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Review Article

Minerals and Sarcopenia; The Role of Calcium, Iron, Magnesium, Phosphorus, Potassium, Selenium, Sodium, and Zinc on Muscle Mass, Muscle Strength, and Physical Performance in Older Adults: A Systematic Review

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A B S T R A C T

Introduction: Minerals may contribute to prevent and treat sarcopenia, the age-related loss of muscle mass, muscle strength, and physical performance. So far, there is no comprehensive review on the impact of minerals on sarcopenia outcomes. The aim of this systematic review is to evaluate the role of calcium, iron, magnesium, phosphorus, potassium, selenium, sodium, and zinc on muscle mass, muscle strength, and physical performance in older adults.

Methods: A systematic search was conducted between March 2016 and July 2016, in the PubMed database using predefined search terms. Articles on the role of dietary mineral intake or mineral serum concentrations on muscle mass, muscle strength, physical performance, and/or the prevalence of sarcopenia in healthy or frail older adults (average age $\geq$ 65 years) were selected. Only original research publications were included. The search and data extraction were conducted in duplicate by 2 independent researchers. The Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) statement was followed in constructing this systematic review. The Effective Public Health Practice Project (EPHPP) Quality Assessment Tool for Quantitative Studies was used to evaluate the quality of the selected articles.

Results: From the 3346 articles found, a total of 10 studies met the inclusion criteria. Observational studies showed that serum selenium (n = 1) and calcium intake (n = 1) were significantly associated with muscle mass, and magnesium (n = 1), selenium (n = 1), iron (n = 1), and zinc (n = 1) intake were significantly and positively associated with physical performance in older adults. Furthermore, magnesium (n = 2), selenium (n = 2), calcium (n = 2), and phosphorus (n = 1) intake were associated with the prevalence of sarcopenia. Magnesium supplementation improved physical performance based on one randomized controlled trial. No studies on the role of sodium or potassium on muscle mass, muscle strength, or physical performance were found.

Conclusion: Minerals may be important nutrients to prevent and/or treat sarcopenia. Particularly, magnesium, selenium, and calcium seem to be most promising. Most of the included studies, however, were observational studies. Therefore, more randomized controlled trials are needed to elucidate the potential benefits of mineral intake to prevent and/or treat sarcopenia and support healthy aging.

Aging is associated with sarcopenia, the age-related loss of muscle mass, muscle strength, and physical performance.[1] This loss is associated with dependence, poor quality of life, hospital admission, and premature death.[2] The cause of sarcopenia is multifactorial and includes poor nutritional intake.[3,4] The role of dietary protein and the

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development of sarcopenia has obtained most attention. Minerals, however, may be important nutrients that can contribute to the prevention and treatment of sarcopenia, but are poorly studied.[5]

It is known that several minerals play a role in muscle metabolism and muscle function. For example, calcium, potassium, and sodium are necessary for healthy muscle and nerve activity, and magnesium is thought to have a positive effect on muscle relaxation and could improve muscle function.[6–9] Low iron blood serum concentrations are thought to be associated with poor physical performance.[10] A lack of phosphorus can lead to muscle weakness,[11,12] whereas selenium deficiency is associated with several muscular diseases.[11–15] Zinc is able to delay oxidative processes, which are known to contribute to disuse muscle atrophy.[16–18]

Although it is clear that these minerals play an important role in muscle functioning, a comprehensive overview of their possible effects on sarcopenia outcomes in older adults is lacking. Therefore, the aim of this systematic review is to evaluate the role of calcium, magnesium, iron, sodium, potassium, phosphorus, selenium, and zinc on muscle mass, muscle strength, and physical performance.

Methods

The Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) statement was followed in constructing this systematic review.[19] The PRISMA checklist can be found in Supplemental Material 1.

Search Strategy and Selection

A systematic search in PubMed has been performed between March and July 2016, using predefined search terms deducted from the eligibility criteria. The complete search has been performed in duplicate by 2 independent researchers. Title and abstract were screened for eligibility according to predefined inclusion and exclusion criteria. If eligible, the full-text articles were screened for final inclusion. In addition, a manual search of reference lists of included and other relevant articles has been performed to increase the number of potentially usable articles. In case of discrepancy between inclusion of an article, the 2 investigators discussed the selection until agreement was reached. A standardized data extraction form has been used to summarize the information from the selected articles. A complete overview of the search can be found in Appendix 1.

Eligibility Criteria

The following inclusion criteria were used:

- Publishing date between 2006 and 2016
- Published in the English language
- Studying a human population with an average age of ≥65 years
- Studies on dietary intake or blood serum concentrations of calcium, iron, magnesium phosphorus, potassium, selenium, sodium, and zinc on muscle mass, muscle strength, physical performance, and sarcopenia of any definition
- Muscle mass measured with computed tomography, dual energy X-ray absorptiometry, magnetic resonance imaging, whole-body air plethysmography, bio impedance analysis (BIA), or dual photon absorptiometry
- Muscle strength measured with either hand grip strength, knee/leg extension, leg pressure strength, or elastic bands
- Physical performance measured with Short Physical Performance Battery (SPPB), chair stand, balance test, gait speed test, 400-m walk test, 6-minute walk test (6MWT), or Timed-Up-and-Go test

No criteria were established for study design, the length of follow-up, or the minimal number of participants. Intervention studies that included other macro- and micronutrients than the minerals of interest, exercise, or studies that included subjects with a disease that influences protein synthesis, muscle strength, muscle mass, or physical performance such as muscle disorders, neoplasms, heart failure, cirrhosis, HIV, renal insufficiency, chronic obstructive pulmonary disease, and hyperparathyroidism were excluded.[20–27] Studies evaluating hyponatremia were excluded, because hyponatremia can be achieved independent of sodium intake, for example, because of vomiting. Studies evaluating regular or high blood concentrations of sodium were still of interest. Studies published as letters, commentaries, editorials, case reports, systematic reviews, or duplicate publications from the same studies were also excluded.

Quality Assessment

The Effective Public Health Practice Project (EPHPP) Quality Assessment Tool for Quantitative Studies was used to evaluate the quality of the selected articles.[28,29] Articles were reviewed for risk of bias, study design, confounders, method of blinding, data collection methods, and withdrawals. No additional action was taken upon evaluation outcome.

Results

A total of 3346 articles were identified. After removing duplicates, 2775 articles remained, of which 2727 were excluded after title and abstract screening. The remaining 48 articles were screened on full text, of which 10 studies met the eligibility criteria. A full overview of the selection of articles is summarized in Figure 1.

Study Characteristics

Details of the 10 studies are provided in Table 1. The average age ranged from 66.5 to 76.5 years and 55% of the subjects was female. All studies included community-dwelling older adults. In total, 1 randomized controlled trial,[30] 1 longitudinal study,[31] 1 case-control,[39] 1 cohort,[32] and 6 cross-sectional studies[33–38] were included.

Dietary calcium was evaluated by 5 studies,[33,36–39] dietary iron by 1,[33] serum iron by 1,[31] dietary magnesium by 3,[30,38,39] dietary phosphorus by 1,[32] dietary selenium by 4,[32,34,38,39] serum selenium by 1,[35] and dietary zinc by 3.[33,38,39] No studies on the role of potassium or sodium that met the inclusion criteria were found.

Muscle mass was measured by dual energy x-ray absorptiometry[34,36] or BIA.[35] Muscle strength was measured by isokinetic flexion and extension strength, isometric knee extension torque, and handgrip strength.[30] Physical performance was measured by Short Physical Performance Battery,[30,31] gait speed,[30,32,33] and chair stand.[30,32] In addition, 4 studies evaluated the association between minerals and the prevalence of sarcopenia.[36–39]

Study Quality

Using the Quality Assessment Tool for Quantitative Studies,[28] 6 studies were rated as 1, 3 studies were rated as 2, and 1 study was rated as 3, with rating 1 being weak and 3 being strong (Table 1). The overall quality was rated as 1.5. The quality assessment per article is presented in Appendix 2.

Minerals

Table 2 provides details on the impact of calcium, iron, magnesium, phosphorus, selenium, and zinc on muscle mass, muscle strength, physical performance, and sarcopenia prevalence in older adults.

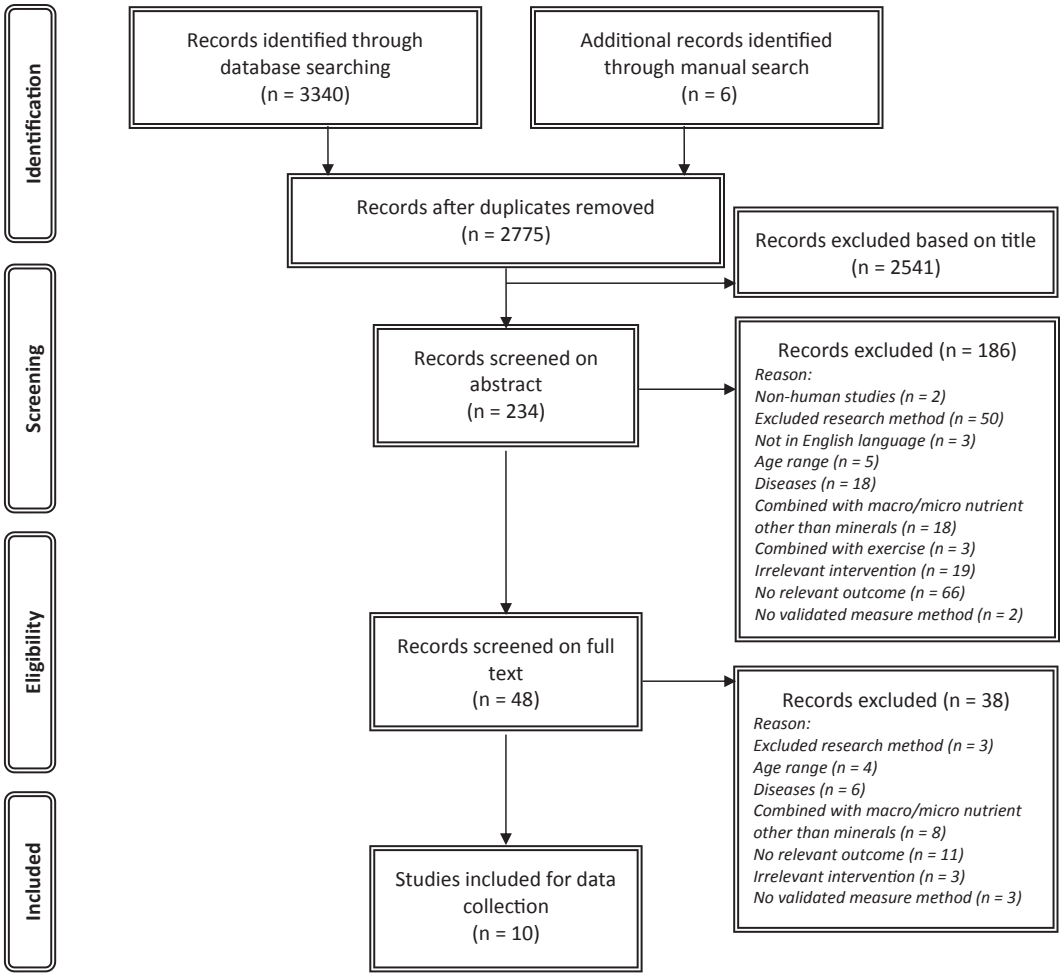

Fig. 1. Flow-chart of search strategy and study selection.

Observational studies showed that serum selenium[35] and calcium intake[36] were significantly associated with muscle mass. Magnesium,[30] selenium,[32] iron,[33] and zinc[33] intake were significantly and positively associated with physical performance in older adults. Furthermore, magnesium,[38,39] selenium,[38,39] calcium,[36,37] and phosphorus[39] intake were associated with the prevalence of sarcopenia. Magnesium supplementation improved physical performance based on one randomized controlled trial.[30] No studies on the role of sodium

Table 1
Study Details and Participant Characteristics of the 10 Included Studies

Author (y)	Mineral Studied	Study Design (Quality)*	Sample Size (% Female)	Mean Age (y)
Veronese et al (2014)[30]	Magnesium	Randomized controlled trial (2)	124 (100)	71.5
Bartali et al (2008)[31]	Serum iron	Longitudinal (3)	698 (54)	73.7
Martin et al (2011)[32]	Selenium	Cohort (2)	628 (45)	67.9
Waters et al (2014)[33]	Calcium Iron Zinc	Cross-sectional (1)	315 (62)	76.5
Chaput et al (2007)[34]	Selenium	Cross-sectional (1)	50 (68)	66.5
Chen et al (2014)[35]	Serum selenium	Cross-sectional (1)	327 (68)	71.5
Seo et al (2013)[36]	Calcium	Cross-sectional (1)	1339 (53)	70.1
Oh et al (2015)[37]	Calcium	Cross-sectional (1)	1433 (54)	68.6
Ter Borg et al (2016)[38]	Calcium Magnesium Serum magnesium Selenium Zinc	Cross-sectional (1)	227 (52)	74.0
Verlaan et al (2017)[39]	Calcium Magnesium Phosphorus Selenium Zinc	Case-control (2)	132 (59)	71.0

*Based on the Effective Public Health Practice Project (EPHPP) quality assessment tool for quantitative studies.

Table 2
Outcomes of the 10 Included Studies

Author (y)	Mineral Studied*	Outcome	Outcome Measurement	Effect Size†	*P* Value†
Veronese et al (2014)[30]	**Magnesium**	Muscle strength	PT isokinetic flex	Δ 2.57 nm	>.05
			PT isokinetic extension	Δ 0.76 nm	>.05
			PT isometric	Δ 13.33 nm	>.05
			Handgrip	Δ 0.51 kg	>.05
		Physical performance	SPPB	**Δ 0.41 points**	**.03**
			Chair stand	**Δ −1.31 s**	**.0001**
			Gait speed	**Δ 0.14 m/s**	**.006**
Bartali et al (2008)[31]	Serum iron	Physical performance	SPPB	OR = 1.10 (95% CI 0.77, 1.59)	>.05
Martin et al (2011)[32]	**Selenium**	Physical performance	Gait speed	Male: β = −0.012 (95% CI −0.065, 0.041)	>.05
				Female: β = −0.091 (95% CI−0.165, −0.018)	**.015**
			Chair stand	Male: β = 0.983 (95% CI 0.961, 1.006)	>.05
				Female: β = 0.983 (95% CI 0.955, 1.012)	>.05
Waters et al (2014)[33]	Calcium	Physical performance	Gait speed	Male: OR = 2.18 (95% CI 0.67, 7.09)	—
				Female: OR = 1.15 (95% CI 0.55, 2.41)	
	Iron			**Male: OR = 4.81 (95% CI 1.51, 15.31)**	
				Female: OR = 0.94 (95% CI 0.44, 2.01)	
	Zinc			**Male: OR = 3.57 (95% CI = 1.14, 11.18)**	
				Female: OR = 2.33 (95% CI = 1.12, 4.85)	
Chaput et al (2007)[34]	Selenium	Muscle mass	DXA	ρ_s = 0.08	>.05
Chen et al (2014)[35]	**Serum selenium**	Muscle mass	BIA	**OR = 4.62 (95% CI 2.11, 10.1)**	**.001**
Seo et al (2013)[36]	**Calcium**	Muscle mass	DXA	**ρ = 0.276**	**<.001**
		Sarcopenia by definition of Lim (2010)		**OR = 0.259 (95% CI 0.087, 0.768)**	***P* for trend = .014**
Oh et al (2015)[37]	**Calcium**	Sarcopenia by definition of Muscaritoli (2010)		—	**Male: .002**
					Female: >.05
Ter Borg et al (2016)[38]	Calcium	Sarcopenia by definition of Cruz-Jentoft (2010)		—	>.05‡
					>.05§
	Magnesium				**.009**‡
					.024§
	Serum magnesium				>.05
	Selenium				**.02**‡
					>.05§
	Zinc				>.05‡
					>.05§
Verlaan et al (2017)[39]	Calcium	Sarcopenia by definition of Cruz-Jentoft (2010)		—	>.05
	Magnesium				**.015**
	Phosphorus				**.014**
	Selenium				**.039**
	Zinc				>.05

BIA, bio impedance analysis; DXA, dual energy x-ray absorptiometry; OR, odds ratio; PT, highest peak torque; ρ_s, Spearman rho; SPPB, Short Physical Performance Battery.
*Statistically significant minerals are shown in bold.
†Statistically significant values are shown in bold.
‡Dietary intake without supplement intake.
§Dietary intake with supplement intake.

or potassium on muscle mass, muscle strength, physical performance, or the prevalence of sarcopenia were found.

Discussion

This review is the first systematic review that provides a comprehensive overview of the role of minerals on muscles mass, muscle strength, and physical performance in relation to sarcopenia in older adults. Magnesium, selenium, and calcium seem to be the most promising minerals to prevent and/or treat sarcopenia.

In this review, magnesium intake was significantly associated with sarcopenia, and one randomized controlled trial showed that magnesium supplementation improved performance in older adults. These findings are supported by studies of Scott et al[40] and Dominguez et al.[41] Magnesium intake was significantly and positively associated with appendicular lean mass, based on a prospective cohort study.[40] Serum magnesium correlated independently with muscle strength.[41] Dietary magnesium intake did significantly differ between sarcopenic subjects and nonsarcopenic subjects.[38,39] Mechanistically, magnesium plays an important role in muscle function and metabolism, along with its involvement in more than 600 enzymic reactions. For example, magnesium is involved in protein synthesis and ATP synthesis, and is responsible for muscle relaxation.[7,8]

Serum magnesium concentrations did not differ between sarcopenic subjects and nonsarcopenic subjects in the study of Ter Borg et al.[38] This might be explained by the strict regulation of serum magnesium by urinary excretion, bone stores, and gastrointestinal tract.[42] This means that serum magnesium concentrations may not be sensitive to small differences in magnesium intake, but is to larger differences in magnesium intake.[42] This finding has been confirmed by the randomized controlled trial of Veronese et al,[30] where a significant increase of serum magnesium concentrations was found after supplementation with 300 mg/d magnesium oxide for 12 weeks. In the same study, the effect of magnesium on physical performance was more evident in subjects with a dietary magnesium intake below the recommended dietary allowance (RDA)[43] at baseline.[30] This finding is in agreement with previous research.[8,44] In addition, the dietary intake of magnesium was below the RDA[43] in sarcopenic older adults in the studies of Ter Borg et al[38] and Verlaan et al.[39] Collectively, magnesium may be an important nutrient to prevent and treat sarcopenia in older adults.

Another potential nutrient that may positively affect sarcopenia outcomes is selenium. In our review, we included 4 studies that showed a positive association of selenium and muscle mass, physical performance, and sarcopenia.[32,35,38,39] These findings are in agreement with the studies of Beck et al[45] and Lauretani et al.[46] However, in the study of Chaput et al,[34] no association was found between

selenium and muscle mass. This could be explained by the high intake of selenium, which was twice the RDA.[43] This is in agreement with the review of Rayman.[14] In the studies that found an association between selenium and muscle mass or physical performance, selenium intakes were below the RDA.[43] Moreover, all subjects had low serum selenium concentrations. In addition, selenium intakes were significantly lower in sarcopenic older adults in comparison with nonsarcopenic older adults.[38,39] These associations may be explained by the potential action of selenium on muscle tissue. Through selenoproteins, selenium is thought to have an effect on muscle synthesis and function, although the exact underlying mechanisms still remain unclear.[47] A selenium deficiency is thought to cause myopathy.[48] All this together indicates that selenium has the potential to prevent and treat sarcopenia.

In this review, the findings on the relation between calcium and sarcopenia were contradictory.[33,36–39] This could be due to the difference in calcium intake of the study populations. The intake was higher in the studies that did not find an association[38,39] than in the studies that did find an association[36,37] between calcium and sarcopenia. In addition, calcium intake was high in the study of Waters et al,[33] who also did not find an association between calcium and physical performance. The calcium intake was low (<415 mg/d) in the study of Seo et al,[36] who did find an association between calcium and muscle mass. This suggests that the role of calcium in the prevention and treatment of sarcopenia seems to be more promising in older adults with a low calcium intake. A hypothesis of the underlying mechanism could be a decreased calcium absorption and an altered calcium homeostasis, which is linked with muscle weakness in the aged muscle, according to recent studies.[49,50] Calcium is highly dependent on the presence of vitamin D for its absorption from the diet. Nevertheless, recent animal research suggests that calcium uptake is also possible through passive absorption.[51] Serum 25-hydroxyvitamin D levels were significantly lower in sarcopenic older adults in the studies that did find an association[36,37] than in the studies that did not find an association[38,39] between calcium and sarcopenia. However, the study of Seo et al[36] showed that after adjusting for serum 25-hydroxyvitamin D, calcium intake was still associated with sarcopenia. The study of Waters et al[33] found a significantly lower vitamin D intake in sarcopenic older adults, but serum 25-hydroxyvitamin D levels were not provided. Clearly, more research is warranted to elucidate the potential role of calcium in the development of sarcopenia.

Zinc and iron may be important in the prevention and treatment of sarcopenia, as they can be linked with oxidative stress.[17,52] Oxidative stress, through accumulation of reactive oxygen species, might cause muscle degeneration and a reduction of muscle strength.[53,54] Studies of Waters et al[33] and Scott et al[40] showed an association between iron and zinc, and physical performance and appendicular lean mass. However, Bartali et al,[31] Ter Borg et al,[38] and Verlaan et al[39] were unable to find an association with sarcopenic outcomes. This inconsistency may be explained by the differences in study design and outcome measures. At this stage, the role of iron and zinc on sarcopenia remains unclear.

The possible effect of phosphorus, potassium, or sodium on sarcopenia remains unclear because of an insufficient amount of articles that met the eligibility criteria.

This present review is, to our knowledge, the first systematic review studying the potential role of minerals on sarcopenia outcomes, giving a clear overview. An additional strength of this review is that we aimed to only include studies that investigated the role of a single mineral. By doing so, the role of the studied minerals on sarcopenia exclusively becomes clear. In addition, the search and selection of the articles were done by 2 independent researchers to limit selection bias. However, there were also some limitations. The studies of Scott et al,[40] Dominguez et al,[41] Beck et al,[45] and Lauretani et al[46] were excluded from this review because of strict criteria on age and underlying disease. However, these studies supported our findings. Most of the studies included in this review scored low on the quality assessment. This is because the design of most of the studies was cross-sectional. Only 1 study was a randomized controlled trial, which produces more sound evidence than cross-sectional studies. This limits the power of the findings. More studies with a strong study design, preferably randomized controlled trials, are warranted to gain insight in the direction of the observed relations and the possible different effects of magnesium, selenium, and calcium on muscle mass, muscle strength, and physical performance.

Conclusion

Based on the current available literature, minerals may be important nutrients to prevent and/or treat sarcopenia. In particular, magnesium, selenium, and calcium are most promising. Most of the included studies, however, were observational studies. Therefore, more randomized controlled trials are needed to elucidate the potential benefits of mineral intake to prevent and/or treat sarcopenia and support healthy aging.

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Appendix 1
Search Strings

Mineral	Search String
Calcium	(Elderly[Title/Abstract] OR "older people"[Title/Abstract] OR older person*[Title/Abstract] OR senior[Title/Abstract] OR aged[MeSH Terms] OR "aging"[MeSH Terms] OR ageing[Title/Abstract] OR "independent living"[MeSH Terms] OR "community dwelling"[Title/Abstract] OR "frail elderly"[MeSH Terms] OR "Aged, 80 and over"[MeSH Terms]) AND ("calcium, dietary"[MeSH Terms] OR calcium[Title/Abstract]) AND ("Muscle mass"[Title/Abstract] OR "muscles"[MeSH Terms] OR "lean body mass"[Title/Abstract] OR "muscle, skeletal"[MeSH Terms] OR "fat free mass"[Title/Abstract] OR "muscular atrophy"[MeSH Terms] OR "muscle waste"[Title/Abstract] OR "muscle loss"[Title/Abstract] OR sarcopenia[MeSH Terms]) OR ("Muscle strength"[MeSH Terms] OR strength[Title/Abstract] OR dynapenia[Title/Abstract] OR "strength loss"[Title/Abstract] OR "muscle weakness"[MeSH Terms]) OR ("Physical performance"[Title/Abstract] OR physical function*[Title/Abstract] OR "functional mobility"[Title/Abstract] OR "activities of daily living"[MeSH Terms] OR "Mobility Limitation"[MeSH Terms] OR "Physical Fitness"[MeSH Terms])) NOT ("rats"[MeSH Terms] OR "rabbits"[MeSH Terms] OR "animals"[Title] OR "mice"[MeSH Terms] OR "in vitro techniques"[MeSH Terms] OR "Neoplasms"[MeSH Terms] OR "Children"[Title])
Magnesium	(Elderly[Title/Abstract] OR "older people"[Title/Abstract] OR older person*[Title/Abstract] OR senior[Title/Abstract] OR aged[MeSH Terms] OR "aging"[MeSH Terms] OR ageing[Title/Abstract] OR "independent living"[MeSH Terms] OR "community dwelling"[Title/Abstract] OR "frail elderly"[MeSH Terms] OR "Aged, 80 and over"[MeSH Terms]) AND ("magnesium"[MeSH Terms] OR "dietary magnesium"[Title/Abstract] OR "magnesium"[Title/Abstract]) AND (("Muscle mass"[Title/Abstract] OR "muscles"[MeSH Terms] OR "lean body mass"[Title/Abstract] OR "muscle, skeletal"[MeSH Terms] OR "fat free mass"[Title/Abstract] OR "muscular atrophy"[MeSH Terms] OR "muscle waste"[Title/Abstract] OR "muscle loss"[Title/Abstract] OR sarcopenia[MeSH Terms]) OR ("Muscle strength"[MeSH Terms] OR strength[Title/Abstract] OR dynapenia[Title/Abstract] OR "strength loss"[Title/Abstract] OR "muscle weakness"[MeSH Terms]) OR ("Physical performance"[Title/Abstract] OR physical function*[Title/Abstract] OR "functional mobility"[Title/Abstract] OR "activities of daily living"[MeSH Terms] OR "Mobility Limitation"[MeSH Terms] OR "Physical Fitness"[MeSH Terms])) NOT ("rats"[MeSH Terms] OR "rabbits"[MeSH Terms] OR "animals"[Title] OR "mice"[MeSH Terms] OR "in vitro techniques"[MeSH Terms] OR "Neoplasms"[MeSH Terms] OR "Children"[Title])
Sodium	(Elderly[Title/Abstract] OR "older people"[Title/Abstract] OR older person*[Title/Abstract] OR senior[Title/Abstract] OR aged[MeSH Terms] OR "aging"[MeSH Terms] OR ageing[Title/Abstract] OR "independent living"[MeSH Terms] OR "community dwelling"[Title/Abstract] OR "frail elderly"[MeSH Terms] OR "Aged, 80 and over"[MeSH Terms]) AND ("Sodium, Dietary"[MeSH Terms] OR "sodium"[Title/Abstract]) AND (("Muscle mass"[Title/Abstract] OR "muscles"[MeSH Terms] OR "lean body mass"[Title/Abstract] OR "muscle, skeletal"[MeSH Terms] OR "fat free mass"[Title/Abstract] OR "muscular atrophy"[MeSH Terms] OR "muscle waste"[Title/Abstract] OR "muscle loss"[Title/Abstract] OR sarcopenia[MeSH Terms]) OR ("Muscle strength"[MeSH Terms] OR strength[Title/Abstract] OR dynapenia[Title/Abstract] OR "strength loss"[Title/Abstract] OR "muscle weakness"[MeSH Terms]) OR ("Physical performance"[Title/Abstract] OR physical function*[Title/Abstract] OR "functional mobility"[Title/Abstract] OR "activities of daily living"[MeSH Terms] OR "Mobility Limitation"[MeSH Terms] OR "Physical Fitness"[MeSH Terms])) NOT ("rats"[MeSH Terms] OR "rabbits"[MeSH Terms] OR "animals"[Title] OR "mice"[MeSH Terms] OR "in vitro techniques"[MeSH Terms] OR "Neoplasms"[MeSH Terms] OR "Children"[Title])
Potassium	(Elderly[Title/Abstract] OR "older people"[Title/Abstract] OR older person*[Title/Abstract] OR senior[Title/Abstract] OR aged[MeSH Terms] OR "aging"[MeSH Terms] OR ageing[Title/Abstract] OR "independent living"[MeSH Terms] OR "community dwelling"[Title/Abstract] OR "frail elderly"[MeSH Terms] OR "Aged, 80 and over"[MeSH Terms]) AND ("Potassium, Dietary"[MeSH Terms] OR "Potassium"[Title/Abstract]) AND (("Muscle mass"[Title/Abstract] OR "muscles"[MeSH Terms] OR "lean body mass"[Title/Abstract] OR "muscle, skeletal"[MeSH Terms] OR "fat free mass"[Title/Abstract] OR "muscular atrophy"[MeSH Terms] OR "muscle waste"[Title/Abstract] OR "muscle loss"[Title/Abstract] OR sarcopenia[MeSH Terms]) OR ("Muscle strength"[MeSH Terms] OR strength[Title/Abstract] OR dynapenia[Title/Abstract] OR "strength loss"[Title/Abstract] OR "muscle weakness"[MeSH Terms]) OR ("Physical performance"[Title/Abstract] OR physical function*[Title/Abstract] OR "functional mobility"[Title/Abstract] OR "activities of daily living"[MeSH Terms] OR "Mobility Limitation"[MeSH Terms] OR "Physical Fitness"[MeSH Terms])) NOT ("rats"[MeSH Terms] OR "rabbits"[MeSH Terms] OR "animals"[Title] OR "mice"[MeSH Terms] OR "in vitro techniques"[MeSH Terms] OR "Neoplasms"[MeSH Terms] OR "Children"[Title])
Selenium	(Elderly[Title/Abstract] OR "older people"[Title/Abstract] OR older person*[Title/Abstract] OR senior[Title/Abstract] OR aged[MeSH Terms] OR "aging"[MeSH Terms] OR ageing[Title/Abstract] OR "independent living"[MeSH Terms] OR "community dwelling"[Title/Abstract] OR "frail elderly"[MeSH Terms] OR "Aged, 80 and over"[MeSH Terms]) AND ("selenium"[Title/Abstract]) AND (("Muscle mass"[Title/Abstract] OR "muscles"[MeSH Terms] OR "lean body mass"[Title/Abstract] OR "muscle, skeletal"[MeSH Terms] OR "fat free mass"[Title/Abstract] OR "muscular atrophy"[MeSH Terms] OR "muscle waste"[Title/Abstract] OR "muscle loss"[Title/Abstract] OR sarcopenia[MeSH Terms]) OR ("Muscle strength"[MeSH Terms] OR strength[Title/Abstract] OR dynapenia [Title/Abstract] OR "strength loss"[Title/Abstract] OR "muscle weakness"[MeSH Terms]) OR ("Physical performance"[Title/Abstract] OR physical function* [Title/Abstract] OR "functional mobility"[Title/Abstract] OR "activities of daily living"[MeSH Terms] OR "Mobility Limitation"[MeSH Terms] OR "Physical Fitness"[MeSH Terms])) NOT ("rats"[MeSH Terms] OR "rabbits"[MeSH Terms] OR "animals"[Title] OR "mice"[MeSH Terms] OR "in vitro techniques"[MeSH Terms] OR "Neoplasms"[MeSH Terms] OR "Children"[Title])
Iron	(Elderly[Title/Abstract] OR "older people"[Title/Abstract] OR older person*[Title/Abstract] OR senior[Title/Abstract] OR aged[MeSH Terms] OR "aging"[MeSH Terms] OR ageing[Title/Abstract] OR "independent living"[MeSH Terms] OR "community dwelling"[Title/Abstract] OR "frail elderly"[MeSH Terms] OR "Aged, 80 and over"[MeSH Terms]) AND ("Iron"[MeSH Terms] OR "Iron, Dietary"[MeSH Terms] OR "ferrum"[Title/Abstract]) AND (("Muscle mass"[Title/Abstract] OR "muscles"[MeSH Terms] OR "lean body mass"[Title/Abstract] OR "muscle, skeletal"[MeSH Terms] OR "fat free mass"[Title/Abstract] OR "muscular atrophy"[MeSH Terms] OR "muscle waste"[Title/Abstract] OR "muscle loss"[Title/Abstract] OR sarcopenia[MeSH Terms]) OR ("Muscle strength"[MeSH Terms] OR strength[Title/Abstract] OR dynapenia[Title/Abstract] OR "strength loss"[Title/Abstract] OR "muscle weakness"[MeSH Terms]) OR ("Physical performance"[Title/Abstract] OR physical function*[Title/Abstract] OR "functional mobility"[Title/Abstract] OR "activities of daily living"[MeSH Terms] OR "Mobility Limitation"[MeSH Terms] OR "Physical Fitness"[MeSH Terms])) NOT ("rats"[MeSH Terms] OR "rabbits"[MeSH Terms] OR "animals"[Title] OR "mice"[MeSH Terms] OR "in vitro techniques"[MeSH Terms] OR "Neoplasms"[MeSH Terms] OR "Children"[Title])
Phosphorus	(Elderly[Title/Abstract] OR "older people"[Title/Abstract] OR older person*[Title/Abstract] OR senior[Title/Abstract] OR aged[MeSH Terms] OR "aging"[MeSH Terms] OR ageing[Title/Abstract] OR "independent living"[MeSH Terms] OR "community dwelling"[Title/Abstract] OR "frail elderly"[MeSH Terms] OR "Aged, 80 and over"[MeSH Terms]) AND ("Phosphorus, Dietary"[MeSH Terms] OR "phosphate"[Title/Abstract] OR "phosphor"[Title/Abstract]) AND (("Muscle mass"[Title/Abstract] OR "muscles"[MeSH Terms] OR "lean body mass"[Title/Abstract] OR "muscle, skeletal"[MeSH Terms] OR "fat free mass"[Title/Abstract] OR "muscular atrophy"[MeSH Terms] OR "muscle waste"[Title/Abstract] OR "muscle loss"[Title/Abstract] OR sarcopenia[MeSH Terms]) OR ("Muscle strength"[MeSH Terms] OR strength[Title/Abstract] OR dynapenia[Title/Abstract] OR "strength loss"[Title/Abstract] OR "muscle weakness"[MeSH Terms]) OR ("Physical performance"[Title/Abstract] OR physical function*[Title/Abstract] OR "functional mobility"[Title/Abstract] OR "activities of daily living"[MeSH Terms] OR "Mobility Limitation"[MeSH Terms] OR "Physical Fitness"[MeSH Terms])) NOT ("rats"[MeSH Terms] OR "rabbits"[MeSH Terms] OR "animals"[Title] OR "mice"[MeSH Terms] OR "in vitro techniques"[MeSH Terms] OR "Neoplasms"[MeSH Terms] OR "Children"[Title])

Appendix 2

Quality Assessment Based on the Effective Public Health Practice Project (EPHPP) Quality Assessment Tool for Quantitative Studies

Author	A Selection Bias	B Design	C Confounders	D Blinding	E Data Collection Methods	F Withdrawals and Drop-outs	Total Score
Bartali et al (2008)[31]	3	2	2	2	3	2	3
Chaput et al (2007)[34]	1	1	1	2	3	NA	1
Chen et al (2014)[35]	1	1	3	2	3	NA	1
Martin et al (2011)[32]	1	2	2	2	3	NA	2
Oh et al (2015)[37]	2	1	1	2	3	NA	1
Seo et al (2013)[36]	1	1	2	2	3	NA	1
Ter Borg et al (2016)[38]	1	1	2	2	3	NA	1
Verlaan et al (2017)[39]	1	2	2	2	3	NA	2
Veronese et al (2014)[30]	1	3	3	2	3	3	2
Waters et al (2014)[33]	1	2	1	1	3	1	1

Supplementary Material 1
PRISMA 2009 Checklist for Minerals and Sarcopenia: A Systematic Review*

Section/topic	#	Checklist Item	Reported on Page#
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	1
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	3
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	3
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (eg, Web address), and, if available, provide registration information including registration number.	-
Eligibility criteria	6	Specify study characteristics (eg, PICOS, length of follow-up) and report characteristics (eg, years considered, language, publication status) used as criteria for eligibility, giving rationale.	4
Information sources	7	Describe all information sources (eg, databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	4
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	A1
Study selection	9	State the process for selecting studies (ie, screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	4
Data collection process	10	Describe method of data extraction from reports (eg, piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	4
Data items	11	List and define all variables for which data were sought (eg, PICOS, funding sources) and any assumptions and simplifications made.	A1
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	5
Summary measures	13	State the principal summary measures (eg, risk ratio, difference in means).	4
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (eg, I^2) for each meta-analysis.	4
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (eg, publication bias, selective reporting within studies).	A2
Additional analyses	16	Describe methods of additional analyses (eg, sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	NA
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	6
Study characteristics	18	For each study, present characteristics for which data were extracted (eg, study size, PICOS, follow-up period) and provide the citations.	6
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	6
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	Table 2
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	NA
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	NA
Additional analysis	23	Give results of additional analyses, if done (eg, sensitivity or subgroup analyses, meta-regression [see Item 16]).	NA
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (eg, healthcare providers, users, and policy makers).	8
Limitations	25	Discuss limitations at study and outcome level (eg, risk of bias), and at review-level (eg, incomplete retrieval of identified research, reporting bias).	10
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	12
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (eg, supply of data); role of funders for the systematic review.	NA

*For more information, visit www.prisma-statement.org.

From Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7):e1000097. http://dx.doi.org/10.1371/journal.pmed1000097.