



Age at natural menopause and physical function in older women from Albania, Brazil, Colombia and Canada: A life-course perspective

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ABSTRACT

Objective: Grip strength and gait speed are objective measures of physical function, which in turn is an indicator of biological aging. We evaluate the association between age at natural menopause (ANM) and physical functioning in a sample of postmenopausal women drawn from the International Mobility in Aging Study (IMIAS). **Study Design:** Retrospective cohort study of 775 women aged 65–74, from Albania, Brazil, Colombia and Canada, who had experienced natural menopause.

Main outcome measures: Gait speed and grip strength were obtained following standardized protocols. The association between self-reported ANM (< 40, 40–44, 45–49, 50–54 and ≥55) and gait speed (m/s) and grip strength (kg) was assessed by linear regression analyses adjusting for several life-course economic and reproductive exposures, height, BMI and smoking.

Results: Overall, women with ANM ≥ 55 had higher gait speed than those with ANM 50–54 ($\beta = 0.05$; 95%CI: 0.01, 0.10). Women with ANM < 40 had significantly lower grip strength compared with all other groups ($\beta = -2.58$; 95%CI: $-4.43, -0.74$). In region-specific analyses, ANM was associated with grip strength in Albania and Latin America and with gait speed in Albania only. No associations were observed in Canada.

Conclusions: ANM is associated with markers of physical functioning. Differences across study sites suggest that women in socially disadvantaged areas may reach menopause with different physiological reserves than those from more advantaged settings, leading to greater losses in muscle strength in postmenopausal years. More work comparing distinct populations is needed to better understand the underlying mechanisms.

1. Introduction

Physical functioning represents an integrated marker of healthy biological aging, capturing the interaction of a broad array of physiological systems [1]. Grip strength and gait speed are two validated measures of physical function [1,2]. Grip strength, a measure of muscle strength, is a key aspect in the definition of frailty [3] and sarcopenia phenotypes [4]. Gait speed, which incorporates many domains of the locomotor function, such as mobility, strength and balance [5], is also a key aspect of sarcopenia and frailty [4], and its association with disability and mortality is also well established [4]. While both sexes

experience functional losses with increasing chronological age, on average, women experience worse physical function and greater physical decline than men at similar ages [6,7]. The reasons for this disparity are poorly delineated, but one hypothesis centers on women's unique life-course reproductive events, including age at natural menopause (ANM) [8].

Observational studies suggest that the transition to menopause is a specific time in which accelerated loss in muscle mass and strength among women occurs [8–14]. For example, studies report lower grip strength among postmenopausal women as compared to premenopausal women [9,10,15] or peri-menopausal women [14]. Gait

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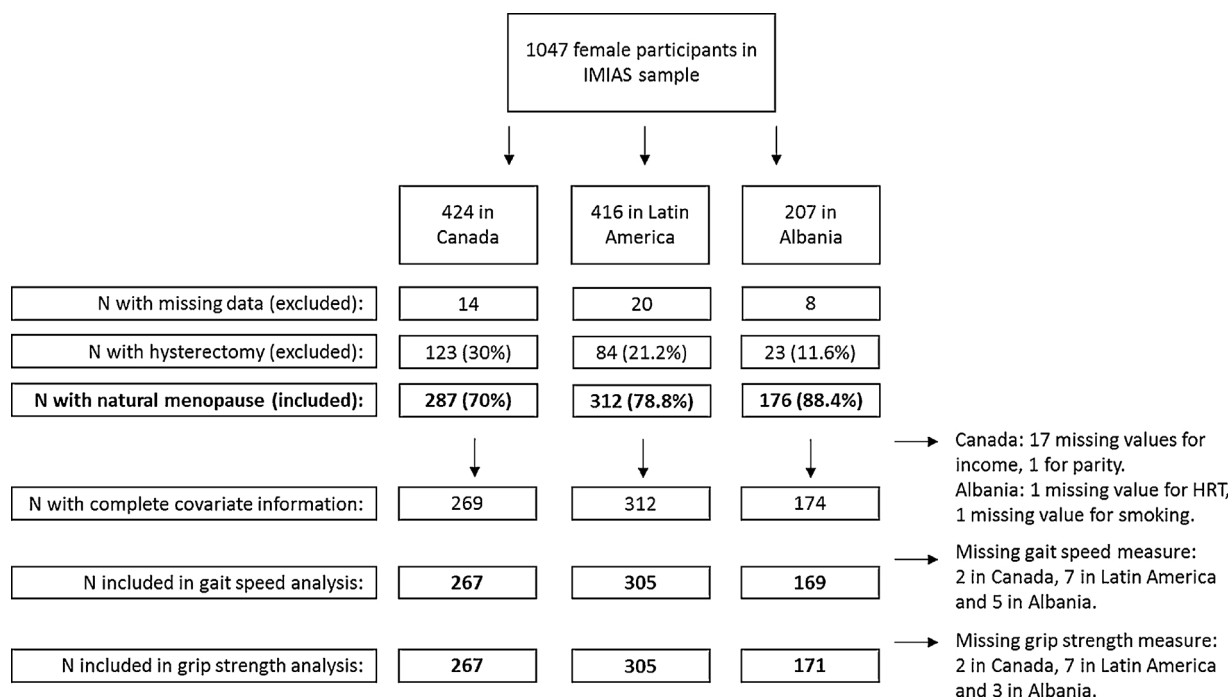


Fig. 1. Flow diagram of participant inclusion for gait speed and grip strength analysis.

speed at one’s usual pace is highly conserved until older adulthood and substantial changes in gait speed manifest only after a substantial reduction of fitness or nerve conduction velocity [16]. Yet, post-menopausal status as compared to pre-menopausal status has been related to lower gait speed in different studies [11–13].

Compared to studies of the menopausal statuses, ANM has been less studied as a reproductive exposure in relation with physical function, and the results are not consistent. Among postmenopausal women, Tom et al. [11] observed that those who transitioned to menopause at later ages had faster walking speed than women who transitioned earlier. For instance, women with natural menopause at 50–54 had a walking speed 0.08 m/s faster than those who experienced menopause at < 45 years. In contrast, an earlier study of a UK birth cohort showed that neither menopausal status nor age at menopause was associated to grip strength [17].

Biologically, estrogen decline after menopause has a negative impact on muscle mass and bone density [7,18,19], and cardiovascular function [12,13,20], which are risk factors for poor physical function. As we have previously reported, childhood social and economic disadvantages are associated with earlier menopause [21], and physical function [22]; however, these factors have not been examined with a life-course perspective with regard to the association between ANM and physical functioning. By life-course perspective, we account for contemporary conditions and prior living circumstances when examining ANM in a cohort of senior women. Moreover, no studies have considered these effects across populations of diverse social backgrounds, and none in women from Latin America or Eastern Europe, despite calls from experts in population aging to conduct investigations of physical function in more ethnically diverse samples and to perform cross-national comparisons [1]. The present study aims to investigate the association of ANM with gait speed and grip strength using a life-course approach, in a socially diverse cohort of women from the International Mobility and Aging Study (IMIAS) [23].

2. Methods

IMIAS is a population-based prospective cohort study amongst community-dwelling older adults [23], conducted in five sites in four

countries: Tirana (Albania), Natal (Brazil), Manizales (Colombia), Kingston (Ontario, Canada), and Saint-Hyacinthe (Quebec, Canada). The IMIAS cohort was established in 2012 at which time participants were 65–74 years old. A detailed description of the recruitment and study procedures for the IMIAS can be obtained from Gomez et al. [23]. Institutional ethics review board approval was obtained from the participating sites. Written informed consent was obtained from all participants.

As part of the Short Physical Performance Battery (SPPB), a timed 3 or 4 m gait speed test was conducted twice and the fastest time was used for these analyses [5]. Further details on administering the SPPB have been published elsewhere [5] and can be viewed on the SPPB website (<http://www.grc.nia.nih.gov/branches/leps/sppb/index.htm>).

Grip strength was measured using a handheld dynamometer (Jamar Hydraulic Hand Dynamometer®). Participants were seated on a chair with no armrest and positioned to flex their elbow at 90°, shoulder adducted and neutrally rotated, and forearm in neutral position. They were asked to grip the handle as hard as they could with their dominant hand for 5 s. Three measurements were carried out, and the highest value was used in the analyses.

Age at natural menopause (ANM) was defined through the following question: 1) *how old were you when you had your last menstrual period?* Women whose last menstrual period was the result of a hysterectomy (with or without oophorectomy) were excluded. Categories of ANM were defined as: < 40 (premature menopause), 40–44 (early menopause), 45–49, 50–54 and ≥ 55. Our reference age category was 50–54 years, based on results from Tom et al. [11] in which women in this age group had faster gait speed than those with a younger ANM.

The following characteristics were considered as potential covariates. Age, which was self-reported. Years of education, categorized into site-specific tertiles as follows: Tirana: < 8, 8–12, ≥ 13; Manizales and Natal: < 4, 4–5, ≥ 6; Kingston: < 15, 15–17, ≥ 18; St Hyacinthe: < 11, 11–12, ≥ 13. Income, classified into ‘poor’, ‘middle to middle high’, and ‘high’ also according to site-specific tertiles as follows: Tirana: annual income of < 1000 USD, 1,000–2,000 USD, ≥ 2000 USD; Manizales and Natal: monthly income of < 1 minimum salary, 1 minimum salary, ≥ 2 minimum salaries; and Canadian sites: annual income of < 20,000 CAD, 20,000–40,000, > 40,000. Height and BMI, measured and

Table 1
Population characteristics by age at natural menopause.

Characteristics	Age at natural menopause - categories										P-value
	< 40 (N = 31)		40-44 (N = 83)		45-49 (N = 237)		50-54 (N = 292)		≥ 55 (N = 132)		
Study site, N, %											
Kingston	6	3.8%	14	8.8%	35	21.9%	67	41.9%	38	23.8%	0.025
St Hyacinthe	3	2.4%	9	7.1%	35	27.6%	51	40.2%	29	22.8%	
Tirana	6	3.4%	17	9.7%	57	32.4%	72	40.9%	24	13.6%	
Manizales	9	5.7%	20	12.7%	55	35.0%	51	32.5%	22	14.0%	
Natal	7	4.5%	23	14.8%	55	35.5%	51	32.9%	19	12.3%	
Age, mean, SD	69.65	3.08	69.20	2.87	69.05	2.77	68.80	2.71	69.07	2.76	0.499
Education, site specific tertiles, N, %											
lowest tertile	15	4.7%	48	15.0%	90	28.0%	120	37.4%	48	15.0%	0.040
middle tertile	8	2.9%	24	8.6%	97	34.6%	99	35.4%	52	18.6%	
highest tertile	8	4.6%	11	6.3%	50	28.7%	73	42.0%	32	18.4%	
Income, N, %											
poor	14	5.8%	27	11.1%	82	33.7%	83	34.2%	37	15.2%	0.373
middle	11	3.1%	43	12.0%	100	28.0%	138	38.7%	65	18.2%	
middle high/high	6	3.8%	12	7.6%	49	31.0%	66	41.8%	25	15.8%	
Height, mean, SD	154.06	6.23	153.66	6.54	153.74	6.8	155.24	7.26	156.2	6.59	0.005
BMI, N, %											
Normal or underweight (< 25)	9	4.3%	23	11.0%	66	31.6%	78	37.3%	33	15.8%	0.816
Overweight (25.0-29.9)	11	3.4%	36	11.0%	95	29.1%	119	36.5%	65	19.9%	
Obese (> = 30)	11	4.6%	24	10.0%	76	31.7%	95	39.6%	34	14.2%	
Hysterectomy (post-menopausal), N, %											
Had hysterectomy	7	9.1%	7	9.1%	29	37.7%	24	31.2%	10	13.0%	0.063
Did not have hysterectomy	24	3.4%	76	10.9%	208	29.8%	268	38.4%	122	17.5%	
HRT, ever, N, %											
no	24	4.4%	65	12.0%	173	31.9%	196	36.2%	84	15.5%	0.089
yes	7	3.0%	18	7.8%	64	27.6%	95	40.9%	48	20.7%	
Smoking, last 15 years N, %											
no	26	3.7%	68	9.7%	217	30.8%	267	37.9%	126	17.9%	0.015
yes	4	5.7%	15	21.4%	20	28.6%	25	35.7%	6	8.6%	
Childhood economic adversity, N, %											
No adversities	16	3.7%	45	10.3%	126	28.9%	171	39.2%	78	17.9%	0.664
One or more adversities	15	4.4%	38	11.2%	111	32.7%	121	35.7%	54	15.9%	
Childhood social adversity, N, %											
No adversities	20	3.4%	57	9.7%	183	31.2%	227	38.7%	100	17.0%	0.258
One or more adversities	11	5.9%	26	13.8%	54	28.7%	65	34.6%	32	17.0%	
Teenage pregnancy, N, %											
No teenage pregnancy	23	3.7%	60	9.6%	190	30.4%	245	39.1%	108	17.3%	0.152
Teenage pregnancy (< 20)	8	5.4%	23	15.4%	47	31.5%	47	31.5%	24	16.1%	
Parity, N, %											
Nulliparous	3	3.4%	5	5.6%	36	40.4%	30	33.7%	15	16.9%	0.018
1 to 3 births	17	4.0%	36	8.5%	122	28.8%	178	42.1%	70	16.5%	
4 or more births	11	4.2%	41	15.6%	79	30.2%	84	32.1%	47	17.9%	

*17 missing values in income, 1 in HRT, 1 in smoking, 1 in parity.

P-values: chi2 for categorical/dichotomous covariates, anova for continuous covariates.

calculated following standard protocols. We categorized BMI into ‘underweight or normal weight’, ‘overweight’ and ‘obese’.

Hormone replacement therapy (HRT), categorized as those who never used HRT and those who had used HRT at some point in their lives. Post-menopausal hysterectomy (with or without oophorectomy), categorized as yes/no. Smoking status, categorized as current smokers or non(current)-smoker. Lastly, we considered four life-course variables; childhood social adversity and childhood economic adversity, lifetime parity and adolescent childbirth. Childhood social adversity encompassed experiences of parental alcohol or drug abuse, witnessing physical violence in the family, and/or physical abuse during childhood. Childhood economic adversity occurred if participants reported poor economic status, hunger, and/or unwanted parental unemployment. Both childhood adversity measures were based on a validation study previously carried out with data from IMIAS [24]. Parity was categorized into nulliparous, 1–3 children, 4 children or more. Adolescent childbirth was defined as giving birth before 20 years of age.

Descriptive analyses included comparison of the sample by outcomes, menopause-related characteristics and covariates using chi² for categorical/dichotomous covariates, and one-way ANOVA for continuous variables. Linear regressions were performed to assess the relationships between ANM and physical function, as linearity diagnosis

met criteria of normality and heteroscedasticity. Analysis was conducted with all sites together as well as separately by region: the Southeastern European site (Tirana, Albania), Latin American sites (Manizales, Colombia and Natal, Brazil), and Canadian sites (Kingston, Ontario and Saint-Hyacinthe, Quebec). Grouping by region increased the sample size for data analyses and interpretation. As we have previously demonstrated in IMIAS, cities in the same country and region may share similar contextual factors [23]. For the combined sites analysis, we increasingly adjusted for covariates in a total of six regression models: 1) age and study site, 2) years of education and income, 3) height and BMI; 4) hysterectomy and HRT, 5) smoking status, and 6) early life-course exposures. For the region-specific analysis, we used a backwards selection procedure to determine covariates relevant to the region and obtain the most parsimonious model [25]. Statistical analysis was conducted using STATA, version 14.

3. Results

Fig. 1 depicts the total number of participants included in our analyses. Mean ANM was 49.0 (SD 4.9) in Albania, 48.11 (SD 5.6) in Latin America, and 50.3 years (SD 5.19) in Canada, ($p < 0.001$). Table 1 shows the distribution of covariates by categories of ANM. For

Table 2
Distribution (or mean) of exposure variable and population characteristics by gait speed and grip strength.

Characteristics	Sites combined (N = 741)					
	Gait Speed			Grip Strength		
	Mean	SD	P-Value	Mean	SD	P-Value
Age at natural menopause			0.035			0.001
< 40	0.8	0.19	0.064	18.44	4.81	0.001
40–44	0.88	0.22	0.69	20.55	6.06	0.061
45–49	0.86	0.27	0.74	20.91	5.38	0.058
50–54	0.89	0.26	ref	21.81	5.07	ref
≥ 55	0.97	0.27	0.005	22.2	5.24	0.493
Study site			< 0.001			< 0.001
Kingston	1.09	0.23	ref	23.07	5.75	ref
St Hyacinthe	1.05	0.22	0.076	24.22	5.12	0.066
Tirana	0.84	0.27	< 0.001	20.75	5.35	< 0.001
Manizales	0.82	0.17	< 0.001	20.31	4.15	< 0.001
Natal	0.74	0.21	< 0.001	19.07	4.68	< 0.001
Age (each additional year)	−0.02		< 0.001	−0.31		< 0.001
Education, site specific tertiles			< 0.001			0.47
lowest tertile	0.85	0.26	< 0.001	21.21	5.60	0.287
middle tertile	0.91	0.27	0.020	21.18	5.42	0.267
highest tertile	0.97	0.25	ref	21.76	4.73	ref
Income*			< 0.001			0.07
poor	0.88	0.24	< 0.001	21.09	4.84	0.046
middle	0.87	0.27	< 0.001	21.10	5.57	0.034
high	0.99	0.25	ref	22.20	5.52	ref
Height (each cm increase)	0.01		< 0.001	0.28		< 0.001
BMI			< 0.001			0.48
Normal or under weight (< 25)	0.96	0.26	ref	21.63	5.21	ref
Overweight (25.0–29.9)	0.90	0.23	0.009	21.37	5.59	0.586
Obese (> = 30)	0.84	0.28	< 0.001	21.01	5.14	0.227
Hysterectomy (post-menopausal)						
Had hysterectomy	0.89	0.26	0.734	21.77	4.79	0.457
Did not have hysterectomy	0.90	0.26	ref	21.28	5.40	ref
HRT, ever						
never (n = 113)	0.85	0.26	< 0.001	20.53	5.08	< 0.001
ever (N = 172)	1.01	0.24	ref	23.24	5.49	ref
Smoking, currently						
no (n = 267)	0.90	0.26	ref	21.41	5.29	ref
yes (n = 18)	0.88	0.25	0.449	20.53	5.87	0.198
Childhood economic adversity						
No adversities	0.95	0.26	ref	21.90	5.31	ref
One or more adversities	0.84	0.25	< 0.001	20.63	5.31	0.001
Childhood social adversity						
No adversities	0.91	0.26	ref	21.45	5.17	ref
One or more adversities	0.87	0.26	0.042	20.94	5.86	0.261
Teenage pregnancy						
No teenage pregnancy	0.92	0.26	ref	21.54	5.47	ref
Teenage pregnancy (< 20)	0.80	0.24	< 0.001	20.42	4.73	0.023
Parity			< 0.001			0.006
Nulliparous	0.95	0.24	0.7	21.89	6.09	0.821
1 to 3 births	0.94	0.27	ref	21.75	5.56	ref
4 or more births	0.82	0.23	< 0.001	20.48	4.61	0.003

all sites combined, those in the lowest education tertile had earlier ages at menopause ($p = 0.04$), as did those who reported currently smoking ($p = 0.02$) and those who gave birth 4 or more times ($p = 0.02$). Taller women had later ANM ($p = 0.01$). Few differences were observed within regions (Supplemental tables A–C).

Table 2 shows differences in gait speed and grip strength by ANM and covariates. For all sites combined, a difference in gait speed was observed across categories of ANM, with women with an ANM of ≥ 55 having higher mean gait speed (0.97 m/s) compared to women with ANM 50–54 (0.89 m/s). Mean grip strength increased progressively

with later ANM (Table 2) and a marked and significant difference was observed between women with ANM < 40 and the reference categories of 50–54, as well as ≥ 55 years. In region-specific analysis (Supplemental material, Table 2A and 2B), no differences in mean of gait speed or mean of grip strength were observed across categories of ANM. However, some pairwise analysis shows that in Albania, women with an ANM of ≥ 55 had higher gait speed compared to women with an ANM of 50–54 (0.94 m/s vs 0.81 m/s, $p = 0.02$). Similarly, women in Latin America with an ANM < 40 had lower grip strength than those 50–54 (Supplemental material, Table 2B).

In combined site analysis, gait speed was associated with education, income, height, BMI, HRT, childhood adversities, teen pregnancy and parity; grip strength was associated with age, height, HRT, childhood economic adversity, teen pregnancy and parity (Table 2). Women in Albania and Latin America had lower gait speed as well as grip strength compared to women in Canada (Supplemental tables 2A, B). Covariates associated with gait speed in all regions were age, education and income (Supplemental Table 2A). In addition, gait speed was associated with height, BMI, smoking and childhood social adversity in Canada, with height, BMI, HRT, and childhood economic adversity in Latin America and with childhood economic and social adversity in Albania (Supplemental Table 2A). In region-specific univariate analyses, height was associated with grip strength in all regions (Supplemental Table 2B). In addition, grip strength was associated with age, and smoking in Canada, with hysterectomy and HRT in Latin America, and with age, income, and childhood economic and social adversity in Albania (Supplemental Table 2B). In multivariable analyses, with sites combined ANM was associated to gait speed in all models (Table 3). Women with ANM ≥ 55 years had higher gait speed compared to 50–54 years, with no differences observed with the other ANM categories. In region-specific analysis (Supplemental Table 3A), Albanian women with ANM ≥ 55 years had a higher gait speed compared to 50–54 years (0.129 m/s, CI: 0.008–0.251). No association was observed in Latin America or Canada, where differences in gait speed between > 55 vs 50–54 category were around 0.03 m/s (Supplemental Table 3A). In the grip strength analysis (Table 4), a borderline association was found in all multivariable models with ANM; with a difference of 2.6 kg observed between women with ANM < 40 compared to the reference group of ANM 50–54. In the region-specific analysis (Supplemental Table 4A), although only in Albania there were a significant effect of ANM on grip strength, women with ANM < 40 had a lower grip strength compared to the reference group of 50–54 years in all sites, 2.74 kg among Canadian women, 2.45 kg in Latin America women, and 5.55 kg, in Albanian women.

4. Discussion

Our study suggests an association between ANM and physical functioning. In the case of gait speed, later ANM results in higher mean gait speed. For grip strength, the difference observed was more evident for women with premature menopause (ANM < 40) compared to older categories (i.e., women with ANM < 40 have a lower grip strength than women with older ANM). To our knowledge, this is the first study to apply a life-course perspective to examine the association between ANM and physical functioning. Our results suggest that the observed associations remain when additional social and economic exposures across the life-course are considered, suggesting that ANM may contribute independently to the physical functioning of older women.

Later transitions to menopause appear to favor better gait speed. This is consistent with Tom et al. [11], who observed differences in gait speed between those with ANM ≥ 55 as compared to ANM at earlier ages. In their case, lower gait speeds were observed in those with ANM < 45, while in our study the differences were significant for premature menopause (ANM < 40).

Our study is the first to show differences in the association of ANM and physical function by social context. Although caution should be

Table 3
Multivariate linear regression models presenting the association of ANM and gait speed.

	Model 1: Age and study site only		Model 2: model 1 + education and income		Model 3: model 2 + height and BMI		Model 4: model 3 + HRT		Model 5: model 4 + smoking		Model 6: model 5 + life-course variables		
	B	95%CI	B	95%CI	B	95%CI	B	95%CI	B	95%CI	B	95%CI	
Age at natural menopause													
< 40	-0.05	-0.13	0.04	0.04	-0.04	-0.12	0.04	0.04	-0.04	-0.12	0.04	-0.03	-0.11
40-44	0.04	-0.02	0.09	0.10	0.05	0.00	0.10	0.10	0.05	0.00	0.10	0.05	0.00
45-49	0.03	-0.01	0.07	0.07	0.03	0.00	0.07	0.07	0.03	-0.01	0.07	0.04	0.00
50-54	<i>ref</i>				<i>ref</i>				<i>ref</i>			<i>ref</i>	
≥55	0.06	0.01	0.10	0.10	0.05	0.01	0.10	0.10	0.05	0.01	0.10	0.05	0.01
Overall P			0.03	0.03			0.04	0.04			0.04		0.04
Age (years)	-0.02	-0.02	-0.01	-0.01	-0.01	-0.02	-0.01	-0.01	-0.01	-0.02	-0.01	-0.01	-0.02
Study site													
Kingston	<i>ref</i>				<i>ref</i>				<i>ref</i>			<i>ref</i>	
St Hyacinthe	-0.06	-0.12	-0.01	0.01	-0.03	-0.08	0.03	0.03	-0.03	-0.08	0.03	-0.03	-0.08
Tirana	-0.26	-0.31	-0.21	-0.21	-0.21	-0.26	-0.16	-0.15	-0.21	-0.27	-0.15	-0.21	-0.27
Manizales	-0.27	-0.32	-0.22	-0.19	-0.20	-0.26	-0.14	-0.14	-0.20	-0.26	-0.14	-0.20	-0.27
Natal	-0.35	-0.40	-0.30	-0.30	-0.30	-0.36	-0.24	-0.24	-0.30	-0.36	-0.24	-0.29	-0.35
Overall P			< 0.001	< 0.001			< 0.001	< 0.001			< 0.001		< 0.001
Education, site specific tertiles													
lowest tertile			-0.09	-0.13	-0.09	-0.13	-0.04	-0.04	-0.09	-0.13	-0.04	-0.08	-0.12
middle tertile			-0.04	-0.08	-0.04	-0.08	0.00	0.00	-0.04	-0.08	0.00	-0.04	-0.08
highest tertile			<i>ref</i>		<i>ref</i>				<i>ref</i>			<i>ref</i>	
Overall P			< 0.001	< 0.001			< 0.001	< 0.001			< 0.001		0.002
Income, site specific													
Low			-0.07	-0.12	-0.06	-0.11	-0.01	-0.01	-0.06	-0.11	-0.01	-0.06	-0.10
Middle			-0.04	-0.08	-0.03	-0.07	0.01	0.01	-0.03	-0.07	0.01	-0.02	-0.07
High			<i>ref</i>		<i>ref</i>				<i>ref</i>			<i>ref</i>	
Overall P			0.02	0.02			0.06	0.06			0.06		0.09
Height (cm)													
BMI													
Normal weight or underweight					<i>ref</i>				<i>ref</i>			<i>ref</i>	
Overweight					-0.03	-0.07	0.01	0.01	-0.03	-0.07	0.01	-0.02	-0.06
Obese					-0.07	-0.11	-0.03	-0.03	-0.07	-0.11	-0.03	-0.07	-0.11
Overall P							0.002	0.002			0.002		0.002
Post-menopausal hysterectomy (ref: no)													
no					0.00	-0.05	0.06	0.06	0.00	-0.05	0.06	0.00	-0.05
yes													
Ever used HRT (ref: yes, ever)													
no					0.00	-0.04	0.04	0.04	0.00	-0.04	0.04	0.00	-0.05
yes													
Currently smoking (ref: no)													
no					0.00	-0.05	0.06	0.06	0.00	-0.05	0.06	0.01	-0.05
yes													
Childhood economic adversity (ref: none)													
no					0.00	-0.04	0.04	0.04	0.00	-0.04	0.04	0.01	-0.05
yes													
Childhood social adversity (ref: none)													
no					0.00	-0.07	0.01	0.01	-0.03	-0.07	0.01	-0.02	-0.06
yes													
Adolescent pregnancy (ref: no)													
no					-0.03	-0.07	-0.03	-0.03	-0.03	-0.07	-0.03	-0.07	-0.11
yes													
Parity													
Nulliparous					0.00	-0.05	0.06	0.06	0.00	-0.05	0.06	0.00	-0.05
1													
2													
3													
4													
5													
Overall P													

(continued on next page)

Table 4
Multivariate linear regression models presenting the association of ANM and grip strength.

	Model 1: Age and study site only		Model 2: model 1 + education and income		Model 3: model 2 + height and BMI		Model 4: model 3 + HRT		Model 5: model 4 + smoking		Model 6: model 5 + life-course variables		
	(N = 743)	95%CI	(N = 743)	95%CI	(N = 743)	95%CI	(N = 743)	95%CI	(N = 743)	95%CI	(N = 743)	95%CI	
Age at natural menopause													
< 40	-2.73	-4.61	-0.84	-0.77	-2.67	-4.51	-0.84	-2.72	-4.55	-0.88	-2.69	-4.52	-0.85
40-44	-0.61	-1.85	0.63	0.68	-0.54	-1.75	0.67	-0.48	-1.69	0.72	-0.43	-1.65	0.78
45-49	-0.43	-1.30	0.45	0.49	-0.29	-1.15	0.56	-0.31	-1.17	0.54	-0.31	-1.17	0.54
50-54	ref				ref			ref			ref		
≥55	0.12	-0.94	1.18	1.18	0.12	-0.91	1.15	0.13	-0.89	1.16	0.11	-0.92	1.14
Overall P		0.05		0.06		0.06			0.05			0.06	
Age (years)	-0.26	-0.39	-0.13	-0.11	-0.23	-0.36	-0.10	-0.23	-0.36	-0.10	-0.23	-0.36	-0.11
Study site													
Kingston	ref				ref			ref			ref		
St Hyacinthe	0.97	-0.23	2.18	2.56	2.05	0.80	3.29	1.76	0.49	3.03	1.81	0.54	3.08
Tirana	-2.28	-3.38	-1.18	-1.15	-0.74	-1.93	0.45	-0.31	-1.57	0.96	-0.27	-1.54	1.00
Manizales	-2.59	-3.73	-1.45	-0.93	0.25	-1.13	1.62	0.49	-0.91	1.90	0.51	-0.89	1.92
Natal	-3.85	-4.98	-2.72	-2.67	-1.71	-3.00	-0.41	-1.45	-2.79	-0.10	-1.43	-2.78	-0.09
Overall P		< 0.001		< 0.001		< 0.001			< 0.001			< 0.001	
Education, site specific tertiles													
lowest tertile				0.96	0.20	-0.75	1.15	0.31	-0.64	1.26	0.34	-0.61	1.30
middle tertile				0.81	-0.06	-1.02	0.89	0.07	-0.89	1.04	0.09	-0.87	1.06
highest tertile				0.90	ref			ref			ref		
Overall P				0.90		0.77			0.74			0.70	
Income, site specific													
Low				-0.02	-1.18	-2.34	0.20	-0.91	-2.03	0.22	-0.92	-2.05	0.21
Middle				0.47	-0.54	-1.54	0.47	-0.30	-1.28	0.68	-0.30	-1.28	0.68
High				0.13	ref			ref			ref		
Overall P				0.13		0.26			0.27			0.26	
Height (cm)					0.22	0.16	0.28	0.22	0.16	0.29	0.22	0.16	0.28
BMI					ref			ref			ref		
Normal weight or underweight					0.07	-0.81	0.94	0.01	-0.87	0.89	-0.02	-0.90	0.86
Overweight					0.05	-0.89	0.99	0.04	-0.90	0.98	0.01	-0.94	0.95
Obese							0.98			0.98			0.99
Overall P						0.98			0.98			0.99	
Post-menopausal hysterectomy (ref: no)					0.80	-0.41	2.01	0.80	-0.41	2.01	0.80	-0.41	2.01
Ever used HRT (ref: yes, ever)													
Currently smoking (ref: no)													
Childhood economic adversity (ref: none)													
Childhood social adversity (ref: none)													
Adolescent pregnancy (ref: no)													
Parity													
Nulliparous													

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Table 4 (continued)

	Model 1: Age and study site only (N = 743)	Model 2: model 1 + education and income (N = 743)	Model 3: model 2 + height and BMI (N = 743)	Model 4: model 3 + HRT (N = 743)	Model 5: model 4 + smoking (N = 743)	Model 6: model 5 + life-course variables (N = 743)
	B	B	B	B	B	B
1-3 births						ref
4 or more births						0.36
Overall P						-0.59
R-squared	0.15	0.15	0.20	0.21	0.21	1.32
Adj R-squared	0.14	0.14	0.19	0.19	0.19	0.68
Constant	41.15	40.57	3.91	3.66	3.93	4.73
	95%CI	95%CI	95%CI	95%CI	95%CI	95%CI

incorporating strategies earlier in life to prevent women from entering menopause with low physiological reserve and to maintain physical function during menopause.

Contributors

Maria P. Velez was responsible for funding acquisition, conceptualization, and drafting of the manuscript.

Nicole Rosendaal was responsible for formal analysis and revision of the manuscript.

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Conflict of interest

The authors declare that they have no conflict of interest.

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Ethical approval

This study abided by the human rights code of ethics and guidelines. Institutional Ethics review board approval was obtained from the participating sites. Written informed consent was obtained from all participants. Ethical approval was obtained from Queen’s University (HSREB 6020804).

Provenance and peer review

This article has undergone peer review.

Research data (data sharing and collaboration)

There are no linked research data sets for this paper. Data will be made available on request to the IMIAS Data Sharing Committee via a standard application procedure.

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