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Authors

Shea, M Kyla
Loeser, Richard F
Hsu, Fang-Chi
et al.

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Research Article

Vitamin K Status and Lower Extremity Function in Older Adults: The Health Aging and Body Composition Study

M. Kyla Shea,[1] Richard F. Loeser,[2] Fang-Chi Hsu,[3] Sarah L. Booth,[1] Michael Nevitt,[4] Eleanor M. Simonsick,[5] Elsa S. Strotmeyer,[6] Cees Vermeer,[7] and Stephen B. Kritchevsky[8] for the Health ABC Study

[1]Tufts University USDA Human Nutrition Research Center on Aging, Boston, Massachusetts. [2]Division of Rheumatology, Allergy and Immunology, University of North Carolina, Chapel Hill. [3]Division of Public Health Sciences, Wake Forest School of Medicine, Winston-Salem North Carolina. [4]Department of Epidemiology and Biostatistics, University of California San Francisco. [5]National Institute on Aging/NIH Baltimore, Maryland. [6]Graduate School of Public Health, University of Pittsburgh, Pennsylvania. [7]VitaK, University of Maastricht, Netherlands. [8]Sticht Center on Aging, Wake Forest School of Medicine, Winston-Salem, North Carolina.

Address correspondence to Kyla Shea, PhD, USDA Human Nutrition Research Center on Aging at Tufts University, 711 Washington St., Boston MA. E-mail: kyla.shea@tufts.edu

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Abstract

Background: While low vitamin K status has been associated with several chronic diseases that can lead to lower extremity disability, it is not known if low vitamin K status is associated with worse lower extremity function.

Methods: Vitamin K status was measured according to plasma phylloquinone (vitamin K1) and dephosphorylated-uncarboxylated MGP (dp-ucMGP) in 1,089 community-dwelling older adults (mean ± SD age =74 ± 3 years; 67% female). Lower extremity function was assessed using the short physical performance battery (SPPB), gait speed, and isokinetic leg strength. Linear regression and mixed models were used to determine the cross-sectional and longitudinal associations between vitamin K status and functional outcome measures.

Results: Cross-sectionally, higher plasma phylloquinone was associated with better SPPB scores and 20-m gait speed ($p \leq .05$). After 4–5 years, those with ≥1.0 nM plasma phylloquinone (the concentration achieved when recommended intakes are met) had better SPPB scores ($p = .03$) and 20-m gait speed ($p < .05$). Lower plasma dp-ucMGP (reflective of better vitamin K status) was associated with better SPPB scores and leg strength cross-sectionally ($p \leq .04$), but not longitudinally. Neither measure of vitamin K status was associated with walking endurance or with the rate of decline in function.

Conclusion: Older adults with higher vitamin K status had better physical performance scores at baseline, but data are less consistent longitudinally. Since lower extremity disability is a common consequence of multiple chronic diseases for which a role of vitamin K has been suggested, future studies are needed to determine if vitamin K supplementation could improve function in those with vitamin K insufficiency and clarify underlying mechanism(s).

Keywords: Physical performance—Nutrition—Physical function—Vitamin K

Vitamin K is an essential fat-soluble nutrient found mainly in green leafy vegetables and vegetable oils that functions primarily as an enzymatic cofactor in the carboxylation of vitamin K-dependent proteins. While the most-known vitamin K-dependent proteins are coagulation proteins, several others are present in vascular, skeletal, and other extra-hepatic tissues, suggesting multiple roles for vitamin K in health and disease (1). For example, matrix gla protein (MGP) is a vitamin K-dependent protein in vascular tissue, cartilage, and bone that inhibits mineralization when it is carboxylated—which requires vitamin K (2). Uncarboxylated MGP does not inhibit soft-tissue mineralization (3). Independent of this enzymatic cofactor role, vitamin K was shown to suppress inflammatory cytokine production in rodent models suggesting it has anti-inflammatory effects (4). At the population level, low vitamin K status has been associated with more cardiovascular disease, osteoarthritis, metabolic syndrome, and inflammation (5–8). These conditions are associated with lower extremity disability (9–11).

Impaired lower extremity function is a risk factor for disability and mortality (12,13) While the etiology of functional impairment is complex, the presence of age-related comorbidities increases the likelihood of developing or having worse impairment (14). More than 75% of adults over age 65 have more than one chronic disease (15) and older adults with multiple chronic disease are more likely to have impaired physical function than those with one condition (14,16). Mechanisms common to chronic diseases associated with impaired function represent possible targets to reduce functional decline. While weight loss and physical activity are two approaches that reduce functional decline in older age (17,18), vitamin K may represent an alternate novel and readily modifiable approach because vitamin K-dependent mechanisms are implicated in multiple comorbidities associated with functional decline (1). To our knowledge the association between vitamin K status and lower extremity function has not yet been reported. The purpose of this study was test the hypothesis that older community-dwelling adults with better vitamin K status would have better lower extremity function and less functional decline.

Methods

A detailed description of participants, outcome, exposure, and covariate measurements, and statistical analyses is included in the Supplementary Methods.

Participants were drawn from the Health, Aging and Body Composition Study (Health ABC, n = 3,075), a prospective longitudinal cohort study designed to examine age-related changes in physical function and body composition in older black and white adults. Health ABC recruitment has been well-described (19). When enrolled, all participants were free of disability in activities of daily living and reported no difficulty walking 1/4 mile or up 10 steps. Vitamin K status was measured in 1,133 participants in the knee osteoarthritis substudy, initiated at the year 2 clinic visit (1998–99) to examine the relationship between knee osteoarthritis and functional decline. The Health ABC knee osteoarthritis substudy included 836 participants with knee pain and 297 randomly selected controls without knee pain. Knee pain was defined as "knee pain, aching, or stiffness on most days for at least 1 month" at some point over the previous year or moderate or worse knee pain during the previous month in association with at least one activity on the WOMAC knee pain scale (8). All participants provided written informed consent and the institutional review boards at both study sites approved all protocols.

Lower Extremity Function

In years 1, 4, and 6 physical performance was assessed using the short physical performance battery (SPPB) (20). To minimize ceiling effects, the Health ABC PPB was also administered (19). Usual gait speed over 20 m and endurance over 400 m was assessed in years 2, 4, and 6 using a 20-m course marked with cones at each end, as described (19). Knee extensor strength was measured at years 2, 4, and 6 using an isokinetic dynamometer (Kin-com, model 125AP, Chattecx Corp., Chattanooga, TN) as described (19). Exclusion criteria for lower extremity function tests are described in detail elsewhere (19).

Vitamin K Status

Vitamin K status was measured according to plasma phylloquinone and desphospho-uncarboxylated MGP (dp-ucMGP) from the same citrated samples collected at the year 2 clinic visit (1998/99) after an overnight fast. All samples were stored at −70°C until analysis. Plasma phylloquinone was measured using reversed-phase HPLC (Tufts University (21)). Plasma dp-ucMGP was measured using a sandwich ELISA (VitaK, University of Maastricht (22)). This form of circulating MGP is reduced in response to phylloquinone supplementation (23).

Covariates

The following covariates were assessed, as described in the Supplementary Methods: age, sex, race, site, education, triglycerides, total cholesterol, smoking, alcohol use, healthy eating index, energy intake, fat intake, 25(OH)D, creatinine, time spent walking per week, depression, diabetes, lipid lowering medication use, antihypertension medication use, BMI, systolic blood pressure, interleukin-6 (IL-6), cognitive status, and anti-inflammatory medication use.

Statistical Analyses

Linear regression and mixed models were used to determine the cross-sectional and longitudinal associations between vitamin K status and lower extremity function. Based on previous work, plasma phylloquinone was categorized as <0.2, 0.2–<1.0, or ≥1.0 nM (8). Concentrations <0.2 nM are generally achieved when dietary intakes are ≤20% of current recommendations and 1.0 nmol/L is the concentration that is generally achieved when adequate intakes are met, based on metabolic feeding studies (24). Given the lack of established dp-ucMGP normal ranges, categories were based on distribution tertiles. All analyses were carried out in SAS v.9.3 (Cary, NC). Significance was set at two-sided alpha of 0.05.

Results

Our study population was 60% female, 47% black, with a mean ± SD BMI of 28.0 ± 5.0 kg/m^2. Over 61% had plasma phylloquinone <1.0 nM and nearly 8% had concentrations <0.2 nM. Participant characteristics according to plasma phylloquinone category are shown in Table 1. Participants with ≥1.0 nM plasma phylloquinone had higher triglycerides and total cholesterol, were more likely to be female, from Memphis, and less likely to smoke. Participant characteristics according to plasma dp-ucMGP tertile are shown in Supplementary Table 1. Those with low dp-ucMGP had lower triglycerides and circulating IL-6, were more likely to be black and less likely to take anti-inflammatory medication.

Cross-sectionally, higher plasma phylloquinone was associated with higher SPPB scores (p < .01) and faster 20-m gait speed (p = .05) after adjustment (Table 2). Lower dp-ucMGP was associated with higher SPPB scores cross-sectionally (p ≤ .05) and with higher isokinetic leg strength (p = .04). Neither vitamin K status measure was significantly associated with 400-m gait speed (both p ≥ .45) nor with ability to complete the 400-m walk (both p ≥ .45).

Longitudinally, participants with plasma phylloquinone ≥1.0 nM had higher physical performance scores and faster usual gait speed at 4–5 years of follow-up, fully-adjusted (Table 3; Figure 1). Plasma phylloquinone was not associated with isokinetic leg strength, 400-m gait speed, or ability to complete 400-m walk longitudinally. Participants in the lower dp-ucMGP tertiles had better Health ABC physical performance scores over time compared to the highest tertile, but plasma dp-ucMGP was not associated with any other performance outcome during follow-up (fully-adjusted) (Table 3; Figure 2). Although all performance outcomes declined over time,

Table 1. Baseline Characteristics of Health ABC Participants According to Plasma Phylloquinone Category

	<0.2 nM *n* = 84	0.2–<1.0 nM *n* = 585	≥1.0 nM *n* = 419	*p**
Age, y	74.8 ± 2.6	74.8 ± 3.0	74.4 ± 2.8	.13
Female (*n* [%])	47 (56)	334 (57)	270 (64)	.05
Black (*n* [%])	43 (51)	265 (45)	200 (48)	.53
Pittsburgh (*n* [%])	56 (67)	331 (57)	190 (45)	<.01
BMI, kg/m^2	27.9 ± 5.2	27.9 ± 5.0	28.4 ± 5.0	.07
Triglycerides, mg/dL†	111 ± 44	129 ± 39	161 ± 100	<.01
Total cholesterol, mg/dl	200 ± 36	205 ± 39	210 ± 42	.04
IL-6, pg/ml†	4.1 ± 4.1	3.6 ± 3.9	2.5 ± 3.8	.11
Creatinine, mg/dl†	1.0 ± 0.3	1.0 ± 0.2	1.0 ± 0.2	.70
25(OH)D, ng/ml	25.4 ± 9.4	25.2 ± 11.1	25.2 ± 10.0	.99
dp-ucMGP, pM†	477 ± 323	508 ± 409	401 ± 339	<.01
Healthy Eating Index score	68 ± 12	69 ± 12	70 ± 12	.23
Energy intake, kcal/day	1872 ± 827	1882 ± 778	1794 ± 653	.30
Fat intake, g/day	71 ± 41	71 ± 37	69 ± 33	.45
Systolic blood pressure, mmHg	132 ± 18	135 ± 21	135 ± 20	.62
Diabetes (*n* [%])	11 (13)	100 (17)	77 (18)	.49
Lipid lowering medication (*n* [%])	13 (15)	90 (15)	69 (16)	.90
Anti-hypertension medication (*n* [%])	40 (47)	325 (56)	265 (63)	<.01
Anti-inflammatory medication (*n*[%])	41 (49)	336 (58)	247 (59)	.23
Cognitive function (3MS score)†	88 ± 8	90 ± 8	90 ± 8	.22
Depression (CESD10 score)†	3.8 ± 4.0	3.2 ± 3.2	3.2 ± 3.5	.96
Walking, min/week				
0	35 (42)	266 (46)	172 (41)	.11
1–149	34 (40)	166 (28)	139 (33)	
≥150	15 (18)	152 (26)	109 (26)	
Smokers (*n* [%])				
Current	12 (14)	59 (10)	28 (7)	.04
Former	40 (48)	254 (43)	172 (41)	
Alcohol intake (*n* [%])				
None	39 (46)	321 (55)	218 (52)	.62
≤7 per week	39 (46)	227 (39)	173 (41)	
>1 per day	6 (7)	34 (6)	27 (7)	
Education				
<High school	29 (35)	153 (26)	114 (39)	.51
High school graduate	22 (27)	196 (34)	141 (34)	
College graduate	32 (39)	235 (40)	164 (39)	
Season (*n* [%])				
Dec–Feb	13 (16)	155 (27)	100 (24)	<.01
Mar–May	5 (6)	171 (29)	134 (32)	
June–Aug	24 (29)	93 (16)	90 (21)	
Sep–Nov	42 (50)	166 (28)	96 (23)	

Note: Mean ± SD unless indicated otherwise.

*Based on one-way ANOVA or Kruskal–Wallis (continuous outcomes) or Chi-square test (categorical outcomes).

†Outcome natural log-transformed for ANOVA, means ± SDs are presented in original scale.

the rate of decline was similar across the plasma phylloquinone groups (phylloquinone category*time interaction all $p > .25$) and dp-ucMGP tertiles (dp-ucMGP tertile*time interaction all $p > .10$). The interaction between sex/race and vitamin K status were not statistically significant (p values for sex interactions >0.32 and for race interactions >0.06).

When unadjusted models were restricted to those with complete covariate data, the results were similar. We also stratified by whether participants had qualifying knee pain or not (on account of this Health ABC subgroup's selection (8)). The results in both groups were generally consistent with the direction of our overall findings, but statistical significance was attenuated because sample sizes were reduced (*n* = 799 with knee pain, 290 without) (data not shown.)

Discussion

We hypothesized higher vitamin K status would be associated with better lower extremity function because higher vitamin K status has been associated with a lower prevalence and progression of several comorbidities that have been associated with impaired function and disability (5–8). We found generally healthy older adults with ≥1.0 nM plasma phylloquinone had better physical performance scores and better usual gait speed cross-sectionally and at 4–5 follow-up years compared to those with <1.0 nM plasma phylloquinone. The rate of decline did not differ by plasma phylloquinone status. Lower plasma dp-ucMGP (reflective of better vitamin K status) was associated with better lower extremity performance and isokinetic leg strength cross-sectionally and with better Health ABC physical performance scores (but not SPPB scores) over time. Neither

Table 2. Cross-Sectional Associations Between Vitamin K Status and Lower Extremity Function in Health ABC

Plasma Phylloquinone	*n*	<0.2 nM	0.2–<1.0 nM	≥1.0 nM	*p* Trend*
SPPB (0–12)					
Unadjusted	1,089	9.61 ± 0.17	9.86 ± 0.06	10.07 ± 0.07	<.01
Adjusted†	982	9.58 ± 0.19	9.74 ± 0.12	9.98 ± 0.13	<.01
Health ABC PPB (0–4)					
Unadjusted	1,059	2.09 ± 0.06	2.13 ± 0.02	2.19 ± 0.03	.05
Adjusted†	954	2.06 ± 0.08	2.10 ± 0.04	2.18 ± 0.04	<.01
Usual 20M walk (m/s)					
Unadjusted	1,079	1.11 ± 0.03	1.10 ± 0.02	1.12 ± 0.02	.21
Adjusted†	980	1.09 ± 0.03	1.09 ± 0.01	1.12 ± 0.02	.05
Isokinetic leg strength (nm/kg lean)					
Unadjusted	924	13.51 ± 0.43	13.17 ± 0.16	13.46 ± 0.19	.53
Adjusted	847	12.94 ± 0.49	12.89 ± 0.30	13.40 ± 0.32	.06
400M walk, m/s‡					
Unadjusted	721	1.27 ± 0.04	1.25 ± 0.02	1.25 ± 0.01	.82
Adjusted†	667	1.21 ± 0.03	1.23 ± 0.03	1.23 ± 0.04	.68
Plasma dp-ucMGP	***n***	**T1: ≤ 267 pM**	**T2: 268–566 pM**	**T3: ≥567 pM**	***p* trend†**
SPPB (0–12)					
Unadjusted	1,089	10.07 ± 0.08	9.96 ± 0.08	9.73 ± 0.08	<.01
Adjusted†	982	9.98 ± 0.13	9.80 ± 0.13	9.57 ± 0.14	<.01
Health ABC PPB (0–4)					
Unadjusted	1,059	2.18 ± 0.03	2.16 ± 0.03	2.11 ± 0.03	.09
Adjusted†	954	2.16 ± 0.04	2.13 ± 0.04	2.08 ± 0.05	.05
Usual 20M walk, m/s					
Unadjusted	1,079	1.10 ± 0.01	1.12 ± 0.01	1.11 ± 0.01	.57
Adjusted†	980	1.10 ± 0.02	1.10 ± 0.02	1.10 ± 0.02	.76
Isokinetic leg strength, nm/kg lean					
Unadjusted	924	13.36 ± 0.20	13.39 ± 0.20	13.18 ± 0.21	.54
Adjusted	847	13.32 ± 0.33	13.10 ± 0.31	12.74 ± 0.34	.04
400M walk, m/s‡					
Unadjusted	721	1.23 ± 0.01	1.26 ± 0.01	1.27 ± 0.02	.10
Adjusted†	667	1.22 ± 0.04	1.23 ± 0.03	1.24 ± 0.04	.45

Note: Data are means (or LS means) ± SEM.

*Trend test based on general linear model using category as an ordinal exposure (1–3).

†Adjusted for age, sex, race, site, education, triglycerides, total cholesterol, smoking, alcohol use, healthy eating index, energy intake, fat intake, 25(OH)D, creatinine, depression, diabetes, lipid-lowering medication use, anti-hypertension medication use, BMI, systolic blood pressure, IL-6, cognitive status, anti-inflammatory medication use, walking time per week.

‡In those who completed the test (66%).

measure of vitamin K status was associated with lower extremity endurance as measured according to 400-m walk gait speed. This may reflect task specificity such that vitamin K status could be more relevant to low-endurance functional tasks (eg, standing from a chair) than to tasks requiring more endurance (eg, walking around the neighborhood).

Our finding that plasma phylloquinone was associated with lower extremity function is novel and suggests plasma phylloquinone ≥1.0 nM is beneficial with respect to maintaining lower extremity physical performance and usual gait speed over 4–5 years. A concentration of ≥1.0 nM is generally achieved when recommended vitamin K intakes (90–120 mcg/day) are met (24). There is not an established threshold of circulating phylloquinone that defines sufficient/insufficient and low circulating phylloquinone has not been consistently defined in population-based studies (5,7,8). Identifying the threshold of circulating vitamin K that is sufficient to meet all physiological needs is an area of research that needs attention. Since low circulating phylloquinone is easily corrected, substantiating our findings in future studies could have an important public-health impact on physical function in older age.

Dp-ucMGP was associated with SPPB cross-sectionally but not longitudinally. However, lower dp-ucMGP was associated with better Health ABC performance scores over time. The Health ABC performance battery was designed to reduce potential ceiling effects of the SPPB since Health ABC participants were well-functioning at baseline (25). This may explain why dp-ucMGP was differentially associated with the two performance batteries. Because the Health ABC performance battery was the only performance measure that was associated with dp-ucMGP longitudinally, chance cannot be ruled out as a possible explanation. In an earlier analysis of this same cohort plasma dp-ucMGP was associated with structural characteristics of knee osteoarthritis cross-sectionally but not over follow-up (8), which may suggest (dp)ucMGP is not causally related to these health outcomes. It is also possible vitamin Ks role in functional decline could be through mechanisms that do not involve MGP. Vitamin K-dependent proteins other than MGP are implicated in physiological processes that lead to functional impairment (26,27). Phylloquinone has been shown to reduce expression of proinflammatory cytokines (4). Low grade inflammation is a characteristic of aging and has been linked to functional impairment (11). This could be an additional mechanism

Table 3. Associations Between Vitamin K Status and Lower Extremity Function Over Time in Health ABC Knee OA Study Participants

		Plasma Phylloquinone			*p* Value		
	n	<0.2 nM	0.2–<1.0 nM	≥1.0 nM	Within year	Plasma phylloquinone × year interaction	Overall plasma phylloquinone
SPPB (0–12)							
Unadjusted							
Year 1	1,088	9.60 (0.17)	9.83 (0.06)	10.05 (0.07)	.013	0.195	0.031
4	964	9.26 (0.25)	9.23 (0.10)	9.42 (0.11)	.448		
6	853	8.49 (0.30)	8.44 (0.12)	8.93 (0.13)	.021		
Adjusted							
Year 1*	987	9.67 (0.18)	9.83 (0.10)	10.07 (0.10)	.017	0.250	0.035
4	843	9.46 (0.24)	9.39 (0.12)	9.54 (0.13)	.580		
6	706	8.61 (0.29)	8.72 (0.13)	9.14 (0.15)	.031		
Health ABC PPB (0–4)							
Unadjusted							
Year 1	1,058	2.09 (0.06)	2.11 (0.02)	2.18 (0.03)	.103	0.380	0.078
4	947	1.93 (0.07)	1.91 (0.03)	1.96 (0.03)	.436		
6	819	1.68 (0.08)	1.69 (0.03)	1.80 (0.03)	.035		
Adjusted							
Year 1*	959	2.07 (0.06)	2.06 (0.03)	2.13 (0.04)	.024	0.259	0.033
4	840	1.90 (0.07)	1.89 (0.04)	1.93 (0.04)	.444		
6	704	1.63 (0.08)	1.68 (0.03)	1.78 (0.03)	.022		
Usual 20M gait speed, m/s							
Unadjusted							
Year 2	1,078	1.11 (0.02)	1.10 (0.01)	1.12 (0.01)	.363	0.547	0.069
4	932	1.09 (0.03)	1.08 (0.01)	1.12 (0.01)	.085		
6	811	1.01 (0.02)	1.03 (0.01)	1.06 (0.01)	.049		
Adjusted							
Year 2*	987	1.10 (0.02)	1.10 (0.01)	1.12 (0.01)	.105	0.925	0.002
4	832	1.10 (0.02)	1.11 (0.01)	1.14 (0.01)	.181		
6	696	1.04 (0.03)	1.06 (0.01)	1.09 (0.01)	.047		
Isokinetic leg strength, nm/kg lean							
Unadjusted							
Year 2	923	13.28 (0.42)	13.11 (0.16)	13.30 (0.18)	.718	0.192	0.602
4	806	12.32 (0.37)	12.44 (0.15)	12.47 (0.17)	.937		
6	742	11.11 (0.40)	11.68 (0.16)	11.93 (0.18)	.153		
Adjusted							
Year 2*	851	12.97 (0.44)	12.87 (0.25)	13.17 (0.27)	.433	0.357	0.296
4	726	11.99 (0.41)	12.22 (0.25)	12.35 (0.26)	.643		
6	643	10.91 (0.44)	11.52 (0.26)	11.82 (0.27)	.105		
400M gait speed, m/s†							
Unadjusted							
Year 2	720	1.26 (0.04)	1.25 (0.02)	1.24 (0.02)	.897	0.985	0.976
4	603	1.21 (0.03)	1.22 (0.01)	1.22 (0.01)	.966		
6	515	1.13 (0.03)	1.14 (0.01)	1.14 (0.01)	.991		
Adjusted							
Year 2*	670	1.22 (0.04)	1.23 (0.02)	1.22 (0.01)	.949	0.934	0.605
4	548	1.17 (0.03)	1.20 (0.02)	1.20 (0.02)	.562		
6	460	1.09 (0.03)	1.13 (0.02)	1.13 (0.02)	.445		

		Plasma dp-ucMGP			*p* value		
	n	T1: ≤267 pM	T2: 268–566 pM	T3: ≥ 567 pM	Within year	Plasma dp-ucMGP*year interaction	Overall dp-ucMGP
SPPB (0–12)							
Unadjusted							
Year 1	1,088	10.04 (0.08)	9.94 (0.08)	9.71 (0.08)	.012	0.592	0.019
4	964	9.37 (0.12)	9.47 (0.12)	9.07 (0.12)	.056		
6	853	8.81 (0.14)	8.71 (0.14)	8.38 (0.15)	.094		
Adjusted							
Year 1*	987	10.07 (0.11)	9.92 (0.11)	9.70 (0.11)	.008	0.578	0.035
4	843	9.48 (0.13)	9.59 (0.13)	9.27 (0.14)	.131		
6	706	8.97 (0.15)	8.97 (0.16)	8.65 (0.17)	.181		

Table 3. *Continued*

		Plasma dp-ucMGP			*p* value		
	n	T1: ≤267 pM	T2: 268–566 pM	T3: ≥ 567 pM	Within year	Plasma dp-ucMGP*year interaction	Overall dp-ucMGP
Health ABC PPB (0–4)							
Unadjusted							
Year 1	1,058	2.16 (0.03)	2.16 (0.03)	2.10 (0.03)	.240	0.281	0.031
4	947	1.95 (0.03)	1.98 (0.03)	1.86 (0.03)	.033		
6	819	1.78 (0.04)	1.77 (0.04)	1.65 (0.04)	.031		
Adjusted							
Year 1*	959	2.10 (0.04)	2.09 (0.04)	2.04 (0.04)	.238	0.338	0.024
4	840	1.93 (0.04)	1.94 (0.04)	1.84 (0.04)	.049		
6	704	1.76 (0.05)	1.73 (0.05)	1.63 (0.05)	.021		
Usual 20M walk, m/s							
Unadjusted							
Year 2	1,078	1.10 (0.01)	1.12 (0.01)	1.11 (0.01)	.523	0.458	0.318
4	932	1.09 (0.01)	1.11 (0.01)	1.10 (0.01)	.426		
6	811	1.03 (0.01)	1.06 (0.01)	1.02 (0.01)	.169		
Adjusted							
Year 2*	987	1.11 (0.01)	1.11 (0.01)	1.11 (0.02)	.895	0.705	0.712
4	832	1.11 (0.01)	1.12 (0.01)	1.13 (0.01)	.529		
6	696	1.07 (0.01)	1.07 (0.01)	1.07 (0.01)	.976		
Isokinetic leg strength, nm/kg lean							
Unadjusted							
Year 2	923	13.18 (0.20)	13.30 (0.20)	13.10 (0.20)	.783	0.722	0.627
4	806	12.59 (0.18)	12.48 (0.18)	12.24 (0.19)	.396		
6	742	11.86 (0.20)	11.71 (0.20)	11.63 (0.20)	.711		
Adjusted							
Year 2*	851	13.11 (0.27)	13.01 (0.27)	12.79 (0.29)	.485	0.905	0.227
4	726	12.49 (0.27)	12.21 (0.27)	11.97 (0.28)	.162		
6	643	11.79 (0.28)	11.50 (0.29)	11.39 (0.30)	.366		
400M walk, m/s†							
Unadjusted							
Year 2	720	1.23 (0.02)	1.25 (0.02)	1.27 (0.02)	.324	0.102	0.301
4	603	1.24 (0.02)	1.24 (0.01)	1.20 (0.01)	.187		
6	515	1.11 (0.01)	1.15 (0.01)	1.14 (0.01)	.202		
Adjusted							
Year 2*	670	1.22 (0.03)	1.22 (0.02)	1.24 (0.03)	.691	0.165	0.856
4	548	1.21 (0.02)	1.21 (0.02)	1.18 (0.02)	.252		
6	460	1.12 (0.02)	1.13 (0.02)	1.13 (0.02)	.658		

*Adjusted for age, sex, race, site, education, triglycerides, total cholesterol, smoking, alcohol use, healthy eating index, energy intake, fat intake, 25(OH)D, creatinine, physical activity, depression, diabetes, lipid lowering medication use, anti-hypertension medication use, and time-varying BMI, systolic blood pressure, IL-6, cognitive status, anti-inflammatory medication use, time spent walking per week.

†In those who completed the test (66%).

through which vitamin K influences physical function. Additional research is needed to clarify the role of MGP and other vitamin K-dependent mechanisms in physical performance.

Our study is strengthened by including cross-sectional and longitudinal components in a well-characterized cohort with multiple measures of lower extremity function. However, the observational design precludes causal inferences. At the time of enrollment, Health ABC participants reported being well-functioning, which could limit the generalizability to less functional groups. Participants included in this analysis were selected because they had qualifying knee pain or were a randomly selected control without knee pain (8). When participants with and without knee pain were analyzed separately, the stratified results were generally consistent to our overall findings (although not statistically significant). Plasma phylloquinone and dp-ucMGP did not differ according to knee pain status (both $p > .38$), but persons with knee pain had worse function. Given our sample size and that the majority of participants in our study had knee pain, larger studies are needed to clarify if vitamin K is more relevant to function in persons with knee pain or in older adults overall. The clinical relevance of our findings is also uncertain. In older adults more functionally impaired than Health ABC participants, a 0.3–0.5 unit difference in SPPB was found to be a minimally meaningful change, and for usual gait speed a 0.04–0.05 m/s difference was considered clinically meaningful (28,29). Our results suggest participants with ≥1.0 nM plasma phylloquinone had a 0.3 unit higher SPPB score at baseline and a 0.4 unit higher SPPB score after 5 years compared to participants with <1.0 nM. The difference in usual gait speed between these two groups after 4 years was 0.04 m/s. At the 2–3-year follow-up, we did not detect differences in any outcome across categories of plasma phylloquinone, although significant differences in SPPB were detected at baseline and after 5 years and differences in usual gait speed were detected after 4-year follow-up as well. The explanation for this observation is unclear. Had our follow-up been limited to 2 years, we would have concluded that plasma phylloquinone was not associated with functional impairment

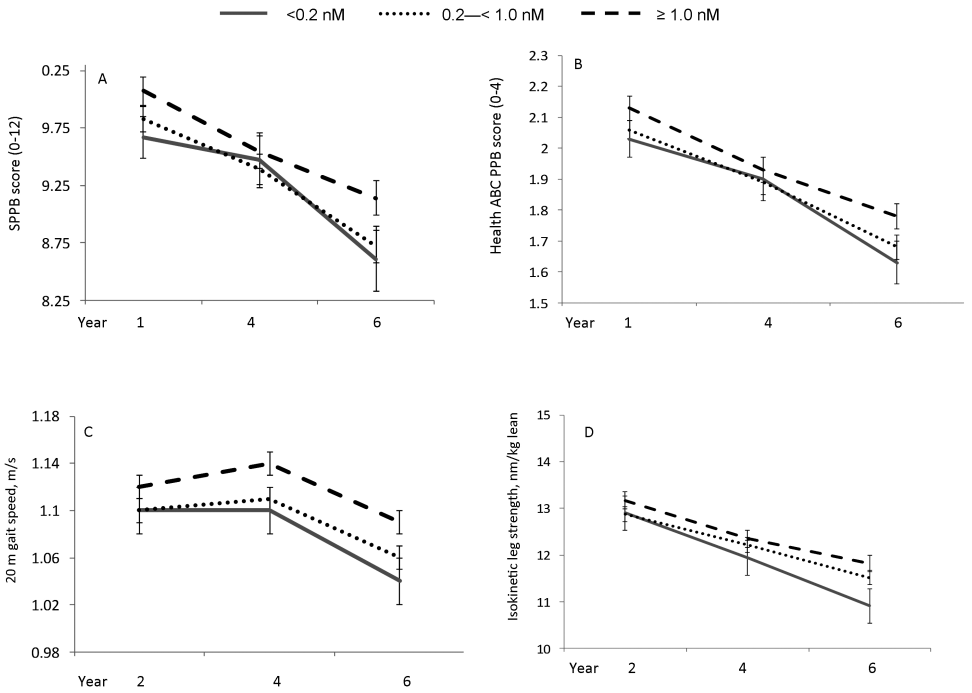

Figure 1. Plasma phylloquinone and (**A**) SPPB score, (**B**) Health ABC PPB score, (**C**) 20-meter gait speed, (**D**) isokinetic leg strength. Data are fully-adjusted LS means, error bars are SEM.

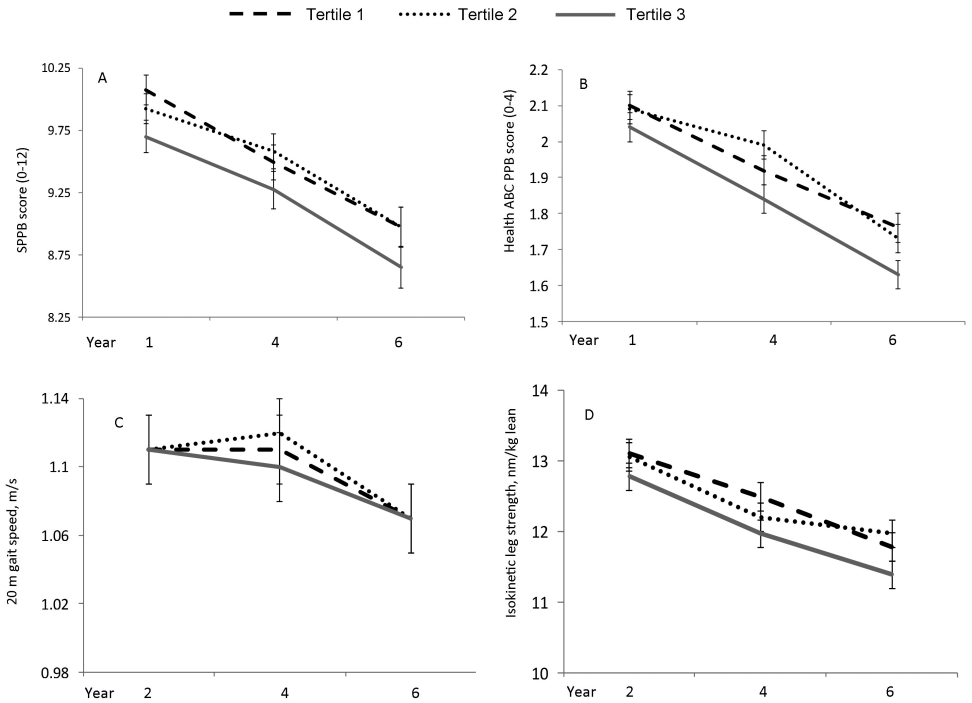

Figure 2. Plasma dp-ucMGP and (**A**) SPPB score, (**B**) Health ABC PPB score, (**C**) 20-meter gait speed, (**D**) isokinetic leg strength. Data are fully-adjusted LS means, error bars are SEM.

longitudinally. With repeated measures we could account for changes in status over time, but vitamin K status measures were only available at a single time point. The primary dietary sources of phylloquinone are characteristic of healthy diets (30) and higher circulating phylloquinone can reflect healthy lifestyles, which could be associated with better function itself. Although we adjusted our models for multiple co-morbidities, medication use, and multiple characteristics that could reflect general good health (diet and physical activity), residual confounding may persist.

In conclusion, older community-dwelling adults with ≥1.0 nM plasma phylloquinone had better physical performance battery scores cross-sectionally and over 4–5 follow-up years. Those with

higher plasma phylloquinone also had better usual gait speed at 4 years of follow-up, but plasma phylloquinone status was not associated with walking endurance. The findings with an independent functional marker of vitamin K status were less consistent. Low vitamin K status has been associated with multiple co-morbidities that lead to impaired function and disability (5–8), so improving vitamin K status may reduce functional decline in older adults with various age-related conditions. Future studies are needed to confirm our findings, establish if vitamin K supplementation reduces lower extremity functional decline in older age and to clarify the mechanism(s) underlying vitamin Ks role in this process.

Supplementary Material

Please visit the article online at http://gerontologist.oxfordjournals.org/ to view supplementary material.

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