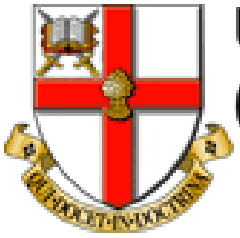

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The effects of magnesium supplementation on muscle strength and body composition: a review of the literature.

Declaration

I hereby declare that I am the legitimate author of this assignment and that it is my original work.

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Table of contents (literature review)

List of abbreviations

Magnesium ..... Mg

Serum Total Magnesium ..... TMg

Erythrocyte Magnesium ..... EMg

Ionic Magnesium ..... iMg

Adenosine Tri-Phosphate ..... ATP

Recommended Daily Allowance ..... RDA

Tolerable Upper Limit ..... TUL

Zinc Magnesium Aspartate ..... ZMA

Leutinising Hormone ..... LH

Insulin-like Growth Factor-1 ..... IGF-1

American College of Sports Medicine ..... ACSM

Fat Free Mass ..... FFM

Lean Body Mass ..... LBM

Abstract

Magnesium plays key roles in several vital reactions within the body, with the roles played in energy production and protein synthesis suggesting a link with muscle strength. Magnesium intake is considered sub-optimal in western populations with certain individuals possibly being predisposed to hypomagnesemia. The determination of magnesium status can be conducted through various methodologies with some considered as being more reflective than others. Magnesium supplementation can be utilised as a method to correct deficiencies, with certain studies suggesting strength augmentations and alterations in body composition as a result. The purpose of this article is to review some of the suggested physiological roles of magnesium, the various options for uncovering whole body status, as well as any possible benefits of supplementation.

Keywords: intake, physiology, whole body status, performance

Introduction

Magnesium (Mg) is a trace mineral and a co-factor for over 300 enzymatic reactions, involved in cellular energy production and storage, protein synthesis cell-growth and reproduction, maintenance of cellular electrolyte composition and stabilisation of mitochondrial membranes (Newhouse & Finstad, 2000). Subsequently Mg is involved in numerous body functions including those controlling neuromuscular transmission, cardiac excitability and vasomotor tone and blood pressure (Altura, 1991). The adult human body contains around 25g of Mg, of which; 50-60% is located within hydroxyl-apatite of the bony skeleton, whereas the rest can mostly be found within muscles and soft tissues with only 1% being present in extracellular fluids (Aikawa, 1981).

The term ‘muscle strength’ was introduced as a medical subject heading (MeSH) term in the PubMed database in 2007; where it is defined as the amount of force generated by muscular contraction (Saey & Toosters, 2008). Muscle strength in different populations is considered an indicator of nutritional status and a suitable predictor of decreased osteoporotic fracture, disability and mortality in both middle-aged and elderly (Rantanen et al., 2000, cited in Moslehi, Vafa, Sarrafzadeh and Foroushani, 2013). Furthermore, studies have also related low levels of muscle strength with an independently increased risk for metabolic syndrome irrespective of age, body size, insulin resistance and central obesity (Jurca et al., 2005). Similarly, increased physical activity has been directly correlated with increased muscle mass (improved body composition) and muscle

strength (Sandler et al., 1991, and Urdiales et al., 2010) and consequently could lead to strength and body composition associated benefits. Body composition can be divided into 2 compartments; either fat-free mass (FFM) and fat or Lean Body Mass (LBM) and lipid. The difference between the 2 classifications is that FFM includes essential fat whereas LBM does not. The difference arises due to the different ways of measuring body composition where measurement through the use of calipers measure FFM and Hydrostatic weighing measures LBM. However, Wang, Piersen and Heymsfield (1992) suggested that due to the minor contribution of essential fat, the terms FFM and LBM, could be used interchangeably.

Magnesium physiology

Mg homeostasis is tightly regulated by the intestines and kidneys, increasing absorption or reabsorption during a deficient period, and increasing excretion during periods of excess, while the skeleton acts as an intrinsic storage for the mineral to buffer acute changes in extracellular Mg levels (Favus, Bushinsky & Lemann, 2006). Of the Mg content of bone (15g), a third (5g) is considered as being readily available to act as a buffer for extracellular hypomagnesemia (Alfrey & Miller, 1973).

Increased levels of physical activity specifically: sustained moderate exercise (Stendig-Lindberg, Shapiro, Tepperberg & Moran, 1999) and short-term high intensity exercise (Meludu et al., 2001) result in a mobilisation of Mg towards

muscle and adipocytes, leading to a transient decrease in serum magnesium (cited in Nielsen & Lukaski, 2006). Synergistically, a study conducted on 13 male athletes performing short-term, high-intensity anaerobic exercise (> 90% $\dot{V}O_{2\,max}$) uncovered that more than 85% of the transient decrease in plasma Mg during exercise could be accounted for by the transient increase in anaerobic metabolism (Deuster, Dolev, Kyle, Anderson & Schoomaker, 1987), as observed through an increase in blood lactate concentration ($r=0.68$, $p<0.01$). Such a metabolic shift precipitates into re-mobilisation of Mg to the plasma from bones, soft-tissues, muscles and adipocytes, following exercise in order to restore plasma pre-exercise Mg levels (Nielsen & Lukaski, 2006). Subsequently, this allows plasma Mg to return to pre-exercise values within 120 minutes, however, urinary excretion of Mg remains elevated by 21% for 24 hours following exercise.

This observation was also seen in Deuster et al (1987) who uncovered significant increases in Mg urinary excretion on the day of exercise (131.5 ± 6.8mg/day) when compared to non-exercise days (108 ± 6.6 mg/day). The authors ultimately postulated that the percentage contribution of anaerobic metabolism to total energy expenditure is positively correlated with the inter-compartmental shift in Mg. Ultimately, this is suggestive that while exercise and muscle strength might be correlated through Mg, higher exercise levels require higher intakes of Mg in order to support the translation into increased muscle strength.

In turn, the roles of Mg in oxygen uptake, energy production and electrolyte balance, further underline the link between Mg and exercise as Mg deficiency has been purported to increase exercise related oxygen requirements, while decreasing adenosine tri-phosphate (ATP) production, leading to decreased efficiency and an attenuation in exercise performance (Lukaski & Nielsen, 2002).

Alcoholism is recognised as the most common cause of disturbed magnesium balance (Galanter, 2013). In fact, increased alcohol intake increases the risk for hypomagnesemia through decreasing intestinal Mg absorption while also acutely stimulating increasing Mg excretion up to 167 to 260% compared to control subjects (Sarai, Tejai, Chan, Kuo, & Li, 2013). Consequently, the increased excretion predisposes chronic alcoholics, to have decreased Mg status as uncovered by lower muscle Mg levels (Jermain, Drimset, & Drisbet, 1992).

Magnesium status

Mg status is generally measured through testing for total Mg (TMg) in serum or plasma and is considered adequate when TMg ranges between 17-23 µg/ml for adults over 17 years of age (Mayo Medical Laboratories, 2015). However, this test in isolation is not necessarily reflective of whole body nutriture (Newhouse and Finstad, 2000), due to the fact that only 1% of total body magnesium is present in the blood of which 0.7% can be found in erythrocytes (EMg) and only 0.3%, within the serum (Fawcett, Haxby & Male, 1999). Furthermore, serum Mg is categorised into three: free/ionised (iMg), bound to proteins, or complexed with

anions such as phosphate, bicarbonate, citrate or sulphate (Maguire & Cowan, 2002). However of all the 3 components within serum, iMg is known to be the most bioactive and is consequently considered to be more representative than TMg (Altura et al., 1994). Comparatively, TMg and EMg are not seriously impacted until severely hypomagnesemic (Altura et al., 1994). This is directly in line with; Galanter (2013), who argued that while serum Mg demonstrates hypomagnesemia in only 25-50% of alcoholics, Mg retention following parenteral Mg administration in alcoholic indicate that the condition is much more prevalent and subsequently, the sole utilisation of TMg is not optimally indicative of total body Mg status.

However, while testing for iMg might be more indicative, the hemodynamic equilibrium aspect of such a component implies accounting for several variables in order to obtain representative results (Newhouse, Johnson, Montelpare & McAuliffe, 2002). In fact recommendations for the test include conducting it in a fasted, non-exercised state, first thing in the morning (Fraser & Harris, 1989).

However, measuring Mg status through iMg also has its downsides. While iMg proved to be more sensitive at reflecting increased Mg intakes through supplementation (4 weeks of 212mg/day Mg oxide), iMg status between baseline and pre-test also varied significantly resulting in a number of participants of previously low status becoming normal (Finstad et al., 2001). The authors ultimately postulated that although the variability in iMg status over time could be due to increased nutritional status awareness within subjects, the physiological

perturbations which could alter iMg status must be researched further to allow the assessment, classification and diagnosis of Mg status through this assay.

Other measurements of Mg status include hair analysis. Hair analysis can be utilised to measure concentration of trace minerals and it is reflective of mineral status over longer time frames, potentially years (Bass, Hickok, Quig & Urek, 2001). Consequently, the authors of this review concluded that hair analysis might be more reflective of long-term trace mineral status in comparison with other analytical methods. However, a review of the method uncovered significant inter-laboratory variation and concluded that standardisation of testing protocols would be paramount to improving inter-laboratory comparability (Seidel, Kreutzer, Smith, McNeel & Gilliss, 2001).

Ultimately, Holm and Jespen ((1987) argue that adequate Mg status could be verified by Mg loading and a subsequent urinalysis. Consequently, Newhouse and Finstad (2000) conclude that in order for the analysis of Mg status to optimally reflect whole body Mg status, an iMg test validated by Mg loading and subsequent 24 hour urinalysis should be undertaken.

Dietary sources and recommended intakes

Magnesium can be found in a variety of plant and animal sources namely; nuts, wholegrains, fish and seafood and also several vegetables, legumes berries and

bananas while Recommended Daily Allowances (RDAs) for Mg in adults stand at 400 and 310 mg/day, respectively, for males and females aged 19-30 years (EFSA, 2015). Also, high intakes of alcohol, fibre and calcium (>2600mg/day), and low protein intakes (<30g/day) were found to negatively impact Mg absorption and retention through phosphate binding, competitive inhibition and increased renal excretion, respectively. Additionally poor Mg status was also a predictor for hypocalcaemia and hypovitaminosis D (FNB, 2006).

Supplementation

Mg status can also be effected through supplementation. Oral Mg supplementation can be utilised and it is present as several salts and chelates including: oxide, chloride and citrate. Following a comparison of different oral magnesium supplements for bioavailability, similarly high bioavailabilities were uncovered for Mg contained in Mg citrate (50%) and chloride preparations, when compared with Mg oxide (4%) (Firoz & Graber, 2001). Additionally, some studies state that soluble preparations tend to be better absorbed than capsulated ones (Ranande & Somberg, 2001).

However, while oral Mg supplementation is possible, successful remineralisation through this method could take a long time depending on the form of Mg utilised (Ford, 1999). Contributing factors to this include the absorption physiology of oral Mg; being absorbed largely in the small bowel by a combination of passive diffusion and saturable active transport mechanisms, suggesting; limited

absorption rates and increased risk of adverse effects such as osmotic retention in the colon, leading to diarrhoea, as dosages of Mg increase (Graham, Caesar & Burgen, 1960, cited in Quamme, 2008). Subsequently, in view of the increased risk for possible associated effects of high doses, Tolerable Upper Limits (TULs) for supplemental Mg have been established. TULs stand at 350 mg of supplemental Mg/day for adults of both genders (Institute of Medicine, 1997).

Alternatively, in view of the many interferences to oral supplementation, topical and transdermal supplementation of Mg might be considered, through the utilisation of a variety of solutions, creams and bath salts (Nica et al., 2015). The authors of a pilot study (9 participants: 2 males, 7 females, aged 22-69 years; mean age 48.5 years) utilised a 12 week application of a 31% Mg chloride solution through 20 sprays/day and a 20 minute foot soak with 100ml oil twice weekly and uncovered an increase in Mg levels between 2-262% (calculated through hair analysis) in 8 of 9 participants, one of which stopped the application at 2 weeks prior testing (Watkins & Josling, 2010). An average increase of 59.7% in Mg levels was observed in this study, and it was compared to the effects of 9-24 months of oral Mg supplementation in Nica et al. (2015).

Dietary intake

However, prior to suggesting supplementation, a rigorous assessment regarding present intake should be conducted. Almost half (48%) of the US population was found to be consuming less than the RDA in 2005-2006 (Rosanoff, Weaver &

Rude, 2012). Concomitantly, in an analysis of 24-h dietary recall data of 4257 participants (age > 20 years) from the National Health and Nutrition Examination Survey (1999-2000) in the US, median and mean intakes for all the different ethnic groups, were all undistinctively found to be below RDA levels of Mg; with the highest mean daily Mg intake being in Caucasian men (352 mg), and the lowest mean daily Mg intake in African American men (278 mg) (Ford & Mokdad, 2003). In the same study, females were also found to be having magnesium deficient diets with Caucasian women having mean Mg intakes of 256 mg/day and Mg intakes for African American women standing at 202 mg/day. Upon analysis of a 7-day food record, populations in other developed countries (France), were found to have even lower intakes of Mg with 71.7% of French males aged between 15-92 years not meeting daily RDA for Mg (Touvier et al., 2006).

Additionally with regards to physically active individuals increased excretory losses observed following acute bouts of physical activity may be suggestive of increased requirements (Buchman et al., 1998). Furthermore, Lukaski (2000) reported decreased intakes (< 69%) in athletes participating in certain sports including basketball, soccer and gymnastics. Similarly, Santos et al. (2011) following an analysis of dietary intakes in 26, male elite volleyball, handball and basketball players uncovered that Mg intakes varied between 42-80% of RDA (mean ± SD: 244.7 ± 78.8 mg/day) indicating marginal deficiency.

Furthermore, given dietary Mg is positively correlated with increased energy intake; voluntary food restriction, and certain food choices, coupled with high levels of physical activity, as practiced in certain sports, linked with varying degrees of aesthetic appearance (such as; gymnastics, dancing, wrestling and bodybuilding), could lead to increased risk of low dietary intakes and effectively hypomagnesemia (Lukaski, 2000).

Wolinsky 1997 reported Mg intakes for strength athletes specifically: American Football players, weightlifters and bodybuilders. Data is available for pre-competition, competition and post-competition seasons in female bodybuilders and for pre-competition and competition season in male bodybuilders (Table 1). Bodybuilders achieve low body fat levels for competition through a combination of dietary manipulation and increased exercise volumes (Helms, Aragon & Fitschen, 2014). Furthermore, Wolinsky (1997) also reported dietary Mg intakes for weightlifters at amateur and elite levels. As observed (Table 1) Mg intakes are very close to RDA levels for female bodybuilders, especially in competition season. The trend of female athletes having close to RDA or lower intakes of has been observed even in other sport disciplines and was attributed, at least in part, to women having lower overall energy intakes and possibly making different food choices (Lukaski, 2000).

Subsequently, given that exercise was uncovered to increase Mg turnover (Deuster, 1987), pre-competition Mg intake in female bodybuilders would be

considered sub-optimal. The increase in Mg during competition might be attributed to an alteration in food choices. In turn, Bazzarre et al. (1993) reported that 100% of female athletes use mineral-vitamin supplements compared to only 51% of male athletes.

Table 1: Summary of dietary Mg intakes in Bodybuilders, Weightlifters and American Football Players.

	Males	Females
	Bodybuilders	Bodybuilders
	Magnesium (mg/day)	Magnesium (mg/day)
Pre-Competition	631	276
Competition	569	314
Post-Competition	/	341
	Weightlifters	
Elite level	777	
Amateur level	374	
	American Football	
	558	

Adapted from: 'Nutrition and Strength' by Wolinsky, I., 1997, *Nutrition in Exercise and Sport* (3rd ed.), p. 382-383.

Magnesium, strength and body composition

Dominquez et al. (2006) analysed data from the InCHIANTI study, encompassing around 1138 elderly subjects (mean ± SD age: 66.7 ± 15.2 years). The authors uncovered that total serum Mg was positively correlated with different measures of muscle strength, specifically; grip strength ($p = 0.0002$), lower-leg muscle power ($p = 0.0001$), knee extension torque ($p = 0.0001$), and ankle extension strength ($p = 0.0001$). A similar study was conducted by Santos et al (2011) analysing the correlation between dietary Mg intake and strength in 26 male professional volleyball, basketball and handball players. The authors reported significant correlation between daily Mg intake and trunk flexion ($p = 0.025$), squat jump ($p = 0.02$), counter-movement jump Abalakov ($p = 0.012$), and peak torque measurements for both extension and flexion ($p < 0.02$). Furthermore, strength measurements were still significant following adjustments for energy intakes: trunk flexion ($p = 0.028$), handgrip ($p = 0.027$), peak torque $180^{o}{}_{\text{extension}}$ ($p < 0.001$) and peak torque $180^{o}{}_{\text{flexion}}$ ($p < 0.001$). Also, in a study by Poikolainen and Alho (2008), encompassing alcoholics (n = 118, 81 males, 37 females; aged 20-64 years), the subjects were found to have lower than average strength levels (analysed through handgrip strength) in comparison with age-matched reference values, published by the Institute for Occupational Health in Finland. Subsequently, the decreased strength levels could be directly correlated with the limitations presented by low Mg levels, present in this population (Jermain et al., 1992), and in turn an increase in Mg intake, coupled with a decrease in alcohol intake, could assist in reversing decreased muscle Mg levels and strength.

Lukaski and Nielsen (2002) conducted a 3 month depletion-repletion Mg study, with 312mg/day the first month, to stabilise Mg status, then 112mg/day of Mg the second month to deplete Mg, and a repletion with 312mg/day of Mg. Exercise included cycling at increasing intensities until 80% max heart rate was reached. The researchers uncovered that, when in a Mg depleted state; 80% max heart rate was reached at lower intensities, while, peak oxygen uptake, total cumulative net oxygen utilisation and heart rate were elevated for a given workload. The effects were directly correlated with the extent of Mg depletion while Mg repletion allowed a gradual return of the aforementioned variables to pre-depletion values.

Brilla & Haley (1992) analysed whether supplementing additional Mg (261 mg/day) (total of 8 mg/kg bodyweight/day) would warrant more strength improvement compared to individuals who were consuming around 246 mg/day (70% RDA) through diet and placebo. Both groups also conducted leg strength training exercise of 3 sets of 10 repetitions, 3 times per week. In this study, the participants who supplemented with Mg experienced significantly greater leg strength gains than those in the control group. The authors concluded that Mg coupled with strength exercise, may potentiate greater strength gains through an increase in protein synthesis which would in turn enable a faster increase in muscle protein density, in previously untrained individuals. The increase in protein density would subsequently enable higher numbers of actin-myosin bridges, resulting in greater force production and ultimately higher strength levels (Rude & Singer, 1981).

However, while the above studies support the claim that sub-RDA Mg intakes could negatively impact improvements in strength performance, evidence to support a benefit in adding supplemental Mg to a non-Mg deficient diet on strength is lacking. A study conducted by Brilla and Conte (2000) supplemented American football players (n=57) with either a daily dose of Zinc Magnesium Aspartate (ZMA; 30 mg zinc, 450 mg Mg and 10.5 mg vitamin B_6) or a placebo for 8 weeks. There were no intra-group differences prior to the trial and mean group results (TMg) indicate adequate zinc and Mg status. Both groups increased in strength however, the ZMA group experienced higher strength increases measured by a dynamometer. Two other studies (Wilborn et al., 2004, and Moezzi, Peeri & Homaei, 2013) attempted to replicate these results in trained and untrained populations, with no significant effect for ZMA on strength levels, compared to placebo.

Subsequently, following an analysis of the results in Deuster et al (1987) and other studies, Nielsen and Lukaski (2006) stated that the increased excretion of Mg in sweat and urine, justifies Mg requirements for exercising populations standing at 10-20% higher than those for statistically-matched sedentary individuals. Alternatively, these conclusions are directly in contrast with those of Newhouse and Finstad (2000), who; following a systematic review of the literature, observed that magnesium supplementation failed to augment exercise performance in trained populations. The authors suggested that Mg might work by addressing a weak link in the physiology of untrained subjects, while previous training would have already strengthened this weak link in trained athletes.

Following the theory of Brilla and Haley (1992) where Mg was theorised to play a role in protein synthesis; protein turnover was found to be lower in trained versus untrained ($p < 0.01$) individuals following resistance exercise (Phillips, Tipton, Ferrando & Wolfe, 1999). Subsequently, the observed reduced rate of protein breakdown following resistance exercise in trained subjects could indicate decreased Mg requirements in trained populations. Concomitantly, the transient increase in muscle Mg during exercise related with compartmental shifting could sufficiently act to negate the need for additional Mg in supporting exercise performance in trained populations (Newhouse & Finstad, 2000).

Magnesium, anabolic hormones and antioxidant capacity

Testosterone is an anabolic steroid hormone, and released by a cascade mechanism, following the pulsatile release of Leutinising Hormone (LH). Testosterone carriage within the blood generally consists of 53% free testosterone (95% of which is bound to albumin) and 47% bound to Sex-Hormone Binding Globulin (SHGB), which is considered biologically inert (Stanworth & Jones, 2008).

Mg was suggested to potentiate strength augmentations through modulating anabolic hormones, specifically testosterone and insulin-like growth factor-1 (IGF-1). Excoffon, Guillaume, Woronoff-Lemsi and Andre (2009), uncovered that Mg in biological concentrations, acts as an uncompetitive inhibitor to testosterone binding, increasing free testosterone within the body. This was supported by the

study of Brilla and Conte (2000) were the ZMA supplemented group exhibited increases in testosterone and also in IGF-1 which translated into strength augmentations. However, this increase in anabolic hormones was not replicable in 3 other studies supplementing with ZMA (Wilborn et al., 2004, Koehler et al., 2009, and Moezzi, Peeri & Homaei, 2013).

The American College of Sports Medicine (ACSM, 2006) states that; testosterone, whether endogenous or exogenous in origin, creates advantages in sport, implying an impact on strength levels. Similarly, chronically higher levels of endogenous testosterone in older men (70+ years) have been linked with lower BMI, lower fat mass index and higher strength and power levels but not increased lean body mass (Orwoll et. al., 2006). Natural variations in testosterone levels are believed to lead to an athletic advantage in the athletic world, as observed by the International Association of Athletics Federation banning women with testosterone levels > 10 nmol/L from competing (Karkazis, Jordan-Young, Davis & Camporesi, 2012).

However, elevated resting testosterone for athletes, has been reported in some studies (Cinar, Polat, Baltaci, & Mogulkoc, 2011) but not in others (Kraemer & Ratamess, 2005). Following studies; Athiainen, Pakarinen, Alen, Kraemer, and Hakkinen (2003), and Kraemer et al (unpublished), observed an increase and a no change in free and total testosterone, following 7 and 2 weeks of high volume training, respectively, whereas testosterone levels decreased following a

decreased volume, high intensity training period (cited in Kraemer & Ratamess, 2005). Similarly, a decrease in free testosterone (12%) was observed during 2 weeks heavy training (Raastad, Glomsheller, Bjoro & Hallen, 2001), possibly due to a decrease in secretion of Leutinizing Hormone (LH) (Nindl et al., 2001). Subsequently, while increased Mg intake could be positively correlated with testosterone levels, exercise could also potentially modulate testosterone levels.

Furthermore, Mg status has also been strongly and independently associated with serum IGF-1, and total testosterone levels in older (65+ years) men (Maggio et al., 2011). IGF-1 is considered another anabolic hormone of importance, given its role in the mediation of growth, cellular transformation and regeneration, as well as immune function, musculoskeletal development (Yakar, Wu, Setsen & Rosen, 2002). IGF-1, exerts an anabolic action similar to insulin by increasing amino acid uptake and stimulating protein synthesis, while suppressing protein degradation, directly contributing to skeletal muscle hypertrophy (Yarasheski, 1994, cited in Ratzin-Jackson, 2000). Alternatively, rather than increased circulating IGF-1 contributing to increments in strength and muscle mass, hypertrophy itself is what leads to increased IGF-1 expression within skeletal muscle, via the mobilisation of satellite cells during the remodelling process (Ratzin-Jackson, 2000). Similarly, Stewart and Pell (2010) uncovered that IGFs contribute to myofibrillar protein accretion and satellite cell proliferation, differentiation, survival and recruitment, ultimately leading to fibre hypertrophy. Furthermore, IGF-1 within muscle has been shown to activate quiescent satellite cells and also act as an anabolic factor for differentiated muscle fibres

(Jacquemin, Furling, Bigot, Butler-Browne & Mouly, 2004). Subsequently, through increasing of IGF-1, increased Mg intakes could be positively correlated with an increase in lean body mass.

Similarly, athletes performing resistance-training for >13 weeks were found to have 20% higher IGF-1 levels than their untrained counterparts (Borst et. al., 2001). An acute rise in IGF-1 (13-26%) was also reported following 10 minutes after the initiation of high-intensity exercise however, IGF-1 levels were unchanged exactly after or in the 24 hours following exercise (Jenkins, 1999). Alternatively, a chronic decrease in IGF-1 (11%) was reported during a period of training intensity or volume overreaching (Raastad et al., 2001).

Furthermore, Mg also plays an active role in decreasing oxidative stress within the human body (Dickens et al., 1992, cited in Maggio et al., 2011). Demirbag et al. (2005) uncovered that while total antioxidant capacity is positively correlated with endogenous testosterone and IGF-1 levels, the respective concentrations of anabolic hormones decrease after exposure to stress. Consequently, Maggio et al. (2011) proposed that Mg, through its antioxidant capacity, aids in the downregulation of oxidative stress, attenuating stress related decreases in anabolic hormone levels. Both aerobic and nonaerobic exercise have been classified as contributors to oxidative stress (Alessio et al., 2000). Consequently, Mg, through its antioxidant capacity, could contribute to a decrease in exercise associated oxidative stress, attenuating the related downregulation of anabolic

hormones. This might be especially useful during periods of training intensity or volume overloading such as those reported in Raastad et al. (2001), which downregulated anabolic hormone production, specifically free testosterone (-12%) and IGF-1 (11%) and consequently could potentially lead to decreased exercise performance. Therefore, higher Mg intakes for athletes, could serve as a warrant to enable athletes to tolerate higher exercise volumes and consequently, increase exercise performance.

Conclusion

Muscular strength has been independently correlated with longevity and increased quality of life. Similarly, adequate Mg status has been associated with muscular strength in some studies, but not in others. Population studies suggest that a considerable amount of the population exhibits marginal Mg deficiency as exhibited by suboptimal Mg intakes. Therefore, improving Mg status could directly imply decreasing the risk for the eventualities associated with decreased muscular strength and consequently, improving health and longevity. Several studies have concluded that Mg, through its roles in improving anabolic hormone profiles and increased antioxidant capacity, could augment strength performance while improving body composition and therefore, prove especially useful to exercising populations who require frequent high energy outputs and exhibit increased oxidative stress (Alves et al., 2012, Prasad et al., 1996, Maret & Sandstead, 2006, Lukaski & Nielsen, 2002). Furthermore, while increased food intake generally observed in athletes, could warrant increased Mg intakes, given

adequate food choices, studies analysing Mg intakes of athletes report that a considerable proportion demonstrate Mg intakes lower than RDA. Subsequently, athletes exhibiting increased physical activity and decreased food intake, might be at a higher risk of deficiencies of these minerals (Lukaski, 2000).

Mg supplementation is an available option for those opting to increase intake of the respective mineral. Supplementation is available through various forms, ranging from oral supplements to soluble powders and topical solutions. Alternatively, while several supplemental options are available, their efficacy at raising Mg status, as assessed by common measurements of Mg status, varies for different forms and different compounds. Alternatively, given the fluctuating physiology of Mg amongst different body pools, the adequacy of the single use of any present method at determining Mg status has been questioned by several authors. Subsequently, numerous authors suggest the adoption of two or more measurements of Mg status to improve the reflection on whole body nutriture.

In turn, based on present observations, some authors have reported that Mg physiology suggests increased requirements for populations undertaking regular bouts of physical activity at high intensities and training volumes, as justified by the increased utilisation and excretion of the mineral (Nielsen & Lukaski, 2006, McDonald & Keen, 1988). This is directly in contrast with suggestions made by other authors (Newhouse and Finstad, 2000); who argued that while increased

Mg intake may benefit untrained individuals, physiological remodelling in trained populations could negate the requirement for increased Mg intake.

Subsequently, while supplementation has been provided as an option for populations not meeting adequate intakes of the mineral, given the positive link with Mg status, could potentially lead to strength increments. However, the evidence regarding the link is inconsistent. Consequently a systematic review; examining present literature could assist in analysing the possibility of a correlation between Mg supplementation and muscle strength, while underlining any existing confounding variables and gaps in the literature, and making suggestions for future research.

References

Aikawa, J.K. (1981). *Magnesium: Its Biological Significance*. Florida: CRC Press

Alessio, H.M., Hagerman, A.E., Fulkerson, B.K., Ambrose, J., Rice, R.E., & Wiley, R.L. (2000). Generation of reactive oxygen species after exhaustive aerobic and isometric exercise. *Medicine and Science in Sports and Exercise, 32(9), 1576-1581.* DOI: 10.1097/00005768-200009000-00008

Alfrey, A.C., & Miller, N.L. (1973). Bone magnesium pools in uremia. *Journal of Clinical Investigations,* 52, 3019-3027.

Altura, B.M. (1991). Basic biochemistry and physiology of magnesium: A brief review. *Magnesium and Trace Elements,* 10, 167-171.

Altura, B.T., Shirey, T.L., Young, C.C., Dellorfano, K., Hiti, J., … Altura, B.M. (1994). Characterization of a new ion selective electrode for ionised magnesium in whole blood, plasma, serum and aqueous samples. *Scandinavian Journal of Clinical and Laboratory Investigation 54*(217), 21-36. doi: 10.3109/00365519409095208

American College of Sports Medicine. (2006). Position Statement: *Senate Hearing on the Abuse of Anabolic Steroids and their precursors by adolescent athletes*.

Athiainen, J.P., Pakarinen, A., Alen, M., Kraemer, W.J., & Hakkinen, K. (2003). Muscle hypertrophy, hormonal adaptations and strength development during

strength training in strength-trained and untrained men. *European Journal of Applied Physiology, Aug 89*(6), 555-563. PMID: 12734759.

Bass, D.A., Hickok, D., Quig, D., & Urek, K. (2001). Trace element analysis in hairL factors determining accuracy, precision and reliability. *Alternative Medicine Review, 6*(5), 472-481.

Bazzarre, T.L., Scarpino, A., Sigmon, R., Marquart, L.F., Wu, S.M., & Izurieta, M. (1993). Vitamin-mineral supplement use and nutritional status of athletes. *Journal of American College of Nutrition, Apr 12*(2), 162-169. PMID: 8463514.

Bhasin, S. Woodhouse, L., Casaburi, R., Singh, A.B., Bhasin, D., … Storer, T.W. (2001). Testosterone dose-response relationships in healthy young men. *American Journal of Physiology Endocrinology and Metabolism 281*(6), E1172-81.

Borst, S.E., De Hoyos, D.V., Garzarella, L., Vincent, K., Pollock, B.H., Lowenthal, D.T., & Pollock, M.L. (2001). Effects of resistance training on insulin-like growth factor-1 and IGF binding proteins. *Medicine and Science in Sports and Exercise 33*(4), 648-653. PMID: 11283443

Brilla, L.R., & Conte, V. (2000). Effects of a novel zinc-magnesium formulation on hormones and strength. *Journal of Exercise Physiology, 3*(4), 26-36.

Brilla, L.R., & Haley, T.F. (1992). Effect of magnesium supplementation on strength training in humans. *Journal of the American College of Nutrition, 11*(3), 326-329. PMID: 1619184.

Buchman, A.L., Keen, C., Commisso, J., Killip, D., Ou, C., … Dunn, J.K. (1998). The effect of a marathon run on plasma and urine mineral and metal concentrations. *Journal of the American College of Nutrition,* 17, 124-127.

Cinar, V., Polat, Y., Baltaci, A.K., & Mogulkoc, R. (2011). Effects of magnesium supplementation on testosterone levels of athletes and sedentary subjects at rest and after exhaustion. *Biological Trace Elements Research,* 140, 18-23. doi: 10.1007/s12011-010-8676-3.

Clemmons, D.R. (2004). The relative roles of growth hormone and IGf-1 in controlling insulin sensitivity. *Journal of Clinical Investigations, Jan1; 113*(1), 25-27. doi: 10.1172/JCI200420660

Dabbs, J.M. (1990). Salivary testosterone measurements: reliability across hours, days, and weeks. *Physiology and Behaviour, Jul 48*(1), 83-86. PMID: 2236282.

Dabbs, J.M., & de la Rue, D. (1991). Salivary testosterone measurements among women: relative magnitude of circadian and menstrual cycles. *Hormone Research, 35*(5), 182-184. PMID: 1802820.

Demirbag, R., Yilmaz, R., & Erel, O., (2005). The association of total antioxidant capacity with sex hormones. *Scandinavian Cardiovascular Journal, 39*(3), 172-176. doi: 10.1080/14017430510035862

Deuster, P.A., Dolev, E., Kyle, S.B., Anderson, R.A., & Schoomaker, E.B. (1987). Magnesium homeostasis during high-intensity anaerobic exercise in men. *Journal of Applied Physiology, 62*(2), 545-550. PMID: 3553215.

Dominquez, L.J., Barbagallo, M., Lauretani, F., Bandinelli, S., Bos, A., … Ferrucci, L. (2006). Magnesium and muscle performance in older persons: the InCHIANTI study. *American Journal of Clinical Nutrition 84*(2), 419-426. PMID: 168955893.

Eisinger, J., & Dagorn, J. (1986). Vitamin B6 and magnesium. *Magnesium* 5(1), 27-32. PMID: 3959594.

Elis, S., Wu, Y., Courtland, H.W., Cannata, D., Sun, H., … Yakar, S. (2011). Unbound (bioavailable) IGF1 enhances somatic growth. *Diseases Models and Mechanics, Sep 4*(5), 649-658. doi:10.1242/dmm.006775

European Food Safety Authority. (2015). Scientific opinion on dietary reference values for magnesium. *EFSA Journal, 13*(7): 4186, 1-63. doi:10.2903/j.efsa.2015.4186. Retrieved from: www.efsa.europa.eu/efsajournal

Excoffon, L., Guillaume, Y.C., Woronoff-Lemsi, M.C., & Andre, C. (2009). Magnesium effect on testosterone-SHBG association studied by a novel molecular chromatography approach. *Journal of Pharmaceutical and Biomedical Analysis*, 49, 175-180.

Favus, M.J., Bushinsky, D.A., & Lemann, J. (2006). Regulation of calcium, magnesium, and phosphate metabolism. In: American Society for Bone and Mineral Research (Ed.), *Primer on the metabolic bone diseases and disorders of mineral metabolism* (6th ed., pp. 76-83.). Washington DC, U.S.A: Retrieved from: http://www.homepages.ucl.ac.uk

Fawcett, W.J., Haxby, E.J., & Male, D.A. (1999). Magnesium: Physiology and pharmacology. *British Journal of Anaestesiology,* 83, 302-320.

Firoz, M., & Graber, M. (2001). Bioavailability of US commercial magnesium preparations. *Magnesium Research, Dec* 14(4), 257-262. PMID: 11794633.

Food and Nutrition Board. (2006). *Dietary reference intakes: The essential guide to nutrient requirements.* National Academies Press: Washington DC. Retrieved from: http://www.nap.edu

Ford, E.S. (1999). Serum magnesium and ischemic heart disease: findings from a national sample of US adults. *International Epidemiological Association,* 28, 645-651.

Ford, E.S., & Mokdad, A.H. (2003). Dietary magnesium intake in a national sample of US adults. *The Journal of Nutrition, Sep 133*(9), 2879-2882.

Fraser, C.G., & Harris, E.K. (1989). Generation and application of data on biological variation in clinical chemistry. *Critical Reviews in Clinical Laboratory Sciences,* 27, 409-437.

Galanter, M. (2013). *Recent developments in alcoholism: Combined alcohol and drug abuse typologies of alcoholics, the withdrawal syndrome renal and electrolyte consequences*. Springer Science and Business Media: Boston, U.S.A.

Helms, E.R., Aragon, A., & Fitschen, P.J. (2014). Evidence-based recommendation for natural bodybuilding contest-preparation: nutrition and

supplementation. *Journal of the International Society of Sports Nutrition 11*(20). doi:10.1186/1550-2783-11-20

Institute of Medicine (IOM) (1997). Food and Nutrition Board. *Dietary Reference Intakes: Calcium, Phosphorus, Magnesium, Vitamin D and Fluoride.* Washington, DC: National AcademyPress.

Jacquemin, V., Furling, D., Bigot, A., Butler-Browne, G.S., & Mouly, V. (2004). IGF-1 induces human myotube hypertrophy by increasing cell recruitment. *Expreimental Cell Research, 299*(1), 148-158. doi:10.1016/j.yexcr.2004.05.023

Jenkins, P.J. (1999). Growth hormone and exercise. *Clinical Endocrinology, Jun 50*(6), 683-689. Doi: 10.1046/j.1365-2265.199.00784x

Jermain, D.M., Drismon, M.L., & Nisbet, R.B. (1992). Controversies over the use of magnesium sulphate in delirium tremens. *Annals of Pharmacotherapy, 26*, 650-652.

Jurca, R., Lamonte, M.J., Barlow, C.E., Kampert, J.B., Church, T.S., & Blair, S.N. (2005). Association of muscular strength with incidence of metabolic syndrome in men. *Medicine and Science in Sports and Exercise*, 37, 1849–1855.

Karkazis, K., Jordan-Young, R., Davis, G., & Camporesi S. (2012). Out of bounds? A critique of the new policies on hyperandrogenism in elite female athletes. *American Journal of Bioethics 12*(7), 3-16. doi: 10.1080/15265161.2012.680533.

Kraemer, W.J., & Ratamess, N.A. (2005). Hormonal responses and adaptations to resistance exercise and training. *Sports Medicine 35*(4), 339-361. doi: 0112-1642/05/0004-0339/$34.95/0

Lukaski, H.C. (2000). Magnesium, zinc and chromium nutriture and physical activity. *American Journal of Clinical Nutrition,* 72(suppl), 585s-593s.

Lukaski, H.C., & Nielsen, F.H. (2002). Dietary magnesium depletion affects metabolic responses during submaximal exercise in postmenopausal women. *Journal of Nutrition, 132*(5), 930-935.

Maggio, M., Ceda, G.P., Lauretani, F., Cattabiani, C., Avantaggiato, E., … Ferrucci, L., (2011). Magnesium and anabolic hormones in older men. *International Journal of Andrology,* 34, e594-e600. doi:10.1111/j.1365-2605.2011.01193.x

Maguire, M.E., & Cowan, J.A. (2002). Magnesium chemistry and biochemistry. *Biometals,* 15, 203-210.

Matias, C.N., Monteiro, C.P., Silva, A.M., Rocha, P.M., Minderico, C.S., … Laires, M.J. (2011). Magnesium intake is associated with strength performance in elite basketball, handball and volleyball players. *Magnesium Research, xx* (x), 1-5. doi:10.1684/mrh.2011.0290

Mayo Medical Laboratories (2015[b]). *Test ID; MGS: Magnesium, Serum.* Retrieved from: http://www.mayomedicallaboratories.com

McCormick, D. (2006). Vitamin B6. In: B. Bowman., & R. Russell., (Eds.). *Present Knowledge in Nutrition* (9th ed.). Washington, DC, USA: International life Sciences Institute.

McDonald, R., & Keen, C.L. (1988). Iron, zinc and magnesium nutrition and athletic performance. *Sports Medicine*, 5, 171–84.

Newhouse, I.J., & Finstad, E.W. (2000). The effects of magnesium supplementation on exercise performance. *Clinical Journal of Sport Medicine*, 10, 195-200.

Newhouse, I.J., Johnson, K.P., Montelpare, W.J., & McAuliffe, J.E. (2002). Variability within individuals of plasma ionic magnesium concentrations. *BMC Physiology, 2*(6). PMCID: 113254.

Nielsen, F.H., & Lukaski, H.C. (2006). Update on the relationship between magnesium and exercise. *Magnesium Research, Sep 19*(3), 180-189. PMID: 17172008.

Nindl, B.C., Kraemer, W.J., Deaver, D.R., Peters, J.L., Marx, J.O. Heckman, J.T., & Loomis, G.A. (2001). LH secretion and testosterone are blunted after resistance exercise in men. *Journal of Applied Physiology, 91*(3), 1251-1258. PMID: 11509523.

Nishida, Y., Matsubara, T., Tobina, T., Shindo, M., Tokuyama, K., … Tanaka, H. (2010). Effect of low-intensity aerobic exercise on insulin-like growth factor-I and insulin-like growth factor-binding proteins in healthy men. *International Journal*

of Endocrinology, 2010(2010), Arcticle ID: 452820. Retrieved from: http://www.hindawi.com

Orwoll, E., Lambert, L.C., Marshall, L.M., Blank, J., Barrett-Connor, E., … Cummings, S.R. (2006). Endogenous testosterone levels, physical performance, and fall risk in older men. *Archives of Internal Medicine 166*(19), 2124-2131. doi:10.1001/archinte.166.19.2124

Phillips, S.M., Tipton, K.D., Ferrando, A.A., & Wolfe, R.R. (1999). Resistance training reduces the acute exercise-induced increase in muscle protein turnover. *American Journal of Physiology, Jan 276*(1 Pt 1), E118-124.

Poikolainen, K., & Alho, H. (2008). Magnesium treatment in alcoholics: a randomised controlled trial. *Substance abuse treatment, prevention, and policy 3*(1). Doi: 10.1186/1747-597X-3-1

Quamme, G.A. (2008). Recent developments in intestinal magnesium absorption. Current Opinions in Gastroenterology, Mar 24(2), 230-235. doi: 10.1097/MOG.0b013e3282f37b59.

Raastad,T., Glomsheller, T., Bjøro, T., & Hallén, J. (2001). Changes in human skeletal muscle contractility and hormone status during 2 weeks of heavy strength training. *European Journal of Applied Physiology, Jan-Feb 84*(1-2), 54-63.

Ranande, V.V., & Somberg, J.C. (2001). Bioavailability and pharmacokinetics of magnesium after administration of magnesium salts to humans. *American Journal of Thermodynamics*, 8, 345-357.

Ratzin-Jackson, C.G. (2000). *Nutrition and the Strength Athlete.* CRC Press: New York, USA.

Rosanoff, A., Weaver, C.M., & Rude, R.K. (2012). Suboptimal magnesium status in the United States: are health consequences underestimated?

Rude, R.K., & Singer, F.R. (1981). Magnesium deficiency and excess. *Annual Reviews of Medicine*, 32, 245-259.

Saey, D., & Troosters, T. (2008). Measuring skeletal muscle strength and endurance: from bench to bedside. *Clinical and Investigative Medicine 31*(5), E307-E311.

Sandler, R.B., Burdett, R., Zaleskiwicz, M., Repcheck, C.S., & Harwell, M. (1991). Muscle strength as an indicator of habitual level of physical activity. *Medicine and Science in Sports and Exercise, Dec 23*(12), 1375, 1381.

Sarai, M., Tejani, A.M., Chan, A.H.W., Kuo, I.F., & Li, J. (2013). Magnesium for alcohol withdrawal. *Cochrane Database of Systematic Reviews, 6,* Art. No.: CD008358. Doi: 10.1002/14651858.CD008358.pub2.

Saris, N.E., Mervaala, E., Karppanen, Khawaja, J.A., & Lewenstam, A. (2000). Magnesium: an update on physiological, clinical and analytical aspects. *Clinica Chimica Acta, 294*(1-2), 1-26.

Seidel, S., Kreutzer, R., Smith, D., McNeel, S., & Gilliss, D. (2001). Assessment of commercial laboratories performing hair mineral analysis. *Journal of the American Medical Association, Jan 3, 285*(1), 67-72. PMID: 11150111.

Stanworth, R.D., & Jones, R.H. (2008). Testosterone for the aging male; current evidence and recommended practice. *Clinical Interventions in Aging, 3*(1), 25-44. PMCID: PMC2544367.

Stewart, C.E., & Pell, J.M. (2010). Point: IGF is the major physiological regulator of muscle mass. *Journal of Applied Physiology, 108*(6), 1820-1821. Doi: 10.1152/japplphysiol.01246.2009

Strauss, J. F., & Barbieri, R.L. (1999). *Yen and Jaffe's reproductive endocrinology: Physiology, pathophysiology, and clinical management*. Philadelphia, PA: Saunders/Elsevier.

Touvier, M., Lioret, S. Vanrullen, I., Bocle, J.C., Boutron-Ruault, M.C., … Volatier, J.L. (2006). Vitamin and mineral inadequacy in the French population: estimation and application for the optimisation of food fortification. *International Journal of Vitamin and Nutrition Research, Nov 76*(6), 343-351.

Urdiales, D.M., Ortega, F.B., Rodriguez, G.V., Lopez, J.P.R., Marco, L.G., … Ruiz, J.R. (2010). Association of physical activity with muscular strength and fat-free mass in adolescents: the HELENA study. *European Journal of Applied Physiology, Aug 109*(6), 1119-1127 doi: 10.1007/s00421-010-1457-z. Epub 2010 Apr 7.

van Anders, S.M., Hampson, E., & Watson, N.V. (2006). Seasonality, waist-to-hip ratio, and salivary testosterone. *Psychoneuroendocrinology, Aug 31*(7), 895-899. PMID: 16675146.

Wang, Z.M., Piersen, R.M., & Heymsfield, S.B. (1992). The five-level model: a new approach to organising body composition research. *American Journal of Clinical Nutrition, 56*, 19-28.

Watkins, K., & Josling, P.D. (2010). A Pilot Study to determine the impact of Transdermal Magnesium treatment on serum levels and whole body Ca/Mg Ratios *European Journal of Nutraceutical Research. Retrieved from: www.aucoeurdestraditions.com/*

Wolinsky, I. (Ed.). (1997). *Nutrition in Exercise and Sport.* (3rd ed.). USA: CRC Press.

Yakar, S., Wu, Y., Setser, J., & Rosen, C.J. (2002). The role of circulating IGF-1: lessons from human and animal models. *Endocrine,* 19, 239-248.

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The effects of magnesium supplementation on strength and body composition: a systematic review

Intended publication

This systematic review is intended for publication in the Biological Trace Element Research Journal. The respective journal is an international journal, publishing high quality studies elucidating the important roles of trace elements for human health. The journal specifically publishes studies analysing the effects of deficiency, supra-nutritional, pharmacological and toxicological expects of trace elements. Minimal modifications, including a slight alteration in referencing style and addition of the author's details to the title page, would be required prior to publishing in the aforementioned journal.

Contents

List of abbreviations

Medical Subject Headings ..... MeSH

European Food Safety Authority ..... EFSA

Magnesium ..... Mg

Recommended Daily Allowance ..... RDA

Randomised Controlled Trial ..... RCT

Population Intervention Comparison Outcome ..... PICO

WHO International Controlled Trials Registry Platform ..... WHO-ICTRP

Physiotherapy Evidence Database Scale ..... PEDro Scale

One-Repetition Maximum 1-RM

Dual X-Ray Absorptiometry ..... DXA

Bioelectrical Impedance Analysis ..... BIA

Body Mass Index ..... BMI

Serum Ionic Magnesium ..... iMg

Abstract

Background

Magnesium physiology suggests a possible benefit for supplementation on strength and body composition, however evidence for a direct correlation is incoherent.

Objectives

To systematically analyse trials for evidence regarding the effects of magnesium supplementation on strength and body composition.

Search methods

Searches were conducted in Google Scholar, Sport Discus, Pubmed, WHO-ICTRP, University of Chester Library, and databases of Italian journals. Authors were also contacted. There were no date restrictions.

Selection criteria

Trials supplementing with magnesium supplementation (any form) and measuring muscle strength or body composition, in comparison with a placebo or no treatment were included.

Data collection and analysis

Risk of bias was assessed using the PEDro scale. Data was collected from the retrieved version of the studies.

Main results

A total of 9 studies, encompassing 522 participants were included for muscle strength. 4 of these studies (298 participants) also analysed changes in body composition. There was a variety in dosing, form and duration of

supplementation. 3 studies were conducted on alcoholics, 3 on physically active individuals, 1 on elderly and 2 on untrained populations. Only 3 studies displayed a strength benefit for magnesium over placebo; 1 in alcoholics, untrained and physically active. Body composition changes were only significant in 1 study conducted on overweight, untrained middle-aged women.

Conclusion

The strength of the evidence points towards no benefit for magnesium supplementation on strength performance or body composition in normomagnesemic populations.

Keywords: bioavailability, exercise, mineral status, muscle mass

Background

Information regarding the trace element

Magnesium (Mg) is an essential mineral and cofactor for over 300 enzymatic reactions involved in neuromuscular transmission, muscular contraction, oxygen uptake, energy production and electrolyte balance (Altura, 1991). Recommended Daily Allowances (RDAs) for Mg in adults stand at 400 and 310 mg/day, for males and females respectively (European Food Safety Authority, EFSA, 2015). Despite several dietary sources, subclinical or marginal Mg deficiency is prevalent worldwide (Nielsen, 2010). Supplemental Mg is available as capsules containing various salts of Mg such as; oxide, aspartate and citrate, with organic salts and chloride displaying higher bioavailabilities (Firoz & Graber, 2001). Soluble preparations, for intravenous (Garrison, Allan, Sekhon, Musini & Khan, 2012), topical and transdermal supplemental methods are also available (Nica et al., 2015).

Description of considered outcomes

'Muscle strength' is defined in the medical subject heading (MeSH) PubMed database as; the amount of force generated by muscular contraction (Saey & Toosters, 2008). It is considered an indicator of nutritional status and predictor of decreased osteoporotic fracture, disability and mortality in both middle-aged and elderly (Rantanen et al., 2000, cited in Moslehi, Vafa, Sarrafzadeh and Foroushani, 2013). Also decreased muscle strength is directly correlated with an

independently increased risk for metabolic syndrome irrespective of age, body size, insulin resistance and central obesity (Jurca et al., 2005). Body composition is outlined as either; Fat Free Mass (FFM) and fat, or Lean Body Mass (LBM) and fat, with the difference between FFM and LBM being that, FFM includes essential fat around the organs, unlike LBM (Wang, Piersen & Heymsfield, 1992).

Trace element physiology and the considered outcomes

The positive association of Mg with energy production, protein synthesis (Brilla & Haley, 1992), anabolic hormone levels and antioxidant capacity (Maggio et al., 2011), suggest that Mg supplementation may improve muscle strength and body composition. Consequently, while supplemented Mg can correct a deficiency it can also exhibit a pharmacological action if supplemented to non-deficient individuals (Lukaski, 2000).

Rationale for review

Supplementation with Mg has been suggested to be positively correlated with increases in strength performance in some studies but not in others (Newhouse & Finstad, 2000). Consequently a systematic review, assembling key articles, could assist towards outlining any related ergogenic benefits, while identifying gaps within the literature for future research.

Aims

1. To investigate for any ergogenic effects of Mg supplementation on strength and body composition.

Objectives

1. To systematically analyse randomised controlled trials (RCTs) which utilise Mg supplementation and include strength performance or body composition as an outcome measure.

Methods

This section has been provided to clearly outline the search methods used to retrieve the relevant articles; including the relative search term/s, keywords, search engines and the associated inclusion/exclusion criteria.

Formulating a focused research question

Prior to conducting any literature search a research question should be formulated. The research question needs to be properly framed in order to enable the researcher to retrieve specific findings. Consequently, given a focused question, the results of the searches will be narrowed down to include as much relevant findings as possible (Aslam & Emmanuel, 2010). Given, the nature of the review question is similar to one conducted in clinical research, and some of

the best studies for such questions definitely include RCTs (Simon, 2001). PICO framework was adopted for the formulation of the research question. PICO stands for Population, Intervention, Comparison and Outcome and it was formulated for use in evidence-based medicine (Huang, Lin & Demner-Fushman, 2006). Furthermore, the PICO framework has shown to improve precision at retrieving high quality studies in widely utilised databases (Schardt, Adams, Owens, Keitz & Fontelo, 2007).

Criteria for considering studies for this review

Types of studies included

RCTs comparing Mg supplementation with placebo or no supplementation were included. Other forms of trials, including RCTs with a cross-over design were also included. Retrieved studies had to be available in English or Italian language to be included. No date restrictions were applied.

Types of participants

The upcoming review included participants who were aged over 15 years of age. No restrictions of gender, ethnicity, health and physical activity status were applied.

Types of interventions

Controlled trials utilising supplementation with Mg as an intervention were included. Control groups of studies could include supplementation with a matched-placebo or no supplementation.

Interventions considered

Magnesium supplementation: any form, duration and pattern of administration

Comparators considered

1. Adequate placebo
    - Not containing Mg or other minerals

2. No supplementation
    - Control group not given a placebo

Outcome measures

1. Strength

The use of dynamometry and One-Repetition Maximum (1-RM) testing, being gold-standards for strength testing in-vivo (Verdijk, van Loon, Meijer & Savelberg, 2009), and outside a lab (Levinger et al., 2009), respectively; were the preferred methods of measurement of strength performance. Grip strength though not being a gold-standard, was still considered an adequate measure of strength; as it can be particularly useful in measuring strength in older or hospitalised populations (Roberts et al., 2011). Maximal isometric contraction as a measure of strength testing has been validated for use in specialised populations (Visser et al., 2003 & Zimmer et al., 2013) and consequently, was also included. Subsequently, the strength measures considered, included:

- Handgrip strength
- 5-second isometric bench press contractions
- Isometric strength
- Isokinetic torque
- 1-RM Bench press

2. Body Composition

The validity of any given body composition test varies for different populations, (Heymsfield, Lohman & Wang, 2005, cited in Duren et al., 2008) as those considered in this review. Consequently a variety of body composition tests were

included ranging from Dual X-Ray Absorptiometry (DXA) to Bioelectrical Impedance Analysis (BIA). One study also included measurement of muscle mass through 24-hour creatinine excretion. Subsequently, outcomes included consisted of the measurement of;

- LBM
- FFM
- Fat mass
- Muscle mass (through biochemical analysis)

The Search strategy

Identification of keywords

Following the formulation of the question, keywords were generated and placed within the different sections of the PICO paradigm (Table 1). The words within the table represent the study characteristics considered, their respective synonyms and truncations, as well as their placement within the PICO paradigm. Subsequently, studies considered were to fit a minimum of 1 characteristic under every column in order to be included.

Table 1: Keywords utilised during the search for articles, within the PICO paradigm

Population	**Intervention**	**Comparison**	**Outcome**
‘adult’	‘magnesium supplementation’	‘placebo’	‘strength’
‘adults’	‘Mg’	‘no supplementation’	‘body composition’
‘athlete’		‘control group’	‘resistance training’
‘athlete’			‘body fat’

The search strategy was developed utilising guidelines from Cochrane (2007). PubMed’s Medical Subject Headings (MeSH) database was used to uncover any further relevant synonyms in the process. The MeSH database is the U.S. National Library of Medicine controlled thesaurus (U.S. National Library of Medicine, 2015).

From the Intervention section, the term ‘Magnesium’ is considered a wide term due to the wide variety of salts available, however, all synonyms uncovered through Pubmed’s MeSH database contained the aforementioned word. The term ‘Mg’ was also utilised as it sometimes is used as an acronym for the element.

From the ‘Population’ section; the term ‘adults’, was inserted in PubMed’s MeSH database, however no other relevant synonyms that did not contain the word ‘adult’ were uncovered. Finally given inclusion criteria included some form of ‘strength’ measurement the term was entered in the MeSH database. This term

uncovered several terms including: ‘muscle strength’, ‘resistance training’, ‘athletes’, ‘strength training’, ‘grip strength’ and ‘hand strength’. The term strength was kept when retrieved keywords contained the word. Alternatively, synonyms devoid of the respective word were also utilised. The term ‘athletes’ was then controlled for truncations to uncover the term ‘athlete’. These 2 terms were then placed under their respective subheading: ‘Population’.

A preliminary search was then conducted in Google Scholar. Following this, subsequent searches were conducted utilising online databases; Medline, Wiley Online Library, SPORTDiscus, University of Chester Library, Research Gate, World Health Organisation-International Controlled Trials Registry Platform (WHO-ICTRP), Medicina dello Sport and Sport & Medicina. Boolean search phrases, filters and wildcard searches were utilised when possible to enable the search to be more refined. No restrictions regarding publication date and publication status were applied. Articles available in English and Italian languages were considered

Electronic searches

Google Scholar

The database was searched utilising a total of 3 keywords from the ‘Intervention’ and ‘Outcome’ sections. In order to allow a focused search, settings were applied so that keywords entered had to be present in the title.

SPORTDiscus (January 1975 to August 2015)

SPORTDiscus was searched using a combination of the one of the keywords under the 'Intervention' heading in Table 1 combined with those under the 'Outcome' heading.

Free text = 'magnesium supplementation' or 'Mg' AND 'strength*' or 'body composition' or 'body fat' or 'resistance training'.

Keyword = 'Mg' AND Free text = 'strength*' or 'body composition' or 'body fat' or 'resistance training'.

Medline through Pubmed (January 1966 to August 2015)

Keywords from the 'Intervention' and 'Outcome' section were utilised. Some searches are very wide when applied to Medline. However, the Dietary Supplements filter was applied and 'Title/Abstract' was selected in the search builder. The Boolean search phrase AND was also used. Searches were conducted as follows:

Title/abstract = 'magnesium supplementation' or 'Mg' AND

Title/Abstract = 'strength*' or 'body composition' or 'body fat' or 'resistance training'.

The publication type: 'Randomized Controlled Trial' could have been utilised in Medline to exclude only such types of studies. However, it was not used as,

according to Glanville, Lefebvre, Miles and Camosso-Stefinovic (2006) this could discriminate against potential such studies, if they are not classified under the respective section.

University of Chester Library

The University of Chester has a unique feature ‘Library Search’, enabling the user to search the entire library including books, journals and dissertations. The aforementioned search feature was used and filters for; ‘Electronic resources’, ‘Dissertation’, ‘Journal/eJournal’ and ‘Journal Articles’ were selected. Also, the ‘diet and clinical nutrition’ discipline was selected. Consequently, searches were conducted utilising keywords from the ‘Intervention’ (present in the Title) in combination with keywords from the ‘Outcome’ section, (present in the abstract) as follows:

Title = ‘magnesium supplementation’ OR ‘Mg’ AND

Abstract = ‘strength*’ or ‘body composition’ or ‘resistance training’ or ‘body composition’ or ‘body fat’.

WHO-ICTRP

The database WHO-ICTRP was searched utilising combinations of keywords from ‘Intervention’ and ‘Outcome’ sections, in an attempt to uncover any further published, unpublished or ongoing trials.

Other electronic searches

Research Gate and Wiley Online Library were also searched for any published or unpublished studies meeting the inclusion criteria, utilising a combination of keywords from the Intervention and Outcome sections.

Italian journal databases

The database of the Italian journals ‘Medicina dello sport’ and ‘Sport & Medicina’ were also searched. Searches uncovering any articles containing any combination of a keyword from the ‘Intervention’ column and a keyword from the ‘Outcome’ column were conducted.

Personal Communication

Researchers in the field were contacted through ‘Research Gate’ for additional information regarding the respective inclusion criteria. Authors of articles in other languages, apart from the ones included, were also contacted and asked regarding any available versions in one of the included languages.

Handsearching

Retrieved studies, conferences proceedings, major textbooks and previous systematic reviews available in included languages were checked for further published or unpublished research.

Data collection and analysis

Selection of studies

Any studies which met the inclusion criteria were considered and their respective full texts were retrieved. Inclusion criteria consisted of:

- RCTs or cross-over trials
- Considered an intervention group supplemented solely with Mg
- Utilised one or more strength performance measures as an outcome
- Participants aged over 15 years of age

The studies generated by the search methods were reviewed primarily based on title and abstract. Subsequently, retrieved articles were re-assessed based on respective inclusion criteria. When duplicate publications were present only one was included.

Data extraction

Data regarding study variables was extracted from selected studies, including:

- study design
- participant characteristics (age, sex, physical activity status, comorbidities)
- any assessment for dietary Mg
- any measurements of Mg status
- intervention details (dose and duration of supplementation)
- any exercise regimen performed in conjunction with supplementation
- outcome measures of interest (strength and body composition)
- comparator details

Methodological quality assessment

The Physiotherapy Evidence Database, PEDro scale (1999) was utilised as a tool to assess methodological quality of included studies. The PEDro scale rates quality of trials on 11 criteria and a ‘yes’ answer for any of criteria 2-11 involves adding 1 to the score. It was developed using the Delphi tool, which in turn was rated as the highest of 7 most commonly utilised trial assessment tools in systematic reviews (Berger & Alperson, 2009). The tool enables the user to account for: selection, performance, attrition, detection, and reporting biases within each study.

Cross-over trials

A concern with cross-over trials might be the carry-over effect. This due to the fact that physiological differences related to any treatment in the first phase, might increase the risk of bias during the second phase. A washout period to ensure homogeneity of subjects prior to the initiation of the second-phase, was considered adequate.

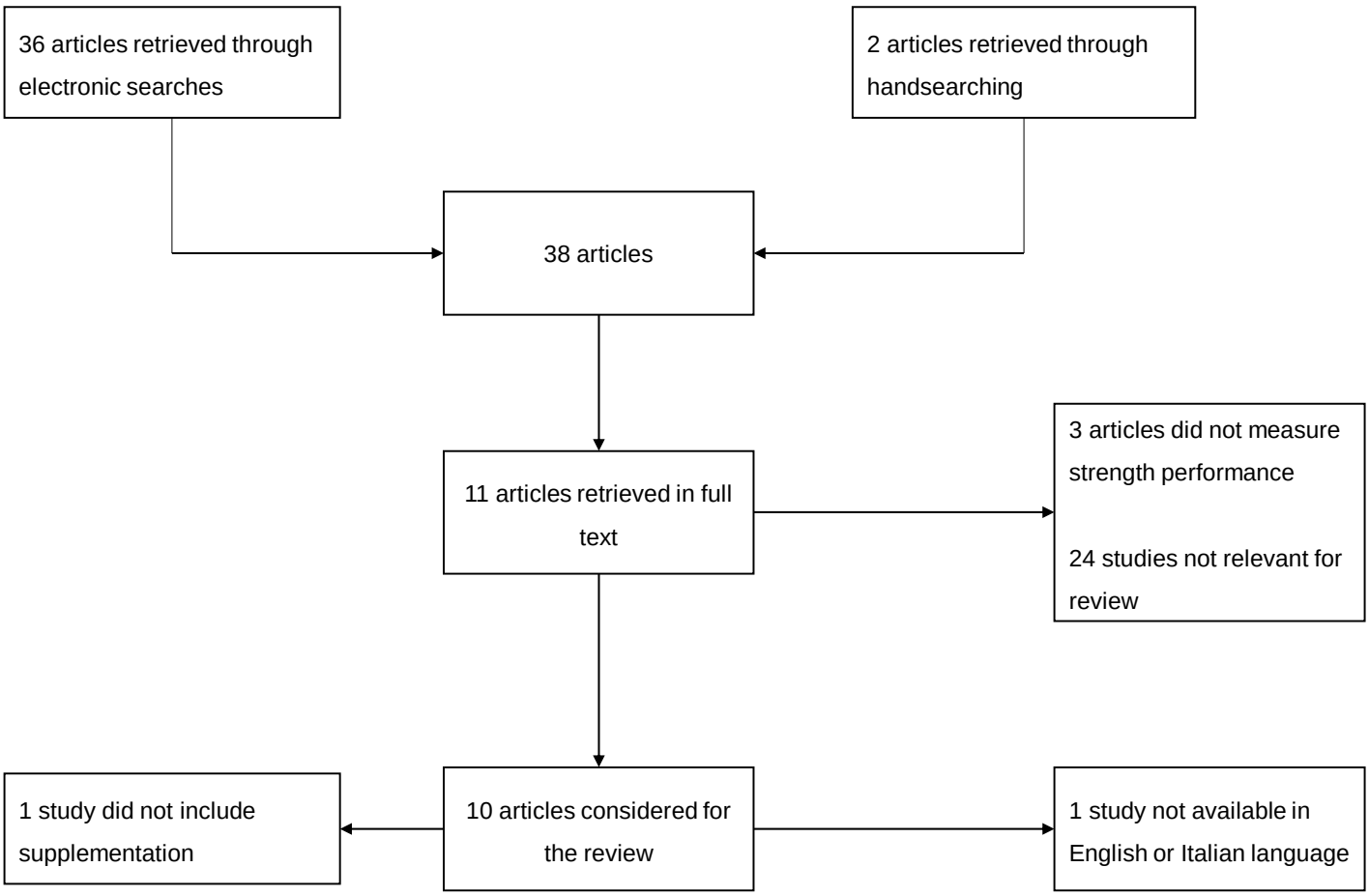
Results

Description of studies

Results of the search

Through an analysis of the title, electronic searches retrieved 36 studies: 6, 7, 12, 5, 1, and 5 in Google Scholar, SportDiscus, MEDLINE, University of Chester Library, WHO-ICTRP and Research Gate, respectively. Handsearching of retrieved articles uncovered 2 more potential studies. Following the reading of abstracts 27 studies were excluded. Authors were contacted when full-text was not retrieved, or retrieved versions were not in English or Italian language version. 11 studies available in full-text were retrieved. Of these; the author of 1 study confirmed it was not available in English language and another did not include a supplementation protocol. The remaining 9 studies were further evaluated, met the inclusion criteria and were considered for this review. (Figure 1)

Figure 1: Flow diagram



Included studies

A summary of the characteristics for each of the included studies can be found in Appendix 1 (Characteristics and risk of bias of included studies). Below is the summation of all the global characteristics for all studies included in this review, by study variable.

Study designs

Included studies consisted of randomised controlled trials (RCTs), one of which had a cross-over design. The control group was either supplemented with a placebo or not supplemented, and in the cross-over design a 1 week washout period was allowed in between.

Sample sizes

A total of 522 participants were included. Sample size in studies varied from 139 (Veronese et al., 2014) to 13 (Kass & Poeira, 2015).

Participant characteristics

Age of participants between 15-20 years of age in Setaro et al. (2014) to mean age in Veronese et al. (2014) being 71.5 years. Certain studies included solely female subjects (Moslehi, Vafa, Sarrafzadeh & Rahimi-Foroushani, 2013 and Veronese et al., 2014), others included exclusively male participants (Kass, Skinner & Poeira, 2013 and Setaro et al., 2014) while others included participants of both sexes. One study did not mention gender of participants (Brilla and Haley, 1992). Physical activity status of participants also varied from professional athletes in Setaro et al. (2014), to untrained populations in Brilla and Haley (1992). Also, participants were of varying health status from with some studies including exclusively: alcoholics (Gullestad et al., 1992 and Poikolanen & Alho, 2008) and patients with alcoholic liver disease (Aagaard et al., 2005). Other

studies included solely overweight participants (Body Mass Index (BMI): 25-30 kg/m^2).

Dietary assessments

Dietary magnesium could act as a confounding variable which could buffer or augment the ergogenic effect of supplementation. The majority of studies (5 studies) included some form of dietary assessment to analyse dietary magnesium intake. Others (3 studies) did not. For one study (Gullestad et al., 1992) the authors reported that all participants were told to minimise alcohol and magnesium-rich food consumption.

Magnesium status

Mg status would be considered as another confounding variable. Consequently, measuring such could ensure homogeneity between groups. Serum magnesium was taken in 4 studies to ensure homogeneity among groups. Other studies utilised different measures including muscle magnesium (Aagaard et al., 2005) and plasma magnesium (Setaro et al., 2014). 3 studies did not measure magnesium levels.

Intervention and comparators

Dosing of oral magnesium varied from 250 mg/day (Moslehi, Vafa, Sarrafzadeh & Rahimi-Foroushani, 2013) to 500 mg/day (Poikolanen & Alho, 2008). One study reported total dietary and supplemented magnesium as being 8 mg/kg bodyweight/day in intervention group (Brilla & Haley, 1992). Another study utilised exclusively 728mg of intravenous Mg sulfate on the first 2 days, followed by solely oral supplementation (Aagaard et al., 2005). Different magnesium salts were supplemented, the most common being oxide, citrate and sulfate.

Training regimens conducted

The majority of studies did not alter physical activity, for the duration of the study. One study included a strength training program consisting of 3 sets of 10 repetitions leg press and leg extension 3 times per week. For the remaining 8 studies participants either were advised to keep a constant level of physical activity or physical activity was not measured.

Excluded studies

Excluded studies were either; not available in English or Italian languages, did not include a magnesium treatment arm, or did not consider strength or body composition as an outcome measure.

Risks of bias in included studies

The judgement for the risk of bias for separate studies can be found in Appendix 1 (Characteristics and Risks of bias in included studies). Below is a summative report of the measures, taken by the authors of the included studies, which could affect the risks of bias.

Randomisation

Randomisation in most studies (8 studies) was done utilising participants as the unit of randomisation. One study (Setaro et al., 2014) utilised urinary magnesium as the unit of randomisation.

Allocation (selection bias)

Only 2 studies (Aagaard et al., 2005 and Veronese et al., 2014) mentioned some form of allocation concealment, stating that allocation sequence was kept confidential.

Blinding (performance and detection bias)

Participants in studies which did not include a placebo-controlled group, were not considered as being blinded, as subjects would have been able to distinguish whether they were supplementing or not (Veronese et al., 2014 and Kass &

Poeira, 2013). Furthermore, in some of the studies it was unclear whether assessors were blinded or not.

Attrition bias

Some studies had high rates of dropouts: 28% (Aagard et al., 2005) and 50.8% (Poikolainen & Alho, 2008). The latter study conducted an intention-to-treat analysis.

Other potential sources of bias

One study (Gullestad et al., 1992) advised all participants to minimise alcohol and magnesium-rich food consumption. No dietary assessment was conducted before or after the trial.

Effects of treatment

A summary of the effects of treatment for the separate considered outcomes can be found in Appendix 2

Strength

Strength increase was found to be significantly higher in 3 studies (Gullestad et al., 1992, Brilla & Haley, 1992, and Kass & Poeira, 2015), when compared to respective control groups.

Body composition

Only 1 study uncovered significantly different body composition between intervention and control groups at the end of the trial (Moslehi, Vafa, Sarrafzadeh & Foroushani, 2013).

Discussion

Magnesium supplementation and strength

Gullestad et al. (1992), after conducting a study on alcoholics, uncovered a significantly higher increase in strength for the Mg supplemented (375 mg/day) group, however, no dietary assessment was conducted, and prior to the study, all participants were advised to reduce alcohol and intake of Mg-rich foods. Mean serum Mg levels decreased (0.84 to 0.79 mmol/L), in the control group and increased (0.86 to 0.88 mmol/L) in the treated group. Subsequently, the positive effect for Mg supplementation on strength could be explained, at least in part, by the uncompensated decreased dietary Mg, which reflected through a reduction in Mg status in the control group, while Mg supplementation addressed the

deficiency in the intervention group and therefore, indicating a disruption in synergy between groups.

Some studies did not account for dietary Mg and Mg status which could act as confounding variables. The study conducted by Brilla and Haley (1992) suggests that; Mg supplementation could exhibit an ergogenic effect and potentiate further augmentations in strength performance, when combined with a resistance training program, in untrained subjects. However, the control group of this study was only having 246mg (70% RDA, as stated by authors), while the intervention group was having 504mg (144% RDA). Kass and Poeira (2015) also uncovered significantly higher (17.7%) increases in strength (1-RM bench press) for 1 week (300mg/day or 300mg prior to exercise on exercise days) Mg supplementation when compared to placebo. The results of this study could be explained by the use of Mg citrate which is known to have improved absorption (50%) when compared to 4% for Mg oxide (Firoz & Graber, 2001). Measures of Mg status were not included, however, both acute intervention and acute placebo groups had dietary Mg intakes positive of 350 mg/day at baseline. Alternatively, another arm of the latter study included participants (mean dietary Mg; 361mg/day) supplementing with Mg (300mg/day) for 4 weeks and did not find a difference in strength (1-RM bench press) when compared with a control group (mean dietary Mg; 551 mg/day). Subsequently, the effects of Mg supplementation in the chronic (4 week) arm of the study could have been buffered by the higher dietary Mg in the control group. Another study, (Moslehi, Vafa, Sarrafzadeh & Foroushani, 2013) considering participants (150 < mean Mg dietary intake (mg/day) < 200),

but were considered of normal Mg status (according to serum Mg), found no significant difference in strength between treated and control groups, following 8 weeks of Mg supplementation (250 mg/day).

Alternatively, Mg's role in protein synthesis would suggest that optimal intakes of Mg may assist strength augmentations, stimulated through physical activity (Brilla & Haley, 1992). However, training-associated compartmental shifting of Mg, could increase Mg muscle content, negating the requirement for additional Mg, especially in trained athletes (Newhouse & Finstad, 2000). This is directly in line with the observations of Setaro et al. (2014), the only included study, on professional athletes.

Magnesium supplementation and body composition

Only one of the included studies uncovered a significant increase and decrease in mean lean body mass (0.7 kg, $p = 0.05$) and fat mass (1 kg, $p = 0.02$), respectively, following Mg supplementation (250 mg/day for 8 weeks) when compared to baseline. Alternatively, body composition changes in the control group of the respective study were not significant. Mean physical activity decreased in both intervention (438 to 363 Met-min/week) and placebo (420 to 383 Met-min/week) groups, however this change was not-significant. Alternatively, all other studies following supplementation with higher doses of supplemental Mg (271<Mg mg/day<300), some of which for longer periods of time (12 weeks in Veronese et al., 2014), and combined with an increase in

physical activity (Brilla & Haley, 1992), uncovered no significant differences in body composition. However, while mean BMI of participants in Moslehi, Vafa, Sarrafzadeh and Foroushani (2013) and Veronese et al. (2014) were similar (28 and 27.4 (kg/m^2), respectively), Moslehi, Vafa, Sarrafzadeh and Foroushani (2013) was the only study which included solely overweight women.

Suggestions for future research

The lack of significant results for strength outcomes could be attributable to numerous factors. Oral supplementation with Mg oxide, as utilised in the majority of studies, is poorly absorbed (4%) when compared to other Mg salts, such as Mg citrate (50%) (Firoz & Graber, 2001). Alternatively, Mg supplementation through transdermal application of 31% Mg chloride formulation was found to be more effective at raising serum Mg than oral supplementation. Furthermore, as also argued in Newhouse, Johnson, Montelpare, and McAuliffe (2002), serum and plasma TMg are not necessarily reflective of whole Mg status. Subsequently, multiple tests of higher reliability such as ionic Mg (iMg) validated against Mg loading with 24 hour urinalysis, could prove more useful for the determination of Mg status (Newhouse & Finstad, 2000).

Conclusion

The conclusions are in line with those of other authors, where majority of the evidence indicates no strength performance benefit related with supplementing

normomagnesemic populations with oral Mg. Some salts of Mg, including Mg citrate, could possibly be correlated with some degree of ergogenesis on strength performance, following acute supplementation. Body composition in overweight populations might be positively affected following Mg supplementation. However, further research; with more participants, of different athletic levels, controlling for confounding variables such as dietary Mg and Mg status through more than one method, and utilising more bioavailable sources of Mg, would be suggested to aid ascertain any possible correlations between ergogenic strength benefits and all forms of supplementation.

References

Aagard, N.K., Andersen, H., Vilstrup, H., Clausen, T., Jakobsen, J., & Dorup, I. (2005). Magnesium supplementation and muscle function in patients with alcoholic liver disease: A randomised placebo-controlled trial. *Scandinavian Journal of Gastroeneterology,* 40, 972-979.

Aslam, S., & Emmanuel, P. (2010). Formulating a researchable question: A critical step for facilitating good clinical research. *Indian Journal of Sexually Transmitted Diseases, Jan-Jun 31*(1), 47-50. doi: 10.4103/0253-7184.69003

Berger, V.W., & Alperson, F.Y., (2009). A general framework for the evaluation of clinical trial quality*. Reviews on Recent Clinical Trials, May 4*(2), 79-88.

Brilla, L., & Haley, T.F. (1992). Effect of magnesium supplementation on strength training in humans. *Journal of the American College of Nutrition, 11*(3), 326-329. Doi: 10.1080/07315724.1992.10718233.

Cochrane (2007). How to develop a search strategy for a cochrane review. *Cochrane Haematological Malignancies Group, Naumann*, 1-10. Retrieved from: http://chmg.cochrane.org

Duren, D.L., Sherwood, R.J., Czerwinski, S.A., Lee, M., Choh, A.C., … Chumlea, W.C. (2006). Body composition methods: comparisons and interpretation. *Journal of Diabetes Science and Techonology, 2*(6), 1139-1146.

Firoz, M., & Graber, M. (2001). Bioavailability of US commercial magnesium preparations. *Magnesium Research*, 14, 257-262.

Garrison, S.R., Allan, G.M., Sekhon, R.K., Musini, V.M., & Khan, K.M. (2012). Magnesium for skeletal muscle cramps. *Cochrane Database of Systematic Reviews (Online). Doi: 10.1002/14651858.CD009402.pub2*

Glanville, J.M., Lefebvre, C., Miles, J.N., & Camosso-Stefinovic, J. (2006). How to identify randomized controlled trials in MEDLINE: ten years on. *Journal of the Medical Library Association, 94*(2), 130-136.

Gullestad, L., Dolva, O.L., Soyland, E., Manger, A.T., Falch, D., & Kjekshus, J. (1992). Oral magnesium supplementation improves metabolic variables and muscle strength in alcoholics. *Alcoholism: Clinical and Experimental Research 16*(5), 986-990. Doi: 0145-6008/92/1065-098653.00/0

Huang, X., Lin, J., & Demner-Fushman, D. (2006). Evaluation of PICO as a knowledge representation for clinical questions. *AMIA Annual Symposium Proceedings,* 359-363. PMCID: PMC1839740.

Jurca, R., Lamonte, M.J., Barlow, C.E., Kampert, J.B., Church, T.S., & Blair, S.N. (2005). Association of muscular strength with incidence of metabolic syndrome in men. *Medicine and Science in Sports and Exercise*, 37, 1849–1855.

Kass, L., & Poeira, F. (2015). The effect of acute vs chronic magnesium supplementation on exercise and recovery on resistance exercise, blood pressure and total peripheral resistance on normotensive adults. *Jopurnal of the Internation Society of Sports Nutrition 12*(19). Doi: 10.1186/s12970-015-0081-z

Kass, L., Skinner, P., & Poeira, F. (2013). A pilot study on the effects of magnesium supplementation with high and low habitual dietary magnesium intake on resting and recovery from aerobic and resistance exercise and systolic blood pressure. *Journal of Sports Science and Medicine,* 12, 144-150

Levinger, I., Goodman, C., Hare, D.L., Jerums, G., Toia, D. and Selig, S. (2009). The reliability of the 1RM strength test for untrained middle-aged individuals. *Journal of Science and Medicine in Sport 12* (3), 310-316.

Lukaski, H.C. (2000). Magnesium, zinc and chromium nutriture and physical activity. *American Journal of Clinical Nutrition,* 72(suppl), 585s-593s.

Maggio, M., Ceda, G.P., Lauretani, F., Cattabiani, C., Avantaggiato, E., … Ferrucci, L., (2011). Magnesium and anabolic hormones in older men. *International Journal of Andrology,* 34, e594-e600. doi:10.1111/j.1365-2605.2011.01193.x

Moslehi, N., Vafa, M., Sarrafzadeh, J., & Foroushani, A. (2013). Does magnesium supplementation improve body composition and muscle strength in middle-aged overweight women? A double-blind, placebo-controlled, randomised clinical trial. *Biological Trace Element Research,* 153, 111-118. Doi: 10.1007/s12011-013-9672-1.

Newhouse, I.J., & Finstad, E.W. (2000). The effects of magnesium supplementation on exercise performance. *Clinical Journal of Sport Medicine*, 10, 195-200.

Newhouse, I.J., Johnson, K.P., Montelpare, W.J., & McAuliffe, J.E. (2002). Variability within individuals of plasma ionic magnesium concentrations. *BMC Physiology, 2*(6). PMCID: 113254.

Nica, A.S., Caramoci, A., Vasilescu, M., Ionescu, A.M., Paduraru, D., & Mazilu, V. (2015). Magnesium supplementation in top athletes – effects and recommendations. *Journal of the Romanian Sports Medicine Society, Medicina Sportiva, vol. XI*(1), 2482-2494

Nielsen, F.H. (2010). Magnesium, inflammation and obesity in chronic disease. *Nutrition Reviews,* 68, 333-340.

Physiotherapy Evidence Database (1990). *PEDro Scale*. Retrieved from Physiotherapy Evidence Database website: http://www.pedro.org.au/

Poikolainen, K., & Alho, H. (2008). Magnesium treatment in alcoholics: A randomised clinical trial. *Substance Abuse Treatment, Prevention and Policy*, *3*(1). Retrieved from: http://www.substanceabusepolicy.com/content/3/1/1

Roberts, H.C., Denison, H.J., Martin, H.J., Patel, H.P., Syddall, H., … Sayer, A.A., (2011). A review of the measurement of grip strength in clinical and epidemiological studies: towards a standardised approach. *Age Ageing, 40*(4), 423-429. doi: 10.1093/ageing/afr051

Saey, D., & Troosters, T. (2008). Measuring skeletal muscle strength and endurance: from bench to bedside. *Clinical and Investigative Medicine 31*(5), E307-E311.

Schardt, C., Adams, M.B., Owens, T., Keitz, S., & Fontelo, P. (2007). Utilization of the PICO framework to improve searching PubMed for clinical questions. *BMC Medical Informatics and Decision Making 7*(16). doi: 10.1186/1472-6947-7-16

Setaro, L., Santos-Silva, P.R., Nakano, E.Y., Sales, C.H., Nunes, N., … Colli, C. (2014). Magnesium status and the physical performance of volleyball players: effects of magnesium supplementation. *Journal of Sport Sciences 32*(5), 438-445. Doi: 10.1080/0264014.2013.828847

Simon, S.D. (2001). Is the randomised clinical trial the gold standard of research? *Journal of Andrology, Nov-Dec 22*(6), 938-943. PMID: 11700857.

U.S. National Library of Medicine. (2015). Introduction: What is MeSH? Retrieved from: http://www.nlm.nih.gov/

Verdijk, L.B., van Loon, L., Meijer, K., & Savelberg, H.H. (2009). One-repetition maximum strength test represents a valid means to assess leg strength in vivo in humans. *Journal of Sports Science, Jan 1; 27*(1), 59-68. doi:10.1080/02640410802428089.

Veronese, N., Berton, L., Carraro, S., Bolzetta, F., De Rui, M., ... Sergi, G. (2014). Effect of oral magnesium supplementation on physical performance in healthy elderly women involved in a weekly exercise program: a randomised controlled trial[1-3]. *The American Journal of Clinical Nutrition*, 100, 974-981.

Visser, J., Mans, E., de Visser, M., van den-Berg-Vos, R.M., Franssen, H., … de Haan, R.J. (2003). Comparison of maximal voluntary isometric contraction and hand-held dynamometry in measuring muscle strength of patients with progressive lower motor neuron syndrome. *Neuromuscular Disorders, Nov 13*(9), 744-750.

Wang, Z.M., Piersen, R.M., & Heymsfield, S.B. (1992). The five-level model: a new approach to organising body composition research. *American Journal of Clinical Nutrition, 56*, 19-28.

Wilson, J. W., Enns, C. W., Goldman, J. D., Tippett, K. S., Mickle, S. J., Cleveland, L. E. & Chahil, P. S. (1997). *Data tables: combined results from USDA's 1994 and 1995 Continuing Survey of Food Intakes by Individuals and 1994 and 1995 Health Knowledge Survey.* United States Department of Agriculture, Agricultural Research Service, Food Surveys Research Group, Beltsville, MD. Retrieved from: http://www.ars.usda.gov

Zimmer, P., Baumann, F.T., Ebel, J., Zopf, E.M., Bloch, W., & Elter, T. (2013). Feasibility of an isometric maximal voluntary contraction test in haematological cancer patients during thrombocytopenia. *Journal of Sports Medicine, 2013*, 1-6. Article ID: 470489.

Appendix 1: Characteristics and Risks of bias of Included studies

Study 1: Characteristics of study

Author/s: Moslehi, Vafa, Sarrafzadeh & Foroushani, 2013

Design	Randomised, double-blind, placebo-controlled trial
Participants	74 females, aged 40-55 years (mean ± SD age: 46.3 ± 4.2 years), overweight (25≤BMI≤30 kg/m²), healthy and not suffering from any chronic diseases, non-smokers and not taking magnesium-containing medications.
Dietary assessment (magnesium mg/day)	24-hour food recalls for 2 days (1 weekday and 1 weekend day); mean ± SD: 158.1 ± 61.9 in intervention and 154 ± 58.4 in control, at baseline. After 8 weeks: 157.2 ± 55.6 in intervention and 150.6 ± 49.8 in control
Magnesium status	Serum magnesium (mmol/L); mean ± SD: 0.9 ± 0.1 in intervention and 0.9 ± 0.1 in control. No changes reported after 8 weeks.
Intervention	250 mg/day magnesium oxide for 8 weeks
Comparator	placebo containing cornstarch, lactose and stearic acid
Training regimen	No specific training regimen but a physical activity questionnaire was used to report physical activity (Met-Min/Weeks), and subjects were advised to maintain same level of physical activity. (Activity levels decreased)
Outcomes of interest	Handgrip strength test in dominant hand using a calibrated (DIGI-II, Korea) digital hand-held dynamometer, highest of 3 measurements. Isometric knee extension strength (kg) in dominant leg using a Nicholas Manual Muscle Tester; Lafayette Inc, highest of 3 measurements. Body Composition measured using a Quad Scan 4000; Bodystat, Bioelectrical Impedance Analyser

Study 1: Risk of bias assessment

Item	Answer
Were eligibility criteria specified?	Yes
Were subjects randomly allocated to groups?	Yes
Was allocation concealed?	Don't know
Were groups similar at baseline for the most prognostic indicators?	Yes
Was there blinding of all subjects?	Yes
Was there blinding of all therapists?	Yes
Was there blinding of all assessors?	Yes
Were measures of at least one key outcome available for over 85% of initial subjects?	Yes
Was there an intention-to-treat analysis?	No
Was there a between-group statistical comparison?	Yes
Does the study provide point measures and measures of variability for at least one key outcome?	Yes

Appendix 1: Characteristics and Risks of bias of Included studies

Study 2: Characteristics of study

Author/s: Brilla and Haley, 1992

Design	Randomised, double-blind, placebo-controlled trial
Participants	26 untrained subjects, aged 18-30 years old
Dietary assessment (magnesium mg/day)	3-day measured diet record (246 mg/day; 70% of RDA as stated by authors)
Magnesium status	Not measured
Intervention	Participants in the intervention group were supplemented accordingly with magnesium oxide to reach total oral magnesium intake of 8 mg/kg bodyweight/day for 7 weeks (approx. 261 mg/day)
Comparator	sugar caplet as placebo
Training regimen	3 sets of 10 reps leg press and leg extension at 70% maximum voluntary contraction, 3 times per week
Outcomes of interest	Isokinetic quadriceps torque (Nm) measured with Orthotron dynamometer. Body composition measured with Bodycomp Light unit, Biolelectrical Impedance Analyser

Study 2: Risk of bias assessment

Item	Answer
Were eligibility criteria specified?	Yes
Were subjects randomly allocated to groups?	Yes
Was allocation concealed?	Don't know
Were groups similar at baseline for the most prognostic indicators?	Yes
Was there blinding of all subjects?	Yes
Was there blinding of all therapists?	Yes
Was there blinding of all assessors?	Yes
Were measures of at least one key outcome available for over 85% of initial subjects?	Yes
Was there an intention-to-treat analysis?	Don't know
Was there a between-group statistical comparison?	Yes
Does the study provide point measures and measures of variability for at least one key outcome?	Yes

Appendix 1: Characteristics and Risks of bias of Included studies

Study 3: Characteristics of study

Author/s: Setaro et al., 2010

Design	Randomised, double-blind, placebo-controlled trial
Participants	25 professional male, (15-20 years of age) volleyball players
Dietary assessment (magnesium mg/day)	None
Magnesium status	Plasma magnesium (mmol/L); mean ± SD: 0.9 ± 0.17 in intervention and 0.99 ± 0.2 in control, at baseline. After 4 weeks; 0.82 ± 0.7 in treated and 0.85 ± 0.07 in control.
Intervention	175 mg twice daily (350 mg/day) of magnesium oxide for 4 weeks
Comparator	250 mg twice daily (500 mg/day) of maltodextrin
Training regimen	no change (6 hours per day of volleyball training)
Outcomes of interest	Isokinetic torque (Nm) in knee flexors and extensors measured with Biodex Medical Systems Pro® dynamometer

Study 3: Risk of bias assessment

Item	Answer
Were eligibility criteria specified?	Yes
Were subjects randomly allocated to groups?	Yes
Was allocation concealed?	Don't know
Were groups similar at baseline for the most prognostic indicators?	Yes
Was there blinding of all subjects?	Yes
Was there blinding of all therapists?	Yes
Was there blinding of all assessors?	Yes
Were measures of at least one key outcome available for over 85% of initial subjects?	Yes
Was there an intention-to-treat analysis?	Yes
Was there a between-group statistical comparison?	Yes
Does the study provide point measures and measures of variability for at least one key outcome?	Yes

Appendix 1: Characteristics and Risks of bias of Included studies

Study 4: Characteristics of study

Author/s: Kass and Poeira, 2015

Design	Randomised, double-blind, placebo-controlled, cross-over trial
Participants	13 subjects, (7 males, 6 females), (mean ± SD age: 38.3 ± 5.3 years) recruited from recreational running, cycling and triathlete clubs, (45 ml/kg < $\dot{V}O_2$ max for males; 35 ml/kg < $\dot{V}O_2$ max for females)
Dietary assessment (magnesium mg/day)	4-day weighed food and beverage diary, including 3 weekdays and 1 weekend day (mean ± SD magnesium intake at baseline; 375 ± 104 in chronic treatment, 368 ± 173 in acute treatment, 551 ± 347 in chronic placebo control, 378 ± 79 acute placebo control (all groups had intakes above RDA for magnesium)
Magnesium status	Not taken
Intervention	Acute (1 week) 75mg four times daily (300 mg/day) magnesium citrate, or Chronic (4 weeks) 75mg four times daily (300 mg/day) magnesium citrate on non-testing days or 300 mg magnesium citrate 3 hours before exercise testing
Comparator	1 week washout period followed by a cross-over. Cornflour was used as a placebo.
Training regimen	Not reported
Outcomes of interest	1-RM bench press measured through 5-RM

Study 4: Risk of bias assessment

Item	Answer
Were eligibility criteria specified?	Yes
Were subjects randomly allocated to groups?	Yes
Was allocation concealed?	Don't know
Were groups similar at baseline for the most prognostic indicators?	Yes
Was there blinding of all subjects?	Yes
Was there blinding of all therapists?	Yes
Was there blinding of all assessors?	Yes
Were measures of at least one key outcome available for over 85% of initial subjects?	Yes
Was there an intention-to-treat analysis?	No
Was there a between-group statistical comparison?	Yes
Does the study provide point measures and measures of variability for at least one key outcome?	Yes

Appendix 1: Characteristics and Risks of bias of Included studies

Study 5: Characteristics of study

Author/s: Kass, Skinner and Poeira, 2013

Design	Randomised, controlled, trial
Participants	16 males, 19-24 years old, > 4 hours/week aerobic exercise at >13 Borg Rating of Perceived Exertion Scale (RPE), normotensive (110/70 mmHg - 135/85 mmHg)
Dietary assessment (magnesium mg/day)	3-day dietary recall to assess habitual magnesium intake
Magnesium status	Not taken
Intervention	150 mg twice daily (300 mg/day) magnesium oxide for 14 days
Comparator	No supplementation
Training regimen	> 4 hours/week aerobic exercise at > 13 Borg RPE
Outcomes of interest	mean of 3, 5-second maximal isometric bench press on a Marcy Smith Machine Plus measured by a Digital Analyser Isometric Transducer

Study 5: Risk of bias assessment

Item	Answer
Were eligibility criteria specified?	Yes
Were subjects randomly allocated to groups?	Yes
Was allocation concealed?	Don't know
Were groups similar at baseline for the most prognostic indicators?	Yes
Was there blinding of all subjects?	No
Was there blinding of all therapists?	No
Was there blinding of all assessors?	Don't know
Were measures of at least one key outcome available for over 85% of initial subjects?	Yes
Was there an intention-to-treat analysis?	Yes
Was there a between-group statistical comparison?	Yes
Does the study provide point measures and measures of variability for at least one key outcome?	Yes

Appendix 1: Characteristics and Risks of bias of Included studies

Study 6: Characteristics of study

Author/s: Veronese et al., 2014

Design	Randomised Controlled Trial
Participants	139 healthy women, > 65 years (mean ± SD age: 71.5 ± 5.2 years) attending a mild fitness program
Dietary assessment (magnesium mg/day)	Estimated 3 day record and food frequency questionnaire (not reported but stated that 24 participants in intervention and 30 in control group had below RDA intakes of Mg (p = 0.86)
Magnesium status	Serum magnesium (mmol/L); mean ± SD: 0.83 ± 0.04 in intervention and 0.84 ± 0.06 in control at baseline. Increase observed at 12 weeks (0.009 ± 0.04 in control and 0.03 ± 0.04 in treated)
Intervention	300 mg/day, magnesium oxide for 12 weeks
Comparator	no placebo
Training regimen	twice weekly mild fitness program
Outcomes of interest	Taken at baseline and at 12 weeks: Isometric knee extension torque (Nm) and isokinetic knee flexion and extension (Nm) using Easytech dynamometer chair, highest peak torque out of 3, for each. Handgrip (kg) measured with DynEx hand dynamometer, highest of 3. Body composition using Hologic Discovery A, DXA scan with fan-beam technology

Study 6: Risk of bias assessment

Item	Answer
Were eligibility criteria specified?	Yes
Were subjects randomly allocated to groups?	Yes
Was allocation concealed?	Yes
Were groups similar at baseline for the most prognostic indicators?	Yes
Was there blinding of all subjects?	No
Was there blinding of all therapists?	Yes
Was there blinding of all assessors?	Yes
Were measures of at least one key outcome available for over 85% of initial subjects?	Yes
Was there an intention-to-treat analysis?	Yes
Was there a between-group statistical comparison?	Yes
Does the study provide point measures and measures of variability for at least one key outcome?	Yes

Appendix 1: Characteristics and Risks of bias of Included studies

Study 7: Characteristics of study

Author/s: Gullestad et al., 1992

Design	Randomised, double-blind, placebo-controlled, trial
Participants	52 (17 females and 35 males) chronic (> 10 years) alcoholics, mean age: 57 years, serum creatinine < 150 μmol/L, no cardiac A-V disturbances and no previous Mg supplementation, hepatitis A and B negative.
Dietary assessment (mg/day)	None but all participants were told to minimise alcohol consumption and avoid magnesium rich foods
Magnesium status	Serum magnesium (mmol/L); mean ± SD: 0.86 ± 0.12 in intervention and 0.84 ± 0.15 in control, at baseline. Change after 6 weeks: 0.02 ± 0.02 in treated and -0.05 ± 0.03 in control
Intervention	125 mg three times daily (375 mg/day) magnesium lactate-citrate for 6 weeks
Comparator	matched placebo
Training regimen	None
Outcomes of interest	Handgrip strength (bar) measured with a Martin strain-gauge dynamometer, highest of 3 readings.

Study 7: Risk of bias assessment

Item	Answer
Were eligibility criteria specified?	Yes
Were subjects randomly allocated to groups?	Yes
Was allocation concealed?	Don't know
Were groups similar at baseline for the most prognostic indicators?	Yes
Was there blinding of all subjects?	Yes
Was there blinding of all therapists?	Yes
Was there blinding of all assessors?	Yes
Were measures of at least one key outcome available for over 85% of initial subjects?	Yes
Was there an intention-to-treat analysis?	No
Was there a between-group statistical comparison?	Yes
Does the study provide point measures and measures of variability for at least one key outcome?	Yes

Appendix 1: Characteristics and Risks of bias of Included studies

Study 8: Characteristics of study

Author/s: Aagaard et al., 2005

Design	Randomised, placebo-controlled trial
Participants	59 patients (49 males, 10 females), age range: (34-61) with alcoholic liver disease and mean daily alcohol consumption of 187 g/day for more than 5 years.
Dietary assessment (magnesium mg/day)	Not measured
Magnesium status	Muscle magnesium (μmol/g wet weight), reported instead. After 7 weeks; increased by 7% in treatment group
Intervention	728 mg intravenous magnesium sulphate diluted in 1litre 5% glucose solution on days 1 and 2 followed by 7 weeks of 150 mg twice daily (300 mg/day) magnesium oxide
Comparator	1L of 5% glucose solution on days 1 and 2 followed by 7 weeks of a mixture of lactulose, gelatine and stearate
Training regimen	None required
Outcomes of interest	Isokinetic knee extension strength (Nm) measured with Lido Active Muscle Joint dynamometer, largest peak torque of 8. Muscle mass (kg) determined through 24-hour urinary creatinine excretion.

Study 8: Risk of bias assessment

Item	Answer
Were eligibility criteria specified?	Yes
Were subjects randomly allocated to groups?	Yes
Was allocation concealed?	Yes
Were groups similar at baseline for the most prognostic indicators?	Yes
Was there blinding of all subjects?	Yes
Was there blinding of all therapists?	Don't know
Was there blinding of all assessors?	Don't know
Were measures of at least one key outcome available for over 85% of initial subjects?	Yes
Was there an intention-to-treat analysis?	Don't know
Was there a between-group statistical comparison?	Yes
Does the study provide point measures and measures of variability for at least one key outcome?	Yes

Appendix 1: Characteristics and Risks of bias of Included studies

Study 9: Characteristics of study

Author/s: Poikolainen and Alho, 2008

Design	Randomised, double-blind, placebo-controlled, trial
Participants	118 participants (81 males, 37 females), 20-64 years (mean ± SD age: 45.3 ± 10 years) with acute alcohol withdrawal symptoms or elevated Serum Gamma-Glutamyltransferase, < 10 tablets of 250mg Mg over the previous 2 months, no history of heart rhytm disturbances, Mg not contraindicated, normal serum creatinine
Dietary assessment (magnesium mg/day)	Not measured
Magnesium status	Serum magnesium (mmol/L):Taken at baseline and at 8 weeks, only changes reported (mean ± SD: 0.06 ± 0.12 in treated and 0.01 ± 0.08 in placebo)
Intervention	8 weeks of 250mg twice daily magnesium (500 mg/day), consisting of a mixture of magnesium carbonate, acetate and hydroxide
Comparator	matched placebo
Training regimen	None
Outcomes of interest	Maximal handgrip strength measured in sitting position with Martin strain-gauge dynamometer, mean of three measurements

Study 9: Risk of bias assessment

Item	Answer
Were eligibility criteria specified?	Yes
Were subjects randomly allocated to groups?	Yes
Was allocation concealed?	Don't know
Were groups similar at baseline for the most prognostic indicators?	Don't know
Was there blinding of all subjects?	Yes
Was there blinding of all therapists?	Yes
Was there blinding of all assessors?	Yes
Were measures of at least one key outcome available for over 85% of initial subjects?	No
Was there an intention-to-treat analysis?	Yes
Was there a between-group statistical comparison?	Yes
Does the study provide point measures and measures of variability for at least one key outcome?	Yes

Appendix 2: Tables of Effect

Table 1: Effects of Magnesium Supplementation on Strength

Author	PEDro Score/ 10	Subjects (n) and age	Health status	Dietary Mg intake at baseline	Changes in Magnesium status	Treatment details	Mg supplement	Duration	Physical activity	Compliance to treatment	Outcome/s considered	Treatment effect
Moslehi, Vafa, Sarraf-zadeh & Foroush ani (2013)	8	74 females, aged 40-55 years	Overweight but healthy	156.05 ± 60.15 mg/day	No changes reported after 8 weeks	250 mg/day	MgO	8 weeks	No significant changes in mean physical activity	93%	Handgrip strength and Isometric knee extension	No significant differences
Brilla & Haley (1992)	8	26 subjects, aged 18-30	Untrained	Mean of 246 mg/day	Not measured	Total of dietary and supplemented 8 mg/kg bodyweight/day (Around 271 mg/day)	MgO	7 weeks	3 X 10 repetitions leg press and leg extension, 3 times per week	Not measured	Isokinetic knee extension strength	Mg supplemented gained more strength ($p < 0.05$)
Setaro et al. (2014)	9	25 males, aged 15-20	Healthy	Not measured	Plasma Mg decreased more in treatment arm	350 mg/day	MgO	4 weeks	6 hours professional volleyball off-season training/day	Not measured	Isokinetic knee flexion and extension	Both groups gained strength. No significant difference between groups
Kass & Poeira (2015)	8	13 subjects (7 males, 6 females), mean age: 38.3 years	Healthy	All groups > 350 mg/day. Chronic placebo group > 550 mg/day	Not measured	300 mg/day	Magnesium citrate	Acute (1 week); Chronic (4 weeks)	Recreational runners, cyclists and triathletes	Not measured	1-RM bench press	Strength increase in acute intervention

Appendix 2: Tables of Effect

Table 1: Effects of Magnesium Supplementation on Strength (Continued [1])

Author	PEDro Score/10	Subjects (n) and age	Health status	Dietary Mg intake at baseline	Changes in Magnesium status	Treatment details	Mg supplement	Duration	Physical activity	Compliance to treatment	Outcome/s considered	Treatment effect
Kass, Skinner & Poeira (2013)	6	16 males, aged 19-24	Healthy	6 subjects < 300 mg/day; 10 subjects > 300 mg/day	Not measured	300 mg/day	MgO	2 weeks	>4 hours/week aerobic exercise	Not measured	5 second maximal isometric bench press contraction	No significant differences
Veronese et al. (2014)	9	139 women, aged >65 years	Healthy	24 in intervention, 30 in control had < 320 mg of Mg/day	Serum Mg increased in intervention group	300 mg/day	MgO	12 weeks	Mild fitness program	85-95%	Isometric knee extension. Isokinetic knee extension and flexion. Handgrip strength.	Both groups gained strength. No difference significant between groups
Gullestad et al. (1992)	8	52 (17 females, 35 males), mean age: 57 years	Chronic (> 10 years) alcoholics	Participants advised to reduce alcohol and magnesium-rich foods	Serum Mg increased slightly in treated and decreased in control	375 mg/day	Magnesium lactate-citrate	6 weeks	None specified	Not measured	Handgrip strength	Increased significantly in intervention group
Aagard et al. (2005)	7	59 patients (49 males, 10 females), aged 34-61 years	Alcoholic liver disease. Mean daily alcohol 168g/day for > 5 years	Not measured	Muscle Mg increased 7% in intervention	728 mg/day IV Mg for 2 days and 7 weeks 300mg/day oral Mg	IV $MgSO_4$ and oral MgO	7 weeks	None specified	16 dropouts	Isokinetic knee extension	Both groups gained strength. No significant difference between groups

Appendix 2: Tables of Effect

Table 1: Effects of Magnesium Supplementation on Strength (Continued [2])

Author	PEDro Score/10	Subjects (n) and age	Health status	Dietary Mg intake at baseline	Changes in Magnesium status	Treatment details	Mg supplement	Duration	Physical activity	Compliance to treatment	Outcome/s considered	Treatment effect
Poikolainen & Alho (2008)	7	118 subjects (81 males, 37 females), aged 20-64 years	Acute alcohol withdrawal symptoms. Elevated S-GGT	Not measured	Serum Mg; increased in both groups but more in supplemented	500 mg/day	Mixture of magnesium carbonate, acetate and hydroxide	8 weeks	None specified	83.40%	Handgrip strength	No significant differences

Appendix 2: Tables of Effect

Table 2: Effects of Magnesium Supplementation on Body Composition

Author	PEDro Score /10	Subjects (n) and age	Health status	Dietary Mg intake at baseline	Changes in Magnesium status	Treatment details	Mg supplement	Duration	Physical activity	Compliance to treatment	Body composition outcomes	Treatment effect
Moslehi, Vafa, Sarrafzadeh & Foroushani (2013)	8	74 females, aged 40-55 years	Overweight but healthy	156.05 ± 60.15 mg/day	No changes reported after 8 weeks	250 mg/day	MgO	8 weeks	No significant changes in mean physical activity	93%	Lean Body Mass and Fat Mass (BIA)	Increase in lean body mass and reduction in fat mass
Brilla & Haley (1992)	8	26 subjects, aged 18-30	Untrained	Mean of 246 mg/day	Not measured	Total of dietary and supplemented Mg 8 mg/kg bodyweight/day (Around 271 mg/day)	MgO	7 weeks	3 X 10 repetitions leg press and leg extension, 3 times per week	Not measured	Lean Body Mass and Fat Mass (BIA)	No significant differences
Veronese et al. (2014)	9	139 women, aged >65 years	Healthy	24 in intervention, 30 in control had intakes < 320 mg of Mg/day	Serum Mg significantly increased in intervention group	300 mg/day	MgO	12 weeks	Mild fitness program	85-95%	Fat-free mass and Fat Mass (DXA scan)	No significant differences
Aagard et al. (2005)	7	59 patients (49 males, 10 females), aged 34-61 years	Alcoholic liver disease. Mean daily alcohol 168g/day for > 5 years	Not measured	Muscle Mg increased 7% in intervention	728 mg/day IV Mg for 2 days and 7 weeks 300mg/day oral Mg	IV $MgSO_4$ and oral MgO	7 weeks	None specified	16 dropouts	Muscle mass (24-hour urinary creatinine excretion)	Both groups gained muscle mass. No significant difference between groups