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## Prevalence, incidence and natural history of simple ovarian cysts among women over age 55 in a large cancer screening trial

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### Abstract

**Objective**—To measure the occurrence and natural history of simple ovarian cysts in a cohort of older women.

**Study Design**—Simple cysts were ascertained among a cohort of 15,735 women from the intervention arm of the Prostate, Lung, Colorectal and Ovarian (PLCO) Cancer Screening Trial, through 4 years of transvaginal ultrasound screening.

**Results**—Simple cysts were seen in 14% of women the first time their ovaries were visualized. The one-year incidence of new simple cysts was 8%. Among ovaries with one simple cyst at the first

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Preliminary results of this study were presented in abstract form at the 2008 annual meeting of the American Society of Clinical Oncology, May 31-June 3, 2008, in Chicago, IL.

screen, 54% retained one simple cyst, and 32% had no cyst one year later. Simple cysts did not increase risk of subsequent invasive ovarian cancer.

**Conclusions**—Simple ovarian cysts are fairly common among post-menopausal women, and most appear stable or resolve by the next annual exam. These findings support recent recommendations to follow unilocular simple cysts in post-menopausal women without intervention.

### Keywords

ovarian cancer; ovarian cysts; transvaginal ultrasound

## INTRODUCTION

With frequent use of transvaginal ultrasound (TVU), clinicians are detecting many simple ovarian cysts among post-menopausal women. Because the natural history of simple ovarian cysts is not fully understood, the proper management of incidental simple cysts in post-menopausal women has been uncertain.<sup>1</sup> Aggressive surgical approaches for simple cyst management have given way to recommendations for careful monitoring,<sup>2-5</sup> and some have raised the question of whether simple cysts need to be monitored at all.<sup>1</sup> We evaluated the prevalence, incidence, and natural history of simple cysts within a cohort of mostly post-menopausal women receiving serial TVU examinations in the intervention arm of the Prostate, Lung, Colorectal, and Ovarian (PLCO) Cancer Screening Trial.<sup>6</sup>

## METHODS

Prorok, et al. have previously described the design and methods of PLCO<sup>6</sup>, which is the setting and source population for this observational cohort analysis. Briefly, PLCO is a prospective evaluation of whether screening with a posterioranterior chest x-ray, flexible sigmoidoscopy, and CA-125 plus transvaginal ultrasound (TVU) can reduce mortality for lung, colon and ovarian cancers respectively in women. Comparable questions are being investigated for lung, colon, and prostate cancer among men. Women were eligible if they were between ages 55 and 74, and had no previous lung, colon or ovarian cancer diagnosis. Women receiving cancer treatment or participating in another screening or prevention trial were not eligible. Women who had undergone prior oophorectomy were excluded from ovarian cancer screening in the trial.

Recruitment occurred from November 1993 to July 2001. Women were randomly assigned either to the intervention or control arm after stratification by age, gender, and Screening Center (see appendix). Participants responded to a self-administered general risk factor questionnaire at entry.<sup>7</sup> Ovarian cancer screening in PLCO included a CA-125 blood test and TVU at baseline, an annual TVU for three additional years, and annual CA-125 tests for five years beyond baseline.<sup>6</sup> For TVU screening, qualified sonographers used a 5 to 7.5 MHz transvaginal probe to measure each ovary and describe any observed abnormalities. The examiner spent at least five minutes searching for each ovary, although the examiner could end the search if the iliac vessels were visualized and the ovaries were not observable. Ovaries were measured along major and minor axes of both transverse and longitudinal planes, and the prolate ellipsoid formula (width × height × thickness × 0.523) was used to calculate the volume of each ovary and/or cyst. Quality assurance procedures on a sample of participants included either repeating the screening examination, independent observation of the exam, or independent review of TVU films at a later time.

In the trial, the TVU screening examination was considered positive (abnormal and suspicious for ovarian cancer) when findings included: 1) ovarian volume greater than 10 cubic cm; 2) cyst volume greater than 10 cubic cm; 3) any solid area or papillary projection extending into

the cavity of a cystic ovarian tumor of any size; or, 4) any mixed (solid/cystic) component within a cystic ovarian tumor. As part of the trial protocol, women with positive screening exams were referred to regular medical care for follow-up investigation. Ovarian cysts with volume less than 10 cubic cm and no solid areas, septae, or papillary projections noted in the cyst cavity, were not considered a positive screening exam in the trial. These simple cysts are, however, the subject of this cohort analysis. Ovarian cancers were ascertained in PLCO through review of medical records and pathology reports following a positive screen or a report of cancer on annual study surveys.<sup>6</sup>

### Statistical Analysis

This analysis is based on the subset of intervention arm women with both ovaries visualized one or more times during TVU screenings. As in a previous PLCO report, women were classified by the most serious abnormality present.<sup>8</sup> Prevalence was the proportion of women having a simple cyst discovered at the screening in which both ovaries were visualized for the first time (prevalent cyst). Most of these were discovered during the baseline screen, but for some women, the first informative screen was in a later round. A one-year incidence rate was the proportion of women who developed a new simple cyst in their second screen with visualized ovaries, after no cysts had been discovered one year before in their first screen with visualized ovaries (incident cyst).

Descriptive evaluation of the natural history of simple cysts was performed by examining the status of all ovaries visualized in 2 consecutive study years (baseline to year 1, year 1 to year 2, or year 2 to year 3). For this particular analysis, each ovary was counted as a separate unit of evaluation. One year change in CA125 levels were compared, in an analysis of variance, between women with simple cysts who had more extensive findings (increased number or complexity) one year later and those who did not. Chi-square or Fisher's exact test, and multivariable logistic regression, were used to evaluate the potential association between detection of simple cysts and subsequent discovery of invasive ovarian cancer, through year 7 after baseline.

Chi-square analysis evaluated possible correlates of simple ovarian cyst occurrence, comparing women with prevalent or incident simple cysts to women without detected cysts at the corresponding screen. The primary objective of this analysis was to evaluate whether known or potential ovarian cancer risk factors correlate with simple cyst occurrence, based on the approach of Hartge.<sup>8</sup> Potential predictors in this analysis included age, education, smoking status, number of sisters, first degree family history of ovarian cancer and of breast cancer, number of pregnancies, parity, number of miscarriages, use and duration of oral contraceptives, age at first pregnancy, use of hormone replacement, regular use of non-steroidal anti-inflammatory drugs or aspirin, age at menarche, age at menopause, previous gynecologic surgery, body mass index, history of benign ovarian tumors or cysts, and history of infertility. Multivariable logistic regression models contained factors with P-values less than or equal to 0.2 from the chi-square analyses. All multivariable models also adjusted for race and Screening Center. For dichotomous variables, the 'no' category served as the referent, and for categorical variables, the referent was the most common category. P-values below 0.05 were considered statistically significant. The study was approved by the Marshfield Clinic Research Foundation Institutional Review Board.

## RESULTS

The trial enrolled 78,237 women and randomized 39,115 to the screening arm (Table 1). Of 4895 screening arm women not eligible for TVU, 4892 had prior oophorectomy, two had died, and one had ovarian cancer prior to the baseline screen. Of 34,220 eligible women, 30,389 (89%) received at least one exam. A total of 15,735 women had both ovaries visualized one

or more times during the study. About two-thirds of these women were enrolled between ages 55 and 64, 89% reported their race as Caucasian, and 94% indicated they had received at least a high school diploma (Table 2).

### Prevalence and Incidence of Simple Cysts

Among the 15,735 women, 2,217 (14.1%) had one or more simple cysts detected at their first fully visualized TVU screening (Table 3). In stratified analysis, prevalence varied by age ( $p=0.001$ ), with simple cyst detection slightly more common for women ages 55–59 (16%) than for women in older age groups (13%). Among women without a cyst of any kind on their first fully visualized screen, the rate of having a new simple cyst at the second screen one year later was 8.3% (Table 4). The incidence rate of new cyst development did not vary systematically with age, ranging across age groups from 7–9% ( $p=0.20$ ). When calculating a simple cyst incidence rate for each individual screening year of the trial, the results were 8.4% at year 1 after baseline, 7.4% from year 1 to year 2, and 7.3% from year 2 to year 3.

### Natural History of Simple Cysts

Among ovaries with a simple cyst at the first visualized screen, 79% had just one cyst, while 15% had two, and 7% had 3 or more. For ovaries with a single simple cyst, 54% retained a single simple cyst in the following year, while 32% no longer had a cyst present (Table 5). Regression to having no cysts at all was less common for ovaries containing 2 or more cysts (23%), although more than half of the time, ovaries with multiple simple cysts had a reduced number of simple cysts the following year.

About 8% of ovaries with a single simple cyst presented the following year with multiple simple cysts, and 6% had developed more complex cysts or solid masses. Ovaries that contained multiple simple cysts were somewhat more likely than ovaries with just one simple cyst to present with complex cysts or solid masses the following year (7% for 2 simple cysts, 11% for 3+ simple cysts). Development of complex cysts or solid masses over the course of a year was rare among ovaries starting with no cyst at all (1%). Average CA-125 level changes over the one-year period were not associated with an increase in the number of simple cysts or progression from simple to more complex cysts.

Women whose ultrasound showed one or more simple cysts at their first fully visualized screening were not at significantly increased risk of subsequently developing invasive ovarian cancer (9 of 2217, or 0.41%) compared to their counterparts with no cysts (55 of 12638, or 0.44%),  $p=0.85$ . Women with a new simple cyst at their second fully visualized screening had the same occurrence of subsequent invasive ovarian cancer (1 of 459, or 0.22%) as did women who had no simple cysts on two consecutive screens (11 of 4939, or 0.22%),  $p>0.99$ . Findings did not change upon multivariable analysis adjusting for ovarian cancer risk factors: OR (95% CI) comparing those with prevalent cysts to those without, 0.84 (0.41–1.73); comparing those with incident cysts to those without, 0.95 (0.12–7.46).

### Potential Correlates of Simple Cysts

In multivariable analysis, a modestly reduced risk of simple cysts at the prevalence screen was found in women age 60–64 (OR compared to women age 55–59 0.83, 0.73–0.94), current smokers (OR compared to never smokers 0.75, 0.61–0.91), and women with first pregnancy at age 25–29 (OR 0.85) or age 30+ (OR 0.71). Women with a college (OR 1.32, 1.14–1.53) or post graduate education (OR 1.19, 1.02–1.40) had an elevated odds of a prevalent simple cyst, as did women with previous history of benign ovarian cysts (OR 1.29, 1.09–1.52) and women with previous gynecologic surgery (OR 1.48, 1.33, 1.66). Menopause before age 40 was strongly associated with elevated odds of a simple cyst compared to women whose last menstruation was between ages 50 and 54 (OR 2.09, 1.77–2.46). Current and former smokers

were each at about 25% increased risk of having an ovarian cyst at the incidence screen, although this was of borderline significance only for former smokers (OR 1.25, 1.00–1.56). Associations with menopause and gynecologic surgery were similar to those observed for simple cyst prevalence. There was a suggestion that women with post-high school education had a higher incidence, but this was only significant among women with some college (OR 1.36, 1.03–1.79).

## COMMENT

In our analysis of four serial TVU examinations within a large cancer screening trial of mostly post-menopausal women, we determined that simple ovarian cysts are a common incidental finding upon ultrasonography. Increases over time in the number or complexity of cysts were infrequent, and many cysts fully resolved between annual exams. Greater numbers of simple cysts correlated with subsequent development of complex cysts, but simple cysts were not associated with development of ovarian cancer, an outcome actively ascertained in the PLCO trial.

Prevalence of simple cysts in this analysis (14%), based on a participant's first screening with fully visualized ovaries, is just slightly lower than previous baseline results from PLCO (15.7%).<sup>8</sup> These values fall within, but near the high end, of the range of prevalence estimates from the published literature. Much of the knowledge gained about the occurrence and course of simple ovarian cysts in post-menopausal women comes from smaller case series.<sup>9–10</sup> Oyelese<sup>11</sup> summarized the results of 5 studies from the late 1980s and 1990s,<sup>10, 12–15</sup> with numbers of post-menopausal women examined ranging from 149 to 7705, and simple cyst prevalence ranging from 3.3 to 14.8%. Levine found 17% of 184 women had simple adnexal cysts following first examination with transvaginal and transabdominal ultrasound.<sup>16</sup> More recently, in a large ovarian cancer screening study at the University of Kentucky, 18% of 15,106 women had unilocular ovarian cysts discovered during the course of the screening program.<sup>17</sup>

Estimates of the incidence of simple ovarian cysts are lacking in the published literature. A major strength of the present study was the use of serial TVU examinations to assess the development of new cysts among women whose ovaries had been cyst-free in previous screenings. The incidence of simple cysts was about 8% per year and remained fairly constant over the course of the trial, even among older women in the study. The expectation of continued simple cyst detection even after multiple clear screens, and even as women approach their late 70s, reinforces the importance of a sound strategy for managing simple ovarian cysts when incorporating repeated TVU examinations in clinical practice.

Serial screenings at standard intervals also provided insight into the natural history of simple ovarian cysts. One third of ovaries with simple cysts were cyst-free the next year. Even ovaries with 3 or more simple cysts were cyst-free one year later 25% of the time. Previous studies report resolution rates ranging upward from 23%. The proportion of simple cysts resolving spontaneously over an average of 4.6 years of followup in the University of Kentucky trial was 83%.<sup>18</sup> The most common outcome for ovaries with simple cysts in the PLCO study a year later was to have the same number of simple cysts. Finding 54% of simple cysts persisting a year later is comparable to the 49% reported among 134 women followed for a mean of 3 years<sup>1</sup> and the 56% persistence over 2 years reported by Castillo<sup>19</sup> among 104 women. In our study, only 6% of ovaries progressed from having a single simple cyst to having a more complex cyst a year later, although this was somewhat more common within ovaries with multiple simple cysts. In the University of Kentucky trial, over 22% of cysts developed septae or solid areas upon followup.<sup>17</sup>

Surgical intervention for abnormal findings in a post-menopausal ovary had been the standard of care for decades.<sup>20,21</sup> In the 1980s, the necessity for a surgical approach was questioned based on small study results. A recent evidence-based report was not able to draw definitive conclusions on the sensitivity and specificity of periodic monitoring of simple cysts for cancer detection, but suggested that prolonged followup of simple cysts with interval TVU was likely a safe approach.<sup>22</sup> The American College of Obstetricians and Gynecologists subsequently stated that simple cysts found on ultrasound ‘may be safely followed without intervention, even in post-menopausal women’.<sup>4</sup> Our study results reinforce the belief that simple cysts are not likely cancer precursors, nor markers of increased risk, and can be managed conservatively. In our study, women with and without simple cysts developed invasive ovarian cancer at an equivalent rate after nearly 8 years of followup. These findings are also consistent with the University of Kentucky report, where only 10 ovarian cancers were detected among 2,700 women with simple cysts after 6 years on average, and none developed among women with an isolated simple cyst.<sup>17</sup> Also, while potential correlates of prevalent simple cysts were identified in our study, including higher risk among women that were younger, well-educated, and had early menopause, traditional ovarian cancer risk factors (increasing age, family history of breast or ovarian cancer, nulliparity, infertility, etc.) were not associated with simple cysts, reinforcing a previous baseline report.<sup>8</sup>

It is a limitation that results were restricted to women with both ovaries visualized during TVU screening. Only 52% of screened women had both ovaries visualized, and occurrence rates of simple cysts may not be the same in women whose ovaries were not visualized. By incorporating simple cysts observed among the 26% of women with only one ovary visualized, and assuming the remaining 22% of women with ovaries never visualized were all cyst free, a lower bound of 11% can be placed on the prevalence among all screened women in the trial. Some ‘persistent’ cysts may reflect cyst resolution and replacement in the same ovary. In a previous study, half of simple cysts resolved within 60 days, and in another, two-thirds of resolving cysts did so within 3 months, suggesting resolution and replacement may have been occurring in some ovaries during the year between screens.<sup>15</sup> Also, data for this study do not clearly distinguish whether a complex cyst found following a simple cyst on a previous screen represents morphological progression or the independent appearance of a complex cyst in the same ovary. PLCO quality assessment results do indicate TVU examinations had reasonably good reproducibility. If no cysts were visualized on the TVU, 99% of the time no cysts were seen on the quality assurance examination. If the initial examiner saw a simple cyst it was seen 84% of the time on the quality assurance examination. Finally, the PLCO trial protocol did not include systematic followup of the care received in response to the detection of simple cysts, since simple cysts were not considered positive screens. Therefore we do not have useful data on simple cyst surgeries or pathological interpretation of simple cyst tissue.

In summary, TVU data from participants in a large cancer screening trial confirm that simple ovarian cysts are common incidental findings among women over age 55 upon transvaginal ultrasonography, and remain common after several screening rounds and as women age. Simple cysts frequently resolve or persist without progression. Women with simple ovarian cysts do not appear to be at increased risk of developing invasive ovarian cancer. These findings support recent recommendations to follow unilocular simple cysts in post-menopausal women without intervention.<sup>4</sup>

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## ABBREVIATION LIST

NSAID	Non-Steroidal Anti-inflammatory Drug
PLCO	Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial
TVU	Transvaginal Ultrasound

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## APPENDIX

PLCO Screening Centers and their locations include:

University of Colorado, Denver, Colorado  
Georgetown University Medical Center, Washington, DC  
Pacific Health Research Institute, Honolulu, Hawaii  
Henry Ford Health System, Detroit, Michigan  
University of Minnesota, Minneapolis, Minnesota  
Washington University, St. Louis, Missouri  
University of Pittsburgh, Pittsburgh, Pennsylvania  
University of Utah, Salt Lake City, Utah  
Marshfield Clinic Research Foundation, Marshfield, Wisconsin  
University of Alabama at Birmingham, Birmingham, Alabama



**Table 1**

Identification of study populations for simple cyst prevalence and incidence analyses from the intervention arm of the PLCO Cancer Screening Trial

39115	women randomized to the screening arm
	4895 not eligible for TVU
	3831 not compliant with TVU
	239 with inadequate TVU(s)
30150	received at least one adequate TVU
	6610 with ovaries never visualized
	7805 at most one ovary visualized
15735	with a qualifying TVU for prevalence estimation*
	3097 with cysts/solid masses on prevalence TVU
	7137 other reasons for no TVU for incidence estimation**
5501	with a qualifying TVU for incidence estimation***

\* prevalence TVU = first screen with both ovaries visualized

\*\* no longer eligible, not compliant, inadequate screen, both ovaries not visualized, or prevalence TVU occurred during last screening round (year 3)

\*\*\* incidence TVU = second exam with both ovaries visualized, one year after prevalence exam, no cysts on prevalence exam

**Table 2**

## Select Characteristics of Simple Ovarian Cyst Study Cohort\*

	Number	%
Total Study Population	15735	100.0
Age		
55–59	5679	36.1
60–64	4994	31.7
65–69	3260	20.7
70–74	1802	11.5
Race/Ethnicity		
White	14068	89.4
Black	508	3.2
Hispanic	218	1.4
Asian	717	4.6
Pacific Islander	84	0.5
American Indian	34	0.2
Missing	106	0.7
Education		
<12 years	796	5.1
12 yrs/Completed High School	6204	39.4
Some College	3526	22.4
College Graduate	2602	16.5
Post Graduate	2492	15.8
Missing	115	0.7
Cigarette Use		
Never Smoked	8876	56.4
Current Smoker	1348	8.6
Former Smoker	5406	34.4
Missing	105	0.7
First Degree Family History of Breast Cancer		
No	12613	80.2
Yes	2238	14.2
Unknown	541	3.4
Missing	343	2.2
Total Years of Oral Contraceptive use		
0	7178	45.6
<1	2214	14.1
2–3	1731	11.0
4–5	1174	7.5
6–9	1421	9.0
10+	1888	12.0

		Number	%
	Missing	129	0.8
Age at First Pregnancy	Never pregnant	1105	7.0
	less than 20	3308	21.0
	20–24	7313	46.5
	25–29	2958	18.8
	30+	907	5.8
	Missing	144	0.9
Number of Pregnancies	Never pregnant	1105	7.0
	1	892	5.7
	2	2800	17.8
	3–4	6481	41.2
	5–9	4046	25.7
	10+	277	1.8
	Missing	134	0.9
Hormone Replacement	No	5437	34.6
	Yes	10131	64.4
	Don't Know	52	0.3
	Missing	115	0.7
Age at Menopause	<40	1576	10.0
	40–44	1730	11.0
	45–49	3536	22.5
	50–54	6579	41.8
	55+	2072	13.2
	Missing	242	1.5
Previous Gynecologic Surgery	No	9406	59.8
	Yes	6159	39.1
	Don't Know	32	0.2
	Missing	138	0.9
History of Benign Ovarian Tumors or Cysts	No	14101	89.6
	Yes	1236	7.9
	Missing	398	2.5
Use of NSAIDs or aspirin	No	6798	43.2
	Yes	8769	55.7
	Missing	168	1.1

	<b>Number</b>	<b>%</b>
History of Infertility		
No	13374	85.0
Yes	2218	14.1
Missing	143	0.9

NSAID - Non-steroidal anti-inflammatory drugs

\* PLCO Trial women in intervention arm with both ovaries visualized by transvaginal ultrasound one or more times from baseline (T0) through the Year 3 (T3) screening

**Table 3**

Simple Ovarian Cyst Prevalence and Multivariable Modeling Results

	Prevalent Simple Cysts		Adjusted Association*	
	# Women	Rate (%)	Odds Ratio	95% CI
Overall	2217	14.1		
Age				
55–59	884	15.6	ref.	
60–64	658	13.2	<b>0.83</b>	<b>(0.73, 0.94)</b>
65–69	434	13.3	0.97	(0.84, 1.12)
70–74	241	13.4	1.01	(0.84, 1.22)
Education				
<12 years	94	11.8	0.85	(0.66, 1.09)
12 yrs/Completed High School	842	13.6	ref.	
Some College	515	14.6	1.11	(0.97, 1.26)
College Graduate	411	15.8	<b>1.32</b>	<b>(1.14, 1.53)</b>
Post Graduate	338	13.6	<b>1.19</b>	<b>(1.02, 1.40)</b>
Missing	17	14.8	NA	
Cigarette Use				
Never Smoked	1248	14.1	ref.	
Current Smoker	155	11.5	<b>0.75</b>	<b>(0.61, 0.91)</b>
Former Smoker	797	14.7	1.04	(0.93, 1.15)
Missing	17	16.2	NA	
First Degree Family History of Breast Cancer				
No	1739	13.8	ref.	
Yes	342	15.3	1.12	(0.98, 1.28)
Unknown	81	15.0	NA	
Missing	55	16.0	NA	
Total Years of Oral Contraceptive Use				
0	946	13.2	ref.	

	Prevalent Simple Cysts		Adjusted Association*	
	# Women	Rate (%)	Odds Ratio	95% CI
Age at First Pregnancy	<1	337	15.2	1.02 (0.88, 1.18)
	2-3	254	14.7	0.95 (0.80, 1.13)
	4-5	179	15.2	0.94 (0.77, 1.14)
	6-9	212	14.9	0.94 (0.78, 1.13)
	10+	266	14.1	0.97 (0.83, 1.15)
	Missing	23	17.8	NA
	Never pregnant	135	12.2	0.82 (0.60, 1.12)
	less than 20	516	15.6	1.04 (0.91, 1.19)
	20-24	1078	14.7	ref.
	25-29	366	12.4	<b>0.85</b> <b>(0.74, 0.98)</b>
Number of Pregnancies	30+	102	11.2	<b>0.71</b> <b>(0.55, 0.91)</b>
	Missing	20	13.9	NA
	Never pregnant	135	12.2	NA
	1	120	13.5	1.25 (0.99, 1.58)
	2	359	12.8	0.97 (0.84, 1.12)
	3-4	938	14.5	ref.
	53-9	612	15.1	0.97 (0.86, 1.09)
	10+	34	12.2	0.72 (0.49, 1.06)
	Missing	19	14.2	NA
	Hormone Replacement	No	682	12.5
Yes		1512	14.9	1.09 (0.98, 1.22)
Don't Know		6	11.5	NA
Missing		17	14.8	NA
<40		390	24.7	<b>2.09</b> <b>(1.77, 2.46)</b>
40-44	272	15.7	<b>1.26</b> <b>(1.07, 1.49)</b>	

	Prevalent Simple Cysts		Adjusted Association*	
	# Women	Rate (%)	Odds Ratio	95% CI
45–49	410	11.6	0.93	(0.82, 1.07)
50–54	786	11.9	ref.	
55+	313	15.1	<b>1.24</b>	<b>(1.07, 1.44)</b>
Missing	46	19.0	NA	
Previous Gynecologic Surgery				
No	1070	11.4	ref.	
Yes	1124	18.2	<b>1.48</b>	<b>(1.33, 1.66)</b>
Don't Know	1	3.1	NA	
Missing	22	15.9	NA	
History of Benign Ovarian Tumors or Cysts				
No	1934	13.7	ref.	
Yes	220	17.8	<b>1.29</b>	<b>(1.09, 1.52)</b>
Missing	63	15.8	NA	
Use of NSAIDs or aspirin				
No	920	13.5	ref.	
Yes	1268	14.5	1.00	(0.91, 1.10)
Missing	29	17.3	NA	
History of Infertility				
No	1862	13.9	ref.	
Yes	335	15.1	0.95	(0.69, 1.30)
Missing	20	14.0	NA	

\* Model adjusts for all factors shown, plus race and screening center

NSAID - Non Steroidal Anti-Inflammatory Drug

ref. - Referent Category

NA - Not Available

**Table 4**  
One Year Incidence of Simple Ovarian Cysts and Multivariable Modeling Results

	Incident Simple Cysts		Adjusted Association*	
	Count	Rate (%)	Odds Ratio	95% CI
Overall	459	8.3		
Age				
55–59	179	8.7	ref.	
60–64	141	7.9	0.98	(0.76, 1.27)
65–69	102	9.4	1.26	(0.93, 1.78)
70–74	37	6.6	0.91	(0.60, 1.39)
Education				
<12 years	21	7.5	0.99	(0.60, 1.64)
12 yrs/Completed High School	167	7.4	ref.	
Some College	116	10.0	<b>1.36</b>	<b>(1.03, 1.79)</b>
College Graduate	75	8.4	1.29	(0.94, 1.78)
Post Graduate	77	8.8	1.35	(0.98, 1.88)
Missing	3	11.1	NA	
Cigarette Use				
Never Smoked	230	7.4	ref.	
Current Smoker	49	9.7	1.26	(0.88, 1.79)
Former Smoker	177	9.5	<b>1.25</b>	<b>(1.00, 1.56)</b>
Missing	3	11.5	NA	
First Degree Family History of Breast Cancer				
No	352	7.9	ref.	
Yes	75	9.6	1.18	(0.89, 1.55)
Unknown	22	12.2	NA	
Missing	10	11.2	NA	
Ever Used Oral Contraceptives				
No	198	7.8	ref.	
Yes	258	8.8	1.07	(0.85, 1.34)



	Incident Simple Cysts		Adjusted Association*	
	Count	Rate (%)	Odds Ratio	95% CI
Age at First Pregnancy				
Missing	3	10.3	NA	
Never pregnant	42	10.1	1.27	(0.86, 1.88)
less than 20	97	8.4	1.01	(0.77, 1.33)
20-24	220	8.8	ref.	
25-29	71	6.7	0.85	(0.62, 1.15)
30+	25	7.6	1.03	(0.65, 1.64)
Missing	4	10.5	NA	
Age at Menopause				
<40	56	14.1	<b>1.92</b>	<b>(1.32, 2.80)</b>
40-44	46	9.2	1.35	(0.94, 1.95)
45-49	109	8.6	1.27	(0.97, 1.66)
50-54	168	6.7	ref.	
55+	68	9.1	<b>1.43</b>	<b>(1.05, 1.95)</b>
Missing	12	15.8	NA	
Previous Gynecologic Surgery				
No	255	7.2	ref.	
Yes	201	10.6	<b>1.52</b>	<b>(1.21, 1.92)</b>
Don't Know	0	0.0	NA	
Missing	3	8.3	NA	
History of Benign Ovarian Tumors or Cysts				
No	414	8.2	ref.	
Yes	39	10.2	1.25	(0.86, 1.82)
Missing	6	6.0	NA	

\* Model adjusts for all factors shown, plus race and screening center

ref. - Referent Category

NA - Not Available

**Table 5**

One year change in Ovary\* status

Ovary Status at Screening	Ovary Status at Screening One Year Later												
	No Cyst	1 Simple Cyst	2 Simple Cysts	3 or more Simple Cysts	Solid Mass	Complex Cyst	Number	%	Number	%			
No Cyst	32264	1745	255	95	138	248	34745	92.9	5.0	0.7	0.3	0.4	0.7
1 Simple Cyst	1487	2533	276	89	23	245	4653	32.0	54.4	5.9	1.9	0.5	5.3
2 Simple Cysts	203	242	268	93	1	62	869	23.4	27.8	30.8	10.7	0.1	7.1
3 or more Simple Cysts	92	62	71	132	4	39	400	23.0	15.5	17.8	33.0	1.0	9.8
<b>Total</b>							<b>40667</b>						

\* Ovaries visualized by transvaginal ultrasound in two consecutive screening years, showing no cysts or only simple cysts in the former year (n=40,667).