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Impact of genetic testing on endometrial cancer risk-reducing practices in women at risk for Lynch syndrome

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Abstract

OBJECTIVE—Due to the increased lifetime risk of endometrial cancer (EC), guidelines recommend that women with Lynch syndrome (LS) age ≥35 undergo annual EC surveillance or prophylactic hysterectomy (PH). The aim of this study was to examine the uptake of these risk-reducing strategies.

METHODS—The study population included women meeting clinical criteria for genetic evaluation for LS. Data on cancer risk-reducing behaviors were collected from subjects enrolled in two distinct studies: (1) a multicenter cross-sectional study involving completion of a one-time questionnaire, or (2) a single-center longitudinal study in which subjects completed questionnaires before and after undergoing genetic testing. The main outcome was uptake of EC risk-reducing practices.

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RESULTS—In the cross-sectional cohort, 58/77 (75%) women at risk for LS-associated EC reported engaging in EC risk-reduction. Personal history of genetic testing was associated with uptake of EC surveillance or PH (OR 17.1; 95% CI 4.1–70.9). Prior to genetic testing for LS, 26/40 (65%) women in the longitudinal cohort reported engaging in EC risk-reduction. At one-year follow-up, 16/16 (100%) mismatch repair (MMR) gene mutation carriers were adherent to guidelines for EC risk-reduction, 9 (56%) of whom had undergone PH. By three-year follow-up, 11/16 (69%) MMR mutation carriers had undergone PH. Among women with negative or uninformative genetic test results, none underwent PH after testing.

CONCLUSIONS—Genetic testing for LS is strongly associated with uptake of EC risk-reducing practices. Women found to have LS in this study underwent prophylactic gynecologic surgery at rates comparable to those published for *BRCA1/2* mutation carriers.

INTRODUCTION

Lynch syndrome (LS), also known as hereditary nonpolyposis colorectal cancer (HNPCC), is a highly-penetrant genetic condition associated with an increased risk of gastrointestinal, gynecologic, and other malignancies.[1–6] Individuals with LS carry a germline mutation in one of the DNA mismatch repair (MMR) genes (*hMLH1, hMSH2, hMSH6*, *hPMS2*, and *TACSTD1*).[7–12] After colorectal carcinoma (CRC), endometrial carcinoma (EC) is the second most common LS-associated malignancy among female mutation carriers, and 2% of all EC diagnoses are attributable to LS.[1–3, 13–15] Prior studies have estimated that women with LS have a 16–71% lifetime risk of EC with a median age of diagnosis below 50 years.[1, 2, 12–15]

Published guidelines recommend that women with LS undergo annual EC surveillance with endometrial biopsy and/or transvaginal ultrasound (TVUS) starting at age 30–35, and/or consider prophylactic hysterectomy (PH) after the completion of childbearing.[16–18] Although prior studies have suggested that women with LS underestimate their risk for extracolonic cancers compared to CRC,[19] there are few data regarding the uptake of EC risk-reducing strategies. The aim of our study was to examine factors associated with uptake of EC risk-reduction practices among women at risk for LS-associated EC.

METHODS

We conducted a survey of health behaviors in two distinct cohorts of patients:

Cohort 1 – Multicenter cross-sectional cohort

Individuals with a personal or family history of cancer fulfilling Bethesda guidelines[20] for evaluation of LS were identified through cancer genetics clinics at four different sites (Dana-Farber Cancer Institute, Boston, MA; Massachusetts General Hospital Cancer Center, Boston, MA; University of California San Francisco, San Francisco, CA; and University of Michigan, Ann Arbor, MI) between 2002–2006. Potential subjects included individuals who personally visited one of the clinics or who were referred to the study by a family member who had been seen at one of the clinics. Participants were limited to those ≥18 years of age who could read and write in English. Subjects completed a onetime written self-administered questionnaire, which collected standard demographic information as well as data regarding their medical history, family history, cancer surveillance practices, and personal history of genetic evaluation.[21] All subjects provided informed consent and the study was approved by the Institutional Review Board at all participating sites.

Cohort 2 – Single-center longitudinal cohort

Individuals referred for genetic testing for LS at a single center (Dana-Farber Cancer Institute, Boston, MA) were invited to enroll in a prospective longitudinal study between 2003–2009. Eligible subjects included individuals ≥18 years of age who met clinical criteria for evaluation for LS and chose to proceed with genetic testing. Participants completed self-administered questionnaires prior to genetic testing, and at one-year intervals for up to three years after the disclosure of test results. All individuals who underwent genetic testing met with a physician and genetic counselor before testing and received additional counseling following the disclosure of test results. For subjects whose testing confirmed a diagnosis of LS, post-test counseling included discussion about the risks of LS-associated malignancies, recommendations about cancer surveillance guidelines, and discussion about potential surgical options to reduce cancer risks. All subjects provided informed consent and the study was approved by the Dana-Farber Cancer Institute's Institutional Review Board.

In addition to standard demographic information, questionnaires collected data regarding participants' medical history, use of specific cancer screening practices (including colonoscopy, TVUS, and endometrial biopsy), and prior surgical history. Subjects reporting a prior hysterectomy and/or salpingo-oophorectomy (BSO) were asked whether these had been performed "for cancer prevention," "for cancer treatment," or "for reasons other than cancer treatment or prevention." Annual follow-up questionnaires asked if participants had undergone any screening tests and/or surgeries in the preceding 12 months. At baseline, participants provided a detailed family history, including specific cancer diagnoses among first-, second-, and third-degree relatives. Subjects were asked whether any family member had previously had genetic testing which identified a pathogenic MMR gene mutation.

Study population

Subjects in both cohorts were considered to be at risk for LS if their family history (1) fulfilled Amsterdam I or II criteria[22, 23] or (2) included a known, pathogenic MMR gene mutation. Cohort 1 participants with a personal history of prior genetic testing confirming that they did not carry the family's known MMR gene mutation ("true negative" test results) were excluded; individuals in Cohort 2, by definition, had not had prior genetic testing for LS. For the purposes of examining risk-reducing behaviors among women at risk for LS-associated EC, subjects were excluded if they had previously been diagnosed with EC and/or reported having a prior hysterectomy for reasons other than cancer prevention.

Outcomes

For both cohorts, the primary outcome measure of uptake of EC risk-reduction was defined as having had at least one of the following: (1) a prophylactic hysterectomy ("for cancer prevention"), (2) annual surveillance endometrial biopsy, or (3) annual TVUS. Women age ≥35 who did not undergo at least one of these procedures were classified as not engaging in EC risk-reduction. Since published guidelines[16–18] recommend that women with LS initiate EC surveillance between ages 30–35, all women age <35 in our cohorts were classified as engaging in EC risk-reduction. Since all subjects were considered to be at risk for having LS, adequate CRC surveillance was defined as undergoing colonoscopy at least every 2 years for individuals age >25.

Statistical analysis

Potential relationships between clinical and demographic factors and uptake of EC risk-reduction were examined using univariate tests of association (Fisher's exact and *t*-tests). Age was studied as both a continuous and categorical (<40, 40–49, and ≥50 years old) variable. Factors found to be statistically significant on univariate analysis were considered

for inclusion in multivariable logistic regression models in order to detect those with an independent association with uptake of EC risk-reduction. Generalized estimating equations were used to account for potential clustering of results among members of the same family. Analyses were performed using SAS Version 9.1 (Cary, NC) software. All *p*-values were two-sided and *p*-values <0.05 were considered statistically significant.

RESULTS

Cohort 1

Two-hundred seventy (58%) of the 462 potentially eligible individuals who were invited to participate in the study due to a personal and/or family history fulfilling Bethesda guidelines[20] completed the one-time questionnaire.[21] Of these, 77/270 (29%) were at risk for LS-associated EC (Figure 1) and were included in the analysis. Subject demographics, personal history and health practices, family history, and prior genetic evaluation data are presented in Table 1.

Overall, 58/77 (75%) women at risk for LS-associated EC reported engaging in EC risk-reduction with 42 reporting annual EC surveillance with TVUS and/or endometrial biopsy, and 16 reporting having undergone PH. Twelve (75%) of the 16 women who had PH carried a pathogenic MMR gene mutation. Compared to those reporting annual EC surveillance, women who had undergone PH were more likely to have had a prior cancer diagnosis (non-EC) (p=0.02) and be compliant with CRC surveillance (p=0.03). Only one woman under age 40 had undergone PH.

Factors associated with uptake of EC risk-reduction on univariate analysis (Table 2) included having visited a cancer genetics/high-risk clinic (p=0.01), having undergone genetic testing (p<0.01), testing positive for a pathogenic MMR gene mutation (p=0.04), having a known pathogenic MMR gene mutation in the family (p=0.01), and uptake of LS-specific guidelines for colonoscopic surveillance (p=0.03). Subjects' educational level, income, marital status, health insurance carriage, personal history of cancer, and family history of EC were not significantly associated with uptake of EC risk-reduction.

In our multivariable logistic regression, the final model was limited to two variables due to constraints imposed by the cohort's size. We used "genetic testing status" ("have had genetic testing" versus "have not had genetic testing") as a surrogate for other correlated variables that were found to have a significant association on univariate analysis ("genetic testing status", "genetic test result", "visit to a high-risk clinic", and "known mutation in the family") to avoid overfitting the model. Controlling for subject age, "genetic testing status" remained strongly associated with uptake of EC risk-reduction (OR 17.1, 95% CI 4.1–70.9; p<0.01). Age as a categorical variable (<40, 40–49, and ≥50 years old) was not significant on multivariable analysis (p=0.10).

Cohort 2

Of the 162 subjects who completed a baseline questionnaire prior to genetic testing for LS, 40 (25%) were at risk for LS-associated EC (Figure 1) and included in the analysis. Subject demographics, medical history and health practices, family history, and prior genetic evaluation data are presented in Table 1.

Of these 40 women, 26 (65%) engaged in EC risk-reduction prior to undergoing genetic testing for LS: 6 (15%) reported a prior PH, 13 (33%) were undergoing annual EC surveillance with TVUS and/or endometrial biopsy, and an additional 7 (18%) were age <35 and had not reached the age at which EC surveillance or prophylactic surgery would be recommended (Figure 2A).

Genetic test results were available for all 40 women. Sixteen (40%) were found to carry a pathogenic MMR gene mutation ("positive" results), 9 (23%) tested negative for their family's known mutation ("true negative" results), 14 (35%) had indeterminate results, and 1 (3%) was found to have a variant of uncertain significance. At the time of analysis, one-, two-, and three-year follow-up questionnaires were available on 30 (75%), 21 (53%), and 8 (20%) of the 40 subjects, respectively. No subjects reported being diagnosed with EC at any of the follow-up intervals.

At one-year follow-up after genetic testing, all 16 MMR gene mutation carriers were adherent to EC risk-reducing guidelines. Four (25%) of the 16 mutation carriers had undergone PH prior to testing, 5 (31%) underwent PH in the year following testing (4 of whom had reported no EC surveillance at baseline), 5 (31%) reported undergoing EC surveillance in the year after testing, and the remaining 2 (13%) were under age 35 (Figure 2A–C). Three mutation carriers did not return one-year questionnaires but were still considered adherent to EC risk-reducing guidelines since two of them had undergone PH prior to genetic testing and the third would have been 23 years old at the time of one year follow-up. By three-year follow-up, an additional 2 subjects reported having undergone PH, thereby giving a cumulative total of 11/16 (69%) mutation carriers who underwent PH (Figure 2B).

Four (27%) of the 15 women found to have indeterminate or variant genetic test results reported engaging in EC risk-reduction at one-year follow-up with 3 (20%) having annual EC surveillance (1 of whom was not having EC surveillance at baseline) and 1 (7%) having undergone PH prior to testing. None reported having undergone PH on follow-up.

One (11%) of the 9 women who received "true negative" test results reported continuing her EC surveillance in the year after testing. Although 1/9 (11%) had undergone PH prior to testing, none of the remaining women who received "true negative" results underwent PH on follow-up.

DISCUSSION

Our study found that uptake of interventions to reduce EC risk is high among women at risk for LS. In the cross-sectional cohort, personal history of genetic testing was strongly associated with uptake of surveillance and/or prophylactic surgery for EC risk-reduction. In our longitudinal cohort, all subjects confirmed to carry a MMR gene mutation were compliant with guidelines for EC risk-reduction in the first year after genetic testing, with nearly 70% opting for PH by three-year follow-up. In contrast, the majority of women who received negative or uninformative genetic test results did not continue EC surveillance and none underwent PH. We believe that our study provides an important and updated contribution to our understanding of how women at risk for LS-associated EC choose to manage this risk, since the increase in EC risk-reduction was driven largely by uptake of PH among mutation carriers.

Most of the existing data regarding the uptake of prophylactic gynecologic surgery among women with hereditary cancer syndromes come from studies of *BRCA1* and *BRCA2* gene mutation carriers. Women with such mutations have an estimated 18–62% lifetime risk of ovarian, fallopian tube, and primary peritoneal cancer.[24–26] Although gynecologic cancer surveillance is considered to be ineffective, studies have shown that prophylactic BSO significantly reduces the risk of gynecologic cancer, and women with *BRCA1/2* mutations are thus counseled to undergo BSO at age 35–40.[24–29] In a prospective, multi-center, United States study, Kauff et al reported that 509/792 (64%) *BRCA1/2* mutation carriers underwent prophylactic BSO after genetic testing, with most having surgery in the year

following testing.[30] Numerous smaller studies have described similar rates of uptake of prophylactic BSO among *BRCA1/2* mutation carriers after genetic testing.[31, 32] In our own cohort of women undergoing genetic testing for *BRCA1/2* mutations (studied in parallel with the longitudinal cohort (Cohort 2) reported here), we found that 18/30 (60%) *BRCA1/2* mutation carriers underwent prophylactic BSO in the year following testing (unpublished data).

Prior studies examining the uptake of EC risk-reducing behaviors among women with LS have observed comparably lower rates of prophylactic gynecologic surgery. In a cohort of 17 Australian women confirmed to have LS between 1998–2002, Collins et al reported that 0, 8 (47%), and 9 (53%) went on to have PH, TVUS, and endometrial biopsy, respectively, in the year following genetic testing.[33] In a study of 103 Finnish women found to carry a MMR gene mutation between 1995–1999 and managed through a centralized registry, Jarvinen at el found that 97% of their cohort had EC surveillance at some point after genetic testing.[5] By a median follow-up of 11 years after testing, 48/103 (47%) had undergone a hysterectomy, although half of these might not be considered prophylactic in nature since they were performed for management of specific gynecologic diagnoses, including ovarian cancer and endometrial hyperplasia.[5] By contrast, in the only prior study of EC risk-reducing practices among women with LS in the United States, Hadley et al found that, among a cohort of 28 women confirmed to have LS on genetic testing performed between 1997–2002, only 2 (7%) and 15 (54%) underwent PH and EC surveillance, respectively, after testing.[19]

With nearly 70% of genetically-confirmed women with LS in our longitudinal cohort undergoing PH, our study population had a strikingly higher rate of prophylactic gynecologic surgery compared to prior reports, with an uptake comparable to what has been described among *BRCA1/2* mutation carriers. While this high uptake of PH could simply be a result of institutional bias, an alternate hypothesis is that our findings reflect an evolving understanding as to how women with LS can best reduce their risk of EC. Numerous studies over the past decade have failed to demonstrate any meaningful efficacy from EC surveillance in women with LS with regards to cancer detection or survival outcomes.[34–40] A recent systematic literature review[40] concluded that available published data are insufficient to provide evidence-based recommendations about the benefit of EC surveillance in women with LS, due to the observational nature of most of the relevant studies, their lack of a control group, and a paucity of information on subjects' compliance with surveillance.[34–38] Likewise, guidelines put forth by the National Comprehensive Cancer Network (NCCN) cite a lack of evidence to support routine EC surveillance in women with LS.[41]

While the value of EC surveillance in women with LS remains unproven, evidence supporting the efficacy of prophylactic gynecologic surgery continues to emerge. Most notably, in their landmark 2006 study, Schmeler et al reported that 0/61 women with LS in a retrospective cohort were diagnosed with EC after undergoing PH (with or without BSO), whereas 69/210 (33%) women who had not had prophylactic surgery were eventually diagnosed with EC.[42] Although subsequent data have shown that PH with BSO is not 100% protective against LS-associated gynecologic cancer,[43] this nonetheless remains the strongest evidence to date supporting the efficacy of prophylactic gynecologic surgery in LS. Furthermore, recent cost-effectiveness analyses have supported the use of PH as a primary component of the management of women with LS.[44, 45]

Our study's main strength is its use of both cross-sectional and longitudinal designs for studying the behaviors of women at risk for LS-associated EC. Our cross-sectional cohort enabled us to identify that having had genetic testing was strongly associated with uptake of

EC risk-reduction, and then our longitudinal cohort allowed us to prospectively study the impact of genetic testing on medical decision-making among women at risk for LS and demonstrate the sustainability of this effect through three years of follow-up.

We recognize that our study has limitations. Although our sample size is comparable to prior studies of women with LS, our cohorts' small size hinders our ability to detect significant associations between various clinical factors and the uptake of EC risk-reducing practices. The study's questionnaire format is also inherently reliant on subjects' self-reporting of their health behaviors, and we were unable to verify their accuracy by medical record review. Our study population was demographically homogeneous with a significant majority having health insurance, a college education, and relatively high income, and was presumably enriched with highly-motivated subjects with a particular interest in their personal and/or family history of cancer. We also recognize that LS-associated EC is generally a much less lethal disease than *BRCA1/2*-associated gynecologic cancer, which could theoretically lead to a higher degree of institutional variability in how patients' LS-associated gynecologic cancer risk is managed. We acknowledge that using Amsterdam criteria to define subjects at risk for LS is likely to also capture individuals with Familial Colorectal Cancer Type X who would not be at increased risk of gynecologic cancer.[46] Uncertainty regarding EC risk along with questions regarding the effectiveness of EC screening may have contributed to a lower uptake of EC risk-reducing measures among women without a genetically-confirmed diagnosis.

In summary, women at risk for LS-associated EC are more likely to follow published EC risk-reduction guidelines if they have undergone genetic testing. Among women confirmed to carry a pathogenic MMR gene mutation in our study, adherence to guidelines was high with nearly 70% opting for PH by three years after genetic testing. The uptake of PH among women with LS in our study is markedly higher than in previous reports, but is comparable to rates of prophylactic BSO among *BRCA1/2* carriers. We hypothesize that these findings might reflect an emerging trend of prophylactic surgery, rather than cancer surveillance, being the preferred method of gynecologic cancer risk-reduction among women with LS.

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Highlights

- We studied endometrial cancer risk-reducing practices in women at risk for LS.
- Having genetic testing for LS is strongly associated with adherence to guidelines.
- Women confirmed to have LS have high uptake of prophylactic hysterectomy.

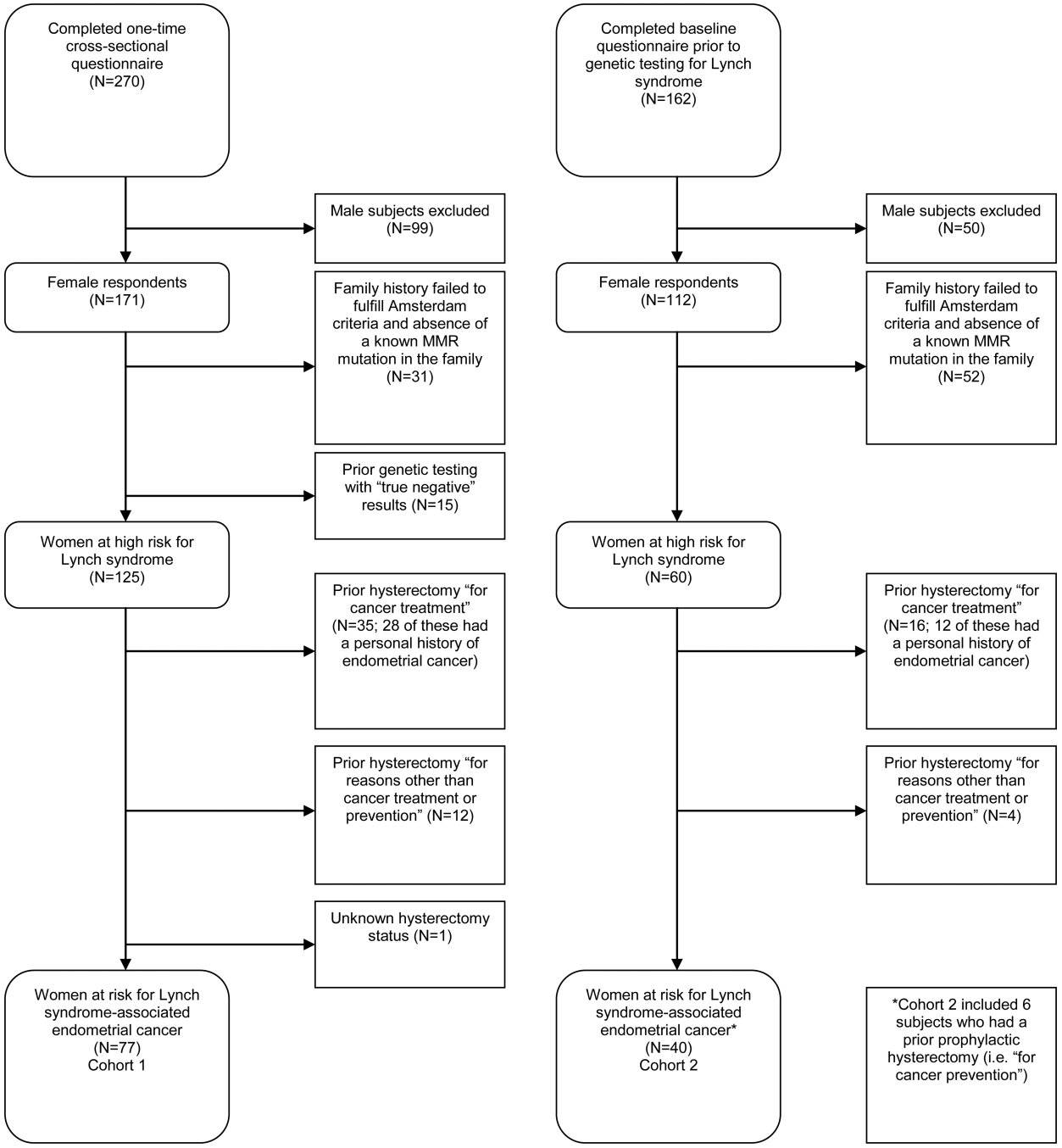
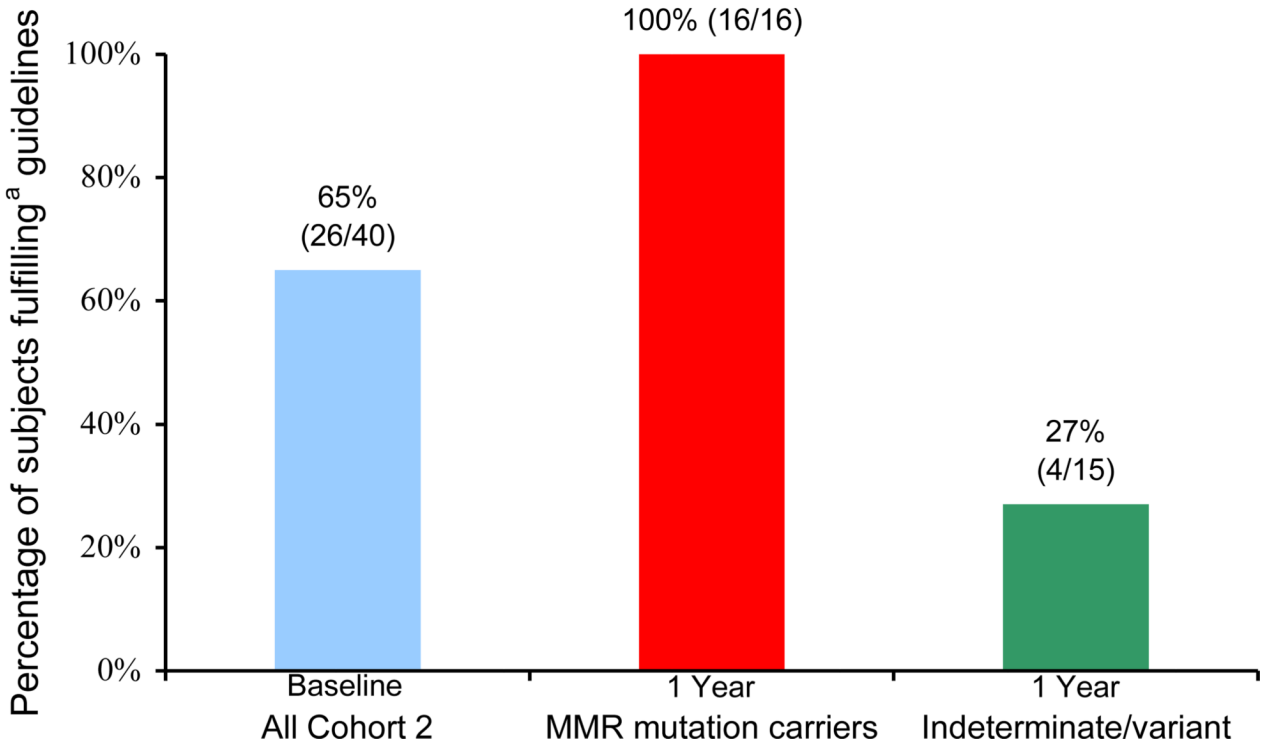


Figure 1.
CONSORT diagram for Cohort 1 and Cohort 2.

A



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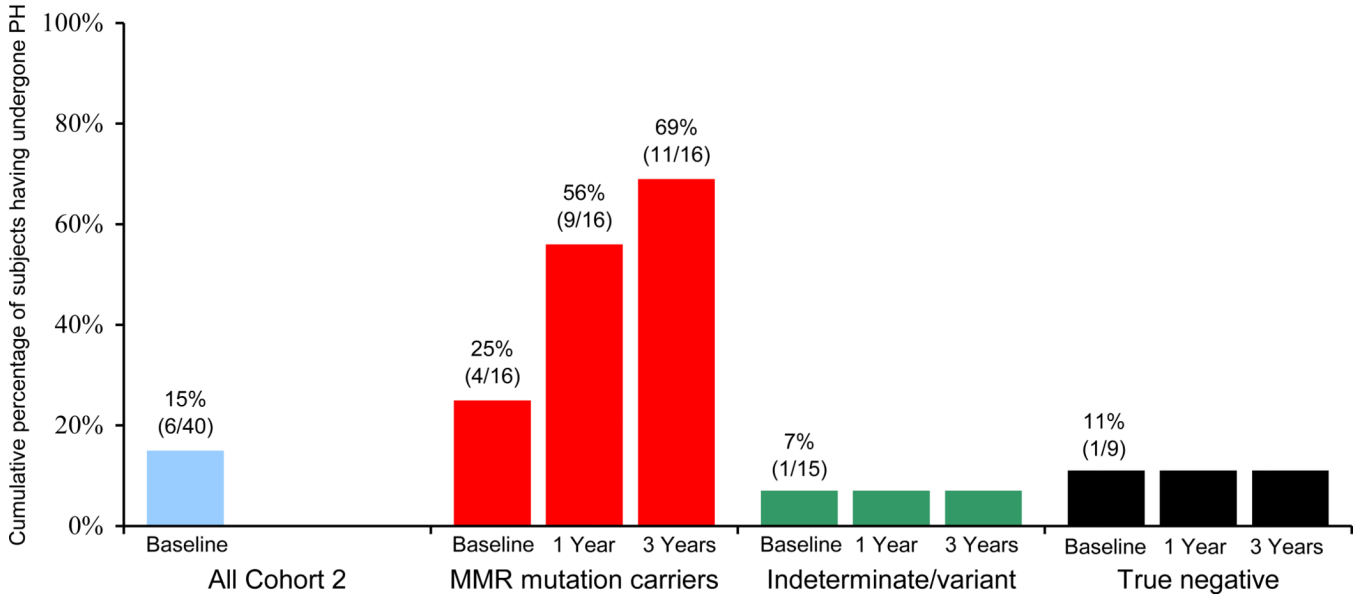

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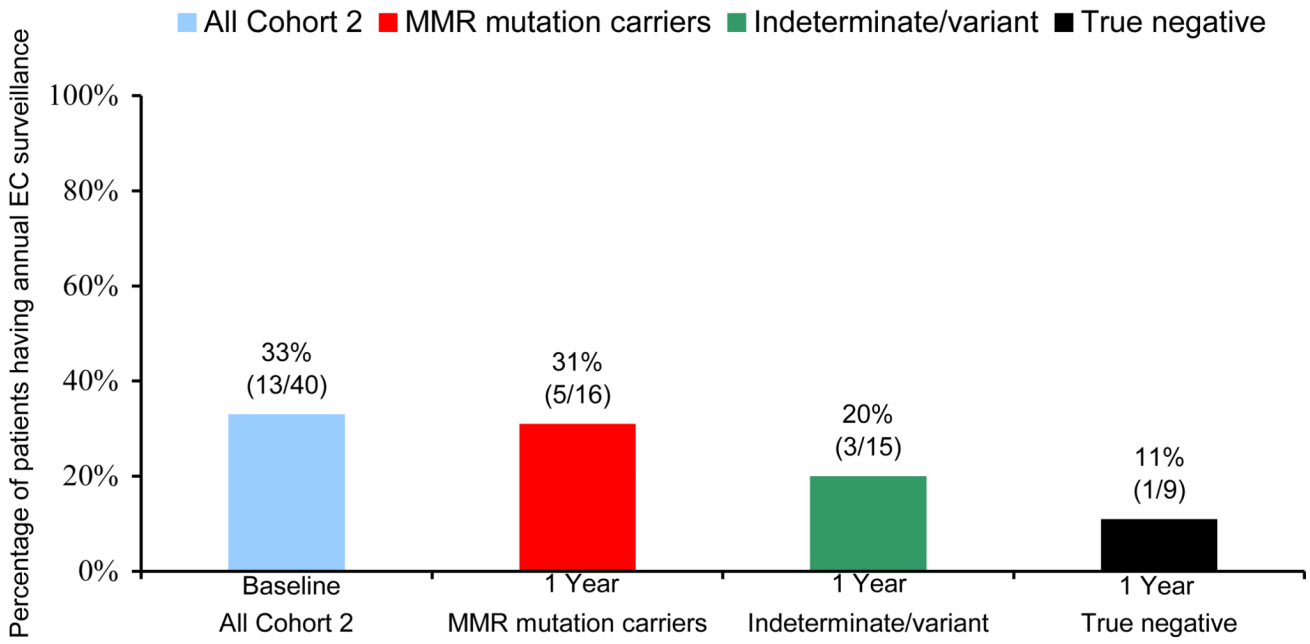

Figure 2.

Endometrial cancer (EC) risk-reducing practices in a longitudinal cohort of women before and after genetic testing for Lynch syndrome. (A) Overall percentage of subjects engaging in EC risk-reductiona at baseline and one yearb after genetic testing. (B) Cumulative rates of prophylactic hysterectomy (PH) at baseline and at one- and three-year follow-up. (C) Rates of annual EC surveillance at baseline and at one-year follow-up.

[a] "Engaging in EC risk-reduction" defined as either (1) having had a PH, (2) reporting annual EC surveillance by transvaginal ultrasound and/or endometrial biopsy, and/or (3) age <35 years old.

[b] Uptake in EC risk-reduction at one-year follow-up is not reported for subjects found to have "true negative" genetic test results, since they would no longer be considered at risk for Lynch-associated EC.

Table 1

Demographics of two distinct cohort of women at high risk for Lynch syndrome (LS) -associated endometrial cancer (EC)

Variable	Cohort 1 (cross-sectional cohort) N=77 Number (column %)	Cohort 2 at baseline (longitudinal cohort) N=40 Number (column %)
Demographics		
Mean age (range)	41.4 (20–70)	43.6 (20–70)
<40 Years old	35 (45)	13 (33)
40–49 Years old	24 (31)	18 (45)
≥50 Years old	17 (22)	9 (23)
Unknown/missing	1(1)	0 (0)
Educational level		
Less than college graduate	23 (30)	3 (8)
At least college graduate	54 (70)	26 (90)
Unknown/missing	0 (0)	1 (3)
Annual income		
<$50,000	15 (19)	5 (13)
>$50,000	57 (74)	33 (83)
Unknown/missing	5 (6)	2 (5)
Marital status		
Married	58 (75)	30 (75)
Not married	18 (23)	9 (23)
Unknown/missing	1 (1)	1 (3)
Health insurance		
Yes	76 (99)	40 (100)
No	1 (1)	0 (0)
Personal history and health practices		
Personal cancer history		
Have had any cancer	30 (39)	17 (43)
Have not had any cancer	47 (61)	22 (55)
Unknown/missing	0 (0)	1 (3)
Personal colorectal cancer (CRC) history		
Have had CRC	27 (35)	9 (23)
Have not had CRC	50 (65)	31 (78)
Physician visits in the past year		
0	1 (1)	1 (3)
1–6	58 (75)	26 (65)
≥7	18 (23)	11 (28)
Unknown/missing	0 (0)	2 (5)
Physician discussed cancer risk		
Yes	66 (86)	33 (83)

Variable	Cohort 1 (cross-sectional cohort) N=77 Number (column %)	Cohort 2 at baseline (longitudinal cohort) N=40 Number (column %)
No	11 (14)	7 (18)
CRC surveillance practices[a]		
Adequate CRC surveillance[a]	55 (71)	21 (53)
Inadequate CRC surveillance[a]	22 (29)	19 (48)
Family history		
Fulfills Amsterdam Criteria		
Yes	65 (84)	33 (83)
No	12 (16)	7 (18)
Known MMR mutation in the family		
Yes	49 (64)	19 (48)
No	28 (36)	21 (53)
Family history of any LS cancer		
Yes	73 (95)	39 (98)
No	4 (5)	1 (3)
1st/2nd degree relative with EC		
Yes	33 (43)	16 (40)
No	44 (57)	24 (60)
Genetic evaluation		
Visited high-risk clinic		
Yes	64 (83)	40 (100)
No	13 (17)	0 (0)
Genetic testing status		
Had genetic testing	58 (75)	0 (0)
Have not had genetic testing	19 (25)	40 (100)
Genetic test result		
Positive	45 (58)	0 (0)
Indeterminate/variant	13 (17)	0 (0)
True negative	0 (0)	0 (0)
Have not had genetic testing	19 (25)	40 (100)

[a]"Adequate colorectal cancer surveillance" defined as having colonoscopy at least every 2 years or being age <25

Table 2

Factors associated with fulfillment of endometrial cancer (EC) risk-reducing guidelines[a] among women at risk for Lynch syndrome (LS)-associated EC (Cohort 1 - cross-sectional cohort)

Variable	Fulfilling guidelines [a] Number (row %)	Not fulfilling guidelines [a] Number (row %)	*P* value[b]
Total cohort 1 (N=77)	58 (75)	19 (25)	
Demographics			
Mean age (± SD)	39.5 ± 11.1	47.3 ±9.9	0.01
<40 Years old	30 (86)	5 (14)	0.04
40–49 Years old	18 (75)	6 (25)	
≥50 Years old	9 (53)	8 (47)	
Unknown/missing	1(--)	0(--)	
Educational level			
Less than college graduate	14 (61)	9 (39)	0.08
At least college graduate	44 (81)	10 (19)	
Annual income			
<$50,000	12 (80)	3 (20)	0.75
≥$50,000	42 (74)	15 (26)	
Unknown/missing	4(--)	1(--)	
Marital status			
Married	46 (79)	12 (21)	0.13
Not married	11 (61)	7 (39)	
Unknown/missing	1 (--)	0 (--)	
Personal history and health practices			
Personal cancer history			
Have had any cancer	25 (83)	5 (17)	0.28
Have not had any cancer	33 (70)	14 (30)	
Personal colorectal cancer (CRC) history			
Have had CRC	22 (81)	5 (19)	0.42
Have not had CRC	36 (72)	14 (28)	
Physician visits in the past year			
0	1 (100)	0 (0)	0.82
1–6	44 (76)	14 (24)	
≥7	13 (72)	5 (28)	
Physician discussed cancer risk			
Yes	48 (73)	18 (27)	0.28
No	10 (91)	1 (9)	
CRC surveillance practices[c]			
Adequate CRC surveillance[c]	47 (85)	8 (15)	0.03

Variable	Fulfilling guidelines [a] Number (row %)	Not fulfilling guidelines [a] Number (row %)	*P* value[b]
Inadequate CRC surveillance[c]	11 (50)	11 (50)	
Family history			
Fulfills Amsterdam			
Criteria			
Yes	48 (74)	17 (26)	0.72
No	10 (83)	2 (17)	
Known MMR mutation in the family			
Yes	42 (86)	7 (14)	0.01
No	16 (57)	12 (43)	
1st/2nd degree relative with EC			
Yes	27 (82)	6 (18)	0.30
No	31 (70)	13 (30)	
Genetic evaluation			
Visited high-risk clinic			
Yes	52 (81)	12 (19)	0.01
No	6 (46)	7 (54)	
Genetic testing status			
Had genetic testing	51 (88)	7 (12)	<0.001
Have not had genetic testing	7 (37)	12 (63)	
Genetic test result			
Positive	42 (93)	3 (7)	0.04
Indeterminate/variant	9 (69)	4 (31)	

[a] "Fulfilling guidelines" defined as either (1) having had a prophylactic hysterectomy, (2) reporting annual EC surveillance by transvaginal ultrasound and/or endometrial biopsy, and/or (3) age <35 years old

[b] Fisher's exact test was used for categorical values, and *t*-test was used for continuous variables

[c] "Adequate colorectal cancer surveillance" defined as having colonoscopy at least every 2 years or being age <25