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Menopausal status and physical performance in midlife: findings from a British birth cohort study

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Abstract

Objective—To test the associations of menopausal status, timing of menopause and hysterectomy with physical performance at age 53y

Design—Using data on women participating in the MRC National Survey of Health and Development who have been followed up since birth in March 1946 (N=1386) associations of interest were examined. Menopausal status, grip strength, chair rises and standing balance time were assessed at age 53y and covariates were measured across life.

Results—Women who were post-menopausal and not using hormone replacement therapy (HT) at age 53y had lower mean grip strength than women who were still pre- or peri-menopausal at this age. However, this trend of decreasing grip strength across the three natural menopausal categories (from pre- to post-menopausal) was explained by current body size. Those women who had undergone hysterectomy before age 40y had significantly weaker grip strength than women who had undergone hysterectomy at later ages - in fully adjusted analyses those women who had a hysterectomy before age 40y had a mean grip strength 5.21kg (95% CI: 2.18, 8.25) lower than women who had a hysterectomy between ages 50 and 53y. There were no significant associations between menopausal status or age at hysterectomy and chair rise or standing balance time and also no significant associations between timing of menopause and any of the performance measures.

Conclusions—Women who have hysterectomies at young ages represent a group who may require more support than other women to achieve and maintain good physical performance, especially muscle strength, in mid-life.

Keywords

menopause; hysterectomy; grip strength; chair rises; standing balance; physical performance

Introduction

Poor physical performance predicts frailty, disability and loss of independence in old-age,¹⁻³ all outcomes which are causing growing public health concern as populations age. Physical performance is also a significant predictor of subsequent mortality even in non-disabled populations.^{2,4-6}

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The poorer physical performance of women when compared to men^{7,8} suggests that sex-specific factors across life may influence maximum levels of physical performance achieved and also rates of decline with age. One factor that has been implicated is menopause, because physical performance begins to decline at a greater rate than previously from midlife onwards among women and may be affected by changes in hormonal exposure.^{9,10} The association between menopause and physical performance has been examined in a limited number of studies.^{8,11-13} These studies have used a range of outcome measures including grip, pinch and quadricep strength^{8,12} and self-reports of physical function and functional limitations.^{11,13} There is some evidence from these studies that post-menopausal women have lower levels of muscle strength and physical function than pre-menopausal women,^{12,13} although this has not been consistently shown.⁸ It is also unclear whether the associations found are independent of changes in performance associated with general ageing. Further, existing studies have paid little attention to variation in associations by timing of menopause or in the potentially modifiable components of menopause including hormone therapy (HT) use and hysterectomy, with authors often excluding women who have undergone hysterectomy or who take HT. Findings from studies focusing on the association between HT use and components of physical performance are inconsistent, with some finding evidence of a benefit^{10,14,15} but others finding no such effects.¹⁶⁻¹⁹

Using data from a nationally representative British birth cohort study we have examined the association between menopausal status and objective measures of physical performance at age 53y. We have also investigated whether there is variation in physical performance by age at menopause and hysterectomy. As the cohort members were all born in the same week of the same year we have been able to examine the effect of menopause independently of any general age-related effects. Further, as information has been collected prospectively across life we have been able to take into account a range of potential confounding factors.

Methods

The Medical Research Council National Survey of Health and Development (NSHD) is a socially stratified sample of all births that occurred during one week in March 1946 across England, Scotland and Wales. This cohort has been followed-up prospectively at over 20 time points across life from birth onwards. The most recent data collection involving all cohort members was in 1999 (age 53 years) when nurses surveyed study participants in their homes.²⁰ Women in the study have also completed postal questionnaires sent annually between 1993 (age 47y) and 2000 (age 54y) and in 2003 (age 57y) which focused on women's health.²¹ Of 2547 females in the original cohort, by age 53y 154 (6%) had died, 232 (9%) were living abroad, 296 (12%) had refused to participate and 87 (3%) were untraced. Relevant ethical approval was received for this study.

Ascertainment of physical performance

Physical performance levels were assessed during home visits at age 53y using three tests: chair rising; standing balance and grip strength. Trained nurses conducted these tests using standardised protocols as described elsewhere⁷ and summarised here.

Grip strength was measured isometrically using an electronic handgrip dynamometer. Two values were recorded for each hand and the highest used in analyses. Standing balance time was measured, using a stopwatch, as the longest time, up to a maximum of 30 seconds, for which participants could maintain a one-legged stance in a standard position with their eyes closed. The distribution of these times was positively skewed and so they were normalised using a natural logarithm transformation. Chair rise time was measured, using a stopwatch, as the time taken to rise from a sitting to a standing position with straight back and legs and then sit down again ten complete times. In order for high scores to indicate good

performance as for the other two tests the reciprocal of the time taken (multiplied by 100) was used.

All three outcomes were modelled as continuous variables. This was to provide maximal statistical power and because there are expected to be linear increases in disability across each of the outcome measures.

Ascertainment of menopausal status

Using information on menstrual characteristics, hysterectomy and HT use provided by women in response to the annual women's health postal questionnaires sent between ages 47 and 54y and from similar data obtained during home visits at ages 43 and 53y the menopausal status of women at age 53y was derived. This was categorised into six groups. The first three groups comprised women not using HT who were classified, by the same method used in the Massachusetts Women's Health Study,^{22;23} as pre-menopausal (still menstruating and no changes in regularity of menstruation), peri-menopausal (periods ceased for between 3 and 12 months or menstruation reported to have become less regular) or post-menopausal (no menstruation for over 12 months). The fourth category consisted of women who had undergone hysterectomy and/or bilateral oophorectomy and were not using HT. The fifth category comprised women who had undergone these procedures but were using HT. The sixth category included other women using HT. Women were excluded from analyses if they had an unknown menopausal status at age 53y or if their periods had stopped because of chemotherapy or other treatment. Age at menopause was categorised into three groups: 45; 46-49; 50-53y and age at hysterectomy into four groups: < 40; 40-44; 45-49; 50-53y.

Covariates

Factors that could potentially confound the main associations of interest were identified *a priori* based on previous research.^{7;24-29}

As current height has previously been found to be strongly positively associated with grip strength and balance time and current weight has been found to be negatively associated with balance and chair rise time in women in the NSHD⁷ these were considered to be the two most important covariates. Height (m) and weight (kg) were measured by nurses during the home visit at age 53y.

Father's occupational class at age 11y and head of household occupational class at age 53y (or if not available, the most recent measure in adulthood) were categorised using the Registrar General's Social Classification. Cognitive ability at age 8y, which has been shown to be associated with timing of menopause^{24;30} and also with physical performance,^{28;29} was assessed using tests of reading comprehension, pronunciation, vocabulary, and nonverbal reasoning designed for the study by the National Foundation for Educational Research in England and Wales. The average score from this battery of tests was transformed into a standardised score that was then categorised into quartiles for the purposes of these analyses. Smoking status at age 53y was assessed during the home visit at this age and supplemented with information from previous data collections where necessary. Parity at age 53y was ascertained from information on children updated at each data collection across adulthood.

Statistical analysis

Linear regression was used to test the unadjusted associations between menopausal status and each of the three continuous outcome measures, treating the post-menopausal group as the reference category. Tests for trend were performed across the three categories of natural

menopause (i.e. pre-, peri- and post-menopause). Multiple linear regression was then used to model the effect of menopausal status adjusting for each covariate separately (i.e. height and weight at age 53y, father's occupational class, head of household occupational class, cognitive function at age 8y, smoking status at age 53y and parity at age 53y). Both measures of current body size were then adjusted for simultaneously and in a final model all covariates were included. To ensure comparability of models all analyses were performed on the sample of women with complete data on all covariates.

In sub-group analyses linear regression models were used to test the unadjusted associations between age at menopause and each of the three outcome measures among the naturally post-menopausal group and, between age at hysterectomy and each of the outcome measures among the women who had undergone hysterectomy. In both sets of models age 50-53y was treated as the reference category. Tests for trend across the different categories of age were performed. Multiple linear regression models were then run in which adjustments were made for the covariates listed above plus HT use.

Results

Of the 1778 women in the NSHD not lost to follow-up by age 53y 1386 had complete data on menopausal status and at least one physical performance measure. Of these women, at age 53y 76 (5.5%) were still pre-menopausal, 214 (15.4%) were peri-menopausal, 460 (33.2%) were post-menopausal, 310 (22.4%) had undergone a hysterectomy or bilateral oophorectomy and the remaining 326 (23.5%) were using HT (table 1).

In unadjusted analyses women who were pre-menopausal at age 53y had higher mean grip strength than women who were post-menopausal, whereas women who had undergone a hysterectomy prior to age 53y and were not using HT had lower mean grip strength (tables 2 and 3) however, these differences were not statistically significant at conventional levels (table 3). Peri-menopausal women had a mean grip strength between that of pre- and post-menopausal women and there was some evidence of a trend in grip strength across these three categories of natural menopause ($p=0.07$). Women using HT, whether they had undergone hysterectomy or not, had a similar mean grip strength to post-menopausal women. After adjustment for current height the differences in mean grip strength between menopausal groups attenuated, with only small additional attenuation after adjustment for current weight and other covariates (table 3). There was no evidence of an association between menopausal status and chair rise or standing balance time in unadjusted or adjusted analyses.

While women who had become post-menopausal at or before age 45y had lower mean grip strength and standing balance time than women who had become post-menopausal at later ages, these differences in performance by age at menopause were not significant (table 2) and adjustment for potential confounders did not alter this finding (results not shown).

There was a significant trend across categories of age at hysterectomy whereby mean grip strength decreased with decreasing age at hysterectomy (tables 2 and 4). Although these associations attenuated slightly after adjustment for covariates they remained significant (table 4). For example, in fully adjusted analyses those women who had a hysterectomy before age 40y had a mean grip strength 5.21kg (95% CI: 2.18, 8.25) lower than women who had a hysterectomy after age 50y. There was no significant variation in chair rise or standing balance time by age at hysterectomy (table 2).

Discussion

In a British birth cohort there was evidence to suggest that women who had undergone hysterectomy before age 40y had significantly weaker grip strength in mid-life than women who had undergone hysterectomy at later ages. This association was maintained after a range of adjustments. While women who were post-menopausal by age 53y had weaker grip strength at this age than women who were still pre- or peri-menopausal these differences were not statistically significant at conventional levels and attenuated after adjustment for current height. There was no evidence of variation in physical performance by age at menopause or, of associations between menopausal status or timing of hysterectomy and the other measures of physical performance, standing balance and chair rise time.

Comparison with other studies

Our findings are consistent with a study of American women which also found that while not statistically significant post-menopausal women did have weaker grip strength than pre-menopausal women.¹² However, this study did not adjust for height or include women who had undergone hysterectomy. Another study which considered muscle strength reported no significant variation by menstrual status however, these analyses may have been underpowered (n=229) and standard definitions of menopausal status were not used.

It has been shown that the objective measures of physical performance measured in the NSHD are associated with self-reported functional limitations.⁷ Consistent with our finding of no association between menopausal status and chair rise or balance time, menopausal status was not associated with self-reports of functional limitations at age 53y (i.e. difficulties walking 400 yards on the level or climbing stairs) in our study (results not shown). Findings from an American study of women aged 40 to 55y¹³ which found increased odds of self-reported substantial physical limitations across the three categories of natural menopause (from pre- to post-menopause) even in adjusted models are therefore not fully consistent with our findings. This inconsistency could be because the findings from the American study, which was cross-sectional and included women of a range of ages, are explained by general age-related changes in the self-report of limitations or because our study had insufficient statistical power to detect the levels of effect which exist. Our findings are consistent with another British study¹¹ which did not find associations between the menopausal transition and decline in self-reported physical functioning (as measured using the appropriate sections of the SF-36) except among those women who reported vasomotor symptoms and menopause associated depression.

Women in the NSHD using HT had similar levels of physical performance to post-menopausal women not using HT, supporting evidence from those studies which have found no protective benefit to physical performance of HT use.¹⁶⁻¹⁹

While few studies previously have considered variation in physical performance by hysterectomy status and timing of hysterectomy our finding of poorer physical performance among women with young age at hysterectomy is consistent with the finding that these women also have poorer levels of other health outcomes including psychological health at age 53y.³¹

Explanations

Grip strength is arguably the simplest of the three physical performance measures - it is an isometric test of upper body muscle strength whereas chair rise and standing balance times test lower body muscle strength, neuromuscular speed and control and appropriate processing by the central nervous system (CNS) and will be more greatly affected by cardiovascular and respiratory function.⁷ As there was some evidence that menopausal

status may be associated with grip strength but not chair rise or balance time, our findings therefore suggest that any association between menopausal status and physical performance in mid-life in the NSHD is acting through the musculoskeletal system, specifically muscle strength, rather than other systems, such as the CNS or cardiovascular and respiratory systems. That the associations we have found are specific to grip strength also suggests that the association between menopausal status and physical performance is unlikely to be mediated by poor mental health as the fact that women with poor mental health may be less motivated than other women to produce a maximal performance would be expected to affect all outcomes.

One of the most striking findings of our study is the greater risk of weak grip strength in middle-age among women who underwent a hysterectomy in earlier adulthood. It is possible that there is something particularly harmful to subsequent physical performance about having a hysterectomy at a young age. If hysterectomy is associated with reductions in oestrogen and testosterone exposure, women exposed to these reductions at younger ages and further from the time that these would be expected to occur naturally (i.e. with menopause) may be at higher risk of conditions influenced by such reductions, including loss of muscle strength. However, if this premature reduction in hormone exposure fully explained the association it would have been expected that women who had a young age at natural menopause would also have had significantly poorer physical performance than women who had later ages at natural menopause and this was not found, although this may be because of the small number of women who underwent early menopause in the NSHD. If this was the explanation it would also have been expected that women who took HT would be at least partially protected from such effects but in analyses examining variation in physical performance by age at hysterectomy adjustment for HT use had only small effects and there was no evidence of interaction between HT use and age at hysterectomy.

Women in the NSHD who had hysterectomies earlier in adulthood are known to have had higher levels of risk factors for a range of poor health outcomes in mid-life than women who had hysterectomies at later ages or did not have a hysterectomy, including lower lifetime socioeconomic position. The higher risk profile of women who underwent hysterectomies at young ages may therefore be expected to explain their poorer physical performance in mid-life. While this explanation is partially supported by the slight changes in the size of associations between young age at hysterectomy and grip strength after adjustment for potential confounders, even after taking such factors into account the associations retained significance. Further, the risk profile of women with young age at hysterectomy would also have been expected to have put them at higher risk of poor performance in chair rising and standing balance tests and as variations in these two measures by age at hysterectomy were not significant, this suggests that their higher risk profile is not fully responsible for the associations found.

A further possibility is that early age at hysterectomy is part of a complex of factors which indicate premature ovarian ageing.³² As there is thought to be a link between ovarian and general ageing³³ factors which indicate premature ovarian ageing could also be indicators of premature general ageing. If this were the case then early age at hysterectomy would not itself precipitate subsequent poor physical performance in middle-age but would indicate women who had a higher risk of health outcomes usually associated with ageing, occurring. This requires further investigation.

Methodological considerations

The measures of physical performance used in these analyses were recorded for the first time at age 53y and so it was not possible to make adjustments in our analyses for earlier life levels of these measures. We are thus unable to establish whether those groups of women

with poorer mean levels of physical performance at age 53y performed more poorly in these specific tests earlier in life, even before the menopausal transition, hysterectomy or HT use, or whether these differences have developed only since and possibly as a consequence of the menopausal status they had achieved by age 53y.

A further limitation of having data on physical performance at only one time point is that we are unable to assess whether the menopausal transition and hysterectomy are directly associated with declines in performance within individuals.

Women were excluded from analyses of the three individual physical performance measures if they were unable to attempt or complete the tests. While the women unable to perform the tests had poorer general health, were more likely to be inactive and of lower SEP⁷ than women who did complete the tests, they did not have significantly different distributions of menopausal status, age at menopause, age at hysterectomy or prevalence of hysterectomy (results not shown) and so any bias introduced is likely to have been minimal. Further, we also examined the association between menopause and a composite summary performance score which did include women unable to do the tests and this produced consistent results. To ensure comparability of models women were also excluded from analyses if they had missing data. While this could have introduced bias, analyses run using maximum available samples produced similar results.

A major strength of these analyses is that it has been possible to examine the effect of menopausal status on a range of physical performance measures in a large study population, who despite losses to follow-up remain nationally representative.³⁴ Another strength is that the measures of physical performance were taken by trained health professionals using standardised protocols rather than self-reported. Data on menopausal status, timing of menopause and hysterectomy were collected regularly during the time period when women were most likely to be undergoing hysterectomy or the menopausal transition. Further, as a wealth of information about the NSHD has been prospectively collected at time points across life it has been possible to adjust for a range of factors from across life which could confound the main associations of interest.

Conclusions

The differences in physical performance between menopausal status groups found in these analyses were small and whether they are clinically relevant is not yet known. As the cohort ages and the incidence of clinical musculoskeletal outcomes such as osteoporosis, osteoarthritis and sarcopaenia increases it will be possible to identify whether these small differences do translate into differences in the incidence of clinically important outcomes and levels of disability in later life. It will also only be by following up the women until all those currently pre- or peri-menopausal are post-menopausal that we will be able to establish whether the differences that currently exist between these three groups persist.

Our study suggests that women who have hysterectomies at young ages represent a group who may require more support than other women to achieve and maintain good physical performance, especially muscle strength, in mid-life.

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Table 1

Characteristics of the study population (sample with complete data on menopausal status and at least one physical performance measure (N=1386))

Characteristic	Total N	N (%) or mean (sd)
Menopausal status at 53y	1386	
Pre-menopausal		76 (5.48)
Peri-menopausal		214 (15.44)
Post-menopausal		460 (33.19)
Hysterectomy, no HT		114 (8.23)
Hysterectomy, HT		196 (14.14)
Other HT users		326 (23.52)
Age at menopause (y)	442	48.71 (3.00) (median: 49)
Age at hysterectomy (y)	307	43.26 (5.86)
Physical performance at 53y		
Chair rise time ((1/s)×100) [*]	1292	5.03 (1.58)
Standing balance time (s) [†]	1306	4.57 (2.12)
Grip strength (kg)	1334	27.79 (7.85)
Father's occupational class	1386	
Non-manual		557 (40.19)
Manual		746 (53.82)
Other		83 (5.99)
Head of household occupational class in adulthood	1376	
Non-manual		980 (71.22)
Manual		396 (28.78)
Smoking status at 53y	1386	
Never		678 (48.92)
Former		395 (28.50)
Current		313 (22.58)
Parity at 53y	1385	
0		169 (12.20)
1		173 (12.49)
2		614 (44.33)
3		309 (22.31)
4		120 (8.66)
Weight at 53y (kg)	1374	71.55 (14.24)
Height at 53y (cm)	1380	161.64 (5.96)

^{*} Reciprocal of time taken for 10 chair rises × 100

[†] Geometric mean and standard deviation

Table 2

Mean levels of physical performance at age 53y by menopausal status, timing of menopause and timing of hysterectomy

	Grip strength (kg)		Chair rise time ((1/s)×100)*		Standing balance (s)	
	N	Mean (sd)	N	Mean (sd)	N	Geometric mean (sd)
Menopausal status at 53y						
Pre-menopausal	69	28.71 (7.17)	69	5.17 (1.69)	70	5.29 (2.23)
Peri-menopausal	207	28.52 (7.88)	206	4.92 (1.47)	205	4.67 (2.11)
Post-menopausal	434	27.42 (7.99)	411	5.06 (1.53)	417	4.53 (2.04)
Hysterectomy, no HT	110	25.83 (7.05)	108	4.85 (1.47)	108	3.80 (2.02)
Hysterectomy, HT	186	28.20 (8.98)	179	5.01 (1.65)	182	4.61 (2.16)
Other HT users	305	27.99 (7.32)	299	5.13 (1.67)	305	4.61 (2.18)
<i>p</i> -value [†]		0.048		0.51		0.09
Age at menopause, y						
45	50	26.29 (8.36)	50	5.46 (1.31)	51	3.83 (2.06)
46-49	159	27.32 (8.25)	153	4.96 (1.61)	156	4.50 (2.09)
50-53	209	27.80 (7.71)	196	5.05 (1.52)	197	4.67 (1.94)
<i>p</i> -value [†]		0.47		0.13		0.20
Age at hysterectomy, y						
< 40	79	25.57 (7.72)	78	4.64 (1.38)	80	4.07 (2.26)
40-44	77	27.49 (7.92)	73	5.16 (1.36)	72	4.06 (2.16)
45-49	93	27.05 (8.14)	88	4.99 (1.74)	90	4.45 (2.01)
50-53	44	30.87 (10.00)	45	5.05 (1.88)	45	4.73 (2.04)
<i>p</i> -value [†]		0.01		0.22		0.63

* Reciprocal of time taken for 10 chair rises × 100

[†] from test of analysis of variance

Table 3

Unadjusted and adjusted differences in mean levels of physical performance (95% CI) at age 53y by menopausal status at age 53y

Menopausal status at 53y							p-value (overall)	p-value test for trend [*]
Pre-menopausal	Peri-menopausal	Post-menopausal	Hysterectomy, no HT	Hysterectomy, HT	Other HT users			
Grip strength (kg) (N=1311) [†]								
Model 1	1.29 (−0.71, 3.28)	1.10 (−0.20, 2.40)	0.00	−1.59 (−3.24, 0.06)	0.78 (−0.57, 2.13)	0.57 (−0.58, 1.72)	0.048	0.07
Model 2	0.95 (−1.00, 2.89)	1.06 (−0.20, 2.33)	0.00	−1.12 (−2.72, 0.48)	0.94 (−0.37, 2.26)	0.38 (−0.74, 1.50)	0.14	0.12
Model 3	0.93 (−1.01, 2.88)	1.09 (−0.18, 2.36)	0.00	−1.09 (−2.70, 0.52)	0.95 (−0.36, 2.27)	0.36 (−0.77, 1.48)	0.14	0.12
Model 4	0.86 (−1.09, 2.82)	0.93 (−0.35, 2.22)	0.00	−1.21 (−2.83, 0.41)	0.86 (−0.47, 2.19)	0.22 (−0.91, 1.35)	0.17	0.21
Chair rise time ((1/s)×100) (N=1272) [†]								
Model 1	0.11 (−0.29, 0.52)	−0.14 (−0.40, 0.12)	0.00	−0.21 (−0.54, 0.13)	−0.05 (−0.33, 0.23)	0.07 (−0.17, 0.30)	0.51	0.92
Model 2	0.14 (−0.26, 0.54)	−0.14 (−0.40, 0.13)	0.00	−0.26 (−0.59, 0.08)	−0.07 (−0.34, 0.21)	0.08 (−0.15, 0.31)	0.34	0.99
Model 3	0.12 (−0.27, 0.52)	−0.06 (−0.32, 0.20)	0.00	−0.17 (−0.50, 0.16)	−0.04 (−0.31, 0.23)	0.04 (−0.19, 0.27)	0.81	0.84
Model 4	0.04 (−0.36, 0.43)	−0.13 (−0.39, 0.13)	0.00	−0.19 (−0.52, 0.14)	−0.09 (−0.36, 0.19)	0.02 (−0.21, 0.25)	0.75	0.75
Standing balance (log_e(s)) (N=1287) [†]								
Model 1	0.15 (−0.04, 0.34)	0.03 (−0.09, 0.16)	0.00	−0.18 (−0.34, −0.02)	0.02 (−0.11, 0.15)	0.02 (−0.09, 0.13)	0.09	0.14
Model 2	0.15 (−0.04, 0.34)	0.03 (−0.09, 0.15)	0.00	−0.17 (−0.32, −0.01)	0.02 (−0.11, 0.15)	0.01 (−0.10, 0.12)	0.12	0.16
Model 3	0.13 (−0.05, 0.31)	0.07 (−0.05, 0.20)	0.00	−0.12 (−0.27, 0.04)	0.04 (−0.09, 0.16)	−0.01 (−0.12, 0.10)	0.19	0.10
Model 4	0.08 (−0.10, 0.27)	0.04 (−0.08, 0.16)	0.00	−0.12 (−0.27, 0.03)	0.04 (−0.09, 0.16)	−0.03 (−0.13, 0.08)	0.34	0.19

Model 1 – unadjusted

Model 2 – adjusted for height at age 53y

Model 3 – adjusted for height and weight at age 53y

Model 4 – adjusted for height and weight at age 53y and father's occupational class, head of household occupational class, cognition at age 8y, smoking at age 53y and parity

^{*} Test for trend across the 3 categories of natural menopause (pre-, peri- and post-menopausal)[†] Models 1 to 4 are all based on the same N

Table 4

Unadjusted and adjusted differences in mean grip strength (kg) (95% CI) at age 53y by age at hysterectomy (y) (N=293)

	Age at hysterectomy (y)				p-value (overall)	p-value test for trend
	< 40	40-44	45-49	50-53		
Model 1	-5.30 (-8.36, -2.23)	-3.38 (-6.46, -0.30)	-3.82 (-6.80, -0.84)	0.00	0.01	0.004
Model 2	-5.23 (-8.24, -2.23)	-3.58 (-6.60, -0.56)	-3.81 (-6.73, -0.89)	0.00	0.01	0.004
Model 3	-5.16 (-8.15, -2.16)	-3.53 (-6.54, -0.51)	-3.81 (-6.72, -0.89)	0.00	0.01	0.004
Model 4	-5.21 (-8.25, -2.18)	-3.27 (-6.37, -0.17)	-3.50 (-6.45, -0.54)	0.00	0.01	0.003

Model 1 – unadjusted

Model 2 – adjusted for height at 53y

Model 3 – adjusted for height and weight at 53y

Model 4 – adjusted for height and weight at 53y and father's occupational class, head of household occupational class, cognition at age 8y, smoking at age 53y and parity