Published in final edited form as:

Female Pelvic Med Reconstr Surg. 2011 March ; 17(2): 80–90. doi:10.1097/SPV.0b013e31820e5d06.

RISK FACTORS FOR PROLAPSE DEVELOPMENT IN WHITE, BLACK, AND HISPANIC WOMEN

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Abstract

Objectives—To examine risk factors for prevalence and incidence of pelvic organ prolapse (POP) in whites, Hispanics, and blacks.

Methods—This is a secondary analysis of the Women's Health Initiative (WHI) Estrogen plus Progestin Clinical Trial. Out of the original E+P trial population of 16,608, 12,667 (78.3%) women (11,194 Whites, 804 Blacks, 669 Hispanics) were included in the final study sample and evaluated over the 5 year period. The outcomes evaluated were any prolapse (WHI Prolapse Grades 1–3) and WHI Prolapse Grades 2 or 3. Descriptive analyses, logistic regression and proportional hazard modeling were performed.

Results—Increasing parity correlates with increasing WHI Prolapse Grades (0–3) in Whites and Blacks but not Hispanics. The incidence of Grade 2/3 POP increased by 250% in white women with one child (HR 2.50, 1.68–3.71) in comparison to nulliparous women and grew with higher parity. For Blacks, a weak association between the parity and Grade 2/3 POP was noted only in women who had 5 or more kids (HR 10.41, 1.38–78.77). Blacks were less likely (HR 0.53, 0.40–0.71) to develop Grade 2/3 POP compared to whites. For Grade 2/3 POP, age was found to be a

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Presented at the 30th Annual Scientific Meeting of American Urogynecologic Society, September 24–26, 2009, Hollywood, Florida.

risk factor in whites (OR 1.03, 1.02–1.04) only and BMI ($\geq 25\text{kg/m}^2$, $<30\text{kg/m}^2$) in whites (OR 1.64, 1.34–2.02) and Hispanics (OR 2.87, 1.03–2.02).

Conclusions—White women are at a much greater risk for developing Grade 2/3 POP compared to blacks. Parity correlates most strongly with the risk of prolapsed development in whites and possibly in grand multiparous blacks.

Keywords

prolapse incidence; prolapse development; parity; race; ethnicity

Introduction

Pelvic organ prolapse (POP) affects up to 50% of women in the United States¹ and varies widely among different ethnic populations, with ranges from 30 to 93%.² These variations are a reflection of the differences in the definition of prolapse, examination techniques, diagnostic criteria and population characteristics. According to the US National Center for Health Statistics, POP is one of the three most common reasons for hysterectomy, with white women having the highest number of POP surgeries. Based on the 2003 US National Hospital Discharge Survey, white women undergo an average of 14.8 prolapse-related surgical procedures per 10,000 women, which is almost three times that of black women and almost double that of other races.³

Despite recent literature on this topic, both the epidemiology and pathogenesis of POP are not well understood. In particular, there are limited data evaluating risk factors for POP in racial groups. Most information is restricted to either surveys or cross-sectional studies. In one such cross-sectional study, the Women's Health Initiative (WHI) Hormone Therapy (HT) clinical trials, African American women had a lower rate of uterine prolapse, cystocele, and rectocele compared with white women (OR 0.63, 95% CI 0.50–0.79).¹ In another population-based study, Rortveit et al. noted that symptomatic prolapse was twice as high in white as compared to black women.⁴ In addition to race, other risk factors have been associated with pelvic organ prolapse,^{1, 5} including age, parity, body mass index (BMI), estrogen status, and history of hysterectomy.^{6, 7} While there is a paucity of literature on the natural history of prolapse in general, even less is known about prolapse and race. Therefore, examining the relative role of risk factors for POP in various racial groups is of critical importance. The WHI HT clinical trial offers a unique opportunity to examine risk factors for prevalence and incidence of pelvic organ prolapse (POP) in whites, Hispanics, and blacks.

Materials and Methods

This secondary analysis was approved by the Human Subjects Review Committee of the Medstar Research Institute, Washington, DC. All postmenopausal women (with a uterus) enrolled in the WHI Estrogen plus Progestin (E+P) Clinical Trial⁸ between 1993 and 1998 were included in the study. This was a randomized, double-blinded trial of the effects of E+P on coronary heart disease, fractures, and malignancies in postmenopausal women, ages 50 to 79. Sixteen percent of the study participants were from ethnic minority groups.⁹ At

baseline, women completed screening and enrollment questionnaires by interview and self-report, a physical examination, and blood specimen collection.

Information obtained at baseline included age, age at last delivery, race/ethnicity, education, occupation, overall quality of life, chronic medical morbidities, time since menopause, parity, duration of prior hormone use, hysterectomy status, constipation, current and past smoking, and physical activity. Route of childbirth (vaginal or cesarean) was not recorded. As part of the baseline physical examination, weight (kg), height (cm), and waist and hip circumferences (cm), and findings from a pelvic examination were recorded.

A baseline pelvic examination of the woman in the supine lithotomy position with/without valsalva was performed using standardized procedures by a gynecologist, experienced nurse, or physician assistant performed the pelvic examination (<http://whiscience.org/about/collection.php>). The pelvic examination included an assessment of uterine prolapse, cystocele, and rectocele using the WHI Prolapse Classification System (grades: 0, no prolapse; 1, prolapse in vagina; 2, prolapse to introitus; and 3, prolapse outside vagina). Centralized training of the personnel provided a review of the examination procedure, the definitions of prolapse, and how to record the results on standardized forms. A WHI clinic gynecologist certified and oversaw all midlevel providers to ensure proper performance of the examination. Annual pelvic evaluation was performed along with follow-up standardized physical examinations, with each participant having between 1 and 10 visits.

Descriptive analyses were performed and recorded in the form of frequencies and corresponding percentages by racial category (white, black, Hispanic, American Indian, Asian). Waist circumference was dichotomized based on the cutoff point of 88cm; this cutoff has been shown to correctly identify 88.5% of women who are obese and to be a risk factor for hypertension.^{10, 11} Explanatory variables found to be statistically ($p<0.1$) and clinically significant from logistic regression modeling in our previously published study¹² on the same WHI E+P Clinical Trial cohort were included as adjustment covariates in logistic regression modeling for each ethnic category at baseline to examine risk factors for the prevalence of prolapse. The outcomes evaluated were any prolapse (WHI Prolapse Grades 1–3) and WHI Prolapse Grades 2 or 3. Finally, we used a series of proportional hazard models to examine the risk of development (incidence) of any prolapse and Grade 2/3 prolapse over the 5-year period in women without prolapse at baseline for each racial/ethnic category. We excluded any ethnic category from these analyses with too low study participant numbers, less than 5% of the final sample size, to provide any meaningful conclusions. Of note, the impact of the E+P therapy was not one of the secondary outcomes; the placebo group that did not receive the E+P therapy was used as a reference group in the analyses.

Missing data were treated in the following manner. At baseline all participants had known prolapse data. At year 5, the numbers were reduced to 5,375 for uterine prolapse, 6,401 for cystocele, and 6,380 for rectocele. For the purposes of this manuscript, all participants with missing covariate data ($n=3589$) were excluded from all analyses, leaving a final sample of 12,667 with Asian ($N=318$) and American Indian ($N=39$) women being excluded because of a small sample size. Participants who were still alive at a given time point but missing

prolapse data were classified based on their previous examination for the hazard models. Thus, out of the original E+P trial population of 16,608, 12,667 (78.3%) women were included in our final study sample.

All statistical analyses were completed with SAS 9.1 (SAS Institute, Cary, NC).

Results

Over the 5-year time period, trends in prolapse progression and regression are shown in Figures 1A–1C for whites, blacks, and Hispanics. Specifically, 881 out of 5,442 (16.2%) white women without prolapse at baseline developed WHI Prolapse Grades 1–3 (Figure 1A); 41 out of 436 (9.4%) black women without prolapse at baseline developed POP (Figure 1B); and 65 out of 323 (20.1%) Hispanic women without prolapse at baseline developed POP (Figure 1C). The incidence of new Grade 2/3 prolapse in the three racial/ethnic groups is presented in Table 1.

Baseline demographic and clinical data, including prevalence of cystocele, rectocele, and uterine prolapse, for these women, self-assigned to the five ethnic categories, are presented in Table 2. More complete analysis of baseline characteristics of the WHI E+P participants has been published previously.⁹ The black and Hispanic groups were younger and had more participants who were less than 60 years old (47% and 54.7%) compared to whites (30.1%). The vast majority of participants had 2 or more children.

The associations between prolapse (WHI grades 1 through 3) prevalence and potential covariates were examined within each ethnic category at baseline. While increasing parity was found to be a risk factor for any POP in all racial groups (p-trend <0.03), this factor appeared to most strongly correlate with Grade 2/3 POP in whites. Specifically, in white participants one delivery was associated with a 2-fold increase in the risk of any POP (Grade 1–3) compared to nulliparous women with an almost linear increase in the risk of POP with each higher order of pregnancies. In a subanalysis of WHI Grade 2/3 POP, this trend was even more dramatic (one delivery: OR 4.7 to 5 deliveries: OR 10.04) (Table 3). Age was a weak correlate (OR 1.01–1.03 per 1 year increase) for any POP in all groups. BMI (<25kg/m², ≥30kg/m²) was found to be a risk factor in whites and trended toward significance in Hispanics. WC ≥88cm correlated with an increase in the risk for any POP in whites only. In whites, urge (OR 1.47, 1.21–1.79) and mixed (OR 1.27, 1.01–1.60) urinary incontinence were associated with any prolapse as well as Grade 2, 3 POP while stress urinary incontinence was associated with any prolapse, but not Grade 2/3 POP.

Subsequently, we constructed two proportional hazard models to evaluate predictors of the rate of any prolapse and WHI Grade 2/3 Prolapse development (POP incidence) in each of the three racial/ethnic groups (whites, blacks, and Hispanics). Within our sample, black women were significantly less likely (HR 0.70 (0.60–0.81) to develop Grade 2/3 POP in comparison to white women (Table 4). The Kaplan-Meier estimates of cumulative hazards for any prolapse and Grade 2/3 POP indicate that the difference in POP incidence between the racial groups persists beyond the 5-year period (Figure 2A and 2B) with black women

having the least cumulative hazard for any or Grade 2/3 POP over time in comparison to other racial groups.

Finally, to examine the risk factors for any and WHI Grades 2/3 prolapse development within each racial group, we constructed two other models. Findings are presented for Grade 2/3 POP because it has been shown that prolapse to or beyond the (level of the) hymen is often symptomatic and may necessitate intervention (Table 5).^{13, 14} The incidence of Grade 2/3 POP in white women was increased by 250% in those who had one child (HR 2.50, 1.68–3.71) compared to nulliparous women and continued to increase with each additional delivery. A similar trend with respect to parity was not observed for black women. There were an insufficient number of cases within each parity subgroup to evaluate such associations within the Hispanic group (Table 1). With respect to being overweight or obese, the incidence of Grade 2/3 POP increased by 25% in white women only. Additionally, the incidence of Grade 2/3 POP was increased by 17% in whites only who were randomized to estrogen and progestin compared to placebo. These associations were not observed for either past or current hormone users.

When we evaluated the risk factors for the incidence of WHI Prolapse Grade 3 (prolapse outside vagina) compared to Grades 0–2 (prolapse inside vagina or at the introitus), parity remained to be a risk factor in white participants: compared to nulliparas, a linear increase in hazard ratios from 2.32 for primiparas to 9.4 for quintiparas and women of higher order parity ($p < 0.0001$) was noted. However, we are unable to comment on the association of parity and Grade 3 prolapse in Blacks and Hispanics due to insufficient numbers of participants with Grade 3 prolapse in each parity subgroup in these three racial/ethnic groups. The E+P treatment assignment did not impact the incidence of Grade 3 prolapse in white, black, or Hispanic participants.

Discussion

The key findings of this study are that white women are at a much greater risk for developing WHI Grades 2/3 Prolapse in comparison to blacks. We were unable to fully examine associations with prolapse in Hispanics because of the limited sample size. Increasing parity appears to most strongly correlate with the risk of POP in whites. Parity is a risk factor for having prolapse (POP prevalence) in whites only and for developing prolapse (POP incidence) in whites and possibly in grand multiparous blacks. The incidence of WHI Grades 2/3 Prolapse in white women was increased by 250% in those who had one child (HR 2.50, 1.68–3.71) compared to nulliparous participants and continued to rise with increasing parity. Additionally, black women had the least cumulative hazard for developing Grade 2/3 POP over time in comparison to other racial groups after adjusting for parity. These findings may suggest that the currently accepted notion of the first delivery carrying the greatest risk for POP development appears to be primarily driven by the risk of such an event in white women rather than in other racial groups. However, because the study was performed using the data collected on postmenopausal women, our findings should be confirmed for women younger than 50 years of age.

A recent study by Handa et al. revealed that white women have a wider pelvic inlet/outlet, shallower anteroposterior outlet and less pelvic floor mobility after vaginal delivery compared to African-American women, which may contribute to observed racial differences in obstetric outcomes and in the development of pelvic floor disorders.¹⁵ These findings support our study's epidemiologic observations and suggest that the pelvic bony morphology might play a role in the mechanism of pelvic floor dysfunction.

Our study adds important information to the existing literature on the risk of POP among various racial groups. The possible etiologic role of racial/ethnic differences is a major epidemiologic question in the area of pelvic floor disorders. Previous studies have shown that white women are at a higher risk for POP than black women^{1, 4} as supported by the distribution of POP surgery by race.³ In a cross-sectional study of women who enrolled in the WHI HT clinical trials, African American women had lower rates of uterine prolapse, cystocele, and rectocele compared with white women (OR 0.63, 95% CI 0.50–0.79).¹ Another population-based study of 2001 randomly selected women at Kaiser by Rortveit et al revealed African-American women were significantly less likely to report symptomatic prolapse compared with white women (OR 0.4, 95% CI 0.2–0.8).⁴ However, other studies have not confirmed these findings.^{16–18} The POSST study revealed a strong association between an increased risk for POP in the Hispanic participants (OR 4.29, 1.80–10.2) in comparison to whites on multivariate logistic regression analysis. Furthermore, Bump et al. found that the prevalence of severe prolapse was the same for blacks and whites in the analyzed referral population, although black women had significantly more vaginal deliveries.¹⁸ Hence, some studies suggest that being white and Hispanic may predispose to having (symptomatic) pelvic organ prolapse in comparison to blacks ^{1, 7, 17, 19} while others do not.¹⁸

A similar controversy regarding the role of racial background is found for lower urinary tract dysfunction. Graham and Mallett demonstrated that being white was the most significant predictor of stress urinary incontinence (OR 2.21, 95% CI 1.31–3.73).⁵ More recently, in a subanalysis of the Reproductive Risks for Incontinence Study, Thom et al. showed that, compared to white nonHispanic women, black women were less likely to have incontinence progression (OR 0.46, 95% CI 0.24–0.88).²⁰ Similarly, in the Nurse's Health study, Grodstein et al found that black and Hispanic women were at much lower risk for urinary leakage (OR 0.54, 0.43–0.67 and OR 0.67, 0.49–0.91) in comparison to white women.²¹

Unfortunately, with the exception of POSST study (424 white, 242 black, 289 Hispanic and 31 other)¹⁷ and a subanalysis of the Reproductive Risks for Incontinence Study (569 white, 209 black, 159 Asian, and 199 other, including Hispanics),⁷ the vast majority of studies on pelvic floor dysfunction, including the Nurse's Health study (10675 white, 97 black, 50 Hispanic, 79 Asian)²¹ are underpowered to make any reproducible, meaningful conclusions about the role of racial/ethnic background in the prevalence of pelvic floor disorders as these studies contain a very small percentage of other than white participants.

While the primary aim of this study was not to evaluate estrogen or progestin effect on POP, the finding that the incidence of WHI POP Grade 2/3 was increased by 17% in whites only,

who were randomized to estrogen and progestin compared to placebo, is interesting (Table 5). We can hypothesize that progestin might promote soft tissue relaxation, resulting in more cases of Grade 2/3 POP in this ethnic group. However, this finding cannot be explained with any certainty, especially since this effect was not found in white women with Grade 3 prolapse only. Though, the latter finding might be due to low numbers of white women with Grade 3 prolapse compared to women with Grades 0–2.

The important strengths to this study include a large sample size and prospectively collected data from multiple centers, allowing for longitudinal observations, which were performed in a standardized fashion. Finally, the proportion of racial/ethnic minority participants was higher than in most studies and thus afforded an opportunity to make comparisons among races undergoing identical protocols.

Limitations of our study are that the WHI E+P Trial was designed primarily to examine the effects of hormone therapy on incidence and death from coronary heart disease in women, many of whom were more than 10 years postmenopausal, and not to evaluate the risk of POP among racial/ethnic groups. Hence, the measure (WHI Prolapse Classification) chosen to quantify the prolapse might not have been optimal (more simplistic) as compared with the Pelvic Organ Prolapse Quantification system. Additionally, although the prolapse assessment was done during Valsalva maneuver, the participants were in a supine position rather than in a birthing chair at a 45 degree angle or standing that allows for a significantly higher detection of stage 2 or greater prolapse, which is frequently found to be symptomatic. This report may underestimate the effect of vaginal delivery on prolapse because the study questionnaires did not capture the type of delivery. Additionally, the samples of black and Hispanic women are likely not representative of the African American and Hispanic women in the US of this age group. The racial/ethnic status of study participants was assigned by self-report; thus, possibly decreasing the number of ethnic minorities in the study and making the associations less pronounced. We are also unable to comment on possibly different risk factors for prolapse in white versus non-white Hispanic participants. Furthermore, the information that was collected on any surgical procedures performed to correct POP at baseline and throughout the WHI study period was limited by the participant's response rate on the study forms. This factor might have allowed for underestimation of the rate of prolapsed and might have possibly contributed to a less accurate picture. Finally, our findings are restricted to women with a uterus and might not apply to women with prior hysterectomy.

In conclusion, our data indicate that the assumption that the findings derived mainly from the white population are applicable to other racial/ethnic groups should be questioned. We believe that understanding racial and ethnic differences in pelvic bony architecture and morphology, pelvic muscle and connective tissue properties may provide clues to the pathophysiology of POP. Large prospective studies, specifically designed to target certain racial/ethnic groups as well as to evaluate the differential effect of risk factors for pelvic floor dysfunction (PFD) within various racial/ethnic groups, are imperative for risk stratification, effective patient counseling and possibly treatment.

Acknowledgements

The WHI program is funded by the National Heart, Lung, and Blood Institute, National Institutes of Health, U.S. Department of Health and Human Services through contracts N01WH22110, 24152, 32100-2, 32105-6, 32108-9, 32111-13, 32115, 32118-32119, 32122, 42107-26, 42129-32, and 44221.

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1A

1B

1C

Figure 1.

A, WHI grades 0 to 3 prolapse dynamic during the 5-year period in white participants. B, WHI grades 0 to 3 prolapse dynamic during the 5-year period in black participants. C, WHI grades 0 to 3 prolapse dynamic during the 5-year period in Hispanic participants.

2A

2B

Figure 2.

A, Kaplan-Meier estimates of cumulative hazards for WHI grades 1 to 3 prolapse in white, black, and Hispanic participants during the 9-study observational period. “0” years on the x axis (Time) refer to baseline evaluation. B, Kaplan-Meier estimates of cumulative hazards for WHI grade 2 or 3 prolapse in white, black, and Hispanic participants during the 5-year study observational period. “0” years on the x axis (Time) refer to baseline evaluation.

Figure 2A:

* Kaplan-Meier estimates of cumulative hazards for WHI Grade 1–3 Prolapse in white, black, and Hispanic participants over the 9-study observational period

* “0” years on the x -axis (Time) refer to baseline evaluation

Figure 2B:

5* Kaplan-Meier estimates of cumulative hazards for WHI Grade 2/3 Prolapse in white, black, and Hispanic participants over the 5-year study observational period

* “0” years on the x -axis (Time) refer to baseline evaluation

Table 1

Incidence of New WHI Grade 2 or 3 Prolapse by Ethnicity

	Year 1	Year 2	Year 3	Year 4	Year 5
Ethnicity	n / N*	n / N*	n / N*	n / N*	n / N*
White	353 / 8557	275 / 7600	219 / 7454	227 / 6727	172 / 4622
Black	18 / 617	11 / 539	11 / 525	4 / 476	3 / 317
Hispanic	20 / 496	10 / 452	8 / 442	9 / 404	13 / 272

n = participants reporting WHI Grade 2 or 3 prolapse for the first time

N = evaluable participants with prolapse data at the given time point and no history of WHI Grade 2 or 3 prolapse

Table 2

Baseline demographics and health characteristics by racial/ethnic groups

Baseline Characteristic	Ethnicity											
	White (11,194)		Black (804)		Hispanic (669)		Am. Indian (39)		Asian (318)			
	N	%	N	%	N	%	N	%	N	%	N	%
Age												
<50–59	3366	30.1	378	47.0	366	54.7	14	35.9	118	37.1		
60–69	5182	46.3	325	40.4	245	36.6	17	43.6	129	40.6		
70–79+	2646	23.6	101	12.6	58	8.7	8	20.5	71	22.3		
Parity												
Never pregnant	875	7.8	45	5.6	44	6.6	3	7.7	33	10.4		
Never had term pregnancy	240	2.1	44	5.5	16	2.4	0	0.0	4	1.3		
1	848	7.6	113	14.1	60	9.0	5	12.8	27	8.5		
2	2483	22.2	190	23.6	137	20.5	6	15.4	83	26.1		
3	2757	24.6	162	20.1	132	19.7	4	10.3	78	24.5		
4	1974	17.6	88	10.9	121	18.1	6	15.4	45	14.2		
5+	2017	18.0	162	20.1	159	23.8	15	38.5	48	15.1		
Waist circumference												
88 cm												
No	6411	57.3	354	44.0	369	55.2	17	43.6	265	83.3		
Yes	4783	42.7	450	56.0	300	44.8	22	56.4	53	16.7		
Smoking												
Never smoked	5448	48.7	376	46.8	436	65.2	19	48.7	206	64.8		
Past smoker	4612	41.2	303	37.7	181	27.1	12	30.8	88	27.7		
Current smoker	1134	10.1	125	15.5	52	7.8	8	20.5	24	7.5		
Total hormone usage												
Never used	8240	73.6	632	78.6	508	75.9	31	79.5	232	73.0		
Past user	2250	20.1	127	15.8	115	17.2	6	15.4	55	17.3		

Baseline Characteristic	Ethnicity											
	White (11,194)			Black (804)			Hispanic (669)			Am. Indian (39)		
	N	%	N	N	%	N	N	%	N	N	%	N
Current user	701	6.3	44	5.5	45	6.7	2	5.1	31	9.7		
Constipation												
No	10458	93.4	722	89.8	564	84.3	36	92.3	298	93.7		
Yes	736	6.6	82	10.2	105	15.7	3	7.7	20	6.3		
Any urinary incontinence												
No	3004	26.8	402	50.0	254	38.0	11	28.2	147	46.2		
Yes	8190	73.2	402	50.0	415	62.0	28	71.8	171	53.8		
Cystocele												
Grade 0	7355	65.7	584	72.6	389	58.1	28	71.8	163	51.3		
Grade 1	3249	29.0	180	22.4	236	35.3	11	28.2	101	31.8		
Grade 2	551	4.9	37	4.6	41	6.1	0	0.0	54	17.0		
Grade 3	39	0.3	3	0.4	3	0.4	0	0.0	0	0.0		
Rectocele												
Grade 0	9020	80.6	697	86.7	531	79.4	36	92.3	241	75.8		
Grade 1	1846	16.5	99	12.3	122	18.2	1	2.6	63	19.8		
Grade 2	309	2.8	8	1.0	15	2.2	2	5.1	13	4.1		
Grade 3	19	0.2	0	0.0	1	0.1	0	0.0	1	0.3		
Uterine Prolapse												
Grade 0	9413	84.1	706	87.8	533	79.7	37	94.9	276	86.8		
Grade 1	1654	14.8	87	10.8	125	18.7	2	5.1	40	12.6		
Grade 2	106	0.9	8	1.0	10	1.5	0	0.0	2	0.6		
Grade 3	21	0.2	3	0.4	1	0.1	0	0.0	0	0.0		

* p-value for all category comparisons by Chi-Square tests is <0.01

Table 3
Predictors of having (prevalence) WHI Prolapse Grade 2 or 3 in whites, blacks, and Hispanics

Baseline Characteristic	White			Black			Hispanic		
	OR*	95% CI	p-value	OR*	95% CI	p-value	OR*	95% CI	p-value
Age	1.03	(1.02, 1.04)	<.0001	1.01	(0.97, 1.06)	0.66	1.02	(0.98, 1.07)	0.38
Parity (vs. Never had a term pregnancy)			<.0001			0.10			0.11
1	4.70	(2.56, 8.63)		0.98	(0.21, 4.64)		2.00	(0.36, 11.05)	
2	5.74	(3.31, 9.97)		1.61	(0.43, 6.03)		2.07	(0.43, 10.05)	
3	6.27	(3.63, 10.84)		1.21	(0.30, 4.89)		1.07	(0.20, 5.65)	
4	7.63	(4.40, 13.22)		1.08	(0.21, 5.64)		2.67	(0.56, 12.75)	
5+	10.04	(5.82, 17.32)		3.39	(0.93, 12.30)		3.52	(0.78, 15.92)	
Smoking (vs. Never smoked)			<.0001			0.50			0.51
Past smoker	0.76	(0.65, 0.88)		0.70	(0.35, 1.38)		1.28	(0.68, 2.43)	
Current smoker	0.60	(0.44, 0.81)		0.66	(0.23, 1.84)		1.75	(0.60, 5.06)	
Moderate/Severe constipation	0.83	(0.62, 1.11)	0.20	1.73	(0.68, 4.43)	0.27	0.62	(0.25, 1.53)	0.28
Asthma	1.10	(0.83, 1.47)	0.51	1.95	(0.69, 5.47)	0.23	1.63	(0.65, 4.05)	0.31
Emphysema	1.15	(0.77, 1.71)	0.50	-	-	0.04	1.60	(0.32, 8.11)	0.59
Total hormone usage (vs. Never used)			0.36			0.42			0.45
Past user	0.89	(0.74, 1.07)		0.91	(0.37, 2.28)		0.95	(0.45, 2.02)	
Current user	0.88	(0.63, 1.23)		2.22	(0.71, 6.96)		0.41	(0.09, 1.89)	
Incontinence (vs. Never)			<.0001			0.52			0.27
Stress	0.97	(0.79, 1.20)		0.91	(0.32, 2.58)		1.83	(0.93, 3.62)	
Urge	1.47	(1.21, 1.79)		1.27	(0.59, 2.73)		1.22	(0.53, 2.83)	
Mixed	1.27	(1.01, 1.60)		2.12	(0.65, 6.85)		0.76	(0.21, 2.76)	
Other	1.38	(0.99, 1.93)		2.34	(0.73, 7.52)		2.46	(0.71, 8.51)	
Waist circumference > 88 cm	1.19	(0.98, 1.45)	0.08	1.81	(0.75, 4.40)	0.19	1.60	(0.75, 3.39)	0.22

Baseline Characteristic	White			Black			Hispanic		
	OR*	95% CI	p-value	OR*	95% CI	p-value	OR*	95% CI	p-value
Physical activity	0.97	(0.92, 1.03)	0.36	1.12	(0.89, 1.41)	0.34	1.18	(0.96, 1.45)	0.13
BMI (vs. <25 kg/m ²)			<.0001			0.10			0.09
25-<30 kg/m ²	1.64	(1.34, 2.02)		0.72	(0.29, 1.79)		2.87	(1.03, 8.05)	
30 kg/m ²	1.87	(1.44, 2.43)		0.32	(0.10, 1.02)		2.22	(0.67, 7.33)	

* multi-variable adjusted OR from multi-variate logistic regression analysis

* predictors and outcome measured at baseline

Table 4

Results of Proportional Hazards Model With all Ethnicities

Baseline Characteristic	Any Prolapse			WHI Prolapse Grade 2/3		
	HR*	95% CI	p-value	HR*	95% CI	p-value
Ethnicity (vs. White)			<.0001			<.0001
Black	0.70	(0.60, 0.81)		0.53	(0.40, 0.71)	
Hispanic	1.10	(0.94, 1.29)		0.88	(0.69, 1.12)	
Age	1.00	(1.00, 1.01)	0.11	1.01	(1.00, 1.02)	0.002
Parity (vs. Never had a term pregnancy)			<.0001			<.0001
1	1.20	(1.03, 1.40)		2.44	(1.66, 3.60)	
2	1.43	(1.26, 1.61)		3.49	(2.51, 4.87)	
3	1.53	(1.36, 1.72)		3.91	(2.82, 5.42)	
4	1.60	(1.40, 1.81)		5.09	(3.66, 7.08)	
5+	1.70	(1.49, 1.93)		5.87	(4.24, 8.14)	
Smoking (vs. Never smoked)			<.0001			<.0001
Past smoker	0.87	(0.81, 0.93)		0.75	(0.67, 0.84)	
Current smoker	0.78	(0.69, 0.87)		0.52	(0.42, 0.66)	
Moderate/Severe constipation	1.00	(0.88, 1.14)	0.94	0.99	(0.81, 1.21)	0.91
Asthma	1.16	(1.01, 1.32)	0.03	0.97	(0.78, 1.21)	0.81
Emphysema	1.10	(0.91, 1.32)	0.33	1.20	(0.89, 1.62)	0.23
Total hormone usage (vs. Never used)			0.37			0.14
Past user	1.02	(0.94, 1.10)		1.09	(0.95, 1.24)	
Current user	0.91	(0.80, 1.05)		1.20	(0.97, 1.49)	
E-P Treatment (vs. Placebo)	1.07	(1.00, 1.14)	0.04	1.14	(1.03, 1.27)	0.01
Incontinence (vs. Never)			0.0007			0.00
Stress	1.17	(1.07, 1.28)		1.11	(0.96, 1.29)	
Urge	1.18	(1.08, 1.29)		1.32	(1.14, 1.53)	

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Baseline Characteristic	Any Prolapse			WHI Prolapse Grade 2/3		
	HR*	95% CI	p-value	HR*	95% CI	p-value
Mixed	1.17	(1.05, 1.31)		1.23	(1.03, 1.46)	
Other	1.22	(1.05, 1.42)		1.04	(0.80, 1.36)	
Waist circumference > 88 cm	1.10	(1.00, 1.21)	0.06	1.21	(1.04, 1.41)	0.01
Physical activity	1.00	(0.97, 1.02)	0.76	0.99	(0.95, 1.03)	0.55
BMI (vs. <25 kg/m ²)			0.06			0.01
25<30 kg/m ²	1.07	(0.99, 1.17)		1.25	(1.08, 1.44)	
30 kg/m ²	1.16	(1.02, 1.30)		1.27	(1.05, 1.54)	

* multi-variable adjusted Hazard Ratios

Table 5
Results of Proportional Hazards Model for WHI Prolapse Grade 2 or 3 in Whites, Blacks, and Hispanics

Baseline Characteristic	White N=11,185			Black N=800			Hispanic N=665		
	HR*	95% CI	p-value	HR*	95% CI	p-value	HR*	95% CI	p-value
Age	1.01	(1.00, 1.02)	0.01	1.05	(1.01, 1.09)	0.03	1.05	(1.01, 1.09)	0.17
Parity (vs. Never had a term pregnancy)			<.0001			0.008			0.004
1	2.50	(1.68, 3.71)		0.77	(0.05, 12.40)		-	-	
2	3.31	(2.36, 4.63)		4.35	(0.56, 33.97)		-	-	
3	3.75	(2.69, 5.23)		3.86	(0.48, 30.77)		-	-	
4	4.86	(3.48, 6.80)		6.12	(0.75, 50.21)		-	-	
5+	5.29	(3.79, 7.38)		10.41	(1.38, 78.77)		-	-	
Smoking (vs. Never smoked)			<.0001			0.06			0.33
Past smoker	0.74	(0.66, 0.83)		0.48	(0.25, 0.92)		1.33	(0.79, 2.24)	
Current smoker	0.52	(0.41, 0.66)		0.48	(0.16, 1.44)		0.50	(0.12, 2.15)	
Moderate/Severe constipation	1.04	(0.84, 1.29)	0.70	0.99	(0.38, 2.55)	0.98	0.50	(0.22, 1.11)	0.09
Asthma	0.95	(0.75, 1.20)	0.68	2.16	(0.91, 5.14)	0.08	0.62	(0.19, 2.06)	0.43
Emphysema	1.18	(0.86, 1.62)	0.31	1.44	(0.40, 5.13)	0.58	1.27	(0.29, 5.66)	0.75
Total hormone usage (vs. Never used)			0.33			0.06			0.77
Past user	1.06	(0.93, 1.21)		1.37	(0.67, 2.82)		1.23	(0.68, 2.22)	
Current user	1.17	(0.93, 1.46)		3.33	(1.22, 9.06)		0.92	(0.33, 2.59)	
E+P Treatment (vs. Placebo)	1.17	(1.05, 1.30)	0.005	1.02	(0.58, 1.80)	0.95	0.74	(0.45, 1.20)	0.22
Incontinence (vs. Never)			0.002			0.99			0.78
Stress	1.15	(0.98, 1.34)		0.91	(0.39, 2.12)		0.73	(0.39, 1.36)	
Urge	1.36	(1.17, 1.59)		0.94	(0.49, 1.82)		1.07	(0.56, 2.03)	
Mixed	1.27	(1.06, 1.52)		0.71	(0.17, 3.09)		0.96	(0.41, 2.24)	
Other	1.09	(0.82, 1.43)		-	-		1.33	(0.40, 4.48)	
Waist circumference	1.24	(1.06, 1.45)	0.007	0.67	(0.31, 1.44)	0.30	1.02	(0.48, 2.16)	0.96

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Baseline Characteristic	White N=11,185			Black N=800			Hispanic N=665		
	HR *	95% CI	p-value	HR *	95% CI	p-value	HR *	95% CI	p-value
> 88 cm									
Physical activity	0.99	(0.94, 1.03)	0.53	1.01	(0.80, 1.27)	0.92	1.07	(0.88, 1.31)	0.50
BMI (vs. <25 kg/m ²)			0.01			0.29			0.3909
25-<30 kg/m ²	1.25	(1.08, 1.46)		1.23	(0.47, 3.24)		1.13	(0.53, 2.42)	
30 kg/m ²	1.23	(1.00, 1.50)		2.12	(0.73, 6.19)		1.82	(0.70, 4.73)	

* multi-variable adjusted HR