Hysterectomy and perceived physical function in middle-aged Australian women: a 20-year population-based prospective cohort study

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ABSTRACT

PURPOSE: Hysterectomy is one of the most common gynaecological procedures worldwide. Changes in endocrine function may impact on age-associated decline in physical function and these changes may be accelerated by hysterectomy. The aim of this study was to investigate associations between hysterectomy status and self-reported physical function limitations.

METHODS: Our study sample (n=8,624) came from the mid-cohort (born 1945-50) of the Australian Longitudinal Study on Women's Health (ALSWH). Self-report of physical function was measured by the Physical Functioning (PF) subscale of the Medical Outcomes Study Short-Form Health Survey (SF-36) over seven surveys (1998-2016), categorised into substantial, moderate and minimal PF-limitations. The associations between hysterectomy status and *de novo* substantial or moderate PF-limitations versus minimal PF-limitations were investigated using log multinomial regression.

RESULTS: By Survey 8 (2016), 20% of the study sample had a hysterectomy with ovarian conservation (hysterectomy only) and 9% had a hysterectomy and both ovaries removed (hysterectomy-bilateral oophorectomy). Women with a hysterectomy only had a small increase in risk of substantial PF-limitations (versus minimal PF-limitations) compared to women with no hysterectomy (relative risk [RR]: 1.13; 95% confidence interval [95% CI] 1.00-1.27); the point estimate was stronger for women with a hysterectomy-bilateral oophorectomy (RR: 1.26; 95% CI 1.09-1.46). In a supplementary analysis, the increased risk of substantial PF-limitations was seen only in women who had surgery before the age of 45 years.

CONCLUSIONS: Compared to women with no hysterectomy, women with hysterectomy-bilateral oophorectomy were at increased risk of substantial PF-limitations versus minimal PF-limitations over eighteen years of follow-up.

Keywords: Hysterectomy, physical function, bilateral oophorectomy, SF36, women's health

INTRODUCTION

Ageing has consistently been associated with a decline in physical function due to physiological changes including loss of bone mineral density, muscle strength and muscle mass [1]. Evidence suggests that women are more likely than men of the same age to report physical function limitations [2, 3]; this difference may be due to women experiencing more dramatic changes in endocrine function as they age, particularly around the time of menopause [1, 4]. These changes in endocrine function may be accelerated by hysterectomy, with potential effects on age-associated decline in physical function.

Hysterectomy remains a common gynaecological procedure [5]. Between 20 and 40% of women in middle and high income countries will have a hysterectomy by the time they are 60 years old [6, 7]. Hysterectomy with the surgical removal of both ovaries (bilateral oophorectomy) results in immediate menopause and an abrupt reduction in hormone levels. Moreover, even when ovaries are conserved, hysterectomy has been associated with earlier menopause[8] and changes in hormone levels [9, 10], however this effect is not consistent across the literature [11, 12]. Women who had hysterectomy (with or without bilateral oophorectomy) have consistently had more self-reported limitations in physical function in studies using pre-menopausal women as the reference group [13-16]. However, only two of these studies were longitudinal, assessing physical function at multiple time-points [13, 15]. In contrast, one cross-sectional study (in women 60 years and older) found no difference in self-reported physical function limitations among women who had a hysterectomy compared to women who experienced natural menopause [17].

To our knowledge, no studies have investigated limitations in physical function, comparing women with a hysterectomy to women without a hysterectomy (in the same birth cohort) as they age over the longer term i.e. beyond the menopause transition. In addition, no

longitudinal studies have presented results that stratify hysterectomy status by whether or not both ovaries have been removed. Due to the inconsistencies in the literature on hormonal changes after hysterectomy with ovarian conservation, and the observed differences in a range of health outcomes for women with a hysterectomy with and without ovarian conservation [18], we hypothesised that there might also be differences between these two groups in the development of physical function limitations.

In summary, the aim of this study was to investigate the association between hysterectomy status and self-reported physical function limitations over an 18-year period in a mid-aged cohort of Australian women, and whether the relationships depended on their ovarian conservation status.

METHODS

Study setting and population

The Australian Longitudinal Study on Women's Health (ALSWH) is a longitudinal population-based study exploring factors that influence women's health across the life course. Recruitment methods and response rates for the study have been described in detail elsewhere [19, 20]. In summary, women were sampled from the Medicare Australia database (which covers all citizens and permanent residents of Australia, including refugees and immigrants), from three cohorts of women born in 1973-1978, 1946-1951 and 1921-1926. Sampling was random within each cohort, except that women from rural and remote areas were sampled at twice the rate of women in urban areas. Participants in the baseline surveys conducted in 1996 have been followed up approximately every three years. A fourth cohort born 1989-95 was recruited in 2013.

Our analyses included data from the 1946-1951 cohort. The 1996 baseline survey (Survey 1) was completed by 13,715 women when they were aged 45-50 years. Seven follow-up surveys (Surveys 2-8) took place in 1998 (47-52 years, n=12,338), 2001 (50-55 years, n=11,226), 2004 (53-58 years, n=10,905), 2007 (56-61 years, n=10,638), 2010 (59-64 years, n=10,011), 2013 (62-67 years, n=9151) and 2016 (65-70 years, n=8,622).

Hysterectomy status

At each survey women were asked a series of questions about their hysterectomy and bilateral oophorectomy status. At Survey 1, participants were asked whether they had ever had a hysterectomy and whether they had ever had both ovaries removed. At all subsequent surveys, participants were asked if they had either of these procedures in the intervening period. We created a three-category time-dependent variable reflecting a woman's hysterectomy status at each survey. *A priori* we excluded women who only reported having a bilateral oophorectomy (Survey 1 through to Survey 8, n=195) and women who reported a hysterectomy at one survey and both ovaries removed at a subsequent survey (n=247). Women who reported having a hysterectomy, but did not report having both ovaries removed, formed the hysterectomy with ovarian conservation group ('hysterectomy only' group). Women who reported having a hysterectomy and both ovaries removed at the same survey formed the "hysterectomy - bilateral oophorectomy" group. Women did not report having either a hysterectomy or both ovaries removed formed the 'no hysterectomy' group. A woman's status could change from 'no hysterectomy' to either 'hysterectomy only' or 'hysterectomy-bilateral oophorectomy' at a subsequent survey, but once in either of the hysterectomy groups, a woman's status could not change further.

Age at hysterectomy

At Surveys 7 and 8 women were asked the age they had their hysterectomy. We derived a five-category time-independent variable by combining a woman's reported age at hysterectomy with her reported hysterectomy status at each survey ("no hysterectomy", "hysterectomy only < 45 years old", "hysterectomy only 45+ years old", "hysterectomy-bilateral oophorectomy < 45 years old", "hysterectomy-bilateral oophorectomy 45+ years old"). For a woman to be included in the < 45 year age categories, she had to report a hysterectomy age younger than 45 years and also report that she had a hysterectomy (with or without both ovaries removed) at Survey 1 (when all participants were aged between 45 and 50 years). The women in the 'no hysterectomy' group were women who did not report a hysterectomy at any survey.

Physical function

Information on physical function was collected at each survey using the well-validated Physical Functioning (PF) subscale of the Medical Outcomes Study Short-Form Health Survey (SF-36).[21] The PF subscale asks ten questions about the degree of physical limitation experienced doing the following activities: bathing/dressing, walking 100 metres/500 metres/more than one kilometre, bending/kneeling/stooping, climbing one/ several flights of stairs, lifting/carrying groceries, moderate and vigorous activities. Response options are "yes, limited a lot", "yes, limited a little" or "no, not limited at all". The raw score of the PF subscale is transformed to a 0 to 100 scale with lower values indicating poorer perceived physical function [21]. Because scores on the PF subscale are not normally distributed, we categorised the PF subscale into three categories based on the cut-offs for the 5^{th} and 25^{th} percentiles (PF scores of 50 and 80 respectively) in women in the no hysterectomy group at Survey 1 [22]. Women with a score of 50 or lower were classified as having "substantial physical function (PF) limitations"; those with a score between 51 and 80

were classified as having "moderate PF-limitations", and those with a score of 81 to 100 as having "minimal PF-limitations".

When considering covariates for our analysis, we included those we thought would potentially affect both our exposure of interest (hysterectomy status) and outcome (PF-limitations). We tested for these relationships in univariate models.

Sociodemographic factors

The age of women, measured at Survey 1, was included as a continuous variable. Highest education level was measured at Survey 1 and categorized as 'less than high school', 'high school/trade/diploma' and 'degree or higher'. Area of residence ('urban' and 'rural/remote') and partner status ('living with partner' and 'not living with partner') were time-dependent variables measured at each survey.

Lifestyle factors

All of the lifestyle factors were measured at each survey and were included in the analysis as time-dependent variables. Body mass index (BMI; kg/m^2) was calculated from self-reported weight (kg) and height (cm) and categorized into '<25 kg/m^2' (under/healthy weight), '25-29.9 kg/m^2' (overweight) and '≥30 kg/m^2' (obese) [23]. Smoking status was categorized as 'never smoker', 'ex-smoker' and 'current smoker'. Physical activity levels were categorized according to average minutes of moderate intensity activity per week: 'none/low level' (< 150 minutes), 'moderate level' (150-300 minutes) and 'high level' (>300 minutes) [24].

Reproductive factors

Current use of menopausal hormone therapy (MHT) was reported at each survey (yes/no). Women were also asked about menopausal symptoms at each survey: 'in the last 12 months have you had any of the following – (a) hot flushes and (b) night sweats?' Response options

were ‘never’, ‘rarely’, ‘sometimes’ and ‘often’. We combined the hot flushes and night sweats variables into a vasomotor menopausal symptoms variable. Women responding as ‘often’ experiencing hot flushes and/or night sweats were categorised as ‘often’ reporting vasomotor menopausal symptoms at that survey. Otherwise they were categorised as ‘not often’ experiencing vasomotor menopausal symptoms. Current MHT use and vasomotor menopausal symptoms were time-dependent variables. Parity was measured at Survey 1 (‘no children’, ‘1 child’, ‘2 children’, ‘3 children’ and ‘4 or more children’). Age at menarche was measured at Survey 2 and categorised into ‘< 12 years’, ’12 years’, ’13 years’, ’14 years or older’.

Chronic conditions

We created a time-dependent chronic conditions variable by counting the number of chronic conditions a woman reported at each survey from the following list: diabetes, asthma, bronchitis/emphysema, cardiovascular disease, hypertension, cancer (excluding skin cancer), osteoporosis, arthritis and mental disorders (anxiety, depression, or other psychiatric disorder). We dichotomised the variable into ‘no chronic conditions’ and ‘one or more chronic conditions’.

Statistical analysis

We excluded women from our analysis if they reported substantial or moderate PF-limitations at survey 1 (n= 3,634). Characteristics of participants were described by PF-limitation category at Survey 2 (the baseline for this study), with percentages weighted by area of residence to account for over-sampling in rural areas. Differences between groups were assessed by the χ^2 test.

We assessed the impact of missing data on our analysis in three ways: 1) we compared the characteristics (at Survey 2) of those included in the analysis (n = 8,624) with those excluded due to missing information (n = 1,015). Differences between groups were assessed by the χ^2 test; 2) we performed a complete case analysis on women who had complete information on all variables at every survey (n= 2,913); and 3) we imputed missing data using the two-fold Fully Conditional Specification (FCS) algorithm method for longitudinal data which imputes missing values at a given survey, conditional on information at the same survey and immediately adjacent surveys [25]. Full details of our imputation analysis are provided in Online Resource 1.

As our outcome was not rare, we used log-multinomial regression to estimate relative risks (RRs) with 95% confidence intervals (CIs) for the association between hysterectomy status and incidence (across Surveys 2-8) of substantial and moderate PF-limitations versus minimal PF-limitations, using the cluster option to account for repeated measurements [26]. A woman could change PF-limitation category from survey to survey. To reduce the possibility of reduced PF being due to post-surgical recovery (i.e. that women who have a hysterectomy may experience a decline in physical function in time period immediately surrounding the surgery), and to avoid reverse causation, we ascertained hysterectomy status at the survey prior to measurement of physical function. Consequently, the hysterectomy would have occurred at a minimum of two years prior to measurement of physical function. In our primary analysis, the time-dependent covariates included in the model were measured at the same time as physical function, recognising that factors such as MHT use, physical activity and BMI are likely to have fairly immediate impacts on physical function (i.e. measurement at the same survey would therefore be a better reflection of any recent changes). To test this assumption we conducted two sensitivity analyses. First, we measured both hysterectomy and the time-dependent covariates at the survey prior to self-report of

physical function (time-lagged) and second, we performed the analysis with hysterectomy and the time-dependent covariates measured at the same survey as physical function (no time-lag).

Our base model included hysterectomy status, age, current MHT use and area of residence (to account for over-sampling of women in rural areas). We then assessed the impact of adding lifestyle, socioeconomic factors, presence of chronic conditions and reproductive factors to our base model in separate blocks. Our final model included all of the variables considered, except for the reproductive factors (vasomotor menopausal symptoms, age at menarche, parity) as these did not attenuate any of the base model effect estimates for hysterectomy by more than 5%. In a supplementary analysis, we stratified hysterectomy status by age at hysterectomy using the sub-sample of women we had this information for (n=5,624).

Analysis for descriptive characteristics were done using SAS software, Version 9.4 of the SAS system for windows Copyright © 2002-2012 by SAS Institute Inc. SAS and all other SAS Institute Inc. product or service names are registered trademarks or trademarks of SAS Institute Inc., Carey, NC, USA. Multiple imputation and log-multinomial regression analyses were done in Stata/SE 12.1 for Windows [27].

RESULTS

Our analysis included 8,624 participants with complete information at one or more surveys. Of the 13,715 women recruited at survey 1 (1996), 4,105 were excluded *a priori*. Fig.1 shows the number of women included at each survey, and those excluded due to missing data. Overall, the women with missing data were more likely to be older, overweight or obese, have a less than high school education, living without a partner, have one or more chronic conditions, have a younger age at menarche and often experience vasomotor symptoms (Online Resource 2 Supplemental Table 1).

Descriptive characteristics of the women included in our analysis at our study baseline (Survey 2) are summarised in Table 1. Women who reported new onset of substantial or moderate PF-limitations at survey 2 were more likely to have a hysterectomy (with and without bilateral oophorectomy), lower education levels, and one or more chronic conditions. They were also more likely to have poorer lifestyle habits, live without a partner, experience vasomotor menopausal symptoms often and be MHT users (Table 1). Over 50% of women in the substantial and moderate PF-limitation categories reported at study baseline they were "limited a lot" doing vigorous activities compared to only 7% of women in the no PF-limitations category (Online Resource 2 Supplemental Table 2). More than 50% of women in the substantial PF-limitations category also reported they were "limited a lot" climbing several flights of stairs; bending, kneeling or stooping, and walking more than half a kilometre. None of the women in the no PF-limitations category reported being "limited a lot" doing these activities (Online Resource 2 Supplemental Table 2). At study baseline, 13% of women had a hysterectomy only and 5% had a hysterectomy-bilateral oophorectomy; by 2016 this percentage had increased to 20% and 9% respectively. Between Survey 2 and Survey 8 an increasing percentage of all women, regardless of hysterectomy status, experienced moderate and substantial PF-limitations, with a corresponding decrease in the percentage experiencing minimal PF-limitations (Online Resource 2 Supplemental Table 3). However, at each survey, a higher percentage of women with a hysterectomy (with and without bilateral oophorectomy) experienced both substantial and moderate PF-limitations than women with no hysterectomy (Fig. 2).

In our minimally-adjusted base model, women with a hysterectomy only and women with a hysterectomy-bilateral oophorectomy had a significantly higher risk of both moderate and substantial PF-limitations (versus minimal PF-limitations) compared to women with no hysterectomy (Table 2). Adjustment for lifestyle factors substantially attenuated these risks,

but they remained statistically significant (Table 2). In the final model (with additional adjustment for the presence of chronic conditions and socioeconomic factors), there was no longer an association between hysterectomy status and moderate PF-limitations versus minimal PF-limitations. Women with a hysterectomy only had a small increase in risk of substantial PF-limitations (versus minimal limitations) compared to women with no hysterectomy (relative risk [RR]: 1.13; 95% confidence interval [95% CI] 1.00-1.27); the point estimate was stronger for women with a hysterectomy-bilateral oophorectomy (RR: 1.26; 95% CI 1.09-1.46) (Table 2). The RRs were very similar in the sensitivity analyses where we used different time-lags between the measurement of hysterectomy status and covariates and the measurement of the outcome (Online Resource 2 Supplemental Table 4).

When we stratified our analysis by age at hysterectomy for women who provided this information at Surveys 7 and 8 (n=5,264), there were differences in the strength of point estimates across age strata for substantial PF-limitations (versus minimal PF-limitations) for both hysterectomy groups, with statistically significant associations seen in women who had surgery before the age of 45 years (RR 1.26, 95% CI: 1.07-1.48 hysterectomy only; RR 1.41, 95% CI: 1.16, 1.72 hysterectomy-bilateral oophorectomy) (Fig. 3).

DISCUSSION

Compared to women with no hysterectomy, women with a hysterectomy were at increased risk of *de novo* substantial PF-limitations versus minimal PF-limitations over nearly two decades of follow-up. To our knowledge, this is the first study in this area that has presented results for hysterectomy stratified by bilateral oophorectomy status. We found that compared to women with no hysterectomy, women with a hysterectomy-bilateral oophorectomy had an increased risk of substantial PF-limitations versus minimal PF-limitations; for women with a hysterectomy only, the increase in risk was lower. In a sub-sample of women, where our

analysis was further stratified by age at hysterectomy, women who had a hysterectomy (with/without bilateral oophorectomy) before the age of 45 years had an increased risk of substantial PF-limitations.

Key strengths of the study include the large community-based sample of ALSWH and the longitudinal nature of the analysis. Perceptions of physical function were consistently measured using the same validated instrument, and the questions about hysterectomy/bilateral oophorectomy and the time-dependent covariates were repeated, at each survey. We time-lagged our analysis so that measures of physical function occurred at least two years after hysterectomy, so any physical function limitations that were reported were unlikely to be directly related to the surgery. We had a large number of women with a hysterectomy, with sufficient numbers to stratify by bilateral oophorectomy status; by the end of the follow-up period 20% of women had a hysterectomy with ovarian conservation (n=1,148) and 9% of women had a hysterectomy with bilateral oophorectomy (n=483). In addition, in a sub-sample of women (n=5,264) we were able to further stratify our results by age at surgery.

Limitations of the study are that all data were collected by self-report, which may introduce bias into the analysis. In particular, while the validity of self-report of hysterectomy is consistently high [28-30], the validity of self-reported bilateral oophorectomy may be less reliable [28, 30], and would affect the distribution between the two hysterectomy groups. We did not have information on whether women in the "hysterectomy only" group retained both ovaries or had one ovary removed, so we could not further stratify our analysis by unilateral oophorectomy status. As women were not asked the reason for their hysterectomy, we were also unable to explore potential differences in physical function limitations by indication for hysterectomy. Although we had missing data through loss to follow-up, our results remained robust in the complete case analysis and when we imputed the missing data (Online Resource 2 Supplemental Table 5).

Women were not asked about the age they had their hysterectomy until Surveys 7 and 8, therefore women who had been lost to follow-up would not have responded to these questions. We investigated the differences between women with a hysterectomy who responded to the age at hysterectomy questions at either Survey 7 or Survey 8 and those that did not participate in Surveys 7 and 8 (n=1,013 in our study sample). Women with a hysterectomy who had been lost to follow-up were more likely to be smokers and have lower education levels at Survey 1 (results not shown). Responses to the questions about age at hysterectomy may also be prone to recall bias as many women would have had their hysterectomy more than 15 years before responding to the question. The results of this sub-analysis should therefore be treated with caution.

There have only been two longitudinal studies published on the associations between hysterectomy and perceived physical function. Both of these studies have focused on comparisons between menopausal states. In the Michigan Bone Health and Metabolism Study (MBHMS)[15], self-reported physical function was assessed at two time-points, five years apart. Compared to pre- and peri-menopausal women, women with a hysterectomy (with and without oestrogen from ovarian conservation or MHT use) had reduced levels of self-reported physical function. In the Study of Women's Health Across the Nation (SWAN)[13], in a longitudinal analysis over a 15 year period (with five repeated measures of physical function), women with a hysterectomy and naturally menopausal women not using hormone therapy had higher odds of substantial functional limitation compared to pre-menopausal women. Our results, while consistent with these studies, are not directly comparable as we took a different approach, investigating the association between hysterectomy status (irrespective of menopausal status) and perceived physical function limitations over an 18 year period. Because the women in our study were in the same 5-year age group and likely to move through different life-stages within similar timeframes, we were able to assess whether

differences between women with and without a hysterectomy persisted beyond the menopause transition.

The physiological mechanisms behind women with a hysterectomy experiencing greater physical function limitations than women without a hysterectomy remain unclear. Reductions in oestrogens and androgens are a result of the surgery are an obvious explanation, however, it is possible that other mechanisms are also at play. We hypothesised that women with a hysterectomy only would differ from women with a hysterectomy-bilateral oophorectomy, due to the more abrupt changes in hormone levels in the latter. We found only a small increase in risk of substantial PF-limitations in women with a hysterectomy only; the point estimate was stronger (and statistically significant) for women with a hysterectomy-bilateral oophorectomy. Of note was our finding that the higher ris k of substantial PF-limitations was confined to women who had surgery before the age of 45 (irrespective of bilateral oophorectomy status). This finding is consistent with those of other studies [17, 31], perhaps suggesting surgery prior to menopause has a more substantial impact on hormonal and other changes, and that these reductions, experienced when a woman is pre-menopausal have a greater cumulative impact on physical function over time. Similar to other studies [15, 31], adjustment for exogenous MHT use did not attenuate our estimates, suggesting that factors other than oestrogen are also impacting upon levels of physical function. Some theories hypothesised in the literature include an increase in oxidative stress around menopause, along with declining levels of hormones such as testosterone, growth hormone (GH), dehydroepiandrosterone (DHEA) and insulin-like growth factor-1 (IGF-I) [1, 13], with suggestions that these changes may be mitigated by increased physical activity, reductions in body weight, and increased vitamin D and protein intake [4].

Conclusion

We identified that compared to women no hysterectomy, women with a hysterectomy with bilateral oophorectomy are at increased risk of substantial PF-limitations in the longer term. Further research on age at hysterectomy is needed to build the evidence-base in this area. Future research should investigate whether the indications for hysterectomy (such as endometriosis, fibroids and dysfunctional uterine bleeding) play a differential role in limitations in physical function.

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Compliance with ethical standards

Disclosure of interests

All authors declare that they have no conflict of interest.

Details of Ethics Approval

The ALSWH has been granted ethics clearance by the Universities of Newcastle and Queensland (Ethics approvals H0760795 and 2004000224). Ethics for the longitudinal study was approved on 26 July 1995. All procedures (surveys) performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. The article does not contain any studies with animals performed by any of the authors.

Informed consent

Informed consent was obtained from all individual participants included in the study.

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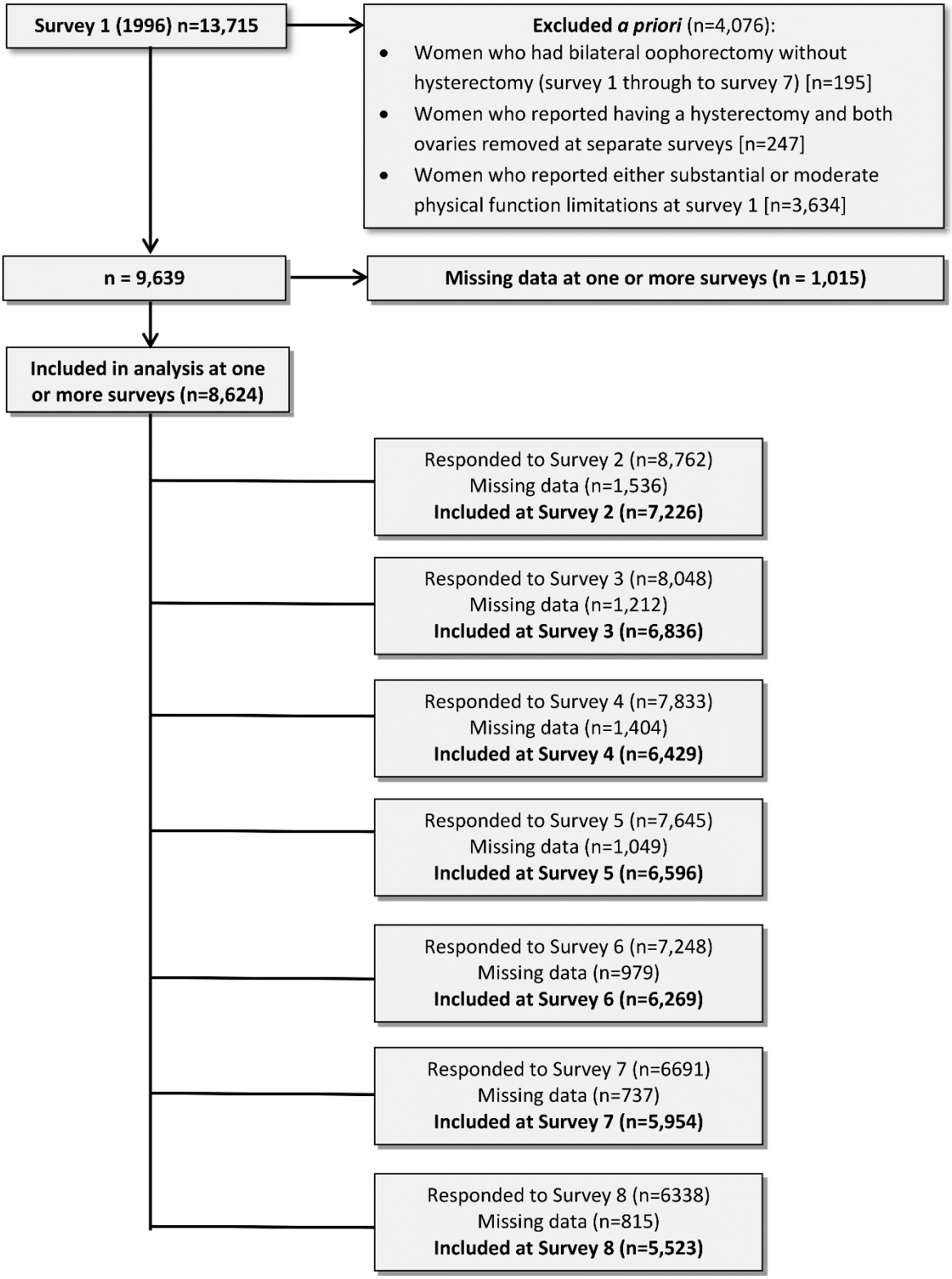
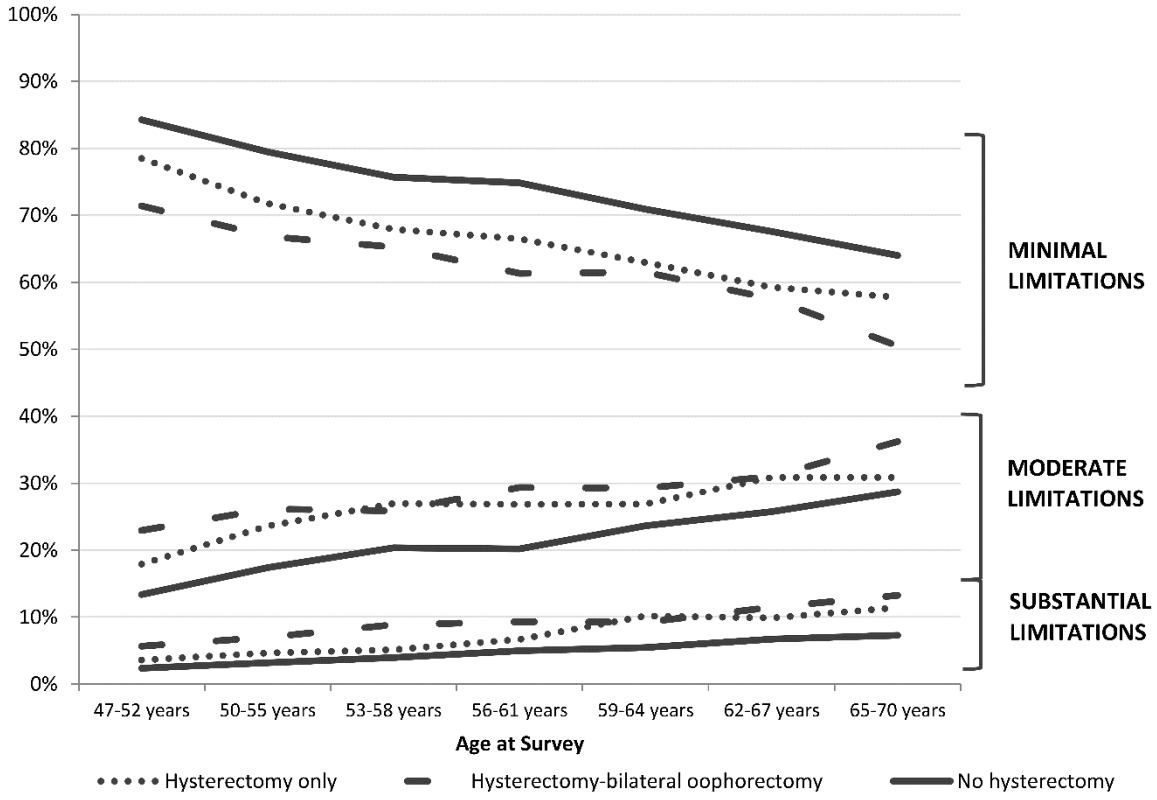
Fig. 1 Flowchart of participants included in the analysis at each survey. Participants who met *a priori* exclusion criteria or who had missing data at each survey were excluded

Fig. 2 Percent of women who reported minimal, moderate and substantial physical function limitations at each survey by hysterectomy status

Fig. 3 Forest plot showing associations between age at hysterectomy and substantial and moderate physical function limitations versus minimal physical function limitations (n=5,264)


Survey 1 (1996) n=13,715
Excluded *a priori* (n=4,076):
Women who had bilateral oophorectomy without hysterectomy (survey 1 through to survey 7) [n=195]
Women who reported having a hysterectomy and both ovaries removed at separate surveys [n=247]
Women who reported either substantial or moderate physical function limitations at survey 1 [n=3,634]
n = 9,639
Missing data at one or more surveys (n = 1,015)
Included in analysis at one or more surveys (n=8,624)
Responded to Survey 2 (n=8,762)
Missing data (n=1,536)
Included at Survey 2 (n=7,226)
Responded to Survey 3 (n=8,048)
Missing data (n=1,212)
Included at Survey 3 (n=6,836)
Responded to Survey 4 (n=7,833)
Missing data (n=1,404)
Included at Survey 4 (n=6,429)
Responded to Survey 5 (n=7,645)
Missing data (n=1,049)
Included at Survey 5 (n=6,596)
Responded to Survey 6 (n=7,248)
Missing data (n=979)
Included at Survey 6 (n=6,269)
Responded to Survey 7 (n=6691)
Missing data (n=737)
Included at Survey 7 (n=5,954)
Responded to Survey 8 (n=6338)
Missing data (n=815)
Included at Survey 8 (n=5,523)


100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
47-52 years
50-55 years
53-58 years
56-61 years
59-64 years
62-67 years
65-70 years
Age at Survey
MINIMAL LIMITATIONS
MODERATE LIMITATIONS
SUBSTANTIAL LIMITATIONS
Hysterectomy only
Hysterectomy-bilateral oophorectomy
No hysterectomy

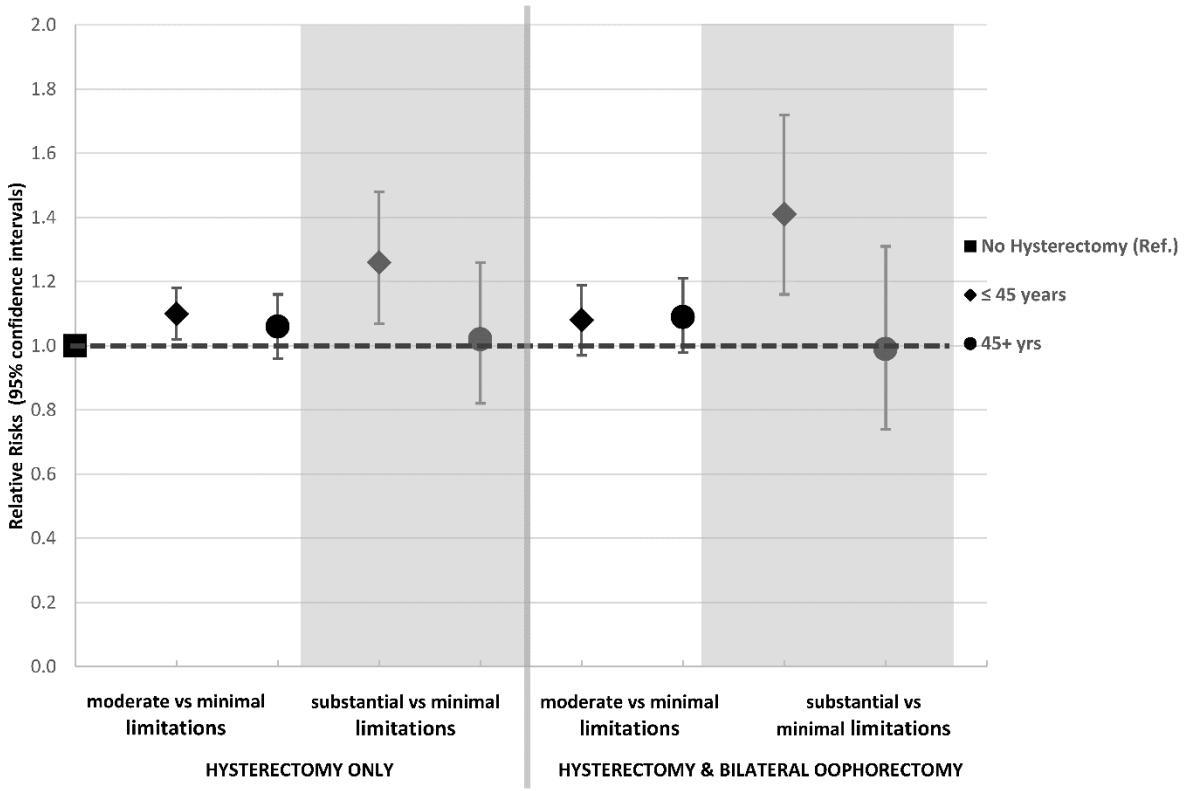

2.0
1.8
1.6
1.4
1.2
1.0
0.8
0.6
0.4
0.2
0.0
Relative Risks (95% confidence intervals)
No Hysterectomy (Ref.)
≤ 45 years
45+ yrs
moderate vs minimal limitations
substantial vs minimal limitations
moderate vs minimal limitations
substantial vs minimal limitations
HYSTERECTOMY ONLY
HYSTERECTOMY & BILATERAL OOPHORECTOMY

Table 1 Characteristics of women[a] at study baseline (Survey 2) by self-reported level of physical function limitation (n=7,226)

	Substantial limitations[b] (n=195)		Moderate limitations[c] (n=1045)		Minimal limitations[d] (n=5986)		
	n[e]	%[f]	n[e]	%[f]	n[e]	%[f]	p-value
Hysterectomy status (at Survey 1)							
Hysterectomy only	36	3.1	180	18.0	789	78.9	<.0001
Hysterectomy and both ovaries removed	20	5.5	81	23.1	252	71.4	
No hysterectomy	139	2.4	784	13.4	4965	84.3	
Age (at Survey 1)							
45-46 years	47	2.2	264	13.0	1715	84.9	0.145
47-48 years	77	2.8	413	14.2	2400	83.0	
49-50 years	71	2.8	368	16.0	1871	81.3	
Area of residence							
Urban	66	2.6	367	14.4	2144	83.0	0.955
Rural/remote	129	2.7	678	14.6	3842	82.8	
Body mass index							
< 25 kg/m^2	74	2.0	423	11.3	3334	86.7	<.0001
25-29.9 kg/m^2	55	2.2	353	15.4	1823	82.4	
≥ 30 kg/m^2	66	5.7	269	24.2	829	70.1	
Physical activity level							
None/low level	111	2.9	660	17.0	3082	80.1	<.0001
Moderate level	25	1.8	129	10.9	936	87.3	
High level	50	2.5	256	11.6	1968	85.9	
Smoking status							
Never smoker	94	2.1	579	14.1	3499	83.8	0.009
Former smoker	61	3.1	264	13.5	1611	83.5	
Current smoker	40	3.7	202	17.3	876	79.0	
Highest qualification							
Less than high school	114	3.3	540	16.6	2636	80.2	<.001
High school/trade/diploma	61	2.5	374	13.4	2337	84.2	
Degree or higher	20	1.5	131	12.0	1013	86.5	
Partner status							
Living with partner	150	2.4	851	13.9	5088	83.6	0.017
Not living with partner	45	3.6	194	16.8	898	79.7	
Current MHT use							
No	135	2.3	801	13.9	4803	83.8	0.003
Yes	60	3.9	244	16.3	1183	79.8	
Age at menarche							
< 12 years	33	2.9	213	16.0	1005	81.0	0.344
12 years	35	1.8	220	15.2	1277	83.0	
13 years	56	2.5	269	13.3	1703	84.2	
≥ 14 years	66	2.9	329	14.3	1916	82.9	
Experience vasomotor symptoms often							
No	150	2.3	821	13.3	5171	84.4	<.0001
Yes	42	4.1	221	21.8	760	74.1	
Number of children							
None	17	2.7	76	15.1	445	82.1	0.779
One	16	3.2	91	15.4	483	81.4	
Two	73	2.5	366	13.2	2290	84.3	
Three	48	2.5	292	15.0	1636	82.5	
Four or more	30	2.5	175	15.8	858	81.7	
Presence of chronic conditions							
No	80	2.3	402	10.8	3314	86.9	<.0001
Yes	115	3.0	643	18.4	2672	78.6	

ABBREVIATIONS: n = number; % = percent; MHT = menopausal hormone therapy

[a] Women who had not reported substantial or moderate limitations in physical function at Survey 1

[b] Substantial limitations defined as a score of ≤ 50 on the physical function subscale of the SF-36

[c] Moderate limitations defined as a score of 51 to ≤ 80 on the physical function subscale of the SF-36

[d] Minimal limitations defined as a score of > 80 on the physical function subscale of the SF-36

[e] Numbers for each characteristic will differ due to missing values at Survey 2

f Weighted for participants' area of residence

Table 1 Relative risks and 95% confidence intervals (Cis) for the associations between hysterectomy status and moderate and substantial physical function (PF) limitations versus minimal PF-limitations (n=8,624)

	Minimal PF-limitations versus			
	Moderate PF-limitations		Substantial PF-limitations	
	RR	(95% CI)	RR	(95 % CI)
Base model [a]				
No hysterectomy	1.00		1.00	
Hysterectomy only	1.22	(1.14, 1.30)	1.50	(1.31, 1.71)
Hysterectomy and both ovaries removed	1.30	(1.29, 1.42)	1.83	(1.53, 2.20)
Base model + chronic conditions [b]				
No hysterectomy	1.00		1.00	
Hysterectomy only	1.15	(1.08, 1.22)	1.37	(1.20, 1.56)
Hysterectomy and both ovaries removed	1.21	(1.12, 1.31)	1.64	(1.37, 1.96)
Base model + socio-economic factors [c]				
No hysterectomy	1.00		1.00	
Hysterectomy only	1.19	(1.11, 1.26)	1.43	(1.25, 1.63)
Hysterectomy and both ovaries removed	1.26	(1.15, 1.37)	1.69	(1.42, 2.02)
Base model + lifestyle factors [d]				
No hysterectomy	1.00		1.00	
Hysterectomy only	1.11	(1.05, 1.17)	1.24	(1.10, 1.39)
Hysterectomy and both ovaries removed	1.12	(1.04, 1.21)	1.38	(1.17, 1.62)
Base model + reproductive factors [e]				
No hysterectomy	1.00		1.00	
Hysterectomy only	1.20	(1.12, 1.28)	1.48	(1.28, 1.71)
Hysterectomy and both ovaries removed	1.25	(1.13, 1.37)	1.77	(1.45, 2.16)
Fully-adjusted model [f]				
No hysterectomy	1.00		1.00	
Hysterectomy only	1.05	(1.00, 1.11)	1.13	(1.00, 1.27)
Hysterectomy and both ovaries removed	1.07	(0.99, 1.15)	1.26	(1.09, 1.46)

ABBREVIATIONS: PF = physical function; RR = relative risk; 95% CI = 95% confidence interval

[a] Base model: adjusted for age at survey 1, area of residence and current MHT use

[b] Base model + chronic diseases: adjusted for age at survey 1, area of residence, current MHT use, presence of chronic conditions

[c] Base model + socioeconomic factors: adjusted for age at survey 1, area of residence, current MHT use, highest qualification level, partner status

[d] Base model + lifestyle factors: adjusted for age at survey 1, area of residence, current MHT use, BMI, smoking status, physical activity level

[e] Base model + reproductive factors: adjusted for age at survey 1, area of residence, current MHT use, parity, vasomotor menopausal symptoms, age at menarche

[f] Fully-adjusted model: adjusted for age at survey 1, area of residence, current MHT use, presence of chronic conditions, highest qualification level, partner status, BMI, smoking status, physical activity level