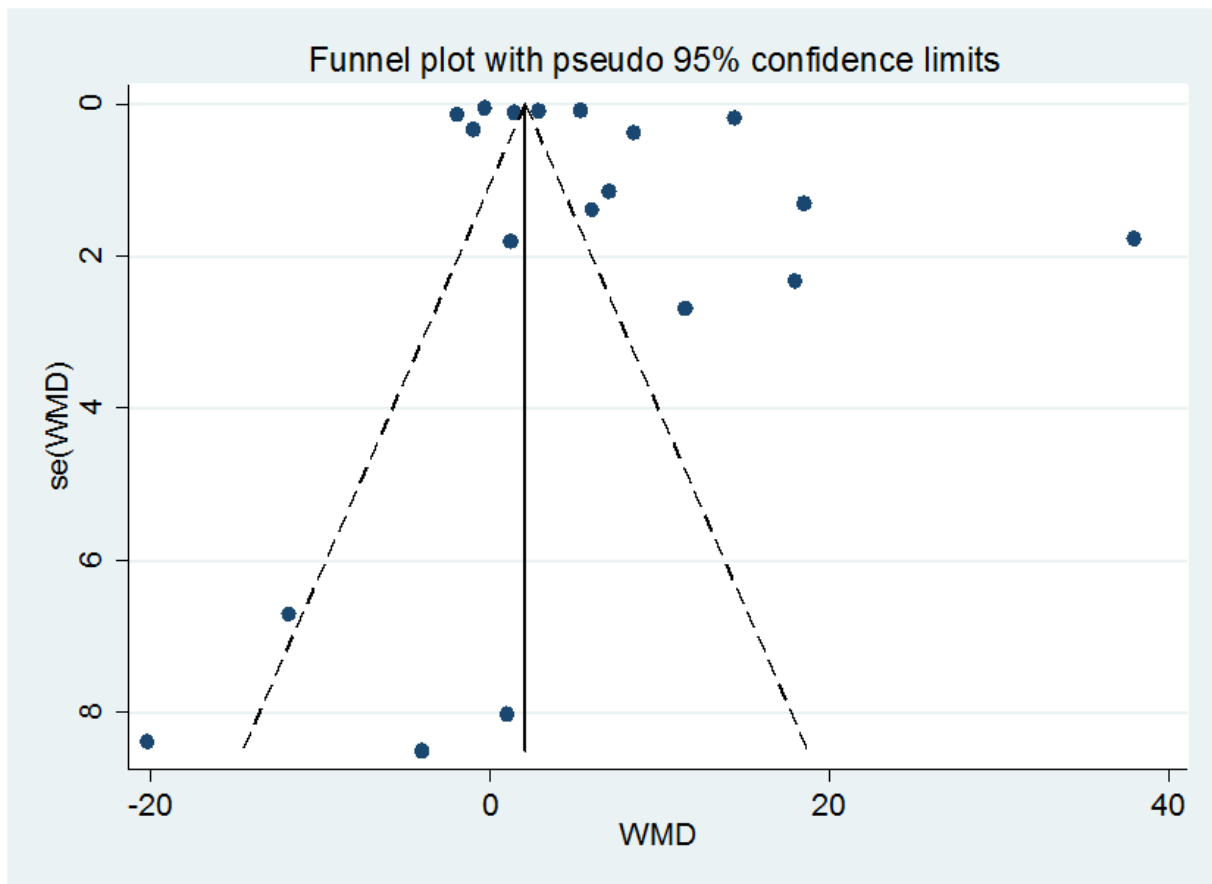
Figure 35. Funnel plot of the effect of WPS on insulin (μU/ml) published studies.

## b) Cortisol

A total of seven studies met the inclusion criteria for cortisol, as shown in Figure 36. The overall of cortisol level decrease in the intervention group by 5.40 nmol/L (CI = -10.14, -0.66, $I^2$ = 75.9%, p = 0.000) than in the control group, although heterogeneity was detected (Appendix 5: 8.5.5. b). Only two studies were favourable to the intervention group with light weighted influence: Hansen (2015) (weight = 2.29) and Kraemer (2015) (weight = 0.06%). While, five studies were favourable to the control group: Shing (2013) study carried the highest (32.32%) weighted influences and Hansen (2016) carried the lowest study (8.87%) weighted influences. For the subgroup analyses, the cycle subgroup was no heterogeneity ($I^2$ = 0%; CI = -8.56, -5.62) (Figure 37). However, other subgroup did not explain the heterogeneity the $I^2$ value stayed high and standalone study (Appendix 5: 8.5.5. b) iii).
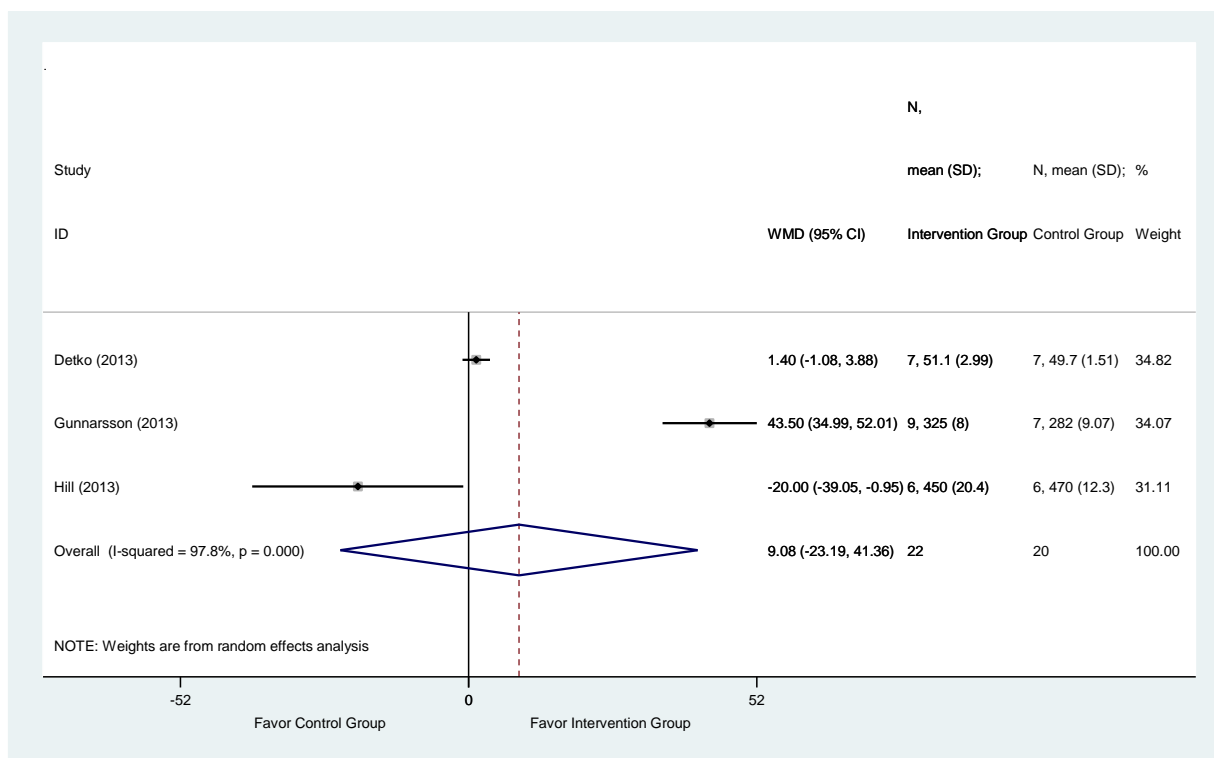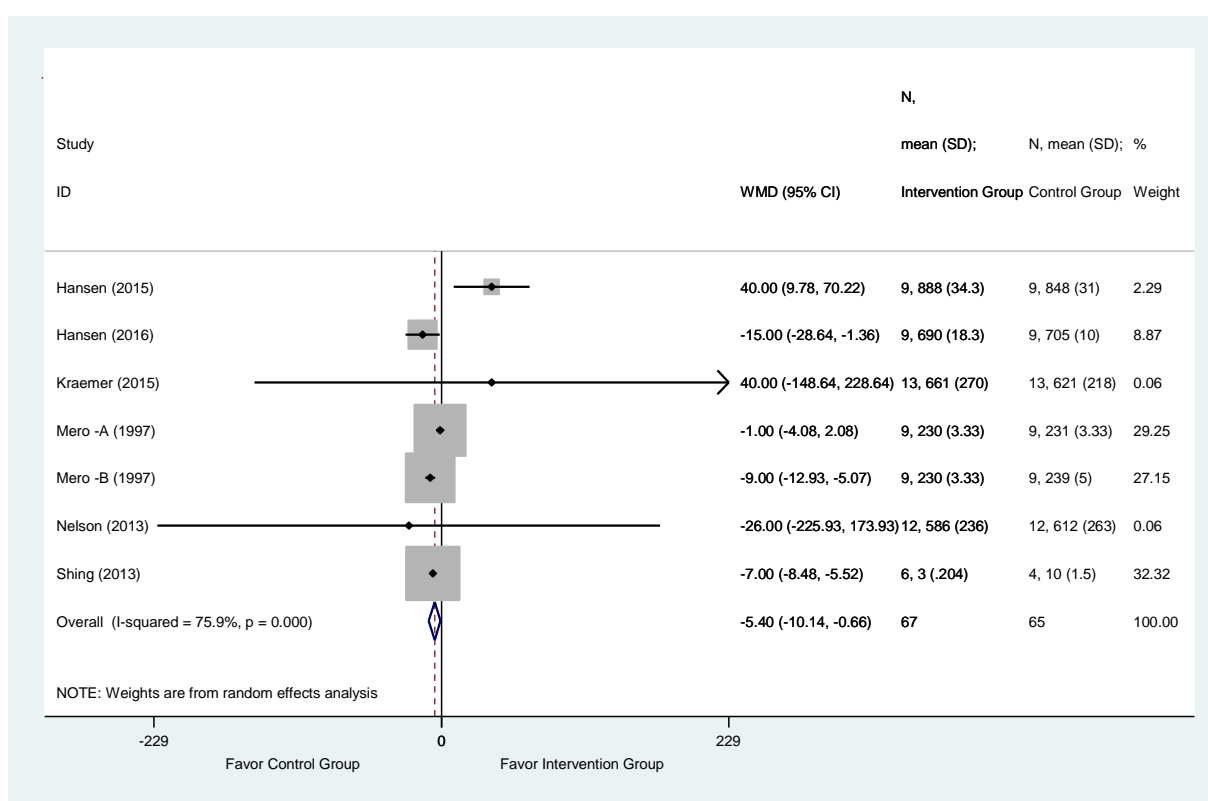


Figure 36. Forest plot of the effect of WPS on cortisol (nmol/L).
Mero -A (1997) = WP vs 125-ml Bioenervi,
Mero -B (1997) = WP vs 25-ml Bioenervi.

| Study ID | WMD (95% CI) | N, mean (SD); Intervention Group | N, mean (SD); Control Group | % Weight |
|---|---|---|---|---|
| **run** | | | | |
| Hansen (2015) | 40.00 (9.78, 70.22) | 9, 888 (34.3) | 9, 848 (31) | 100.00 |
| Subtotal (I-squared = .%, p = .) | 40.00 (9.78, 70.22) | 9 | 9 | 100.00 |
| . | | | | |
| **cycle** | | | | |
| Hansen (2016) | -15.00 (-28.64, -1.36) | 9, 690 (18.3) | 9, 705 (10) | 1.16 |
| Kraemer (2015) | 40.00 (-148.64, 228.64) | 13, 661 (270) | 13, 621 (218) | 0.01 |
| Nelson (2013) | -26.00 (-225.93, 173.93) | 12, 586 (236) | 12, 612 (263) | 0.01 |
| Shing (2013) | -7.00 (-8.48, -5.52) | 6, 3 (.204) | 4, 10 (1.5) | 98.83 |
| Subtotal (I-squared = 0.0%, p = 0.664) | -7.09 (-8.56, -5.62) | 40 | 38 | 100.00 |
| . | | | | |
| **leg** | | | | |
| Mero -A (1997) | -1.00 (-4.08, 2.08) | 9, 230 (3.33) | 9, 231 (3.33) | 51.21 |
| Mero -B (1997) | -9.00 (-12.93, -5.07) | 9, 230 (3.33) | 9, 239 (5) | 48.79 |
| Subtotal (I-squared = 89.9%, p = 0.002) | -4.90 (-12.74, 2.93) | 18 | 18 | 100.00 |
| . | | | | |
| NOTE: Weights are from random effects analysis | | | | |

Favor Control Group     -229     0     229     Favor Intervention Group

Figure 37. Forest plot of subgroup by physical activities on the effect of WPS on cortisol (nmol/L).
Mero -A (1997) = WP vs 125-ml Bioenervi,
Mero -B (1997) = WP vs 25-ml Bioenervi.

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### c) Testosterone

Four studies (Figure 38) reported that testosterone level decreased in the intervention group with the overall of 0.37 nmol/L (CI = -0.86, 0.12; $I^2$ = 90.8%; p = 0.000) compared to in the control group, though presented of heterogeneity (Appendix 5: 8.5.5. c). Kraemer (2015) only study that favourable to the intervention group with light weighted influences of 1.36%. Three studies were favourable to the control group: Shing (2013) study carried the highest (36.04%) weighted influences and Mero -A (1997) study carried the lowest (29.40%) weighted influences. For the subgroup analyses, the cycle subgroup was homogeneity ($I^2$ = 0%; CI = -0.14, -0.041). However, other subgroup did not explain the heterogeneity as the $I^2$ value remained high (Appendix 5: 8.5.5. c) iii).
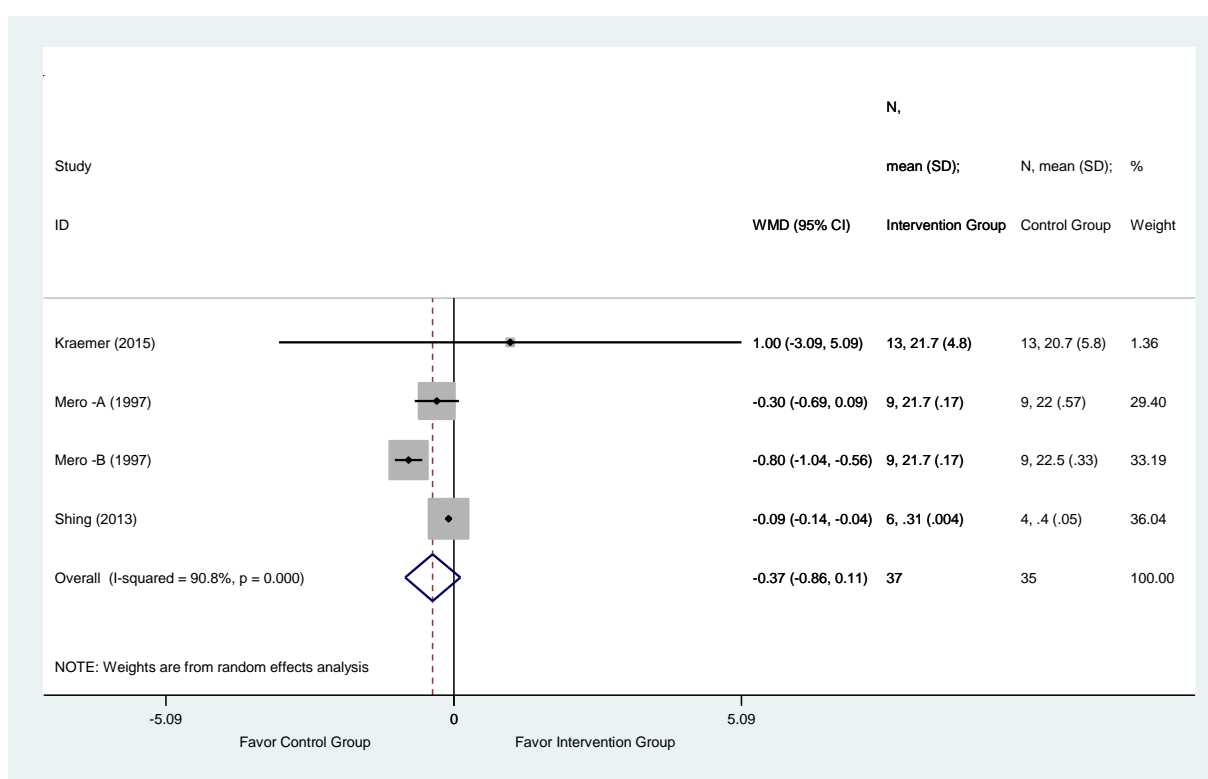


Figure 38. Forest plot of the effect of WPS on testosterone (nmol/L).
Mero -A (1997) = WP vs 125-ml Bioenervi,
Mero -B (1997) = WP vs 25-ml Bioenervi.

# CHAPTER 5: DISCUSSION

## 5    Chapter 5 Discussion

The purpose of the systematic review and meta-analysis study was to evaluate the clinical evidence on the efficacy and safety of WPS on sports performance and recovery among athletes. This study is unique as it focused the meta-analysis of the clinical evidence on the efficacy and safety of WPS among athletes' sports performance and recovery by reflecting on vital signs, serum protein, strength and body composition, blood profile and hormone outcomes. Then again, the intervention described as WPS, while others as comparators.

### 5.1    Quality of the studies

The search strategy was robust and unlikely to have missed eligible studies. With the comprehensive search strategy, a total of 50 studies have included in this systematic review and meta-analysis. Of the collected studies, 45 (95%) of the included studies were RCTs which many sources of bias had removed from the process (Higgins & Green, 2011). The implemented of the Cochrane Risk of Bias Assessment tool table (Appendix 3) and the ROBINS-I tool had evaluated the overall quality and reliability of the pooled studies (Figure 2, Figure 3, Figure 4 and Figure 5). Moreover, almost half of the 45 RCTs have low RoB. Therefore, the RCTs are considerate high quality studies.

For ROBINS-I tool assessment (Appendix 4), 4 of total non-RCTs (Fahlström et al., 2006; Kraemer et al., 2015; Morifuji et al., 2012; Witard et al., 2014) are high quality as well as the overall assessments had low RoB. Furthermore, this indicated that the 4 non-RCTs comparable to RCTs. However, there were 8 (7 RCTs and 1 non-RCTs) studies have overall of

high and serious RoB that cause the slight decline in the quality. Though, there is a small number of studies have high and serious RoB, while the majority quality of the studies is valid and reliable in supporting the overall effect and safety of WPS on performance and recovery among athletes.

There is methodological heterogeneity because of differences risks of bias and study design. The methodological heterogeneity can assist in explaining the variation of the heterogeneity that could not be sufficiently explained in the subgroup analyses (Fletcher, 2007; Pigott & Shepperd, 2013). The differences could be in binding allocation, a washout period of time and data analysis strategy. For instant, although Areta et al. (2014) and Breen et al. (2011) were RCTs, Areta et al. (2014) on 60 days of intervention period that was non-blinding and had washout period while Breen et al. (2011) on 28 days of intervention period that was single-blinding and no washout period (Table 3). Moreover, in the calculation, the publication bias from the pooled estimates was assessed by the funnel plot and Egger test. From the assessed results, three of the five parameters (creatine kinase, glucose and insulin) seem to have a noticeable presence of publication bias (Figure 29, Figure 32 and Figure 35) as most of the studies were not within 95% confidence limits. Therefore, there is variation in the study design and risk of bias may influence the overall meta-analysis results.

## 5.2 Subgroup analysis

The subgroups meta-analysis were conducted to investigate heterogeneous on each parameter of the outcomes. The subgroup analysis was conducted by physical activities and intervention period range (day). These two variables were selected because nutrient needed in athletes' body depends on how deficient is their body. Physical activities direct causes of deficient in athletes' body (Jani, Coakley, Douglas, & Singh, 2017). During repeated days of high intensity exercise, athletes may have enhanced their performance and may prevent from the fatigue (McInerney et al., 2005).

Apparently, heart rate subgroup analysis managed to explain the differences as the $I^2$ value is low in both subgroups meta-analysis (Figure 8 and Figure 9). However, most of the outcome subgroups analyses heterogeneity remain high and standalone study (Appendix 5). One of the main reason is because of clinical heterogeneity (Fletcher, 2007; Pigott & Shepperd, 2013). The studies data were extracted and analysed without controlling the individual study characteristic as they are different in nature. Nonetheless, the difference dosages and formulation of supplements given to athletes, and protocol of the individual studies also have affected the bioavailability and outcomes (Burke et al., 2012; Lollo et al., 2014). The Table 3 has provide a comprehensive summary of the characteristic and the use of supplements by athletes. Thus, these clinical aspect have contributed to the heterogeneity (Fletcher, 2007). Although there is heterogeneity, this study is worthwhile as explained about the efficacy and safety of WPS on sports performance and recovery among athletes.

## 5.3    Vital signs outcome

### 5.3.1    Heart rate

Heart rate for athletes is an instrument to determine and monitor their daily right effort for every training and how hard their body is being train. A slower increase heart rate while performing training acts as a proof that athletes are physically fit (Aubert, Seps, & Beckers, 2003; M. Li & Kim, 2017). There was an overall slight increase in heart rate (0.52 bpm) when consumed WPS was observed based on the heart rate meta-analysis (Figure 6). Although a slower heart rate is preferable, the small differences between both groups have indicated that WPS is capable and comparable to the comparators.

Rapid absorption of fluids and nutrition assist on better cardiovascular performance in athletes (Oosthuyse & Millen, 2016). These twelve studies have individually shown that WPS and comparators were comparably absorbed rapidly. For WPS is known competent absorbed rapidly more than most protein sources as it appears to resist coagulation in the stomach and surpass intestines relatively quickly (Frank et al., 2017). Whereby, Breen et al. (2011), Li and Zhao (2007) and Impey at al. (2015) studies have shown slower heart rate in WPS compare to carbohydrate supplements. However, among these three studies, two studies heaviest weighted influence studies (Breen et al., 2011; Impey et al., 2015) (Figure 6), and Breen et al. (2011) study has high RoB secondary to the allocation concealment (Figure 3).

The benefits associated with consumed of WPS in context of heart rate may not be significant while consumed comparators (carbohydrate, casein, L-alanine, maltodextrin supplements and placebo). Oosthuyse and Millen (2016) studied specifically the effect of supplements (WPS and comparators) and placebo. This study has the carbohydrate-casein only supplement that intended to maintain all measures of systolic function, yet, these supplements were parallel consistently ingestion.

Based on these findings on examined all supplements with similar heart rate results, therefore, WPS is capable to act as ergogenic aids in athletes' heart rate. Nevertheless, athletes must be mindful about continuous of having low heart rates as their heart enlarged over a prolonged period of time (Dixon, Kamath, McCartney, & Fallen, 1992; Imai et al., 1994). This may lead to suffering from athletic heart syndrome and they would need pacemaker later in life.

### 5.3.2 Respiratory exchange ratio

Respiratory exchange ratio is one of the most metabolic measurements that indicates fuel (mainly carbohydrate or lipid) is being metabolized to supply energy. When RER value is high, carbohydrates are being utilized. On the other hand, when RER value is low, lipid oxidation (Bergman & Brooks, 1999). From the RER meta-analysis (Figure 10) shows WPS has slightly higher RER value compare to the comparators. This implies that the athletes will benefit from WPS as fuel being metabolized to supply energy (mainly from the utilization of carbohydrates) better than the comparators.

Furthermore, the individual studies of RER values are between 0.8 and 0.9 which corresponds to 50% fat and 50% carbohydrate metabolism (M. T. Nelson, Biltz, & Dengel, 2015). Vegge et al. (2012) examined WPS and maltodextrin supplements were associated RER had similar RER values throughout the prolonged submaximal exercise, while Schroer et al. (2014) studied that WPS did not influence RER or performance. Surprisingly, even though Breen et al. (2011) examined on carbohydrate contain supplements, the results of RER value were not extraordinary high, though the study has high RoB (Figure 3). Therefore, athletes consumed WPS has contributed to a higher RER value for better generation of energy.

### 5.3.3  Rate perceived exertion

Rate perceived exertion is a method to quantify internal training load or intensity of exercise for athletes. Normally, it is a scale measurement that runs from 0 to 10 rating. Whereby, 0 is no training is done and 10 extremely heavy training that athletes are able to cope (Amtmann, Amtmann, & Spath, 2008; Ekblom & Golobarg, 1971; Iellamo et al., 2014). The meta-analysis of RPE (Figure 11) shows that WPS has lower RPE value, though there is a slight difference between both groups and a study has high Rob (Breen et al., 2011) (Figure 3). This indicates that WPS group have lower RPE compare to comparators with the similar workload done. Hence, athletes who consume WPS able to have lower RPE and better in coping with the intensity of physical exercise.

Moreover, Highton et al. (2012) reported that athletes who consumed WPS were exercising at a higher exercise intensity compare to carbohydrate, yet both groups RPE value has no great difference. Additionally, Naclerio et al. (2015) examined that WPS provided a lower of RPE values beginning and toward the end of soccer compared to carbohydrate alone or a low calorie placebo. The lower of RPE especially on the end of exercising suggested that availability of glycogen would attenuate the rise in fatigue (Naclerio et al., 2015). These findings suggested that the effect of WPS on a lower RPE value allows athletes greatly increasing physical performance, also known as pacing strategy.

### 5.3.4   Maximum volume of oxygen

Maximum volume of oxygen is defined as the highest rate of oxygen consumption attainable during the incremental or intensity of physical activities (Dlugosz et al., 2013). It also reflects the cardiorespiratory fitness associated with endurance capacity during the prolonged physical activities (Ross et al., 2016). In general, the more $VO_{2max}$ is consume, the athletes are performing more intensely (Dlugosz et al., 2013). Based on the meta-analysis on $VO_{2max}$ (Figure 12), the analysis shows slightly more oxygen when consumption of WPS which supports the motion that WPS allows athletes to attain more $VO_{2max}$ while increase the intensity of physical activities.

The individual included studies agreed to the meta-analysis, though Breen et al. (2011) has high RoB (Figure 3). Coombes et al. (2002) studied that WPS had similar performance benefits with bovine colostrum alone. Similar to Shing et al. (2006) and Schroer et al. (2014) examined that at the beginning of intensity, there may vary in intake $VO_{2max}$, but, at longer duration, there was no difference in improving intake of oxygen and performance. Thus, this may be may be one of causes to the huge amount of 95% CI in the meta-analysis for Schroer (2014) study, but this study has the least weighted influence (Figure 12). On the other hand, Smith et al. (2010) studied that 90%-115% of $VO_{2max}$ during for higher-intensity exercise when consuming caffeine supplementation. The study may have increase the performance although caffeine is an illegal substance that prohibited by WADA (WADA, 2017b). With these findings, WPS is better ergogenic effect in $VO_{2max}$ that allows athletes to have cardiorespiratory fitness while perform intensively.

## 5.4    Serum protein outcome

## 5.4.1    Myoglobin

Released and elevation of myoglobin level indicated the presence of muscle damage or Inflammation after over-exercise (Ramos-Campo et al., 2016). For myoglobin act as direct blood markers of muscle damage (Thomas Jr & Motley, 1984). Moreover, kidneys impair function can build up when extremely myoglobin level release known as rhabdomyolysis (Petejova & Martinek, 2014). For athletes, they seek for aids to prevent the increase of myoglobin concentration during the intensive muscle actions. According to the meta-analysis of myoglobin (Figure 15), athletes who consumed WPS observed to have lower myoglobin level. Surprisingly, WPS seems to have ergogenic aids as it a lower level of myoglobin while athletes drive their strength. Subsequently, athletes are able to diminish muscle fatigue to muscle damage by consuming WPS (Ramos-Campo et al., 2016).

The positive effect of WPS on myoglobin level may be due to ample supply of sources in WP (Nilsson, Holst, & Bjorck, 2007; Sindayikengera & Xia, 2006). Naclerio et al. (2015) examined that a multi-ingredient supplement that contains L-glutamine and L-carnitine L-tartrate did not have any additional effect on performance or recovery. Instead, possibility WP in the supplements that impact on lower myoglobin level. Additionally, Gunnarsson et al. (2013) studied simple ingredients between WPS (WP and carbohydrate) and placebo, thus, WPS result of a lower myoglobin level as well. Based on these findings, for consumption of WPS has shown that it can lower myoglobin level, athletes are able to go beyond their potential maximum aerobic threshold while delaying muscle damage and injuries (Thomas Jr & Motley, 1984).

### 5.4.2 Muscle glycogen

Muscle glycogen is essential substrate sources during prolonged moderate to high intensity exercise. Yet, muscle glycogen degenerate when perform the intensity exercise over a long period of time. It requires replenishing to able to recover from the intensity exercise as well as repair and heal damaged muscle (Gunnarsson et al., 2013). Protein will be an absolute aid for stimulating muscle glycogen synthesis also known as proteolysis (Hardin et al., 1995). From the meta-analysis of muscle glycogen (Figure 16), the analysis illustrates that athletes who consumed WPS has enhanced or better in regenerate of muscle glycogen level compare to the comparators. Therefore, WPS has ergogenic aid athletes for rapid recovery from fatigue and muscle damage.

Even though it is only three studies which also have a high RoB study (Hill et al., 2013) caused by allocation concealment (Figure 3), Gunnarsson et al. (2013) and Detko et al. (2013) discussed positively specifically on the enhancement of muscle glycogen content by consumed WPS. Gunnarsson et al. (2013) study observed the resynthesise appeared in both type I and type II muscle fibres. Additionally, the rate of glycogen rebuilding higher after the 90-minutes soccer match compared to the 60-minutes soccer match. However, Hill et al. (2013) experimented that WPS did not influence muscle glycogen levels, yet, had enhances recovery at end of 6 hours cycling. Based on these findings, WPS improved muscle glycogen level can delay the time to fatigue during exertion. Hence, consumption of WPS, higher muscle glycogen level, athletes can focus more at higher intensity levels as well as improves their performance.

## 5.5    Strength and body composition outcome

### 5.5.1    Maximum and average power

To perform in sports, strength is key performance measurement and one of the main interest that athletes seek for ergogenic aids (Al-Nawaiseh et al., 2016; Lemon, Tarnopolsky, MacDougall, & Atkinson, 1992; Tarnopolsky et al., 1992). The meta-analyses on maximum and average power (Figure 17 and Figure 20) show slight differences between both groups. This indicates that WPS has the ergogenic effect to the maximum and average power are equivalent to the control groups. Thus, WPS is comparable to be capable as ergogenic aids in strength for athletes.

Four of the included studies agreed there no difference between both groups (Coombes et al., 2002; Hansen et al., 2016; Hoffman et al., 2009; Joy et al., 2013), which may explain the low value of subgroup analysis heterogeneity (Figure 17 and Figure 20). Moreover, Shing et al. (2006) examined that athletes consume WPS experienced decrease in strength in the beginning, but they recovered from any residual fatigue and remained unchanged at following the 5-6 days. Moreover, Highton et al. (2012) discovered that WPS ingestion enabled a small increase in exercise intensity in the latter stages of the sports exercise compared to carbohydrate. Al-Nawaiseh et al. (2016) also investigated that average power recovered better and managed bout 4 higher for athletes consumed WPS than placebo. Hence, WPS would assist athletes in strength at a longer period of consumption with the physical activities.

### 5.5.2 Body mass

The central of athletes' development and well-being are body composition. One of the important body composition measures is body mass (Anding & Oliver, 2015). Based on the body mass meta-analysis (Figure 23), the analysis has illustrated that WPS improved athletes' body mass by lowering their body mass better than the comparators, though marginal difference. When both groups exercising at the similar workload, WPS group intend to have lower body mass. Thus, the results suggested that athletes who need to achieved Ideal weight by losing their body mass for the sports performance are encouraged to consumed WPS (Brukner & Khan, 2009).

Additionally, the individual studies explained that WPS is ergogenic aids body composition as a whole. The relationship of WPS with body mass is well studied and elaborated by Lollo et al. (2011, 2014). Additionally, according to the finding Lollo et al. (2011) examined that WPS provided beneficial for maintaining and gaining muscle mass in athletes, while Lollo et al. (2014) further assessed that WPS has a net effect on muscle mass gain over prolonged exercise. Both studies have the highest weighted influence (Figure 23). Moreover, Taylor et al. (2016) reported particularly on female athletes who improved lean body mass and reduces fat mass. Hence, WPS has ergogenic aids effect in body composition by lowering body mass while maintaining or gaining muscle mass.

## 5.6 Blood profile outcome

### 5.6.1 Amino acid

Whey protein supplements have high levels of serum amino acids of both EAA and BCAA are well-known and has described them in Chapter 2.4 (Frank et al., 2017). Furthermore, the meta-analyses results (Figure 25 and Figure 27) illustrated robust evidence that athletes who consumed WPS had higher levels of serum amino acids than comparators. Essential amino acids of WPS was believed to retain and growth of muscle, while BCAA of WPS was believed to delay the onset of fatigue during prolonged endurance exercise (Chang et al., 2015; Ha & Zemel, 2003; Tang et al., 2007).

Moreover, Areta et al. (2014) investigated that amino acids of WPS support muscle protein while Impey et al. (2015) examined WPS enhanced post-exercise muscle protein synthesis rates. Tang et al. (2007) also investigated that a small dose of WP (10 g) able to stimulate muscle protein synthesis athletes after exercise. Therefore, serum amino acid from WPS absolute ergogenic benefit for athletes on delay and recovery from the sports injuries and fatigue (Chang et al., 2015; Kingsbury et al., 1998).

### 5.6.2 Creatine kinase

Creatine kinase appearing in blood is considered as a marker of indirect muscle damage (Al-Nawaiseh et al., 2016). The level is to assist in detecting athletes' body condition of tissue damage. It is reasonable for creatine kinase level to elevate temporary due to the eccentric muscle actions (Cepero et al., 2010; Hansen et al., 2016), but the level should not raise up until a condition that could damage the skeletal muscles, heart or brain (O'Gorman, Beutner, Wallimann, & Brdiczka, 1996). Based on the meta-analysis of creatine kinase (Figure 28), WPS has lower creatine kinase level in athletes, though Hansen et al. (2015, 2016) have high RoB (Figure 3). This indicates that WPS can attenuate muscle fatigue and reduce the risk of sports injuries better than the comparator groups (Jauhari et al., 2014; Lollo et al., 2014). Therefore, WPS is beneficial for athletes by having a lower creatine kinase level while driving their physical strength.

Creatine kinase seems to be the most attractive biomarker for athletes as it has the most studies in the meta-analysis among the biomarkers parameter. Most of the individual studies concluded that WPS had the positive effect of WPS on prevented Increase in creatine kinase level - which may explain the low value of the cycle subgroup analysis heterogeneity (Figure 30). Moreover, Kraemer et al. (2015) observed that WPS delay in muscle soreness as well as improved intensity of the physical performance. Lollo et al. (2014) also studied that the positive effect of WPS on attenuated creatine kinase level could be because properties of WPS has antioxidant capacity. Hence, lower in creatine kinase when consuming WPS will aid athlete to prolong time to fatigue and better maintain or improve exercise performance.

### 5.6.3   Glucose

Glucose is one of the main energizers for athletes to optimize their performance (Breen et al., 2011; Cepero et al., 2010). Additionally, after heavy physical activities, glucose assists to regenerate muscle glycogen level that leads to better recovery. Based on the meta-analysis of glucose (Figure 31), the analysis has illustrated that WPS has energetically enhanced glucose level as there are marginal differences between both groups, though the analysis shows slightly higher in the control group. Therefore, WPS has efficient glucose level to provide energy for athletes.

Glucose parameter is one of the parameters that has most eligible studied across all the outcomes. Cepero et al. (2010) examined that due to the utilization of the added WP in the supplement has hepatic glucose output. Morifuji et al. (2012) studied that this because of WPS contains large amounts of BCAA that containing bioactive peptides. However, Detko et al. (2013) concluded that both treatment groups had enhanced glucose concentrations. The study also examined there is a possible reflection of a reduced rate of glucose production rather than glucose disposal by WPS. According to the findings, WPS is able to provide athletes essential fuel and restore of glucose concentrations. Yet, athletes must be mindful about glucose levels which remain high over a prolonged period of time can develop diabetes, damage your eyes, kidneys, nerves and blood vessels (Kavey et al., 2006).

### 5.7 Hormones outcome

### 5.7.1 Insulin

Insulin is a hormone made by the pancreas that allows the body to use glucose for energy or to store glucose for future use. Sufficient of insulin level enabling to restore of the muscle glycogen before and between strenuous muscle events (Detko et al., 2013). Based on the meta-analysis of insulin (Figure 34), WPS has enhanced glucose level compared to the comparators. Athletes will have sufficient and storage of energy to performance when consuming WPS. Thus, WPS enhanced insulin concentration for athletes which act as a bolster of stamina.

Of all the parameters across all the outcomes, insulin has the most number of studies, yet, there are three studies have high RoB (Breen et al., 2011; Burke et al., 2012; Hill et al., 2013) caused by allocation concealment and selective outcome reporting (Figure 3). Cepero et al. (2010) concluded that sometimes seem with WPS has a positive physiological effect with greater significant values for serum insulin especially at 165 and 180 minutes of performance. However, in the meta-analysis shows that insulin level is higher in comparators. Hill et al. (2013) explained that WPI has better insulinotrophic property compare to the comparator (i.e. caseins and proteins of vegetable origin). Morifuji et al. (2012) discussed in depth that WP fraction was more efficient insulin secretagogue than comparators (i.e. casein with/and carbohydrate). However, Mero et al. (1997) reported that insulin curve is typical of physical exercise. Bovine colostrum supplementation provides better insulin concentration by strengthening the effects of IGF-I and insulin on protein anabolism in athletes. Hence, WPS is a nutritional strategy to maximize insulin levels in athletes. However, direct use of insulin is prohibited by WADA (WADA, 2017b). This is

because an overdose of insulin causes a fatal coma by clearing glucose from blood brain which starved of energy and oxygen (Beigelman, 1971).

### 5.7.2 Cortisol

Cortisol acted as a marker of exercise recovery from hormones. Cortisol is one of the important markers because it has a catabolic effect on tissue and decrease in anabolic hormones (Powell, DiLeo, Roberge, Coca, & Kim, 2015). From the meta-analysis of cortisol (Figure 36), the analysis shows an overall cortisol level was slightly lower when consuming WPS compared to comparators, though there are two high RoB studies (Hansen et al., 2015; Hansen et al., 2016) caused by allocation concealment (Figure 3). The impact of WPS on cortisol level may be small but it is significant. This is because a lower of cortisol level is ideal for athletes on achieving recovery and regenerate of tissue (Powell et al., 2015).

The beneficial effect of WPS may due to the effect of reduction in circulating cortisol. This may cause changes in recovery concentrations of neutrophil-priming plasma fatty acid and amino acid metabolites (A. R. Nelson et al., 2013). Furthermore, Kraemer et al. (2015) had observed that WPS responses may occur in muscle tissue but there are relatively small increases in circulating beta-hydroxy-beta-methylbutyrate after ingestion of interventions, thus, no evident effects on circulating hormone concentrations. On the other hand, Shing et al. (2013) believe that interventions had no relationship between cortisol because of imbalance of anabolic and catabolic process. Additionally, Hansen et al. (2015) had an interesting observation that sustains the sense of performance capacity, though cortisol level is higher after the athletes consumed WPS compared to carbohydrate. Hence, with

these findings, the effect of WPS on cortisol level sustains performance of athletes and aids on the muscle recovery, though it has a small impact.

### 5.7.3 Testosterone

Testosterone is a hormone that assists in increasing lean muscle mass and bone density (Maïmoun et al., 2003). Testosterone can influence muscles protein synthesise by promote growth hormone responses in the pituitary (Rickenlund, Thorén, Carlström, von Schoultz, & Hirschberg, 2004). According to the meta-analysis of testosterone (Figure 38), there is slight differences between both groups of testosterone concentrations, though comparators has slightly higher. Therefore, WPS is effective on induce testosterone level for muscles protein synthesise. Especially for athletes who want to increase lean muscle mass and bone density.

Testosterone has the least interest and included studies among the hormones outcome. Yet, the results add on value towards athletes' recovery as may produce hypertrophied muscles (Maïmoun et al., 2003). One of the study, Kraemer et al. (2015), has discussed generally on hormones testosterone concentrations were similar between WPS and comparators as the stability of beta-hydroxy-betamethylbutyrate in cell membrane. Hence, the effect of WPS on level of testosterone has influence on the development of strength and muscle mass.

## 5.8    Safety

There was no relevant data was available on the safety and no side effect reported in all the included studies. Therefore, this systematic review and meta-analysis study are not in the position to discuss about it. Nonetheless, although WP is recognised as safe supplements for athletes (Bolster et al., 2005; Tipton et al., 2004), concern arises from WADA insight whereby illegal substances can be found in the interventions from the included studies. Four studies reported intervention contained caffeine (Fahlström et al., 2006; Gunnarsson et al., 2013; Impey et al., 2015; Smith et al., 2010) and a study had intervention contained alcohol (Parr et al., 2014). Hence, it can be concluded in the light of these reports that athletes shall be cautious while taking WPS in the content of not violating WADA rule; however the safety profile of these WPS (WADA, 2017b).

# CHAPTER 6: CONCLUSION AND RECOMMENDATIONS

## 6 Chapter 6: Conclusion and recommendations

### 6.1 Conclusion

The systematic review and meta-analysis study has attempted on the clinical evidence efficacy and safety of WPS on performance and recovery among athletes is promising. First of all, the quality of studies has delivered assure validity and reliability of the clinical evidence. Whereby, most of all the studies were RCTs, thus, many sources of biases have omitted. Furthermore, from the RoB assessment of the Cochrane Risk of Bias Assessment and the ROBIN-I tools, the majority of the studies shows low RoB and non-RCTs were comparable to RCTs. Therefore, athletes and their support staff such as physicians, coaches, trainers, therapists and nurses can have sureness on the evidence with regards WPS for sports performance and recovery.

Athletes who aiming to have cardiorespiratory fitness during intense performance, may consumed WPS as it has better ergogenic aids on the vital signs outcome than comparators. The assessment effect of WPS on the vital signs outcome has improves RPE (overall WMD = 0.258; CI = -1.09, 0.57; $I^2$ = 95.1%; p = 0.00) and $VO_{2max}$ (overall WMD = 1.33; CI = 4.71, 7.36; $I^2$ = 98.8%; p = 0.00). These parameters indicate that WPS allows athletes inhale more oxygen while increase intensely of the physical performance. Furthermore, WPS has increase RER (overall WMD = 0.004; CI = -0.003, 0.01; $I^2$ = 14.5%; p = 0.32) that improve generation of energy. However, consuming WPS has slight increase of heart rate (overall WMD = 0.52; CI = -1.07, 2.11; $I^2$ = 62.3%; p = 0.002) which may shortage in contribute to the physically fitness. Although the parameters results are marginal differences, WPS is capable and comparable to the comparators for the vital signs outcome.

The assessment of the effect of WPS on the serum protein outcome revealed to be an absolute advantage than comparators. The advantage contribute especially for athletes who performing prolonged intensity exercise will able to have lower (overall WMD = 11.74; CI=-30.24, 6.76; $I^2$ = 79.6%; p = 0.007) myoglobin level and enhancement of muscle glycogen level (overall WMD = 9.08; CI =-23.19, 41.36: $I^2$ = 97.8%; p = 0.00). Hence, athletes can focus on prolonged higher intensity level exercise while delaying muscle damage and injuries.

For athletes who need to achieve their ideal weight by losing weight, may consider consuming WPS which seem to reduce body mass (overall 4.1 kg CI = -5.84, -2.36; $I^2$ = 47.9%; p = 0.04) than comparators. When athletes on diet to lose weight, their strength to perform may be affectedly. However, this situation did not occur for athletes who consumed WPS, their strength is sustainable. Although decrease of strength on parameter average power (overall WMD = 2.57; CI = -1.07, 2.11; $I^2$ = 62.3%; p = 0.002) and maximum power (overall WMD = 3.14; CI = -129.47, 123.2; $I^2$ = 97.4%; p = 0.00) meta-analysis, they are merely slight decrease. Thus, athletes is able to maintain their strength for performance while losing weight.

Athletes who are hinder from recovery process, the results of WPS has demonstrated that it has ample supply of sources from WPS for the blood profile outcome to enhance the recovery process. As it is well-known to have high amino acid parameters that aids in muscle growth: EAA (overall WMD = 624.03; CI = 169.27, 1078.8; $I^2$= 100%; p = 0.00) and BCAA (overall WMD = 458.57; CI=179.96, 737.18; $I^2$=100%; p = 0.00). Subsequently, speedy recovery of muscle damage as the creatine kinase level have seen to be reduced (overall

WMD = 47.05; CI= -129.47, 35.37; $I^2$ =98.4%; p = 0.000). Furthermore, to re-establishment of strength during recovery, WPS has supply energy the body with essential glucose (overall WMD = 0.17; CI=-0.33, -0.01; $I^2$ = 99.1%; p = 0.000) for athletes, though glucose concentrations slightly lower than comparators. Therefore, athletes who are seeking ergogenic aids in recovery from sport injuries may consider WPS as it has enhances recovery and supply of energy for re-establishment of strength.

The assessment of the ergogenic effect of WPS on the hormone outcome has benefit athletes on recovery and performance. The effect of insulin level was higher that bolster of stamina (overall WMD = 7.13; CI = 5.00, 9.25; $I^2$ = 99.8%; p = 0.00) than comparators. Moreover, testosterone induce (overall WMD = 0.37; CI = -0.86, 0.12; $I^2$ = 90.8%; p = 0.000) which allows growth of lean muscle mass and bone density. While, having lower (overall WMD = 5.40; CI = -10.14, -0.66, $I^2$ = 75.9%, p = 0.000) cortisol level lower on achieving recovery and regenerate of tissue. Therefore, athletes should consider WPS as ergogenic aid on corresponding to hormone outcome. Athletes will have speedy recovery for their next performance.

## 6.2 Limitation

Several limitations of this systematic review and meta-analysis are worth considering. Foremost, the high level of heterogeneity between studies was found in most of the parameters. Thus, subgroup analyses were conducted, yet, heterogeneity remains high in some scenario of the parameters. Moreover, the funnel plot and Egger test were performed to identify the publication bias, and the analyses discovered that creatine kinase, glucose and insulin parameters have the presence of publication bias which may influence the heterogeneity. Therefore, this systematic review and meta-analysis study are not in a position to identify the main causes of the high heterogeneity.

However, the variable or the characteristic of the participants possibly contributed to the high heterogeneity. Although inclusion criteria have defined to ensure that the participants of included studies were as similar as possible, factors such as geographical, ethnicity, categorical of athletes, weight, heights and age still varied (Table 3). For instant, Oosthuyse et al. (2016) studied on cyclist athletes on average age of 38.9, average weight of 78.5 kg and average heights of 179.8 cm that conducted study in South Africa, while Taylor et al. (2016) examined on basketball players who have average age of 20.5, average weight of 67.1 kg and average heights of 169.5 cm. Therefore, it is difficult to generalise the outcomes due to the diverse characteristics of athletes.

Nevertheless, variation in study design may also influence the result of high heterogeneity. Although inclusion criteria on the type of study design were placed and most studies are RCTs, there are different from one trial to another. Additionally, the high and serious risk of bias from the assessment of RoB (Chapter 4.3) may contribute to the high heterogeneity.

For example, Hoffman et al (2009) and Yang (2014) had only randomisation state as their descriptive study design. On the other hand, many studies had more features and blinding of study design such as crossover (Highton et al., 2012), counterbalanced (Impey et al., 2015), placebo controlled (Schroer et al., 2014) and parallel (Detko et al., 2013). Therefore, study design varies across the parameters of the outcomes may have influenced the heterogeneity.

Furthermore, clinical heterogeneity (e.g. a dose of supplements, setting and protocol) have added to the heterogeneity. In margin situation, Schroer et al. (2014) have participants consumed supplements every 15 minutes within a day for 16 days, while Joy et al. (2013) has participants consumed supplements once a day for 56 days. For settings and protocol which has different in strenuous, Impey et al. (2015) instructed that participants cycling and consume supplements before exercise, whereas Lollo et al. (2014) has participants consume supplements before and after their usual soccer training. Even though subgroup analyses were performed to investigate to interrelate to these situations, the high heterogeneity remains in some parameters. Thus, it is difficult to identify the true causes of the high heterogeneity.

This variation may influence correlated independently or dependently between the variables. Hence, researchers or readers (especially athletes and their support staff) should carry in mind that these factors and parameters when clinical interpretability the results of this systematic review and meta-analysis.

On top of that, the discussion and conclusion draw from this systematic review and meta-analysis upon the sports performance and recovery among athletes are at the time they were measured. Therefore, this review cannot establish the causation between the parameters and long-term performances and recovery progress for athletes. As abovementioned (Chapter 5.3.1 and 5.6.3), athletes must be mindful of continuous of having low heart rates and remain of glucose levels over a prolonged period of time.

## 6.3    Recommendations

Future directions for research and conducting research that includes larger sample sizes, the inclusion of both gender (especially on female athletes), ages, geographical, type of sport and categories of athletes. Interventions that are consumed before, during and/or after sports performances and recovery process also deserve further considering the effectiveness of improving athletes' sports performances and recovery. Additionally, follow-up studies could establish effectiveness for the relation between interventions and long-term performances recovery progress for athletes.

Athletes and their providers must utilise the most effective interventions to assist in the process of injuries recovery and their returns for the sports performance and activities. This study contributes the most up-to-date information available with respect to the efficacy and safety of WPS and comparators for athletes' sports performance and recovery. Besides, although the study demonstrates has small size effect on certain parameters, the included studies examined as close as possible to real life conditions of sports performances and competition for athletes. Therefore, the study can be used as a guide for better decision-making especially when working with multidisciplinary approach between cardiologists,

physiologists and coaches. Importantly, it is highly recommended for athletes and their

providers are well-inform and updated on WADA guidelines that updated annually before

consuming any WPS. These findings are worthy of further inquiry and investigation.

# CHAPTER 7: REFERENCES

## 7    Chapter 7: References

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**APPENDICES**

**Table of Appendices**

## 8    Appendices

### 8.1    Appendix 1: PRISMA Checklist

| Section/topic | # | Checklist item | Reported on page # |
|---|---|---|---|
| **TITLE** | | | |
| Title | 1 | Identify the report as a systematic review, meta-analysis, or both. | 23 |
| **ABSTRACT** | | | |
| Structured summary | 2 | Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number. | 3 |
| **INTRODUCTION** | | | |
| Rationale | 3 | Describe the rationale for the review in the context of what is already known. | 23 |
| Objectives | 4 | Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS). | 26 |
| **METHODS** | | | |
| Protocol and registration | 5 | Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number. | 43 |
| Eligibility criteria | 6 | Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale. | 45-47 |
| Information sources | 7 | Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched. | 44-47 |
| Search | 8 | Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated. | 44-47 |
| Study selection | 9 | State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis). | 44-47 |
| Data collection process | 10 | Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators. | 47-48 |
| Data items | 11 | List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made. | 48 |
| Risk of bias in individual studies | 12 | Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis. | 49-47 |
| Summary measures | 13 | State the principal summary measures (e.g., risk ratio, difference in means). | 51-54 |

| Section/topic | # | Checklist item | Reported on page # |
|---|---|---|---|
| Synthesis of results | 14 | Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I$^2$) for each meta-analysis. | 51-54 |
| Risk of bias across studies | 15 | Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies). | 51-54 |
| Additional analyses | 16 | Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified. | 51-54 |
| **RESULTS** | | | |
| Study selection | 17 | Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram. | 56-54 |
| Study characteristics | 18 | For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations. | 58-71 |
| Risk of bias within studies | 19 | Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12). | 75-76 |
| Results of individual studies | 20 | For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot. | 80-115 |
| Synthesis of results | 21 | Present results of each meta-analysis done, including confidence intervals and measures of consistency. | 80-115 |
| Risk of bias across studies | 22 | Present results of any assessment of risk of bias across studies (see Item 15). | 80-115 |
| Additional analysis | 23 | Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]). | 80-115 |
| **DISCUSSION** | | | |
| Summary of evidence | 24 | Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers). | 121 |
| Limitations | 25 | Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias). | 144 |
| Conclusions | 26 | Provide a general interpretation of the results in the context of other evidence, and implications for future research. | 141 |
| **FUNDING** | | | |
| Funding | 27 | Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review. | Not Applicable |

Source from  (Moher et al., 2009)

## 8.2   Appendix 2: Stata Syntax to install meta-analysis packages

update all

///metan

net install sbe24_3, from(http://www.stata-journal.com/software/sj9-2) replace


///mvmeta

net install mvmeta, from(http://www.mrc-bsu.cam.ac.uk/IW_Stata/meta) replace


///metareg

net install sbe23_1, from (http://www.stata-journal.com/software/sj8-4) replace


///network

net from http://www.mrc-bsu.cam.ac.uk/IW_Stata/


///produce graph for meta-analysis

ssc install metafunnel

search metan

which metan

ssc install metaaggr, all replace

ssc install metabias

## 8.3 Appendix 3: Cochrane Risk of Bias tool for RCTs

### 8.3.1 Guideline

Use the modified Cochrane Collaboration tool to assess risk of bias for randomized controlled trials. Bias is assessed as a judgment (high, low, or unclear) for individual elements from five domains (selection, performance, attrition, reporting, and other) (McPheeters et al., 2012).

| Domain | Description | High Risk of Bias | Low Risk of Bias | Unclear Risk of Bias | Reviewer Assessment |
|---|---|---|---|---|---|
| Selection bias **Random sequence generation** | Described the method used to generate the allocation sequence in sufficient detail to allow an assessment of whether it should produce comparable groups | Selection bias (biased allocation to interventions) due to inadequate generation of a randomized sequence | Random sequence generation method should produce comparable groups | Not described in sufficient detail | High Low Unclear |
| Selection bias **Allocation concealment** | Described the method used to conceal the allocation sequence in sufficient detail to determine whether intervention allocations could have been foreseen before or during enrollment | Selection bias (biased allocation to interventions) due to inadequate concealment of allocations prior to assignment | Intervention allocations likely could not have been foreseen in before or during enrollment | Not described in sufficient detail | High Low Unclear |
| Reporting bias **Selective reporting** | Stated how the possibility of selective outcome reporting was examined by the authors and what was found | Reporting bias due to selective outcome reporting | Selective outcome reporting bias not detected | Insufficient information to permit judgment† | High Low Unclear |

| Other bias **Other sources of bias** | Any important concerns about bias not addressed above* | Bias due to problems not covered elsewhere in the table | No other bias detected | There may be a risk of bias, but there is either insufficient information to assess whether an important risk of bias exists or insufficient rationale or evidence that an identified problem will introduce bias | High Low Unclear |
|---|---|---|---|---|---|
| Performance bias **Blinding (participants and personnel)** | Described all measures used, if any, to blind study participants and personnel from knowledge of which intervention a participant received. Provided any information relating to whether the intended blinding was effective. | Performance bias due to knowledge of the allocated interventions by participants and personnel during the study. | Blinding was likely effective. | Not described in sufficient detail | High Low Unclear |
| Detection bias **Blinding (outcome assessment)** | Described all measures used, if any, to blind outcome assessors from knowledge of which intervention a participant received. Provided any information relating to whether the intended blinding was effective. | Detection bias due to knowledge of the allocated interventions by outcome assessors. | Blinding was likely effective. | Not described in sufficient detail | High Low Unclear |

| | | | | |
|---|---|---|---|---|
| Attrition bias **Incomplete outcome data** | Described the completeness of outcome data for each main outcome, including attrition and exclusions from the analysis. Stated whether attrition and exclusions were reported, the numbers in each intervention group (compared with total randomized participants), reasons for attrition/exclusions where reported. | Attrition bias due to amount, nature or handling of incomplete outcome data. | Handling of incomplete outcome data was complete and unlikely to have produced bias | Insufficient reporting of attrition/exclusions to permit judgment (e.g., number randomized not stated, no reasons for missing data provided) | High Low Unclear |

* If particular questions/entries were pre-specified in the study's protocol, responses should be provided for each question/entry.

† It is likely that the majority of studies will fall into this category.

Assess each main or class of outcomes for each of the following. Indicate the specific outcome.

## 8.3.2 The assessment judgment outcomes of RCTs

| Author name | Year | Title | Sequence generation | Description | Allocation concealment | Description | Blinding of participants and personnel | Description | Blinding of outcome assessors | Description | Incomplete outcome data | Description | Selective outcome reporting | Description | Other sources of bias | Description | Overall |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Al-Nawaiseh | 2016 | Enhancing Short-Term Recovery After High-Intensity Anaerobic Exercise | Low Risk | random & crossover, counterbalanced | Unclear Risk | didn't mention about blinding | Unclear Risk | didn't mention about blinding | Unclear Risk | didn't mention about blinding | Low Risk | No missing outcome data or loss to follow-up | Low risk | The study protocol is available and all of the study's pre-specified outcomes of interest have been reported in the pre-specified way | Low risk | The study appears to be free of other sources of bias. | Unclear Risk of Bias |

| | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Areta | 2014 | Reduced resting skeletal muscle protein synthesis is rescued by resistance exercise and protein ingestion following short-term energy deficit | Low Risk | random & within-subject, counterbalanced | Unclear Risk | didn't mention about blinding | Unclear Risk | didn't mention about blinding | Unclear Risk | didn't mention about blinding | Low Risk | No missing outcome data or loss to follow-up | Low risk | The study protocol is available and all of the study's pre-specified outcomes of interest have been reported in the pre-specified way | Low risk | The study appears to be free of other sources of bias. | Unclear Risk of Bias |
| Breen | 2011 | The influence of carbohydrate-protein co-ingestion following endurance exercise on myofibrillar and mitochondrial protein synthesis | Low Risk | random & counterbalanced | High Risk | Single Blinding (participants or investigators enrolling participants could possibly foresee assignments) | Low Risk | Although it is single blinding whereby participants or investigators enrolling participants could possibly foresee assignme | Low Risk | Although it is single blinding whereby participants or investigators enrolling participants could possibly foresee assignme | Low Risk | No missing outcome data or loss to follow-up | Low risk | The study protocol is available and all of the study's pre-specified outcomes of interest have been reported in the pre-specified | Low risk | The study appears to be free of other sources of bias. | High Risk of Bias |

| | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | nts. However, there is no incomplete blinding, but in the reviewer's judgment the outcome is not likely to be influenced by lack of blinding | | nts. However, there is no incomplete blinding, but in the reviewer's judgment the outcome is not likely to be influenced by lack of blinding | | | | way | | | |
| Brinkworth | 2002 | Oral bovine colostrum supplementation enhances buffer capacity but not rowing performance in elite female rowers | Low Risk | random & placebo-controlled, parallel | Low Risk | Double Blinding | Low Risk | Double Blinding | Low Risk | Double Blinding | Low Risk | No missing outcome data or loss to follow-up | Low risk | The study protocol is available and all of the study's pre-specified outcomes of interest have been reported in the pre-specified | Low risk | The study appears to be free of other sources of bias. | Low Risk of Bias |

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|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | | | | | way | | | |
| Brown | 2004 | Soy versus whey protein bars: Effects on exercise training impact on lean body mass and antioxidant status | Unclear Risk | random & without providing the details of what was done | Low Risk | Double Blinding | Low Risk | Double Blinding | Low Risk | Double Blinding | Low Risk | No missing outcome data or loss to follow-up | Low risk | The study protocol is available and all of the study's pre-specified outcomes of interest have been reported in the pre-specified way | Low risk | The study appears to be free of other sources of bias. | Unclear Risk of Bias |
| Buckley | 2000 | Does a diet of colostrum improve athletic performance? | Low Risk | random & placebo controlled, parallel | Low Risk | Double Blinding | Low Risk | Double Blinding | Low Risk | Double Blinding | Low Risk | No missing outcome data or loss to follow-up | Low risk | The study protocol is roughly explain but it is clear that the published reports include all expected outcomes, including those that were pre-specified | Low risk | The study appears to be free of other sources of bias. | Low Risk of Bias |

| | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Burke | 2012 | Preexercise aminoacidemia and muscle protein synthesis after resistance exercise | Low Risk | random & placebo controlled, counterbalanced | Low Risk | Double Blinding | Low Risk | Double Blinding | Low Risk | Double Blinding | Low Risk | No missing outcome data or loss to follow-up | High Risk | One or more primary outcomes are reported using measurements, | Low risk | The study appears to be free of other sources of bias. | High Risk of Bias |
| Cepero | 2010 | INFLUENCE OF INGESTING CASEIN PROTEIN AND WHEY PROTEIN CARBOHYDRATE BEVERAGES ON RECOVERY AND PERFORMANCE OF AN ENDURANCE CYCLING TEST | Low Risk | random & counterbalanced | Low Risk | Double Blinding | Low Risk | Double Blinding | Low Risk | Double Blinding | Low Risk | No missing outcome data or loss to follow-up | Low risk | analysis methods or subsets of the data (e.g. subscales) that were not pre-specified | Low risk | The study appears to be free of other sources of bias. | Low Risk of Bias |
| Coombes | 2002 | Dose effects of oral bovine colostrum on physical work capacity in cyclists. / Effets de la prise orale | Low Risk | random & placebo-controlled study | Low Risk | Double Blinding | Low Risk | Double Blinding | Low Risk | Double Blinding | Low Risk | No missing outcome data or loss | Low risk | The study protocol is available and all of the study's pre-specified | Low risk | The study appears to be free of | Low Risk of Bias |

| | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | de colostrum bovin sur les capacites physiques de travail chez des cyclistes | | | | | | | | | | to follow-up | | outcomes of interest have been reported in the pre-specified way | | other sources of bias. | |
| Cribb | 2006 | The effect of whey isolate and resistance training on strength, body composition, and plasma glutamine | Unclear Risk | random & without providing the details of what was done | Low Risk | Double Blinding | Low Risk | Double Blinding | Low Risk | Double Blinding | Low Risk | No missing outcome data or loss to follow-up | Low risk | The study protocol is available and all of the study's pre-specified outcomes of interest have been reported in the pre-specified way | Low risk | The study appears to be free of other sources of bias. | Unclear Risk of Bias |
| Cury-boaventura | 2008 | Effects of exercise on leukocyte death: prevention by hydrolyzed whey protein enriched with glutamine | Low Risk | random & crossover | Low Risk | Double Blinding | Low Risk | Double Blinding | Low Risk | Double Blinding | Low Risk | No missing outcome data or loss to follow- | Low risk | The study protocol is available and all of the study's pre-specified outcomes of interest have been | Low risk | The study appears to be free of other sources of | Low Risk of Bias |

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|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | dipeptide | | | | | | | | | | up | | reported in the pre-specified way | | bias. | |
| Detko | 2013 | Liver and muscle glycogen repletion using 13C magnetic resonance spectroscopy following ingestion of maltodextrin, galactose, protein and amino acids | Low Risk | random & parallel | Low Risk | Double Blinding | Low Risk | Double Blinding | Low Risk | Double Blinding | Low Risk | No missing outcome data or loss to follow-up | Low risk | The study protocol is available and all of the study's pre-specified outcomes of interest have been reported in the pre-specified way | Low risk | The study appears to be free of other sources of bias. | Low Risk of Bias |
| Fukuda | 2010 | The possible combinatory effects of acute consumption of caffeine, creatine, and amino acids on the improvement of anaerobic running performance in | Low Risk | random & placebo-controlled crossover | High Risk | Single Blinding (participants or investigators enrolling participants could possibly foresee assignme | Low Risk | Although it is single blinding whereby participants or investigators enrolling participants could possibly foresee | Low Risk | Although it is single blinding whereby participants or investigators enrolling participants could possibly foresee | Low Risk | No missing outcome data or loss to follow-up | Low risk | The study protocol is available and all of the study's pre-specified outcomes of interest have been reported in the pre-specified | Low risk | The study appears to be free of other sources of bias. | High Risk of Bias |

| | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | humans | | | | nts) | | assignments. However, there is no incomplete blinding, but in the reviewer's judgment the outcome is not likely to be influenced by lack of blinding | | assignments. However, there is no incomplete blinding, but in the reviewer's judgment the outcome is not likely to be influenced by lack of blinding | | | | way | | | |
| Gunnarsson | 2013 | Effect of whey protein- and carbohydrate-enriched diet on glycogen resynthesis during the first 48 h after a soccer game | Unclear Risk | random & without providing the details of what was done | Unclear Risk | didn't mention about blinding | Unclear Risk | didn't mention about blinding | Unclear Risk | didn't mention about blinding | Low Risk | No missing outcome data or loss to follow-up | Low risk | The study protocol is available and all of the study's pre-specified outcomes of interest have been reported in the pre- | Low risk | The study appears to be free of other sources of bias. | Unclear Risk of Bias |

| | | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | | | | | | specified way | | | | |
| Hansen | 2015 | Effect of Whey Protein Hydrolysate on Performance and Recovery of Top-Class Orienteering Runners | Low Risk | random & block | High Risk | Single Blinding (participants or investigators enrolling participants could possibly foresee assignments) | Low Risk | Although it is single blinding whereby participants or investigators enrolling participants could possibly foresee assignments. However, there is no incomplete blinding, but in the reviewer's judgment the outcome is not likely to be influence | Low Risk | Although it is single blinding whereby participants or investigators enrolling participants could possibly foresee assignments. However, there is no incomplete blinding, but in the reviewer's judgment the outcome is not likely to be influence | Low Risk | No missing outcome data or loss to follow-up | Low risk | The study protocol is available and all of the study's pre-specified outcomes of interest have been reported in the pre-specified way | Low risk | The study appears to be free of other sources of bias. | High Risk of Bias |

| | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | d by lack of blinding | | d by lack of blinding | | | | | | | |
| Hansen | 2016 | Protein intake during training sessions has no effect on performance and recovery during a strenuous training camp for elite cyclists | Low Risk | random & block | High Risk | Single Blinding (participants or investigators enrolling participants could possibly foresee assignments) | Low Risk | Although it is single blinding whereby participants or investigators enrolling participants could possibly foresee assignments. However, there is no incomplete blinding, but in the reviewer's judgment the outcome is not likely to be | Low Risk | Although it is single blinding whereby participants or investigators enrolling participants could possibly foresee assignments. However, there is no incomplete blinding, but in the reviewer's judgment the outcome is not likely to be | Low Risk | No missing outcome data or loss to follow-up | Low risk | The study protocol is available and all of the study's pre-specified outcomes of interest have been reported in the pre-specified way | Low risk | The study appears to be free of other sources of bias. | High Risk of Bias |

| Author | Year | Title | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | influenced by lack of blinding | | influenced by lack of blinding | | | | | | | |
| Highton | 2012 | Carbohydrate-protein coingestion improves multiple-sprint running performance | Low Risk | random & crossover | Low Risk | Double Blinding | Low Risk | Double Blinding | Low Risk | Double Blinding | Low Risk | No missing outcome data or loss to follow-up | Low risk | The study protocol is available and all of the study's pre-specified outcomes of interest have been reported in the pre-specified way | Low risk | The study appears to be free of other sources of bias. | Low Risk of Bias |
| Hill | 2013 | Co-ingestion of carbohydrate and whey protein isolates enhance PGC-1α mRNA expression: A randomised, single blind, cross over study | Low Risk | random & crossover | High Risk | Single Blinding (participants or investigators enrolling participants could possibly foresee assignme | Low Risk | Although it is single blinding whereby participants or investigators enrolling participants could possibly foresee | Low Risk | Although it is single blinding whereby participants or investigators enrolling participants could possibly foresee | Low Risk | No missing outcome data or loss to follow-up | Low risk | The study protocol is available and all of the study's pre-specified outcomes of interest have been reported in the pre-specified | Low risk | The study appears to be free of other sources of bias. | High Risk of Bias |

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|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | nts) | | assignments. However, there is no incomplete blinding, but in the reviewer's judgment the outcome is not likely to be influenced by lack of blinding | | assignments. However, there is no incomplete blinding, but in the reviewer's judgment the outcome is not likely to be influenced by lack of blinding | | | | way | | | | | |
| Hoffman | 2009 | Effect of protein-supplement timing on strength, power, and body-composition changes in resistance-trained men | Unclear Risk | random & without providing the details of what was done | Unclear Risk | didn't mention about blinding | Unclear Risk | didn't mention about blinding | Unclear Risk | didn't mention about blinding | Low Risk | No missing outcome data or loss to follow-up | Low risk | The study protocol is available and all of the study's pre-specified outcomes of interest have been reported in the pre- | Low risk | The study appears to be free of other sources of bias. | Unclear Risk of Bias |

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| | | | | | | | | | | | | | | specified way | | | |
| Hofman | 2002 | The effect of bovine colostrum supplementation on exercise performance in elite field hockey players | Low Risk | random & placebo-controlled | High Risk | Single Blinding (participants or investigators enrolling participants could possibly foresee assignments) | Low Risk | Although it is single blinding whereby participants or investigators enrolling participants could possibly foresee assignments. However, there is no incomplete blinding, but in the reviewer's judgment the outcome is not likely to be influence | Low Risk | Although it is single blinding whereby participants or investigators enrolling participants could possibly foresee assignments. However, there is no incomplete blinding, but in the reviewer's judgment the outcome is not likely to be influence | Low Risk | No missing outcome data or loss to follow-up | Low risk | The study protocol is available and all of the study's pre-specified outcomes of interest have been reported in the pre-specified way | Low risk | The study appears to be free of other sources of bias. | High Risk of Bias |

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|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | d by lack of blinding | | d by lack of blinding | | | | | | | |
| Impey | 2015 | Leucine-enriched protein feeding does not impair exercise-induced free fatty acid availability and lipid oxidation: beneficial implications for training in carbohydrate-restricted states | Low Risk | random & counterbalanced (Latin Squares approach) | Unclear Risk | didn't mention about blinding | Unclear Risk | didn't mention about blinding | Unclear Risk | didn't mention about blinding | Low Risk | No missing outcome data or loss to follow-up | Low risk | The study protocol is available and all of the study's pre-specified outcomes of interest have been reported in the pre-specified way | Low risk | The study appears to be free of other sources of bias. | Unclear Risk of Bias |
| Jauhari | 2014 | Effect of administering Tempeh drink on muscle damage recoveries after resistance exercise in student athletes | Unclear Risk | random & without providing the details of what was done | Low Risk | Double Blinding | Low Risk | Double Blinding | Low Risk | Double Blinding | Low Risk | No missing outcome data or loss to follow-up | Low risk | The study protocol is available and all of the study's pre-specified outcomes of interest have been reported in the pre-specified | Low risk | The study appears to be free of other sources of bias. | Unclear Risk of Bias |

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|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | | | | | | way | | |
| Joy | 2013 | The effects of 8 weeks of whey or rice protein supplementation on body composition and exercise performance | Unclear Risk | random & without providing the details of what was done | Low Risk | Double Blinding | Low Risk | Double Blinding | Low Risk | Double Blinding | Low Risk | No missing outcome data or loss to follow-up | Low risk | The study protocol is available and all of the study's pre-specified outcomes of interest have been reported in the pre-specified way | Low risk | The study appears to be free of other sources of bias. | Unclear Risk of Bias |
| Li | 2007 | Effects of carbohydrate and whey protein supplement at appropriate time on physical performance during football game. [Chinese] | Unclear Risk | random & without providing the details of what was done | Unclear Risk | didn't mention about blinding | Unclear Risk | didn't mention about blinding | Unclear Risk | didn't mention about blinding | Low Risk | No missing outcome data or loss to follow-up | Low risk | The study protocol is available and all of the study's pre-specified outcomes of interest have been reported in the pre-specified way | Low risk | The study appears to be free of other sources of bias. | Unclear Risk of Bias |

| Author | Year | Title | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Lollo | 2011 | Physiological and physical effects of different milk protein supplements in elite soccer players | Unclear Risk | random & without providing the details of what was done | Low Risk | Double Blinding | Low Risk | Double Blinding | Low Risk | Double Blinding | Low Risk | No missing outcome data or loss to follow-up | Low risk | The study protocol is available and all of the study's pre-specified outcomes of interest have been reported in the pre-specified way | Low risk | The study appears to be free of other sources of bias. | Unclear Risk of Bias |
| Lollo | 2014 | Hydrolysed whey protein reduces muscle damage markers in Brazilian elite soccer players compared with whey protein and maltodextrin. A twelve-week in-championship intervention | Unclear Risk | random & without providing the details of what was done | Low Risk | Double Blinding | Low Risk | Double Blinding | Low Risk | Double Blinding | Low Risk | No missing outcome data or loss to follow-up | Low risk | The study protocol is available and all of the study's pre-specified outcomes of interest have been reported in the pre-specified way | Low risk | The study appears to be free of other sources of bias. | Unclear Risk of Bias |
| Macdermid | 2006 | A whey-supplemented, high-protein | Low Risk | random & balanced | Unclear | didn't mention about | Unclear | didn't mention about | Unclear | didn't mention about | Low Risk | No missing | Low | The study protocol is available | Low risk | The study appea | Unclear Risk |

| | | | | | Risk | blinding | Risk | blinding | Risk | blinding | | outcome data or loss to follow-up | risk | and all of the study's pre-specified outcomes of interest have been reported in the pre-specified way | k | rs to be free of other sources of bias. | of Bias |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | diet versus a high-carbohydrate diet: effects of endurance cycling performance | | order | | | | | | | | | | | | | |
| Mero | 1997 | Effects of bovine colostrum supplementation on serum IGF-I, IgG, hormone, and saliva IgA during training | Low Risk | random & crossover | Low Risk | Double Blinding | Low Risk | Double Blinding | Low Risk | Double Blinding | Low Risk | No missing outcome data or loss to follow-up | Low risk | The study protocol is available and all of the study's pre-specified outcomes of interest have been reported in the pre-specified way | Low risk | The study appears to be free of other sources of bias. | Low Risk of Bias |
| Naclerio | 2015 | A multi-ingredient containing carbohydrate, proteins L-glutamine and | Low Risk | random & counter balanced, cross over | Low Risk | Double Blinding | Low Risk | Double Blinding | Low Risk | Double Blinding | Low Risk | No missing outcome data | Low risk | The study protocol is available and all of the study's pre- | Low risk | The study appears to be free | Low Risk of Bias |

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|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | L-carnitine attenuates fatigue perception with no effect on performance, muscle damage or immunity in soccer players | | | | | | | | | | | or loss to follow-up | | specified outcomes of interest have been reported in the pre-specified way | | of other sources of bias. | |
| Nelson | 2013 | Effect of post-exercise protein-leucine feeding on neutrophil function, immunomodulatory plasma metabolites and cortisol during a 6-day block of intense cycling | Low Risk | random & crossover | Low Risk | Double Blinding | Low Risk | Double Blinding | Low Risk | Double Blinding | Low Risk | No missing outcome data or loss to follow-up | Low risk | The study protocol is available and all of the study's pre-specified outcomes of interest have been reported in the pre-specified way | Low risk | The study appears to be free of other sources of bias. | Low Risk of Bias |
| Oosthuyse | 2015 | Whey or Casein Hydrolysate with Carbohydrate for Metabolism and Performance in | Low Risk | random & four way crossover | Low Risk | Double Blinding | Low Risk | Double Blinding | Low Risk | Double Blinding | Low Risk | No missing outcome data or loss to | Low risk | The study protocol is available and all of the study's pre-specified outcomes of | Low risk | The study appears to be free of other | Low Risk of Bias |

| Author | Year | Title | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Cycling | | | | | | | | | | follow-up | | interest have been reported in the pre-specified way | | sources of bias. | |
| Oosthuyse | 2016 | Comparison of energy supplements during prolonged exercise for maintenance of cardiac function: carbohydrate only versus carbohydrate plus whey or casein hydrolysate | Low Risk | random & four way crossover | Low Risk | Double Blinding | Low Risk | Double Blinding | Low Risk | Double Blinding | Low Risk | No missing outcome data or loss to follow-up | Low risk | The study protocol is available and all of the study's pre-specified outcomes of interest have been reported in the pre-specified way | Low risk | The study appears to be free of other sources of bias. | Low Risk of Bias |
| Parr | 2014 | Alcohol ingestion impairs maximal post-exercise rates of myofibrillar protein synthesis following a single bout of | Low Risk | random & counter-balanced, crossover | Unclear Risk | didn't mention about blinding | Unclear Risk | didn't mention about blinding | Unclear Risk | didn't mention about blinding | Low Risk | No missing outcome data or loss to follow- | Low risk | The study protocol is available and all of the study's pre-specified outcomes of interest have been | Low risk | The study appears to be free of other sources of | Unclear Risk of Bias |

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|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | concurrent training | | | | | | | | | | up | | reported in the pre-specified way | | bias. | |
| Rankin | 2006 | Energy restriction but not protein source affects antioxidant capacity in athletes | Unclear Risk | random & without providing the details of what was done | Unclear Risk | didn't mention about blinding | Unclear Risk | didn't mention about blinding | Unclear Risk | didn't mention about blinding | Low Risk | No missing outcome data or loss to follow-up | Low risk | The study protocol is available and all of the study's pre-specified outcomes of interest have been reported in the pre-specified way | Low risk | The study appears to be free of other sources of bias. | Unclear Risk of Bias |
| Ronghui | 2015 | The reasearch on the anti-fatigue effect of whey protein powder in basketball training | Unclear Risk | random & without providing the details of what was done | Unclear Risk | didn't mention about blinding | Unclear Risk | didn't mention about blinding | Unclear Risk | didn't mention about blinding | Low Risk | No missing outcome data or loss to follow-up | Low risk | The study protocol is roughly explain but it is clear that the published reports include all expected outcomes, including those that | Low risk | The study appears to be free of other sources of bias. | Unclear Risk of Bias |

| | | | | | | | | | | | | | | | | were pre-specified | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Schroer | 2014 | Cycling Time Trial Performance May Be Impaired by Whey Protein and L-Alanine Intake During Prolonged Exercise | Low Risk | random & counterbalanced, placebo-controlled | Low Risk | Double Blinding | Low Risk | Double Blinding | Low Risk | Double Blinding | Low Risk | No missing outcome data or loss to follow-up | Low risk | The study protocol is available and all of the study's pre-specified outcomes of interest have been reported in the pre-specified way | Low risk | The study appears to be free of other sources of bias. | Low Risk of Bias |
| Shing | 2006 | The influence of bovine colostrum supplementation on exercise performance in highly trained cyclists | Low Risk | random & placebo controlled | Low Risk | Double Blinding | Low Risk | Double Blinding | Low Risk | Double Blinding | Low Risk | No missing outcome data or loss to follow-up | Low risk | The study protocol is available and all of the study's pre-specified outcomes of interest have been reported in the pre-specified way | Low risk | The study appears to be free of other sources of bias. | Low Risk of Bias |

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|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Shing | 2007 | Effects of bovine colostrum supplementation on immune variables in highly trained cyclists | Low Risk | random & placebo controlled | Low Risk | Double Blinding | Low Risk | Double Blinding | Low Risk | Double Blinding | Low Risk | No missing outcome data or loss to follow-up | Low risk | The study protocol is available and all of the study's pre-specified outcomes of interest have been reported in the pre-specified way | Low risk | The study appears to be free of other sources of bias. | Low Risk of Bias |
| Shing | 2013 | A pilot study: bovine colostrum supplementation and hormonal and autonomic responses to competitive cycling | Low Risk | random & placebo controlled | Low Risk | Double Blinding | Low Risk | Double Blinding | Low Risk | Double Blinding | Low Risk | No missing outcome data or loss to follow-up | Low risk | The study protocol is available and all of the study's pre-specified outcomes of interest have been reported in the pre-specified way | Low risk | The study appears to be free of other sources of bias. | Low Risk of Bias |
| Smith | 2010 | The effects of a pre-workout supplement | Low Risk | random & placebo controlled | High Risk | Single Blinding (participa | Low Risk | Although it is single blinding | Low Risk | Although it is single blinding | Low Risk | No missing | Low w | The study protocol is available | Low w ris | The study appea | High Risk of |

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|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | containing caffeine, creatine, and amino acids during three weeks of high-intensity exercise on aerobic and anaerobic performance | | parallel | | nts or investigators enrolling participants could possibly foresee assignments) | | whereby participants or investigators enrolling participants could possibly foresee assignments. However, there is no incomplete blinding, but in the reviewer's judgment the outcome is not likely to be influenced by lack of blinding | | whereby participants or investigators enrolling participants could possibly foresee assignments. However, there is no incomplete blinding, but in the reviewer's judgment the outcome is not likely to be influenced by lack of blinding | | outcome data or loss to follow-up | risk | and all of the study's pre-specified outcomes of interest have been reported in the pre-specified way | k | rs to be free of other sources of bias. | Bias |
| Tang | 2007 | Minimal whey protein with | Low Risk | random & crossover, | Low Risk | Double Blinding | Low Risk | Double Blinding | Low Risk | Double Blinding | Low Risk | No missin | Low | The study protocol is | Low | The study | Low Risk |

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|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | carbohydrate stimulates muscle protein synthesis following resistance exercise in trained young men | | counterbalanced | | | | | | | | g outcome data or loss to follow-up | risk | available and all of the study's pre-specified outcomes of interest have been reported in the pre-specified way | risk | appears to be free of other sources of bias. | of Bias |
| Taylor | 2016 | Eight weeks of pre- and postexercise whey protein supplementation increases lean body mass and improves performance in Division III collegiate female basketball players | Unclear Risk | random & without providing the details of what was done | Low Risk | Double Blinding | Low Risk | Double Blinding | Low Risk | Double Blinding | Low Risk | No missing outcome data or loss to follow-up | Low risk | The study protocol is available and all of the study's pre-specified outcomes of interest have been reported in the pre-specified way | Low risk | The study appears to be free of other sources of bias. | Unclear Risk of Bias |
| Vegge | 2012 | Improved cycling performance with ingestion of hydrolyzed | Low Risk | random & crossedover | Low Risk | Double Blinding | Low Risk | Double Blinding | Low Risk | Double Blinding | Low Risk | No missing outcome me | Low risk | The study protocol is available and all of the study's | Low risk | The study appears to be | Low Risk of Bias |

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| | | marine protein depends on performance level | | | | | | | | | | data or loss to follow-up | | pre-specified outcomes of interest have been reported in the pre-specified way | | free of other sources of bias. | |
| Wilborn | 2013 | The Effects of Pre- and Post-Exercise Whey vs. Casein Protein Consumption on Body Composition and Performance Measures in Collegiate Female Athletes | Unclear Risk | random & without providing the details of what was done | Low Risk | Double Blinding | Low Risk | Double Blinding | Low Risk | Double Blinding | Low Risk | No missing outcome data or loss to follow-up | Low risk | The study protocol is available and all of the study's pre-specified outcomes of interest have been reported in the pre-specified way | Low risk | The study appears to be free of other sources of bias. | Unclear Risk of Bias |
| Yang | 2014 | Research on application of whey protein in sports drink | Unclear Risk | random & without providing the details of what was done | Unclear Risk | didn't mention about blinding | Unclear Risk | didn't mention about blinding | Unclear Risk | didn't mention about blinding | Low Risk | No missing outcome data or loss to | Low risk | The study protocol is available and all of the study's pre-specified outcomes of | Low risk | The study appears to be free of other | Unclear Risk of Bias |

| | | | | | | | | | | | follow-up | | interest have been reported in the pre-specified way | | sources of bias. | |
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**8.4    Appendix 4: ROBINS-I for non-RCTs**

**8.4.1    Study ID: Fahlström 2006**

**Article title:** Positive short-term subjective effect of sports drink supplementation during recovery
**Authors:** Fahlström, M.; Fahlström, P. G.; Lorentzon, R.; Henriksson-Larsén, K.

# The Risk Of Bias In Non-randomized Studies – of Interventions (ROBINS-I) assessment tool
**Version 19 September 2016**

**ROBINS-I tool (Stage I): At protocol stage**
**Specify the review question**

| Participants | Athletes experience recovering from injuries and/or hinder in performance. |
|---|---|
| Experimental intervention | Whey protein or the whey supplements. It can be in form of isolate, concentrate, or hydrolysate. |
| Comparator | Carbohydrate supplement; protein-containing foods include animal sources, and vegetarian sources; vitamins; minerals; placebo |
| Outcomes | level of the protein in blood and creatine kinase activity; development of muscle and bone tissue; the muscle and bone fracture injuries recovery period; pain level; and mobility, strength and performance level |

**List the confounding domains relevant to all or most studies**

| Consume whey protein |
| --- |
| |

**List co-interventions that could be different between intervention groups and that could impact on outcomes**

**ROBINS-I tool (Stage II): For each study**
**Specify a target randomized trial specific to the study**
Design                              Matched (cross-over)

| | |
|---|---|
| Participants | badminton players |
| Experimental intervention | Active drink #751 (Whey Protein) |
| Comparator | Placebo drink #862 |

**Is your aim for this study…?**

☑      to assess the effect of *assignment to* intervention

☐      to assess the effect of *starting and adhering to* intervention

**Specify the outcome**
Specify which outcome is being assessed for risk of bias (typically from among those earmarked for the Summary of Findings table). Specify whether this is a proposed benefit or harm of intervention.

Hemoglobin

**Specify the numerical result being assessed**
In case of multiple alternative analyses being presented, specify the numeric result (e.g. RR = 1.52 (95% CI 0.83 to 2.77) and/or a reference (e.g. to a table, figure or paragraph) that uniquely defines the result being assessed.

Numeric result on Hemoglobin 140±10.8 vs 137.4±8.8, P=0.05; Table II Basic characteristics and training load of the 18 badminton players.

**Preliminary consideration of confounders**

Complete a row for each important confounding domain (i) listed in the review protocol; and (ii) relevant to the setting of this particular study, or which the study authors identified as potentially important.

*"Important" confounding domains are those for which, in the context of this study, adjustment is expected to lead to a clinically important change in the estimated effect of the intervention. "Validity" refers to whether the confounding variable or variables fully measure the domain, while "reliability" refers to the precision of the measurement (more measurement error means less reliability).*

| (i) Confounding domains listed in the review protocol | | | | |
|---|---|---|---|---|
| Confounding domain | Measured variable(s) | Is there evidence that controlling for this variable was unnecessary?* | Is the confounding domain measured validly and reliably by this variable (or these variables)? | OPTIONAL: Is failure to adjust for this variable (alone) expected to favour the experimental intervention or the comparator? |
| Not Applicable (NA) | | | Yes / No / No information | Favour experimental / Favour comparator / No information |
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| (ii) Additional confounding domains relevant to the setting of this particular study, or which the study authors identified as important | | | | |
|---|---|---|---|---|
| Confounding domain | Measured variable(s) | Is there evidence that controlling for this variable was unnecessary?* | Is the confounding domain measured validly and reliably by this variable (or these variables)? | OPTIONAL: Is failure to adjust for this variable (alone) expected to favour the experimental intervention or the comparator? |
| NA | | | Yes / No / No information | Favour experimental / Favour comparator / No information |
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* In the context of a particular study, variables can be demonstrated not to be confounders and so not included in the analysis: (a) if they are not predictive of the outcome; (b) if they are not predictive of intervention; or (c) because adjustment makes no or minimal difference to the estimated effect of the primary parameter. Note that "no statistically significant association" is not the same as "not predictive".

**Preliminary consideration of co-interventions**

Complete a row for each important co-intervention (i) listed in the review protocol; and (ii) relevant to the setting of this particular study, or which the study authors identified as important.

*"Important" co-interventions are those for which, in the context of this study, adjustment is expected to lead to a clinically important change in the estimated effect of the intervention.*

| (i) Co-interventions listed in the review protocol | | |
|---|---|---|
| Co-intervention | Is there evidence that controlling for this co-intervention was unnecessary (e.g. because it was not administered)? | Is presence of this co-intervention likely to favour outcomes in the experimental intervention or the comparator |
| NA | | Favour experimental / Favour comparator / No information |
| | | Favour experimental / Favour comparator / No information |
| | | Favour experimental / Favour comparator / No information |
| | | Favour experimental / Favour comparator / No information |

| (ii) Additional co-interventions relevant to the setting of this particular study, or which the study authors identified as important | | |
|---|---|---|
| Co-intervention | Is there evidence that controlling for this co-intervention was unnecessary (e.g. because it was not administered)? | Is presence of this co-intervention likely to favour outcomes in the experimental intervention or the comparator |
| NA | | Favour experimental / Favour comparator / No information |
| | | Favour experimental / Favour comparator / No information |

|  |  | Favour experimental / Favour comparator / No information |
|---|---|---|
|  |  | Favour experimental / Favour comparator / No information |

**Risk of bias assessment**

Responses <u>underlined in green</u> are potential markers for low risk of bias, and responses in red are potential markers for a risk of bias. Where questions relate only to sign posts to other questions, no formatting is used.

| Signalling questions | Description | Response options |
|---|---|---|
| **Bias due to confounding** | | |
| 1.1 Is there potential for confounding of the effect of intervention in this study?<br><br>If **N/PN** to 1.1: the study can be considered to be at low risk of bias due to confounding and no further signalling questions need be considered | The players were instructed, above their normal nutrition to drink at least one pack of given sports drink immediately after each session of training or physical activity during badminton season. Apart from the instructions concerning consumption of the sport drinks, the players were instructed not to make any changes in their usual habit concerning eating, drinking, resting and training. | <u>N</u> |
| If **Y/PY** to 1.1: determine whether there is a need to assess time-varying confounding: | | |
| 1.2. Was the analysis based on splitting participants' follow up time according to intervention received?<br><br>If **N/PN**, answer questions relating to baseline confounding (1.4 to 1.6)<br><br>If **Y/PY**, go to question 1.3. | | |

| | | |
|---|---|---|
| 1.3. Were intervention discontinuations or switches likely to be related to factors that are prognostic for the outcome?<br><br>**If N/PN**, answer questions relating to baseline confounding (1.4 to 1.6)<br><br>**If Y/PY**, answer questions relating to both baseline and time-varying confounding (1.7 and 1.8) | | |

**Questions relating to baseline confounding only**

| | | |
|---|---|---|
| 1.4. Did the authors use an appropriate analysis method that controlled for all the important confounding domains? | | |
| 1.5. **If Y/PY to 1.4**: Were confounding domains that were controlled for measured validly and reliably by the variables available in this study? | | |
| 1.6. Did the authors control for any post-intervention variables that could have been affected by the intervention? | | |

**Questions relating to baseline and time-varying confounding**

| | | |
|---|---|---|
| 1.7. Did the authors use an appropriate analysis method that controlled for all the important confounding domains and for time-varying confounding? | | |
| 1.8. **If Y/PY to 1.7**: Were confounding domains that were controlled for measured validly and reliably by the variables available in this study? | | |
| **Risk of bias judgement** | | Low |
| Optional: What is the predicted direction of bias due to confounding? | | |

| **Bias in selection of participants into the study** | | |
|---|---|---|
| 2.1. Was selection of participants into the study (or into the analysis) based on participant characteristics observed after the start of intervention?<br><br>**If N/PN to 2.1:** go to 2.4<br><br>2.2. **If Y/PY to 2.1**: Were the post-intervention variables that influenced selection likely to be associated with intervention?<br><br>2.3 **If Y/PY to 2.2**:  Were the post-intervention variables that influenced selection likely to be influenced by the outcome or a cause of the outcome? | An inquiry was made to players in local badminton club with a competitive team in the national elite division (top level) and with well-organized training programs for the players | N |

| 2.4. Do start of follow-up and start of intervention coincide for most participants? | There were 22 players who volunteered of which 18 (82%) completed the whole project. | Y |
|---|---|---|
| 2.5. **If Y/PY to 2.2 and 2.3, or N/PN to 2.4**: Were adjustment techniques used that are likely to correct for the presence of selection biases? | | |
| **Risk of bias judgement** | | Low |
| Optional: What is the predicted direction of bias due to selection of participants into the study? | | |

| **Bias in classification of interventions** | | |
|---|---|---|
| 3.1 Were intervention groups clearly defined? | Table II | Y |
| 3.2 Was the information used to define intervention groups recorded at the start of the intervention? | Table II | Y |
| 3.3 Could classification of intervention status have been affected by knowledge of the outcome or risk of the outcome? | Collection of the information at the time is sufficient | N |
| **Risk of bias judgement** | | Low |
| Optional: What is the predicted direction of bias due to classification of interventions? | | |

**Bias due to deviations from intended interventions**

| | | |
|---|---|---|
| **If your aim for this study is to assess the effect of assignment to intervention, answer questions 4.1 and 4.2** | | |
| 4.1. Were there deviations from the intended intervention beyond what would be expected in usual practice? | The mean consumption of the sports drinks after each training/playing session was 400-450 ml. | N |
| 4.2. **If Y/PY to 4.1**: Were these deviations from intended intervention unbalanced between groups *and* likely to have affected the outcome? | | |
| **If your aim for this study is to assess the effect of starting and adhering to intervention, answer questions 4.3 to 4.6** | | |
| 4.3. Were important co-interventions balanced across intervention groups? | | |
| 4.4. Was the intervention implemented successfully for most participants? | | |
| 4.5. Did study participants adhere to the assigned intervention regimen? | | |
| 4.6. **If N/PN to 4.3, 4.4 or 4.5**: Was an appropriate analysis used to estimate the effect of starting and adhering to the intervention? | | |
| **Risk of bias judgement** | | Low |
| Optional: What is the predicted direction of bias due to deviations from the intended interventions? | | |

| Bias due to missing data | | | |
|---|---|---|---|
| 5.1 Were outcome data available for all, or nearly all, participants? | The results based on 18 participants | | Y |
| 5.2 Were participants excluded due to missing data on intervention status? | Three dropouts reported lack of time or motivation as the main reason for not participating. One player had a serious injury (ankle fracture) in the beginning of the second test period and was excluded | | N |
| 5.3 Were participants excluded due to missing data on other variables needed for the analysis? | The results based on 18 participants | | N |
| 5.4 **If PN/N to 5.1, or Y/PY to 5.2 or 5.3**: Are the proportion of participants and reasons for missing data similar across interventions? | | | |
| 5.5 **If PN/N to 5.1, or Y/PY to 5.2 or 5.3**: Is there evidence that results were robust to the presence of missing data? | | | |
| **Risk of bias judgement** | | | Low |
| Optional: What is the predicted direction of bias due to missing data? | | | |

| Bias in measurement of outcomes |
|---|

| | | |
|---|---|---|
| 6.1 Could the outcome measure have been influenced by knowledge of the intervention received? | Ethical approval and do not involve negligible assessor judgment | N |
| 6.2 Were outcome assessors aware of the intervention received by study participants? | It is double blinded study design | N |
| 6.3 Were the methods of outcome assessment comparable across intervention groups? | Both group outcomes are using the same assessment | Y |
| 6.4 Were any systematic errors in measurement of the outcome related to intervention received? | The method impose are well explain for conducting the study and blinded | N |
| **Risk of bias judgement** | | Low |
| Optional: What is the predicted direction of bias due to measurement of outcomes? | | |

| **Bias in selection of the reported result** | | |
|---|---|---|
| Is the reported effect estimate likely to be selected, on the basis of the results, from... | | |
| 7.1. ... multiple outcome *measurements* within the outcome domain? | The outcome results are reported using specific measurements that have stated in the methodology | N |
| 7.2 ... multiple *analyses* of the intervention-outcome relationship? | The results did not report baseline. However, authors did report the decrease and increase of each outcome with the end results. | PN |
| 7.3 ... different *subgroups*? | No subgroup | N |

| Risk of bias judgement | | Moderate |
|---|---|---|
| Optional: What is the predicted direction of bias due to selection of the reported result? | | |

| Overall bias | | |
|---|---|---|
| Risk of bias judgement | | Low |
| Optional: What is the overall predicted direction of bias for this outcome? | | |

**8.4.2   Study ID: Kraemer 2015**

**Article title**: The addition of beta-hydroxy-beta-methylbutyrate and isomaltulose to whey protein improves recovery from highly demanding resistance exercise.
**Authors**: Kraemer, William J.; Hooper, David R.; Szivak, Tunde K.; Kupchak, Brian R.; Dunn-Lewis, Courtenay; Comstock, Brett A.; Flanagan, Shawn D.; Looney, David P.; Sterczala, Adam J.; DuPont, William H.; Pryor, J. Luke; Luk, Hiu-Ying; Maladoungdock, Jesse; McDermott, Danielle; Volek, Jeff S.; Maresh, Carl M.

## The Risk Of Bias In Non-randomized Studies – of Interventions (ROBINS-I) assessment tool
**Version 19 September 2016**

**ROBINS-I tool (Stage I): At protocol stage**
**Specify the review question**

| | |
|---|---|
| Participants | Athletes experience recovering from injuries and/or hinder in performance. |
| Experimental intervention | Whey protein or the whey supplements. It can be in form of isolate, concentrate, or hydrolysate. |
| Comparator | Carbohydrate supplement; protein-containing foods include animal sources, and vegetarian sources; vitamins; minerals; placebo |
| Outcomes | level of the protein in blood and creatine kinase activity; development of muscle and bone tissue; the muscle and bone fracture injuries recovery period; pain level; and mobility, strength and performance level |

**List the confounding domains relevant to all or most studies**

Consume whey protein

**List co-interventions that could be different between intervention groups and that could impact on outcomes**

None

**ROBINS-I tool (Stage II): For each study**
**Specify a target randomized trial specific to the study**
Design                          Matched (Counterbalanced within-group)

| | |
|---|---|
| Participants | Participants who have resistance training experience |
| Experimental intervention | whey protein (100 kcal, 20 g protein, 2.5 g carbohydrate, 1 g fat) |
| Comparator | RP supplement (260 kcal, 20 g protein, 1.5 g HMB, 41 g carbohydrate, 2 g fat) |

**Is your aim for this study…?**

☑     to assess the effect of *assignment to* intervention

☐     to assess the effect of *starting and adhering to* intervention

**Specify the outcome**
Specify which outcome is being assessed for risk of bias (typically from among those earmarked for the Summary of Findings table). Specify whether this is a proposed benefit or harm of intervention.

Plasma insulin-like growth factor I, Creatine Kinase, Cortisol and Testosterone

**Specify the numerical result being assessed**
In case of multiple alternative analyses being presented, specify the numeric result (e.g. RR = 1.52 (95% CI 0.83 to 2.77) and/or a reference (e.g. to a table, figure or paragraph) that uniquely defines the result being assessed.

Table 2 Hormonal Response Data and Subject Characteristics

**Preliminary consideration of confounders**

Complete a row for each important confounding domain (i) listed in the review protocol; and (ii) relevant to the setting of this particular study, or which the study authors identified as potentially important.

*"Important" confounding domains are those for which, in the context of this study, adjustment is expected to lead to a clinically important change in the estimated effect of the intervention. "Validity" refers to whether the confounding variable or variables fully measure the domain, while "reliability" refers to the precision of the measurement (more measurement error means less reliability).*

| (i) Confounding domains listed in the review protocol | | | | |
|---|---|---|---|---|
| Confounding domain | Measured variable(s) | Is there evidence that controlling for this variable was unnecessary?* | Is the confounding domain measured validly and reliably by this variable (or these variables)? | OPTIONAL: Is failure to adjust for this variable (alone) expected to favour the experimental intervention or the comparator? |
| Not Applicable (NA) | | | Yes / No / No information | Favour experimental / Favour comparator / No information |
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| (ii) Additional confounding domains relevant to the setting of this particular study, or which the study authors identified as important | | | | |
|---|---|---|---|---|
| Confounding domain | Measured variable(s) | Is there evidence that controlling for this variable was unnecessary?* | Is the confounding domain measured validly and reliably by this variable (or these variables)? | OPTIONAL: Is failure to adjust for this variable (alone) expected to favour the experimental intervention or the comparator? |
| NA |  |  | Yes / No / No information | Favour experimental / Favour comparator / No information |
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* In the context of a particular study, variables can be demonstrated not to be confounders and so not included in the analysis: (a) if they are not predictive of the outcome; (b) if they are not predictive of intervention; or (c) because adjustment makes no or minimal difference to the estimated effect of the primary parameter. Note that "no statistically significant association" is not the same as "not predictive".

**Preliminary consideration of co-interventions**

Complete a row for each important co-intervention (i) listed in the review protocol; and (ii) relevant to the setting of this particular study, or which the study authors identified as important.

*"Important" co-interventions are those for which, in the context of this study, adjustment is expected to lead to a clinically important change in the estimated effect of the intervention.*

| (i) Co-interventions listed in the review protocol | | |
|---|---|---|
| Co-intervention | Is there evidence that controlling for this co-intervention was unnecessary (e.g. because it was not administered)? | Is presence of this co-intervention likely to favour outcomes in the experimental intervention or the comparator |
| NA | | Favour experimental / Favour comparator / No information |
| | | Favour experimental / Favour comparator / No information |
| | | Favour experimental / Favour comparator / No information |
| | | Favour experimental / Favour comparator / No information |

| (ii) Additional co-interventions relevant to the setting of this particular study, or which the study authors identified as important | | |
|---|---|---|
| Co-intervention | Is there evidence that controlling for this co-intervention was unnecessary (e.g. because it was not administered)? | Is presence of this co-intervention likely to favour outcomes in the experimental intervention or the comparator |
| NA | | Favour experimental / Favour comparator / No information |
| | | Favour experimental / Favour comparator / No information |

| | | Favour experimental / Favour comparator / No information |
| --- | --- | --- |
| | | Favour experimental / Favour comparator / No information |

**Risk of bias assessment**

Responses <span style="color:green"><u>underlined in green</u></span> are potential markers for low risk of bias, and responses in <span style="color:red">red</span> are potential markers for a risk of bias. Where questions relate only to sign posts to other questions, no formatting is used.

| Signalling questions | Description | Response options |
|---|---|---|
| **Bias due to confounding** | | |
| 1.1 Is there potential for confounding of the effect of intervention in this study?<br><br>**If <span style="color:green"><u>N/PN</u></span> to 1.1:** the study can be considered to be at low risk of bias due to confounding and no further signalling questions need be considered | • Before supplement loading, subjects were asked to complete a trial 3-day diet record, which served as a familiarization.<br>• Subjects were instructed to follow the prescription during the subsequent 2-week supplement loading phase. | <u>N</u> |
| **If <span style="color:red">Y/PY</span> to 1.1**: determine whether there is a need to assess time-varying confounding: | | |
| 1.2. Was the analysis based on splitting participants' follow up time according to intervention received?<br><br>**If N/PN**, answer questions relating to baseline confounding (1.4 to 1.6)<br><br>**If Y/PY**, go to question 1.3. | | |

| | | |
|---|---|---|
| 1.3. Were intervention discontinuations or switches likely to be related to factors that are prognostic for the outcome?<br><br>**If N/PN**, answer questions relating to baseline confounding (1.4 to 1.6)<br><br>**If Y/PY**, answer questions relating to both baseline and time-varying confounding (1.7 and 1.8) | | |

**Questions relating to baseline confounding only**

| | | |
|---|---|---|
| 1.4. Did the authors use an appropriate analysis method that controlled for all the important confounding domains? | | |
| 1.5. **If Y/PY to 1.4**: Were confounding domains that were controlled for measured validly and reliably by the variables available in this study? | | |
| 1.6. Did the authors control for any post-intervention variables that could have been affected by the intervention? | | |

**Questions relating to baseline and time-varying confounding**

| | | |
|---|---|---|
| 1.7. Did the authors use an appropriate analysis method that controlled for all the important confounding domains and for time-varying confounding? | | |
| 1.8. **If Y/PY to 1.7**: Were confounding domains that were controlled for measured validly and reliably by the variables available in this study? | | |
| **Risk of bias judgement** | | Low |
| Optional: What is the predicted direction of bias due to confounding? | | |

| | | |
|---|---|---|
| **Bias in selection of participants into the study** | | |
| 2.1. Was selection of participants into the study (or into the analysis) based on participant characteristics observed after the start of intervention?<br><br>**If N/PN to 2.1:** go to 2.4<br><br>2.2. **If Y/PY to 2.1**: Were the post-intervention variables that influenced selection likely to be associated with intervention?<br><br>2.3 **If Y/PY to 2.2**: Were the post-intervention variables that influenced selection likely to be influenced by the outcome or a cause of the outcome? | All subjects were fully informed of the protocol design and associated risks of this investigation before signing an informed consent approved by the University of Connecticut Institutional Review Board for use of human subjects. | N |

| | | | |
|---|---|---|---|
| 2.4. Do start of follow-up and start of intervention coincide for most participants? | No dropout or withdraw. 100% full participants | | Y |
| 2.5. **If Y/PY to 2.2 and 2.3, or N/PN to 2.4**: Were adjustment techniques used that are likely to correct for the presence of selection biases? | | | |
| **Risk of bias judgement** | | | Low |
| Optional: What is the predicted direction of bias due to selection of participants into the study? | | | |

| **Bias in classification of interventions** | | | |
|---|---|---|---|
| 3.1 Were intervention groups clearly defined? | Thirteen men (age: 22.6 ± 3.9 years; height: 175.3 ± 12.2 cm; weight: 86.2 ± 9.8 kg) with at least one year of resistance training experience volunteered to participate in the study. Height was measured using a stadiometer (Seca, Hamburg, Germany). Weight was measured using a calibrated scale (OHAUS Corp., Florham Park, NJ). | | Y |
| 3.2 Was the information used to define intervention groups recorded at the start of the intervention? | Same as above | | Y |
| 3.3 Could classification of intervention status have been affected by knowledge of the outcome or risk of the outcome? | Collection of the information at the time is sufficient | | N |
| **Risk of bias judgement** | | | Low |

| | | |
|---|---|---|
| Optional: What is the predicted direction of bias due to classification of interventions? | | |

| | | |
|---|---|---|
| **Bias due to deviations from intended interventions** | | |
| **If your aim for this study is to assess the effect of assignment to intervention, answer questions 4.1 and 4.2** | | |
| 4.1. Were there deviations from the intended intervention beyond what would be expected in usual practice? | Crossover study. Each participate receive both supplements. Fig. 1 A | N |
| 4.2. **If Y/PY to 4.1**: Were these deviations from intended intervention unbalanced between groups *and* likely to have affected the outcome? | | |
| **If your aim for this study is to assess the effect of starting and adhering to intervention, answer questions 4.3 to 4.6** | | |
| 4.3. Were important co-interventions balanced across intervention groups? | | |
| 4.4. Was the intervention implemented successfully for most participants? | | |
| 4.5. Did study participants adhere to the assigned intervention regimen? | | |
| 4.6. **If N/PN to 4.3, 4.4 or 4.5**: Was an appropriate analysis used to estimate the effect of starting and adhering to the intervention? | | |

| | | |
|---|---|---|
| **Risk of bias judgement** | | Low |
| Optional: What is the predicted direction of bias due to deviations from the intended interventions? | | |

| **Bias due to missing data** | | |
|---|---|---|
| 5.1 Were outcome data available for all, or nearly all, participants? | Outcomes based on all the participants | Y |
| 5.2 Were participants excluded due to missing data on intervention status? | No participants were excluded | N |
| 5.3 Were participants excluded due to missing data on other variables needed for the analysis? | No participants were excluded | N |
| 5.4 **If PN/N to 5.1, or Y/PY to 5.2 or 5.3**: Are the proportion of participants and reasons for missing data similar across interventions? | | |
| 5.5 **If PN/N to 5.1, or Y/PY to 5.2 or 5.3**: Is there evidence that results were robust to the presence of missing data? | | |
| **Risk of bias judgement** | | Low |
| Optional: What is the predicted direction of bias due to missing data? | | |

| Bias in measurement of outcomes | | |
|---|---|---|
| 6.1 Could the outcome measure have been influenced by knowledge of the intervention received? | informed consent approved by the University of Connecticut Institutional Review Board for use of human subjects and do not involve negligible assessor judgment | N |
| 6.2 Were outcome assessors aware of the intervention received by study participants? | It is double blinded study design | N |
| 6.3 Were the methods of outcome assessment comparable across intervention groups? | Both group outcomes are using the same assessment | Y |
| 6.4 Were any systematic errors in measurement of the outcome related to intervention received? | The method impose are well explain for conducting the study and blinded | N |
| **Risk of bias judgement** | | Low |
| Optional: What is the predicted direction of bias due to measurement of outcomes? | | |

| Bias in selection of the reported result | | |
|---|---|---|
| Is the reported effect estimate likely to be selected, on the basis of the results, from... | | |
| 7.1. ... multiple outcome *measurements* within the outcome domain? | The outcome results are reported using specific measurements that have stated in the methodology | Y / PY / PN / N / NI |
| 7.2 ... multiple *analyses* of the intervention-outcome relationship? | There is no missing of data for the outcomes results | N |

| 7.3 ... different *subgroups*? | No subgroup | N |
|---|---|---|
| **Risk of bias judgement** | | Low |
| Optional: What is the predicted direction of bias due to selection of the reported result? | | |

| Overall bias | | |
|---|---|---|
| **Risk of bias judgement** | | Low |
| Optional: What is the overall predicted direction of bias for this outcome? | | |

### 8.4.3 Study ID: Morifuji 2012

**Article title**: Post-exercise ingestion of different amounts of protein affects plasma insulin concentration in humans
**Authors**: Morifuji, M.; Aoyama, T.; Nakata, A.; Sambongi, C.; Koga, J.; Kurihara, K.; Kanegae, M.; Suzuki, K.; Higuchi, M.

## The Risk Of Bias In Non-randomized Studies – of Interventions (ROBINS-I) assessment tool
**Version 19 September 2016**

**ROBINS-I tool (Stage I): At protocol stage**
**Specify the review question**

| Participants | Athletes experience recovering from injuries and/or hinder in performance. |
|---|---|
| Experimental intervention | Whey protein or the whey supplements. It can be in form of isolate, concentrate, or hydrolysate. |
| Comparator | Carbohydrate supplement; protein-containing foods include animal sources, and vegetarian sources; vitamins; minerals; placebo |
| Outcomes | level of the protein in blood and creatine kinase activity; development of muscle and bone tissue; the muscle and bone fracture injuries recovery period; pain level; and mobility, strength and performance level |

**List the confounding domains relevant to all or most studies**

| Consume whey protein |
|---|

|  |
| --- |
|  |

**List co-interventions that could be different between intervention groups and that could impact on outcomes**

| None |
| --- |
|  |

**ROBINS-I tool (Stage II): For each study**
**Specify a target randomized trial specific to the study**
Design                                      Matched (cross-over)

| Participants | Trained men |
|---|---|
| Experimental intervention | (1) carbohydrate plus a low amount of whey protein (2) carbohydrate plus a high amount of whey protein |
| Comparator | carbohydrate |

**Is your aim for this study…?**

☑       to assess the effect of *assignment to* intervention

☐       to assess the effect of *starting and adhering to* intervention

**Specify the outcome**
Specify which outcome is being assessed for risk of bias (typically from among those earmarked for the Summary of Findings table). Specify whether this is a proposed benefit or harm of intervention.

| Glucose, essential amino acids, branched-chain amino acids, insulin |
|---|

**Specify the numerical result being assessed**
In case of multiple alternative analyses being presented, specify the numeric result (e.g. RR = 1.52 (95% CI 0.83 to 2.77) and/or a reference (e.g. to a table, figure or paragraph) that uniquely defines the result being assessed.

| Figure 1. (A) Blood glucose and (B) plasma insulin concentrations; Figure 2. Plasma concentrations of (B) essential amino acids, and (C) branched-chain amino acids; Table I. Characteristics of participants |
|---|

**Preliminary consideration of confounders**

Complete a row for each important confounding domain (i) listed in the review protocol; and (ii) relevant to the setting of this particular study, or which the study authors identified as potentially important.

*"Important" confounding domains are those for which, in the context of this study, adjustment is expected to lead to a clinically important change in the estimated effect of the intervention. "Validity" refers to whether the confounding variable or variables fully measure the domain, while "reliability" refers to the precision of the measurement (more measurement error means less reliability).*

| (i) Confounding domains listed in the review protocol | | | | |
|---|---|---|---|---|
| Confounding domain | Measured variable(s) | Is there evidence that controlling for this variable was unnecessary?* | Is the confounding domain measured validly and reliably by this variable (or these variables)? | OPTIONAL: Is failure to adjust for this variable (alone) expected to favour the experimental intervention or the comparator? |
| Not Applicable (NA) | | | Yes / No / No information | Favour experimental / Favour comparator / No information |
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| (ii) Additional confounding domains relevant to the setting of this particular study, or which the study authors identified as important | | | | |
|---|---|---|---|---|
| Confounding domain | Measured variable(s) | Is there evidence that controlling for this variable was unnecessary?* | Is the confounding domain measured validly and reliably by this variable (or these variables)? | OPTIONAL: Is failure to adjust for this variable (alone) expected to favour the experimental intervention or the comparator? |
| NA |  |  | Yes / No / No information | Favour experimental / Favour comparator / No information |
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\* In the context of a particular study, variables can be demonstrated not to be confounders and so not included in the analysis: (a) if they are not predictive of the outcome; (b) if they are not predictive of intervention; or (c) because adjustment makes no or minimal difference to the estimated effect of the primary parameter. Note that "no statistically significant association" is not the same as "not predictive".

**Preliminary consideration of co-interventions**

Complete a row for each important co-intervention (i) listed in the review protocol; and (ii) relevant to the setting of this particular study, or which the study authors identified as important.

*"Important" co-interventions are those for which, in the context of this study, adjustment is expected to lead to a clinically important change in the estimated effect of the intervention.*

| **(i) Co-interventions listed in the review protocol** | | |
|---|---|---|
| Co-intervention | Is there evidence that controlling for this co-intervention was unnecessary (e.g. because it was not administered)? | Is presence of this co-intervention likely to favour outcomes in the experimental intervention or the comparator |
| NA | | Favour experimental / Favour comparator / No information |
| | | Favour experimental / Favour comparator / No information |
| | | Favour experimental / Favour comparator / No information |
| | | Favour experimental / Favour comparator / No information |

| **(ii) Additional co-interventions relevant to the setting of this particular study, or which the study authors identified as important** | | |
|---|---|---|
| Co-intervention | Is there evidence that controlling for this co-intervention was unnecessary (e.g. because it was not administered)? | Is presence of this co-intervention likely to favour outcomes in the experimental intervention or the comparator |
| NA | | Favour experimental / Favour comparator / No information |
| | | Favour experimental / Favour comparator / No information |

| | | Favour experimental / Favour comparator / No information |
|---|---|---|
| | | Favour experimental / Favour comparator / No information |

**Risk of bias assessment**

Responses <u>underlined in green</u> are potential markers for low risk of bias, and responses in red are potential markers for a risk of bias. Where questions relate only to sign posts to other questions, no formatting is used.

| Signalling questions | Description | Response options |
|---|---|---|
| **Bias due to confounding** | | |
| 1.1 Is there potential for confounding of the effect of intervention in this study?<br><br>**If N/PN to 1.1:** the study can be considered to be at low risk of bias due to confounding and no further signalling questions need be considered | all participants were instructed to eat the same meals the day before<br><br>the test. The calorific intake in the 24-h period before each time trial was 8700 kJ/day. In the hour preceding the tests, the participants were not allowed to eat but were allowed to drink water. | <u>N</u> |
| **If Y/PY to 1.1**: determine whether there is a need to assess time-varying confounding: | | |
| 1.2. Was the analysis based on splitting participants' follow up time according to intervention received?<br><br>**If N/PN**, answer questions relating to baseline confounding (1.4 to 1.6)<br><br>**If Y/PY**, go to question 1.3. | | |

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| | | |
|---|---|---|
| 1.3. Were intervention discontinuations or switches likely to be related to factors that are prognostic for the outcome?<br><br>**If N/PN**, answer questions relating to baseline confounding (1.4 to 1.6)<br><br>**If Y/PY**, answer questions relating to both baseline and time-varying confounding (1.7 and 1.8) | | |

**Questions relating to baseline confounding only**

| | | |
|---|---|---|
| 1.4. Did the authors use an appropriate analysis method that controlled for all the important confounding domains? | | |
| 1.5. **If Y/PY to 1.4**: Were confounding domains that were controlled for measured validly and reliably by the variables available in this study? | | |
| 1.6. Did the authors control for any post-intervention variables that could have been affected by the intervention? | | |

**Questions relating to baseline and time-varying confounding**

| | | |
|---|---|---|
| 1.7. Did the authors use an appropriate analysis method that controlled for all the important confounding domains and for time-varying confounding? | | |
| 1.8. **If Y/PY to 1.7**: Were confounding domains that were controlled for measured validly and reliably by the variables available in this study? | | |
| **Risk of bias judgement** | | Low |
| Optional: What is the predicted direction of bias due to confounding? | | |

| **Bias in selection of participants into the study** | | |
|---|---|---|
| 2.1. Was selection of participants into the study (or into the analysis) based on participant characteristics observed after the start of intervention?<br><br>**If N/PN to 2.1:** go to 2.4<br><br>2.2. **If Y/PY to 2.1**: Were the post-intervention variables that influenced selection likely to be associated with intervention?<br><br>2.3 **If Y/PY to 2.2**: Were the post-intervention variables that influenced selection likely to be influenced by the outcome or a cause of the outcome? | The selection of participants into study before starting the protocol of the study. For the protocol and potential benefits and risks associated with participation in the study were explained in full before each participant signed an informed consent document. | N |

| 2.4. Do start of follow-up and start of intervention coincide for most participants? | 8 out of 15 participants. | PY |
|---|---|---|
| 2.5. **If Y/PY to 2.2 and 2.3, or N/PN to 2.4**: Were adjustment techniques used that are likely to correct for the presence of selection biases? | | |
| **Risk of bias judgement** | | Low |
| Optional: What is the predicted direction of bias due to selection of participants into the study? | | |

| **Bias in classification of interventions** | | |
|---|---|---|
| 3.1 Were intervention groups clearly defined? | Table I | Y |
| 3.2 Was the information used to define intervention groups recorded at the start of the intervention? | Table I | Y |
| 3.3 Could classification of intervention status have been affected by knowledge of the outcome or risk of the outcome? | Collection of the information at the time is sufficient | N |
| **Risk of bias judgement** | | Low |
| Optional: What is the predicted direction of bias due to classification of interventions? | | |

**Bias due to deviations from intended interventions**

| | | |
|---|---|---|
| **If your aim for this study is to assess the effect of assignment to intervention, answer questions 4.1 and 4.2** | | |
| 4.1. Were there deviations from the intended intervention beyond what would be expected in usual practice? | Crossover study. Each participate receive three supplements | N |
| 4.2. **If Y/PY to 4.1**: Were these deviations from intended intervention unbalanced between groups *and* likely to have affected the outcome? | | |
| **If your aim for this study is to assess the effect of starting and adhering to intervention, answer questions 4.3 to 4.6** | | |
| 4.3. Were important co-interventions balanced across intervention groups? | | |
| 4.4. Was the intervention implemented successfully for most participants? | | |
| 4.5. Did study participants adhere to the assigned intervention regimen? | | |
| 4.6. **If N/PN to 4.3, 4.4 or 4.5**: Was an appropriate analysis used to estimate the effect of starting and adhering to the intervention? | | |
| **Risk of bias judgement** | | Low |
| Optional: What is the predicted direction of bias due to deviations from the intended interventions? | | |

**Bias due to missing data**

| | | |
|---|---|---|
| 5.1 Were outcome data available for all, or nearly all, participants? | The results based on 8 participants | Y |
| 5.2 Were participants excluded due to missing data on intervention status? | Seven participants were subsequently excluded as they were unable to complete the exercise protocol. | PN |
| 5.3 Were participants excluded due to missing data on other variables needed for the analysis? | The results based on 8 participants | N |
| 5.4 **If PN/N to 5.1, or Y/PY to 5.2 or 5.3**: Are the proportion of participants and reasons for missing data similar across interventions? | | |
| 5.5 **If PN/N to 5.1, or Y/PY to 5.2 or 5.3**: Is there evidence that results were robust to the presence of missing data? | | |
| **Risk of bias judgement** | | Low |
| Optional: What is the predicted direction of bias due to missing data? | | |

**Bias in measurement of outcomes**

| | | |
|---|---|---|
| 6.1 Could the outcome measure have been influenced by knowledge of the intervention received? | The study was conducted according to the guidelines of the Declaration of Helsinki and all procedures received approval from the Ethics Committee of the Faculty of Sport Sciences, Waseda University. | N |

| | | |
|---|---|---|
| 6.2 Were outcome assessors aware of the intervention received by study participants? | It is double blinded study design | N |
| 6.3 Were the methods of outcome assessment comparable across intervention groups? | Both group outcomes are using the same assessment | Y |
| 6.4 Were any systematic errors in measurement of the outcome related to intervention received? | The method impose are well explain for conducting the study and blinded | N |
| **Risk of bias judgement** | | Low |
| Optional: What is the predicted direction of bias due to measurement of outcomes? | | |

| **Bias in selection of the reported result** | | |
|---|---|---|
| Is the reported effect estimate likely to be selected, on the basis of the results, from... | | |
| 7.1. ... multiple outcome *measurements* within the outcome domain? | The outcome results are reported using specific measurements that have stated in the section material and method | N |
| 7.2 ... multiple *analyses* of the intervention-outcome relationship? | There is no missing of data for the outcomes results upon the 8 participants | N |
| 7.3 ... different *subgroups*? | No subgroups | N |
| **Risk of bias judgement** | | Low |

| Optional: What is the predicted direction of bias due to selection of the reported result? | | |
|---|---|---|

| **Overall bias** | | |
|---|---|---|
| **Risk of bias judgement** | | Low |
| Optional: What is the overall predicted direction of bias for this outcome? | | |

**8.4.4    Study ID: She 2005**

**Article title:** Changes of hemorrheologic indexes related to the exercise ability in track and field athletes with blood enriching nourishment
**Author**: She, J. B.

# The Risk Of Bias In Non-randomized Studies – of Interventions (ROBINS-I) assessment tool
**Version 19 September 2016**

**ROBINS-I tool (Stage I): At protocol stage**
**Specify the review question**

| | |
|---|---|
| Participants | Athletes experience recovering from injuries and/or hinder in performance. |
| Experimental intervention | Whey protein or the whey supplements. It can be in form of isolate, concentrate, or hydrolysate. |
| Comparator | Carbohydrate supplement; protein-containing foods include animal sources, and vegetarian sources; vitamins; minerals; placebo |
| Outcomes | level of the protein in blood and creatine kinase activity; development of muscle and bone tissue; the muscle and bone fracture injuries recovery period; pain level; and mobility, strength and performance level |

**List the confounding domains relevant to all or most studies**

Consume whey protein

**List co-interventions that could be different between intervention groups and that could impact on outcomes**

None

**ROBINS-I tool (Stage II): For each study**
**Specify a target randomized trial specific to the study**
Design                              Longitudinal study

| | |
|---|---|
| Participants | Track and field athletes |
| Experimental intervention | Whey, sugar, changbai jing xian ling hematopoietic fermin |
| Comparator | changbai jing xian ling; changbai jing xian ling, hematopoietic fermin; changbai jing xian ling, hematopoietic fermin, sugar |

**Is your aim for this study…?**

☑   to assess the effect of *assignment to* intervention

☐   to assess the effect of *starting and adhering to* intervention

**Specify the outcome**
Specify which outcome is being assessed for risk of bias (typically from among those earmarked for the Summary of Findings table). Specify whether this is a proposed benefit or harm of intervention.

| |
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| hemoglobin |

**Specify the numerical result being assessed**
In case of multiple alternative analyses being presented, specify the numeric result (e.g. RR = 1.52 (95% CI 0.83 to 2.77) and/or a reference (e.g. to a table, figure or paragraph) that uniquely defines the result being assessed.

| |
|---|
| Fig 1 and Characteristics of participants |

**Preliminary consideration of confounders**

Complete a row for each important confounding domain (i) listed in the review protocol; and (ii) relevant to the setting of this particular study, or which the study authors identified as potentially important.

*"Important" confounding domains are those for which, in the context of this study, adjustment is expected to lead to a clinically important change in the estimated effect of the intervention. "Validity" refers to whether the confounding variable or variables fully measure the domain, while "reliability" refers to the precision of the measurement (more measurement error means less reliability).*

| (i) Confounding domains listed in the review protocol | | | | |
|---|---|---|---|---|
| Confounding domain | Measured variable(s) | Is there evidence that controlling for this variable was unnecessary?* | Is the confounding domain measured validly and reliably by this variable (or these variables)? | OPTIONAL: Is failure to adjust for this variable (alone) expected to favour the experimental intervention or the comparator? |
| Not Applicable (NA) | | | Yes / No / No information | Favour experimental / Favour comparator / No information |
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| (ii) Additional confounding domains relevant to the setting of this particular study, or which the study authors identified as important | | | | |
|---|---|---|---|---|
| Confounding domain | Measured variable(s) | Is there evidence that controlling for this variable was unnecessary?* | Is the confounding domain measured validly and reliably by this variable (or these variables)? | OPTIONAL: Is failure to adjust for this variable (alone) expected to favour the experimental intervention or the comparator? |
| Not Applicable (NA) | | | Yes / No / No information | Favour experimental / Favour comparator / No information |
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* In the context of a particular study, variables can be demonstrated not to be confounders and so not included in the analysis: (a) if they are not predictive of the outcome; (b) if they are not predictive of intervention; or (c) because adjustment makes no or minimal difference to the estimated effect of the primary parameter. Note that "no statistically significant association" is not the same as "not predictive".

**Preliminary consideration of co-interventions**

Complete a row for each important co-intervention (i) listed in the review protocol; and (ii) relevant to the setting of this particular study, or which the study authors identified as important.

*"Important" co-interventions are those for which, in the context of this study, adjustment is expected to lead to a clinically important change in the estimated effect of the intervention.*

| **(i) Co-interventions listed in the review protocol** | | |
|---|---|---|
| Co-intervention | Is there evidence that controlling for this co-intervention was unnecessary (e.g. because it was not administered)? | Is presence of this co-intervention likely to favour outcomes in the experimental intervention or the comparator |
| Not Applicable (NA) | | Favour experimental / Favour comparator / No information |
| | | Favour experimental / Favour comparator / No information |
| | | Favour experimental / Favour comparator / No information |
| | | Favour experimental / Favour comparator / No information |

| **(ii) Additional co-interventions relevant to the setting of this particular study, or which the study authors identified as important** | | |
|---|---|---|
| Co-intervention | Is there evidence that controlling for this co-intervention was unnecessary (e.g. because it was not administered)? | Is presence of this co-intervention likely to favour outcomes in the experimental intervention or the comparator |
| Not Applicable (NA) | | Favour experimental / Favour comparator / No information |
| | | Favour experimental / Favour comparator / No information |

| | | Favour experimental / Favour comparator / No information |
|---|---|---|
| | | Favour experimental / Favour comparator / No information |

**Risk of bias assessment**

Responses <u>underlined in green</u> are potential markers for low risk of bias, and responses in red are potential markers for a risk of bias. Where questions relate only to sign posts to other questions, no formatting is used.

| Signalling questions | Description | Response options |
|---|---|---|
| **Bias due to confounding** | | |
| 1.1 Is there potential for confounding of the effect of intervention in this study?<br><br>**If N/PN to 1.1:** the study can be considered to be at low risk of bias due to confounding and no further signalling questions need be considered | The athletes were adjusted to have the blood enriching nourishment for more sort groups according to the change of indexes. They are healthy and no heart disease participate | PN |
| **If Y/PY to 1.1**: determine whether there is a need to assess time-varying confounding: | | |
| 1.2. Was the analysis based on splitting participants' follow up time according to intervention received?<br><br>**If N/PN**, answer questions relating to baseline confounding (1.4 to 1.6)<br><br>**If Y/PY**, go to question 1.3. | | |

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| | | |
|---|---|---|
| 1.3. Were intervention discontinuations or switches likely to be related to factors that are prognostic for the outcome?<br><br>**If N/PN**, answer questions relating to baseline confounding (1.4 to 1.6)<br><br>**If Y/PY**, answer questions relating to both baseline and time-varying confounding (1.7 and 1.8) | | |

**Questions relating to baseline confounding only**

| | | |
|---|---|---|
| 1.4. Did the authors use an appropriate analysis method that controlled for all the important confounding domains? | | |
| 1.5. **If Y/PY to 1.4**: Were confounding domains that were controlled for measured validly and reliably by the variables available in this study? | | |
| 1.6. Did the authors control for any post-intervention variables that could have been affected by the intervention? | | |

**Questions relating to baseline and time-varying confounding**

| | | |
|---|---|---|
| 1.7. Did the authors use an appropriate analysis method that controlled for all the important confounding domains and for time-varying confounding? | | |
| 1.8. **If Y/PY to 1.7**: Were confounding domains that were controlled for measured validly and reliably by the variables available in this study? | | |
| **Risk of bias judgement** | | Moderate |
| Optional: What is the predicted direction of bias due to confounding? | | |

| | | |
|---|---|---|
| **Bias in selection of participants into the study** | | |
| 2.1. Was selection of participants into the study (or into the analysis) based on participant characteristics observed after the start of intervention?<br><br>**If N/PN to 2.1:** go to 2.4<br><br>2.2. **If Y/PY to 2.1**: Were the post-intervention variables that influenced selection likely to be associated with intervention?<br><br>2.3 **If Y/PY to 2.2**: Were the post-intervention variables that influenced selection likely to be influenced by the outcome or a cause of the outcome? | The selection of participants into study before starting the protocol of the study as they are 16 participants throughout the 11 month experiments. | PN |

| | | | |
|---|---|---|---|
| | 2.4. Do start of follow-up and start of intervention coincide for most participants? | No dropout or withdraw. 100% full participants | Y |
| | 2.5. **If Y/PY to 2.2 and 2.3, or N/PN to 2.4**: Were adjustment techniques used that are likely to correct for the presence of selection biases? | | |
| | **Risk of bias judgement** | | Low |
| | Optional: What is the predicted direction of bias due to selection of participants into the study? | | |

| | | | |
|---|---|---|---|
| **Bias in classification of interventions** | | | |
| | 3.1 Were intervention groups clearly defined? | Translation documents define clearly | Y |
| | 3.2 Was the information used to define intervention groups recorded at the start of the intervention? | Translation documents define intervention groups recorded at the start of the intervention | Y |
| | 3.3 Could classification of intervention status have been affected by knowledge of the outcome or risk of the outcome? | Collection of the information at the time is sufficient. However, the duration for each supplement differs. | PY |
| | **Risk of bias judgement** | | Moderate |
| | Optional: What is the predicted direction of bias due to classification of interventions? | | |

| **Bias due to deviations from intended interventions** | | |
|---|---|---|
| **If your aim for this study is to assess the effect of assignment to intervention, answer questions 4.1 and 4.2** | | |
| 4.1. Were there deviations from the intended intervention beyond what would be expected in usual practice? | It is longitudinal study. all participants receive all four type of supplements | N |
| 4.2. **If Y/PY to 4.1**: Were these deviations from intended intervention unbalanced between groups *and* likely to have affected the outcome? | | |
| **If your aim for this study is to assess the effect of starting and adhering to intervention, answer questions 4.3 to 4.6** | | |
| 4.3. Were important co-interventions balanced across intervention groups? | | |
| 4.4. Was the intervention implemented successfully for most participants? | | |
| 4.5. Did study participants adhere to the assigned intervention regimen? | | |
| 4.6. **If N/PN to 4.3, 4.4 or 4.5**: Was an appropriate analysis used to estimate the effect of starting and adhering to the intervention? | | |
| **Risk of bias judgement** | | Low |
| Optional: What is the predicted direction of bias due to deviations from the intended interventions? | | |

**Bias due to missing data**

| | | |
|---|---|---|
| 5.1 Were outcome data available for all, or nearly all, participants? | The results based on 16 participants | Y |
| 5.2 Were participants excluded due to missing data on intervention status? | No participants were excluded | N |
| 5.3 Were participants excluded due to missing data on other variables needed for the analysis? | No participants were excluded | N |
| 5.4 **If PN/N to 5.1, or Y/PY to 5.2 or 5.3**: Are the proportion of participants and reasons for missing data similar across interventions? | | |
| 5.5 **If PN/N to 5.1, or Y/PY to 5.2 or 5.3**: Is there evidence that results were robust to the presence of missing data? | | |
| **Risk of bias judgement** | | Low |
| Optional: What is the predicted direction of bias due to missing data? | | |

**Bias in measurement of outcomes**

| | | |
|---|---|---|
| 6.1 Could the outcome measure have been influenced by knowledge of the intervention received? | The lack of information due to partially translation | NI |

| | | |
|---|---|---|
| 6.2 Were outcome assessors aware of the intervention received by study participants? | It is not blinded study | Y |
| 6.3 Were the methods of outcome assessment comparable across intervention groups? | The lack of information due to partially translation | NI |
| 6.4 Were any systematic errors in measurement of the outcome related to intervention received? | The duration of the given supplement differ and it is not blinding | Y |
| **Risk of bias judgement** | | Serious |
| Optional: What is the predicted direction of bias due to measurement of outcomes? | | |

| **Bias in selection of the reported result** | | |
|---|---|---|
| Is the reported effect estimate likely to be selected, on the basis of the results, from... | | |
| 7.1. ... multiple outcome *measurements* within the outcome domain? | The outcome results may be reported using specific measurements that have stated in the method as at translation has 'duration of testing period' | PN |
| 7.2 ... multiple *analyses* of the intervention-outcome relationship? | | NI |
| 7.3 ... different *subgroups*? | No subgroups | N |
| **Risk of bias judgement** | | Low |

| Optional: What is the predicted direction of bias due to selection of the reported result? | | |
|---|---|---|

| Overall bias | | |
|---|---|---|
| **Risk of bias judgement** | There is a domain that is serious and a lot of information which are unavailable in English | Serious |
| Optional: What is the overall predicted direction of bias for this outcome? | | |

**8.4.5   Study ID: Witard 2014**

**Article title**: Myofibrillar muscle protein synthesis rates subsequent to a meal in response to increasing doses of whey protein at rest and after resistance exercise.

**Authors**: Witard, Oliver C; Jackman, Sarah R; Breen, Leigh; Smith, Kenneth; Selby, Anna; Tipton, Kevin D

## The Risk Of Bias In Non-randomized Studies – of Interventions (ROBINS-I) assessment tool
**Version 19 September 2016**

**ROBINS-I tool (Stage I): At protocol stage**
**Specify the review question**

| Participants | Athletes experience recovering from injuries and/or hinder in performance. |
|---|---|
| Experimental intervention | Whey protein or the whey supplements. It can be in form of isolate, concentrate, or hydrolysate. |
| Comparator | Carbohydrate supplement; protein-containing foods include animal sources, and vegetarian sources; vitamins; minerals; placebo |
| Outcomes | level of the protein in blood and creatine kinase activity; development of muscle and bone tissue; the muscle and bone fracture injuries recovery period; pain level; and mobility, strength and performance level |

**List the confounding domains relevant to all or most studies**

Consume whey protein

**List co-interventions that could be different between intervention groups and that could impact on outcomes**

None

**ROBINS-I tool (Stage II): For each study**
**Specify a target randomized trial specific to the study**
Design                            Matched (parallel)

| | |
|---|---|
| Participants | Weight-lifter |
| Experimental intervention | 10 g, 20 g, 40 g of whey protein |
| Comparator | placebo |

**Is your aim for this study…?**

☑      to assess the effect of *assignment to* intervention

☐      to assess the effect of *starting and adhering to* intervention

**Specify the outcome**
Specify which outcome is being assessed for risk of bias (typically from among those earmarked for the Summary of Findings table). Specify whether this is a proposed benefit or harm of intervention.

| |
|---|
| Muscle myofibrillar |

**Specify the numerical result being assessed**
In case of multiple alternative analyses being presented, specify the numeric result (e.g. RR = 1.52 (95% CI 0.83 to 2.77) and/or a reference (e.g. to a table, figure or paragraph) that uniquely defines the result being assessed.

| |
|---|
| Basic characteristics ; 'Overall, across all dose conditions combined, the myofibrillar FSR was greater in the exercised than in nonexercised muscle (main effect of muscle, P , 0.05; Figure 7). Although no dose 3 muscle interaction was detected (P = 0.437), a main effect of dose was observed across both muscles (rested and exercised) combined (P , 0.05). The myofibrillar FSR was increased (P , 0.05) above the 0WP (0.041 6 0.015%/h) by w49% andw56% in the 20WP and 40WP, respectively, whereas no difference |

was observed between the 0WP and 10WP (P . 0.05). In addition, the myofibrillar FSR was increased (P , 0.05) above the 10WP by w22% and w28% in the 20WP and 40WP, respectively. No difference in myofibrillar MPS was observed between the 20WP and 40WP (P . 0.05)'

**Preliminary consideration of confounders**

Complete a row for each important confounding domain (i) listed in the review protocol; and (ii) relevant to the setting of this particular study, or which the study authors identified as potentially important.

*"Important" confounding domains are those for which, in the context of this study, adjustment is expected to lead to a clinically important change in the estimated effect of the intervention. "Validity" refers to whether the confounding variable or variables fully measure the domain, while "reliability" refers to the precision of the measurement (more measurement error means less reliability).*

| (i) Confounding domains listed in the review protocol | | | | |
|---|---|---|---|---|
| Confounding domain | Measured variable(s) | Is there evidence that controlling for this variable was unnecessary?* | Is the confounding domain measured validly and reliably by this variable (or these variables)? | OPTIONAL: Is failure to adjust for this variable (alone) expected to favour the experimental intervention or the comparator? |
| Not Applicable (NA) | | | Yes / No / No information | Favour experimental / Favour comparator / No information |
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| (ii) Additional confounding domains relevant to the setting of this particular study, or which the study authors identified as important | | | | |
|---|---|---|---|---|
| Confounding domain | Measured variable(s) | Is there evidence that controlling for this variable was unnecessary?* | Is the confounding domain measured validly and reliably by this variable (or these variables)? | OPTIONAL: Is failure to adjust for this variable (alone) expected to favour the experimental intervention or the comparator? |
| Not Applicable (NA) |  |  | Yes / No / No information | Favour experimental / Favour comparator / No information |
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* In the context of a particular study, variables can be demonstrated not to be confounders and so not included in the analysis: (a) if they are not predictive of the outcome; (b) if they are not predictive of intervention; or (c) because adjustment makes no or minimal difference to the estimated effect of the primary parameter. Note that "no statistically significant association" is not the same as "not predictive".

**Preliminary consideration of co-interventions**

Complete a row for each important co-intervention (i) listed in the review protocol; and (ii) relevant to the setting of this particular study, or which the study authors identified as important.

"Important" co-interventions are those for which, in the context of this study, adjustment is expected to lead to a clinically important change in the estimated effect of the intervention.

| (i) Co-interventions listed in the review protocol | | |
|---|---|---|
| Co-intervention | Is there evidence that controlling for this co-intervention was unnecessary (e.g. because it was not administered)? | Is presence of this co-intervention likely to favour outcomes in the experimental intervention or the comparator |
| Not Applicable (NA) | | Favour experimental / Favour comparator / No information |
| | | Favour experimental / Favour comparator / No information |
| | | Favour experimental / Favour comparator / No information |
| | | Favour experimental / Favour comparator / No information |

| (ii) Additional co-interventions relevant to the setting of this particular study, or which the study authors identified as important | | |
|---|---|---|
| Co-intervention | Is there evidence that controlling for this co-intervention was unnecessary (e.g. because it was not administered)? | Is presence of this co-intervention likely to favour outcomes in the experimental intervention or the comparator |
| Not Applicable (NA) | | Favour experimental / Favour comparator / No information |
| | | Favour experimental / Favour comparator / No information |

| | | Favour experimental / Favour comparator / No information |
| --- | --- | --- |
| | | Favour experimental / Favour comparator / No information |

**Risk of bias assessment**

Responses <u>underlined in green</u> are potential markers for low risk of bias, and responses in red are potential markers for a risk of bias. Where questions relate only to sign posts to other questions, no formatting is used.

| Signalling questions | Description | Response options |
|---|---|---|
| **Bias due to confounding** | | |
| 1.1 Is there potential for confounding of the effect of intervention in this study?<br><br>If **N/PN** to **1.1:** the study can be considered to be at low risk of bias due to confounding and no further signalling questions need be considered<br><br>If **Y/PY** to **1.1**: determine whether there is a need to assess time-varying confounding: | There is protocol explain in details under the protocol section. | <u>N</u> |
|     1.2. Was the analysis based on splitting participants' follow up time according to intervention received?<br><br>        If **N/PN**, answer questions relating to baseline confounding (1.4 to 1.6)<br><br>        If **Y/PY**, go to question 1.3. | | |

| 1.3. Were intervention discontinuations or switches likely to be related to factors that are prognostic for the outcome?<br><br>**If N/PN**, answer questions relating to baseline confounding (1.4 to 1.6)<br><br>**If Y/PY**, answer questions relating to both baseline and time-varying confounding (1.7 and 1.8) | | |
| --- | --- | --- |

| **Questions relating to baseline confounding only** | | |
| --- | --- | --- |
| 1.4. Did the authors use an appropriate analysis method that controlled for all the important confounding domains? | | |
| 1.5. **If Y/PY to 1.4**: Were confounding domains that were controlled for measured validly and reliably by the variables available in this study? | | |
| 1.6. Did the authors control for any post-intervention variables that could have been affected by the intervention? | | |
| **Questions relating to baseline and time-varying confounding** | | |

| | | |
|---|---|---|
| 1.7. Did the authors use an appropriate analysis method that controlled for all the important confounding domains and for time-varying confounding? | | |
| 1.8. **If Y/PY to 1.7**: Were confounding domains that were controlled for measured validly and reliably by the variables available in this study? | | |
| **Risk of bias judgement** | | Low |
| Optional: What is the predicted direction of bias due to confounding? | | |

| **Bias in selection of participants into the study** | | |
|---|---|---|
| 2.1. Was selection of participants into the study (or into the analysis) based on participant characteristics observed after the start of intervention?<br><br>**If N/PN to 2.1:** go to 2.4<br><br>2.2. **If Y/PY to 2.1**: Were the post-intervention variables that influenced selection likely to be associated with intervention?<br><br>2.3 **If Y/PY to 2.2**: Were the post-intervention variables that influenced selection likely to be influenced by the outcome or a cause of the outcome? | Written informed consent was provided by all participants before beginning the study. | N |

| | | | |
|---|---|---|---|
| | 2.4. Do start of follow-up and start of intervention coincide for most participants? | No dropout or withdraw. 100% full participants. 12 participants for each supplement | Y |
| | 2.5. **If Y/PY to 2.2 and 2.3, or N/PN to 2.4**: Were adjustment techniques used that are likely to correct for the presence of selection biases? | | |
| | **Risk of bias judgement** | | Low |
| | Optional: What is the predicted direction of bias due to selection of participants into the study? | | |

| Bias in classification of interventions | | |
|---|---|---|
| 3.1 Were intervention groups clearly defined? | Table 1 | Y |
| 3.2 Was the information used to define intervention groups recorded at the start of the intervention? | Table 1 | Y |
| 3.3 Could classification of intervention status have been affected by knowledge of the outcome or risk of the outcome? | Collection of the information at the time is sufficient and even timeframe (Figure 1) | N |
| **Risk of bias judgement** | | Low |
| Optional: What is the predicted direction of bias due to classification of interventions? | | |

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**Bias due to deviations from intended interventions**

| | | |
|---|---|---|
| **If your aim for this study is to assess the effect of assignment to intervention, answer questions 4.1 and 4.2** | | |
| 4.1. Were there deviations from the intended intervention beyond what would be expected in usual practice? | 12 participants for each supplement | <u>N</u> |
| 4.2. **If Y/PY to 4.1**: Were these deviations from intended intervention unbalanced between groups *and* likely to have affected the outcome? | | |
| **If your aim for this study is to assess the effect of starting and adhering to intervention, answer questions 4.3 to 4.6** | | |
| 4.3. Were important co-interventions balanced across intervention groups? | | |
| 4.4. Was the intervention implemented successfully for most participants? | | |
| 4.5. Did study participants adhere to the assigned intervention regimen? | | |
| 4.6. **If N/PN to 4.3, 4.4 or 4.5**: Was an appropriate analysis used to estimate the effect of starting and adhering to the intervention? | | |
| **Risk of bias judgement** | | Low |
| Optional: What is the predicted direction of bias due to deviations from the intended interventions? | | |

| Bias due to missing data | | |
|---|---|---|
| 5.1 Were outcome data available for all, or nearly all, participants? | The results based on 48 participants | Y |
| 5.2 Were participants excluded due to missing data on intervention status? | No participants were excluded | N |
| 5.3 Were participants excluded due to missing data on other variables needed for the analysis? | No participants were excluded | N |
| 5.4 **If PN/N to 5.1, or Y/PY to 5.2 or 5.3**: Are the proportion of participants and reasons for missing data similar across interventions? | | |
| 5.5 **If PN/N to 5.1, or Y/PY to 5.2 or 5.3**: Is there evidence that results were robust to the presence of missing data? | | |
| **Risk of bias judgement** | | Low |
| Optional: What is the predicted direction of bias due to missing data? | | |

| Bias in measurement of outcomes |
|---|

| | | |
|---|---|---|
| 6.1 Could the outcome measure have been influenced by knowledge of the intervention received? | Procedures followed were in accordance with the ethical standards of the National Research Ethics Service ethics board, Black Country, Birmingham (Research Ethics Committee number: 08/H1202/131) and the Helsinki Declaration of 1975 as revised in 1983. Written informed consent was provided by all participants before beginning the study. | N |
| 6.2 Were outcome assessors aware of the intervention received by study participants? | It is single blinded study design | Y |
| 6.3 Were the methods of outcome assessment comparable across intervention groups? | All group outcomes are using the same assessment | Y |
| 6.4 Were any systematic errors in measurement of the outcome related to intervention received? | The method impose are well explain for conducting the study and blinded | N |
| **Risk of bias judgement** | | Low |
| Optional: What is the predicted direction of bias due to measurement of outcomes? | | |

| Bias in selection of the reported result | | |
|---|---|---|
| Is the reported effect estimate likely to be selected, on the basis of the results, from... | | |
| 7.1. ... multiple outcome *measurements* within the outcome domain? | The outcome results are reported using specific measurements that have stated in the section material and method | N |
| 7.2 ... multiple *analyses* of the intervention-outcome relationship? | The results did not report baseline. However, authors did report the decrease and increase of each outcome with the end results | PN |

| 7.3 … different *subgroups*? | No subgroup | N |
|---|---|---|
| **Risk of bias judgement** | | Moderate |
| Optional: What is the predicted direction of bias due to selection of the reported result? | | |

| **Overall bias** | | |
|---|---|---|
| **Risk of bias judgement** | | Low |
| Optional: What is the overall predicted direction of bias for this outcome? | | |

### 8.5 Appendix 5: Meta-analysis all outputs and plots

### 8.5.1 Vital signs

#### a) Heart rate

##### i. Data

| Study | Intervention | n1 | m1 | s1 | Control | n2 | m2 | s2 |
|---|---|---|---|---|---|---|---|---|
| **Breen (2011)** | whey contain | 10 | 171 | 2 | carbohydrate | 10 | 172 | 1 |
| **Gunnarsson (2013)** | whey contain | 9 | 166 | 0.67 | placebo | 7 | 164 | 0.76 |
| **Highton (2012)** | whey contain | 9 | 163 | 7 | carbohydrate | 9 | 162 | 7 |
| **Impey (2015)** | whey contain | 9 | 163 | 1 | leucine | 9 | 164 | 1.33 |
| **Li (2007)** | whey contain | 8 | 138.3 | 11.6 | carbohydrate | 8 | 139.3 | 12.2 |
| **Oosthuyse -A (2016)** | whey contain | 8 | 87 | 7 | carbohydrate | 8 | 84 | 9 |
| **Oosthuyse _B (2016)** | whey contain | 8 | 87 | 7 | casein | 8 | 85 | 8 |
| **Oosthuyse -C (2016)** | whey contain | 8 | 87 | 7 | placebo | 8 | 84 | 15 |
| **Schroer (2014)** | whey contain | 8 | 146 | 13 | L-alanine | 8 | 141 | 7 |
| **Schroer (2014)** | whey contain | 8 | 146 | 13 | placebo | 8 | 144 | 13 |
| **Vegge (2012)** | whey contain | 12 | 150 | 12 | maltodextrin | 12 | 149 | 12 |
| **Vegge (2012)** | whey contain | 12 | 150 | 9 | maltodextrin | 12 | 149 | 12 |

n1 = number of intervention participants on the outcome
m1 = mean of intervention on the outcome
s1 = standard deviation of intervention on the outcome
n2 = number of control participant on the outcome
m2 = mean of control on the outcome
s2 = standard deviation of control on the outcome

##### ii. Forest Plot

```
         Study      |    WMD    [95% Conf. Interval]    % Weight
-------------------+-------------------------------------------------
Breen (2011)       | -1.000    -2.386     0.386          23.19
Gunnarsson (2013)  |  2.000     1.287     2.713          26.65
Highton (2012)     |  1.000    -5.468     7.468           4.96
Impey (2015)       | -1.000    -2.087     0.087          24.88
Li (2007)          | -1.000   -12.665    10.665           1.74
Oosthuyse -A (2016)|  3.000    -4.901    10.901           3.53
Oosthuyse -B (2016)|  2.000    -5.366     9.366           3.98
Oosthuyse -C (2016)|  3.000    -8.470    14.470           1.79
Schroer -A (2014)  |  5.000    -5.231    15.231           2.22
Schroer -B (2014)  |  2.000   -10.740    14.740           1.47
Vegge -A (2012)    |  1.000    -8.602    10.602           2.49
Vegge -B (2012)    |  1.000    -7.487     9.487           3.11
-------------------+-------------------------------------------------
D+L pooled WMD     |  0.520    -1.066     2.106         100.00
-------------------+-------------------------------------------------

  Heterogeneity chi-squared =  29.21 (d.f. = 11) p = 0.002
  I-squared (variation in WMD attributable to heterogeneity) =  62.3%
  Estimate of between-study variance Tau-squared =  2.3256

  Test of WMD=0 : z=   0.64 p = 0.521
```

| Study ID | WMD (95% CI) | N, mean (SD); Intervention Group | N, mean (SD); Control Group | % Weight |
|---|---|---|---|---|
| Breen (2011) | -1.00 (-2.39, 0.39) | 10, 171 (2) | 10, 172 (1) | 23.19 |
| Gunnarsson (2013) | 2.00 (1.29, 2.71) | 9, 166 (.67) | 7, 164 (.76) | 26.65 |
| Highton (2012) | 1.00 (-5.47, 7.47) | 9, 163 (7) | 9, 162 (7) | 4.96 |
| Impey (2015) | -1.00 (-2.09, 0.09) | 9, 163 (1) | 9, 164 (1.33) | 24.88 |
| Li (2007) | -1.00 (-12.67, 10.67) | 8, 138 (11.6) | 8, 139 (12.2) | 1.74 |
| Oosthuyse -A (2016) | 3.00 (-4.90, 10.90) | 8, 87 (7) | 8, 84 (9) | 3.53 |
| Oosthuyse -B (2016) | 2.00 (-5.37, 9.37) | 8, 87 (7) | 8, 85 (8) | 3.98 |
| Oosthuyse -C (2016) | 3.00 (-8.47, 14.47) | 8, 87 (7) | 8, 84 (15) | 1.79 |
| Schroer -A (2014) | 5.00 (-5.23, 15.23) | 8, 146 (13) | 8, 141 (7) | 2.22 |
| Schroer -B (2014) | 2.00 (-10.74, 14.74) | 8, 146 (13) | 8, 144 (13) | 1.47 |
| Vegge -A (2012) | 1.00 (-8.60, 10.60) | 12, 150 (12) | 12, 149 (12) | 2.49 |
| Vegge -B (2012) | 1.00 (-7.49, 9.49) | 12, 150 (9) | 12, 149 (12) | 3.11 |
| Overall  (I-squared = 62.3%, p = 0.002) | 0.52 (-1.07, 2.11) | 109 | 107 | 100.00 |

NOTE: Weights are from random effects analysis

-15.2          0          15.2

Favor Control Group          Favor Intervention Group

Impey  (2015) = WP vs carbohydrate
Oosthuyse -A (2016) = WP with carbohydrate vs carbohydrate
Oosthuyse -B (2016) = WP with carbohydrate vs carbohydrate-casein
Oosthuyse -C (2016) = WP with carbohydrate vs placebo
Schroer -A (2014) = WP vs L-alanine
Schroer -B (2014) = WP vs placebo
Vegge -A (2012) = WP with maltodextrin vs maltodextrin
Vegge -B (2012) = WP with nutripeptin and maltodextrin vs maltodextrin

### iii. Funnel Plot



Funnel plot with pseudo 95% confidence limits

### iv. Egger test

```
Egger test for small-study effects:
Regress standard normal deviate of intervention
effect estimate against its standard error

Number of studies =  12                          Root MSE      =   1.708
-------------------------------------------------------------------------
    Std_Eff |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
------------+------------------------------------------------------------
      slope |   .8425302   .6025494     1.40   0.192    -.5000337    2.185094
       bias |  -.0627918   .6329321    -0.10   0.923    -1.473052    1.347469
-------------------------------------------------------------------------

Test of H0: no small-study effects          P = 0.923
```

Publication Bias of Whey Protein on Heart Rate (bpm)

### v. Subgroup

#### • Subgroup by physical activities

```
           Study       |    WMD    [95% Conf. Interval]
--------------------+-----------------------------------------------
     cycle
Breen (2011)           |   -1.000    -2.386     0.386
Impey (2015)           |   -1.000    -2.087     0.087
Oosthuyse -A (2016)    |    3.000    -4.901    10.901
Oosthuyse -B (2016)    |    2.000    -5.366     9.366
Oosthuyse -C (2016)    |    3.000    -8.470    14.470
Schroer -A (2014)      |    5.000    -5.231    15.231
Schroer -B (2014)      |    2.000   -10.740    14.740
Vegge -A (2012)        |    1.000    -8.602    10.602
Vegge -B (2012)        |    1.000    -7.487     9.487
 Sub-total             |
  D+L pooled WMD       |   -0.810    -1.641     0.020
--------------------+-----------------------------------------------
     soccer
Gunnarsson (2013)      |    2.000     1.287     2.713
 Sub-total             |
  D+L pooled WMD       |    2.000     1.287     2.713
--------------------+-----------------------------------------------
     gym
Highton (2012)         |    1.000    -5.468     7.468
 Sub-total             |
  D+L pooled WMD       |    1.000    -5.468     7.468
--------------------+-----------------------------------------------
     cycle and resistance
Li (2007)              |   -1.000   -12.665    10.665
 Sub-total             |
  D+L pooled WMD       |   -1.000   -12.665    10.665
--------------------+-----------------------------------------------
```

Test(s) of heterogeneity:

| | Heterogeneity statistic | degrees of freedom | P | I-squared** | Tau-squared |
|---|---|---|---|---|---|
| cycle | 3.80 | 8 | 0.874 | 0.0% | 0.0000 |
| soccer | 0.00 | 0 | . | .% | 0.0000 |
| gym | 0.00 | 0 | . | .% | 0.0000 |
| cycle and resistance | 0.00 | 0 | . | .% | 0.0000 |

** I-squared: the variation in WMD attributable to heterogeneity)

Significance test(s) of WMD=0

```
cycle                 z=  1.91    p = 0.056
soccer                z=  5.50    p = 0.000
gym                   z=  0.30    p = 0.762
cycle and resistance  z=  0.17    p = 0.867
```

| Study ID | WMD (95% CI) | N, mean (SD); Intervention Group | N, mean (SD); Control Group | % Weight |
|---|---|---|---|---|
| **cycle** | | | | |
| Breen (2011) | -1.00 (-2.39, 0.39) | 10, 171 (2) | 10, 172 (1) | 35.92 |
| Impey (2015) | -1.00 (-2.09, 0.09) | 9, 163 (1) | 9, 164 (1.33) | 58.38 |
| Oosthuyse -A (2016) | 3.00 (-4.90, 10.90) | 8, 87 (7) | 8, 84 (9) | 1.11 |
| Oosthuyse -B (2016) | 2.00 (-5.37, 9.37) | 8, 87 (7) | 8, 85 (8) | 1.27 |
| Oosthuyse -C (2016) | 3.00 (-8.47, 14.47) | 8, 87 (7) | 8, 84 (15) | 0.52 |
| Schroer -A (2014) | 5.00 (-5.23, 15.23) | 8, 146 (13) | 8, 141 (7) | 0.66 |
| Schroer -B (2014) | 2.00 (-10.74, 14.74) | 8, 146 (13) | 8, 144 (13) | 0.43 |
| Vegge -A (2012) | 1.00 (-8.60, 10.60) | 12, 150 (12) | 12, 149 (12) | 0.75 |
| Vegge -B (2012) | 1.00 (-7.49, 9.49) | 12, 150 (9) | 12, 149 (12) | 0.96 |
| Subtotal (I-squared = 0.0%, p = 0.874) | -0.81 (-1.64, 0.02) | 83 | 83 | 100.00 |
| **soccer** | | | | |
| Gunnarsson (2013) | 2.00 (1.29, 2.71) | 9, 166 (.67) | 7, 164 (.76) | 100.00 |
| Subtotal (I-squared = .%, p = .) | 2.00 (1.29, 2.71) | 9 | 7 | 100.00 |
| **gym** | | | | |
| Highton (2012) | 1.00 (-5.47, 7.47) | 9, 163 (7) | 9, 162 (7) | 100.00 |
| Subtotal (I-squared = .%, p = .) | 1.00 (-5.47, 7.47) | 9 | 9 | 100.00 |
| **cycle and resistance training** | | | | |
| Li (2007) | -1.00 (-12.67, 10.67) | 8, 138 (11.6) | 8, 139 (12.2) | 100.00 |
| Subtotal (I-squared = .%, p = .) | -1.00 (-12.67, 10.67) | 8 | 8 | 100.00 |

NOTE: Weights are from random effects analysis

Oosthuyse -A (2016) = WP with carbohydrate vs carbohydrate
Oosthuyse -B (2016) = WP with carbohydrate vs carbohydrate-casein
Oosthuyse -C (2016) = WP with carbohydrate vs placebo
Schroer -A (2014) = WP vs L-alanine
Schroer -B (2014) = WP vs placebo
Vegge -A (2012) = WP with maltodextrin vs maltodextrin
Vegge -B (2012) = WP with nutripeptin and maltodextrin vs maltodextrin

## • Subgroup by intervention period range (day)

```
          Study       |    WMD    [95% Conf. Interval]
--------------------+-------------------------------------------------
     21-40
Breen (2011)          |   -1.000    -2.386     0.386
Oosthuyse -A (2016)   |    3.000    -4.901    10.901
Oosthuyse -B (2016)   |    2.000    -5.366     9.366
Oosthuyse -C (2016)   |    3.000    -8.470    14.470
 Sub-total            |
  D+L pooled WMD      |   -0.734    -2.067     0.599
--------------------+-------------------------------------------------
      1-20
Gunnarsson (2013)     |    2.000     1.287     2.713
Highton (2012)        |    1.000    -5.468     7.468
Impey (2015)          |   -1.000    -2.087     0.087
Schroer -A (2014)     |    5.000    -5.231    15.231
Schroer -B (2014)     |    2.000   -10.740    14.740
 Sub-total            |
  D+L pooled WMD      |    0.855    -1.571     3.281
--------------------+-------------------------------------------------
     61-80
Li (2007)             |   -1.000   -12.665    10.665
 Sub-total            |
  D+L pooled WMD      |   -1.000   -12.665    10.665
--------------------+-------------------------------------------------
     41-60
Vegge -A (2012)       |    1.000    -8.602    10.602
Vegge -B (2012)       |    1.000    -7.487     9.487
 Sub-total            |
  D+L pooled WMD      |    1.000    -5.359     7.359
--------------------+-------------------------------------------------
```

```
Test(s) of heterogeneity:
          Heterogeneity  degrees of
            statistic     freedom      P     I-squared**   Tau-squared

21-40            1.94          3      0.586      0.0%         0.0000
1-20            21.03          4      0.000     81.0%         3.5602
61-80            0.00          0        .         .%          0.0000
41-60            0.00          1      1.000      0.0%         0.0000
** I-squared: the variation in WMD attributable to heterogeneity)
```

```
Significance test(s) of WMD=0

21-40                 z=  1.08    p = 0.281
1-20                  z=  0.69    p = 0.490
61-80                 z=  0.17    p = 0.867
41-60                 z=  0.31    p = 0.758
```

| Study ID | WMD (95% CI) | N, mean (SD); Intervention Group | N, mean (SD); Control Group | % Weight |
|---|---|---|---|---|
| **21-40** | | | | |
| Breen (2011) | -1.00 (-2.39, 0.39) | 10, 171 (2) | 10, 172 (1) | 92.53 |
| Oosthuyse -A (2016) | 3.00 (-4.90, 10.90) | 8, 87 (7) | 8, 84 (9) | 2.85 |
| Oosthuyse -B (2016) | 2.00 (-5.37, 9.37) | 8, 87 (7) | 8, 85 (8) | 3.28 |
| Oosthuyse -C (2016) | 3.00 (-8.47, 14.47) | 8, 87 (7) | 8, 84 (15) | 1.35 |
| Subtotal (I-squared = 0.0%, p = 0.586) | -0.73 (-2.07, 0.60) | 34 | 34 | 100.00 |
| **1-20** | | | | |
| Gunnarsson (2013) | 2.00 (1.29, 2.71) | 9, 166 (.67) | 7, 164 (.76) | 41.48 |
| Highton (2012) | 1.00 (-5.47, 7.47) | 9, 163 (7) | 9, 162 (7) | 10.60 |
| Impey (2015) | -1.00 (-2.09, 0.09) | 9, 163 (1) | 9, 164 (1.33) | 39.60 |
| Schroer -A (2014) | 5.00 (-5.23, 15.23) | 8, 146 (13) | 8, 141 (7) | 4.97 |
| Schroer -B (2014) | 2.00 (-10.74, 14.74) | 8, 146 (13) | 8, 144 (13) | 3.34 |
| Subtotal (I-squared = 81.0%, p = 0.000) | 0.86 (-1.57, 3.28) | 43 | 41 | 100.00 |
| **61-80** | | | | |
| Li (2007) | -1.00 (-12.67, 10.67) | 8, 138 (11.6) | 8, 139 (12.2) | 100.00 |
| Subtotal (I-squared = .%, p = .) | -1.00 (-12.67, 10.67) | 8 | 8 | 100.00 |
| **41-60** | | | | |
| Vegge -A (2012) | 1.00 (-8.60, 10.60) | 12, 150 (12) | 12, 149 (12) | 43.86 |
| Vegge -B (2012) | 1.00 (-7.49, 9.49) | 12, 150 (9) | 12, 149 (12) | 56.14 |
| Subtotal (I-squared = 0.0%, p = 1.000) | 1.00 (-5.36, 7.36) | 24 | 24 | 100.00 |

NOTE: Weights are from random effects analysis

Oosthuyse -A (2016) = WP with carbohydrate vs carbohydrate
Oosthuyse -B (2016) = WP with carbohydrate vs carbohydrate-casein
Oosthuyse -C (2016) = WP with carbohydrate vs placebo
Schroer -A (2014) = WP vs L-alanine
Schroer -B (2014) = WP vs placebo
Vegge -A (2012) = WP with maltodextrin vs maltodextrin
Vegge -B (2012) = WP with nutripeptin and maltodextrin vs maltodextrin

**b) Respiratory exchange ratio**

   **i. Data**

| Study | intervention | n1 | m1 | s1 | control | n2 | m2 | s2 |
|-------|-------------|----|----|----|---------|----|----|----|
| **Breen (2011)** | whey contain | 10 | 18 | 0.32 | carbohydrate | 10 | 17 | 0.32 |
| **Highton (2012)** | whey contain | 9 | 17.6 | 1 | carbohydrate | 9 | 17.8 | 1 |
| **Impey -A (2015)** | whey contain | 9 | 15 | 0.33 | Protein+Caffeine | 9 | 14 | 0.33 |
| **Impey -B (2015)** | whey contain | 9 | 15 | 0.33 | placebo | 9 | 16 | 0.33 |
| **Naclerio -A (2015)** | whey contain | 16 | 15.9 | 1.4 | carbohydrate | 16 | 17.1 | 1.9 |
| **Naclerio -B (2015)** | whey contain | 16 | 15.9 | 1.4 | placebo | 16 | 17.8 | 1.4 |
| **Schroer -A (2014)** | whey contain | 8 | 13.3 | 1.3 | L-alanine | 8 | 13.3 | 1.3 |
| **Schroer -B (2014)** | whey contain | 8 | 13.3 | 1.3 | placebo | 8 | 13.4 | 1.2 |

   **ii. Forest Plot**

```
          Study      |    WMD    [95% Conf. Interval]     % Weight
--------------------+------------------------------------------------
Breen (2011)        |   0.000    -0.004     0.004          66.20
Schroer -A (2014)   |   0.000    -0.029     0.029           4.08
Schroer -B (2014)   |   0.010    -0.015     0.035           5.57
Vegge -A (2012)     |   0.020    -0.005     0.045           5.43
Vegge -B (2012)     |   0.010    -0.003     0.023          18.72
--------------------+------------------------------------------------
D+L pooled WMD      |   0.004    -0.003     0.010         100.00
--------------------+------------------------------------------------


  Heterogeneity chi-squared =   4.68 (d.f. = 4) p = 0.322
  I-squared (variation in WMD attributable to heterogeneity) =  14.5%
  Estimate of between-study variance Tau-squared =  0.0000

  Test of WMD=0 : z=   1.14 p = 0.256
```
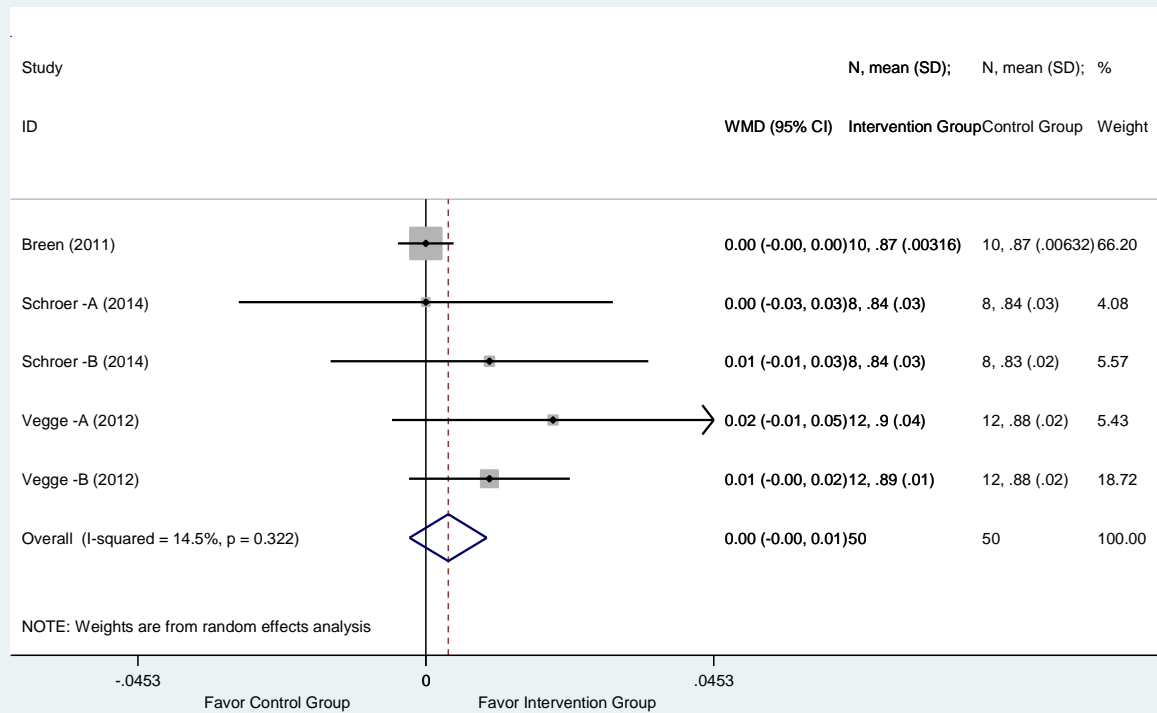
| Study | | | | | |
|---|---|---|---|---|---|
| | | N, mean (SD); | | N, mean (SD); | % |
| ID | | WMD (95% CI) | Intervention Group | Control Group | Weight |
| Breen (2011) | | 0.00 (-0.00, 0.00) | 10, .87 (.00316) | 10, .87 (.00632) | 66.20 |
| Schroer -A (2014) | | 0.00 (-0.03, 0.03) | 8, .84 (.03) | 8, .84 (.03) | 4.08 |
| Schroer -B (2014) | | 0.01 (-0.01, 0.03) | 8, .84 (.03) | 8, .83 (.02) | 5.57 |
| Vegge -A (2012) | | 0.02 (-0.01, 0.05) | 12, .9 (.04) | 12, .88 (.02) | 5.43 |
| Vegge -B (2012) | | 0.01 (-0.00, 0.02) | 12, .89 (.01) | 12, .88 (.02) | 18.72 |
| Overall (I-squared = 14.5%, p = 0.322) | | 0.00 (-0.00, 0.01) | 50 | 50 | 100.00 |

NOTE: Weights are from random effects analysis

-.0453        0        .0453

Favor Control Group        Favor Intervention Group

Schroer -A (2014) = WP vs L-alanine
Schroer -B (2014) = WP vs placebo
Vegge -A (2012) = WP with maltodextrin vs maltodextrin
Vegge -B (2012) = WP with nutripeptin and maltodextrin vs maltodextrin

### c) Rate perceived exertion

#### i. Data

| Study | intervention | n1 | m1 | s1 | control | n2 | m2 | s2 |
|---|---|---|---|---|---|---|---|---|
| **Breen (2011)** | whey contain | 10 | 0.87 | 0.003162 | carbohydrate | 10 | 0.87 | 0.01 |
| **Schroer -A (2014)** | whey contain | 8 | 0.84 | 0.03 | L-alanine | 8 | 0.84 | 0.03 |
| **Schroer -B (2014)** | whey contain | 8 | 0.84 | 0.03 | placebo | 8 | 0.83 | 0.02 |
| **Vegge -A (2012)** | whey contain | 12 | 0.9 | 0.04 | maltodextrin | 12 | 0.88 | 0.02 |
| **Vegge -B (2012)** | whey contain | 12 | 0.89 | 0.01 | maltodextrin | 12 | 0.88 | 0.02 |

#### ii. Forest Plot

```
          Study      |    WMD    [95% Conf. Interval]    % Weight
--------------------+-------------------------------------------------
Breen (2011)        |   1.000     0.720     1.280         14.22
Highton (2012)      |  -0.200    -1.124     0.724         12.26
Impey -A (2015)     |   1.000     0.695     1.305         14.18
Impey -B (2015)     |  -1.000    -1.305    -0.695         14.18
Naclerio -A (2015)  |  -1.200    -2.356    -0.044         11.29
Naclerio -B (2015)  |  -1.900    -2.870    -0.930         12.08
Schroer -A (2014)   |   0.000    -1.274     1.274         10.79
Schroer -B (2014)   |  -0.100    -1.326     1.126         11.00
--------------------+-------------------------------------------------
D+L pooled WMD      |  -0.258    -1.089     0.573        100.00
--------------------+-------------------------------------------------

  Heterogeneity chi-squared = 141.55 (d.f. = 7) p = 0.000
  I-squared (variation in WMD attributable to heterogeneity) =  95.1%
  Estimate of between-study variance Tau-squared =  1.2431

  Test of WMD=0 : z=   0.61 p = 0.542
```
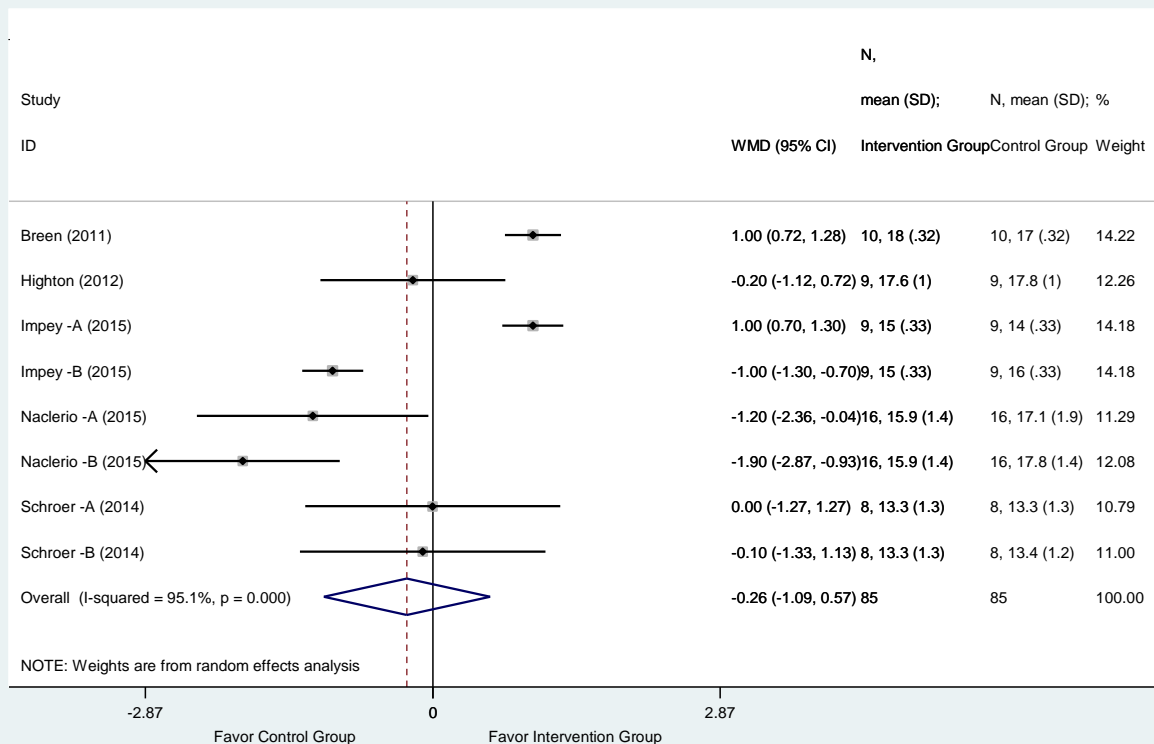
Impey -A (2015) = WP vs carbohydrate
Impey -B (2015) = WP with caffeine vs carbohydrate
Naclerio -A (2015) = WP with multi-ingredient vs carbohydrate
Naclerio -B (2015) = WP with multi-ingredient vs placebo
Schroer -A (2014) = WP vs L-alanine
Schroer -B (2014) = WP vs placebo

### iii. Subgroup

- **Subgroup by physical activities**

```
            Study      |    WMD    [95% Conf. Interval]
-------------------+------------------------------------------------
    cycle
Breen (2011)           |   1.000     0.720     1.280
Impey -A (2015)        |   1.000     0.695     1.305
Impey -B (2015)        |  -1.000    -1.305    -0.695
Schroer -A (2014)      |   0.000    -1.274     1.274
Schroer -B (2014)      |  -0.100    -1.326     1.126
 Sub-total             |
  D+L pooled WMD       |   0.205    -0.805     1.215
-------------------+------------------------------------------------
    run
Highton (2012)         |  -0.200    -1.124     0.724
Naclerio -A (2015)     |  -1.200    -2.356    -0.044
Naclerio -B (2015)     |  -1.900    -2.870    -0.930
 Sub-total             |
  D+L pooled WMD       |  -1.087    -2.122    -0.053
-------------------+------------------------------------------------


Test(s) of heterogeneity:
            Heterogeneity  degrees of
              statistic     freedom      P     I-squared**   Tau-squared

cycle          114.20          4       0.000     96.5%         1.1750
```

```
run                        6.26        2     0.044     68.1%        0.5677
** I-squared: the variation in WMD attributable to heterogeneity)


Significance test(s) of WMD=0

cycle                  z=  0.40    p = 0.691
run                    z=  2.06    p = 0.039
```
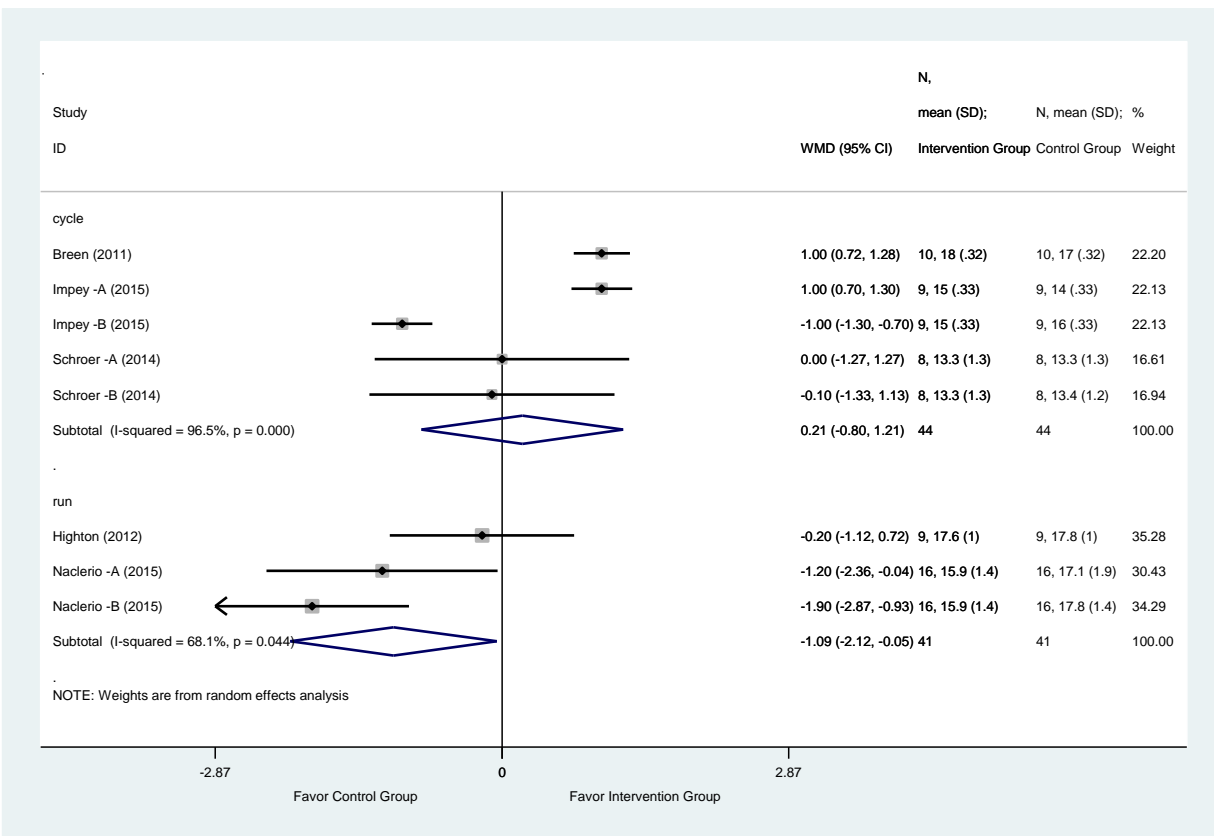


Impey -A (2015) = WP vs carbohydrate
Impey -B (2015) = WP with caffeine vs carbohydrate
Naclerio -A (2015) = WP with multi-ingredient vs carbohydrate
Naclerio -B (2015) = WP with multi-ingredient vs placebo
Schroer -A (2014) = WP vs L-alanine
Schroer -B (2014) = WP vs placebo

- **Subgroup by intervention period range (day)**

```
          Study      |   WMD    [95% Conf. Interval]
-------------------+-------------------------------------------------
    21-40
Breen (2011)       |   1.000    0.720    1.280
 Sub-total         |
  D+L pooled WMD   |   1.000    0.720    1.280
-------------------+-------------------------------------------------
    1-20
Highton (2012)     |  -0.200   -1.124    0.724
Impey -A (2015)    |   1.000    0.695    1.305
Impey -B (2015)    |  -1.000   -1.305   -0.695
Naclerio -A (2015) |  -1.200   -2.356   -0.044
Naclerio -B (2015) |  -1.900   -2.870   -0.930
Schroer -A (2014)  |   0.000   -1.274    1.274
Schroer -B (2014)  |  -0.100   -1.326    1.126
 Sub-total         |
  D+L pooled WMD   |  -0.470   -1.435    0.495
-------------------+-------------------------------------------------


Test(s) of heterogeneity:
            Heterogeneity  degrees of
              statistic     freedom     P    I-squared**   Tau-squared

21-40            0.00          0         .         .%         0.0000
1-20           100.18          6      0.000     94.0%        1.4726
** I-squared: the variation in WMD attributable to heterogeneity)


Significance test(s) of WMD=0

21-40              z=  6.99    p = 0.000
1-20               z=  0.95    p = 0.340
```

| Study ID | WMD (95% CI) | N, mean (SD); Intervention Group | N, mean (SD); Control Group | % Weight |
|---|---|---|---|---|
| **21-40** | | | | |
| Breen (2011) | 1.00 (0.72, 1.28) | 10, 18 (.32) | 10, 17 (.32) | 100.00 |
| Subtotal (I-squared = .%, p = .) | 1.00 (0.72, 1.28) | 10 | 10 | 100.00 |
| . | | | | |
| **1-20** | | | | |
| Highton (2012) | -0.20 (-1.12, 0.72) | 9, 17.6 (1) | 9, 17.8 (1) | 14.31 |
| Impey -A (2015) | 1.00 (0.70, 1.30) | 9, 15 (.33) | 9, 14 (.33) | 16.21 |
| Impey -B (2015) | -1.00 (-1.30, -0.70) | 9, 15 (.33) | 9, 16 (.33) | 16.21 |
| Naclerio -A (2015) | -1.20 (-2.36, -0.04) | 16, 15.9 (1.4) | 16, 17.1 (1.9) | 13.32 |
| Naclerio -B (2015) | -1.90 (-2.87, -0.93) | 16, 15.9 (1.4) | 16, 17.8 (1.4) | 14.12 |
| Schroer -A (2014) | 0.00 (-1.27, 1.27) | 8, 13.3 (1.3) | 8, 13.3 (1.3) | 12.80 |
| Schroer -B (2014) | -0.10 (-1.33, 1.13) | 8, 13.3 (1.3) | 8, 13.4 (1.2) | 13.02 |
| Subtotal (I-squared = 94.0%, p = 0.000) | -0.47 (-1.44, 0.50) | 75 | 75 | 100.00 |

NOTE: Weights are from random effects analysis

-2.87    0    2.87

Favor Control Group    Favor Intervention Group

Impey -A (2015) = WP vs carbohydrate
Impey -B (2015) = WP with caffeine vs carbohydrate
Naclerio -A (2015) = WP with multi-ingredient vs carbohydrate
Naclerio -B (2015) = WP with multi-ingredient vs placebo
Schroer -A (2014) = WP vs L-alanine
Schroer -B (2014) = WP vs placebo

### d) Maximum volume of oxygen

#### i. Data

| Study | intervention | n1 | m1 | s1 | control | n2 | m2 | s2 |
|---|---|---|---|---|---|---|---|---|
| **Breen (2011)** | whey contain | 10 | 50.9 | 0.82 | carbohydrate | 10 | 50.9 | 0.63 |
| **Coombes -A (2002)** | pure whey | 10 | 56 | 2 | bovine colostrum | 9 | 60 | 7 |
| **Coombes -B (2002)** | whey contain | 9 | 59 | 4 | bovine colostrum | 9 | 60 | 7 |
| **Schroer -A (2014)** | whey contain | 8 | 2740 | 310 | L-alanine | 8 | 2680 | 300 |
| **Schroer -B (2014)** | whey contain | 8 | 2740 | 310 | placebo | 8 | 2710 | 290 |
| **Shing (2006)** | whey contain | 15 | 4930 | 520 | bovine colostrum | 14 | 4930 | 520 |
| **Smith (2010)** | whey contain | 13 | 56.2 | 0.75 | maltodextrin | 11 | 45.3 | 0.69 |
| **Vegge -A (2012)** | whey contain | 12 | 41.3 | 3.2 | maltodextrin | 12 | 40.9 | 3.4 |
| **Vegge -B (2012)** | whey contain | 12 | 41.5 | 4.8 | maltodextrin | 12 | 40.9 | 3.4 |

#### ii. Forest Plot

```
              Study     |    WMD    [95% Conf. Interval]     % Weight
--------------------+-----------------------------------------------
Breen (2011)        |   0.000     -0.641      0.641         17.50
Coombes -A (2002)   |  -4.000     -8.738      0.738         15.82
Coombes -B (2002)   |  -1.000     -6.267      4.267         15.47
Schroer -A (2014)   |  60.000   -238.935    358.935          0.04
Schroer -B (2014)   |  30.000   -264.158    324.158          0.04
Shing (2006)        |   0.000   -378.740    378.740          0.03
Smith (2010)        |  10.900     10.323     11.477         17.50
Vegge -A (2012)     |   0.400     -2.242      3.042         16.96
Vegge -B (2012)     |   0.600     -2.728      3.928         16.64
--------------------+-----------------------------------------------
D+L pooled WMD      |   1.325     -4.714      7.364        100.00
--------------------+-----------------------------------------------

  Heterogeneity chi-squared = 663.20 (d.f. = 8) p = 0.000
  I-squared (variation in WMD attributable to heterogeneity) =  98.8%
  Estimate of between-study variance Tau-squared = 54.1514

  Test of WMD=0 : z=   0.43 p = 0.667
```
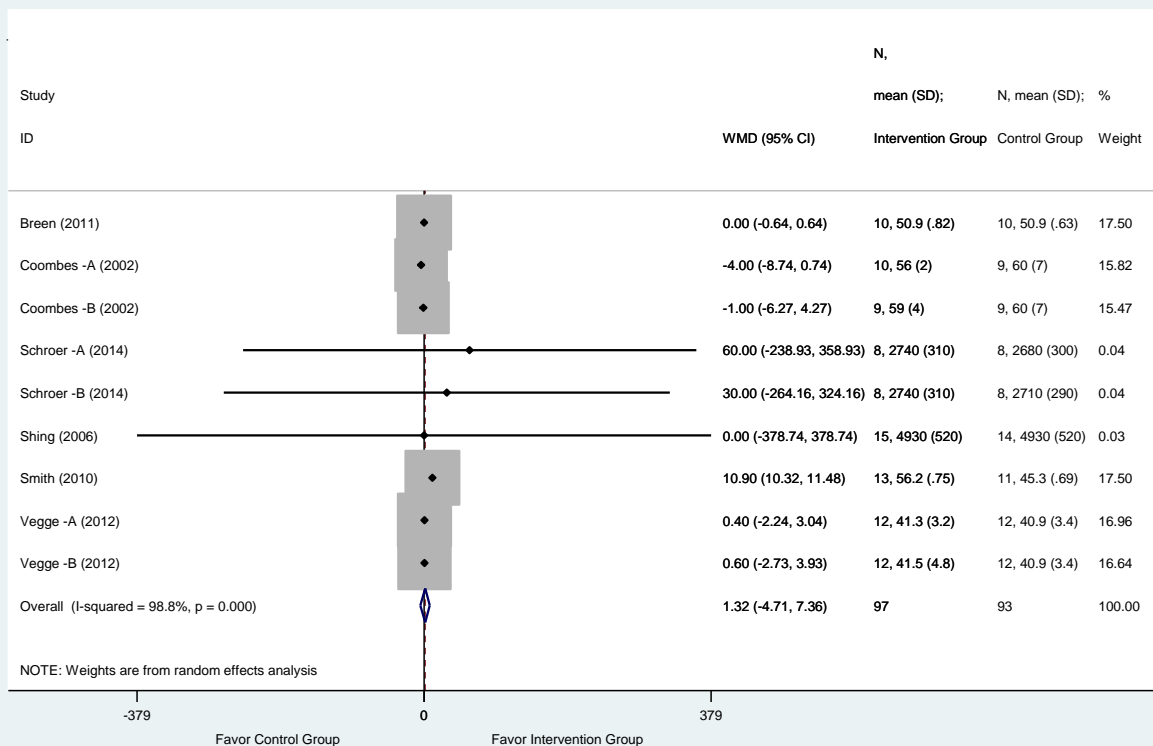
| Study ID | WMD (95% CI) | N, mean (SD); Intervention Group | N, mean (SD); Control Group | % Weight |
|----------|--------------|----------------------------------|------------------------------|----------|
| Breen (2011) | 0.00 (-0.64, 0.64) | 10, 50.9 (.82) | 10, 50.9 (.63) | 17.50 |
| Coombes -A (2002) | -4.00 (-8.74, 0.74) | 10, 56 (2) | 9, 60 (7) | 15.82 |
| Coombes -B (2002) | -1.00 (-6.27, 4.27) | 9, 59 (4) | 9, 60 (7) | 15.47 |
| Schroer -A (2014) | 60.00 (-238.93, 358.93) | 8, 2740 (310) | 8, 2680 (300) | 0.04 |
| Schroer -B (2014) | 30.00 (-264.16, 324.16) | 8, 2740 (310) | 8, 2710 (290) | 0.04 |
| Shing (2006) | 0.00 (-378.74, 378.74) | 15, 4930 (520) | 14, 4930 (520) | 0.03 |
| Smith (2010) | 10.90 (10.32, 11.48) | 13, 56.2 (.75) | 11, 45.3 (.69) | 17.50 |
| Vegge -A (2012) | 0.40 (-2.24, 3.04) | 12, 41.3 (3.2) | 12, 40.9 (3.4) | 16.96 |
| Vegge -B (2012) | 0.60 (-2.73, 3.93) | 12, 41.5 (4.8) | 12, 40.9 (3.4) | 16.64 |
| Overall (I-squared = 98.8%, p = 0.000) | 1.32 (-4.71, 7.36) | 97 | 93 | 100.00 |

NOTE: Weights are from random effects analysis

Coombes -A (2002) = WP alone vs bovine colostrum
Coombes -B (2002) = WP with bovine colostrum vs bovine colostrum
Schroer -A (2014) = WP vs L-alanine
Schroer -B (2014) = WP vs placebo
Vegge -A (2012) = WP with maltodextrin vs maltodextrin
Vegge -B (2012) = WP with nutripeptin and maltodextrin vs maltodextrin

### iii. Subgroup

#### • Subgroup by physical activities

```
            Study      |    WMD   [95% Conf. Interval]
-------------------+-----------------------------------------------------
    cycle
Breen (2011)           |    0.000    -0.641     0.641
Schroer -A (2014)      |   60.000  -238.935   358.935
Schroer -B (2014)      |   30.000  -264.158   324.158
Shing (2006)           |    0.000  -378.740   378.740
Vegge -A (2012)        |    0.400    -2.242     3.042
Vegge -B (2012)        |    0.600    -2.728     3.928
 Sub-total             |
  D+L pooled WMD       |    0.042    -0.570     0.654
-------------------+-----------------------------------------------------
    cycle and resistance
Coombes -A (2002)      |   -4.000    -8.738     0.738
Coombes -B (2002)      |   -1.000    -6.267     4.267
 Sub-total             |
  D+L pooled WMD       |   -2.658    -6.181     0.865
-------------------+-----------------------------------------------------
    run
Smith (2010)           |   10.900    10.323    11.477
 Sub-total             |
```

```
   D+L pooled WMD     |   10.900    10.323    11.477
--------------------+-----------------------------------------------------

Test(s) of heterogeneity:
              Heterogeneity  degrees of
                 statistic     freedom      P    I-squared**   Tau-squared

cycle                  0.39          5      0.996     0.0%        0.0000
cycle and resistance   0.69          1      0.407     0.0%        0.0000
run                    0.00          0       .         .%         0.0000
** I-squared: the variation in WMD attributable to heterogeneity)


Significance test(s) of WMD=0

cycle                  z=  0.13     p = 0.893
cycle and resistance   z=  1.48     p = 0.139
run                    z= 37.05     p = 0.000
```



| Study ID | WMD (95% CI) | N, mean (SD); Intervention Group | N, mean (SD); Control Group | % Weight |
|---|---|---|---|---|
| **cycle** | | | | |
| Breen (2011) | 0.00 (-0.64, 0.64) | 10, 50.9 (.82) | 10, 50.9 (.63) | 91.24 |
| Schroer -A (2014) | 60.00 (-238.93, 358.93) | 8, 2740 (310) | 8, 2680 (300) | 0.00 |
| Schroer -B (2014) | 30.00 (-264.16, 324.16) | 8, 2740 (310) | 8, 2710 (290) | 0.00 |
| Shing (2006) | 0.00 (-378.74, 378.74) | 15, 4930 (520) | 14, 4930 (520) | 0.00 |
| Vegge -A (2012) | 0.40 (-2.24, 3.04) | 12, 41.3 (3.2) | 12, 40.9 (3.4) | 5.37 |
| Vegge -B (2012) | 0.60 (-2.73, 3.93) | 12, 41.5 (4.8) | 12, 40.9 (3.4) | 3.38 |
| Subtotal (I-squared = 0.0%, p = 0.996) | 0.04 (-0.57, 0.65) | 65 | 64 | 100.00 |
| **cycle and resistance training** | | | | |
| Coombes -A (2002) | -4.00 (-8.74, 0.74) | 10, 56 (2) | 9, 60 (7) | 55.27 |
| Coombes -B (2002) | -1.00 (-6.27, 4.27) | 9, 59 (4) | 9, 60 (7) | 44.73 |
| Subtotal (I-squared = 0.0%, p = 0.407) | -2.66 (-6.18, 0.86) | 19 | 18 | 100.00 |
| **run** | | | | |
| Smith (2010) | 10.90 (10.32, 11.48) | 13, 56.2 (.75) | 11, 45.3 (.69) | 100.00 |
| Subtotal (I-squared = .%, p = .) | 10.90 (10.32, 11.48) | 13 | 11 | 100.00 |

NOTE: Weights are from random effects analysis

-379     0     379

Favor Control Group     Favor Intervention Group

Coombes -A (2002) = WP alone vs bovine colostrum
Coombes -B (2002) = WP with bovine colostrum vs bovine colostrum
Schroer -A (2014) = WP vs L-alanine
Schroer -B (2014) = WP vs placebo
Vegge -A (2012) = WP with maltodextrin vs maltodextrin
Vegge -B (2012) = WP with nutripeptin and maltodextrin vs maltodextrin

## • Subgroup by intervention period range (day)

```
         Study       |    WMD    [95% Conf. Interval]
-------------------+-----------------------------------------------
     21-40
Breen (2011)         |    0.000    -0.641     0.641
Smith (2010)         |   10.900    10.323    11.477
 Sub-total           |
  D+L pooled WMD     |    5.451    -5.231    16.133
-------------------+-----------------------------------------------
     41-60
Coombes -A (2002)    |   -4.000    -8.738     0.738
Coombes -B (2002)    |   -1.000    -6.267     4.267
Vegge -A (2012)      |    0.400    -2.242     3.042
Vegge -B (2012)      |    0.600    -2.728     3.928
 Sub-total           |
  D+L pooled WMD     |   -0.327    -2.111     1.457
-------------------+-----------------------------------------------
     1-20
Schroer -A (2014)    |   60.000  -238.935   358.935
Schroer -B (2014)    |   30.000  -264.158   324.158
 Sub-total           |
  D+L pooled WMD     |   44.758  -164.911   254.428
-------------------+-----------------------------------------------
     61-80
Shing (2006)         |    0.000  -378.740   378.740
 Sub-total           |
  D+L pooled WMD     |    0.000  -378.740   378.740
-------------------+-----------------------------------------------

Test(s) of heterogeneity:
          Heterogeneity  degrees of
            statistic     freedom     P    I-squared**  Tau-squared

21-40            614.07          1    0.000    99.8%       59.3083
41-60              2.96          3    0.398     0.0%        0.0000
1-20               0.02          1    0.889     0.0%        0.0000
61-80              0.00          0      .        .%         0.0000
** I-squared: the variation in WMD attributable to heterogeneity)


Significance test(s) of WMD=0

21-40                   z=  1.00    p = 0.317
41-60                   z=  0.36    p = 0.719
1-20                    z=  0.42    p = 0.676
61-80                   z=  0.00    p = 1.000
```

| Study ID | WMD (95% CI) | N, mean (SD); Intervention Group | N, mean (SD); Control Group | % Weight |
|---|---|---|---|---|
| **21-40** | | | | |
| Breen (2011) | 0.00 (-0.64, 0.64) | 10, 50.9 (.82) | 10, 50.9 (.63) | 49.99 |
| Smith (2010) | 10.90 (10.32, 11.48) | 13, 56.2 (.75) | 11, 45.3 (.69) | 50.01 |
| Subtotal (I-squared = 99.8%, p = 0.000) | 5.45 (-5.23, 16.13) | 23 | 21 | 100.00 |
| **41-60** | | | | |
| Coombes -A (2002) | -4.00 (-8.74, 0.74) | 10, 56 (2) | 9, 60 (7) | 14.18 |
| Coombes -B (2002) | -1.00 (-6.27, 4.27) | 9, 59 (4) | 9, 60 (7) | 11.47 |
| Vegge -A (2012) | 0.40 (-2.24, 3.04) | 12, 41.3 (3.2) | 12, 40.9 (3.4) | 45.61 |
| Vegge -B (2012) | 0.60 (-2.73, 3.93) | 12, 41.5 (4.8) | 12, 40.9 (3.4) | 28.74 |
| Subtotal (I-squared = 0.0%, p = 0.398) | -0.33 (-2.11, 1.46) | 43 | 42 | 100.00 |
| **1-20** | | | | |
| Schroer -A (2014) | 60.00 (-238.93, 358.93) | 8, 2740 (310) | 8, 2680 (300) | 49.19 |
| Schroer -B (2014) | 30.00 (-264.16, 324.16) | 8, 2740 (310) | 8, 2710 (290) | 50.81 |
| Subtotal (I-squared = 0.0%, p = 0.889) | 44.76 (-164.91, 254.43) | 16 | 16 | 100.00 |
| **61-80** | | | | |
| Shing (2006) | 0.00 (-378.74, 378.74) | 15, 4930 (520) | 14, 4930 (520) | 100.00 |
| Subtotal (I-squared = .%, p = .) | 0.00 (-378.74, 378.74) | 15 | 14 | 100.00 |

NOTE: Weights are from random effects analysis

-379    0    379

Favor Control Group    Favor Intervention Group

Coombes -A (2002) = WP alone vs bovine colostrum
Coombes -B (2002) = WP with bovine colostrum vs bovine colostrum
Schroer -A (2014) = WP vs L-alanine
Schroer -B (2014) = WP vs placebo
Vegge -A (2012) = WP with maltodextrin vs maltodextrin
Vegge -B (2012) = WP with nutripeptin and maltodextrin vs maltodextrin

### 8.5.2 Serum protein

#### a) Myoglobin

##### i. Data

| Study | intervention | n1 | m1 | s1 | control | n2 | m2 | s2 |
|---|---|---|---|---|---|---|---|---|
| **Gunnarsson (2013)** | whey contain | 9 | 69 | 7 | placebo | 7 | 69 | 14 |
| **Naclerio -A (2015)** | whey contain | 16 | 4.7 | 7.8 | carbohydrate | 16 | 8.9 | 15.2 |
| **Naclerio -B (2015)** | whey contain | 16 | 4.7 | 7.8 | placebo | 16 | 70.5 | 80.5 |

##### ii. Forest Plot

```
          Study        |    WMD    [95% Conf. Interval]     % Weight
-------------------+---------------------------------------------------
Gunnarsson (2013)      |   0.000    -11.335    11.335          40.95
Naclerio -A (2015)     |  -4.200    -12.571     4.171          44.02
Naclerio -B (2015)     |-65.800    -105.429   -26.171          15.03
-------------------+---------------------------------------------------
D+L pooled WMD         |-11.737     -30.239     6.765         100.00
-------------------+---------------------------------------------------

  Heterogeneity chi-squared =   9.80 (d.f. = 2) p = 0.007
  I-squared (variation in WMD attributable to heterogeneity) =  79.6%
  Estimate of between-study variance Tau-squared = 184.1681

  Test of WMD=0 : z=   1.24 p = 0.214
```
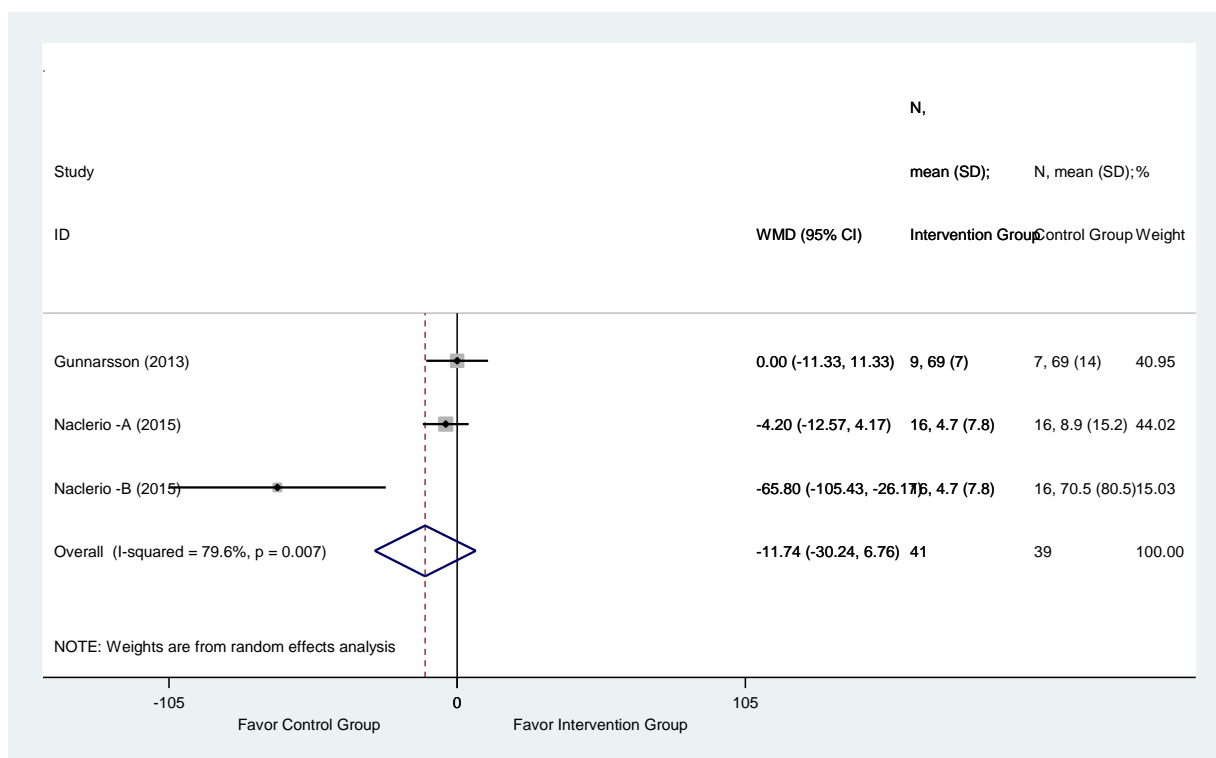


Naclerio -A (2015) = WP with multi-ingredient vs carbohydrate
Naclerio -B (2015) = WP with multi-ingredient vs placebo

### iii. Subgroup

- **Subgroup by physical activities**

```
            Study      |    WMD    [95% Conf. Interval]
-------------------+------------------------------------------------
     soccer game
Gunnarsson (2013)   |   0.000    -11.335    11.335
 Sub-total          |
  D+L pooled WMD    |   0.000    -11.335    11.335
-------------------+------------------------------------------------
     run, jogging
Naclerio -A (2015)  |  -4.200    -12.571     4.171
Naclerio -B (2015)  | -65.800   -105.429   -26.171
 Sub-total          |
  D+L pooled WMD    | -31.830    -91.876    28.217
-------------------+------------------------------------------------

Test(s) of heterogeneity:
              Heterogeneity  degrees of
                statistic     freedom      P     I-squared**   Tau-squared

soccer game         0.00          0          .        .%        0.0000
run, jogging        8.89          1        0.003     88.7%      1.7e+03
** I-squared: the variation in WMD attributable to heterogeneity)


Significance test(s) of WMD=0

soccer game            z=  0.00     p = 1.000
run, jogging           z=  1.04     p = 0.299
```
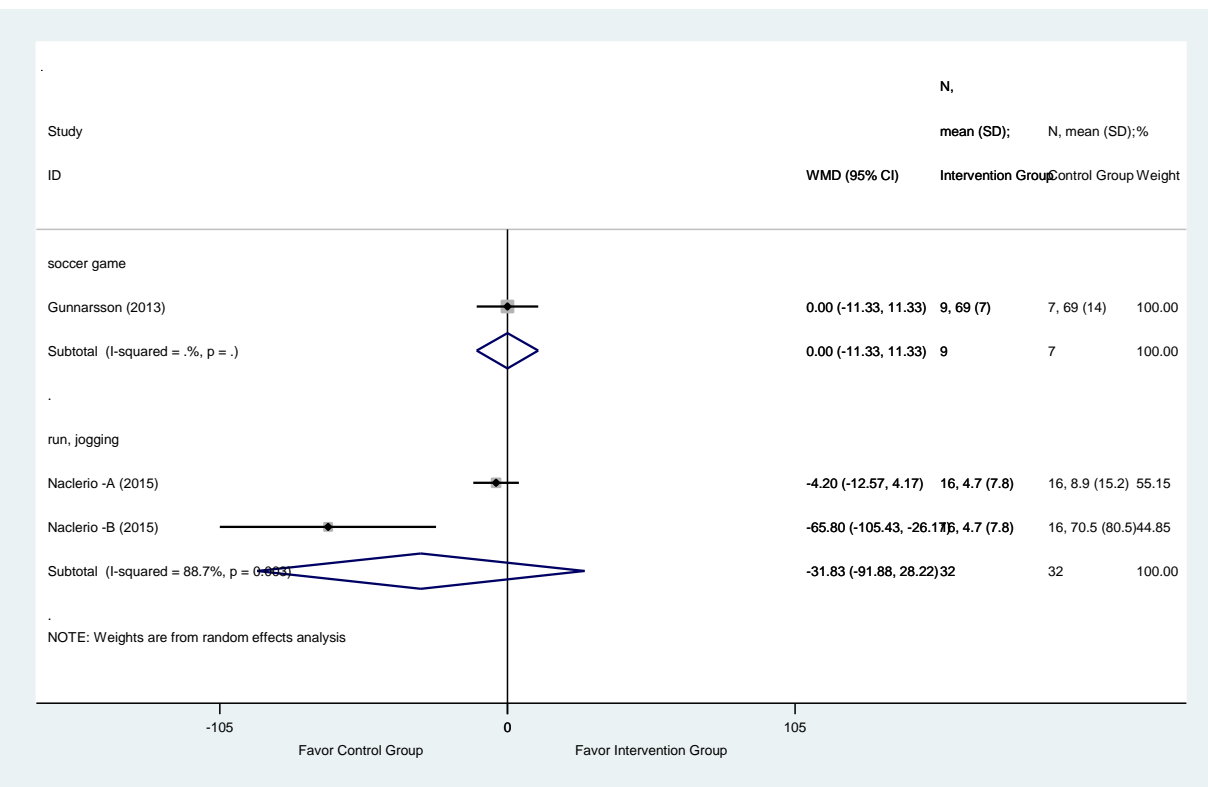


Naclerio -A (2015) = WP with multi-ingredient vs carbohydrate
Naclerio -B (2015) = WP with multi-ingredient vs placebo

- **Subgroup by intervention period range (day)**

```
          Study        |    WMD    [95% Conf. Interval]
-------------------+------------------------------------------------
      1-20
Gunnarsson (2013)      |    0.000   -11.335    11.335
Naclerio -A (2015)     |   -4.200   -12.571     4.171
Naclerio -B (2015)     |  -65.800  -105.429   -26.171
 Sub-total             |
  D+L pooled WMD       |  -11.737   -30.239     6.765
-------------------+------------------------------------------------

Test(s) of heterogeneity:
              Heterogeneity  degrees of
                statistic      freedom      P     I-squared**   Tau-squared

1-20                 9.80          2       0.007     79.6%      184.1681
** I-squared: the variation in WMD attributable to heterogeneity)


Significance test(s) of WMD=0

1-20                     z=  1.24     p = 0.214
```
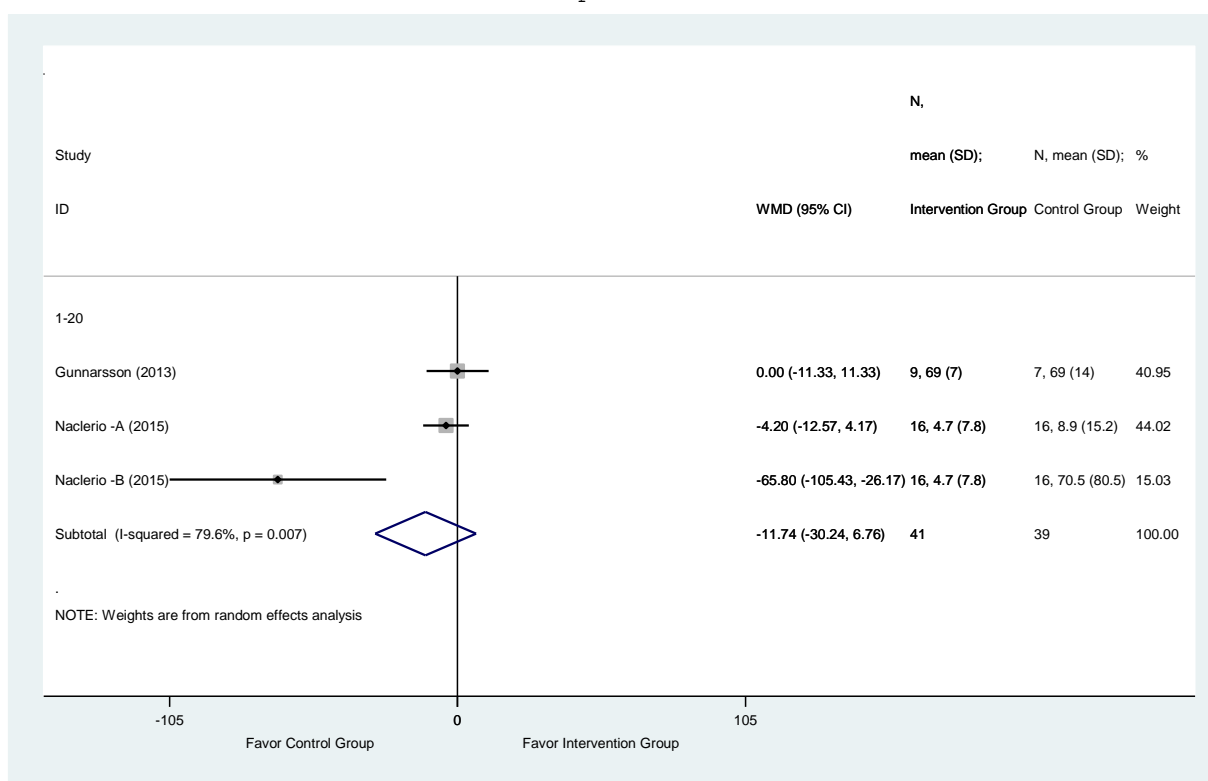


Naclerio -A (2015) = WP with multi-ingredient vs carbohydrate
Naclerio -B (2015) = WP with multi-ingredient vs placebo

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## b) Muscle glycogen

### i. Data

| Study | intervention | n1 | m1 | s1 | control | n2 | m2 | s2 |
|---|---|---|---|---|---|---|---|---|
| **Detko (2013)** | whey contain | 7 | 51.10 | 2.99 | maltodextrin + GAL | 7 | 49.70 | 1.51 |
| **Gunnarsson (2013)** | whey contain | 9 | 325.28 | 8 | placebo | 7 | 281.78 | 9.07 |
| **Hill (2013)** | whey contain | 6 | 450 | 20.41 | protein + carbohydrate + fat | 6 | 470 | 12.25 |

### ii. Forest Plot

```
          Study      |    WMD    [95% Conf. Interval]      % Weight
--------------------+-------------------------------------------------
Detko (2013)        |   1.400    -1.081     3.881           34.82
Gunnarsson (2013)   |  43.500    34.988    52.012           34.07
Hill (2013)         | -20.000   -39.047    -0.953           31.11
--------------------+-------------------------------------------------
D+L pooled WMD      |   9.084   -23.188    41.356          100.00
--------------------+-------------------------------------------------

  Heterogeneity chi-squared =  92.96 (d.f. = 2) p = 0.000
  I-squared (variation in WMD attributable to heterogeneity) =  97.8%
  Estimate of between-study variance Tau-squared = 776.9901

 Test of WMD=0 : z=   0.55 p = 0.581
```
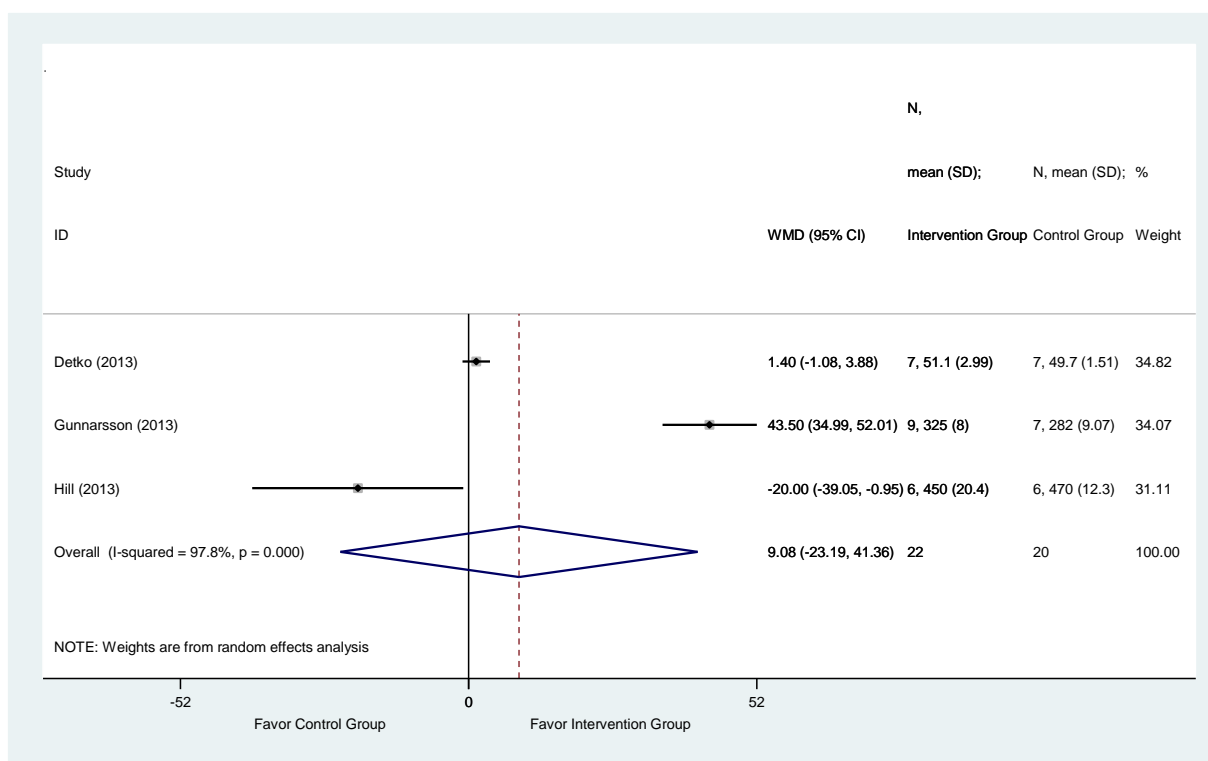
### iii. Subgroup

- **Subgroup by physical activities**

```
            Study       |    WMD    [95% Conf. Interval]
--------------------+--------------------------------------------------
     cycle
Detko (2013)            |   1.400    -1.081     3.881
Hill (2013)             | -20.000   -39.047    -0.953
 Sub-total              |
  D+L pooled WMD        |  -7.131   -27.667    13.405
--------------------+--------------------------------------------------
     soccer game
Gunnarsson (2013)       |  43.500    34.988    52.012
 Sub-total              |
  D+L pooled WMD        |  43.500    34.988    52.012
--------------------+--------------------------------------------------

Test(s) of heterogeneity:
           Heterogeneity  degrees of
             statistic     freedom       P     I-squared**   Tau-squared

cycle             4.77          1       0.029     79.0%       180.9591
soccer game       0.00          0         .         .%         0.0000
** I-squared: the variation in WMD attributable to heterogeneity)


Significance test(s) of WMD=0

cycle                  z=  0.68    p = 0.496
soccer game            z= 10.02    p = 0.000
```
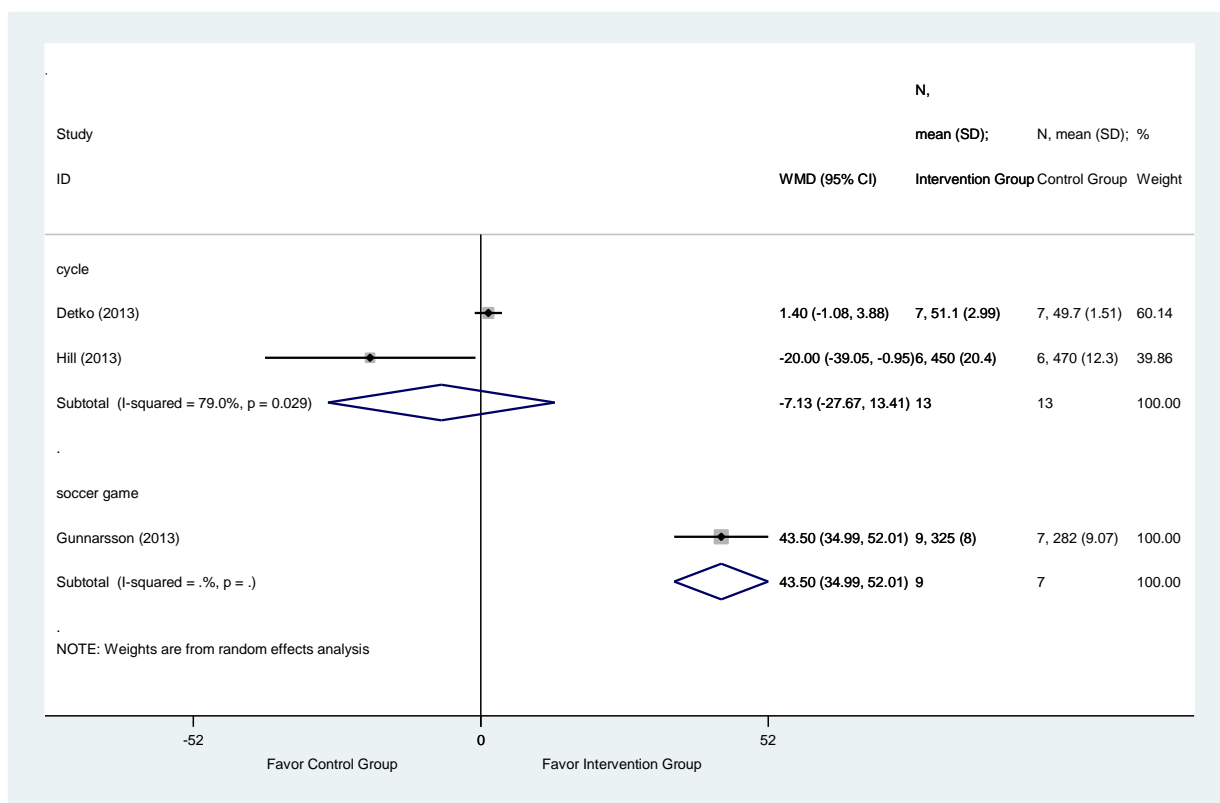
- **Subgroup by intervention period range (day)**

```
              Study       |    WMD    [95% Conf. Interval]
--------------------------+-----------------------------------------------
      1-20
Detko (2013)              |   1.400    -1.081     3.881
Gunnarsson (2013)         |  43.500    34.988    52.012
 Sub-total                |
  D+L pooled WMD          |  22.245   -19.010    63.500
--------------------------+-----------------------------------------------
      41-60
Hill (2013)               | -20.000   -39.047    -0.953
 Sub-total                |
  D+L pooled WMD          | -20.000   -39.047    -0.953
--------------------------+-----------------------------------------------

Test(s) of heterogeneity:
                 Heterogeneity  degrees of
                    statistic     freedom      P     I-squared**   Tau-squared

1-20                   86.60          1       0.000     98.8%        875.9719
41-60                   0.00          0         .          .%         0.0000
** I-squared: the variation in WMD attributable to heterogeneity)


Significance test(s) of WMD=0

1-20                   z=  1.06     p = 0.291
41-60                  z=  2.06     p = 0.040
```
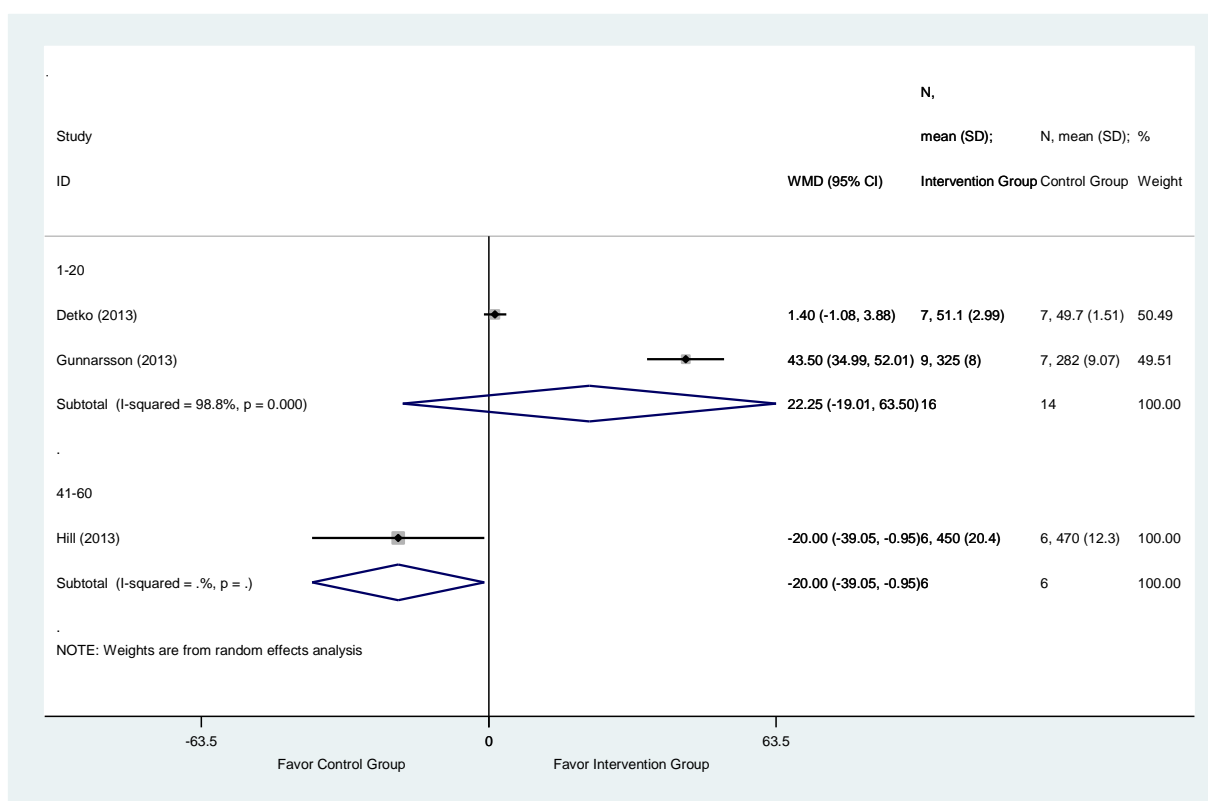
### 8.5.3  Strength and body composition

#### a)  Maximum power

##### i.  Data

| Study | intervention | n1 | m1 | s1 | control | n2 | m2 | s2 |
|---|---|---|---|---|---|---|---|---|
| **Al-Nawaiseh (2016)** | whey contain | 22 | 833 | 199 | placebo | 22 | 813 | 188 |
| **Hansen (2016)** | whey contain | 9 | 1090 | 16.67 | carbohydrate | 9 | 1350 | 33.33 |
| **Hoffman -A (2009)** | whey contain | 13 | 683 | 149 | placebo | 7 | 612 | 126 |
| **Hoffman -B (2009)** | whey contain | 13 | 733 | 167 | placebo | 7 | 612 | 126 |
| **Joy (2013)** | whey contain | 12 | 785 | 101.1 | rice | 12 | 753.9 | 115.6 |
| **Li (2007)** | whey contain | 8 | 920.1 | 127.8 | carbohydrate | 8 | 869.6 | 63.10 |
| **Macdermid (2006)** | whey contain | 7 | 230 | 100 | carbohydrate | 7 | 275 | 100 |
| **Shing (2006)** | whey contain | 15 | 462 | 38 | bovine colostrum | 14 | 448 | 37 |

##### ii.  Forest Plot

```
          Study       |    WMD    [95% Conf. Interval]     % Weight
--------------------+--------------------------------------------------
Al-Nawaiseh (2016)  | 20.000    -94.395   134.395           12.12
Hansen (2016)       |-260.000  -284.348  -235.652           13.39
Hoffman -A (2009)   | 71.000    -52.583   194.583           11.92
Hoffman -B (2009)   |121.000     -9.206   251.206           11.78
Joy (2013)          | 31.100    -55.790   117.990           12.65
Li (2007)           | 50.500    -48.266   149.266           12.44
Macdermid (2006)    |-45.000   -149.764    59.764           12.32
Shing (2006)        | 14.000    -13.303    41.303           13.38
--------------------+--------------------------------------------------
D+L pooled WMD      | -3.137   -129.467   123.192          100.00
--------------------+--------------------------------------------------

  Heterogeneity chi-squared = 271.97 (d.f. = 7) p = 0.000
  I-squared (variation in WMD attributable to heterogeneity) =  97.4%
  Estimate of between-study variance Tau-squared =  3.1e+04

  Test of WMD=0 : z=   0.05 p = 0.961
```
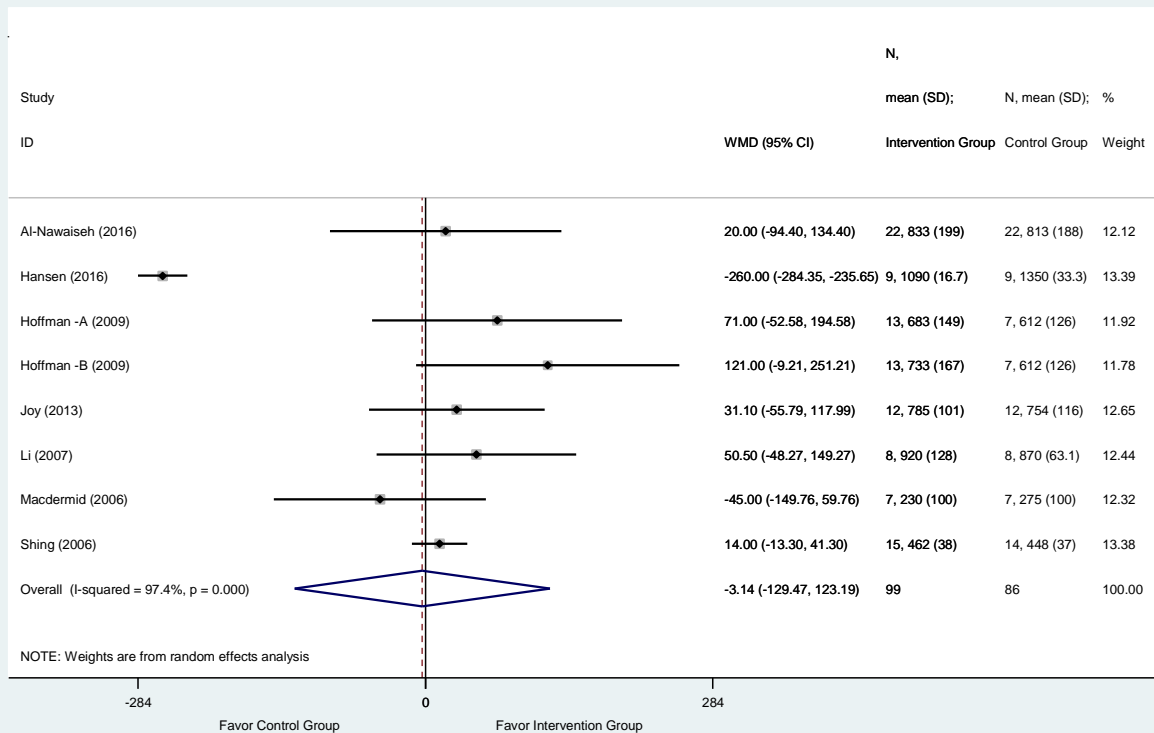
Hoffman -A (2009) = WP with carbohydrate vs placebo
Hoffman -B (2009) = WP with fat and carbohydrate vs placebo

### iii. Subgroup

- #### Subgroup by physical activities

```
            Study      |    WMD    [95% Conf. Interval]
-------------------+-----------------------------------------------
    cycle and resistance
Al-Nawaiseh (2016) |   20.000   -94.395    134.395
Hansen (2016)      | -260.000  -284.348   -235.652
Joy (2013)         |   31.100   -55.790    117.990
Li (2007)          |   50.500   -48.266    149.266
 Sub-total         |
  D+L pooled WMD   |  -42.913  -242.890    157.064
-------------------+-----------------------------------------------
    gym
Hoffman -A (2009)  |   71.000   -52.583    194.583
Hoffman -B (2009)  |  121.000    -9.206    251.206
 Sub-total         |
  D+L pooled WMD   |   94.696     5.060    184.332
-------------------+-----------------------------------------------
    cycle
Macdermid (2006)   |  -45.000  -149.764     59.764
Shing (2006)       |   14.000   -13.303     41.303
 Sub-total         |
  D+L pooled WMD   |    7.069   -30.166     44.303
-------------------+-----------------------------------------------

Test(s) of heterogeneity:
```

```
                      Heterogeneity  degrees of
                        statistic     freedom      P    I-squared**  Tau-squared

cycle and resistance 87.90              3        0.000     96.6%       4.0e+04
gym                   0.30              1        0.585      0.0%       0.0000
cycle                 1.14              1        0.285     12.3%       214.9024
** I-squared: the variation in WMD attributable to heterogeneity)



Significance test(s) of WMD=0

cycle and resistance  z=  0.42     p = 0.674
gym                   z=  2.07     p = 0.038
cycle                 z=  0.37     p = 0.710
-----------------------------------------------------------------------
```
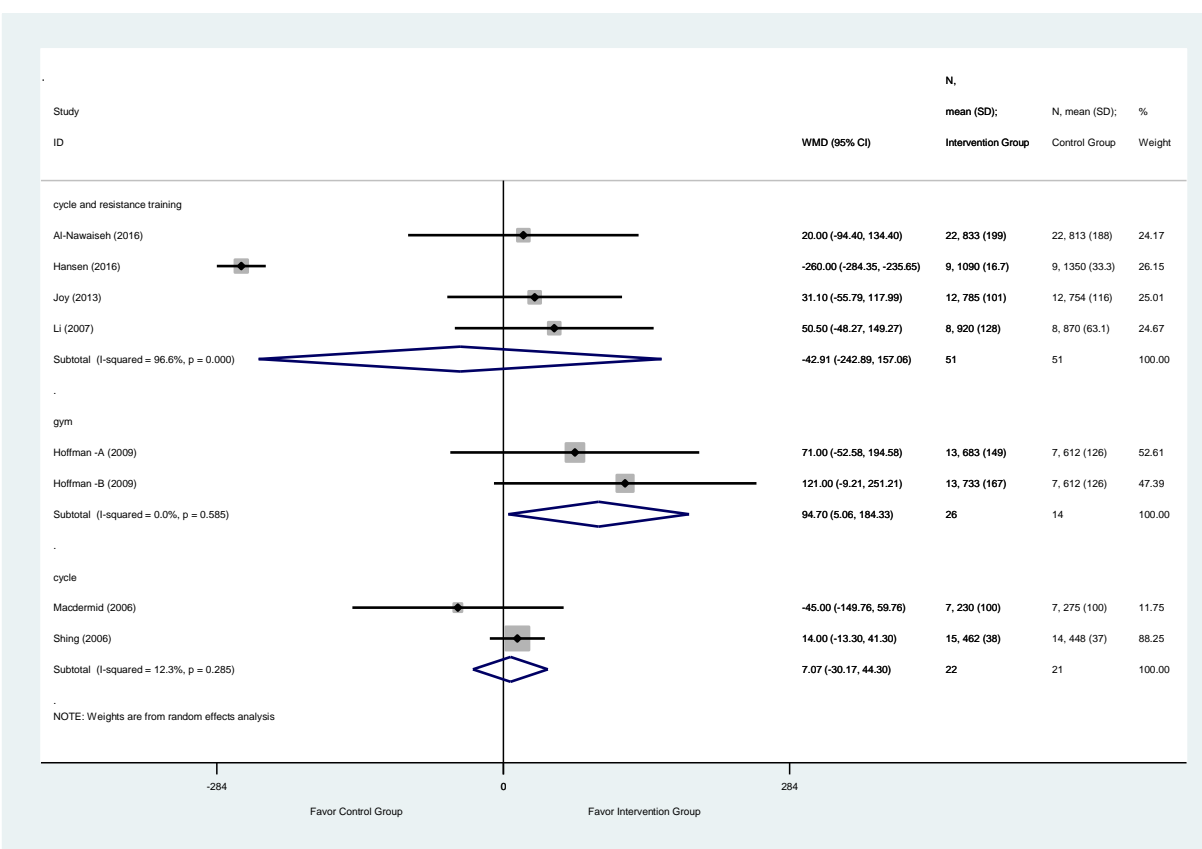


Hoffman -A (2009) = WP with carbohydrate vs placebo
Hoffman -B (2009) = WP with fat and carbohydrate vs placebo

- **Subgroup by intervention period range (day)**

```
         Study      |    WMD    [95% Conf. Interval]
-------------------+-----------------------------------------------
    1-20
Al-Nawaiseh (2016) |   20.000   -94.395   134.395
Hansen (2016)      | -260.000  -284.348  -235.652
Macdermid (2006)   |  -45.000  -149.764    59.764
 Sub-total         |
  D+L pooled WMD   | -100.779  -297.338    95.781
-------------------+-----------------------------------------------
    61-80
Hoffman -A (2009)  |   71.000   -52.583   194.583
Hoffman -B (2009)  |  121.000    -9.206   251.206
Li (2007)          |   50.500   -48.266   149.266
Shing (2006)       |   14.000   -13.303    41.303
 Sub-total         |
  D+L pooled WMD   |   31.304    -5.566    68.175
-------------------+-----------------------------------------------
    41-60
Joy (2013)         |   31.100   -55.790   117.990
 Sub-total         |
  D+L pooled WMD   |   31.100   -55.790   117.990
-------------------+-----------------------------------------------

Test(s) of heterogeneity:
          Heterogeneity  degrees of
            statistic     freedom      P    I-squared**   Tau-squared

1-20            35.71         2       0.000     94.4%        2.8e+04
61-80            3.47         3       0.325     13.6%        299.2044
41-60            0.00         0         .         .%           0.0000
** I-squared: the variation in WMD attributable to heterogeneity)



Significance test(s) of WMD=0

1-20                  z=  1.00    p = 0.315
61-80                 z=  1.66    p = 0.096
41-60                 z=  0.70    p = 0.483
-----------------------------------------------------------------------
```

| Study ID | WMD (95% CI) | N, mean (SD); Intervention Group | N, mean (SD); Control Group | % Weight |
|---|---|---|---|---|
| **1-20** | | | | |
| Al-Nawaiseh (2016) | 20.00 (-94.40, 134.40) | 22, 833 (199) | 22, 813 (188) | 31.92 |
| Hansen (2016) | -260.00 (-284.35, -235.65) | 9, 1090 (16.7) | 9, 1350 (33.3) | 35.59 |
| Macdermid (2006) | -45.00 (-149.76, 59.76) | 7, 230 (100) | 7, 275 (100) | 32.49 |
| Subtotal (I-squared = 94.4%, p = 0.000) | -100.78 (-297.34, 95.78) | 38 | 38 | 100.00 |
| . | | | | |
| **61-80** | | | | |
| Hoffman -A (2009) | 71.00 (-52.58, 194.58) | 13, 683 (149) | 7, 612 (126) | 8.28 |
| Hoffman -B (2009) | 121.00 (-9.21, 251.21) | 13, 733 (167) | 7, 612 (126) | 7.51 |
| Li (2007) | 50.50 (-48.27, 149.27) | 8, 920 (128) | 8, 870 (63.1) | 12.47 |
| Shing (2006) | 14.00 (-13.30, 41.30) | 15, 462 (38) | 14, 448 (37) | 71.75 |
| Subtotal (I-squared = 13.6%, p = 0.325) | 31.30 (-5.57, 68.17) | 49 | 36 | 100.00 |
| . | | | | |
| **41-60** | | | | |
| Joy (2013) | 31.10 (-55.79, 117.99) | 12, 785 (101) | 12, 754 (116) | 100.00 |
| Subtotal (I-squared = .%, p = .) | 31.10 (-55.79, 117.99) | 12 | 12 | 100.00 |
| . | | | | |
| NOTE: Weights are from random effects analysis | | | | |

Favor Control Group     Favor Intervention Group

-297     0     297

Hoffman -A (2009) = WP with carbohydrate vs placebo
Hoffman -B (2009) = WP with fat and carbohydrate vs placebo

## b) Average power

### i. Data

| Study | intervention | n1 | m1 | s1 | control | n2 | m2 | s2 |
|-------|-------------|----|----|----|---------|----|----|----|
| **Al-Nawaiseh (2016)** | whey contain | 22 | 498 | 121 | placebo | 22 | 486 | 115 |
| **Coombes -A (2002)** | pure whey | 10 | 288 | 78 | bovine colostrum | 9 | 400 | 89 |
| **Coombes -B (2002)** | whey contain | 9 | 381 | 62 | bovine colostrum | 9 | 400 | 89 |
| **Hansen (2016)** | whey contain | 9 | 404 | 3.67 | carbohydrate | 9 | 409 | 2.67 |
| **Highton (2012)** | whey contain | 9 | 8.1 | 0.3 | carbohydrate | 9 | 7.9 | 0.5 |
| **Hoffman -A (2009)** | whey contain | 13 | 463 | 84 | placebo | 7 | 463 | 81 |
| **Hoffman -B (2009)** | whey contain | 13 | 483 | 91 | placebo | 7 | 463 | 81 |
| **Li (2007)** | whey contain | 8 | 823.8 | 65.4 | carbohydrate | 8 | 784.1 | 100.8 |
| **Macdermid (2006)** | whey contain | 7 | 220 | 150 | carbohydrate | 7 | 270 | 200 |

### ii. Forest Plot

```
            Study     |    WMD   [95% Conf. Interval]     % Weight
--------------------+------------------------------------------------
Al-Nawaiseh (2016)  | 12.000   -57.755    81.755          0.64
Coombes -A (2002)   |-112.000  -187.618   -36.382         0.55
Coombes -B (2002)   |-19.000   -89.864    51.864          0.62
Hansen (2016)       | -5.000    -7.965    -2.035         45.12
Highton (2012)      |  0.200    -0.181     0.581         51.46
Hoffman -A (2009)   |  0.000   -75.403    75.403          0.55
Hoffman -B (2009)   | 20.000   -57.766    97.766          0.52
Li (2007)           | 39.700   -43.563   122.963          0.45
Macdermid (2006)    |-50.000  -235.199   135.199          0.09
--------------------+------------------------------------------------
D+L pooled WMD      | -2.570    -8.195     3.055         100.00
--------------------+------------------------------------------------

  Heterogeneity chi-squared =  21.86 (d.f. = 8) p = 0.005
  I-squared (variation in WMD attributable to heterogeneity) =  63.4%
  Estimate of between-study variance Tau-squared = 15.9676

  Test of WMD=0 : z=   0.90 p = 0.371
```
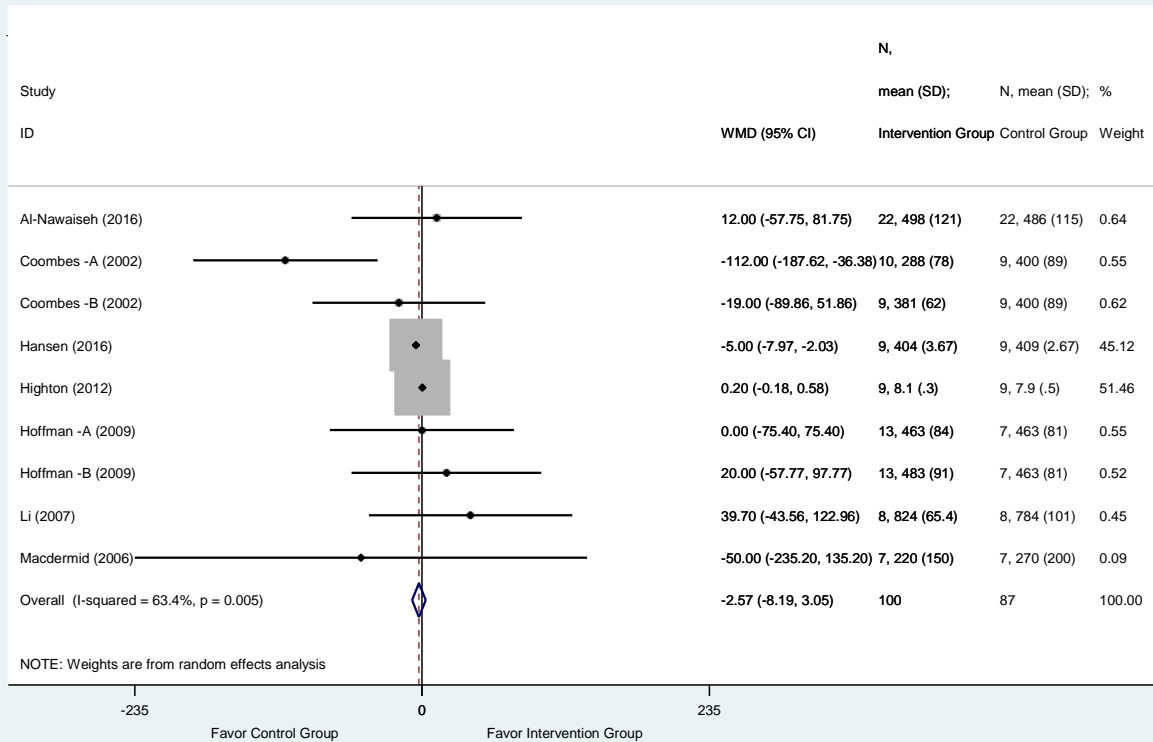
| Study ID | WMD (95% CI) | N, mean (SD); Intervention Group | N, mean (SD); Control Group | % Weight |
|---|---|---|---|---|
| Al-Nawaiseh (2016) | 12.00 (-57.75, 81.75) | 22, 498 (121) | 22, 486 (115) | 0.64 |
| Coombes -A (2002) | -112.00 (-187.62, -36.38) | 10, 288 (78) | 9, 400 (89) | 0.55 |
| Coombes -B (2002) | -19.00 (-89.86, 51.86) | 9, 381 (62) | 9, 400 (89) | 0.62 |
| Hansen (2016) | -5.00 (-7.97, -2.03) | 9, 404 (3.67) | 9, 409 (2.67) | 45.12 |
| Highton (2012) | 0.20 (-0.18, 0.58) | 9, 8.1 (.3) | 9, 7.9 (.5) | 51.46 |
| Hoffman -A (2009) | 0.00 (-75.40, 75.40) | 13, 463 (84) | 7, 463 (81) | 0.55 |
| Hoffman -B (2009) | 20.00 (-57.77, 97.77) | 13, 483 (91) | 7, 463 (81) | 0.52 |
| Li (2007) | 39.70 (-43.56, 122.96) | 8, 824 (65.4) | 8, 784 (101) | 0.45 |
| Macdermid (2006) | -50.00 (-235.20, 135.20) | 7, 220 (150) | 7, 270 (200) | 0.09 |
| Overall (I-squared = 63.4%, p = 0.005) | -2.57 (-8.19, 3.05) | 100 | 87 | 100.00 |

NOTE: Weights are from random effects analysis

Coombes -A (2002) = WP alone vs bovine colostrum
Coombes -B (2002) = WP with bovine colostrum vs bovine colostrum
Hoffman -A (2009) = WP with carbohydrate vs placebo
Hoffman -B (2009) = WP with fat and carbohydrate vs placebo

### iii. Subgroup

- **Subgroup by physical activities**

```
         Study     |    WMD   [95% Conf. Interval]
-------------------+-------------------------------------------------
    cycle and resistance
Al-Nawaiseh (2016) |   12.000   -57.755    81.755
Coombes -A (2002)  | -112.000  -187.618   -36.382
Coombes -B (2002)  |  -19.000   -89.864    51.864
Hansen (2016)      |   -5.000    -7.965    -2.035
Li (2007)          |   39.700   -43.563   122.963
Macdermid (2006)   |  -50.000  -235.199   135.199
 Sub-total         |
  D+L pooled WMD   |  -15.297   -49.847    19.252
-------------------+-------------------------------------------------
    gym
Highton (2012)     |    0.200    -0.181     0.581
Hoffman -A (2009)  |    0.000   -75.403    75.403
Hoffman -B (2009)  |   20.000   -57.766    97.766
 Sub-total         |
  D+L pooled WMD   |    0.200    -0.180     0.581
-------------------+-------------------------------------------------

Test(s) of heterogeneity:
```

321

```
                  Heterogeneity  degrees of
                  statistic      freedom      P      I-squared**    Tau-squared

cycle and resistance  9.40         5         0.094      46.8%        763.3865
gym                   0.25         2         0.883      0.0%         0.0000
** I-squared: the variation in WMD attributable to heterogeneity)



Significance test(s) of WMD=0

cycle and resistance  z=  0.87     p = 0.385
gym                   z=  1.03     p = 0.302
```
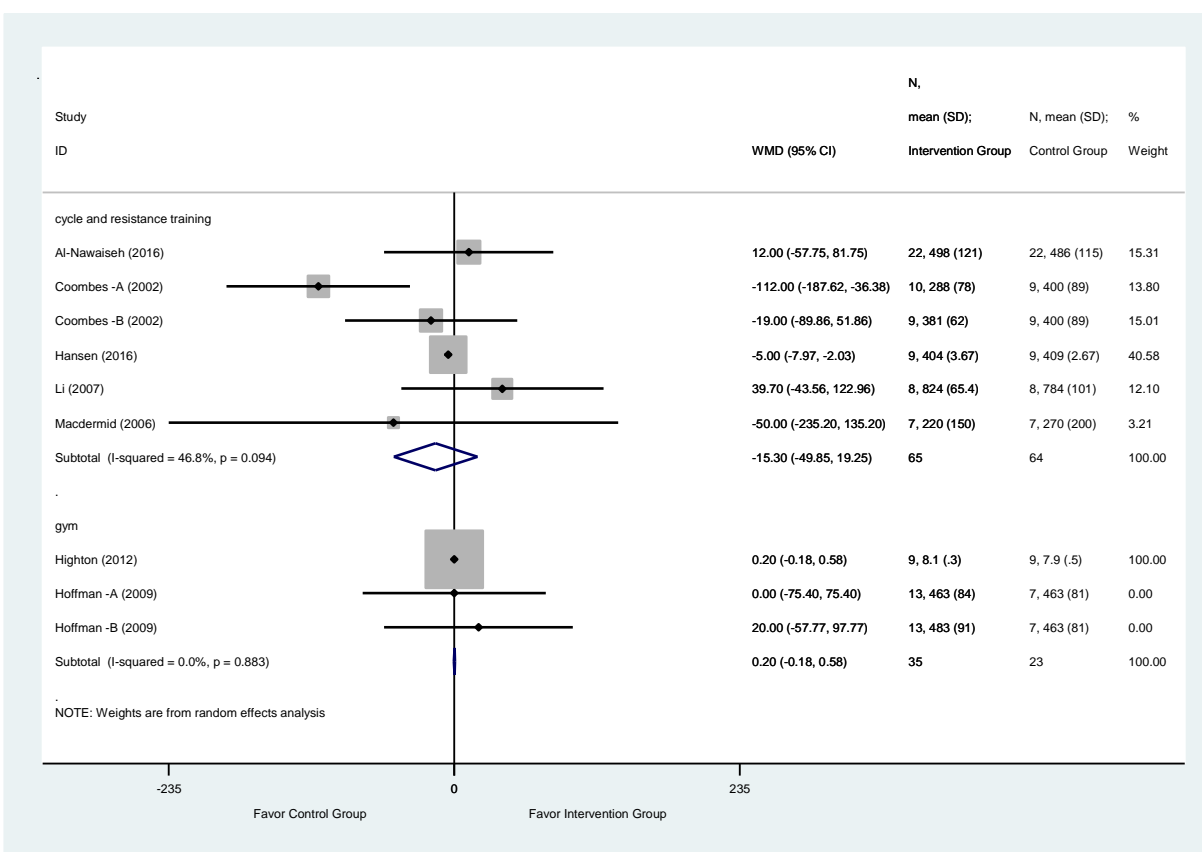


Coombes -A (2002) = WP alone vs bovine colostrum
Coombes -B (2002) = WP with bovine colostrum vs bovine colostrum
Hoffman -A (2009) = WP with carbohydrate vs placebo
Hoffman -B (2009) = WP with fat and carbohydrate vs placebo

- **Subgroup by intervention period range (day)**

```
          Study     |    WMD    [95% Conf. Interval]
------------------+------------------------------------------------
     1-20
Al-Nawaiseh (2016) |   12.000   -57.755    81.755
Hansen (2016)      |   -5.000    -7.965    -2.035
Highton (2012)     |    0.200    -0.181     0.581
Macdermid (2006)   |  -50.000  -235.199   135.199
 Sub-total         |
   D+L pooled WMD  |   -2.116    -6.807     2.576
------------------+------------------------------------------------
     41-60
Coombes -A (2002)  | -112.000  -187.618   -36.382
Coombes -B (2002)  |  -19.000   -89.864    51.864
 Sub-total         |
   D+L pooled WMD  |  -64.525  -155.644    26.593
------------------+------------------------------------------------
     61-80
Hoffman -A (2009)  |    0.000   -75.403    75.403
Hoffman -B (2009)  |   20.000   -57.766    97.766
Li (2007)          |   39.700   -43.563   122.963
 Sub-total         |
   D+L pooled WMD  |   18.607   -26.778    63.992
------------------+------------------------------------------------
```

```
Test(s) of heterogeneity:
          Heterogeneity  degrees of
            statistic     freedom      P     I-squared**   Tau-squared

1-20            12.02         3       0.007     75.0%        10.4657
41-60            3.09         1       0.079     67.7%        2.9e+03
61-80            0.48         2       0.786      0.0%        0.0000
** I-squared: the variation in WMD attributable to heterogeneity)


Significance test(s) of WMD=0

1-20                    z=  0.88    p = 0.377
41-60                   z=  1.39    p = 0.165
61-80                   z=  0.80    p = 0.422
```

| Study ID | WMD (95% CI) | N, mean (SD); Intervention Group | N, mean (SD); Control Group | % Weight |
|---|---|---|---|---|
| **1-20** | | | | |
| Al-Nawaiseh (2016) | 12.00 (-57.75, 81.75) | 22, 498 (121) | 22, 486 (115) | 0.45 |
| Hansen (2016) | -5.00 (-7.97, -2.03) | 9, 404 (3.67) | 9, 409 (2.67) | 44.93 |
| Highton (2012) | 0.20 (-0.18, 0.58) | 9, 8.1 (.3) | 9, 7.9 (.5) | 54.56 |
| Macdermid (2006) | -50.00 (-235.20, 135.20) | 7, 220 (150) | 7, 270 (200) | 0.06 |
| Subtotal (I-squared = 75.0%, p = 0.007) | -2.12 (-6.81, 2.58) | 47 | 47 | 100.00 |
| **41-60** | | | | |
| Coombes -A (2002) | -112.00 (-187.62, -36.38) | 10, 288 (78) | 9, 400 (89) | 48.95 |
| Coombes -B (2002) | -19.00 (-89.86, 51.86) | 9, 381 (62) | 9, 400 (89) | 51.05 |
| Subtotal (I-squared = 67.7%, p = 0.079) | -64.53 (-155.64, 26.59) | 19 | 18 | 100.00 |
| **61-80** | | | | |
| Hoffman -A (2009) | 0.00 (-75.40, 75.40) | 13, 463 (84) | 7, 463 (81) | 36.23 |
| Hoffman -B (2009) | 20.00 (-57.77, 97.77) | 13, 483 (91) | 7, 463 (81) | 34.06 |
| Li (2007) | 39.70 (-43.56, 122.96) | 8, 824 (65.4) | 8, 784 (101) | 29.71 |
| Subtotal (I-squared = 0.0%, p = 0.786) | 18.61 (-26.78, 63.99) | 34 | 22 | 100.00 |

NOTE: Weights are from random effects analysis

Coombes -A (2002) = WP alone vs bovine colostrum
Coombes -B (2002) = WP with bovine colostrum vs bovine colostrum
Hoffman -A (2009) = WP with carbohydrate vs placebo
Hoffman -B (2009) = WP with fat and carbohydrate vs placebo

### c) Body mass

#### i. Data

| Study | intervention | n1 | m1 | s1 | control | n2 | m2 | s2 |
|---|---|---|---|---|---|---|---|---|
| **Coombes -A (2002)** | pure whey | 10 | 75 | 17 | bovine colostrum | 9 | 73 | 10 |
| **Coombes -B (2002)** | whey contain | 9 | 73 | 7 | bovine colostrum | 9 | 73 | 10 |
| **Hoffman -A (2009)** | whey contain | 13 | 102 | 18.5 | placebo | 7 | 100.1 | 27.7 |
| **Hoffman -B (2009)** | whey contain | 13 | 96.3 | 14.1 | placebo | 7 | 100.1 | 27.7 |
| **Lollo -A (2011)** | whey contain | 8 | 71.08 | 1.41 | casein | 8 | 77.97 | 1.34 |
| **Lollo -B (2011)** | whey contain | 8 | 73.67 | 1.38 | casein | 8 | 77.97 | 1.34 |
| **Lollo -A (2014)** | whey contain | 8 | 73.6 | 3 | maltodextrin | 8 | 76 | 3.1 |
| **Lollo -B (2014)** | whey contain | 8 | 71.8 | 3.2 | maltodextrin | 8 | 76 | 3.1 |
| **Macdermid (2006)** | whey contain | 7 | 67.8 | 35.1 | carbohydrate | 7 | 67.6 | 5 |
| **Taylor (2016)** | whey contain | 8 | 67 | 10 | maltodextrin | 6 | 65.8 | 5 |

#### ii. Forest Plot

```
          Study      |    WMD    [95% Conf. Interval]    % Weight
--------------------+-------------------------------------------------
Coombes -A (2002)   |   2.000   -10.398    14.398          1.86
Coombes -B (2002)   |   0.000    -7.975     7.975          4.17
Hoffman -A (2009)   |   1.900   -20.952    24.752          0.57
Hoffman -B (2009)   |  -3.800   -25.705    18.105          0.62
Lollo -A (2011)     |  -6.890    -8.242    -5.538         27.56
Lollo -B (2011)     |  -4.300    -5.634    -2.966         27.68
Lollo -A (2014)     |  -2.400    -5.389     0.589         16.75
Lollo -B (2014)     |  -4.200    -7.287    -1.113         16.21
Macdermid (2006)    |   0.200   -26.064    26.464          0.43
Taylor (2016)       |   1.200    -6.802     9.202          4.14
--------------------+-------------------------------------------------
D+L pooled WMD      |  -4.097    -5.839    -2.355         100.00
--------------------+-------------------------------------------------

  Heterogeneity chi-squared =  17.28 (d.f. = 9) p = 0.044
  I-squared (variation in WMD attributable to heterogeneity) =  47.9%
  Estimate of between-study variance Tau-squared =  2.3897

  Test of WMD=0 : z=   4.61 p = 0.000
```

| Study ID | WMD (95% CI) | N, mean (SD); Intervention Group | N, mean (SD); Control Group | % Weight |
|---|---|---|---|---|
| Coombes -A (2002) | 2.00 (-10.40, 14.40) | 10, 75 (17) | 9, 73 (10) | 1.86 |
| Coombes -B (2002) | 0.00 (-7.97, 7.97) | 9, 73 (7) | 9, 73 (10) | 4.17 |
| Hoffman -A (2009) | 1.90 (-20.95, 24.75) | 13, 102 (18.5) | 7, 100 (27.7) | 0.57 |
| Hoffman -B (2009) | -3.80 (-25.70, 18.10) | 13, 96.3 (14.1) | 7, 100 (27.7) | 0.62 |
| Lollo -A (2011) | -6.89 (-8.24, -5.54) | 8, 71.1 (1.41) | 8, 78 (1.34) | 27.56 |
| Lollo -B (2011) | -4.30 (-5.63, -2.97) | 8, 73.7 (1.38) | 8, 78 (1.34) | 27.68 |
| Lollo -A (2014) | -2.40 (-5.39, 0.59) | 8, 73.6 (3) | 8, 76 (3.1) | 16.75 |
| Lollo -B (2014) | -4.20 (-7.29, -1.11) | 8, 71.8 (3.2) | 8, 76 (3.1) | 16.21 |
| Macdermid (2006) | 0.20 (-26.06, 26.46) | 7, 67.8 (35.1) | 7, 67.6 (5) | 0.43 |
| Taylor (2016) | 1.20 (-6.80, 9.20) | 8, 67 (10) | 6, 65.8 (5) | 4.14 |
| Overall (I-squared = 47.9%, p = 0.044) | -4.10 (-5.84, -2.36) | 92 | 77 | 100.00 |

NOTE: Weights are from random effects analysis

Coombes -A (2002) = WP alone vs bovine colostrum
Coombes -B (2002) = WP with bovine colostrum vs bovine colostrum
Hoffman -A (2009) = WP with carbohydrate vs placebo
Hoffman -B (2009) = WP with fat and carbohydrate vs placebo
Lollo -A (2011) = 91.4% of WP vs casein
Lollo -B (2011) = 87 % of WP vs casein
Lollo -A (2014) = WP concentrate vs maltodextrin
Lollo -B (2014) = WP hydrolysed vs maltodextrin

### iii. Funnel Plot



Funnel plot with pseudo 95% confidence limits

### iv. Egger test

```
Egger test for small-study effects:
Regress standard normal deviate of intervention
effect estimate against its standard error

Number of studies =  10                         Root MSE      =   1.185
------------------------------------------------------------------------------
     Std_Eff |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
       slope | -6.080575   .7276823    -8.36   0.000    -7.758614   -4.402537
        bias |  1.096185   .5277698     2.08   0.071    -.1208543    2.313225
------------------------------------------------------------------------------

Test of H0: no small-study effects            P = 0.071
```

Publication Bias of Whey Protein on Body Mass (Kg)

### 8.5.4 Blood profile

#### a) Essential amino acid

##### i. Data

| Study | intervention | n1 | m1 | s1 | control | n2 | m2 | s2 |
|-------|-------------|----|----|----|---------|----|----|----|
| Areta -A (2014) | whey contain | 15 | 1500 | 800 | placebo | 15 | 800 | 10 |
| Areta -B (2014) | whey contain | 15 | 1800 | 850 | placebo | 16 | 800 | 10 |
| Impey -A (2015) | whey contain | 9 | 1700 | 13.33 | protein + Caffeine | 9 | 1650 | 13.33 |
| Impey -B (2015) | whey contain | 9 | 1700 | 13.33 | placebo | 9 | 498 | 5 |
| Parr (2014) | whey contain | 8 | 1200 | 10 | maltodextrin with alcohol | 8 | 798 | 20 |
| Tang (2007) | whey contain | 8 | 1150 | 14.14 | carbohydrate + maltodextrin | 8 | 700 | 10.61 |

##### ii. Forest Plot

```
          Study     |    WMD    [95% Conf. Interval]    % Weight
-------------------+----------------------------------------------
Areta -A (2014)    |700.000     295.120   1104.880        15.30
Areta -B (2014)    |1000.000    569.821   1430.179        15.06
Impey -A (2015)    | 50.000      37.684     62.316        17.41
Impey -B (2015)    |1202.000   1192.699   1211.301        17.41
Parr (2014)        |402.000     386.505    417.495        17.41
Tang (2007)        |450.000     437.750    462.250        17.41
-------------------+----------------------------------------------
D+L pooled WMD     |624.035     169.270   1078.799       100.00
-------------------+----------------------------------------------

  Heterogeneity chi-squared = 24656.96 (d.f. = 5) p = 0.000
  I-squared (variation in WMD attributable to heterogeneity) = 100.0%
  Estimate of between-study variance Tau-squared =  3.1e+05

  Test of WMD=0 : z=   2.69 p = 0.007
```
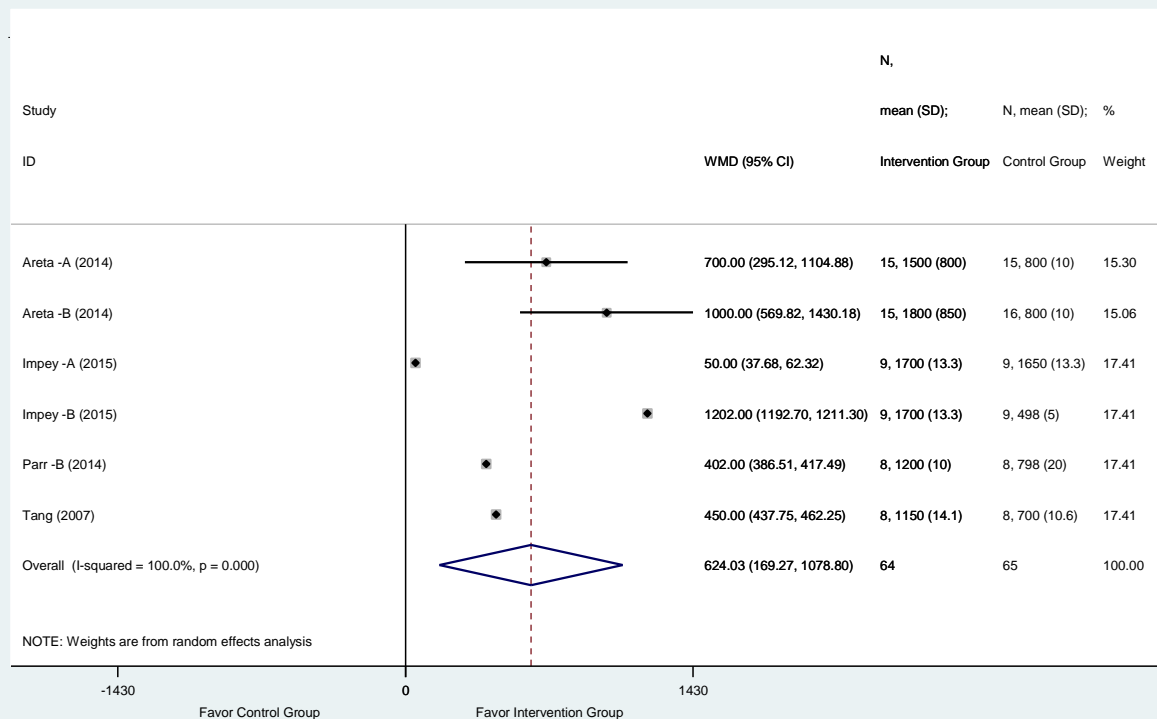
Areta -A (2014) = 15 g WP vs placebo
Areta -B (2014) = 30 g WP vs placebo
Impey -A (2015) = WP vs carbohydrate
Impey -B (2015) = WP with caffeine vs carbohydrate

### iii. Subgroup

- **Subgroup by physical activities**

```
        Study       |    WMD    [95% Conf. Interval]
--------------------+-------------------------------------------------
    leg
Areta -A (2014)     |  700.000   295.120   1104.880
Areta -B (2014)     | 1000.000   569.821   1430.179
Parr (2014)         |  402.000   386.505    417.495
 Sub-total          |
  D+L pooled WMD    |  653.764   277.576   1029.952
--------------------+-------------------------------------------------
    cycle
Impey -A (2015)     |   50.000    37.684     62.316
Impey -B (2015)     | 1202.000  1192.699   1211.301
 Sub-total          |
  D+L pooled WMD    |  626.007  -502.932   1754.947
--------------------+-------------------------------------------------
    gym
Tang (2007)         |  450.000   437.750    462.250
 Sub-total          |
  D+L pooled WMD    |  450.000   437.750    462.250
--------------------+-------------------------------------------------
```

```
Test(s) of heterogeneity:
              Heterogeneity  degrees of
              statistic      freedom      P    I-squared**   Tau-squared

leg                9.48         2        0.009     78.9%        8.5e+04
cycle          21402.34         1        0.000    100.0%        6.6e+05
gym                0.00         0          .         .%         0.0000
** I-squared: the variation in WMD attributable to heterogeneity)



Significance test(s) of WMD=0

leg                    z=  3.41      p = 0.001
cycle                  z=  1.09      p = 0.277
gym                    z= 72.00      p = 0.000
```
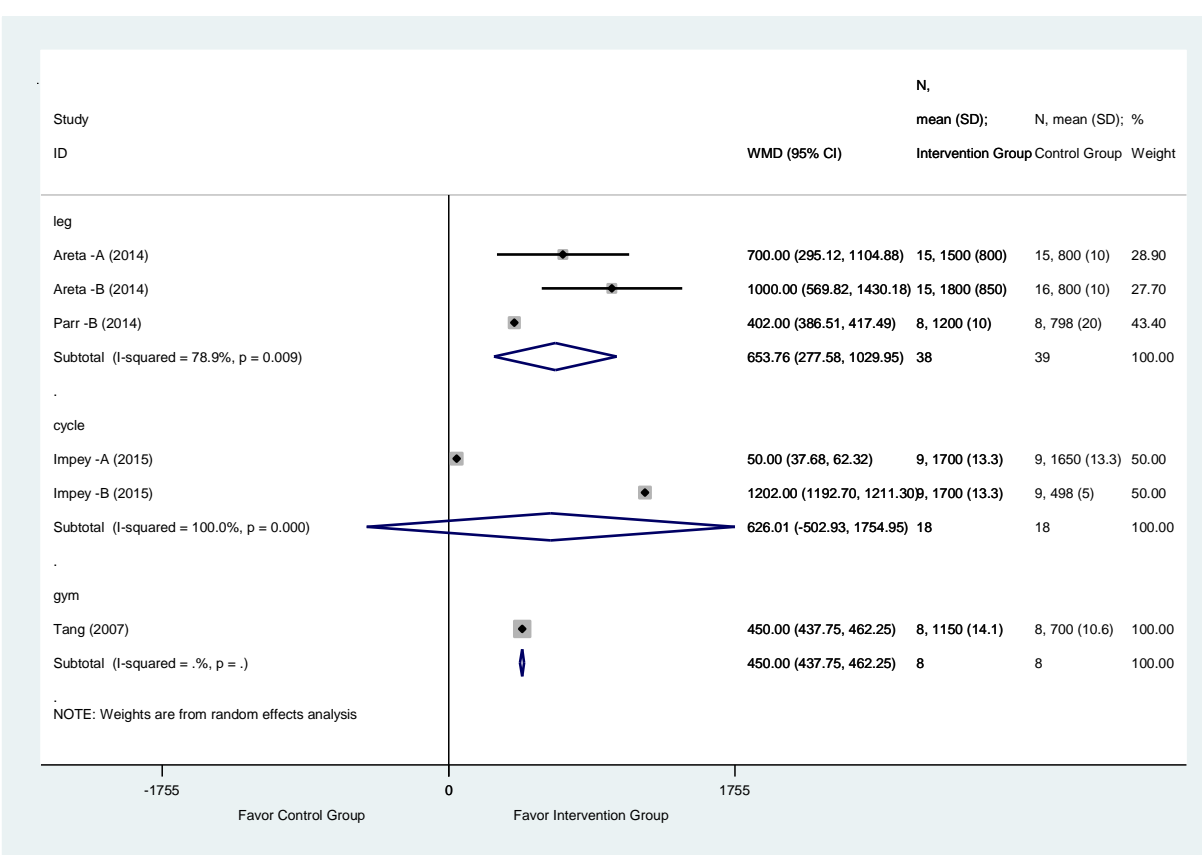


Areta -A (2014) = 15 g WP vs placebo
Areta -B (2014) = 30 g WP vs placebo
Impey -A (2015) = WP vs carbohydrate
Impey -B (2015) = WP with caffeine vs carbohydrate

- **Subgroup by intervention period range (day)**

```
         Study      |    WMD    [95% Conf. Interval]
-------------------+----------------------------------------------
     41-60
Areta -A (2014)    |  700.000   295.120   1104.880
Areta -B (2014)    | 1000.000   569.821   1430.179
 Sub-total         |
  D+L pooled WMD   |  840.919   546.088   1135.751
-------------------+----------------------------------------------
     1-20
Impey -A (2015)    |   50.000    37.684     62.316
Impey -B (2015)    | 1202.000  1192.699   1211.301
Parr (2014)        |  402.000   386.505    417.495
Tang (2007)        |  450.000   437.750    462.250
 Sub-total         |
  D+L pooled WMD   |  526.012   -19.143   1071.167
-------------------+----------------------------------------------
```

```
Test(s) of heterogeneity:
          Heterogeneity  degrees of
            statistic     freedom      P    I-squared**   Tau-squared

41-60             0.99         1      0.320     0.0%        0.0000
1-20          24654.40         3      0.000   100.0%        3.1e+05
** I-squared: the variation in WMD attributable to heterogeneity)
```

```
Significance test(s) of WMD=0

41-60                 z=  5.59    p = 0.000
1-20                  z=  1.89    p = 0.059
```

| Study ID | WMD (95% CI) | N, mean (SD); Intervention Group | N, mean (SD); Control Group | % Weight |
|---|---|---|---|---|
| **41-60** | | | | |
| Areta -A (2014) | 700.00 (295.12, 1104.88) | 15, 1500 (800) | 15, 800 (10) | 53.03 |
| Areta -B (2014) | 1000.00 (569.82, 1430.18) | 15, 1800 (850) | 16, 800 (10) | 46.97 |
| Subtotal (I-squared = 0.0%, p = 0.320) | 840.92 (546.09, 1135.75) | 30 | 31 | 100.00 |
| . | | | | |
| **1-20** | | | | |
| Impey -A (2015) | 50.00 (37.68, 62.32) | 9, 1700 (13.3) | 9, 1650 (13.3) | 25.00 |
| Impey -B (2015) | 1202.00 (1192.70, 1211.30) | 9, 1700 (13.3) | 9, 498 (5) | 25.00 |
| Parr -B (2014) | 402.00 (386.51, 417.49) | 8, 1200 (10) | 8, 798 (20) | 25.00 |
| Tang (2007) | 450.00 (437.75, 462.25) | 8, 1150 (14.1) | 8, 700 (10.6) | 25.00 |
| Subtotal (I-squared = 100.0%, p = 0.000) | 526.01 (-19.14, 1071.17) | 34 | 34 | 100.00 |

NOTE: Weights are from random effects analysis

-1430    0    1430

Favor Control Group    Favor Intervention Group

Areta -A (2014) = 15 g WP vs placebo
Areta -B (2014) = 30 g WP vs placebo
Impey -A (2015) = WP vs carbohydrate
Impey -B (2015) = WP with caffeine vs carbohydrate

## b) Branched-chain amino acid

### i. Data

| Study | intervention | n1 | m1 | s1 | control | n2 | m2 | s2 |
|---|---|---|---|---|---|---|---|---|
| **Areta -A (2014)** | whey contain | 15 | 600 | 70 | placebo | 15 | 290 | 10 |
| **Areta -B (2014)** | whey contain | 15 | 900 | 150 | placebo | 15 | 290 | 10 |
| **Impey -A (2015)** | whey contain | 9 | 1150 | 5 | protein + Caffeine | 9 | 1100 | 5 |
| **Impey -B (2015)** | whey contain | 9 | 1150 | 5 | placebo | 9 | 490 | 5 |
| **Morifuji -A (2012)** | whey contain | 8 | 1200 | 3.53 | carbohydrate | 8 | 700 | 0.35 |
| **Morifuji -B (2012)** | whey contain | 8 | 2000 | 5.32 | carbohydrate | 8 | 700 | 0.35 |
| **Parr -B (2014)** | whey contain | 8 | 600 | 100 | maltodextrin + alcohol | 8 | 490 | 100 |
| **Parr -B (2014)** | whey contain | 8 | 700 | 100 | maltodextrin + alcohol | 8 | 490 | 100 |
| **Tang (2007)** | whey contain | 8 | 630 | 3.54 | carbohydrate + maltodextrin | 8 | 260 | 3.54 |

### ii. Forest Plot

```
          Study       |    WMD    [95% Conf. Interval]     % Weight
--------------------+-------------------------------------------------
Areta -A (2014)     |310.000    274.216    345.784         11.14
Areta -B (2014)     |610.000    533.922    686.078         11.07
Impey -A (2015)     | 50.000     45.380     54.620         11.16
Impey -B (2015)     |660.000    655.380    664.620         11.16
Morifuji -A (2012)  |500.000    497.535    502.465         11.16
Morifuji -B (2012)  |1300.000  1296.306   1303.694         11.16
Parr -A (2014)      |110.000     12.002    207.998         11.01
Parr -B (2014)      |210.000    112.002    307.998         11.01
Tang (2007)         |370.000    366.531    373.469         11.16
--------------------+-------------------------------------------------
D+L pooled WMD      |458.572    179.959    737.184        100.00
--------------------+-------------------------------------------------

  Heterogeneity chi-squared =  2.2e+05 (d.f. = 8) p = 0.000
  I-squared (variation in WMD attributable to heterogeneity) = 100.0%
  Estimate of between-study variance Tau-squared =  1.8e+05

  Test of WMD=0 : z=   3.23 p = 0.001
```
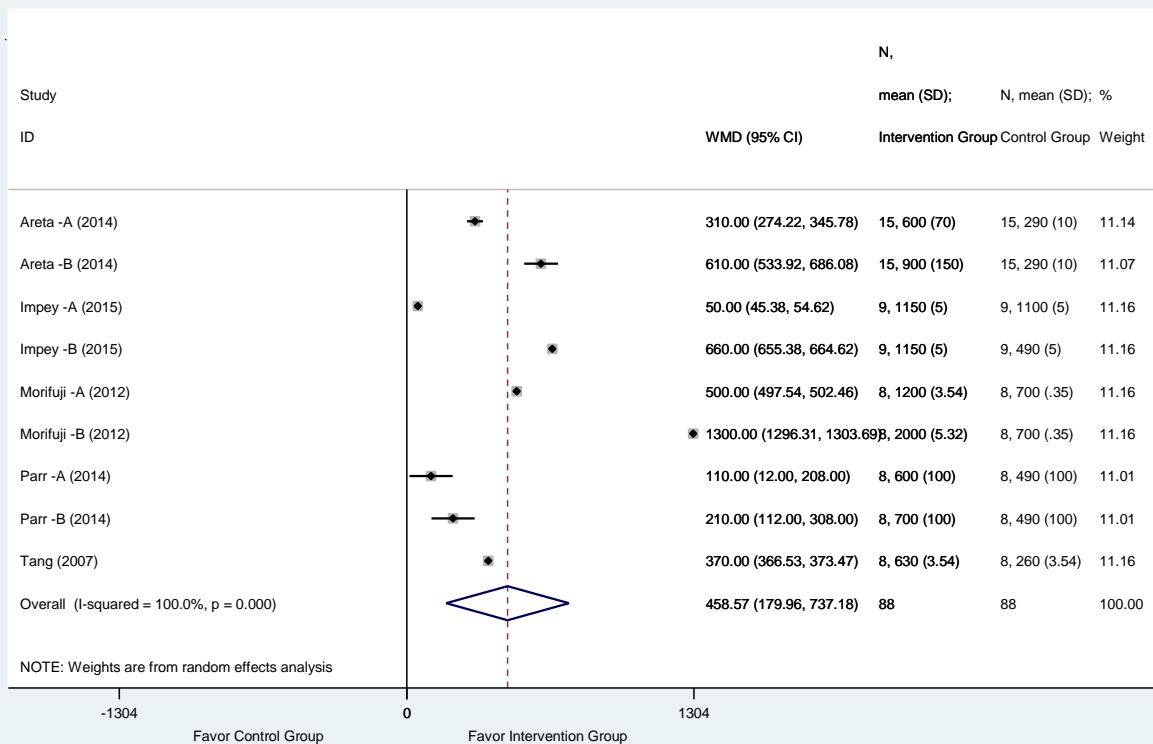
Areta -A (2014) = 15 g WP vs placebo
Areta -B (2014) = 30 g WP vs placebo
Impey -A (2015) = WP vs carbohydrate
Impey -B (2015) = WP with caffeine vs carbohydrate
Morifuji -A (2012) = 3.0 g WP vs carbohydrate
Morifuji -B (2012) = 8.0 g WP vs carbohydrate
Parr -A (2014) = 25 g WP vs maltodextrin with alcohol
Parr -B (2014) = 25 g WP with alcohol vs maltodextrin with alcohol

### iii. Subgroup

- **Subgroup by physical activities**

```
           Study      |    WMD    [95% Conf. Interval]
-------------------+--------------------------------------------------
      leg
Areta -A (2014)     |  310.000   274.216    345.784
Areta -B (2014)     |  610.000   533.922    686.078
Parr -A (2014)      |  110.000    12.002    207.998
Parr -B (2014)      |  210.000   112.002    307.998
 Sub-total          |
  D+L pooled WMD    |  312.105   129.371    494.838
-------------------+--------------------------------------------------
      cycle
Impey -A (2015)     |   50.000    45.380     54.620
Impey -B (2015)     |  660.000   655.380    664.620
Morifuji -A (2012)  |  500.000   497.535    502.465
Morifuji -B (2012)  | 1300.000  1296.306   1303.694
 Sub-total          |
  D+L pooled WMD    |  627.501   153.985   1101.016
-------------------+--------------------------------------------------
      gym
```

```
Tang (2007)              |  370.000   366.531   373.469
 Sub-total               |
  D+L pooled WMD         |  370.000   366.531   373.469
---------------------+------------------------------------------------
```

Test(s) of heterogeneity:

```
              Heterogeneity  degrees of
                 statistic     freedom      P    I-squared**  Tau-squared

leg                78.33          3        0.000     96.2%       3.3e+04
cycle             2.0e+05         3        0.000    100.0%       2.3e+05
gym                0.00           0          .         .%        0.0000
```
** I-squared: the variation in WMD attributable to heterogeneity)


Significance test(s) of WMD=0

```
leg                      z=   3.35     p = 0.001
cycle                    z=   2.60     p = 0.009
gym                      z= 209.04     p = 0.000
```
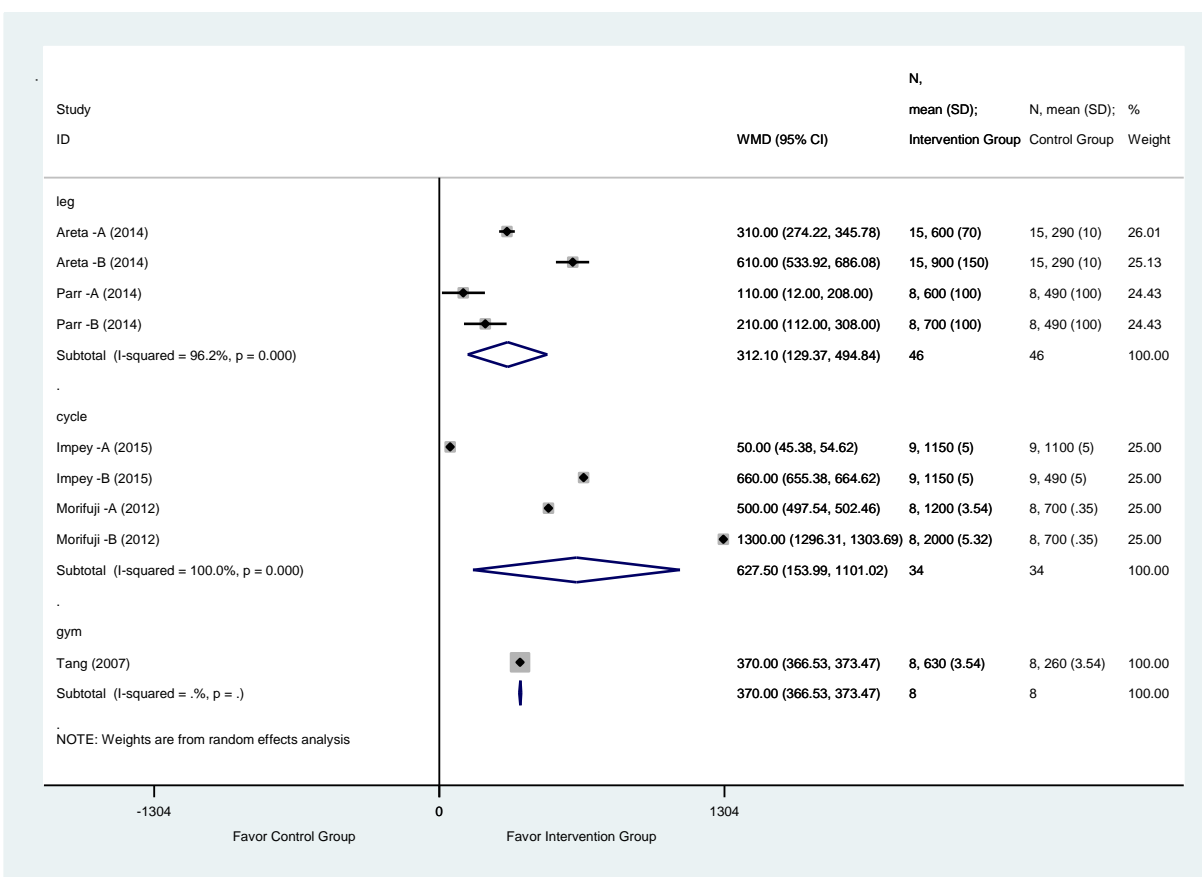


Areta -A (2014) = 15 g WP vs placebo
Areta -B (2014) = 30 g WP vs placebo
Impey -A (2015) = WP vs carbohydrate
Impey -B (2015) = WP with caffeine vs carbohydrate
Morifuji -A (2012) = 3.0 g WP vs carbohydrate
Morifuji -B (2012) = 8.0 g WP vs carbohydrate
Parr -A (2014) = 25 g WP vs maltodextrin with alcohol
Parr -B (2014) = 25 g WP with alcohol vs maltodextrin with alcohol

- **Subgroup by intervention period range (day)**

```
            Study     |    WMD   [95% Conf. Interval]
--------------------+-----------------------------------------------
     41-60
Areta -A (2014)       |  310.000  274.216   345.784
Areta -B (2014)       |  610.000  533.922   686.078
 Sub-total            |
  D+L pooled WMD      |  458.044  164.075   752.014
--------------------+-----------------------------------------------
     1-20
Impey -A (2015)       |   50.000   45.380    54.620
Impey -B (2015)       |  660.000  655.380   664.620
Morifuji -A (2012)    |  500.000  497.535   502.465
Morifuji -B (2012)    | 1300.000 1296.306  1303.694
Parr -A (2014)        |  110.000   12.002   207.998
Parr -B (2014)        |  210.000  112.002   307.998
Tang (2007)           |  370.000  366.531   373.469
 Sub-total            |
  D+L pooled WMD      |  458.299  141.976   774.621
--------------------+-----------------------------------------------


Test(s) of heterogeneity:
          Heterogeneity  degrees of
            statistic     freedom      P    I-squared**  Tau-squared

41-60            48.91         1      0.000     98.0%       4.4e+04
1-20            2.2e+05        6      0.000    100.0%       1.8e+05
** I-squared: the variation in WMD attributable to heterogeneity)


Significance test(s) of WMD=0

41-60                  z=  3.05    p = 0.002
1-20                   z=  2.84    p = 0.005
```

| Study ID | WMD (95% CI) | N, mean (SD); Intervention Group | N, mean (SD); Control Group | % Weight |
|---|---|---|---|---|
| **41-60** | | | | |
| Areta -A (2014) | 310.00 (274.22, 345.78) | 15, 600 (70) | 15, 290 (10) | 50.65 |
| Areta -B (2014) | 610.00 (533.92, 686.08) | 15, 900 (150) | 15, 290 (10) | 49.35 |
| Subtotal (I-squared = 98.0%, p = 0.000) | 458.04 (164.07, 752.01) | 30 | 30 | 100.00 |
| . | | | | |
| **1-20** | | | | |
| Impey -A (2015) | 50.00 (45.38, 54.62) | 9, 1150 (5) | 9, 1100 (5) | 14.34 |
| Impey -B (2015) | 660.00 (655.38, 664.62) | 9, 1150 (5) | 9, 490 (5) | 14.34 |
| Morifuji -A (2012) | 500.00 (497.54, 502.46) | 8, 1200 (3.54) | 8, 700 (.35) | 14.34 |
| Morifuji -B (2012) | 1300.00 (1296.31, 1303.69) | 8, 2000 (5.32) | 8, 700 (.35) | 14.34 |
| Parr -A (2014) | 110.00 (12.00, 208.00) | 8, 600 (100) | 8, 490 (100) | 14.15 |
| Parr -B (2014) | 210.00 (112.00, 308.00) | 8, 700 (100) | 8, 490 (100) | 14.15 |
| Tang (2007) | 370.00 (366.53, 373.47) | 8, 630 (3.54) | 8, 260 (3.54) | 14.34 |
| Subtotal (I-squared = 100.0%, p = 0.000) | 458.30 (141.98, 774.62) | 58 | 58 | 100.00 |

NOTE: Weights are from random effects analysis

Areta -A (2014) = 15 g WP vs placebo
Areta -B (2014) = 30 g WP vs placebo
Impey -A (2015) = WP vs carbohydrate
Impey -B (2015) = WP with caffeine vs carbohydrate
Morifuji -A (2012) = 3.0 g WP vs carbohydrate
Morifuji -B (2012) = 8.0 g WP vs carbohydrate
Parr -A (2014) = 25 g WP vs maltodextrin with alcohol
Parr -B (2014) = 25 g WP with alcohol vs maltodextrin with alcohol

### c) Creatine kinase

#### i. Data

| Study | intervention | n1 | m1 | s1 | control | n2 | m2 | s2 |
|---|---|---|---|---|---|---|---|---|
| **Cepero -A (2010)** | whey contain | 15 | 156.27 | 77.85 | carbohydrate + energy + vitamins | 15 | 132.47 | 63.88 |
| **Cepero -B (2010)** | whey contain | 15 | 156.27 | 77.85 | casein | 15 | 140.87 | 52.12 |
| **Gunnarsson (2013)** | whey contain | 9 | 395 | 29 | placebo | 7 | 324 | 28.73 |
| **Hansen (2015)** | whey contain | 9 | 250 | 0.67 | carbohydrate | 9 | 680 | 50 |
| **Hansen (2016)** | whey contain | 9 | 200 | 11.67 | carbohydrate | 9 | 200 | 11.67 |
| **Jauhari -A (2014)** | whey contain | 6 | 20 | 55 | tempeh | 6 | -2 | 2 |
| **Jauhari -B (2014)** | whey contain | 6 | 20 | 55 | placebo | 6 | 97 | 190 |
| **Kraemer (2015)** | whey contain | 13 | 270 | 60 | HMB + carbohydrate + fat | 13 | 170 | 20 |
| **Lollo -A (2014)** | whey contain | 8 | 250.8 | 13.93 | maltodextrin | 8 | 363.17 | 71.24 |
| **Lollo -B (2014)** | whey contain | 8 | 198.38 | 21.50 | maltodextrin | 8 | 363.17 | 71.24 |
| **Naclerio -A (2015)** | whey contain | 16 | 552.6 | 285 | carbohydrate | 16 | 469.1 | 206.8 |
| **Naclerio -B (2015)** | whey contain | 16 | 552.6 | 285 | placebo | 16 | 589.9 | 348.8 |
| **Yang (2014)** | whey contain | 10 | 305.86 | 1.82 | placebo | 10 | 382.33 | 55.2 |

#### ii. Forest Plot

```
        Study       |    WMD    [95% Conf. Interval]    % Weight
--------------------+-----------------------------------------------
Cepero -A (2010)    | 23.800    -27.162     74.762       8.13
Cepero -B (2010)    | 15.400    -32.011     62.811       8.16
Gunnarsson (2013)   | 71.000     42.506     99.494       8.30
Hansen (2015)       |-430.000   -462.669   -397.331      8.28
Hansen (2016)       |  0.000    -10.782     10.782       8.38
Jauhari -A (2014)   | 22.000    -22.037     66.037       8.19
Jauhari -B (2014)   |-77.000    -235.270    81.270       6.41
Kraemer (2015)      |100.000     65.620    134.380       8.27
Lollo -A (2014)     |-112.370   -162.671   -62.069       8.13
Lollo -B (2014)     |-164.790   -216.355   -113.225      8.12
Naclerio -A (2015)  | 83.500    -89.038    256.038       6.13
Naclerio -B (2015)  |-37.300    -258.006   183.406       5.24
Yang (2014)         |-76.470    -110.701   -42.239       8.27
--------------------+-----------------------------------------------
D+L pooled WMD      |-47.049    -129.465    35.367      100.00
--------------------+-----------------------------------------------

  Heterogeneity chi-squared = 766.54 (d.f. = 12) p = 0.000
  I-squared (variation in WMD attributable to heterogeneity) =  98.4%
  Estimate of between-study variance Tau-squared =  2.1e+04

  Test of WMD=0 : z=   1.12 p = 0.263
```

| Study ID | WMD (95% CI) | N, mean (SD); Intervention Group | N, mean (SD); Control Group | % Weight |
|---|---|---|---|---|
| Cepero -A (2010) | 23.80 (-27.16, 74.76) | 15, 156 (77.8) | 15, 132 (63.9) | 8.13 |
| Cepero -B (2010) | 15.40 (-32.01, 62.81) | 15, 156 (77.8) | 15, 141 (52.1) | 8.16 |
| Gunnarsson (2013) | 71.00 (42.51, 99.49) | 9, 395 (29) | 7, 324 (28.7) | 8.30 |
| Hansen (2015) | -430.00 (-462.67, -397.33) | 9, 250 (.67) | 9, 680 (50) | 8.28 |
| Hansen (2016) | 0.00 (-10.78, 10.78) | 9, 200 (11.7) | 9, 200 (11.7) | 8.38 |
| Jauhari -A (2014) | 22.00 (-22.04, 66.04) | 6, 20 (55) | 6, -2 (2) | 8.19 |
| Jauhari -B (2014) | -77.00 (-235.27, 81.27) | 6, 20 (55) | 6, 97 (190) | 6.41 |
| Kraemer (2015) | 100.00 (65.62, 134.38) | 13, 270 (60) | 13, 170 (20) | 8.27 |
| Lollo -A (2014) | -112.37 (-162.67, -62.07) | 8, 251 (13.9) | 8, 363 (71.2) | 8.13 |
| Lollo -B (2014) | -164.79 (-216.36, -113.22) | 8, 198 (21.5) | 8, 363 (71.2) | 8.12 |
| Naclerio -A (2015) | 83.50 (-89.04, 256.04) | 16, 553 (285) | 16, 469 (207) | 6.13 |
| Naclerio -B (2015) | -37.30 (-258.01, 183.41) | 16, 553 (285) | 16, 590 (349) | 5.24 |
| Yang (2014) | -76.47 (-110.70, -42.24) | 10, 306 (1.82) | 10, 382 (55.2) | 8.27 |
| Overall (I-squared = 98.4%, p = 0.000) | -47.05 (-129.47, 35.37) | 140 | 138 | 100.00 |

NOTE: Weights are from random effects analysis

Cepero -A (2010) = WP vs carbohydrate
Cepero -B (2010) = WP vs casein
Jauhari -A (2014) = WP vs tempeh
Jauhari -B (2014) = WP vs placebo
Lollo -A (2014) = WP concentrate vs maltodextrin
Lollo -B (2014) = WP hydrolysed vs maltodextrin
Naclerio -A (2015) = WP with multi-ingredient vs carbohydrate
Naclerio -B (2015) = WP with multi-ingredient vs placebo

### iii. Funnel Plot



Funnel plot with pseudo 95% confidence limits

### iv. Egger test

```
Egger test for small-study effects:
Regress standard normal deviate of intervention
effect estimate against its standard error

Number of studies =  13                         Root MSE      =   8.219
------------------------------------------------------------------------
    Std_Eff |      Coef.   Std. Err.      t    P>|t|    [95% Conf. Interval]
------------+-----------------------------------------------------------
      slope | -1.055819   54.17511    -0.02   0.985    -120.2944    118.1828
       bias | -2.103328   3.568176    -0.59   0.567    -9.956831    5.750175
------------------------------------------------------------------------

Test of H0: no small-study effects          P = 0.567
```
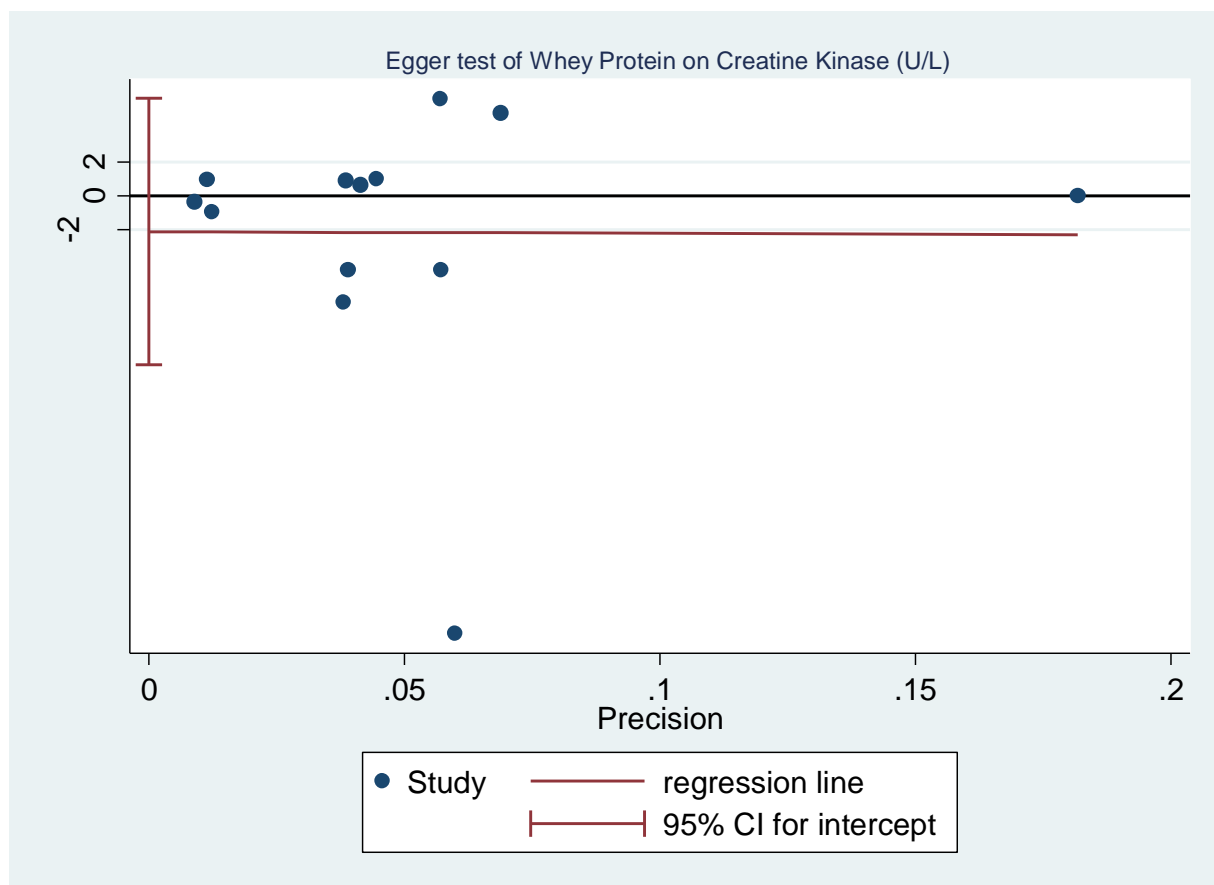
Egger test of Whey Protein on Creatine Kinase (U/L)

### v. Subgroup

#### • Subgroup by physical activities

```
         Study        |   WMD    [95% Conf. Interval]
--------------------+---------------------------------------------------
    cycle
Cepero -A (2010)      |   23.800   -27.162    74.762
Cepero -B (2010)      |   15.400   -32.011    62.811
 Sub-total            |
  D+L pooled WMD      |   19.297   -15.415    54.009
--------------------+---------------------------------------------------
    soccer
Gunnarsson (2013)     |   71.000    42.506    99.494
Lollo -A (2014)       | -112.370  -162.671   -62.069
Lollo -B (2014)       | -164.790  -216.355  -113.225
 Sub-total            |
  D+L pooled WMD      |  -67.582  -225.190    90.026
--------------------+---------------------------------------------------
    run
Hansen (2015)         | -430.000  -462.669  -397.331
Naclerio -A (2015)    |   83.500   -89.038   256.038
Naclerio -B (2015)    |  -37.300  -258.006   183.406
Yang (2014)           |  -76.470  -110.701   -42.239
 Sub-total            |
  D+L pooled WMD      | -124.302  -376.917   128.314
--------------------+---------------------------------------------------
    cycle and resistance
Hansen (2016)         |    0.000   -10.782    10.782
```

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```
Kraemer (2015)        |  100.000    65.620   134.380
 Sub-total            |
  D+L pooled WMD      |   48.613   -49.348   146.573
--------------------+-----------------------------------------------
     resistance exercise
Jauhari -A (2014)     |   22.000   -22.037    66.037
Jauhari -B (2014)     |  -77.000  -235.270    81.270
 Sub-total            |
  D+L pooled WMD      |    2.884   -73.707    79.475
--------------------+-----------------------------------------------

Test(s) of heterogeneity:
             Heterogeneity  degrees of
              statistic      freedom      P     I-squared**   Tau-squared

cycle                0.06        1       0.813     0.0%         0.0000
soccer              81.57        2       0.000    97.5%         1.9e+04
run                233.21        3       0.000    98.7%         6.2e+04
cycle and resistance 29.59       1       0.000    96.6%         4.8e+03
resistance exercise  1.40        1       0.238    28.3%         1.4e+03
** I-squared: the variation in WMD attributable to heterogeneity)


Significance test(s) of WMD=0

cycle                 z=  1.09    p = 0.276
soccer                z=  0.84    p = 0.401
run                   z=  0.96    p = 0.335
cycle and resistance  z=  0.97    p = 0.331
resistance exercise   z=  0.07    p = 0.941
```

| Study ID | WMD (95% CI) | N, mean (SD); Intervention Group | N, mean (SD); Control Group | % Weight |
|---|---|---|---|---|
| **cycle** | | | | |
| Cepero -A (2010) | 23.80 (-27.16, 74.76) | 15, 156 (77.8) | 15, 132 (63.9) | 46.39 |
| Cepero -B (2010) | 15.40 (-32.01, 62.81) | 15, 156 (77.8) | 15, 141 (52.1) | 53.61 |
| Subtotal (I-squared = 0.0%, p = 0.813) | 19.30 (-15.42, 54.01) | 30 | 30 | 100.00 |
| **soccer** | | | | |
| Gunnarsson (2013) | 71.00 (42.51, 99.49) | 9, 395 (29) | 7, 324 (28.7) | 33.87 |
| Lollo -A (2014) | -112.37 (-162.67, -62.07) | 8, 251 (13.9) | 8, 363 (71.2) | 33.09 |
| Lollo -B (2014) | -164.79 (-216.36, -113.22) | 8, 198 (21.5) | 8, 363 (71.2) | 33.04 |
| Subtotal (I-squared = 97.5%, p = 0.000) | -67.58 (-225.19, 90.03) | 25 | 23 | 100.00 |
| **run** | | | | |
| Hansen (2015) | -430.00 (-462.67, -397.33) | 9, 250 (.67) | 9, 680 (50) | 26.85 |
| Naclerio -A (2015) | 83.50 (-89.04, 256.04) | 16, 553 (285) | 16, 469 (207) | 23.95 |
| Naclerio -B (2015) | -37.30 (-258.01, 183.41) | 16, 553 (285) | 16, 590 (349) | 22.36 |
| Yang (2014) | -76.47 (-110.70, -42.24) | 10, 306 (1.82) | 10, 382 (55.2) | 26.83 |
| Subtotal (I-squared = 98.7%, p = 0.000) | -124.30 (-376.92, 128.31) | 51 | 51 | 100.00 |
| **cycle and resistance training** | | | | |
| Hansen (2016) | 0.00 (-10.78, 10.78) | 9, 200 (11.7) | 9, 200 (11.7) | 51.39 |
| Kraemer (2015) | 100.00 (65.62, 134.38) | 13, 270 (60) | 13, 170 (20) | 48.61 |
| Subtotal (I-squared = 96.6%, p = 0.000) | 48.61 (-49.35, 146.57) | 22 | 22 | 100.00 |
| **resistance exercise** | | | | |
| Jauhari -A (2014) | 22.00 (-22.04, 66.04) | 6, 20 (55) | 6, -2 (2) | 80.69 |
| Jauhari -B (2014) | -77.00 (-235.27, 81.27) | 6, 20 (55) | 6, 97 (190) | 19.31 |
| Subtotal (I-squared = 28.3%, p = 0.238) | 2.88 (-73.71, 79.47) | 12 | 12 | 100.00 |

NOTE: Weights are from random effects analysis

-463     0     463

Favor Control Group     Favor Intervention Group

Cepero -A (2010) = WP vs carbohydrate
Cepero -B (2010) = WP vs casein
Jauhari -A (2014) = WP vs tempeh
Jauhari -B (2014) = WP vs placebo
Lollo -A (2014) = WP concentrate vs maltodextrin
Lollo -B (2014) = WP hydrolysed vs maltodextrin
Naclerio -A (2015) = WP with multi-ingredient vs carbohydrate
Naclerio -B (2015) = WP with multi-ingredient vs placebo

- **Subgroup by intervention period range (day)**

```
          Study      |    WMD   [95% Conf. Interval]
--------------------+------------------------------------------------
     1-20            |
Cepero -A (2010)     |   23.800   -27.162    74.762
Cepero -B (2010)     |   15.400   -32.011    62.811
Gunnarsson (2013)    |   71.000    42.506    99.494
Hansen (2015)        | -430.000  -462.669  -397.331
Hansen (2016)        |    0.000   -10.782    10.782
Jauhari -A (2014)    |   22.000   -22.037    66.037
Jauhari -B (2014)    |  -77.000  -235.270    81.270
Naclerio -A (2015)   |   83.500   -89.038   256.038
Naclerio -B (2015)   |  -37.300  -258.006   183.406
Yang (2014)          |  -76.470  -110.701   -42.239
 Sub-total           |
  D+L pooled WMD      |  -43.120  -144.598    58.358
--------------------+------------------------------------------------
     41-60           |
Kraemer (2015)       |  100.000    65.620   134.380
 Sub-total           |
  D+L pooled WMD      |  100.000    65.620   134.380
--------------------+------------------------------------------------
     161-180         |
Lollo -A (2014)      | -112.370  -162.671   -62.069
Lollo -B (2014)      | -164.790  -216.355  -113.225
 Sub-total           |
  D+L pooled WMD      | -138.260  -189.627   -86.893
--------------------+------------------------------------------------

Test(s) of heterogeneity:
          Heterogeneity  degrees of
             statistic     freedom      P    I-squared**   Tau-squared

1-20            675.73         9       0.000    98.7%       2.4e+04
41-60             0.00         0         .        .%        0.0000
161-180           2.03         1       0.154    50.8%       698.5175
** I-squared: the variation in WMD attributable to heterogeneity)


Significance test(s) of WMD=0

1-20                  z=  0.83    p = 0.405
41-60                 z=  5.70    p = 0.000
161-180               z=  5.28    p = 0.000
```

| Study ID | WMD (95% CI) | N, mean (SD); Intervention Group | N, mean (SD); Control Group | % Weight |
|---|---|---|---|---|
| **1-20** | | | | |
| Cepero -A (2010) | 23.80 (-27.16, 74.76) | 15, 156 (77.8) | 15, 132 (63.9) | 10.69 |
| Cepero -B (2010) | 15.40 (-32.01, 62.81) | 15, 156 (77.8) | 15, 141 (52.1) | 10.73 |
| Gunnarsson (2013) | 71.00 (42.51, 99.49) | 9, 395 (29) | 7, 324 (28.7) | 10.89 |
| Hansen (2015) | -430.00 (-462.67, -397.33) | 9, 250 (.67) | 9, 680 (50) | 10.86 |
| Hansen (2016) | 0.00 (-10.78, 10.78) | 9, 200 (11.7) | 9, 200 (11.7) | 10.97 |
| Jauhari -A (2014) | 22.00 (-22.04, 66.04) | 6, 20 (55) | 6, -2 (2) | 10.76 |
| Jauhari -B (2014) | -77.00 (-235.27, 81.27) | 6, 20 (55) | 6, 97 (190) | 8.67 |
| Naclerio -A (2015) | 83.50 (-89.04, 256.04) | 16, 553 (285) | 16, 469 (207) | 8.34 |
| Naclerio -B (2015) | -37.30 (-258.01, 183.41) | 16, 553 (285) | 16, 590 (349) | 7.23 |
| Yang (2014) | -76.47 (-110.70, -42.24) | 10, 306 (1.82) | 10, 382 (55.2) | 10.85 |
| Subtotal (I-squared = 98.7%, p = 0.000) | -43.12 (-144.60, 58.36) | 111 | 109 | 100.00 |
| . | | | | |
| **41-60** | | | | |
| Kraemer (2015) | 100.00 (65.62, 134.38) | 13, 270 (60) | 13, 170 (20) | 100.00 |
| Subtotal (I-squared = .%, p = .) | 100.00 (65.62, 134.38) | 13 | 13 | 100.00 |
| . | | | | |
| **161-180** | | | | |
| Lollo -A (2014) | -112.37 (-162.67, -62.07) | 8, 251 (13.9) | 8, 363 (71.2) | 50.61 |
| Lollo -B (2014) | -164.79 (-216.36, -113.22) | 8, 198 (21.5) | 8, 363 (71.2) | 49.39 |
| Subtotal (I-squared = 50.8%, p = 0.154) | -138.26 (-189.63, -86.89) | 16 | 16 | 100.00 |

NOTE: Weights are from random effects analysis

Favor Control Group — Favor Intervention Group

-463    0    463

Cepero -A (2010) = WP vs carbohydrate
Cepero -B (2010) = WP vs casein
Jauhari -A (2014) = WP vs tempeh
Jauhari -B (2014) = WP vs placebo
Lollo -A (2014) = WP concentrate vs maltodextrin
Lollo -B (2014) = WP hydrolysed vs maltodextrin
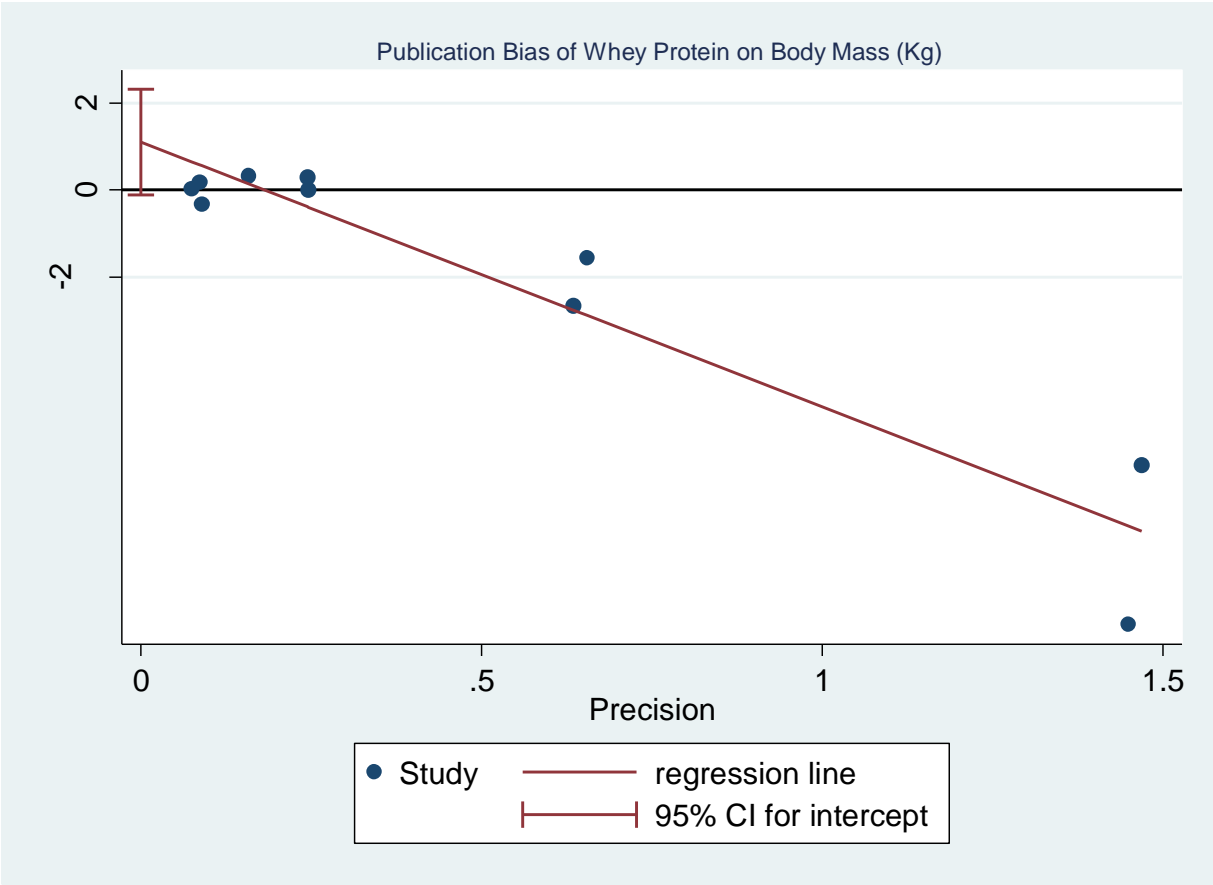Naclerio -A (2015) = WP with multi-ingredient vs carbohydrate
Naclerio -B (2015) = WP with multi-ingredient vs placebo

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## d) Glucose

### i. Data

| Study | intervention | n1 | m1 | s1 | control | n2 | m2 | s2 |
|---|---|---|---|---|---|---|---|---|
| **Cepero -A (2010)** | whey contain | 15 | 6.67 | 1.56 | carbohydrate + energy + vitamins | 15 | 7.66 | 2.02 |
| **Cepero -A (2010)** | whey contain | 15 | 6.67 | 1.56 | casein | 15 | 7.39 | 2.60 |
| **Cury-boaventura (2008)** | whey contain | 9 | 7.83 | 0.19 | maltodextrin | 9 | 7.44 | 0.19 |
| **Detko (2013)** | whey contain | 7 | 5.50 | 0.08 | maltodextrin + GAL | 7 | 6.00 | 0.11 |
| **Hill (2013)** | whey contain | 6 | 5.20 | 0.08 | protein + carbohydrate + fat | 6 | 6.00 | 0.12 |
| **Impey -A (2015)** | whey contain | 9 | 4.80 | 0.03 | protein + Caffeine | 9 | 4.80 | 0.03 |
| **Impey -B (2015)** | whey contain | 9 | 4.80 | 0.03 | placebo | 9 | 5.20 | 0.03 |
| **Lollo -A (2011)** | whey contain | 8 | 4.53 | 0.03 | casein | 8 | 4.62 | 0.03 |
| **Lollo -B (2011)** | whey contain | 8 | 4.67 | 0.03 | casein | 8 | 4.62 | 0.03 |
| **Macdermid (2006)** | whey contain | 7 | 3.50 | 0.50 | carbohydrate + energy + vitamins | 7 | 3.40 | 0.80 |
| **Morifuji -A (2012)** | whey contain | 8 | 5.50 | 0.04 | maltodextrin | 8 | 5.09 | 0.04 |
| **Morifuji -B (2012)** | whey contain | 8 | 4.70 | 0.02 | maltodextrin | 8 | 5.09 | 0.04 |
| **Parr -A (2014)** | whey contain | 8 | 5.00 | 1.00 | maltodextrin + alcohol | 8 | 5.30 | 1.00 |
| **Parr -B (2014)** | whey contain | 8 | 5.20 | 1.00 | maltodextrin + alcohol | 8 | 5.30 | 1.00 |
| **Schroer -A (2014)** | whey contain | 8 | 3.99 | 0.10 | L-alanine | 8 | 4.07 | 0.22 |
| **Schroer -B (2014)** | whey contain | 8 | 3.99 | 0.10 | placebo | 8 | 4.24 | 0.37 |
| **Tang (2007)** | whey contain | 8 | 5.50 | 0.18 | fructose + maltodextrin | 8 | 6.70 | 0.35 |
| **Yang (2014)** | whey contain | 10 | 4.52 | 0.49 | placebo | 10 | 3.55 | 0.41 |

### ii. Forest Plot

| Study | WMD | [95% Conf. Interval] | | % Weight |
|---|---|---|---|---|
| Cepero -A (2010) | -0.960 | -2.252 | 0.332 | 1.25 |
| Cepero -B (2010) | -0.690 | -2.224 | 0.844 | 0.93 |
| Cury-boaventura (2008 | 0.360 | 0.184 | 0.536 | 6.89 |
| Detko (2013) | -0.500 | -0.601 | -0.399 | 7.30 |
| Hill (2013) | -0.800 | -0.915 | -0.685 | 7.24 |
| Impey -A (2015) | 0.000 | -0.028 | 0.028 | 7.51 |
| Impey -B (2015) | -0.400 | -0.428 | -0.372 | 7.51 |
| Lollo -A (2011) | -0.120 | -0.149 | -0.091 | 7.51 |
| Lollo -B (2011) | 0.080 | 0.051 | 0.109 | 7.51 |
| Macdermid (2006) | 0.100 | -0.599 | 0.799 | 3.05 |
| Morifuji -A (2012) | 0.410 | 0.371 | 0.449 | 7.49 |
| Morifuji -B (2012) | -0.390 | -0.421 | -0.359 | 7.50 |
| Parr -A (2014) | -0.300 | -1.280 | 0.680 | 1.94 |
| Parr -B (2014) | -0.100 | -1.080 | 0.880 | 1.94 |
| Schroer -A (2014) | -0.080 | -0.247 | 0.087 | 6.94 |
| Schroer -B (2014) | -0.250 | -0.516 | 0.016 | 6.21 |
| Tang (2007) | -1.200 | -1.473 | -0.927 | 6.15 |
| Yang (2014) | 0.970 | 0.574 | 1.366 | 5.12 |
| D+L pooled WMD | -0.170 | -0.328 | -0.011 | 100.00 |

Heterogeneity chi-squared = 1945.50 (d.f. = 17) p = 0.000
I-squared (variation in WMD attributable to heterogeneity) = 99.1%
Estimate of between-study variance Tau-squared = 0.0867

Test of WMD=0 : z= 2.10 p = 0.036

| Study ID | WMD (95% CI) | N, mean (SD); Intervention Group | N, mean (SD); Control Group | % Weight |
|---|---|---|---|---|
| Cepero -A (2010) | -0.96 (-2.25, 0.33) | 15, 6.7 (1.56) | 15, 7.66 (2.02) | 1.25 |
| Cepero -B (2010) | -0.69 (-2.22, 0.84) | 15, 6.7 (1.56) | 15, 7.39 (2.6) | 0.93 |
| Cury-boaventura (2008) | 0.36 (0.18, 0.54) | 9, 7.8 (.19) | 9, 7.44 (.19) | 6.89 |
| Detko (2013) | -0.50 (-0.60, -0.40) | 7, 5.5 (.08) | 7, 6 (.11) | 7.30 |
| Hill (2013) | -0.80 (-0.92, -0.68) | 6, 5.2 (.08) | 6, 6 (.12) | 7.24 |
| Impey -A (2015) | 0.00 (-0.03, 0.03) | 9, 4.8 (.03) | 9, 4.8 (.03) | 7.51 |
| Impey -B (2015) | -0.40 (-0.43, -0.37) | 9, 4.8 (.03) | 9, 5.2 (.03) | 7.51 |
| Lollo -A (2011) | -0.12 (-0.15, -0.09) | 8, 4.5 (.03) | 8, 4.62 (.03) | 7.51 |
| Lollo -B (2011) | 0.08 (0.05, 0.11) | 8, 4.7 (.03) | 8, 4.62 (.03) | 7.51 |
| Macdermid (2006) | 0.10 (-0.60, 0.80) | 7, 3.5 (.5) | 7, 3.4 (.8) | 3.05 |
| Morifuji -A (2012) | 0.41 (0.37, 0.45) | 8, 5.5 (.04) | 8, 5.09 (.04) | 7.49 |
| Morifuji -B (2012) | -0.39 (-0.42, -0.36) | 8, 4.7 (.02) | 8, 5.09 (.04) | 7.50 |
| Parr -A (2014) | -0.30 (-1.28, 0.68) | 8, 5 (1) | 8, 5.3 (1) | 1.94 |
| Parr -B (2014) | -0.10 (-1.08, 0.88) | 8, 5.2 (1) | 8, 5.3 (1) | 1.94 |
| Schroer -A (2014) | -0.08 (-0.25, 0.09) | 8, 3.99 (.1) | 8, 4.07 (.22) | 6.94 |
| Schroer -B (2014) | -0.25 (-0.52, 0.02) | 8, 3.99 (.1) | 8, 4.24 (.37) | 6.21 |
| Tang (2007) | -1.20 (-1.47, -0.93) | 8, 5.5 (.18) | 8, 6.7 (.35) | 6.15 |
| Yang (2014) | 0.97 (0.57, 1.37) | 10, 4.52 (.49) | 10, 3.55 (.41) | 5.12 |
| Overall (I-squared = 99.1%, p = 0.000) | -0.17 (-0.33, -0.01) | 159 | 159 | 100.00 |

NOTE: Weights are from random effects analysis

Favor Control Group          Favor Intervention Group

Cepero -A (2010) = WP vs carbohydrate
Cepero -B (2010) = WP vs casein
Impey -A (2015) = WP vs carbohydrate
Impey -B (2015) = WP with caffeine vs carbohydrate
Lollo -A (2011) = 91.4% WP vs casein
Lollo -B (2011) = 87 % WP vs casein
Morifuji -A (2012) = 3.0 g WP vs carbohydrate
Morifuji -B (2012) = 8.0 g WP vs carbohydrate
Parr -A (2014) = 25 g WP vs maltodextrin with alcohol
Parr -B (2014) = 25 g WP with alcohol vs maltodextrin with alcohol
Schroer -A (2014) = WP vs L-alanine
Schroer -B (2014) = WP vs placebo

### iii. Funnel Plot



Funnel plot with pseudo 95% confidence limits

### iv. Egger test

```
Egger test for small-study effects:
Regress standard normal deviate of intervention
effect estimate against its standard error

Number of studies =  18                          Root MSE     =   11.01
-----------------------------------------------------------------------------
     Std_Eff |      Coef.    Std. Err.       t    P>|t|     [95% Conf. Interval]
-------------+---------------------------------------------------------------
       slope |  -.1056601    .0935429    -1.13    0.275     -.3039622    .0926419
        bias |   -.751875    3.587015    -0.21    0.837     -8.356007    6.852257
-----------------------------------------------------------------------------

Test of H0: no small-study effects          P = 0.837
```
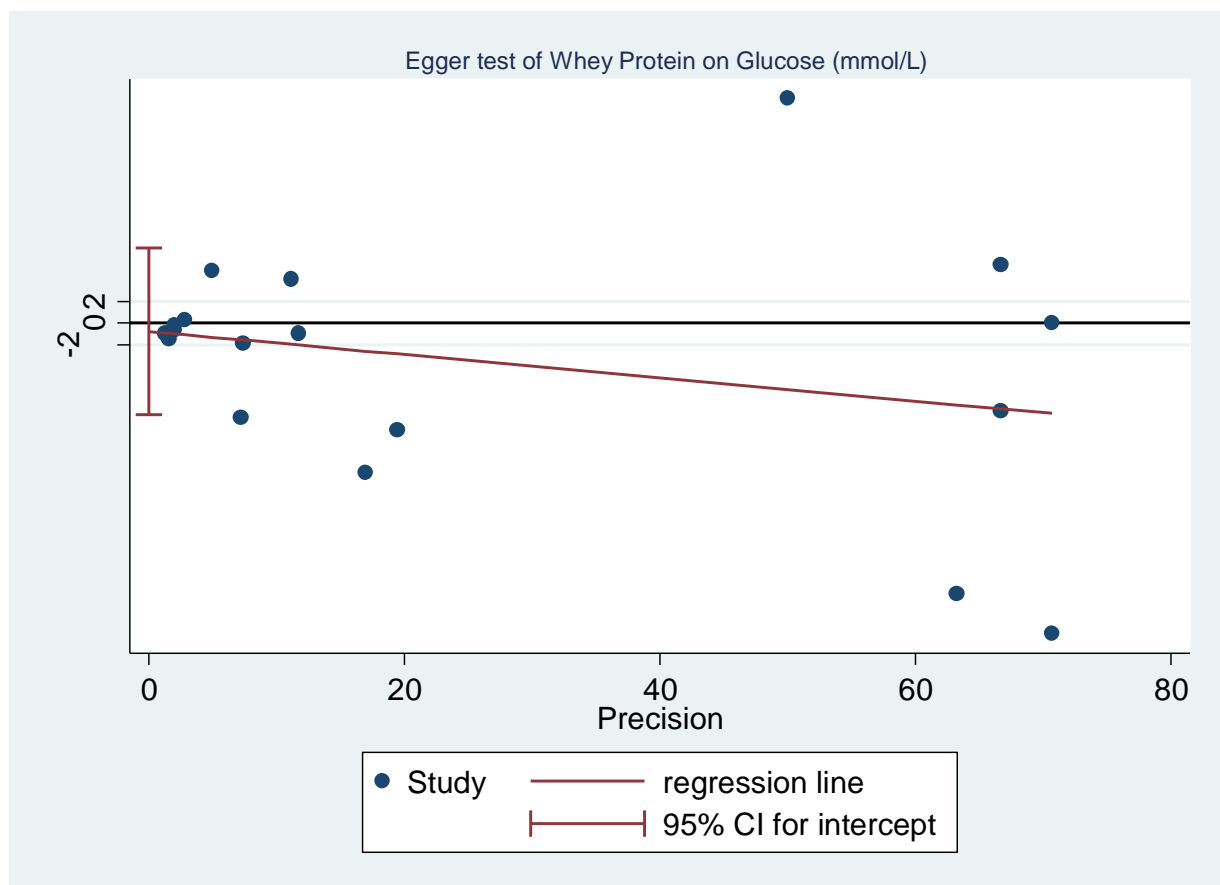
Egger test of Whey Protein on Glucose (mmol/L)

**v. Subgroup**

- **Subgroup by physical activities**

```
          Study      |   WMD    [95% Conf. Interval]
--------------------+-----------------------------------------------
    cycle
Cepero -A (2010)    |  -0.960   -2.252     0.332
Cepero -B (2010)    |  -0.690   -2.224     0.844
Detko (2013)        |  -0.500   -0.601    -0.399
Hill (2013)         |  -0.800   -0.915    -0.685
Impey -A (2015)     |   0.000   -0.028     0.028
Impey -B (2015)     |  -0.400   -0.428    -0.372
Macdermid (2006)    |   0.100   -0.599     0.799
Morifuji -A (2012)  |   0.410    0.371     0.449
Morifuji -B (2012)  |  -0.390   -0.421    -0.359
Schroer -A (2014)   |  -0.080   -0.247     0.087
Schroer -B (2014)   |  -0.250   -0.516     0.016
 Sub-total          |
  D+L pooled WMD    |  -0.257   -0.489    -0.025
--------------------+-----------------------------------------------
    gym
Cury-boaventura (2008|   0.360    0.184     0.536
Tang (2007)         |  -1.200   -1.473    -0.927
 Sub-total          |
  D+L pooled WMD    |  -0.416   -1.945     1.112
--------------------+-----------------------------------------------
```

```
    cycle, soccer
Lollo -A (2011)       |   -0.120    -0.149    -0.091
Lollo -B (2011)       |    0.080     0.051     0.109
 Sub-total            |
  D+L pooled WMD      |   -0.020    -0.216     0.176
-------------------+------------------------------------------------
    leg
Parr -A (2014)        |   -0.300    -1.280     0.680
Parr -B (2014)        |   -0.100    -1.080     0.880
 Sub-total            |
  D+L pooled WMD      |   -0.200    -0.893     0.493
-------------------+------------------------------------------------
    run
Yang (2014)           |    0.970     0.574     1.366
 Sub-total            |
  D+L pooled WMD      |    0.970     0.574     1.366
-------------------+------------------------------------------------

Test(s) of heterogeneity:
            Heterogeneity  degrees of
              statistic     freedom      P    I-squared**   Tau-squared

cycle          1603.16        10        0.000    99.4%         0.1207
gym              88.87         1        0.000    98.9%         1.2031
cycle, soccer    88.89         1        0.000    98.9%         0.0198
leg               0.08         1        0.777     0.0%         0.0000
run               0.00         0          .        .%         0.0000
** I-squared: the variation in WMD attributable to heterogeneity)


Significance test(s) of WMD=0

cycle                 z=  2.17    p = 0.030
gym                   z=  0.53    p = 0.593
cycle, soccer         z=  0.20    p = 0.841
leg                   z=  0.57    p = 0.572
run                   z=  4.80    p = 0.000
```

| Study ID | WMD (95% CI) | N, mean (SD); Intervention Group | N, mean (SD); Control Group | % Weight |
|---|---|---|---|---|
| **cycle** | | | | |
| Cepero -A (2010) | -0.96 (-2.25, 0.33) | 15, 6.7 (1.56) | 15, 7.66 (2.02) | 2.52 |
| Cepero -B (2010) | -0.69 (-2.22, 0.84) | 15, 6.7 (1.56) | 15, 7.39 (2.6) | 1.91 |
| Detko (2013) | -0.50 (-0.60, -0.40) | 7, 5.5 (.08) | 7, 6 (.11) | 11.35 |
| Hill (2013) | -0.80 (-0.92, -0.68) | 6, 5.2 (.08) | 6, 6 (.12) | 11.27 |
| Impey -A (2015) | 0.00 (-0.03, 0.03) | 9, 4.8 (.03) | 9, 4.8 (.03) | 11.58 |
| Impey -B (2015) | -0.40 (-0.43, -0.37) | 9, 4.8 (.03) | 9, 5.2 (.03) | 11.58 |
| Macdermid (2006) | 0.10 (-0.60, 0.80) | 7, 3.5 (.5) | 7, 3.4 (.8) | 5.65 |
| Morifuji -A (2012) | 0.41 (0.37, 0.45) | 8, 5.5 (.04) | 8, 5.09 (.04) | 11.56 |
| Morifuji -B (2012) | -0.39 (-0.42, -0.36) | 8, 4.7 (.02) | 8, 5.09 (.04) | 11.57 |
| Schroer -A (2014) | -0.08 (-0.25, 0.09) | 8, 3.99 (.1) | 8, 4.07 (.22) | 10.94 |
| Schroer -B (2014) | -0.25 (-0.52, 0.02) | 8, 3.99 (.1) | 8, 4.24 (.37) | 10.07 |
| Subtotal (I-squared = 99.4%, p = 0.000) | -0.26 (-0.49, -0.02) | 100 | 100 | 100.00 |
| . | | | | |
| **gym** | | | | |
| Cury-boaventura (2008) | 0.36 (0.18, 0.54) | 9, 7.8 (.19) | 9, 7.44 (.19) | 50.23 |
| Tang (2007) | -1.20 (-1.47, -0.93) | 8, 5.5 (.18) | 8, 6.7 (.35) | 49.77 |
| Subtotal (I-squared = 98.9%, p = 0.000) | -0.42 (-1.95, 1.11) | 17 | 17 | 100.00 |
| **cycle, soccer** | | | | |
| Lollo -A (2011) | -0.12 (-0.15, -0.09) | 8, 4.5 (.03) | 8, 4.62 (.03) | 50.00 |
| Lollo -B (2011) | 0.08 (0.05, 0.11) | 8, 4.7 (.03) | 8, 4.62 (.03) | 50.00 |
| Subtotal (I-squared = 98.9%, p = 0.000) | -0.02 (-0.22, 0.18) | 16 | 16 | 100.00 |
| . | | | | |
| **leg** | | | | |
| Parr -A (2014) | -0.30 (-1.28, 0.68) | 8, 5 (1) | 8, 5.3 (1) | 50.00 |
| Parr -B (2014) | -0.10 (-1.08, 0.88) | 8, 5.2 (1) | 8, 5.3 (1) | 50.00 |
| Subtotal (I-squared = 0.0%, p = 0.777) | -0.20 (-0.89, 0.49) | 16 | 16 | 100.00 |
| . | | | | |
| **run** | | | | |
| Yang (2014) | 0.97 (0.57, 1.37) | 10, 4.52 (.49) | 10, 3.55 (.41) | 100.00 |
| Subtotal (I-squared = .%, p = .) | 0.97 (0.57, 1.37) | 10 | 10 | 100.00 |

NOTE: Weights are from random effects analysis

Favor Control Group    Favor Intervention Group

Cepero -A (2010) = WP vs carbohydrate
Cepero -B (2010) = WP vs casein
Impey -A (2015) = WP vs carbohydrate
Impey -B (2015) = WP with caffeine vs carbohydrate
Lollo -A (2011) = 91.4% WP vs casein
Lollo -B (2011) = 87 % WP vs casein
Morifuji -A (2012) = 3.0 g WP vs carbohydrate
Morifuji -B (2012) = 8.0 g WP vs carbohydrate
Parr -A (2014) = 25 g WP vs maltodextrin with alcohol
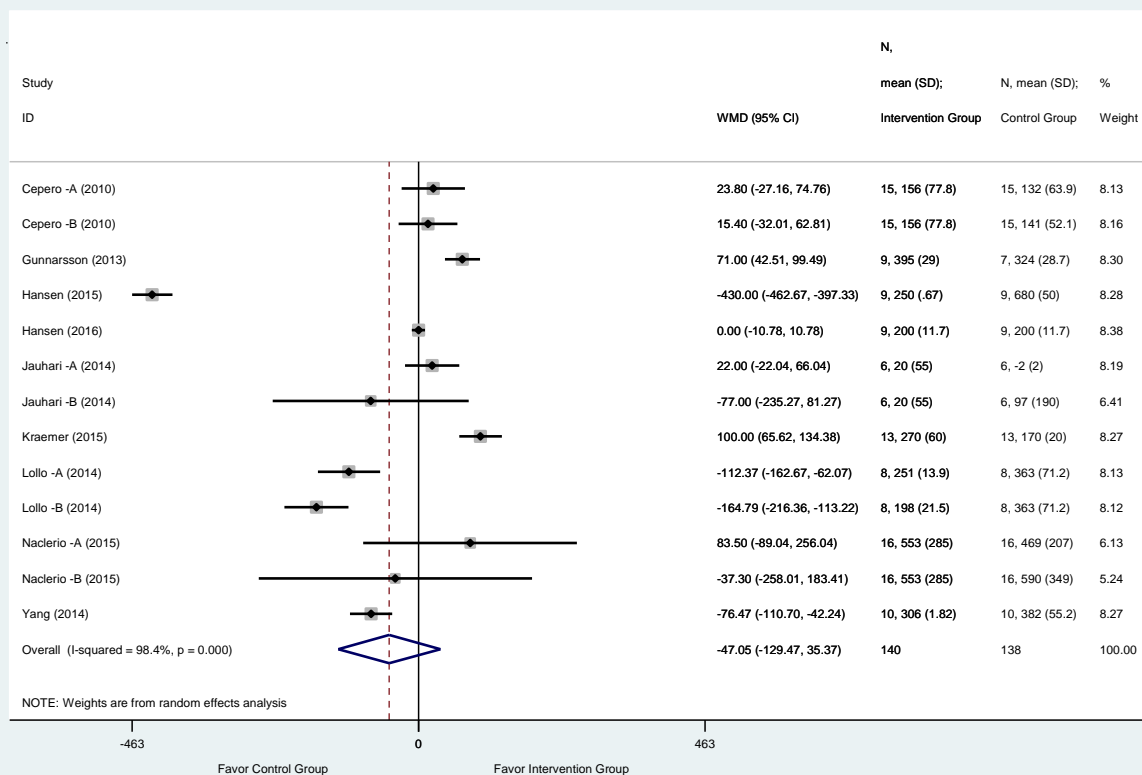Parr -B (2014) = 25 g WP with alcohol vs maltodextrin with alcohol
Schroer -A (2014) = WP vs L-alanine
Schroer -B (2014) = WP vs placebo

- **Subgroup by intervention period range (day)**

```
         Study      |    WMD   [95% Conf. Interval]
-------------------+-------------------------------------------------
     1-20
Cepero -A (2010)    |   -0.960    -2.252     0.332
Cepero -B (2010)    |   -0.690    -2.224     0.844
Cury-boaventura (2008|    0.360     0.184     0.536
Detko (2013)        |   -0.500    -0.601    -0.399
Impey -A (2015)     |    0.000    -0.028     0.028
Impey -B (2015)     |   -0.400    -0.428    -0.372
Macdermid (2006)    |    0.100    -0.599     0.799
Morifuji -A (2012)  |    0.410     0.371     0.449
Morifuji -B (2012)  |   -0.390    -0.421    -0.359
Parr -A (2014)      |   -0.300    -1.280     0.680
Parr -B (2014)      |   -0.100    -1.080     0.880
Schroer -A (2014)   |   -0.080    -0.247     0.087
Schroer -B (2014)   |   -0.250    -0.516     0.016
Tang (2007)         |   -1.200    -1.473    -0.927
Yang (2014)         |    0.970     0.574     1.366
 Sub-total          |
  D+L pooled WMD    |   -0.142    -0.349     0.066
-------------------+-------------------------------------------------
     41-60
Hill (2013)         |   -0.800    -0.915    -0.685
Lollo -A (2011)     |   -0.120    -0.149    -0.091
Lollo -B (2011)     |    0.080     0.051     0.109
 Sub-total          |
  D+L pooled WMD    |   -0.270    -0.533    -0.007
-------------------+-------------------------------------------------
```

```
Test(s) of heterogeneity:
          Heterogeneity  degrees of
            statistic     freedom    P    I-squared**  Tau-squared

1-20          1608.29       14     0.000    99.1%       0.1217
41-60          258.87        2     0.000    99.2%       0.0528
** I-squared: the variation in WMD attributable to heterogeneity)
```

```
Significance test(s) of WMD=0

1-20                  z=  1.34    p = 0.180
41-60                 z=  2.01    p = 0.044
```

| Study ID | WMD (95% CI) | N, mean (SD); Intervention Group | N, mean (SD); Control Group | % Weight |
|---|---|---|---|---|
| **1-20** | | | | |
| Cepero -A (2010) | -0.96 (-2.25, 0.33) | 15, 6.7 (1.56) | 15, 7.66 (2.02) | 2.02 |
| Cepero -B (2010) | -0.69 (-2.22, 0.84) | 15, 6.7 (1.56) | 15, 7.39 (2.6) | 1.53 |
| Cury-boaventura (2008) | 0.36 (0.18, 0.54) | 9, 7.8 (.19) | 9, 7.44 (.19) | 8.64 |
| Detko (2013) | -0.50 (-0.60, -0.40) | 7, 5.5 (.08) | 7, 6 (.11) | 9.01 |
| Impey -A (2015) | 0.00 (-0.03, 0.03) | 9, 4.8 (.03) | 9, 4.8 (.03) | 9.19 |
| Impey -B (2015) | -0.40 (-0.43, -0.37) | 9, 4.8 (.03) | 9, 5.2 (.03) | 9.19 |
| Macdermid (2006) | 0.10 (-0.60, 0.80) | 7, 3.5 (.5) | 7, 3.4 (.8) | 4.50 |
| Morifuji -A (2012) | 0.41 (0.37, 0.45) | 8, 5.5 (.04) | 8, 5.09 (.04) | 9.18 |
| Morifuji -B (2012) | -0.39 (-0.42, -0.36) | 8, 4.7 (.02) | 8, 5.09 (.04) | 9.19 |
| Parr -A (2014) | -0.30 (-1.28, 0.68) | 8, 5 (1) | 8, 5.3 (1) | 3.01 |
| Parr -B (2014) | -0.10 (-1.08, 0.88) | 8, 5.2 (1) | 8, 5.3 (1) | 3.01 |
| Schroer -A (2014) | -0.08 (-0.25, 0.09) | 8, 3.99 (.1) | 8, 4.07 (.22) | 8.69 |
| Schroer -B (2014) | -0.25 (-0.52, 0.02) | 8, 3.99 (.1) | 8, 4.24 (.37) | 8.00 |
| Tang (2007) | -1.20 (-1.47, -0.93) | 8, 5.5 (.18) | 8, 6.7 (.35) | 7.94 |
| Yang (2014) | 0.97 (0.57, 1.37) | 10, 4.52 (.49) | 10, 3.55 (.41) | 6.89 |
| Subtotal (I-squared = 99.1%, p = 0.000) | -0.14 (-0.35, 0.07) | 137 | 137 | 100.00 |
| . | | | | |
| **41-60** | | | | |
| Hill (2013) | -0.80 (-0.92, -0.68) | 6, 5.2 (.08) | 6, 6 (.12) | 32.03 |
| Lollo -A (2011) | -0.12 (-0.15, -0.09) | 8, 4.5 (.03) | 8, 4.62 (.03) | 33.99 |
| Lollo -B (2011) | 0.08 (0.05, 0.11) | 8, 4.7 (.03) | 8, 4.62 (.03) | 33.99 |
| Subtotal (I-squared = 99.2%, p = 0.000) | -0.27 (-0.53, -0.01) | 22 | 22 | 100.00 |

NOTE: Weights are from random effects analysis

-2.25    0    2.25

Favor Control Group          Favor Intervention Group

Cepero -A (2010) = WP vs carbohydrate
Cepero -B (2010) = WP vs casein
Impey -A (2015) = WP vs carbohydrate
Impey -B (2015) = WP with caffeine vs carbohydrate
Lollo -A (2011) = 91.4% WP vs casein
Lollo -B (2011) = 87 % WP vs casein
Morifuji -A (2012) = 3.0 g WP vs carbohydrate
Morifuji -B (2012) = 8.0 g WP vs carbohydrate
Parr -A (2014) = 25 g WP vs maltodextrin with alcohol
Parr -B (2014) = 25 g WP with alcohol vs maltodextrin with alcohol
Schroer -A (2014) = WP vs L-alanine
Schroer -B (2014) = WP vs placebo

### 8.5.5 Hormones

#### a) Insulin

##### i. Data

| Study | intervention | n1 | m1 | s1 | control | n2 | m2 | s2 |
|---|---|---|---|---|---|---|---|---|
| **Areta -A (2014)** | whey contain | 15 | 10 | 5 | placebo | 15 | 4 | 2 |
| **Areta -B (2014)** | whey contain | 15 | 11 | 4 | placebo | 15 | 4 | 2 |
| **Breen (2011)** | whey contain | 10 | 33 | 4 | carbohydrate | 10 | 14.5 | 1 |
| **Burke -A (2012)** | whey contain | 12 | 5.40 | 0.21 | placebo | 12 | 7.34 | 0.42 |
| **Burke -B (2012)** | whey contain | 12 | 15.84 | 1.25 | placebo | 12 | 7.34 | 0.42 |
| **Cepero -A (2010)** | whey contain | 15 | 27.24 | 16.88 | carbohydrate + energy + vitamins | 15 | 39.08 | 19.75 |
| **Cepero -B (2010)** | whey contain | 15 | 27.24 | 16.88 | casein | 15 | 47.43 | 27.72 |
| **Detko (2013)** | whey contain | 7 | 63 | 4.54 | protein + carbohydrate + fat | 7 | 25 | 1.13 |
| **Highton (2012)** | whey contain | 9 | 7.53 | 3.99 | carbohydrate | 9 | 6.31 | 3.67 |
| **Hill (2013)** | whey contain | 6 | 28.80 | 5.88 | protein + carbohydrate + fat | 6 | 17.28 | 2.94 |
| **Impey -A (2015)** | whey contain | 9 | 8.21 | 0.24 | protein + Caffeine | 9 | 6.77 | 0.24 |
| **Impey -B (2015)** | whey contain | 9 | 8.21 | 0.24 | placebo | 9 | 2.88 | 0.00 |
| **Mero -A (1997)** | whey contain | 9 | 3.80 | 0.02 | bovine colostrum | 9 | 4.10 | 0.17 |
| **Mero -B (1997)** | whey contain | 9 | 3.80 | 0.02 | bovine colostrum | 9 | 4.8 | 1 |
| **Morifuji -A (2012)** | whey contain | 8 | 15.84 | 0.25 | carbohydrate + energy + vitamins | 8 | 12.96 | 0.10 |
| **Morifuji -B (2012)** | whey contain | 8 | 27.36 | 0.51 | carbohydrate + energy + vitamins | 8 | 12.96 | 0.10 |
| **Oosthuyse -A (2015)** | whey contain | 8 | 27 | 17 | casein + fructose | 8 | 26 | 15 |
| **Oosthuyse -B (2015)** | whey contain | 8 | 27 | 17 | carbohydrate | 8 | 31 | 17 |
| **Tang (2007)** | whey contain | 8 | 45 | 5.30 | carbohydrate + maltodextrin | 8 | 27 | 3.89 |

### ii. Forest Plot

```
            Study     |    WMD   [95% Conf. Interval]    % Weight
--------------------+----------------------------------------------------
Areta -A (2014)     |  6.000      3.275     8.725         6.10
Areta -B (2014)     |  7.000      4.737     9.263         6.29
Breen (2011)        | 18.500     15.945    21.055         6.17
Burke -A (2012)     | -1.940     -2.206    -1.674         6.77
Burke -B (2012)     |  8.500      7.754     9.246         6.72
Cepero -A (2010)    |-11.840    -24.988     1.308         1.89
Cepero -B (2010)    |-20.190    -36.614    -3.766         1.35
Detko (2013)        | 38.000     34.534    41.466         5.74
Highton (2012)      |  1.220     -2.322     4.762         5.70
Hill (2013)         | 11.520      6.260    16.780         4.79
Impey -A (2015)     |  1.440      1.218     1.662         6.77
Impey -B (2015)     |  5.330      5.173     5.487         6.77
Mero -A (1997)      | -0.300     -0.412    -0.188         6.77
Mero -B (1997)      | -1.000     -1.653    -0.347         6.73
Morifuji -A (2012)  |  2.880      2.693     3.067         6.77
Morifuji -B (2012)  | 14.400     14.040    14.760         6.76
Oosthuyse -A (2015) |  1.000    -14.710    16.710         1.44
Oosthuyse -B (2015) | -4.000    -20.660    12.660         1.32
Tang (2007)         | 18.000     13.444    22.556         5.17
--------------------+----------------------------------------------------
D+L pooled WMD      |  7.126      4.997     9.254        100.00
--------------------+----------------------------------------------------

  Heterogeneity chi-squared = 9905.77 (d.f. = 18) p = 0.000
  I-squared (variation in WMD attributable to heterogeneity) =  99.8%
  Estimate of between-study variance Tau-squared = 17.4143

  Test of WMD=0 : z=   6.56 p = 0.000
```

| Study ID | WMD (95% CI) | N, mean (SD); Intervention Group | N, mean (SD); Control Group | % Weight |
|---|---|---|---|---|
| Areta -A (2014) | 6.00 (3.27, 8.73) | 15, 10 (5) | 15, 4 (2) | 6.10 |
| Areta -B (2014) | 7.00 (4.74, 9.26) | 15, 11 (4) | 15, 4 (2) | 6.29 |
| Breen (2011) | 18.50 (15.94, 21.06) | 10, 33 (4) | 10, 14.5 (1) | 6.17 |
| Burke -A (2012) | -1.94 (-2.21, -1.67) | 12, 5.4 (.21) | 12, 7.34 (.42) | 6.77 |
| Burke -B (2012) | 8.50 (7.75, 9.25) | 12, 15.8 (1.25) | 12, 7.34 (.42) | 6.72 |
| Cepero -A (2010) | -11.84 (-24.99, 1.31) | 15, 27.2 (16.9) | 15, 39.1 (19.8) | 1.89 |
| Cepero -B (2010) | -20.19 (-36.61, -3.77) | 15, 27.2 (16.9) | 15, 47.4 (27.7) | 1.35 |
| Detko (2013) | 38.00 (34.53, 41.47) | 7, 63 (4.54) | 7, 25 (1.13) | 5.74 |
| Highton (2012) | 1.22 (-2.32, 4.76) | 9, 7.53 (3.99) | 9, 6.31 (3.67) | 5.70 |
| Hill (2013) | 11.52 (6.26, 16.78) | 6, 28.8 (5.88) | 6, 17.3 (2.94) | 4.79 |
| Impey -A (2015) | 1.44 (1.22, 1.66) | 9, 8.21 (.24) | 9, 6.77 (.24) | 6.77 |
| Impey -B (2015) | 5.33 (5.17, 5.49) | 9, 8.21 (.24) | 9, 2.88 (.0048) | 6.77 |
| Mero -A (1997) | -0.30 (-0.41, -0.19) | 9, 3.8 (.02) | 9, 4.1 (.17) | 6.77 |
| Mero -B (1997) | -1.00 (-1.65, -0.35) | 9, 3.8 (.02) | 9, 4.8 (1) | 6.73 |
| Morifuji -A (2012) | 2.88 (2.69, 3.07) | 8, 15.8 (.25) | 8, 13 (.1) | 6.77 |
| Morifuji -B (2012) | 14.40 (14.04, 14.76) | 8, 27.4 (.51) | 8, 13 (.1) | 6.76 |
| Oosthuyse -A (2015) | 1.00 (-14.71, 16.71) | 8, 27 (17) | 8, 26 (15) | 1.44 |
| Oosthuyse -B (2015) | -4.00 (-20.66, 12.66) | 8, 27 (17) | 8, 31 (17) | 1.32 |
| Tang (2007) | 18.00 (13.44, 22.56) | 8, 45 (5.3) | 8, 27 (3.89) | 5.17 |
| Overall (I-squared = 99.8%, p = 0.000) | 7.13 (5.00, 9.25) | 192 | 192 | 100.00 |

NOTE: Weights are from random effects analysis

-41.5     0     41.5

Favor Control Group     Favor Intervention Group

Areta -A (2014) = 15 g WP vs placebo
Areta -B (2014) = 30 g WP vs placebo
Burke -A (2012) = 500 ml WP vs placebo
Burke -B (2012) = 33 ml WP vs placebo
Cepero -A (2010) = WP vs carbohydrate
Cepero -B (2010) = WP vs casein
Impey -A (2015) = WP vs carbohydrate
Impey -B (2015) = WP with caffeine vs carbohydrate
Morifuji -A (2012) = 3.0 g WP vs carbohydrate
Morifuji -B (2012) = 8.0 g WP vs carbohydrate
Mero -A (1997) = WP vs 125-ml Bioenervi
Mero -B (1997) = WP vs 25-ml Bioenervi
Oosthuyse -A (2015) = WP vs casein
Oosthuyse -B (2015) = WP vs carbohydrate

### iii. Funnel Plot



Funnel plot with pseudo 95% confidence limits

### iv. Egger test

```
Egger test for small-study effects:
Regress standard normal deviate of intervention
effect estimate against its standard error

Number of studies =  12                          Root MSE      =   1.708
------------------------------------------------------------------------------
    Std_Eff |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
------------+-----------------------------------------------------------------
      slope |   .8425302   .6025494     1.40   0.192    -.5000337    2.185094
       bias |  -.0627918   .6329321    -0.10   0.923    -1.473052    1.347469
------------------------------------------------------------------------------

Test of H0: no small-study effects          P = 0.923
```

Egger test of Whey Protein on Insulin (µU/ml)

**v. Subgroup**

- **Subgroup by physical activities**

```
          Study       |   WMD    [95% Conf. Interval]
--------------------+-------------------------------------------------
      leg           |
Areta -A (2014)     |   6.000    3.275     8.725
Areta -B (2014)     |   7.000    4.737     9.263
Burke -A (2012)     |  -1.940   -2.206    -1.674
Burke -B (2012)     |   8.500    7.754     9.246
Mero -A (1997)      |  -0.300   -0.412    -0.188
Mero -B (1997)      |  -1.000   -1.653    -0.347
 Sub-total          |
  D+L pooled WMD    |   2.779    0.724     4.834
--------------------+-------------------------------------------------
      cycle         |
Breen (2011)        |  18.500   15.945    21.055
Cepero -A (2010)    | -11.840  -24.988     1.308
Cepero -B (2010)    | -20.190  -36.614    -3.766
Detko (2013)        |  38.000   34.534    41.466
Hill (2013)         |  11.520    6.260    16.780
Impey -A (2015)     |   1.440    1.218     1.662
Impey -B (2015)     |   5.330    5.173     5.487
Morifuji -A (2012)  |   2.880    2.693     3.067
Morifuji -B (2012)  |  14.400   14.040    14.760
Oosthuyse -A (2015) |   1.000  -14.710    16.710
Oosthuyse -B (2015) |  -4.000  -20.660    12.660
 Sub-total          |
  D+L pooled WMD    |   9.984    6.966    13.001
--------------------+-------------------------------------------------
```

```
         run
Highton (2012)       |    1.220    -2.322     4.762
  Sub-total          |
   D+L pooled WMD    |    1.220    -2.322     4.762
--------------------+-----------------------------------------------
        gym
Tang (2007)          |   18.000    13.444    22.556
  Sub-total          |
   D+L pooled WMD    |   18.000    13.444    22.556
--------------------+-----------------------------------------------

Test(s) of heterogeneity:
              Heterogeneity  degrees of
                statistic      freedom      P     I-squared**   Tau-squared

leg              743.89           5        0.000     99.3%         6.0823
cycle           4526.94          10        0.000     99.8%        17.4150
run                0.00           0          .         .%          0.0000
gym                0.00           0          .         .%          0.0000
** I-squared: the variation in WMD attributable to heterogeneity)


Significance test(s) of WMD=0

leg                    z=  2.65     p = 0.008
cycle                  z=  6.48     p = 0.000
run                    z=  0.68     p = 0.500
gym                    z=  7.74     p = 0.000
```

| Study ID | WMD (95% CI) | N, mean (SD); Intervention Group | N, mean (SD); Control Group | % Weight |
|---|---|---|---|---|
| **leg** | | | | |
| Areta -A (2014) | 6.00 (3.27, 8.73) | 15, 10 (5) | 15, 4 (2) | 13.71 |
| Areta -B (2014) | 7.00 (4.74, 9.26) | 15, 11 (4) | 15, 4 (2) | 14.82 |
| Burke -A (2012) | -1.94 (-2.21, -1.67) | 12, 5.4 (.21) | 12, 7.34 (.42) | 18.01 |
| Burke -B (2012) | 8.50 (7.75, 9.25) | 12, 15.8 (1.25) | 12, 7.34 (.42) | 17.65 |
| Mero -A (1997) | -0.30 (-0.41, -0.19) | 9, 3.8 (.02) | 9, 4.1 (.17) | 18.06 |
| Mero -B (1997) | -1.00 (-1.65, -0.35) | 9, 3.8 (.02) | 9, 4.8 (1) | 17.75 |
| Subtotal (I-squared = 99.3%, p = 0.000) | 2.78 (0.72, 4.83) | 72 | 72 | 100.00 |
| **cycle** | | | | |
| Breen (2011) | 18.50 (15.94, 21.06) | 10, 33 (4) | 10, 14.5 (1) | 12.40 |
| Cepero -A (2010) | -11.84 (-24.99, 1.31) | 15, 27.2 (16.9) | 15, 39.1 (19.8) | 3.80 |
| Cepero -B (2010) | -20.19 (-36.61, -3.77) | 15, 27.2 (16.9) | 15, 47.4 (27.7) | 2.70 |
| Detko (2013) | 38.00 (34.53, 41.47) | 7, 63 (4.54) | 7, 25 (1.13) | 11.54 |
| Hill (2013) | 11.52 (6.26, 16.78) | 6, 28.8 (5.88) | 6, 17.3 (2.94) | 9.63 |
| Impey -A (2015) | 1.44 (1.22, 1.66) | 9, 8.21 (.24) | 9, 6.77 (.24) | 13.60 |
| Impey -B (2015) | 5.33 (5.17, 5.49) | 9, 8.21 (.24) | 9, 2.88 (.0048) | 13.60 |
| Morifuji -A (2012) | 2.88 (2.69, 3.07) | 8, 15.8 (.25) | 8, 13 (.1) | 13.60 |
| Morifuji -B (2012) | 14.40 (14.04, 14.76) | 8, 27.4 (.51) | 8, 13 (.1) | 13.58 |
| Oosthuyse -A (2015) | 1.00 (-14.71, 16.71) | 8, 27 (17) | 8, 26 (15) | 2.90 |
| Oosthuyse -B (2015) | -4.00 (-20.66, 12.66) | 8, 27 (17) | 8, 31 (17) | 2.64 |
| Subtotal (I-squared = 99.8%, p = 0.000) | 9.98 (6.97, 13.00) | 103 | 103 | 100.00 |
| **run** | | | | |
| Highton (2012) | 1.22 (-2.32, 4.76) | 9, 7.53 (3.99) | 9, 6.31 (3.67) | 100.00 |
| Subtotal (I-squared = .%, p = .) | 1.22 (-2.32, 4.76) | 9 | 9 | 100.00 |
| **gym** | | | | |
| Tang (2007) | 18.00 (13.44, 22.56) | 8, 45 (5.3) | 8, 27 (3.89) | 100.00 |
| Subtotal (I-squared = .%, p = .) | 18.00 (13.44, 22.56) | 8 | 8 | 100.00 |

NOTE: Weights are from random effects analysis

Favor Control Group — Favor Intervention Group

Areta -A (2014) = 15 g WP vs placebo
Areta -B (2014) = 30 g WP vs placebo
Burke -A (2012) = 500 ml WP vs placebo
Burke -B (2012) = 33 ml WP vs placebo
Cepero -A (2010) = WP vs carbohydrate
Cepero -B (2010) = WP vs casein
Impey -A (2015) = WP vs carbohydrate
Impey -B (2015) = WP with caffeine vs carbohydrate
Mero -A (1997) = WP vs 125-ml Bioenervi
Mero -B (1997) = WP vs 25-ml Bioenervi
Morifuji -A (2012) = 3.0 g WP vs carbohydrate
Morifuji -B (2012) = 8.0 g WP vs carbohydrate
Oosthuyse -A (2015) = WP vs casein
Oosthuyse -B (2015) = WP vs carbohydrate

- **Subgroup by intervention period range (day)**

```
         Study      |    WMD   [95% Conf. Interval]
-------------------+------------------------------------------------
     41-60          |
Areta -A (2014)     |   6.000    3.275     8.725
Areta -B (2014)     |   7.000    4.737     9.263
Hill (2013)         |  11.520    6.260    16.780
Mero -A (1997)      |  -0.300   -0.412    -0.188
Mero -B (1997)      |  -1.000   -1.653    -0.347
 Sub-total          |
  D+L pooled WMD    |   3.227    1.210     5.245
-------------------+------------------------------------------------
     21-40          |
Breen (2011)        |  18.500   15.945    21.055
 Sub-total          |
  D+L pooled WMD    |  18.500   15.945    21.055
-------------------+------------------------------------------------
     1-20           |
Burke -A (2012)     |  -1.940   -2.206    -1.674
Burke -B (2012)     |   8.500    7.754     9.246
Cepero -A (2010)    | -11.840  -24.988     1.308
Cepero -B (2010)    | -20.190  -36.614    -3.766
Detko (2013)        |  38.000   34.534    41.466
Highton (2012)      |   1.220   -2.322     4.762
Impey -A (2015)     |   1.440    1.218     1.662
Impey -B (2015)     |   5.330    5.173     5.487
Morifuji -A (2012)  |   2.880    2.693     3.067
Morifuji -B (2012)  |  14.400   14.040    14.760
Oosthuyse -A (2015) |   1.000  -14.710    16.710
Oosthuyse -B (2015) |  -4.000  -20.660    12.660
Tang (2007)         |  18.000   13.444    22.556
 Sub-total          |
  D+L pooled WMD    |   7.367    4.523    10.211
-------------------+------------------------------------------------

Test(s) of heterogeneity:
          Heterogeneity  degrees of
            statistic     freedom      P    I-squared**   Tau-squared

41-60           84.25         4       0.000    95.3%        3.9714
21-40            0.00         0        .        .%          0.0000
1-20          6595.61        12       0.000    99.8%       19.9624
** I-squared: the variation in WMD attributable to heterogeneity)


Significance test(s) of WMD=0

41-60              z=  3.14    p = 0.002
21-40              z= 14.19    p = 0.000
1-20               z=  5.08    p = 0.000
```

| Study ID | WMD (95% CI) | N, mean (SD); Intervention Group | N, mean (SD); Control Group | % Weight |
|---|---|---|---|---|
| **41-60** | | | | |
| Areta -A (2014) | 6.00 (3.27, 8.73) | 15, 10 (5) | 15, 4 (2) | 17.94 |
| Areta -B (2014) | 7.00 (4.74, 9.26) | 15, 11 (4) | 15, 4 (2) | 19.97 |
| Hill (2013) | 11.52 (6.26, 16.78) | 6, 28.8 (5.88) | 6, 17.3 (2.94) | 9.48 |
| Mero -A (1997) | -0.30 (-0.41, -0.19) | 9, 3.8 (.02) | 9, 4.1 (.17) | 26.65 |
| Mero -B (1997) | -1.00 (-1.65, -0.35) | 9, 3.8 (.02) | 9, 4.8 (1) | 25.95 |
| Subtotal (I-squared = 95.3%, p = 0.000) | 3.23 (1.21, 5.24) | 54 | 54 | 100.00 |
| **21-40** | | | | |
| Breen (2011) | 18.50 (15.94, 21.06) | 10, 33 (4) | 10, 14.5 (1) | 100.00 |
| Subtotal (I-squared = .%, p = .) | 18.50 (15.94, 21.06) | 10 | 10 | 100.00 |
| **1-20** | | | | |
| Burke -A (2012) | -1.94 (-2.21, -1.67) | 12, 5.4 (.21) | 12, 7.34 (.42) | 10.54 |
| Burke -B (2012) | 8.50 (7.75, 9.25) | 12, 15.8 (1.25) | 12, 7.34 (.42) | 10.47 |
| Cepero -A (2010) | -11.84 (-24.99, 1.31) | 15, 27.2 (16.9) | 15, 39.1 (19.8) | 3.24 |
| Cepero -B (2010) | -20.19 (-36.61, -3.77) | 15, 27.2 (16.9) | 15, 47.4 (27.7) | 2.33 |
| Detko (2013) | 38.00 (34.53, 41.47) | 7, 63 (4.54) | 7, 25 (1.13) | 9.12 |
| Highton (2012) | 1.22 (-2.32, 4.76) | 9, 7.53 (3.99) | 9, 6.31 (3.67) | 9.06 |
| Impey -A (2015) | 1.44 (1.22, 1.66) | 9, 8.21 (.24) | 9, 6.77 (.24) | 10.54 |
| Impey -B (2015) | 5.33 (5.17, 5.49) | 9, 8.21 (.24) | 9, 2.88 (.0048) | 10.54 |
| Morifuji -A (2012) | 2.88 (2.69, 3.07) | 8, 15.8 (.25) | 8, 13 (.1) | 10.54 |
| Morifuji -B (2012) | 14.40 (14.04, 14.76) | 8, 27.4 (.51) | 8, 13 (.1) | 10.53 |
| Oosthuyse -A (2015) | 1.00 (-14.71, 16.71) | 8, 27 (17) | 8, 26 (15) | 2.50 |
| Oosthuyse -B (2015) | -4.00 (-20.66, 12.66) | 8, 27 (17) | 8, 31 (17) | 2.28 |
| Tang (2007) | 18.00 (13.44, 22.56) | 8, 45 (5.3) | 8, 27 (3.89) | 8.30 |
| Subtotal (I-squared = 99.8%, p = 0.000) | 7.37 (4.52, 10.21) | 128 | 128 | 100.00 |

NOTE: Weights are from random effects analysis

-41.5          0          41.5

Favor Control Group          Favor Intervention Group

Areta -A (2014) = 15 g WP vs placebo
Areta -B (2014) = 30 g WP vs placebo
Burke -A (2012) = 500 ml WP vs placebo
Burke -B (2012) = 33 ml WP vs placebo
Cepero -A (2010) = WP vs carbohydrate
Cepero -B (2010) = WP vs casein
Impey -A (2015) = WP vs carbohydrate
Impey -B (2015) = WP with caffeine vs carbohydrate
Mero -A (1997) = WP vs 125-ml Bioenervi
Mero -B (1997) = WP vs 25-ml Bioenervi
Morifuji -A (2012) = 3.0 g WP vs carbohydrate
Morifuji -B (2012) = 8.0 g WP vs carbohydrate
Oosthuyse -A (2015) = WP vs casein
Oosthuyse -B (2015) = WP vs carbohydrate

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### b) Cortisol

#### i. Data

| Study | intervention | n1 | m1 | s1 | control | n2 | m2 | s2 |
|---|---|---|---|---|---|---|---|---|
| Hansen (2015) | whey contain | 9 | 888 | 34.33 | carbohydrate | 9 | 848 | 31 |
| Hansen (2016) | whey contain | 9 | 690 | 18.33 | carbohydrate | 9 | 705 | 10 |
| Kraemer (2015) | whey contain | 13 | 661 | 270 | HMB + carbohydrate + fat | 13 | 621 | 218 |
| Mero -A (1997) | whey contain | 9 | 230 | 3.33 | bovine colostrum | 9 | 231 | 3.33 |
| Mero -B (1997) | whey contain | 9 | 230 | 3.33 | bovine colostrum | 9 | 239 | 5 |
| Nelson (2013) | whey contain | 12 | 586 | 236 | carbohydrate | 12 | 612 | 263 |
| Shing (2013) | whey contain | 6 | 3 | 0.20 | bovine colostrum | 4 | 10 | 1.5 |

#### ii. Forest Plot

```
         Study     |   WMD    [95% Conf. Interval]    % Weight
-------------------+----------------------------------------------
Hansen (2015)      | 40.000     9.779    70.221          2.29
Hansen (2016)      |-15.000   -28.643    -1.357          8.87
Kraemer (2015)     | 40.000  -148.640   228.640          0.06
Mero -A (1997)     | -1.000    -4.078     2.078         29.25
Mero -B (1997)     | -9.000   -12.926    -5.074         27.15
Nelson (2013)      |-26.000  -225.930   173.930          0.06
Shing (2013)       | -7.000    -8.479    -5.521         32.32
-------------------+----------------------------------------------
D+L pooled WMD     | -5.401   -10.143    -0.659        100.00
-------------------+----------------------------------------------

  Heterogeneity chi-squared =  24.88 (d.f. = 6) p = 0.000
  I-squared (variation in WMD attributable to heterogeneity) =  75.9%
  Estimate of between-study variance Tau-squared = 17.5409

  Test of WMD=0 : z=   2.23 p = 0.026
```

| Study ID | WMD (95% CI) | N, mean (SD); Intervention Group | N, mean (SD); Control Group | % Weight |
|---|---|---|---|---|
| Hansen (2015) | 40.00 (9.78, 70.22) | 9, 888 (34.3) | 9, 848 (31) | 2.29 |
| Hansen (2016) | -15.00 (-28.64, -1.36) | 9, 690 (18.3) | 9, 705 (10) | 8.87 |
| Kraemer (2015) | 40.00 (-148.64, 228.64) | 13, 661 (270) | 13, 621 (218) | 0.06 |
| Mero -A (1997) | -1.00 (-4.08, 2.08) | 9, 230 (3.33) | 9, 231 (3.33) | 29.25 |
| Mero -B (1997) | -9.00 (-12.93, -5.07) | 9, 230 (3.33) | 9, 239 (5) | 27.15 |
| Nelson (2013) | -26.00 (-225.93, 173.93) | 12, 586 (236) | 12, 612 (263) | 0.06 |
| Shing (2013) | -7.00 (-8.48, -5.52) | 6, 3 (.204) | 4, 10 (1.5) | 32.32 |
| Overall (I-squared = 75.9%, p = 0.000) | -5.40 (-10.14, -0.66) | 67 | 65 | 100.00 |

NOTE: Weights are from random effects analysis

-229    Favor Control Group    0    Favor Intervention Group    229

Mero -A (1997) = WP vs 125-ml Bioenervi
Mero -B (1997) = WP vs 25-ml Bioenervi

### iii. Subgroup

- ### Subgroup by physical activities

```
         Study     |    WMD    [95% Conf. Interval]
-------------------+-------------------------------------------------
     run
Hansen (2015)      |   40.000    9.779    70.221
 Sub-total         |
  D+L pooled WMD   |   40.000    9.779    70.221
-------------------+-------------------------------------------------
     cycle
Hansen (2016)      |  -15.000  -28.643    -1.357
Kraemer (2015)     |   40.000 -148.640   228.640
Nelson (2013)      |  -26.000 -225.930   173.930
Shing (2013)       |   -7.000   -8.479    -5.521
 Sub-total         |
  D+L pooled WMD   |   -7.091   -8.561    -5.621
-------------------+-------------------------------------------------
     leg
Mero -A (1997)     |   -1.000   -4.078     2.078
Mero -B (1997)     |   -9.000  -12.926    -5.074
 Sub-total         |
  D+L pooled WMD   |   -4.903  -12.741     2.934
-------------------+-------------------------------------------------

Test(s) of heterogeneity:
           Heterogeneity   degrees of
             statistic       freedom      P    I-squared**   Tau-squared
```

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```
run                     0.00        0        .         .%       0.0000
cycle                   1.58        3     0.664      0.0%       0.0000
leg                     9.88        1     0.002     89.9%      28.7605
** I-squared: the variation in WMD attributable to heterogeneity)


Significance test(s) of WMD=0

run                   z=  2.59    p = 0.009
cycle                 z=  9.45    p = 0.000
leg                   z=  1.23    p = 0.220
```
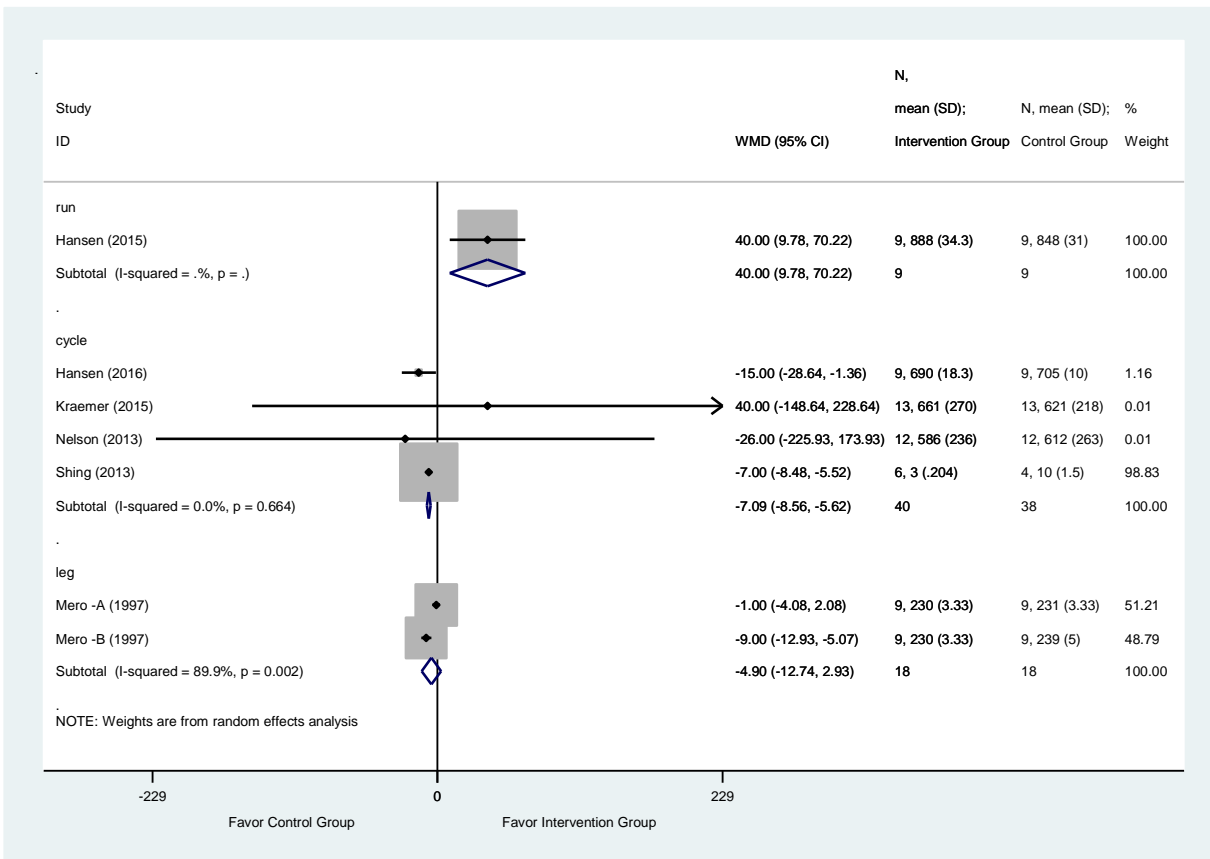


Mero -A (1997) = WP vs 125-ml Bioenervi
Mero -B (1997) = WP vs 25-ml Bioenervi

- **Subgroup by intervention period range (day)**

```
          Study      |    WMD    [95% Conf. Interval]
-------------------+--------------------------------------------------
      1-20          |
Hansen (2015)       |   40.000     9.779    70.221
Hansen (2016)       |  -15.000   -28.643    -1.357
 Sub-total          |
  D+L pooled WMD    |   10.779   -43.014    64.573
-------------------+--------------------------------------------------
      41-60         |
Kraemer (2015)      |   40.000  -148.640   228.640
Mero -A (1997)      |   -1.000    -4.078     2.078
Mero -B (1997)      |   -9.000   -12.926    -5.074
Shing (2013)        |   -7.000    -8.479    -5.521
 Sub-total          |
  D+L pooled WMD    |   -5.604    -9.692    -1.516
-------------------+--------------------------------------------------
      21-40         |
Nelson (2013)       |  -26.000  -225.930   173.930
 Sub-total          |
  D+L pooled WMD    |  -26.000  -225.930   173.930
-------------------+--------------------------------------------------

Test(s) of heterogeneity:
           Heterogeneity  degrees of
             statistic      freedom     P    I-squared**   Tau-squared

1-20             10.57          1      0.001    90.5%        1.4e+03
41-60            14.27          3      0.003    79.0%       10.8606
21-40             0.00          0        .        .%         0.0000
** I-squared: the variation in WMD attributable to heterogeneity)


Significance test(s) of WMD=0

1-20                   z=  0.39    p = 0.695
41-60                  z=  2.69    p = 0.007
21-40                  z=  0.25    p = 0.799
```

| Study ID | WMD (95% CI) | N, mean (SD); Intervention Group | N, mean (SD); Control Group | % Weight |
|---|---|---|---|---|
| **1-20** | | | | |
| Hansen (2015) | 40.00 (9.78, 70.22) | 9, 888 (34.3) | 9, 848 (31) | 46.87 |
| Hansen (2016) | -15.00 (-28.64, -1.36) | 9, 690 (18.3) | 9, 705 (10) | 53.13 |
| Subtotal (I-squared = 90.5%, p = 0.001) | 10.78 (-43.01, 64.57) | 18 | 18 | 100.00 |
| . | | | | |
| **41-60** | | | | |
| Kraemer (2015) | 40.00 (-148.64, 228.64) | 13, 661 (270) | 13, 621 (218) | 0.05 |
| Mero -A (1997) | -1.00 (-4.08, 2.08) | 9, 230 (3.33) | 9, 231 (3.33) | 32.64 |
| Mero -B (1997) | -9.00 (-12.93, -5.07) | 9, 230 (3.33) | 9, 239 (5) | 29.25 |
| Shing (2013) | -7.00 (-8.48, -5.52) | 6, 3 (.204) | 4, 10 (1.5) | 38.06 |
| Subtotal (I-squared = 79.0%, p = 0.003) | -5.60 (-9.69, -1.52) | 37 | 35 | 100.00 |
| . | | | | |
| **21-40** | | | | |
| Nelson (2013) | -26.00 (-225.93, 173.93) | 12, 586 (236) | 12, 612 (263) | 100.00 |
| Subtotal (I-squared = .%, p = .) | -26.00 (-225.93, 173.93) | 12 | 12 | 100.00 |
| . | | | | |

NOTE: Weights are from random effects analysis

Mero -A (1997) = WP vs 125-ml Bioenervi
Mero -B (1997) = WP vs 25-ml Bioenervi

## c) Testosterone

### i. Data

| Study | intervention | n1 | m1 | s1 | control | n2 | m2 | s2 |
|-------|-------------|-----|------|------|---------|-----|------|------|
| **Kraemer (2015)** | whey contain | 13 | 21.7 | 4.8 | HMB + carbohydrate + fat | 13 | 20.7 | 5.8 |
| **Mero -A (1997)** | whey contain | 9 | 21.7 | 0.17 | bovine colostrum | 9 | 22 | 0.57 |
| **Mero -B (1997)** | whey contain | 9 | 21.7 | 0.17 | bovine colostrum | 9 | 22.5 | 0.33 |
| **Shing (2013)** | whey contain | 6 | 0.31 | 0.00 | bovine colostrum | 4 | 0.4 | 0.05 |

### ii. Forest Plot

```
          Study      |    WMD    [95% Conf. Interval]     % Weight
-------------------+------------------------------------------------
Kraemer (2015)      |   1.000      -3.093     5.093          1.36
Mero -A (1997)      |  -0.300      -0.689     0.089         29.40
Mero -B (1997)      |  -0.800      -1.043    -0.557         33.19
Shing (2013)        |  -0.090      -0.139    -0.041         36.04
-------------------+------------------------------------------------
D+L pooled WMD      |  -0.373      -0.860     0.115        100.00
-------------------+------------------------------------------------

  Heterogeneity chi-squared =  32.75 (d.f. = 3) p = 0.000
  I-squared (variation in WMD attributable to heterogeneity) =  90.8%
  Estimate of between-study variance Tau-squared =   0.1708

Test of WMD=0 : z=   1.50 p = 0.134
```
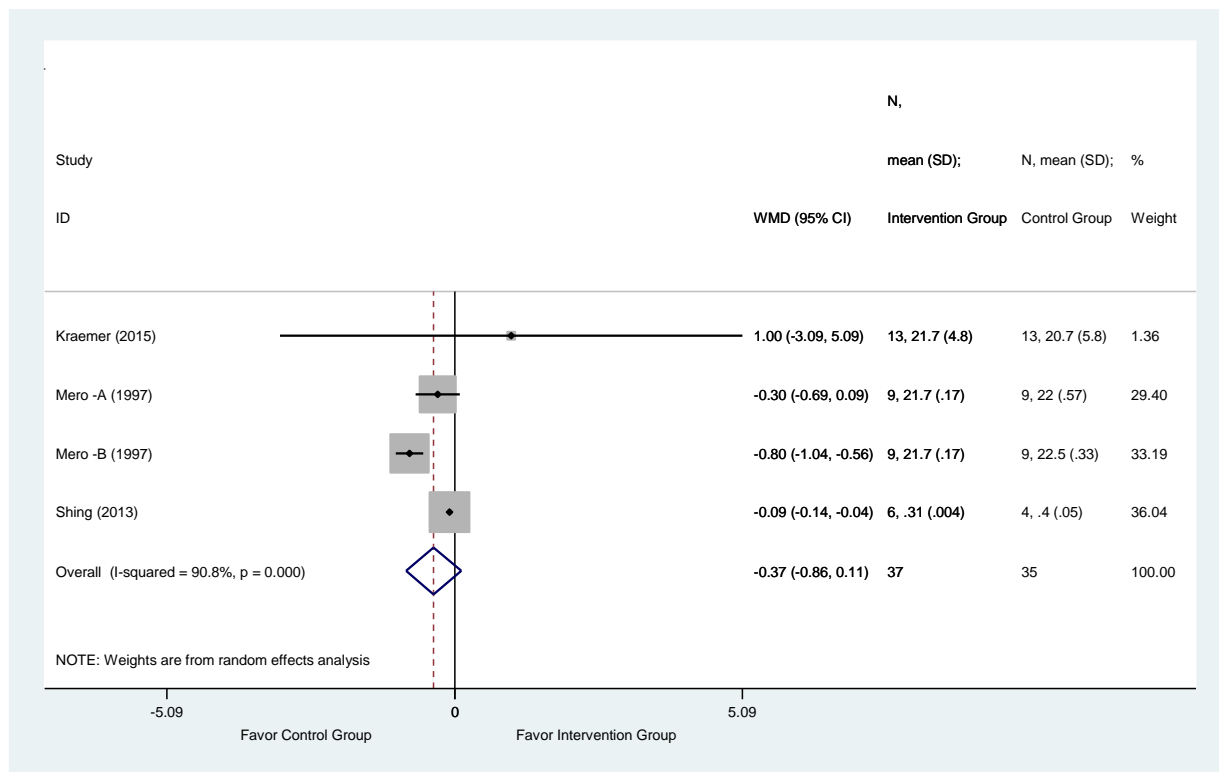


Mero -A (1997) = WP vs 125-ml Bioenervi
Mero -B (1997) = WP vs 25-ml Bioenervi

### iii. Subgroup

- **Subgroup by physical activities**

```
          Study        |   WMD    [95% Conf. Interval]
---------------------+---------------------------------------------------
     cycle
Kraemer (2015)         |   1.000    -3.093     5.093
Shing (2013)           |  -0.090    -0.139    -0.041
 Sub-total             |
  D+L pooled WMD       |  -0.090    -0.139    -0.041
---------------------+---------------------------------------------------
     leg
Mero -A (1997)         |  -0.300    -0.689     0.089
Mero -B (1997)         |  -0.800    -1.043    -0.557
 Sub-total             |
  D+L pooled WMD       |  -0.574    -1.062    -0.086
---------------------+---------------------------------------------------


Test(s) of heterogeneity:
            Heterogeneity  degrees of
              statistic      freedom      P     I-squared**   Tau-squared

cycle           0.27            1        0.602     0.0%         0.0000
leg             4.58            1        0.032    78.2%         0.0977
** I-squared: the variation in WMD attributable to heterogeneity)


Significance test(s) of WMD=0

cycle                 z=  3.59     p = 0.000
leg                   z=  2.31     p = 0.021
```
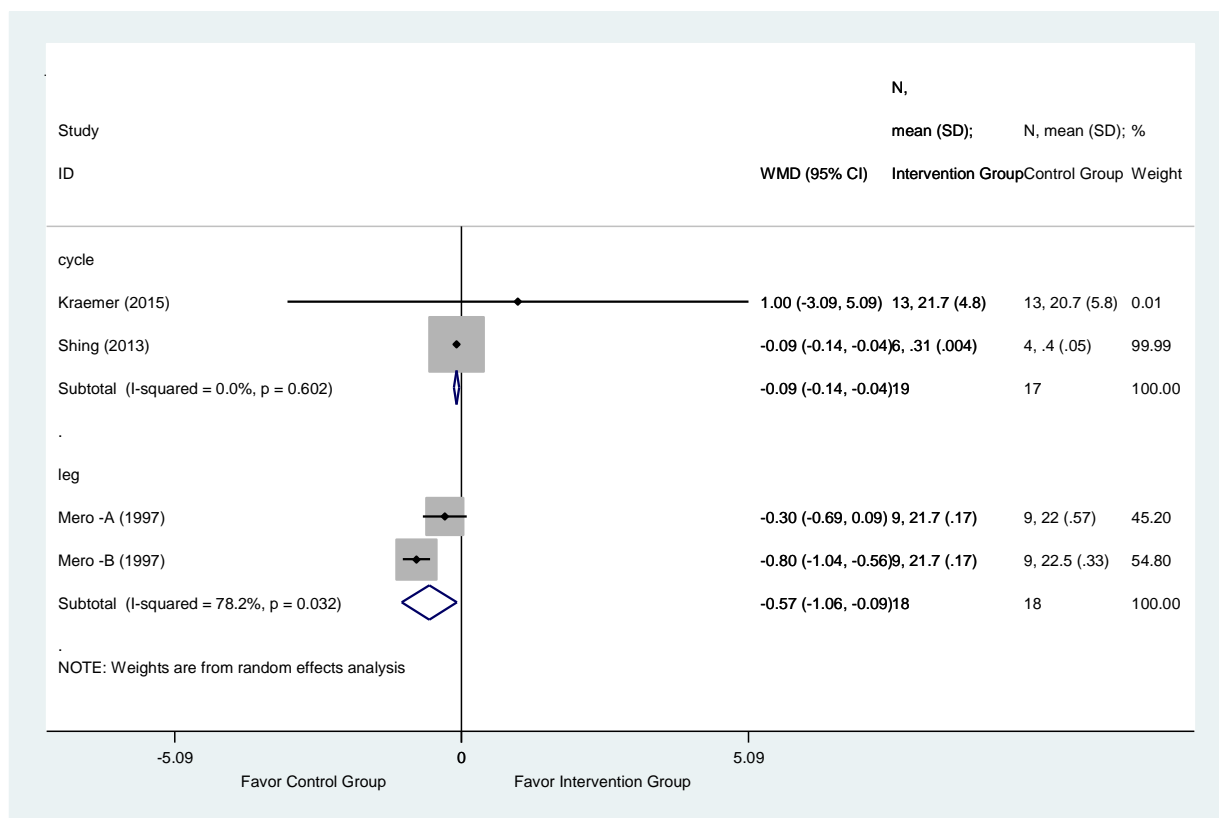


Mero -A (1997) = WP vs 125-ml Bioenervi

- ## Subgroup by intervention period range (day)

```
            Study      |    WMD    [95% Conf. Interval]
--------------------+----------------------------------------------------
       41-60
Kraemer (2015)         |    1.000    -3.093     5.093
Mero -A (1997)         |   -0.300    -0.689     0.089
Mero -B (1997)         |   -0.800    -1.043    -0.557
Shing (2013)           |   -0.090    -0.139    -0.041
 Sub-total             |
  D+L pooled WMD       |   -0.373    -0.860     0.115
--------------------+----------------------------------------------------

Test(s) of heterogeneity:
              Heterogeneity  degrees of
                 statistic     freedom      P     I-squared**   Tau-squared

41-60               32.75         3        0.000     90.8%         0.1708
** I-squared: the variation in WMD attributable to heterogeneity)


Significance test(s) of WMD=0

41-60                   z=  1.50     p = 0.134
```
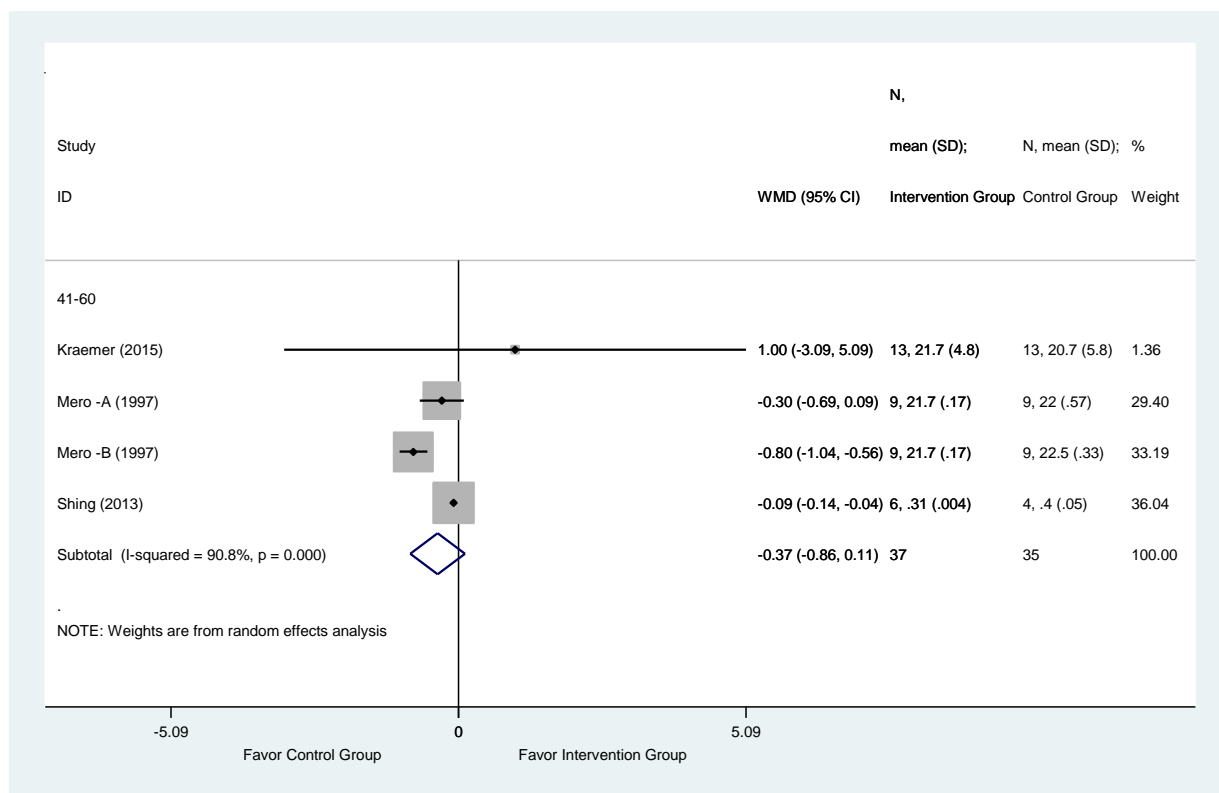


Mero -A (1997) = WP vs 125-ml Bioenervi
Mero -B (1997) = WP vs 25-ml Bioenervi