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Modified panel-based genetic counseling for ovarian cancer susceptibility: A randomized non-inferiority study☆,☆☆

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HIGHLIGHTS

- We evaluated a modified pre-test genetic counseling (GC) model for women undergoing panel-based genetic testing.
- Time spent with a genetic counselor was shorter in the modified pre-test GC compared to traditional pre-test GC.
- Modified pre-test GC was non-inferior to traditional GC on psychosocial outcomes, ovarian cancer knowledge and satisfaction.
- Our modified pre-test GC model provides an efficient and efficacious alternative for individuals undergoing panel testing.
- Further research in a more diverse population and individuals being referred for clinical pre-test GC is needed.

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ABSTRACT

Objective. Genetic testing identifies cancer patients who may benefit from targeted treatment and allows for enhanced cancer screening and risk-reduction in their at-risk relatives. Traditional models of genetic counseling (GC) cannot meet the increasing demand and urgency for genetic testing. The objective of this study was to evaluate a new model of service delivery to improve the efficiency of pre-test GC for panel-based genetic testing.

Methods. A parallel, two-armed, randomized non-inferiority study compared traditional and modified pre-test GC models (1:2) prior to panel-based genetic testing. Participants were adult females, whose first-degree relative died of serous ovarian cancer. In the modified group, participants were emailed a 20-minute presentation prior to a scheduled pre-test GC telephone call. Psychosocial and knowledge questionnaires were provided at baseline (P1) and one week after pre-test GC (P2).

Results. 382 women completed pre-test GC (256 modified, 126 traditional). There were no differences in marital status, education level or household income. Pre-test GC time was shorter in the modified group (average 19 vs. 46 min, $p < 0.001$), with no difference in post-test GC time (average 16 min each, $p = 0.78$). The modified pre-test GC model was found to be non-inferior to traditional GC on measures of cancer-specific distress, depression, anxiety, decisional conflict, ovarian cancer knowledge and satisfaction. Perceived lifetime risk for ovarian cancer decreased to a lesser extent from baseline in women who received modified pre-test GC.

Conclusions. A 20-minute presentation prior to pre-test telephone GC is non-inferior to traditional in-person GC on all variables tested, except for perceived ovarian cancer risk. This modified model improved GC efficiency

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without negatively affecting psychosocial outcomes, providing an alternative strategy to meet the growing demand for genetic testing.

1. Introduction

More than 300,000 women per year in the United States and Canada are diagnosed with breast or ovarian cancer [1,2]. Up to 10% of breast [3] and 30% of ovarian [4–6] cancers are hereditary. Individuals with *BRCA1/2* gene mutations face lifetime risks of ovarian (17–44%) and breast (69–71%) cancers [7]; however, knowledge of their *BRCA1/2* status can provide women with opportunities for personalized cancer treatment or risk reduction. For example, genetic testing may inform treatment and provide survival benefits for women with *BRCA1/2*-related breast cancer who undergo bilateral mastectomy [8,9] and for those with *BRCA1/2* breast/ovarian cancers treated with poly-ADP ribose polymerase (PARP) inhibitors [10,11]. Genetic testing also provides unaffected relatives with opportunities to identify cancer risk and obtain recommendations for enhanced cancer screening and risk-reduction. High risk breast cancer screening, involving annual breast MRI and mammograms, detect the majority of breast cancers at an early stage. In one study of *BRCA1/2* carriers undergoing enhanced surveillance, 97% of screen-detected breast cancers were detected at stage 0-I [12]. *BRCA1/2* carriers may also reduce their breast cancer risk by pursuing prophylactic bilateral mastectomy. A recent meta-analysis reported a significant reduction in breast cancer risk after prophylactic bilateral mastectomy in *BRCA1/2* carriers (RR = 0.11) [13]. A recent simulation by Giannakeas and Narod also reported a substantial mortality benefit of prophylactic mastectomy at age 25, with a 8.7% increased likelihood of being alive at age 80; however, the benefit declined rapidly with increasing age at the time of surgery [14]. Importantly, prophylactic bilateral salpingo-oophorectomy has been associated with an 80% reduction in the risk of ovarian cancer and a 77% reduction in all-cause mortality in *BRCA1/2* carriers [15].

In recent years, enhanced public awareness of hereditary cancer and the development of personalized cancer therapies have resulted in increased requests for genetic testing. Many hereditary cancer clinics noted significant and sustained increases in referrals following Angelina Jolie's decision to undergo prophylactic bilateral mastectomies based on her *BRCA1* carrier status [16,17]. The approval of PARP inhibitors has also improved referral rates for genetic testing [18]; however, current models of genetic service delivery are not sustainable to meet growing demands.

In the traditional GC model, genetic testing for hereditary cancer predisposition involves two in-person visits with a genetic counselor: first to discuss the benefits and limitations of genetic testing and obtain informed consent (pre-test) and second, to review the implications of test results (post-test). Previous research evaluating telephone [19–21], DVD-assisted [22], and printed education [23] models of GC for *BRCA1/2* genetic testing have demonstrated that modified GC models may be non-inferior to standard in-person counseling. To date, we are unaware of any studies that have compared modified GC models to traditional models with regard to panel-based genetic testing, which is the current standard of care in many genetics clinics.

In the present study, a modified GC model for panel-based genetic testing was developed, in which participants watch an online video at home prior to a brief pre-test telephone appointment with a genetic counselor. By eliminating the need for in-person appointments, this model increases patient access to GC and improves the efficiency of the genetics clinic. This is the first randomized study to complete a non-inferiority analysis of a modified GC model for panel-based genetic testing. We hypothesized that, compared to the traditional GC model, the modified GC model would be: 1) non-inferior with respect to psychosocial outcomes, general knowledge about ovarian cancer, and satisfaction and 2) equivalent in terms of the type of genetic results participants would like to receive. Herein, relevant components of the Consolidated Standards of Reporting Trials (CONSORT) extended recommendations for non-inferiority and equivalence trials [24] are reported.

2. Methods

2.1. Study design & participants

From May 2015 to March 2018, participants self-referred into the Prevent Ovarian Cancer Program (www.preventovariancancer.ca) in response to an ongoing educational campaign involving clinical outreach (e.g. information packages to family doctors and genetic counselors) and traditional/social media (e.g. local newspaper articles, TV spots, Facebook) in Ontario, Canada. All Prevent Ovarian Cancer Program participants were enrolled into a parallel, two-armed, randomized non-inferiority study comparing traditional and modified pre-test GC. Eligible participants were female, English-speaking, residents of Ontario, who were at least 18 years of age and had a first-degree relative (FDR) who died of serous ovarian cancer. Participants needed to have a valid email address, as well as telephone and internet access. Participants were excluded if they, or their affected relative, had a known *BRCA1/2* mutation or had previously received negative comprehensive *BRCA1/2* genetic testing (defined as full gene sequencing and deletion duplication analysis). Written informed consent was obtained from all participants. This study was approved by the Research Ethics Board at the University Health Network (UHN).

2.2. Randomization & blinding

All participants were randomized as part of the Prevent Ovarian Cancer Program to receive traditional or modified pre-test GC for ovarian cancer susceptibility using a 1:2 ratio, respectively. A 1:2 ratio was chosen to improve the efficiency of the program. At the time of enrollment into the Prevent Ovarian Cancer Program, participants were blinded to the GC method that they would receive. Randomization was completed sequentially by the research team at the time of pre-test GC appointment booking.

2.3. Intervention

2.3.1. Traditional counseling

Participants received face-to-face pre-test GC. Women living outside of Toronto were given the option of counseling via video conferencing, which is a current standard of care option at the UHN.

2.3.2. Modified counseling

Participants were emailed a password-protected link to a voice-recorded PowerPoint presentation to review prior to a scheduled phone appointment (Supplemental File 1). The presentation included an overview of hereditary ovarian cancer, guidelines for screening/prevention, and the benefits, limitations and possible results of genetic testing.

For both groups, pre-test GC was consistent with published guidelines for hereditary breast and ovarian cancer [25]. Information provided about multigene panel testing was consistent with the binned, tiered approach published by Bradbury et al. [26] Participants were

educated on lifetime cancer risks associated with established genes (e.g. *BRCA1* and *BRCA2*), and brief information about additional gene categories (B, C, D; Supplemental File 2) was provided. Unless indicated by family history, specific cancer risks and screening related to mutations in genes other than *BRCA1* and *BRCA2* were not discussed in detail. Since this study involved genetic testing in a population of unaffected women, the potential for genetic discrimination was routinely discussed with each participant. In May 2017, Canada passed a Genetic Nondiscrimination Act, which was also discussed with each participant [27]. This act protects individuals from the use of genetic test results in areas outside of medical care and medical research, such as insurance and employment. To minimize variability, all pre-test GC was provided by a single board-certified genetic counselor (JM).

2.3.3. Genetic testing

All participants were tested with a 52-gene hereditary cancer panel. Because this panel was designed for studies on cancers of all types at our institution (i.e. not limited to ovarian cancer), it was sub-divided into 4 categories based on clinical actionability and relevance to ovarian cancer (Supplemental File 2). These categories were presented in the genetic consent form as: A) *BRCA1* and *BRCA2* only; B) genes that are known to increase the risk of ovarian and other cancers and where established guidelines for cancer screening are available; C) genes that are thought to increase the risk of ovarian and other cancers but where established guidelines for cancer screening may not be available; D) genes that are known to increase the risks of other cancers (but not ovarian) and where established guidelines for cancer screening are available. The genetic counselor provided all participants with detailed information about the different gene categories. Participants indicated which categories they would like to receive results from on a genetic testing consent form following pre-test GC. All genetic results were disclosed in a post-test phone call with the GC, during which the implications of the genetic result for the participant and their family would be discussed. A tailored result letter would then be sent to the participant dependent on the result (negative, VUS or pathogenic mutation) and gene category.

2.4. Data collection & measures

Non-inferiority was assessed using questionnaire-based data (see Table 1 for measures assessed and Supplemental Files 3–4 for questionnaires). Prior to GC, participants completed a family history questionnaire (Supplemental File 5). Links to psychosocial questionnaires were sent to each participant's email address via LimeSurvey prior to pre-test GC (P1; at time of study enrollment) and one week after pre-test GC (P2).

Psychosocial outcomes were evaluated at P1 and P2. Cancer-specific distress was assessed using the 15-item Impact of Events Scale (IES) [28]. Levels of anxiety and depression were assessed using the 9-item Patient Health Questionnaire (PHQ-9) [29] and the 7-item Generalized Anxiety Disorder (GAD-7) scale [30]. Participants were also asked to report their perceived lifetime risk of ovarian cancer, from 0 to 100%. Conflict about genetic testing was measured using the 11-item Decisional Conflict Scale [31].

Knowledge of hereditary breast and ovarian cancer was obtained at P1 and P2 using a 22-item modified version of the BRCA Knowledge Scale [32]. Questions were modified slightly to focus on ovarian cancer, rather than breast cancer.

Satisfaction with genetic counseling was measured at P2 using the 6-item Genetic Counseling Satisfaction Scale [33].

Information about the choice of result to be disclosed was obtained from genetic testing consent forms. Uptake of genetic testing was determined by the number of patients who provided a blood sample for genetic testing following pre-test GC.

A noticeable time-savings was noted by the genetic counselor during the study. To quantify this, midway through the study, the counselor began recording the length of each appointment. Appointment length was recorded in minutes immediately following each interaction to assess the overall time (pre- and post-test) spent with each participant.

2.5. Statistical methods

A non-inferiority analysis was conducted for all variables assessed at both time points; the purpose of this analysis was to determine if the mean change from baseline for modified pre-test GC (P2-P1) was non-inferior to that observed with the reference model (traditional pre-test GC). Non-inferiority was demonstrated when the one-sided 97.5% confidence limit did not cross the non-inferiority margin. Non-inferiority margins were assigned for each variable based on previous studies (Table 1). Of note, non-inferiority limits for cancer-specific distress and knowledge of hereditary ovarian cancer were based on a similar proportion of change as observed in previous studies [19,21,22,34]. Primary outcome of this study was cancer-specific distress. Based on a non-inferiority margin of 2 and standard deviation of 7, we required data from P1 and P2 from a minimum of 115 participants receiving traditional pre-test GC and 230 participants receiving modified GC for 80% power and a Type-I error of 0.05. Statistical significance was reported using Chi-square test for categorical variables, and student's *t*-test for continuous data. SAS v9.3 or R3.1.3 was used for all statistical analyses.

3. Results

3.1. Demographics and family history

A total of 382 women completed pre-test GC, including 256 modified and 126 traditional (Fig. 1). An overview of participant demographics for the full sample, and within those who received modified or traditional pre-test GC is shown in Table 2. Mean age at consent

Table 1
Overview of study measures. A summary of psychosocial outcomes and additional questions assessed at each time point is shown, including standardized measurement tools, score ranges and non-inferiority limits as applicable. P1 = baseline questionnaire at time of study enrollment; P2 = questionnaire sent to participants 1 week after pre-test genetic counseling.

Question/outcome	Standardized measure	Score range	P1	P2	Non-inferiority limit[a]
Demographics	N/A	–	✓		–
Cancer-specific distress	Impact of Events Scale	0–45	✓	✓	2 [14,16][b]
Depression	PHQ-9	0–27	✓	✓	2 [27][c]
Anxiety	GAD-7	0–21	✓	✓	2 [27]
Decision to have genetic testing	Decisional Conflict Scale	0–64	✓	✓	4 [14,16]
Risk perception (ovarian and breast cancer)	N/A	0–100	✓	✓	7 [17]
Knowledge of hereditary ovarian cancer	Modified BRCA Knowledge Scale	0–22	✓	✓	2 [17,27][d]
Genetic counseling satisfaction	Genetic Counseling Satisfaction Scale	0–24		✓	–

[a] Non-inferiority limits refer to the delta (P2-P1) for modified vs. traditional pre-test genetic counseling.
[b] Limit for cancer-specific distress based on similar proportion of change (25%) used in previous studies.
[c] Non-inferiority limit for depression based on that used for anxiety in previous studies.
[d] Non-inferiority limit for ovarian cancer knowledge based on similar proportion of change (~10%) used in previous studies.

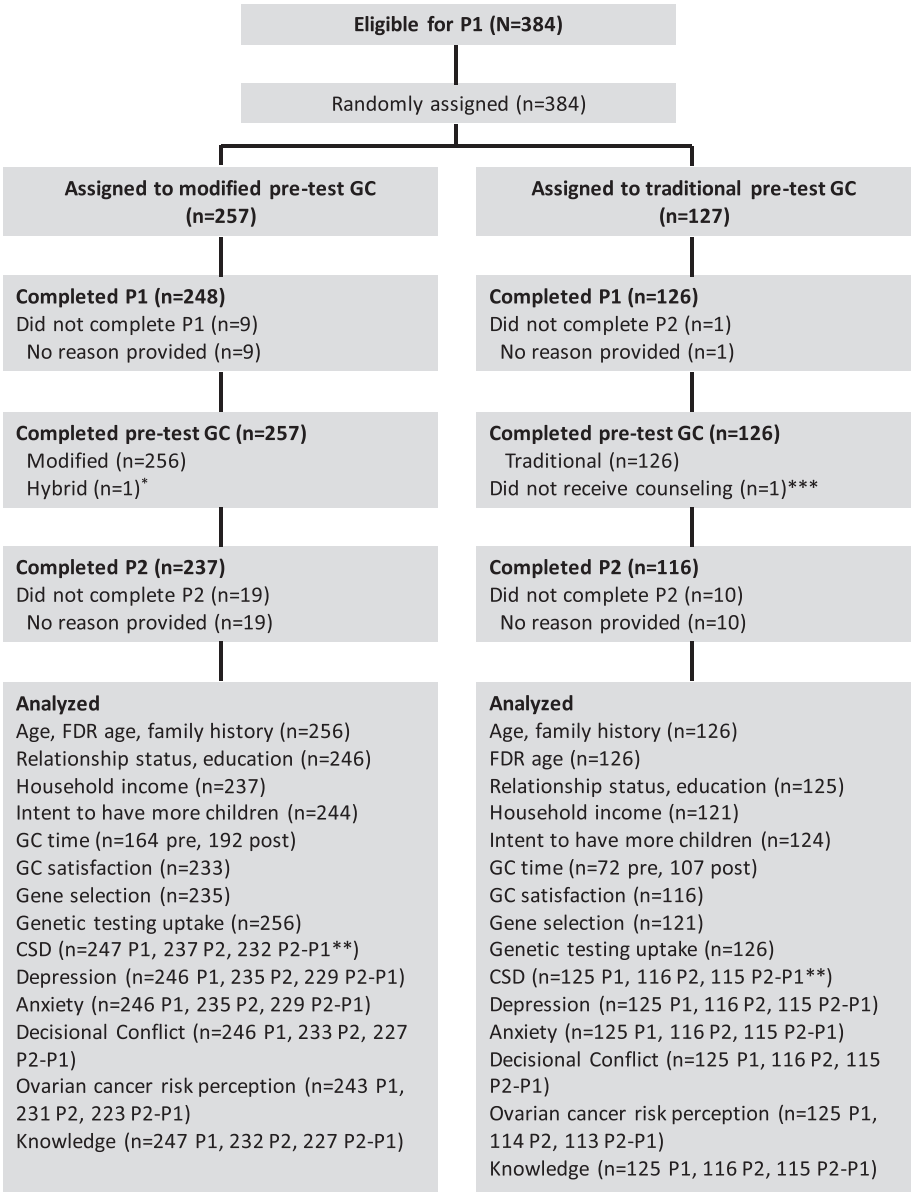

Fig. 1. CONSORT diagram. All prospective participants were enrolled in the Prevent Ovarian Cancer Program between May 8, 2015 and March 8, 2018. To be considered eligible for the current study, participants had to complete a family history questionnaire. P1 (baseline) and P2 (1 week after pre-test genetic counseling) surveys were considered complete if at least the cancer-specific distress portion of the questionnaire was filled out. *Participant ended up both viewing the modified presentation and attending in-person counseling, excluded from subsequent analyses. **Non-inferiority analysis performed on P2-P1 data for all applicable variables. ***Participant donated blood sample prior to planned pre-test genetic counseling appointment, excluded from subsequent analyses. GC = genetic counseling, FDR = first-degree relative, CSD = cancer-specific distress.

was similar in the modified and traditional cohorts (52.1 and 52.4 years, respectively; $p = 0.86$). A high proportion of participants in both groups were married or in a common-law relationship (85% modified vs. 82% traditional), college or university-educated (72% modified vs. 74% traditional), had a household income >$100,000 (52% modified vs. 49% traditional) and did not intend to have more children (95% modified vs. 91% traditional). Self-reported ethnicity was similar for participants in both groups ($p = 0.48$), with the most common including English/Scottish/Irish (48% of cohort), European (including Italian, East European, Other European; combined 25% of cohort), French Canadian (9% of cohort) and Mixed (5% of cohort). Family history of ovarian and/or breast cancer was also similar in participants who received modified vs. traditional pre-test GC ($p = 0.96$), with 70% and 71% of women in each group reporting only one case of ovarian cancer in the family. Mean age of diagnosis in the FDR with ovarian cancer was 63 years in the modified and 63.7 years in the traditional group ($p = 0.57$). Mean pre-test probability of a *BRCA1/2* mutation using the BOADICEA model was not significantly different between groups (3.2 modified vs. 2.2 traditional; $p = 0.1$).

3.2. Non-inferiority analysis

Mean scores for each variable at each time point (overall and within the traditional vs. modified cohorts) and a summary of the non-inferiority analysis results is shown in Table 3 and Fig. 2. Both modified and traditional pre-test GC resulted in a decreased mean score for cancer-specific distress, depression, anxiety, decisional conflict and perceived risk of ovarian/breast cancer. Conversely, a similar increase in knowledge was observed following both models of GC. None of the variables crossed the pre-specified non-inferiority margin, with the exception of ovarian cancer risk perception; while both models decreased perceived risk, this was reduced by a greater extent in participants receiving traditional pre-test GC.

Table 2
Cohort demographics and family history. A summary of participant demographics and family history of ovarian and/or breast cancer in the full sample and within the modified or traditional pre-test genetic counseling cohorts is shown. SD = standard deviation.

Co-variate	Full sample (n = 382)	Modified (n = 256)	Traditional (n = 126)	p-Value
Mean age at consent (SD)	52.2 (10.7)	52.1 (10.4)	52.4 (11.2)	0.86
Relationship status				0.46
Married or in common-law relationship	311 (84%)	209 (85%)	102 (82%)	
Single	60 (16%)	37 (15%)	23 (18%)	
Level of education				0.14
Elementary/middle school/high school	67 (18%)	50 (20%)	17 (14%)	
Certificate program	36 (10%)	20 (8%)	16 (13%)	
College/university/post-graduate degree	268 (72%)	176 (72%)	92 (74%)	
Household income				0.78
<$50,000	44 (12%)	27 (11%)	17 (14%)	
$50,000–$74,999	60 (17%)	41 (17%)	19 (16%)	
$75,000–$99,999	71 (20%)	45 (19%)	26 (21%)	
>$100,000	183 (51%)	124 (52%)	59 (49%)	
Intends to have more children?				0.4
No	344 (93%)	231 (95%)	113 (91%)	
Unsure	10 (3%)	5 (2%)	5 (4%)	
Yes	14 (4%)	8 (3%)	6 (5%)	
Self-reported ethnicity (top 5)				0.48
English/Scottish/Irish	183 (48%)	129 (50%)	54 (43%)	
Other European	48 (13%)	36 (14%)	12 (10%)	
French Canadian	34 (9%)	24 (9%)	10 (8%)	
East European	30 (8%)	16 (6%)	14 (11%)	
Italian	18 (5%)	10 (4%)	8 (6%)	
Mixed	18 (5%)	10 (4%)	8 (6%)	
Mean FDR age at diagnosis (SD)	63.2 (11.5)	63 (11.6)	63.7 (11.4)	0.57
Family history (ovarian/breast cancer)				0.96
Isolated case of ovarian cancer	268 (70%)	178 (70%)	90 (71%)	
2+ cases of ovarian cancer only	22 (6%)	15 (6%)	7 (6%)	
2+ cases of ovarian and breast cancer	92 (24%)	63 (25%)	29 (23%)	
Mean pre-test probability of BRCA mutation using BOADICEA model (SD)	2.9 (5.3)	3.2 (6)	2.2 (3.3)	0.1

3.3. Timing

Mean counseling time for participants randomized to modified vs. traditional pre-test GC is shown in Table 4. As data collection was initiated while the study was already underway, the actual number of observations were as follows: modified (164 pre-test, 192 post-test) and traditional (72 pre-test, 107 post-test). Mean pre-test GC time was significantly shorter in the modified compared to traditional group (19.4 vs. 45.8 min, $p < 0.001$): however, there was no difference in mean post-test GC time (16.1 vs. 16.3 min, $p = 0.78$).

3.4. GC satisfaction, gene selection and genetic testing uptake

A summary of measures assessed following the completion of pre-test GC is also shown in Table 4. Overall, there were no statistically significant differences in mean genetic satisfaction score, gene selection at the time of genetic consent, or uptake of genetic testing. Both cohorts were satisfied with GC, with average scores of 21.2 and 21.9 (out of 24) in participants receiving modified and traditional pre-test GC ($p = 0.12$). At the time of statistical analysis, the vast majority of participants (92% modified vs. 96% traditional) had pursued genetic testing following GC; of note, genetic uptake is likely underestimated as these figures include 11 participants who had only recently attended pre-test GC as part of the study and simply may not have had sufficient time to provide a blood sample for testing. Furthermore, most participants chose to have results from all genes on the panel disclosed, irrespective of GC method (90% modified vs. 86% traditional, $p = 0.24$).

4. Discussion

This is the first randomized non-inferiority study of a modified method of pre-test GC for panel-based genetic testing for hereditary cancer. The use of a 20-minute presentation prior to a pre-test GC telephone call was non-inferior to traditional GC with respect to knowledge, cancer-specific distress, depression, anxiety, and decisional conflict about genetic testing in this low-risk group of women. While both groups had decreases in their perceived ovarian cancer risk, this measure did cross the non-inferiority limit, suggesting that modified GC was inferior on this measure; however, this did not have a negative impact on psychosocial outcomes. Individualized discussions of family history were a component of traditional, but not modified, pre-test GC; this may account for the greater reduction in perceived risk in the traditional cohort. Also of note, there was no statistically significant difference in perceived ovarian cancer risk at P2 (mean score 34.5% modified vs. 31.7% traditional, $p = 0.28$). Importantly, GC satisfaction was high and uptake of genetic testing was >90% in both groups. The modified GC model resulted in a 26-minute reduction in GC time, demonstrating this is an effective and efficient model of pre-test GC.

Other randomized studies comparing modified and traditional models of GC have been reported. In 2014, two randomized non-inferiority trials comparing telephone to in-person GC found the former to be non-inferior on psychosocial outcomes [19–21], knowledge [19–21], and GC satisfaction [19]; these differences persisted one year after pre-test GC [21]. In contrast to the current study in which genetic testing rates were high in both groups, these trials reported lower uptake of testing among patients who received telephone GC. Among 669 women, Schwartz et al. reported that 84.2% of telephone and 90.1% of in-person counselees pursued testing [19]. Among 998 women, Kinney et al. found that 31.8% of in-person and 21.8% of phone counselees pursued testing within the first three months after GC [20] and rates only slightly improved in the following year [21]. Our study cohort consisted of highly motivated, self-referred women which may have inflated genetic testing rates.

Similar to our study, Manchanda et al. evaluated the use of a DVD-assisted model of pre-test GC in a population of low-risk individuals who self-referred for genetic testing following a targeted community campaign [22]. In this study, 936 Ashkenazi Jewish individuals were

Table 3
Mean scores of psychosocial outcomes by time point and pre-test GC method. The mean score and 95% confidence interval for all outcomes in the non-inferiority analysis is shown, including at each time point and by GC method. The change from baseline (P2-P1) for modified vs. traditional GC was used to perform the non-inferiority analysis for each outcome. CSD = cancer-specific distress, "Dep" = depression, "Anx" = anxiety, "Dec Con" = decisional conflict, "Risk (Ov)" = perceived lifetime risk of ovarian cancer, "Risk (Br)" = perceived lifetime risk of breast cancer.

	P1 (baseline)				P2 (after GC)				P2-P1			
	Traditional		Modified		Traditional		Modified		Traditional		Modified	
	N	Mean (95% CI)	N	Mean (95% CI)	N	Mean (95% CI)	N	Mean (95% CI)	N	Mean (95% CI)	N	Mean (95% CI)
CSD	125	**7.81** (6.27–9.35)	247	**7.65** (6.68–8.63)	116	**6.64** (5.33–7.95)	237	**6.19** (5.31–7.08)	115	**−0.65** (1.85 to 0.54)	232	**−1.44** (−2.32 to −0.55)
Dep	125	**3.04** (2.27–3.81)	246	**2.59** (2.11–3.06)	116	**1.71** (1.17–2.25)	235	**2.38** (1.80–2.88)	115	**−0.97** (−1.63 to −0.32)	229	**−0.28** (−0.71 to 0.15)
Anx	125	**2.47** (1.84–3.10)	246	**2.43** (2.02–2.85)	116	**1.59** (1.07–2.12)	235	**2.20** (1.76–2.65)	115	**−0.52** (−0.95 to −0.09)	229	**−0.20** (−0.62 to 0.23)
Dec Con	125	**24.49** (22.1–26.9)	246	**22.1** (20.4–23.9)	116	**9.57** (7.78–11.4)	233	**8.18** (7.02–9.35)	115	**−14.3** (−17.1 to −11.5)	227	**−13.5** (−15.3 to −11.8)
Risk (Ov)	125	**44.6** (40.3–48.9)	243	**42.2** (39.2–45.1)	114	**31.7** (27.8–35.7)	231	**34.5** (31.5–37.4)	113	**−11.9** (−15.6 to −8.25)	223	**−8.47** (−10.9 to −6.06)
Risk (Br)	125	**35.0** (31.4–38.6)	244	**35.5** (32.8–38.3)	114	**29.6** (25.9–33.3)	231	**30.5** (27.9–33.1)	113	**−5.11** (−8.35 to −1.87)	224	**−4.14** (−6.34 to −1.95)
Knowledge	125	**9.62** (8.92–10.3)	247	**9.65** (9.06–10.2)	116	**13.3** (12.6–14.1)	232	**12.95** (12.4–13.5)	115	**3.77** (2.93-4.60)	227	**3.17** (2.64–3.70)

randomized to traditional pre-test GC or a DVD-assisted model, where individuals attended an in-person appointment, which involved a group DVD presentation prior to a one-on-one appointment with a genetic counselor. This group DVD model was non-inferior to the traditional model with respect to knowledge, GC satisfaction, and risk perception [22]. Unlike the aforementioned trials of telephone counseling [19–21], the high rate of genetic testing observed was equivalent between the two groups [22]. Also congruent to our results, the use of a group DVD presentation prior to GC resulted in a 20-minute reduction in time spent with a genetic counselor. Unlike our model, this DVD model still required patients to attend an in-person appointment, limiting its utility in improving access to genetic services among individuals in rural areas.

A number of previous studies have compared patient outcomes of group and individual GC models but none included non-inferiority analyses and most did not randomize patients to an intervention [35–38]. These studies demonstrated improved knowledge scores, high patient satisfaction, and reduced GC time [35–38]; however, when given the choice of group versus individual GC, patients tend to prefer a one-on-one setting [36,38].

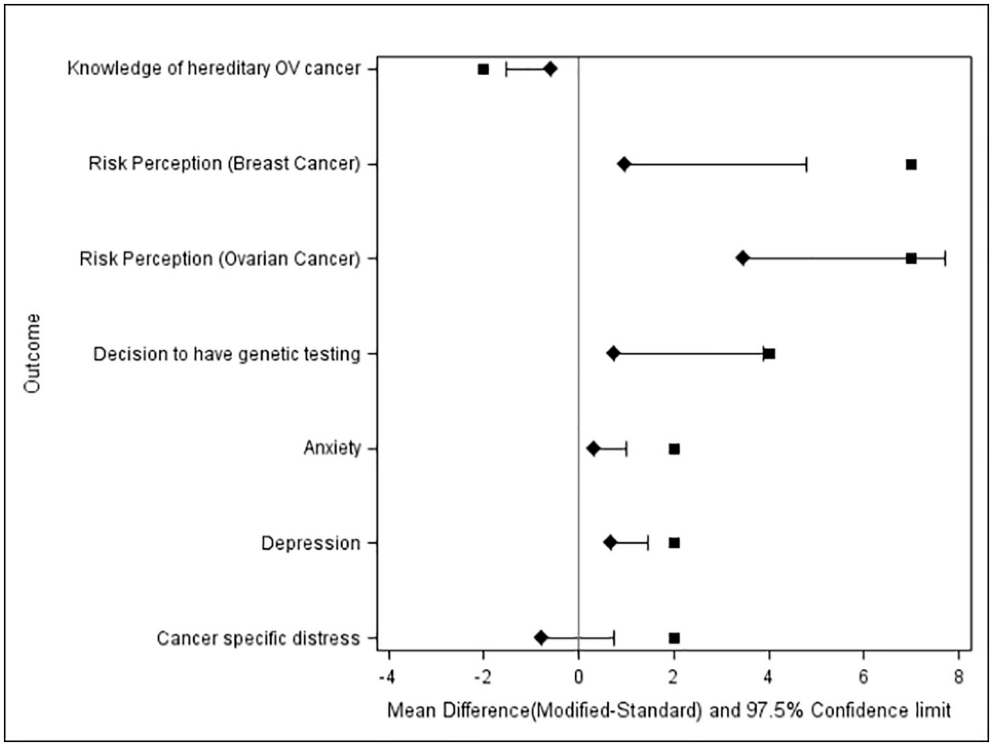

Fig. 2. Summary of non-inferiority analysis. The adjusted mean difference (change from baseline for modified – traditional GC; indicated by diamonds), one-sided 97.5% confidence interval (indicated by lines) and non-inferiority margin (indicated by squares) is shown for each outcome included in the non-inferiority analysis. Outcomes were considered non-inferior if the 97.5% confidence interval crossed the pre-defined non-inferiority margin.

Table 4
Genetic counseling and genetic testing-associated measures. A summary of measures assessed during (time) and after pre-test genetic counseling (satisfaction with the pre-test GC process, gene selection at the time of genetic consent and the proportion of participants who pursue genetic testing) in the full sample and within the modified or traditional pre-test genetic counseling cohorts is shown.

Co-variate	Full sample (n = 382)	Modified (n = 256)	Traditional (n = 126)	p-Value
Mean GC time in min[a] (SD)				
Pre-GC	27.4 (14.6)	19.4 (6.9)	45.8 (9.9)	<0.001
Post-GC	16.1 (6.3)	16.1 (5.9)	16.3 (7)	0.78
Mean GC satisfaction score[b] (SD)	21.4 (3.8)	21.2 (3.8)	21.9 (3.7)	0.12
Gene selection at time of genetic consent[c]				0.24
BRCA1/BRCA2 only (category A)	11 (3%)	8 (3%)	3 (2%)	
Genes with screening guidelines available (categories A, B, D)	25 (7%)	12 (5%)	13 (11%)	
Genes known or thought to increase risk for ovarian cancer (categories A, B, C)	5 (1%)	4 (2%)	1 (1%)	
All genes on panel (categories A, B, C, D)	315 (88%)	211 (90%)	104 (86%)	
Participant pursued testing following pre-test GC				0.14
Yes	356 (93%)	235 (92%)	121 (96%)	
No[d]	26 (7%)	21 (8%)	5 (4%)	

SD = standard deviation.
[a] Actual number of observations for mean genetic counseling time: modified (164 pre-test, 192 post-test) and traditional (72 pre-test, 107 post-test).
[b] Maximum score of 24.
[c] Applicable gene categories listed on the genetic consent form are indicated.
[d] Participants marked as "No" include those who had not submitted genetic consent/blood sample at the time of analysis (N = 15 participants declined, N = 11 recent pre-test appointment).

Despite their benefits, telephone and group GC models do not limit the number of GC visits or number of patients seen by genetics clinics and these models are routinely used by <10% of genetic counselors [39].

Recently, a surge of "mainstreaming" models have been implemented in which genetic testing is ordered without pre-test GC with a genetics professional. In the original mainstreaming model, implemented in the United Kingdom, non-genetics clinicians order genetic testing and only those patients with positive test results or significant family history are seen by a clinical genetics service [40]. The first 207 ovarian cancer patients tested reported high levels of satisfaction with the model [40]. Other mainstreaming models use written information in lieu of pre-test GC, and include post-test GC for either all [23,41] or only positive genetic test results [42].

In a randomized controlled non-inferiority trial comparing a written information model to traditional GC among 135 newly diagnosed breast cancer patients, the written model was non-inferior with respect to decisional conflict about genetic testing [23]. While non-inferiority analyses have not been completed, there do not appear to be differences in the psychosocial outcomes of patients receiving written information or traditional counseling [23,41]. Interestingly, when offered the choice between written information or traditional pre-test GC, the majority of women in one Dutch study chose to receive written information [41]. Reasons included decreased time to genetic test results and minimized travel/hospital visits, while reasons to choose the traditional model included personal contact and the opportunity to ask questions. A recent qualitative study of women using a written model however found that many preferred to talk to a clinician prior to testing [43]. These findings suggest that mainstreamed models of genetic testing and GC may not be equally desired by all patients.

Our model of pre-test GC combines the convenience of telephone counseling with the improved efficiency of group counseling. While mainstreaming models present an opportunity to triage cancer patients who do or do not need to be seen by genetics, it is unclear whether these models are non-inferior to traditional pre-test GC. Furthermore, evaluation of mainstreaming models has predominately focused on genetic testing for cancer patients, whose view about and motivations for genetic testing differ from unaffected individuals who likely require more information and support prior to making a decision about genetic testing. With an average of 3.5 relatives pursuing predictive genetic testing for every individual identified to have a *BRCA1/2* mutation through mainstreaming models [40], genetics clinics will need to embrace more efficient models of pre-test GC. Our model of GC provides an alternative to mainstreaming models for centers who do not have a mainstreaming program and for patients who would like to speak with a genetic counselor. In our model, pre-test GC time was less than half the time of traditional GC. Because the time analysis included the time spent discussing logistics of the research study, the actual time required per patient is likely less than the 19 min reported.

4.1. Limitations and future directions

Several limitations should be noted. First, all participants were enrolled in The Prevent Ovarian Cancer Program, creating a bias of knowledge-seeking, low-risk women. Women at high risk of carrying a *BRCA1/2* mutation would likely have been referred for traditional GC and women who were conflicted about testing would be less likely to enroll. Also, most women were well-educated, Caucasian, of high socioeconomic status and their opinions may not be representative of a wider demographic. Further research in a more diverse population, including in women who have not self-referred, is therefore required to assess the generalizability of our findings. A targeted outreach approach could be used to recruit minority/underserved populations. The acceptability and psychosocial impact of our modified pre-test model could also be tested in individuals being referred for clinical pre-test GC by their healthcare providers based on a family history of hereditary breast and ovarian cancer.

Second, this study did not evaluate outcomes following results disclosure or long-term outcomes; this will be the focus of future studies. It is important to note that previous studies have reported that individuals pursuing genetic testing tend to return to their pre-testing emotional state over time [44].

Third, this study did not include a cost comparison of modified and traditional GC. Cost analyses in other studies have shown alternative models of GC to be cost-effective based on reductions in GC time or number of required GC appointments [19,22,23,40]. Extrapolating from these analyses, the modified GC model used in this study is likely cost-effective given the significant reduction in pre-test GC time. A formal cost analysis will be undertaken in future studies, including whether our modified pre-test GC model increases efficiency for clinical genetic counselors.

5. Conclusion

This is the first study to compare modified and traditional GC for panel-based genetic testing. We have shown that a short presentation prior to pre-test telephone GC is non-inferior to traditional in-person GC and can improve efficiency without negatively impacting psychosocial outcomes in a research setting.

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Conflicts of interest

The authors have no conflicts of interest to disclose.

Author contributions

JM, AT and MB planned the manuscript. JM, AT, TR and NR performed data collection. MM performed statistical analysis. JM, AT and MB drafted the manuscript. All authors reviewed and provided edits to the initial draft. AT submitted the manuscript for publication.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ygyno.2018.12.027.

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