

# NIH Public Access

Author Manuscript

Gynecol Oncol. Author manuscript; available in PMC 2013 August 01.

#### Published in final edited form as:

Gynecol Oncol. 2012 August ; 126(2): 229–235. doi:10.1016/j.ygyno.2012.04.046.

# Prophylactic oophorectomy rates in relation to a guideline update on referral to genetic counseling

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# Abstract

**Objective**—We sought to determine whether prophylactic oophorectomy rates changed after the introduction of a 2007 health plan clinical guideline recommending systematic referral to a genetic counselor for women with a personal or family history suggestive of an inherited susceptibility to breast/ovarian cancer.

**Methods**—We conducted a retrospective cohort study of female members of Group Health, an integrated delivery system in Washington State. Subjects were women aged 35 years during 2004–2009 who reported a personal or family history consistent with an inherited susceptibility to

#### **Conflict of interest statement**

None of the authors have any conflicts of interest.

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breast/ovarian cancer. Personal and family history information was collected on a questionnaire completed when the women had a mammogram. We ascertained oophorectomies from automated claims data and determined whether surgeries were prophylactic by medical chart review. Rates were age-adjusted and age-adjusted incidence rate ratios (IRR) and 95% confidence intervals (CI) were computed using Poisson regression.

**Results**—Prophylactic oophorectomy rates were relatively unchanged after compared to before the guideline change, 1.0 versus 0.8/1,000 person-years, (IRR = 1.2; 95% CI: 0.7–2.0), whereas bilateral oophorectomy rates for other indications decreased. Genetic counseling receipt rates doubled after the guideline change (95% CI: 1.7–2.4) from 5.1 to 10.2/1,000 person-years. During the study, bilateral oophorectomy rates were appreciably greater in women who saw a genetic counselor compared to those who did not regardless of whether they received genetic testing as part of their counseling.

**Conclusion**—A doubling in genetic counseling receipt rates lends support to the idea that the guideline issuance contributed to sustained rates of prophylactic oophorectomies in more recent years.

#### Introduction

The estimated risk of developing ovarian cancer by 70 years of age is 39-46% in women with a *BRCA1* mutation [1-3] and 11-12% in women with a *BRCA2* mutation [1-2], compared to less than 1% in the general female population [4]. Most women with ovarian cancer are diagnosed with advanced stage disease, at which point 5-year relative survival is only about 27% [5]. Removal of the ovaries and fallopian tubes in women with a BRCA1/2 mutation can prevent ovarian cancer [6] and is strongly associated with a decreased risk of death from the disease [7]. Adverse health and quality of life issues are associated with removal of the ovaries before natural menopause [8-9], so it is important that women make surgical decisions based on dependable estimates of cancer risk. As noted by the U.S. Preventive Services Task Force, screening for inherited susceptibility to breast and ovarian cancer is a 2-step process, the first step is to assess the likelihood that a clinically important mutation is present and the second is to genetically test the high-risk women [10]. Genetic counselors have dedicated time to talk with patients to carefully elicit relevant personal and family history information, determine whether genetic testing is indicated, inform patients about the risks and benefits of testing, and interpret uncertain and negative test results. In 2007, Group Health, an integrated health care delivery system updated clinical guidelines to recommend that all women with a personal history of breast cancer before 50 years of age or a strong family history of breast or ovarian cancer be referred to a genetic counselor.

The present study was designed to evaluate whether rates of prophylactic oophorectomy in women at high risk of developing breast or ovarian cancer changed after the guideline update. Secondary goals were to: 1) describe rates of receipt of genetic counseling in high-risk women, and 2) compare bilateral oophorectomy rates in high-risk women with and without prior genetic counseling, as these patterns could potentially explain trends in prophylactic oophorectomy rates.

# **Materials and Methods**

#### Setting and population

We conducted a retrospective cohort study among female members of Group Health, an integrated health care delivery system in Washington state and northern Idaho with about 660,000 members [11]. The study population consisted of women at least 35 years of age who were enrolled in Group Health for any period from January 1, 2004 through August 31, 2009. To be included in the study, women had to have a personal or family history

suggestive of an inherited susceptibility to ovarian cancer (below). Group Health's Institutional Review Board approved all study procedures.

As part of Group Health's Breast Cancer Screening Program (BCSP), women are asked to complete a risk factor questionnaire, which includes extensive family history information, when they come in for a mammogram [12–13]. Any of the following criteria triggered entry into our cohort: a personal history of breast cancer before 50 years of age, a strong family history of ovarian and/or breast cancer (defined in Table 1), or 1 first degree relative diagnosed with both ovarian and breast cancer. A total of 21,984 women met 1 of these criteria and were 35 years of age during their enrollment.

Data from Group Health claims, the western Washington Cancer Surveillance System Surveillance Epidemiology and End Results Program [14], and the BCSP questionnaires were used to assess eligibility. We excluded women with: a prior bilateral oophorectomy (including removal of a remaining ovary) (International Classification of Diseases 9<sup>th</sup> Revision [ICD-9] 65.5, 65.6, 68.8, and Current Procedural Terminology [CPT] 58950– 58952, 58953–58954, and 58956) (n = 2,845) or a prior diagnosis of primary or secondary ovarian cancer, including fallopian tube cancer (Appendix 1 for ICD/CPT codes) (n = 504). We also excluded women with a prior diagnosis of a gynecologic cancer other than ovarian cancer (Appendix 1 for ICD/CPT codes) (n = 927) because ovaries may have been removed as part of, or a consequence of, their treatment. An additional 2 women were excluded from all analyses because they had the same start of follow-up and disenrollment date (i.e., they did not contribute any person-time). After applying these exclusion criteria to the cohort, 18,390 women remained.

In March 2007 Group Health issued a clinical practice guideline for its providers recommending that women with a possible inherited susceptibility to breast or ovarian cancer be referred to a genetic counselor. The criteria were determined by review of available published material [10, 15] and consensus of Group Health's breast cancer screening guideline team, and include those shown in Table 1. Before March 2007, high-risk women were eligible for referral, but there was no guideline describing who should be referred. The guideline was enacted in conjunction with an update to Group Health's breast cancer screening guidelines and was accompanied by seminars for providers about genetic counseling.

#### **Outcomes identification**

We identified bilateral oophorectomies (including removal of a remaining ovary), with or without the concurrent removal of the fallopian tubes, from automated claims data (ICD-9 65.5, 65.6, and V50.42) (n = 242). In order to identify prophylactic opphorectomies separately from oophorectomies for other surgical indications we reviewed the medical records for the reason for the surgery, using information from before the surgery occurred. Medical records were reviewed for: 1) all women with a qualifying ICD-9 code before being censored due to death, a gap in enrollment of at least 60 days, a diagnosis of a gynecologic cancer (Appendix 1 for ICD/CPT codes), surgery for a gynecologic malignancy (Appendix 1 for ICD/CPT codes), or September 1, 2009, whichever occurred first (n = 242); and 2) all women identified as having a bilateral oophorectomy on the same day as a diagnosis of a gynecologic cancer (n = 21). Among the initial 242 women identified from the claims data: the medical chart could not be located for 1 patient; 11 had insufficient information in their medical chart to determine whether or not the surgery had occurred; 4 had evidence of an oophorectomy, but it could not be determined whether an ovary remained following the surgery; and 1 had an intact ovary following the surgery. A total of 225 women were confirmed to have had an oophorectomy that left them with no ovaries and the reason for the surgery was ascertained. Among the 21 women who had a gynecologic cancer diagnosis

code on the same date as their oophorectomy (i.e. it was not clear whether cancer was suspected prior to the surgery or whether an occult tumor was discovered during a surgery intended to be prophylactic), 1 had insufficient information available to determine whether the surgery occurred, and 1 had no evidence that either ovary was removed, leaving a total of 19 women who were confirmed to have had an oophorectomy that left them with no ovaries and for whom we ascertained the reason for the surgery.

Based on medical record abstracted reasons for the bilateral oophorectomy, we classified each oophorectomy into one of three mutually-exclusive groups: prophylactic, hysterectomytreatable, and ovarian-indication. The prophylactic group included women with a surgical indication that did not include treatment for an underlying condition (n = 58), which is similar to the American College of Obstetricians and Gynecologists' (ACOG) definition of risk-reducing salpingo-oophorectomy (the removal of normal ovaries when no other procedure is indicated at that time) [16]. Hysterectomy-treatable included those with a surgical indication that was usually treatable by hysterectomy alone (n = 102) (e.g., uterine fibroids), which is similar to ACOG's definition of elective opphorectomy (the removal of the ovaries at the time of another indicated procedure such as a hysterectomy) [16]. Ovarianindication included women treated for a condition that may have warranted ovary removal (e.g., pelvic pain) (n = 71). If the surgical indication included both hysterectomy-treatable and ovarian-indication, then the woman was categorized into the ovarian-indication group. In 6 of the 19 women who had a gynecologic cancer diagnosis on the same day as their oophorectomy, cancer was not suspected before the surgery, therefore these women were classified in the prophylactic (2/58) or hysterectomy-treatable (4/102) groups. In the remaining 13 of the 19 women, cancer was suspected before the surgery, and so we censored these women.

In our analyses where we did not separate women by the reason for their surgery (i.e. total bilateral oophorectomy), we included the 241 women identified from the administrative data (after excluding the one woman who was found through chart review to have an intact ovary remaining after surgery) in addition to the 2 prophylactic and 4 hysterectomy-treatable ones that occurred on the same day as a gynecologic cancer diagnosis (n = 247).

Receipt of genetic counseling was our secondary outcome. We used Group Health's clinical genetic counseling database to ascertain counseling visits (inpatient, outpatient and phone encounters), any genetic testing, including testing for breast or ovarian cancer risk (a *BRCA* mutation, Lynch Syndrome, or mutations in the genes *PTEN* or *p53*), and test results.

#### Statistical analyses

**Rates of receipt of bilateral oophorectomy and genetic counseling**—Women who completed a BCSP questionnaire before January 1, 2004 that indicated they were at high risk entered the cohort and began contributing person-time starting January 1, 2004. All other women entered the cohort and began contributing person-time as of their first questionnaire identifying them as high-risk. For rates of receipt of bilateral oophorectomy, person-time accrued through the first of the following: receipt of bilateral oophorectomy or censoring (a gap in enrollment of 60 days, a gynecologic cancer diagnosis, surgery for a gynecologic malignancy, death, or September 1, 2009). Genetic counseling receipt rates were computed in the same way except women were necessarily censored upon receipt of a bilateral oophorectomy.

Rates of receipt of bilateral oophorectomy following genetic counseling or

**testing**—In the analyses of receipt of bilateral oophorectomy following genetic counseling, testing or test results, a woman began contributing person-time as of her: first genetic counseling encounter, genetic test, or test result, respectively. In these analyses, we excluded

women with a prior genetic counseling visit (n = 229), leaving 18,161 women for those analyses.

**Analysis**—All rates, except the age-specific ones, were age-adjusted using direct standardization to the 2007 study population. We computed age-adjusted incidence rate ratios (IRR) and 95% confidence intervals (CIs) using Poisson regression. The p-value associated with the exposure variable was computed using the likelihood ratio test by comparing models with and without the exposure variable. We conducted all analyses using Stata/MP 11.1 (College Station, Texas).

# Results

We identified a cohort of 18,390 women with a personal or family history suggestive of an inherited susceptibility to breast or ovarian cancer (not mutually exclusive): 8% had a personal history of breast cancer before 50 years of age, 73% had a strong family history of breast cancer (defined in Table 1), 16% had a strong family history of ovarian cancer, and 7% had at least one first-degree relative diagnosed with both ovarian and breast cancer (Table 1).

During approximately 66,000 person-years of follow-up, with a mean follow-up time of 3.6 years, a total of 247 of the 18,390 women were identified as having received a bilateral oophorectomy, rate = 3.7/1,000 person-years (95% CI: 3.2-4.1/1,000 person-years). Fifty-eight women had a prophylactic oophorectomy, rate = 0.9/1,000 person-years (95% CI: 0.6-1.1/1,000 person-years), 102 had a hysterectomy-treatable oophorectomy, rate = 1.5/1,000 person-years (95% CI: 1.2-1.8/1,000 person-years) and 71 had an ovarian-indication oophorectomy, rate = 1.1/1,000 person-years (95% CI: 0.8-1.3/1,000 person-years). The total bilateral oophorectomy rate was 30% lower after the guideline, age-adjusted IRR = 0.7 (95% CI: 0.6-1.0; p=0.026) (Table 2 and Figure 1). The decrease was due to a decrease in the hysterectomy-treatable and ovarian-indication oophorectomy rates, whereas prophylactic oophorectomy rates were similar before and after the guideline change (Table 2 and Figure 1).

A total of 474 of the 18,161 women received genetic counseling, rate = 7.3/1,000 personyears (95% CI: 6.6–7.9/1,000 person-years). Counseling rates increased about two-fold after the guideline change in all age groups, age-adjusted IRR = 2.0 (95% CI: 1.7–2.4) among all women (Table 3 and Figure 2); however, the absolute increase in rates was greatest in women 35–49 years of age, 11.3/1,000 person-years (Table 3 and Figure 2).

Bilateral oophorectomy rates were greater in women who had genetic counseling during follow-up compared to women who did not, 38.2 versus 2.8/1,000 person-years (Table 4). Over half (61%) of the women who received genetic counseling also received some form of genetic testing (273 had testing for breast or ovarian cancer risk and 14 had other genetic testing) (Table 4). Bilateral oophorectomy rates were higher in women after genetic testing (with prior counseling) compared to women who had counseling but no testing, 44.9 versus 29.0/1,000 person-years (Table 4). Bilateral oophorectomy rates were greater following a positive genetic test result for breast/ovarian cancer risk, 387.8/1,000 person-years compared to a non-positive genetic test result, 25.1/1,000 person-years (Table 4).

# Discussion

A health plan guideline change designed to systematically refer women at high risk for breast and/or ovarian cancer to genetic counseling was associated with increased uptake of genetic counseling. However, we were unable to measure the appropriateness of these

referrals, either before or after the guideline change. Prophylactic oophorectomy rates were largely unchanged following the guideline; although bilateral oophorectomy rates for other surgical indications decreased, attributable to decreases in hysterectomy-treatable and ovarian-indication oophorectomy rates. Among women who received genetic counseling, our findings that bilateral oophorectomy rates were greater among those who had genetic testing compared to those who did not, and were appreciably greater among those who had a positive genetic test for breast/ovarian cancer risk compared to those with a non-positive result, is consistent with the ideas that genetic counseling leads to finer risk stratification and that higher risk women are more likely to have their ovaries removed.

Oophorectomy rates in the general U.S. female population have decreased recently [17, 18]. Based on national hospital discharge data, Oliphant et al. reported that age-adjusted oophorectomy rates in women 18 years of age with any surgical indication decreased from 5.7, to 4.3, then to 3.3/1,000 person-years in 1979, 1993 and 2006, respectively [17]. We are unaware of a study that describes trends over time in prophylactic oophorectomy rates. A study of elective oophorectomy rates (defined similarly to our hysterectomy-treatable oophorectomies) based on national hospital discharge data, reported that age-adjusted rates in women 15 years of age peaked in 2001–2002 at 0.9/1,000 person-years then declined to a low in 2006 of 0.7/1,000 person-years [18].

Although we observed a 2-fold increase in the rate of receipt of genetic counseling after the guideline was issued, this translated to only a small proportion of the cohort receiving counseling. It is not clear to what extent this was due to providers not being aware of the guideline or to women choosing to not obtain counseling even after it was offered or recommended. Financial barriers may not explain these findings as genetic counseling services were covered by Group Health for women who were referred. Some women may have chosen to not have testing done because of fears of future health insurance discrimination [19]. The Genetic Information Nondiscrimination Act (GINA), which prohibits such discrimination, only went into effect in mid-2009, near the end of the study period [20,21]. In a recent survey of 3,200 physicians <65 years of age, 41% self-reported adhering to recommendations for genetic counseling or testing for women who are at high risk of developing ovarian cancer (based on her personal and family history) [22]. In vignettes included in the survey, the physicians were 78% more likely (95% CI: 41%-124%) to recommend referral or testing when the woman in the vignette was younger (35 years of age) versus older (51 years of age) after adjusting for patient race, type of insurance and physician characteristics (physician estimate of woman's risk of ovarian cancer, specialty, and gender) [22]. Other factors that were independently associated with physicians being more likely to recommend genetic counseling or testing included physician's gender being female and physician specialty being obstetrics/gynecology versus family medicine versus [22].

There are several possible reasons why a higher rate of genetic counseling after the guideline change did not translate into a higher bilateral oophorectomy rate. Only a small proportion of the cohort received genetic counseling, making detection of a small increase difficult. Prior studies indicate women without cancer who test positive for a *BRCA* mutation do not, on average, have their ovaries removed immediately. The 2-year cumulative incidence of oophorectomy after testing positive was about 44% in a national cohort of 306 *BRCA1/2* women in Denmark [23], in a cohort of 110 *BRCA1* women in England it was about 46%, and about 20% in 91 *BRCA2* women [24]. In the present study, among the 26 women who tested positive for a *BRCA* mutation, the 2-year cumulative incidence of oophorectomy was 61% (95% CI: 42%–81%). Women who test positive for *BRCA1/2* are recommended to have their ovaries removed for ovarian cancer prevention at

35–40 years of age if childbearing is not an issue [16]. The youngest women who tested positive for BRCA in our cohort were aged 37–39 years (n=4).

Several features of the current study strengthen its ability to provide important, populationbased estimates of bilateral oophorectomy rates by indication. We used prospectively collected personal and family history data to identify a large, population-based cohort of women who had a history suggestive of an inherited susceptibility to ovarian cancer. Oophorectomy indication was collected from medical charts so that we could evaluate trends separately for prophylactic, hysterectomy-treatable, and oophorectomies with an ovarian indication. We additionally reviewed charts of all women who were diagnosed with a gynecologic cancer on the same day as they had their bilateral oophorectomy so that all surgeries performed when there was no prior suspicion of cancer would be counted.

There are some limitations to this study that may have affected our ability to accurately measure bilateral oophorectomy rates. Some women who had had a bilateral oophorectomy before enrolling with Group Health may have been included in the cohort; however, we excluded women who reported having a bilateral oophorectomy before enrollment. Excluding women with a prior diagnosis of any gynecologic cancer may have inadvertently excluded some women with gynecologic cancer who did not have a bilateral oophorectomy as part of their treatment. However, we would expect these women to make up a very small proportion of otherwise similar cohorts. Further, our findings may not apply to other populations to the extent that oophorectomy rates differ in those populations. Additionally, some women who tested positive for a BRCA mutation but who did not have a prophylactic oophorectomy during the follow-up period may have eventually gone on to have the procedure after the conclusion of the study follow-up.

After the guideline was issued, rates of prophylactic oophorectomies remained stable whereas rates of bilateral oophorectomies with other surgical indications decreased, among women with a possible inherited susceptibility to developing ovarian cancer. It is unclear whether in the absence of the guideline prophylactic oophorectomy rates would have also decreased, but a doubling in the rate of receipt of genetic counseling lends support to the idea that issuance of the guideline contributed to the sustained rates of prophylactic oophorectomies in more recent years.

#### Acknowledgments

We are grateful to Monica Fujii, MPH, for project management, Mary Lyons and Marta Brakke for medical chart abstraction, and Walter Clinton and Tyler Ross, MA, for data compilation.

#### Financial support:

This work was funded by the Centers for Disease Control & Prevention (Award number R18DP001142 to N.U.). The data collection was supported by a grant from the National Cancer Institute (Award number CA63731 to D.S.M.B) as part of the Breast Cancer Surveillance Consortium. The collection of cancer incidence data used in this study was supported by the Cancer Surveillance System of the Fred Hutchinson Cancer Research Center, which is funded by Contract No. N01-CN-67009 and N01-PC-35142 from the Surveillance, Epidemiology and End Results (SEER) Program of the National Cancer Institute with additional support from the Fred Hutchinson Cancer Research Center and the State of Washington.

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# Appendix 1

Variable definitions based on administrative data codes.

Variable	Description of code	Code
Bilateral oophorectomy		
Bilateral oophorectom	у	
	Bilateral oophorectomy (ICD-9 <sup>a</sup> )	65.51, 65.53
	Removal of remaining ovary (ICD-9)	65.52, 65.54
	Prophylactic ovary removal (ICD-9)	V50.42
Bilateral salpingo-oop	horectomy	
	Bilateral salpingo-oophorectomy (ICD-9)	65.61, 65.63
	Removal of remaining ovary and tube (ICD-9)	65.62, 65.64
A diagnosis of a gynecol	ogic cancer	
	Malignant neoplasm of female genital organ (ICD-9)	179–184
	Malignant neoplasm of female genital organ (SEER <sup>b</sup> , ICD-10)	C51–C58
	Secondary malignant neoplasm of the ovary (ICD-9)	198.6, 198.82
	Personal history of female genital cancer (ICD-9)	V10.40-V10.44
Surgery for a gynecologie	c malignancy	
	Pelvic evisceration (ICD-9)	68.8
	Radical trachelectomy, with bilateral total pelvic lymphadenectomy and para-aortic lymph node sampling biopsy, with or without removal of tube(s), with or without removal of ovary(s) ( $CPT^{C}$ )	57531
	Total abdominal hysterectomy, including partial vaginectomy, with para- aortic and pelvic lymph node sampling, with or without removal of tube(s), with or without removal of ovary(s) (CPT)	58200
	Radical abdominal hysterectomy, with bilateral total pelvic lymphadenectomy and para-aortic lymph node sampling (biopsy), with or without removal of tube(s), with or without removal of ovary(s) (CPT)	58210

Variable	Description of code	Code
	Pelvic exenteration for gynecologic malignancy, with total abdominal hysterectomy or cervicectomy, with or without removal of tube(s), with or without removal of ovary(s), with removal of bladder and ureteral transplantations, and/or abdominoperineal resection of rectum and colon and colostomy, or any combination thereof (CPT)	58240
	Laparascopy, surgical, with radical hysterectomy, with bilateral total pelvic lymphadenectomy and para-aortic lymph node sampling (biopsy), with removal of tube(s) and ovary(s), if performed (CPT)	58548
	Oophorectomy, partial or total, unilateral or bilateral; for ovarian, tubal or primary peritoneal malignancy, with para-aortic and pelvic lymph node biopsies, peritoneal washings, peritoneal biopsies, diaphragmatic assessments, with or without salpingectomy(s), with or without omentectomy (CPT)	58943
	Resection (initial) of ovarian, tubal or primary peritoneal malignancy with bilateral salpingo-oophorectomy and omentectomy (CPT)	58950–58952
	Bilateral salpingo-oophorectomy with omentectomy, total abdominal hysterectomy and radical dissection for debulking (CPT)	58953, 58954
	Bilateral salpingo-oophorectomy with total omentectomy, total abdominal hysterectomy for malignancy (CPT)	58956

<sup>a</sup>International Classification of Diseases 9<sup>th</sup> Revision

<sup>b</sup>Surveillance Epidemiology and End Results (SEER) program

<sup>C</sup>Current Procedural Terminology

# Highlights

In 2007 Group Health issued a clinical guideline recommending genetic counseling for women with possible inherited susceptibility to breast/ovarian cancer.

We compared bilateral oophorectomy rates, by surgical indication, among high risk women before and after the guideline was issued.

After the guideline, prophylactic oophorectomy rates were generally unchanged and rates of bilateral oophorectomies with other surgical indications were lower.

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#### Figure 1.

Annual age-adjusted rates (per 1,000 person-years) of bilateral oophorectomy, by type, Group Health, 2004–2009.a

<sup>a</sup> Total bilateral oophorectomies include all those identified from the administrative data, whether or not the surgical indication could be ascertained from the medical charts.

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#### Figure 2.

Annual age-adjusted and age-specific rates (per 1,000 person-years) of receipt of genetic counseling, Group Health, 2004–2009.

Age and distribution of characteristics suggestive of an inherited susceptibility to breast or ovarian cancer among the study cohort, Group Health, 2004–2009.

	No. of women N = 18,390 (%)
Age, (mean, SD <sup>2</sup> )	58 (13)
Age	
35–39	812 (4)
40-49	4,785 (26)
50–59	5,589 (30)
60–69	3,310 (18)
70–79	2,443 (13)
80	1,451 (8)
Personal history of breast cancer before 50 years of $age^{b}$	1,406 (8)
A strong family history of breast cancer <sup>b</sup>	13,436 (73)
1 first-degree relatives diagnosed before 50 years of $age^{C}$	7,638 (42)
3 first- or second-degree relatives diagnosed at any age $^{\mathcal{C}}$	5,143 (28)
2 second-degree relatives diagnosed before 50 years of age $^{\mathcal{C}}$	1,841 (10)
A male relative diagnosed with breast cancer at any $age^{\mathcal{C}}$	1,081 (6)
A strong family history of ovarian cancer <sup>b</sup>	3,017 (16)
2 first- or second-degree relatives diagnosed at any $age^d$	734 (4)
1 first- or second-degree relative diagnosed with ovarian cancer and 1 first- or second-degree relative diagnosed with breast cancer $^d$	2,508 (14)
A family history of both ovarian and breast cancer <sup><math>b</math></sup> (1 first-degree relatives diagnosed with both ovarian and breast cancer)	1,223 (7)

<sup>a</sup>SD, standard deviation

 $^{b}$ Characteristics are not mutually exclusive thus percent of women with these characteristics sums to greater than 100%.

 $^{c}$ Characteristics are not mutually exclusive thus percent of women in subgroups sums to greater than total.

 $^{d}$ Characteristics are not mutually exclusive thus percent of women in subgroups sums to greater than total.

Rates of bilateral oophorectomy (per 1,000 person-years), by type, before (2004–2007) and after (2007–2009) issuance of a clinical practice guideline on the referral of women to genetic counseling, Group Health.

	Jan. 2004–March 2007 N = 15,388 Person-years = 35,914	April 2007–Aug. 2009 N = 15,118 Person-years = 30,086
Type of bilateral oophorectomy	Mean follow-up = 2.3 years	Mean follow-up = 2.0 years
Prophylactic		
No. of women who had procedure	30	28
Age-adjusted rate (95% CI)	0.8 (0.5–1.1)	1.0 (0.6–1.3)
Age-adjusted rate difference (95% CI)		0.2 (-0.3-0.6)
Age-adjusted IRR <sup>a</sup> (95% CI)	1.0 (Ref)	1.2 (0.7–2.0)
Hysterectomy-treatable		
No. of women who had procedure	71	31
Age-adjusted rate (95% CI)	1.9 (1.4–2.3)	1.1 (0.7–1.4)
Age-adjusted rate difference (95% CI)		-0.8 (-1.40.2)
Age-adjusted IRR (95% CI)	1.0 (Ref)	0.6 (0.4–0.9)
Ovarian-indication		
No. of women who had procedure	46	25
Age-adjusted rate (95% CI)	1.3 (0.9–1.6)	0.8 (0.5–1.2)
Age-adjusted rate difference (95% CI)		-0.4 (-0.9-0.1)
Age-adjusted IRR (95% CI)	1.0 (Ref)	0.7 (0.4–1.1)
$\mathrm{Total}^{\mathcal{C}}$		
No. of women who had procedure	156	91
Age-adjusted rate (95% CI)	4.1 (3.5–4.8)	3.1 (2.5–3.7)
Age-adjusted rate difference (95% CI)		-1.0 (-2.00.1)
Age-adjusted IRR (95% CI)	1.0 (Ref)	0.7 (0.6–1.0) <sup>b</sup>

<sup>a</sup>Incidence rate ratio

 ${}^{b}_{p=0.026}$ 

 $^{c}$ Includes all bilateral oophorectomies identified from the administrative data, whether or not the surgical indication could be ascertained from the medical charts (n = 247 oophorectomies).

Rates (per 1,000 person-years) of receipt of genetic counseling before (2004–2007) and after (2007–2009) issuance of a clinical practice guideline on the referral of women to genetic counseling, Group Health.

	Jan 2004– March 2007	April 2007– August 2009
All ages		
No. of women	15,225	14,783
No. of women-yrs	35,334	29,154
No. of women who received genetic counseling	185	289
Age-adjusted rate (95% CI)	5.1 (4.3–5.8)	10.2 (9.0–11.4)
Age-adjusted rate difference (95% CI)		5.1 (3.7-6.5)
Age-adjusted IRR <sup>a</sup> (95% CI)	1.0 (Ref)	2.0 (1.7–2.4)
35–49 yrs of age		
No. of women	4,319	3,361
No. of women-yrs	7,471	5,005
No. of women who received genetic counseling	66	101
Rate (95% CI)	8.8 (6.9–11.2)	20.2 (16.6–24.5)
Rate difference (95% CI)		11.3 (6.9–15.8)
IRR (95% CI)	1.0 (Ref)	2.3 (1.7-3.1)
50–69 yrs of age		
No. of women	8,439	8,307
No. of women-yrs	18,138	15,351
No. of women who received genetic counseling	105	160
Rate (95% CI)	5.8 (4.8-7.0)	10.4 (8.9–12.2)
Rate difference (95% CI)		4.6 (2.7–6.6)
IRR (95% CI)	1.0 (Ref)	1.8 (1.4–2.3)
70+ yrs of age		
No. of women	4,063	4,343
No. of women-yrs	9,725	8,797
No. of women who received genetic counseling	14	28
Rate (95% CI)	1.4 (0.9–2.4)	3.2 (2.2–4.6)
Rate difference (95% CI)		1.7 (0.3–3.1)
IRR (95% CI)	1.0 (Ref)	2.2 (1.2-4.2)

<sup>a</sup>Incidence rate ratio

Rates of bilateral oophorectomy (per 1,000 person-years),<sup>*f*</sup> by receipt of genetic counseling and genetic testing, Group Health, 2004–2009

	35–49 years of age	50–69 years of age	70 years of age	All ages
All women				
No. of women	5482	10584	4965	18,161
Person-years	12724	34007	18615	65,346
No. of women who had the procedure	87	117	15	219
Rate (95% CI)	6.8 (5.5-8.4)	3.4 (2.9–4.1)	0.8 (0.5–1.3)	3.4 (2.9–3.8)
Age-adjusted rate (95% CI)				3.3 (2.9–3.7)
No genetic counseling				
No. of women	5482	10544	4949	18161
Person-years	12477	33490	18522	64489
No. of women who had the procedure	74	92	14	180
Rate (95% CI)	5.9 (4.7–7.4)	2.8 (2.2–3.4)	0.8 (0.4–1.3)	2.8 (2.4–3.2)
Age-adjusted rate (95% CI)				2.8 (2.4–3.2)
After genetic counseling				
No. of women	167	295	58	474
Person-years	248	517	93	858
No. of women who had the procedure	13	25	1	39
Rate (95% CI)	52.5 (30.5–90.4)	48.4 (32.7–71.6)	10.8 (1.5-76.5)	45.5 (33.2–62.3)
Age-adjusted rate (95% CI)				38.2 (25.7–50.7)
No genetic testing (prior genetic counseling	ng) <sup>a</sup>			
No. of women	85	157	33	254 <sup>b</sup>
Person-years	104	234	47	385
No. of women who had the procedure	4	7	1	12
Rate (95% CI)	38.4 (14.4–102.3)	29.9 (14.3-62.8)	21.5 (30.3–152.6)	31.2 (17.7–55.0)
Age-adjusted rates (95% CI)				29.0 (11.1-46.9)
After genetic testing (prior genetic counse	eling) <sup>C</sup>			
No. of women	99	181	32	287
Person-years	144	284	46	474
No. of women who had the procedure	9	18	0	27
Rate (95% CI)	62.6 (32.6–120.3)	63.4 (39.9–100.6)	0 (-)	56.9 (39.0-83.0)
Age-adjusted rate (95% CI)				44.9 (28.3–61.5)
After a non-positive test result for breast/o	ovarian cancer risk <sup>d</sup>			
No. of women	85	156	27	247
Person-years	120	250	41	411
No. of women who had the procedure	4	9	0	13
Rate (95% CI)	33.2 (12.4-88.6)	36.0 (18.8–69.3)	0 (-)	31.6 (18.4–54.4)
Age-adjusted rate (95% CI)				25.1 (11.6–38.5)

After a positive test result for breast/ovarian cancer  $\mathrm{risk}^d$ 

	35–49 years of age	50–69 years of age	70 years of age	All ages
No. of women	10	15	1	26 <sup>e</sup>
Person-years	14	15	3	31
No. of women who had the procedure	5	9	0	14
Rate (95% CI)	363.5 (151.3-873.3)	613.3 (319.1–1,178.7)	0 (-)	447.1 (264.8–754.9)
Age-adjusted rate (95% CI)				387.8 (177.0–598.7)

<sup>a</sup>No genetic testing of any type

 $b_{\rm This}$  number differs from 474 because 214 women had testing on the same day as their genetic counseling encounter and 6 women had genetic testing done before their genetic counseling encounter. Thus these 220 women did not contribute any person-time.

<sup>c</sup>After genetic testing of any type

 $^{d}_{BRCA}$  mutation, Lynch Syndrome, or mutations in the genes *PTEN* or *p53* 

 $e_{All}$  women were positive for a BRCA mutation

f Includes all bilateral oophorectomies identified from administrative data, whether or not the surgical indication could be ascertained from the medical charts, among women without prior genetic counseling (n = 219 oophorectomies).