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Author(s)
van Dronkelaar, Carliene; Fultinga, Maaike; Hummel, Mitchell; Kruizenga, Hinke; Weijs, Peter J.M. ; Tieland, Michael

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Review Article

Minerals and Sarcopenia in Older Adults: An Updated Systematic Review

Carliene van Dronkelaar MSc [a,b,c,*], Maaike Fultinga BSc [a], Mitchell Hummel BSc [a], Hinke Kruizenga PhD [a,c], Peter J.M. Weijs [a,b], Michael Tieland PhD [a]

[a] Center of Expertise Urban Vitality, Faculty of Sports and Nutrition, Amsterdam University of Applied Sciences, Amsterdam, the Netherlands
[b] Amsterdam Public Health, Aging and Later Life, Amsterdam, the Netherlands
[c] Department of Nutrition and Dietetics, Amsterdam University Medical Centers, Amsterdam, the Netherlands

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A B S T R A C T

Objective: This systematic review aims to reevaluate the role of minerals on muscle mass, muscle strength, physical performance, and the prevalence of sarcopenia in community-dwelling and institutionalized older adults.
Design: Systematic review.
Setting and Participants: In March 2022, a systematic search was performed in PubMed, Scopus, and Web of Sciences using predefined search terms. Original studies on dietary mineral intake or mineral serum blood concentrations on muscle mass, muscle strength, and physical performance or the prevalence of sarcopenia in older adults (average age ≥65 years) were included.
Methods: Eligibility screening and data extraction was performed by 2 independent reviewers. Quality assessment was performed with the Effective Public Health Practice Project (EPHPP) Quality Assessment Tool for Quantitative Studies. Risk of bias was evaluated using the Risk Of Bias In Non-randomized Studies-of Exposure (ROBINS-E) tool.
Results: From the 15,622 identified articles, a total of 45 studies were included in the review, mainly being cross-sectional and observational studies. Moderate quality of evidence showed that selenium (n = 8) and magnesium (n = 7) were significantly associated with muscle mass, strength, and physical performance as well as the prevalence of sarcopenia. For calcium and zinc, no association could be found. For potassium, iron, sodium, and phosphorus, the association with sarcopenic outcomes remains unclear as not enough studies could be included or were nonconclusive (low quality of evidence).
Conclusions and Implications: This systematic review shows a potential role for selenium and magnesium on the prevention and treatment of sarcopenia in older adults. More randomized controlled trials are warranted to determine the impact of minerals on sarcopenia in older adults.

Ageing is associated with various geriatric syndromes, such as sarcopenia. Sarcopenia is defined by age-related loss of muscle mass, muscle strength, and physical performance and is associated with hospitalization, care dependency, and poor quality of life.[1,2] To prevent or treat sarcopenia, exercise and nutrition interventions have been developed and implemented in clinical practice.[3] These nutritional interventions focused predominantly on energy intake, dietary protein, and vitamin D, but much less on minerals.[4,5] Minerals, however, may have a major impact on muscle mass, strength, and physical performance. For example, calcium is involved in muscle contraction and is essential to create muscular force.[6,7] Magnesium is involved in energy metabolism, crucial for muscular performance, and iron has a major impact in the transport of oxygen and therefore may impact muscle functioning.[6] Selenium and zinc both have an antioxidative function.[8,9] Antioxidants counter reactive oxygen species (ROS) released with exercise, which in excess can cause muscle fatigue and contractile dysfunction.[10] Van Dronkelaar et al[11] previously

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* Address correspondence to Carliene van Dronkelaar, MSc, Center of Expertise Urban Vitality, Faculty of Sports and Nutrition, Amsterdam University of Applied Sciences, Dr. Meurerlaan 8, 1067 SM Amsterdam, the Netherlands.
E-mail address: d.c.van.dronkelaar@hva.nl (C. van Dronkelaar).

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investigated the role of minerals on muscle mass, muscle strength, and physical performance in older adults. They found that particularly magnesium, selenium, and calcium seemed promising, but were only able to include 10 studies. This review was published in 2018, and because many articles were published on the matter since, an update is warranted. This systematic review will reevaluate the role of minerals on muscle mass, muscle strength, physical performance, and the prevalence of sarcopenia in community-dwelling and institutionalized older adults.

Methods

Search Strategy and Selection

The systematic search has been performed in PubMed, Scopus, and Web of Science in March 2021, using predefined search terms. The full search strategy for each database can be found in Appendix 1. After removing duplicates, 2 independent reviewers (M.F., M.H.) screened the title and abstract of all found articles for eligibility. An article was eligible if it was published between January 2006 and March 2022. Further inclusion and exclusion criteria can be found in Table 1. Of the eligible articles, full texts were screened for final inclusion. An additional manual search of the reference lists of included articles has been performed to check for more potential useful articles. In case of any discrepancies between the 2 independent reviewers, a third reviewer (C.D.) was consulted and discrepancies were discussed until consensus was reached. To construct this systematic review the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) statement was followed.[12]

Data Extraction

The following data were extracted: author and year of publication, study design, population characteristics [sample size, mean age (SD) in years, gender ratio], type of mineral(s) studied, and note outcomes (outcome category, outcome measurement, effect size, and *P* value). A meta-analysis was considered when study outcomes were comparable.

Table 1
Inclusion and Exclusion Criteria for Eligible Studies

Inclusion criteria	
Participants	Average age ≥65 y, community-dwelling, hospitalized, institutional
Exposure	Dietary intake or blood serum concentrations of calcium, iron, magnesium, phosphorus, potassium, selenium, sodium, zinc
Outcome	Muscle mass
	Computed tomography, magnetic resonance imaging, dual energy x-ray absorptiometry, whole-body air plethysmography, bioelectrical impedance analysis, dual photon absorptiometry
	Muscle strength
	Handgrip; knee, leg, and ankle extension; knee, ankle, and hip flexor; hip abductor; leg press; elastic bands
	Physical performance
	Short Physical Performance Battery, Chair stand, Balance test, Gait speed test, 400-m walk test, 6-minute walk test, Timed Up and Go test
	Sarcopenia of any definition
Exclusion criteria	
Participants	Participants with muscle disorder or disease
	Heart failure, cirrhosis, HIV, neoplasms, renal insufficiency, hyperparathyroidism, chronic obstructive pulmonary disease
Exposure	Intervention mixed with exercise or other macro- or micronutrients, hyponatremia
Design	Conference abstract, letters, comments, editorials, case reports, systematic reviews

Quality Assessment

The quality of included articles was assessed by 2 independent reviewers (M.F., C.D.) with the Effective Public Health Practice Project (EPHPP) Quality Assessment Tool for Quantitative Studies.[13] The tool assesses risk of bias, study design, confounders, method of blinding, data collection methods, and withdrawals. The total score ranges from 1 to 3, with 1 being low quality and 3 being high quality. The quality assessment per included article can be found in Appendix 2. No articles were excluded based on the outcome of the quality assessment. Risk of bias was evaluated using the Risk Of Bias In Non-randomized Studies—of Exposure (ROBINS-E) tool and visualized with robvis.[14,15] The GRADE approach was used to assess the quality of evidence. The protocol of this review is registered in the PROSPERO register under the number 243666 and can be assessed at https://www.crd.york.ac.uk/prospero/display_record.php?RecordID=243666.

Results

Our search identified a total of 15,622 articles. After removing duplicates, 10,481 articles were screened on title and abstract, from which 171 articles were screened on full text. Finally, a total of 45 articles were eligible.[16-60] A full overview of the selection of articles can be found in Figure 1. The overall quality of the included studies was moderate (Appendix 2). The overall risk of bias evaluation indicated that most of the studies showed some concerns, mainly within selection of the reported results or selection of participants into the study/analysis (Figure 2). Evaluation per study can be found in Appendix 3.

Study Characteristics

Characteristics of the included articles can be found in Table 2. Of the 32,982 studied participants, 58% were female and the average age ranged from 65 to 86 years. Most of the participants were community dwelling,[16-29,32,34-41,44-47,49,50,52-60] in 3 studies participants were hospitalized,[33,43,48] in 2 studies participants were institutionalized,[31,42] and in 1 study participants were outpatients.[28] In total, 3 randomized controlled trials (RCTs),[39,46,57] 2 longitudinal studies,[19,41] 1 case-control,[56] 12 cohort,[16-18,29,30,35,38,40,44,47,49,54] 3 prospective observational studies,[27,32,36] 1 observational,[43] and 23 cross-sectional studies[20-26,28,31,33,34,37,42,45,48,50-53,55,58-60] were included.

The included studies evaluated calcium (n = 18),[18,20,21,23,26,28,31,34,38,39,42,45,49,52,55,56,58,60] iron (n = 13),[18,19,21,26,34,35,38,42,43,46,58-60] magnesium (n = 15),[17,18,21,26,27,32,34,38,42,51-53,56,57,60] phosphorus (n = 7)[20,21,34,38,42,55,56] potassium (n = 11),[18,21,26,34,36,38,42,48,50,56,60] selenium (n = 14),[16,22,24,25,29,30,34,37,40,42,47,52,56,60] sodium (n = 10),[18,21,28,34,36,38,42,44,50,60] and zinc (n = 15).[18,26,30,31,33,34,38,41,42,52,54,56,58-60]

Most articles used muscle strength as outcome (n = 21),[20,22,27,29,31,32,37,38,41,43,44,46-48,50,51,53,55,57,59,60] measured by handgrip; knee, leg, and ankle extension; and ankle, knee, and hip flexor or hip abductor strength. Physical performance was measured in 17 studies[16-19,29,31,36,38,40-42,47,53,54,57,58,60] by Short Physical Performance Battery, gait speed, Timed Up and Go test, or the repeated chair-rise test. Studies that assessed muscle mass (n = 7)[24,25,34,39,49,53,60] used either dual-energy x-ray absorptiometry or bioelectrical impedance analysis. A total of 13 studies[21,23,26,28,30,33,35,45,49,51-53,56] evaluated the relationship between a mineral and any definition of sarcopenia.

Minerals

The relationship between minerals and muscle mass, muscle strength and physical performance, and sarcopenia prevalence is

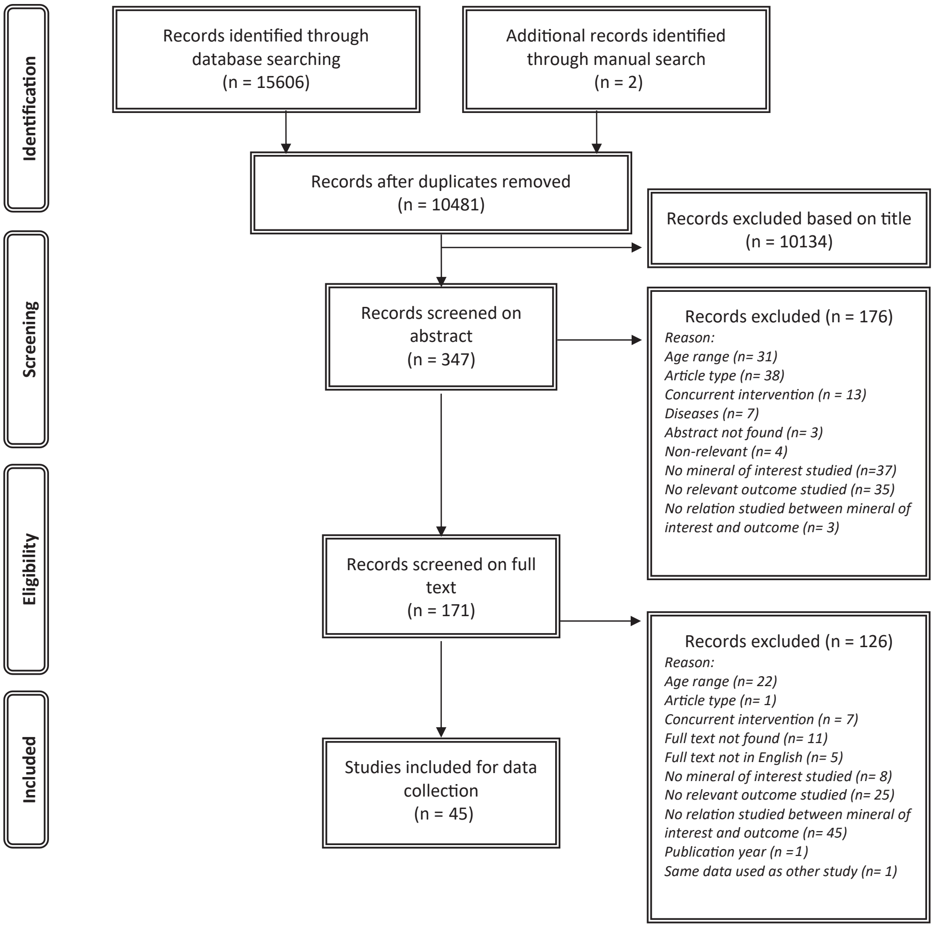

Fig. 1. Flowchart of selection of studies.

provided in Table 3. Of the 7 studies that assessed muscle mass, only 2 studies showed a positive significant association with selenium and calcium.[25,49] Twelve of the 21 studies on muscle strength found a positive significant association with calcium, iron, magnesium, potassium, selenium, and sodium intakes and with serum/plasma phosphorus levels.[20,22,27,29,37,38,43,44,46,50,55,59] Iron and magnesium supplementation each improved muscle strength in an RCT.[46,57] In 9 of 18 studies, a higher physical performance was associated with higher intakes of calcium, iron, magnesium, potassium, selenium, sodium, and zinc and with serum levels of selenium and zinc.[16,17,29,31,36,40,54,57,58] Of the 13 studies that looked at the prevalence of sarcopenia, 10 found an association with lower intakes of magnesium, phosphorus, calcium, iron, zinc, selenium, or potassium or with low serum levels of calcium, ferritin, and zinc.[21,23,26,28,30,35,45,49,52,56]

Discussion

This update on the 2018 systematic review by van Dronkelaar et al[11] provides a comprehensive overview of the current literature on the potential role of minerals on muscle mass, muscle strength, and physical performance and prevalence of sarcopenia in older adults. Selenium and magnesium were associated with muscle mass, strength, performance, and sarcopenia prevalence. The associations

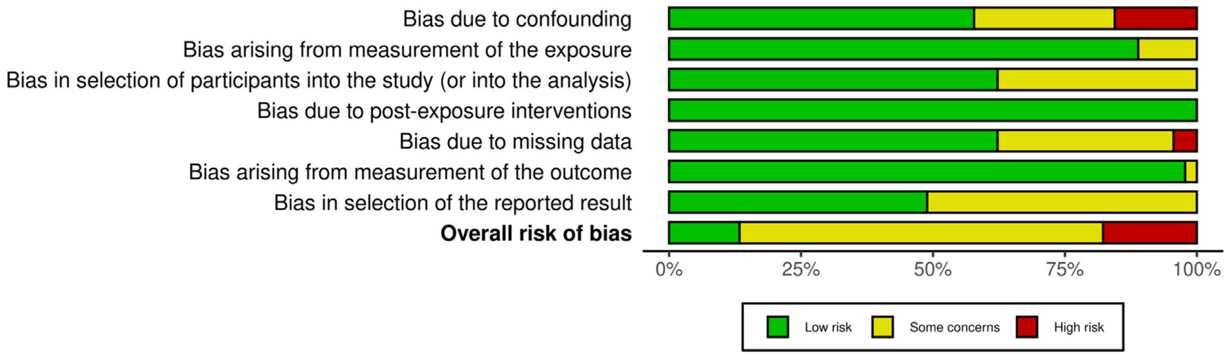

Fig. 2. Overall risk of bias of included studies.

Table 2
Characteristics of Included Studies

Author (y)	Mineral Studied*	Study Design	Sample Size (% Female)	Mean Age (y)
Alipanah et al (2009)[16]	**Serum selenium**	Cohort	687 (100)	>65
Arias-Fernandez et al (2022)[17]	**Magnesium**	Cohort (*Seniors-ENRICA*)	863 (51)	70.5
Asamane et al (2020)[18]	Potassium, magnesium, calcium, iron, zinc, sodium	Cohort	100 (41)	70.8
Bartali et al (2008)[19]	Serum iron	Longitudinal	643 (100)	
Bates et al (2012)[20]	Plasma calcium **Plasma phosphorus**	Cross-sectional	1054 (49)	75.8
Beaudart et al (2019)[21]	Sodium, **potassium, magnesium, phosphorus, iron,** calcium	Cross-sectional	331 (59)	74.8
Beck et al (2007)[22]	**Serum selenium**	Cross-sectional	676 (100)	77.4
Can et al (2017)[23]	**Serum calcium**	Cross-sectional	72 (63)	80.2
Chaput et al (2007)[24]	Selenium	Cross-sectional	50 (68)	66.5
Chen et al (2014)[25]	**Serum selenium**	Cross-sectional	327 (68)	72.1
Das et al (2021)[26]	**Magnesium, calcium, potassium, iron, zinc**	Cross-sectional	794 (0)	81.1
Dominguez et al (2006)[27]	**Serum magnesium**	Prospective (*InCHIANTI*)	1138 (54)	66.7
Fukuoka et al (2019)[28]	Serum sodium Serum potassium **Serum calcium**	Cross-sectional	267 (40)	73.7
Garcia-Esquinas et al (2021)[29]	**Serum selenium**	Cohort (*NHANES; Seniors-ENRICA-2*)	1733 (56) 2548 (53)	≥65
Gariballa et al (2018)[30]	Serum selenium **Serum zinc**	Cohort	432 (49)	≥65
Grieger et al (2007)[31]	**Serum zinc,** calcium	Cross-sectional	115 (68)	80.2
Henderson et al (2010)[32]	Serum magnesium Serum phosphate	Prospective	43 (58)	83.8
Heo et al (2015)[33]	Serum zinc	Cross-sectional	86 (63)	79
Khanal et al (2021)[34]	Calcium, zinc, iron, selenium, potassium, phosphorus, sodium, magnesium	Cross-sectional	281 (100)	70
Kim et al (2014)[35]	**Serum ferritin**	Cohort (*KHANES-IV*)	2332 (59)	M: 69.06 F: 69.36
Lana et al (2020)[36]	**Sodium, potassium**	Prospective	868 (51)	70.5
Lauretani et al (2007)[37]	**Plasma selenium**	Cross-sectional	891 (56)	74.7
Lengelé et al (2020)[38]	Iron, calcium, sodium, **potassium,** magnesium, phosphorus, zinc	Cohort (*Baseline data*)	238 (61)	Median: 72
Lewis et al (2019)[39]	Calcium supplement	RCT	1368 (100)	75.2
Martin et al (2011)[40]	**Selenium**	Cohort	628 (45)	M: 67.8 F: 68.1
Mocchegiani et al (2012)[41]	Plasma zinc	Longitudinal (*iiSIRENTE*)	346 (67)	M: 86.1 F: 85.7
Moradell et al (2021)[42]	Calcium, iron, sodium, magnesium, potassium, iodine, selenium, zinc, phosphorus	Cross-sectional	101 (77)	80.4
Neidlein et al (2021)[43]	**Iron supplement**	Observational	224 (67)	81.4
Noh et al (2019)[44]	**Sodium density** (mg/1000 kcal)	Cohort (*KHANES IV*)	2982 (52)	>65
Oh et al (2015)[45]	**Calcium**	Cross-sectional	1433 (54)	68.6
Oztorun et al (2018)[46]	**Iron supplement**	RCT	81 (69)	76.8
Perri et al (2020)[47]	Selenium	Cohort (*Baseline data*)	791 (62)	>85
Schiara et al (2020)[48]	Serum potassium	Cross-sectional	2166 (54)	>65
Seo et al (2013)[49]	**Calcium**	Cohort (*KHANES IV*)	1339 (53)	70.1
Shimizu et al (2021)[50]	**Serum sodium** Serum potassium	Cross-sectional	246 (0)	65.4
Suranto et al (2020)[51]	Serum magnesium	Cross-sectional	28 (100)	>65
Ter Borg et al (2016)[52]	Calcium, **magnesium,** serum magnesium, **selenium,** zinc	Cross-sectional	227 (52)	Median: 74
Ter Borg et al (2019)[53]	Serum magnesium	Cross-sectional	227 (52)	Median: 74
Vega-Cabello et al (2022)[54]	**Zinc**	Cohort (*Seniors-ENRICA*)	2963 (53)	69
Verde et al (2019)[55]	**Serum calcium** **Serum phosphorus**	Cross-sectional	273 (53)	75.7
Verlaan et al (2017)[56]	Calcium, **magnesium, phosphorus, selenium,** zinc	Case-control	132 (59)	71.0
Veronese et al (2014)[57]	**Magnesium supplement**	RCT	139 (100)	71.5
Waters et al (2014)[58]	Calcium, **iron, zinc**	Cross-sectional	315 (62)	≥60
Yamada et al (2015)[59]	**Serum iron** Serum zinc	Cross-sectional	202 (100)	76.3
Yeung et al (2021)[60]	Sodium, calcium, iron, zinc, potassium, magnesium, selenium	Cross-sectional	58 (66)	77.2

F, female; M, male.
*All minerals listed are dietary intake, unless otherwise indicated. Minerals in bold showed a significant association with sarcopenic outcomes.

Table 3
Overview of Outcome of Included Studies

Author (y)	Mineral Studied*	Outcome	Outcome Measurement	Effect Size	*P*-value	Risk of Bias
Alipanah et al (2009)[16]	**Serum selenium**	Physical performance	Mean walking speed (m/s)	Multivariate (age, BMI, chronic diseases) $\beta = 0.002 \pm 0.00005$	**.0003**	Some concerns
Arias-Fernandez et al (2022)[17] *Seniors-ENRICA*	**Magnesium**	Physical performance	SPPB (points)	$\beta = 1.01$ (95% CI 0.49, 1.52) $\beta = -0.09$ (95% CI −0.59, 0.41)	F: **.001** M: >.05	Some concerns
Asamane et al (2020)[18]	Potassium, magnesium, calcium, iron, zinc, sodium	Muscle strength Physical performance	Hand grip strength (kg) SPPB (points)	$r = 0.101$; $r = 0.106$; $r = -0.011$; $r = -0.083$; $r = -0.187$; $r = 0.012$; $r = 0.179$; $r = 0.139$; $r = -0.009$; $r = -0.001$; $r = -0.122$; $r = -0.162$	>.05 >.05	Some concerns
Bartali et al (2008)[19]	Serum iron	Physical performance	SPPB (points)	OR = 1.10 (95% CI 0.77, 1.59)	>.05	Some concerns
Bates et al (2012)[20]	Plasma calcium	Muscle strength	Hand grip strength (kg)	NR	>.05	Some concerns
	Plasma phosphorus			M: $t = -0.4$; F: $t = -0.8$	**.03**	
				M: t = -2.2; F: t- = -0.9	>.05	
Beaudart et al (2019)[21]	Sodium	Sarcopenia	EWGSOP 1	NA	>.05	Some concerns
	Potassium				**.04**	
	Magnesium				**.03**	
	Phosphorus				**.04**	
	Iron				**.005**	
	Calcium				>.05	
Beck et al (2007)[22]	**Serum selenium**	Muscle strength	Hand grip strength (kg)	$\beta = 2.280 \pm 0.799$	**.005**	High
Can et al (2017)[23]	**Serum calcium**	Sarcopenia	EWGSOP 1	NA	**.008**	Some concerns
Chaput et al (2007)[24]	Selenium	Muscle mass	DEXA (MMI)	$r = 0.08$	>.05	Low
Chen et al (2014)[25]	**Serum selenium**	Muscle mass	BIA (LMM)	OR 4.62 (95% CI 2.11, 10.1)	**<.001**	Some concerns
Das et al (2021)[26]	**Magnesium**	Sarcopenia	FNIH	NA	**<.0001**	Some concerns
	Calcium		EWGSOP 1		**.03**	
	Potassium		EWGSOP 2		**<.0001**	
	Iron				**.03**	
	Zinc				**.02**	
					All > .05	
					>.05	
					>.05	
					>.05	
					>.05	
					.02	
Dominguez et al (2006)[27] *InCHIANTI*	**Serum magnesium**	Muscle strength	Ankle extension isometric (kg)	$\beta = 3.8 \pm 0.5$	**<.0001**	Low
			Hand grip strength (kg)	$\beta = 2.0 \pm 0.5$	**.0002**	
			Knee extension torque (N/dm)	$\beta = 31.2 \pm 7.9$	**<.0001**	
			Lower-leg muscle power (W)	$\beta = 8.8 \pm 2.7$	**.001**	
Fukuoka et al (2019)[28]	Serum sodium	Sarcopenia	AWGS	NA	>.05	Some concerns
	Serum potassium				>.05	
	Serum calcium				**<.05**	
Garcia-Esquinas et al (2021)[29] *NHANES; Seniors-ENRICA-2*	**Whole blood selenium** (per log2)	Muscle strength Physical performance	Low hand grip strength (study specific cut-off; kg) Low SPPB (≤9 points)	OR 0.54 (95% CI 0.32, 0.76) OR 0.59 (95% CI 0.34, 0.82)	NR	Some concerns
Gariballa et al (2018)[30]	Serum selenium	Sarcopenia	EWGSOP 1	NA	>.05	High
	Plasma zinc				**<.05**	
Grieger et al (2007)[31]	Calcium	Muscle strength	Hand grip strength (kg)	NR	>.05	High
	Serum zinc			NR	>.05	
		Physical performance	TUG (s)	NR	>.05	
				$r = 0.449$	**.001**	
Henderson et al (2010)[32]	Serum magnesium, serum phosphate	Muscle strength	Hand grip strength (kg) Leg strength (kg)	$r = -0.03$; $r = 0.13$ $r = -0.01$; $r = 0.10$	All >.05	High
Heo et al (2015)[33]	Serum zinc	Sarcopenia	AWGS	NA	>.05	High

(*continued on next page*)

Table 3 (*continued*)

Author (y)	Mineral Studied*	Outcome	Outcome Measurement	Effect Size	*P*-value	Risk of Bias
Khanal et al (2021)[34]	Calcium, zinc, iron, selenium, potassium, phosphorus, sodium, magnesium	Muscle mass	BIA (relative SMM)	NR	All >.05	Low
Kim et al (2014)[35] *KNHANES-IV*	**Serum ferritin**	Sarcopenia	KNHANES cut-off (ASM %)	M: OR 1.40 (95% CI 0.75, 2.65) F: OR 1.74 (95% CI 1.02, 2.97)	NR	Low
Lana et al (2020)[36]	**Sodium** **Potassium**	Physical performance	SPPB (points)	−0.13 (95% CI −0.26, −0.01) per 1 SD increase 0.19 (95% CI 0.05, 0.34) per 1 SD increase	NR	Some concerns
Lauretani et al (2007)[37]	**Plasma selenium**	Muscle strength	Low hand grip strength (kg) Low hip strength (kg) Low knee strength (kg)	OR 1.94 (95% CI 1.19, 3.16) OR 1.69 (95% CI 1.02, 2.83) OR 1.94 (95% CI 1.18, 3.19)	**.008** **.040** **.009**	Some concerns
Lengelé et al (2020)[38] *(Baseline)*	Iron, calcium, sodium, **Potassium,** magnesium, phosphorus, zinc	Physical performance Muscle strength	Gait speed (m/s) Hand grip strength (kg)	$\beta = -0.005$; $\beta = -9.261 \times x\,10^{-5}$; $\beta = 6.525 \times 10^{-5}$; $\beta = 5.335 \times 10^{-5}$; $\beta = -3.843 \times 10^{-5}$; $\beta = -5.244 \times 10^{-5}$; $\beta = 0.006$; $\beta = -0.179$ $\beta = 0.004$ $\beta = 0.002$ $\beta = 0.003$ $\beta = 0.005$ $\beta = 0.005$ $\beta = 0.119$	All >.05 >.05 >.05 >.05 **.035** >.05 >.05 >.05	Some concerns
Lewis et al (2019)[39]	Calcium supplement	Muscle mass	DEXA (LM)	Placebo: −0.01; calcium: −0.07	>.05	Some concerns
Martin et al (2011)[40]	**Selenium**	Physical performance	Chair rise (s) 3-m walk (s)	M: $\beta = 0.983$ (95% CI 0.961, 1.006) F: $\beta = 0.983$ (95% CI 0.955, 1.012) M: $\beta = -0.012$ (95% CI 0.065, 0.041) F: $\beta =$ -0.091 (95% CI 0.165, 0.018)	>.05 >.05 >.05 **.015**	Some concerns
Mocchegiani et al (2012)[41] *iiSIRENTE*	Plasma zinc	Physical performance Muscle strength	4-m walk (s) SPPB (points) Hand grip strength (kg)	$\beta = 0.013 \times 10^{-2}$ $\beta = 0.167 \times 10^{-2}$ $\beta = 0.167 \times 10^{-2}$	All >.05	Some concerns
Moradell et al (2021)[42]	Calcium, iron, sodium, magnesium, potassium, selenium, zinc, phosphorus	Physical performance	SPPB (groups: dependent, frail, prefrail, robust)	NR	All >.05	Some concerns
Neidlein et al (2021)[43] *(iron-deficient patients)*	**Iron supplement**	Muscle strength	Hand grip strength (kg) Knee extension (kg)	Control: 21.0 ± 9.4; supplement: 23.0 ± 9.4 Control:14.3 ± 6.4; supplement: 19.1 ± 7.8	>.05 **.005**	High
Noh et al (2019)[44] *KNHANES IV*	**Sodium density (mg/ 1000 kcal)**	Muscle strength	Low hand grip strength (kg)	M: Q1: OR 1.08 (95% CI 0.68, 1.72); Q2: OR 1 Q3: OR 0.99 (95% CI 0.68, 1.43) Q4: OR 1.15 (95% CI 0.71, 1.86) F: Q1: OR 1.01 (95% CI 0.74, 1.38); Q2: OR 1 Q3: OR 1.18 (95% CI 0.89, 1.58); Q4: OR 1.51 (95% CI 1.10, 2.07)	NA	Low
Oh et al (2015)[45]	**Calcium**	Sarcopenia	KHANES cut-off (ASM/Wt)	NA	**.002** (M) >.05 (F)	Some concerns
Oztorun et al (2018)[46]	**Iron supplement**	Muscle strength	Hand grip strength (kg)	M: $Z = -2.772$ F: $Z = -3.345$	**.006** **.001**	High

Perri et al (2020)[47]	Selenium	Muscle strength	Hand grip strength (kg)	β = −0.69 SE: 0.65	>.05	Some concerns
(Baseline)		Physical Performance	TUG (log10-s)	β = −0.002 SE:0.024	>.05	
Schiara et al (2020)[48]	Serum potassium	Muscle strength	Hand grip strength (kg)	Normokalemic: 20.4 ± 8.9 hypokalemic: 21.3 ± 8.9	>.05	Some concerns
Seo et al (2013)[49]	**Calcium**	Muscle mass	DEXA	r = 0.276	**<.001**	Some concerns
KNHANES IV		Sarcopenia	KHANES cut-off (ASM/Wt)	OR 0.259 (95% CI 0.087, 0.768)	**.014**	
Shimizu et al (2021)[50]	**Serum sodium**	Muscle strength	Hand grip strength (kg)	Without hypertension	**<.001**	Some concerns
	Serum potassium			r = 0.32; r = 0.08; r = 0.13; r = 0.13	All >.05	
	Serum calcium				All >.05	
	Serum phosphorus			With hypertension r = 0.03; r = 0.07; r = 0.08; r = 0.14		
Suranto et al (2020)[51]	Serum magnesium	Sarcopenia	AWGS	NA	>.05	Some concerns
Ter Borg et al (2016)[52]	Calcium	Sarcopenia	EWGSOP 1	NA	>.05	Low
	Magnesium				**.009**	
	Serum magnesium				>.05	
	Selenium				**.020**	
	Zinc				>.05	
Ter Borg et al (2019)[53]	Serum magnesium	Muscle mass	BIA (SMI)	NR	All >.05	Some concerns
		Muscle strength	Hand grip strength (kg)	NR		
		Physical performance	Gait speed (m/s)	NR		
		Sarcopenia	Chair stand (s)	NR		
			EWGSOP 1	OR 2.663 (95% CI 0.025. 228.118)		
Vega-Cabello et al (2022)[54] *Seniors-ENRICA*	**Zinc**	Physical performance	SPPB (≤6 points)	HR 0.64 (95% CI 0.43, 0.94)	NR	Some concerns
Verde et al (2019)[55]	**Serum calcium**	Muscle strength	Hand grip strength (kg)	OR 1.087 (95% CI 1.028, 1.150)	**.003**	High
	Serum phosphorus			OR 1.263 (95% CI 1.078, 1.480)	**.004**	
Verlaan et al (2017)[56]	Calcium	Sarcopenia	EWGSOP 1	NA	>.05	Some concerns
	Magnesium				**.015**	
	Phosphorus				**.014**	
	Selenium				**.039**	
	Zinc				>.05	
Veronese et al (2014)[57]	**Magnesium supplement**	Physical performance	Chair stand (s)	Δ −1.31	**.0001**	Some concerns
		Muscle strength	Gait speed (m/s)	Δ 0.14	**.006**	
			SPPB (points)	Δ 0.41	**.03**	
			Hand grip strength (kg)	Δ 0.51 kg	>.05	
			Peak torque isokinetic knee flexion (nm)	Δ 2.57 nm	>.05	
				Δ 0.76 nm	>.05	
			Peak torque isokinetic knee extension (nm)	Δ 13.33 nm	>.05	
			PT isometric knee extension (nm)			
Waters et al (2014)[58]	Calcium	Physical performance	Gait speed (m/s)	M: OR 2.18 (95% CI 0.67, 7.09)	NA	Some concerns
	Iron			F: OR 1.15 (95% CI 0.55, 2.41)		
	Zinc			M: OR 4.81 (95% CI 1.51, 15.31)		
				F: OR 0.94 (95% CI 0.44, 2.01)		
				M: OR 3.57 (95% CI 1.14, 11.18)		
				F: OR 2.33 (95% CI 1.12, 4.85)		
Yamada et al (2015)[59]	**Serum iron**	Muscle strength	Hand grip strength (kg)	r = 0.20	**<.05**	Some concerns
	Serum zinc			r = 0.12	>.05	

(*continued on next page*)

Table 3 (*continued*)

Author (y)	Mineral Studied*	Outcome	Outcome Measurement	Effect Size	*P*-value	Risk of Bias
Yeung et al (2021)[60] *SHAPE*	Sodium, calcium, iron, zinc, calcium, magnesium, selenium	Muscle mass	DEXA (SMMI)	β = 0.00 (SE 0.00); β = 0.00 (SE 0.00); β = 0.03 (SE 0.06); β = −0.03 (SE 0.04); β = 0.00 (SE 0.00); β = 0.00 (SE 0.00); β = 0.00 (SE 0.01)	All > .05	Some concerns
		Muscle strength	Hand grip strength (kg)	β = 0.00 (SE 0.00); β = 0.00 (SE 0.00); β = −0.04 (SE 0.06); β = −0.08 (SE 0.05); β = 0.00 (SE 0.00); β = 0.00 (SE 0.00); β = 0.00 (SE 0.01)	All >.05	
		Physical performance	Chair stand (s)	β = 0.00 (SE 0.00); β = 0.00 (SE 0.00); β = −0.05 (SE; 0.06); β = −0.09 (SE 0.05); β = 0.00 (SE 0.00); β = 0.00 (SE 0.00); β = −0.01 (SE 0.01)	All >.05	

ASM, appendicular skeletal muscle mass; AWGS, Asian working group for sarcopenia; BIA, bio-electrical impedance analysis; DEXA, dual-energy x-ray absorptiometry; EWGSOP, European working group on sarcopenia in older people; F, female; LMM, low muscle mass; M, male; MMI, muscle mass index; NA, not applicable; NR, not reported; PT, peak torque; SMM, skeletal muscle mass; SMMI, skeletal muscle mass index; SPPB, short physical performance battery; TUG, Timed up and Go test; Wt, weight.

*All minerals listed are dietary intake, unless otherwise indicated. Minerals in bold indicate a significant association with sarcopenic outcomes.

between calcium and zinc and the sarcopenic outcomes were equivocal. For the other minerals, the potential role remains unclear as not enough studies could be included or were nonconclusive.

Magnesium

Most of the included studies on magnesium intake showed a significant positive relation with muscle mass, muscle strength, physical performance, and/or sarcopenia prevalence. In these studies, the magnesium intake was below Recommend Dietary Allowance (RDA), suggesting a potential role for supplementing or increasing magnesium. Indeed, the only RCT on magnesium supplementation included in this review showed a significant improvement of physical performance in older adults. This was also concluded by a study of Wang et al,[61] who performed a systematic review and meta-analysis of 14 randomized clinical trials on the relation of magnesium supplementation on muscle fitness in younger and older adults. They concluded that magnesium supplementation may benefit individuals with magnesium deficiency, such as in older adults, but may not be of added value for individuals with a relatively high magnesium status.

Studies on serum magnesium on the other hand were not able to support these findings. This might be explained by a tight regulatory control of serum magnesium levels in the body. As thoroughly described by de Baaij et al,[62] magnesium homeostasis is regulated by the intestine, bone, and kidneys. Magnesium is stored mainly in bone tissue, but also in muscle tissue where it antagonizes calcium in muscle contraction. When dietary magnesium intake is inadequate, absorption of magnesium in the intestine can rise from 30%-50% to up to 80%-90%. Also, 90%-95% of daily filtered magnesium in the kidney is resorbed. These 3 systems maintain plasma magnesium homeostasis between 0.65 and 1.05 mmol/L. In the case of older adults, however, osteoporosis, malabsorption, and (chronic) renal failure are prevalent issues.[63,64] A higher dietary magnesium intake might therefore compensate a disrupted absorption, storage, and resorption system and maintain stable serum magnesium levels.

As only 1 RCT was identified in this review, more experimental research is needed to clarify the extent to which higher magnesium intake potentially affects sarcopenic outcomes, especially in older adults with an inadequate magnesium status.

Selenium

Studies included in this review on selenium showed that there is an association between low serum levels and worse sarcopenic outcomes. However, this association was not found for dietary intake of selenium. A possible explanation has not been determined. Although studies on selenium intake included in this review that did not show a significant association with sarcopenic outcomes all had intakes above RDA levels. This could imply that there might be an association between selenium and sarcopenic outcomes in older adults with selenium intake below RDA levels. Patients with selenium deficiency often develop skeletal muscle disorders such as muscle pain, proximal weakness, and fatigue, emphasizing a possible positive relation selenium might have on muscle function.[65] The exact underlying mechanisms, however, remain unclear.

Calcium

The absence of a significant association between calcium and sarcopenia-related outcomes was not expected as calcium has a vital role in muscle function, such as in the activation of the muscle-contraction process, as described by Kuo et al.[66] Without sufficient calcium available, the activation of the contractile apparatus cannot occur, inhibiting muscle contraction and therefore possibly normal muscle function. However, based on studies included in this review it seems that there is no clear role for calcium independently. Calcium homeostasis is regulated by vitamin D, parathyroid hormone (PTH), and calcitonin, with bone as the main storage. Because of interaction between calcium and vitamin D, it could be that they only can play a role in counteracting sarcopenia when both calcium and vitamin D are sufficient.[67] This is also seen in the study by Petermann et al,[68] where 396,283 UK biobank participants with the highest tertile of vitamin D and calcium intake had the lowest odds of sarcopenia. Kim et al[69] were able to show a significant association between low serum calcium levels and ≥5% muscle loss among 3342 participants, aged 50 and over, who were followed for 10 years. However, they did not take vitamin D levels or PTH in consideration as they mention in the limitations of the study. As the underlying mechanisms are complicated, further studies are warranted to explore the role of calcium and vitamin D in the prevention and/or treatment of sarcopenia.[70]

Zinc

Five studies found a significant association between zinc and sarcopenic outcomes, yet a majority of 11 studies did not report any significant association. This is different from the conclusion on zinc of the systematic review performed in 2018, as inconclusive results were reported then. We expected to find an association between low zinc levels or intakes and sarcopenic outcome due to zinc's antioxidative function. As set out by Hernandez-Camacho et al,[9] zinc upregulates the antioxidant system, preventing production of ROS. In excess, ROS can have a negative impact on muscle function.[10] Studies that were able to find a significant association reported low levels of serum zinc. Studies that did not find a significant association all had zinc intakes above RDA or serum levels above the norm. Hence, it seems that if zinc status is sufficient it is able to prevent negative impacts on muscle; however, more RCTs are warranted to determine the exact relation of zinc with sarcopenia-related outcomes.

Potassium, Iron, Sodium, and Phosphorus

The results of included studies on potassium, iron, sodium, and phosphorus were either inconclusive or had indecisive results or there was an insufficient number of articles. The possible relation of these minerals on muscle mass, muscle strength, physical performance, and/or sarcopenia therefore remains unclear.

The 2018 van Dronkelaar et al[11] study on the role of minerals on muscle mass, muscle strength, physical performance, and/or sarcopenia that this update was based on was reported to be the first systematic review presenting a clear overview on this topic. The updated search was performed in 3 databases, whereas the 2018 review only performed the search in 1 database. This update included a total of 45 studies, as opposed to 10 in the original review. Because of the significantly larger number of studies being included, this update presents stronger evidence on the potential role minerals have in the prevention and treatment of sarcopenia. Additionally, the search and selection of articles was performed by 2 independent researchers and discussed with a third researcher, thereby limiting selection bias.

However, there were some limitations to this review. No meta-analysis of the data have been performed because of lack of usable studies per mineral. Furthermore, 3 of the articles included in this study used data from the Korea National Health and Nutrition Examination Study or KHANES IV. Although the included studies using these data focused on different minerals (sodium, iron, and calcium, respectively), these data are derived from the same participants and could therefore be more related to each other. Other minerals such as iodine and manganese were included in the study by Khanal et al,[34] yet these minerals have not been included in this review because of not being defined in advance formulated search strings.

Although we were able to include more articles than in the previous review, the quality of evidence is moderate, because of most data being from observational studies and cross-sectional analyses. This is also reflected by the Quality Assessment scoring of included studies (Appendix 2) and the risk of bias evaluation (Appendix 3). In addition, some of the included studies had a small sample size, which could have affected the findings because of lack of power. More studies with a stronger study design, preferably RCTs, with larger study populations are warranted to gain insight in the direction, size, and strength of the observed relations of calcium, magnesium, selenium, and zinc on muscle mass, strength, physical performance, and the prevalence of sarcopenia.

Conclusion and Implications

This review shows a potential role for selenium and magnesium on the prevention and treatment of sarcopenia in older adults, for example, by increasing mineral intake to recommended daily levels. If more experimental research is performed, this could potentially lead to better interventions for sarcopenia and contribute to healthy ageing and a better quality of life in an increasing older population.

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