Randomized Noninferiority Trial of Telephone Delivery of *BRCA1/2* Genetic Counseling Compared With In-Person Counseling: 1-Year Follow-Up

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ABSTRACT

Purpose

The ongoing integration of cancer genomic testing into routine clinical care has led to increased demand for cancer genetic services. To meet this demand, there is an urgent need to enhance the accessibility and reach of such services, while ensuring comparable care delivery outcomes. This randomized trial compared 1-year outcomes for telephone genetic counseling with in-person counseling among women at risk of hereditary breast and/or ovarian cancer living in geographically diverse areas.

Patients and Methods

Using population-based sampling, women at increased risk of hereditary breast and/or ovarian cancer were randomly assigned to in-person ($n = 495$) or telephone genetic counseling ($n = 493$). One-sided 97.5% CIs were used to estimate the noninferiority effects of telephone counseling on 1-year psychosocial, decision-making, and quality-of-life outcomes. Differences in test-uptake proportions for determining equivalency of a 10% prespecified margin were evaluated by 95% CIs.

Results

At the 1-year follow-up, telephone counseling was noninferior to in-person counseling for all psychosocial and informed decision-making outcomes: anxiety (difference [d], 0.08; upper bound 97.5% CI, 0.45), cancer-specific distress (d, 0.66; upper bound 97.5% CI, 2.28), perceived personal control (d, -0.01; lower bound 97.5% CI, -0.06), and decisional conflict (d, -0.12; upper bound 97.5% CI, 2.03). Test uptake was lower for telephone counseling (27.9%) than in-person counseling (37.3%), with the difference of 9.4% (95% CI, 2.2% to 16.8%). Uptake was appreciably higher for rural compared with urban dwellers in both counseling arms.

Conclusion

Although telephone counseling led to lower testing uptake, our findings suggest that telephone counseling can be effectively used to increase reach and access without long-term adverse psychosocial consequences. Further work is needed to determine long-term adherence to risk management guidelines and effective strategies to boost utilization of primary and secondary preventive strategies.

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INTRODUCTION

Increased awareness of associations between *BRCA1/2* mutations and breast and ovarian cancer¹⁻¹⁰ has led to an increased demand for genetic counseling and testing.^{11,12} If population-wide *BRCA1/2* screening is realized,¹³ the need for evidence-based and efficient counseling care delivery models will also increase. Specialized expertise is required to assess a woman's risk of

hereditary breast and ovarian cancer (HBOC), support informed decision-making, provide risk-appropriate care recommendations, and attend to the potential deleterious psychosocial effects of providing new risk information.¹⁴ Providers often lack this specialized knowledge^{15,16} leading to suboptimal patient informed decision-making and avoidable distress.^{17,18} Increasing access to trained genetic counselors is therefore essential.¹⁹

Telephone counseling can extend the reach of trained genetic counselors and overcome

geographic access barriers^{16,20-26} while reducing costs.^{27,28} Concerns remain, however, about whether telephone counseling can support informed decision-making and minimize adverse psychologic outcomes.^{12,29-31} Recent evidence indicates that in the short term, telephone counseling is noninferior to in-person counseling for key decision-making and psychosocial outcomes.^{27,32} There are no data on longer-term noninferiority for these outcomes after telephone counseling.³³⁻³⁹

To fill this gap, we examined 1-year outcomes from a previously reported randomized trial³² comparing telephone with in-person counseling in a population with potential geographic barriers to care. We hypothesized that telephone counseling would be noninferior to in-person counseling at the 1-year follow-up for psychologic, informed decision-making, quality-of-life, and risk management outcomes. We also assessed geographic differences in follow-up outcomes and described risk management behaviors.

PATIENTS AND METHODS

Research Design and Study Population

A two-armed, parallel-cluster, randomized equivalency/noninferiority trial compared telephone with in-person counseling for deleterious *BRCA1/2* mutations (NCT01346761). Enrollment began August 2010 and ended September 2012. One-year outcome assessments were completed February 2014. Study details and short-term outcomes have been previously published.³²

The Utah Population Database⁴⁰ and Utah Cancer Registry were used to identify and recruit breast and ovarian cancer survivors. At-risk female relatives were recruited through survivors who tested positive for a *BRCA1/2* mutation. Eligible participants were English speaking, 25 to 74 years of age, Utah residents, had personal/family histories meeting HBOC genetic testing guidelines,⁴¹ had telephone access, could travel to in-person counseling at one of 14 clinics, and had no prior genetic counseling and/or *BRCA1/2* testing. The University of Utah and University of New Mexico Institutional Review Boards approved study protocol. All participants provided informed consent.

Randomization and Masking

Participants completed baseline assessments and were randomized by family unit to one of the two study arms using a computer-generated allocation algorithm based on a permuted block randomization plan.³² Study staff who conducted baseline assessments were blinded to the identity of a woman's participating relative(s).

Interventions

In-person counseling. Women assigned to in-person counseling received counseling by a cancer genetic counselor according to a standardized protocol consistent with national guidelines^{32,42,43} and were given an HBOC educational brochure and a copy of the visual aids used during the counseling. Women who decided to have genetic testing could provide a sample at their appointment or bring a *BRCA1/2* buccal test kit home should they decide to test at a later time. Women who chose testing were offered post-test counseling with the same genetic counselor who performed pre-test counseling. Test result-specific visual aids and recommendations for both positive and negative test results were used.

Telephone counseling. Women assigned to telephone counseling received counseling by a cancer genetic counselor according to the same standardized protocol as those in the in-person counseling arm. They were mailed sealed packets containing the same print materials used for in-person counseling, which were to be opened and used at the time of their

telephone counseling session. Women who decided to have genetic testing were mailed a genetic test buccal kit. Post-test counseling was delivered by the same genetic counselor using the same tailored visual aids based on the results. Participants in both arms were mailed a letter summarizing their personalized risk assessment based on family history and/or genetic test result and management recommendations. Both groups were asked to identify their healthcare provider(s) to also receive the letter.

Data collection and measures. Data collectors, who were blinded to intervention assignment, collected self-reported data via telephone, Internet, or mailed surveys. Assessments were done at baseline, 1 week after pre-test and post-test counseling, 6 months, and 1 year after the last counseling session. This study focuses on 1-year outcomes.

Anxiety was measured at baseline and 1 year with the six-item state anxiety subscale of the Brief Symptom Inventory-18.⁴⁴ Higher scores indicate more anxiety (Cronbach's α coefficient = .90 to .91).

Cancer-specific distress was measured at baseline and 1 year with the 15-item Impact of Event Scale.⁴⁵ Higher scores indicate more distress (α = .89 to .90).

Mental and physical health-related quality of life was measured at baseline and 1 year with the 12-item Short Form Health Survey (SF-12, version 2).^{46,47} Higher scores reflect better quality of life for the mental (α = .84) and physical (α = .88) component summary scores.

Perceived control about risk of HBOC (ie, "the problem") was assessed at 1 year with the nine-item Perceived Personal Control Questionnaire.³¹ The questionnaire assesses three dimensions of control: cognitive (eg, "I feel I understand the problem that brought me to genetic counseling"), behavioral (eg, "I know what I can do to alleviate the problem"), and decisional (eg, "I feel I can make decisions that would influence future outcomes"). Higher scores indicate more perceived control (α = .85).

Decisional conflict associated with the *BRCA1/2* testing decision was measured with the 16-item version of the Decisional Conflict Scale at 1 year.^{48,49} Higher scores indicate more decisional conflict (α = .92).

Decisional regret about *BRCA1/2* testing decisions were measured with the five-item Decision Regret Scale at 1 year.⁵⁰ Higher scores indicate more decisional regret (α = .91).

Risk management behaviors. Participants were provided with risk management recommendations, which were based on National Comprehensive Cancer Network guidelines and tailored to their personal cancer status, genetic test results, and presence of breast and ovaries (Appendix Table A1, online only). Counseling recommendations reflected the guidelines for surveillance at the time of the study.^{51,52} Breast cancer screening, prophylactic mastectomy, and oophorectomy were assessed.^{51,53}

Statistical Analysis

The a priori primary noninferiority outcomes were 1-year changes from baseline in anxiety and cancer-specific distress. Noninferiority margins reflected established clinically significant change (cancer-specific distress and decisional conflict: 4 points; mental and physical quality of life: -2.5 points).^{45,46,50} In accordance with other studies and literature on meaningful changes in health,⁵⁴ a margin of no more than 0.5 standard deviation "worse" than the in-person counseling mean value was used for measures without clinical guidelines (decisional regret and anxiety: 5 points; perceived personal control: -0.2 points).

The primary noninferiority analyses were based on the available sample at baseline and 1 year.⁵⁵⁻⁵⁷ Missing scores were substituted with estimates biased toward inferiority: substituting in-person counseling missing observations with the mean of in-person counseling, and replacing telephone counseling missing observations with the mean plus the noninferiority margin of in-person counseling. To test that telephone counseling was not unacceptably worse than in-person counseling, one-sided 97.5% cluster bootstrap CIs with 1,000 replications were used to estimate the noninferiority effects for the between-group intervention differences, while accounting for the potential correlation among subjects within the

family. The same approach was used for the exploratory analysis of the noninferiority effects for geographic (rural v urban) and genetic test status (tester v nontester) subgroups.

The equivalency of genetic testing uptake between telephone and in-person counseling within 1 year of the precounseling session was a secondary outcome. A sensitivity analysis showed that results did not differ when including or excluding women who reported testing outside the study; therefore, testing status included all women who had either study-verified testing ($n = 240$) or testing outside the study ($n = 21$). To test whether the interventions had equivalent rates of genetic testing uptake by 1 year and to exclude a potential clinically relevant difference, a two-sided 95% CI was estimated from 1,000 cluster bootstrap samples for the difference in uptake proportions (equivalence range $\pm 10\%$) for the per-protocol and intent-to-treat equivalency analyses, accounting for the correlation within families.⁵⁸ For the intent-to-treat analysis, the multiple imputation method^{59,60} was used to impute the missing observations using cancer status, number of relatives with cancer, education level, and health insurance status. We also delineated risk management behaviors across the two interventions, by cancer and by genetic testing result status.

All analyses were performed using SAS 9.4 (SAS Institute Inc., Cary, NC) and R 3.2.1 (R Development Core Team, Vienna, Austria).

Sample Size and Power Evaluation

Sample size and power calculations were based on the trial's 6-month primary outcome analysis using NQuery Advisor 7.0.^{32,61} Based on the final randomized sample size of 988, 79% retention, a mean cluster size of 1.02, and an estimated intraclass coefficient of 0.07, our ad hoc power was $> 80\%$ to detect noninferiority in cancer-specific distress and anxiety at 1 year, with an α level of 0.05.

RESULTS

Study enrollment, randomization, and retention data are shown in the CONSORT flow diagram (Fig 1). The study arms did not differ at baseline (Tables 1, 2, and 3).

Psychosocial and Informed Decision-Making Outcomes

Table 2 shows measures of psychologic distress and well-being by telephone and in-person counseling arms for the more conservative per-protocol analysis. The mean differences for participant-reported measures between the arms for noninferiority measures from baseline and 1-year follow-up values were all within the prespecified margins (Fig 2 and Table 4). No differences were observed for noninferiority based on rural versus urban residence or test uptake (Table 3), cancer cases (Appendix Table A2, online only), or uninformative and nontester result status (Appendix Table A3, online only). Results were similar for imputed data (data not shown). Missing data for these analyses ranged from 17% to 28%.

Genetic Testing

At 1 year, 27.9% of telephone counseling and 37.3% of in-person counseling participants underwent genetic testing. A 95% CI of the difference in the testing uptake was 2.2% to 16.8%, which falls outside of the equivalence range (-10% to 10%). Similar results were observed for imputed data (difference = 8.2%; 95% CI, 0.9% to 15.4%). Testing uptake was appreciably higher for rural compared with urban dwellers in both arms (rural telephone counseling: 38.7% [95% CI, 26.2% to 50.0%]; urban telephone

counseling: 25.9% [95% CI, 21.1% to 30.9%]; rural in-person counseling: 41.3% [95% CI, 29.1% to 53.9%]; urban in-person counseling: 36.6% [95% CI, 30.8% to 42.8%]).

Risk Management Behaviors

Risk management behaviors based on testing status and previous cancer diagnosis are shown in Table 5. Three out of 20 women, who were *BRCA1/2* positive and had at least one breast before testing, had a prophylactic mastectomy (telephone counseling: 10% [one of 10 women]; in-person counseling: 20% [two of 10 women]). Six of 10 women ≥ 35 years old, who were *BRCA1/2* positive and had at least one ovary, underwent a prophylactic oophorectomy (telephone counseling: 50% [two of four women]; in-person counseling: 67% [four of six women]). Most women whose test results were uninformative or who did not undergo testing were up to date with breast cancer screening guidelines based on personal and family history. Significance tests were not conducted because of small subgroup sample size.

DISCUSSION

This trial provides important evidence that telephone genetic counseling for HBOC is noninferior to in-person counseling and can be delivered as safely as in-person counseling without an adverse effect on long-term psychologic, quality-of-life, and decision-making outcomes. This conclusion was robust across subgroups of participants, including those living in geographically remote areas and those choosing to be tested or not. The vast majority of participants received uninformative test results. Thus, noninferiority for women with *BRCA1/2* mutations or variants of uncertain significance cannot be certain from our data because of small subgroups.

Overall, our findings are concordant with previous research that established nonequivalency of telephone counseling up to 6 months after genetic counseling^{27,32} and provide further evidence that telephone genetic counseling for HBOC can be delivered safely.⁶² However, consistent with earlier reports focused on shorter-term outcomes,^{27,32} at 12 months, telephone counseling continued to generate lower genetic testing rates (27.9%) than in-person counseling (37.3%) at 1 year. Reasons for this are unclear but may be due to travel time to mail test kits, a delay between telephone counseling and testing at home that might have reduced enthusiasm for testing, or the wait between telephone counseling and testing at home provided opportunity to further consider potential out-of-pocket expenses or to discuss testing with social network members. Future research is needed to better understand how counseling mode might influence testing uptake rates and whether the women at lowest risk are opting appropriately to forgo testing.

Rural women had higher test uptake rates in both the telephone and in-person counseling arms, suggesting that *BRCA1/2* testing interests were satisfied by expanding access to genetic counseling through the two modalities.^{16,22,23} One explanation for this is that urban women most interested in testing may have had access to genetic testing before the study. Many urban women may have been tested and were therefore not eligible for the trial. Thus,

Fig 1. CONSORT diagram. *Seven families had at least one member randomly assigned and one member not randomly assigned. †Total number of participants depends on completion of intervention and completion of measure. ‡Intent-to-treat refers to data analysis after imputation of unknown testing uptake. GC, genetic counseling; HBOC, hereditary breast and ovarian cancer.

Table 1. Characteristics by Overall Sample and by Intervention Group

Characteristic	Overall, % (No.; N = 988)	Telephone, % (No.; n = 493)	In Person, % (No.; n = 495)
Age, years			
Mean $\pm$ SD	56.1 $\pm$ 8.2	56.2 $\pm$ 8.1	55.9 $\pm$ 8.3
Self-reported race/ethnicity			
Non-Hispanic white	94.1 (930)	95.7 (472)	92.5 (458)
Hispanic	3.2 (32)	2.0 (10)	4.4 (22)
Other	2.6 (26)	2.2 (11)	3.0 (15)
Self-reported Ashkenazi Jewish ancestry			
Yes	0.9 (9)	1.2 (6)	0.6 (3)
No	99.1 (979)	98.8 (487)	99.4 (492)
Marital status			
Married or living as married	79.3 (784)	80.1 (395)	78.6 (389)
Single/widowed/separated/divorced	20.6 (204)	19.9 (98)	21.4 (106)
Educational level			
High school or less	21.8 (215)	23.5 (116)	20.0 (99)
Some college, associates degree, or vocational school	37.9 (374)	34.3 (169)	41.4 (205)
Bachelor's degree or higher	40.4 (399)	42.2 (208)	38.6 (191)
Rural v urban residence*			
Urban	85.4 (844)	84.8 (418)	86.1 (426)
Rural	14.6 (144)	15.2 (75)	13.9 (69)
Yearly household income, \$			
$\leq$ 29,999	13.0 (128)	14.0 (69)	11.9 (59)
30,000-49,999	19.2 (190)	17.0 (84)	21.4 (106)
50,000-69,999	19.0 (188)	19.1 (94)	19.0 (94)
$\geq$ 70,000	45.0 (445)	44.8 (221)	45.3 (224)
Missing data	3.7 (37)	5.1 (25)	2.4 (12)
Employment status			
Employed (for wages or self-employed)	62.0 (613)	61.1 (301)	63.0 (312)
Not employed	38.0 (375)	38.9 (192)	37.0 (183)
Health care coverage			
Yes	96.9 (957)	95.5 (471)	98.2 (486)
No	3.1 (31)	4.5 (22)	1.8 (9)
Has a personal health care provider			
Yes	88.7 (876)	88.6 (437)	88.7 (439)
No	11.3 (112)	11.4 (56)	11.3 (56)
Personal history of breast and/or ovarian/fallopian tube/peritoneal cancer			
Yes	97.6 (964)	98.4 (485)	96.8 (479)
No	2.4 (24)	1.6 (8)	3.2 (16)
Recruited relatives of <i>BRCA1/2</i> carriers			
Yes	2.5 (25)	1.6 (8)	3.4 (17)
No	97.5 (963)	98.4 (485)	96.6 (478)
Number of first- and second-degree relatives with breast or ovarian cancer			
0 FDR and 0 SDR	52.2 (516)	51.9 (256)	52.5 (260)
1 FDR or 1 SDR	27.8 (275)	26.6 (131)	29.1 (144)
2 or more FDR/SDR	19.9 (197)	21.5 (106)	18.4 (91)

Abbreviations: FDR, first-degree relative; SDR, second-degree relative.

*Rural or urban residence was based on Rural-Urban Commuting Area (RUCA) codes at the zip code level. RUCA codes were developed by the University of Washington Rural Health Research Center and the United States Department of Agriculture Economic Research Service (ERS), with the support of the federal Health Resource and Service Administration's Office of Rural Health Policy and the ERS, using standard Census Bureau urbanized area and urban cluster definitions in combination with work commuting data to characterize census tracts and then zip codes. The 10 RUCA categories were aggregated into urban (1 to 3) and rural (4 to 10), as recommended by the WWMRI (Washington, Wyoming, Alaska, Montana, and Idaho) Rural Health Research Center.

the urban sample may have been biased toward women who were less interested in testing. Nonetheless, the rates of testing in our study are substantially lower than in other studies where women who were members of families with a known deleterious mutation^{27,63,64} were self- or physician-referred, but similar to a study of African American women.⁶⁵

A contributing factor to the lower overall uptake of testing in this study may be the active recruitment strategy, which identified eligible women from population-based sources without any direct involvement of or referral from their primary health care providers. In general, recommendations from a health care provider strengthen perceptions about the importance of recommendations.⁶⁶

Outcomes of telephone and in-person genetic counseling will likely be optimal when integrated into the health care system and the messages are supported and reinforced by the patient's entire health care team.

To our knowledge, our study is the first to assess risk management outcomes at 1 year after telephone and in-person counseling. The majority of women adhered to screening clinical breast examination and mammography guidelines (although not for breast magnetic resonance imaging [MRI]). Uptake of breast MRI was low, but during the timeframe of the study, guidelines for use of breast MRI only addressed at-risk individuals, and there were no formal guidelines recommending breast MRI

Table 2. Noninferiority of Telephone to In Person Counseling on Psychosocial, Quality-of-Life, and Informed Decision-Making Outcomes by Intervention Arm: 1-Year Follow-Up

Outcome	Baseline						1-Year Follow-Up						1-Year Change From Baseline					
	Overall			In Person			Overall			Telephone			Overall			Telephone		
	No. of Participants	Mean Score (95% CI)	No. of Participants	Mean Score (95% CI)	No. of Participants	Mean Score (95% CI)	No. of Participants	Mean Score (95% CI)	No. of Participants	Mean Score (95% CI)	No. of Participants	Mean Score (95% CI)	No. of Participants	Mean Score (95% CI)	No. of Participants	Mean Score (95% CI)	No. of Participants	Mean Score (95% CI)
Anxiety (possible scores range from 0 to 24)	988	2.69 (2.50 to 2.88)	493	2.76 (2.49 to 3.05)	495	2.61 (2.36 to 2.88)	785	2.56 (2.34 to 2.77)	403	2.74 (2.42 to 3.09)	382	2.37 (2.08 to 2.67)	785	-0.05 (-0.24 to 0.13)	403	-0.01 (-0.26 to 0.24)	382	-0.09 (-0.35 to 0.18)
Cancer-specific distress (possible scores range from 0 to 75)	981	15.43 (14.52 to 16.35)	490	15.41 (14.21 to 16.62)	491	15.45 (14.22 to 16.80)	770	10.64 (9.68 to 11.56)	397	11.19 (9.91 to 12.52)	373	10.06 (8.81 to 11.34)	764	-4.09 (-4.92 to -3.31)	395	-3.77 (-4.84 to -2.69)	369	-4.43 (-5.66 to -3.19)
Quality of life: physical health (possible scores range from 0 to 100)	985	49.61 (49.03 to 50.17)	491	49.55 (48.74 to 50.34)	494	49.67 (48.82 to 50.47)	776	50.14 (49.44 to 50.83)	397	49.75 (48.74 to 50.65)	379	50.54 (49.61 to 51.52)	776	-0.20 (-0.70 to 0.32)	397	-0.39 (-1.10 to 0.32)	379	0 (-0.62 to 0.65)
Quality of life: mental health (possible scores range from 0 to 100)	985	51.13 (50.57 to 51.70)	491	51.34 (50.50 to 52.14)	494	50.91 (50.14 to 51.70)	776	50.63 (49.95 to 51.29)	397	50.74 (49.77 to 51.70)	379	50.51 (49.60 to 51.41)	776	-0.93 (-1.49 to -0.35)	397	-0.79 (-1.58 to 0.04)	379	-1.09 (-1.90 to -0.23)
Decisional conflict (possible scores range from 0 to 100)							734	26.82 (25.70 to 27.95)	379	26.76 (25.19 to 28.38)	355	26.88 (25.32 to 28.62)						
Decisional regret (possible scores range from 0 to 100)							731	21.22 (19.96 to 22.50)	377	21.07 (19.25 to 22.82)	354	21.38 (19.52 to 23.30)						
Perceived personal control (possible scores range from 0 to 2)							786	1.53 (1.50 to 1.55)	405	1.52 (1.49 to 1.56)	381	1.53 (1.49 to 1.57)						

Table 3. Noninferiority of Telephone to In-Person Counseling on Informed Decision Making and Change Between Baseline and 1-Year Follow-Up of Psychosocial and Quality-of-Life Outcomes by Intervention Arm and Urban Versus Rural, Tester Versus Nontester Groups

Outcome	Urban						Rural						Tester						Nontester								
	Telephone			In Person			Difference, Telephone – In Person			Telephone			In Person			Difference, Telephone – In Person			Telephone			In Person			Difference, Telephone – In Person		
	No. of Participants	Mean (95% CI)	Mean (95% CI)	No. of Participants	Mean (95% CI)	Mean (95% CI)	No. of Participants	Mean (95% CI)	Mean (95% CI)	No. of Participants	Mean (95% CI)	Mean (95% CI)	No. of Participants	Mean (95% CI)	Mean (95% CI)	No. of Participants	Mean (95% CI)	Mean (95% CI)	No. of Participants	Mean (95% CI)	Mean (95% CI)	No. of Participants	Mean (95% CI)	Mean (95% CI)	No. of Participants	Mean (95% CI)	Mean (95% CI)
Anxiety*	344	-0.03 (-0.32 to 0.22)	0.00 (-0.30 to 0.30)	321	0.00 (-0.30 to 0.30)	-0.03 (-0.72 to 0.30)	59	0.10 (-0.59 to 0.78)	0.64 (-0.85 to 1.37)	61	-0.54 (-1.17 to 0.13)	0.16 (-0.22 to 0.56)	105	0.16 (-0.22 to 0.56)	-0.45 (-0.85 to -0.01)	130	-0.45 (-0.85 to -0.01)	0.61 (-0.30 to 1.09)	291	-0.12 (-0.41 to 0.20)	0.08 (-0.25 to 0.47)	247	0.08 (-0.41 to 0.20)	-0.19 (-0.93 to 0.19)			
Cancer-specific distress*	337	-3.47 (-4.64 to -2.30)	-4.21 (-5.53 to -2.80)	310	-4.21 (-5.53 to -2.80)	0.74 (-2.30 to 2.15)	58	-5.55 (-8.90 to -2.17)	0.04 (-6.70 to 4.05)	59	-5.59 (-8.95 to -2.61)	-4.80 (-6.80 to -2.76)	102	-4.80 (-6.80 to -2.76)	-4.50 (-6.60 to -2.33)	124	-4.50 (-6.60 to -2.33)	-0.30 (-5.35 to 2.00)	286	-3.59 (-6.14 to -3.07)	-4.63 (-6.14 to -3.07)	240	-3.59 (-6.14 to -3.07)	1.04 (-2.24 to 2.81)			
Quality of life: physical health*	339	-0.29 (-1.06 to 0.51)	0.20 (-0.45 to 0.89)	318	0.20 (-0.45 to 0.89)	-0.49 (-1.36 to 1.29)	58	-1.02 (-2.81 to 0.94)	0.03 (-2.21 to 4.59)	61	-1.05 (-2.90 to 0.78)	-0.67 (-2.28 to 0.82)	104	-0.67 (-2.28 to 0.82)	-0.56 (-1.84 to 0.59)	129	-0.56 (-1.84 to 0.59)	-0.11 (-1.73 to 3.36)	286	-0.24 (-1.11 to 0.53)	0.27 (-0.50 to 1.18)	245	0.27 (-0.50 to 1.18)	-0.51 (-1.51 to 2.18)			
Quality of life: mental health*	339	-0.88 (-1.75 to 0.06)	-1.17 (-2.07 to -0.23)	318	-1.17 (-2.07 to -0.23)	0.29 (-0.80 to 2.30)	58	-0.23 (-2.17 to 1.74)	0.42 (-1.66 to 5.39)	61	-0.65 (-2.35 to 0.98)	-0.26 (-1.92 to 1.34)	104	-0.26 (-1.92 to 1.34)	-0.18 (-1.50 to 1.33)	129	-0.18 (-1.50 to 1.33)	-0.08 (-1.95 to 3.14)	286	-0.89 (-2.54 to -0.47)	-1.45 (-2.54 to -0.47)	245	-1.45 (-2.54 to -0.47)	0.56 (-0.55 to 2.61)			
Decisional conflict	325	27.25 (25.46 to 29.05)	26.41 (24.70 to 28.10)	300	26.41 (24.70 to 28.10)	0.84 (-3.00 to 3.06)	54	23.80 (20.00 to 27.81)	-5.62 (-14.98 to -0.88)	55	29.42 (25.23 to 33.59)	17.43 (14.63 to 20.53)	103	17.43 (14.63 to 20.53)	22.62 (19.88 to 25.70)	120	22.62 (19.88 to 25.70)	-5.19 (-11.29 to -2.05)	270	30.37 (27.38 to 33.35)	29.16 (27.38 to 33.35)	231	29.16 (27.38 to 33.35)	1.21 (-2.76 to 3.55)			
Decisional regret	323	21.53 (19.45 to 23.57)	21.34 (19.10 to 23.52)	300	21.34 (19.10 to 23.52)	0.19 (-4.89 to 2.69)	54	18.33 (13.60 to 23.35)	-3.24 (-15.70 to 2.215)	54	21.57 (17.24 to 25.79)	10.73 (8.08 to 13.44)	103	10.73 (8.08 to 13.44)	12.58 (9.81 to 15.69)	120	12.58 (9.81 to 15.69)	-1.86 (-9.04 to 1.22)	268	25.20 (23.69 to 27.48)	25.95 (23.69 to 27.48)	230	25.20 (23.69 to 27.48)	-0.74 (-6.25 to 2.01)			
Perceived personal control	345	1.52 (1.48 to 1.56)	1.54 (1.50 to 1.58)	320	1.54 (1.50 to 1.58)	-0.02 (-0.06 to 0.06)	60	1.53 (1.44 to 1.63)	0.04 (-0.08 to 0.26)	61	1.49 (1.38 to 1.61)	1.62 (1.57 to 1.69)	107	1.62 (1.57 to 1.69)	1.63 (1.57 to 1.69)	131	1.63 (1.57 to 1.69)	-0.01 (-0.08 to 0.16)	291	1.48 (1.43 to 1.52)	1.48 (1.43 to 1.52)	245	1.48 (1.43 to 1.52)	0.00 (-0.05 to 0.12)			

*Values indicate change from baseline.

Fig 2. Effects and noninferiority ranges 1 year after the last intervention. GC, genetic counseling; IP, in person; TEL, telephone.

for ongoing screening for cancer survivors. Most *BRCA1/2* carriers ≥ 35 years old had a bilateral salpingo-oophorectomy, but only one carrier had a prophylactic mastectomy. Available evidence indicates that women undergo risk-reducing surgeries over time, well beyond the first year.^{67,68} Thus, longer-term assessments of risk management behaviors and decision-making factors postcounseling require further study.

The study's results have implications for care delivery and policy. Noninferiority of telephone counseling at 1 year provides additional evidence that telephone-delivered genetic counseling and testing could expand access to *BRCA1/2* counseling. Telephone counseling can improve access from geographically remote areas, ease the travel and care burden for patients traveling to a clinic, and increase perceived control when patients are given a choice about their preferred counseling mode. It can also address the limited

genetic counseling work force as the demand for clinical genetic services increases.^{20,69} However, it is not clear whether telephone counseling is noninferior for women who test *BRCA1/2* positive, have variants of uncertain significance, and seek multigene testing. Furthermore, telephone counseling strategies would have to be reassessed in the general population in women without a previous diagnosis of cancer.

National best practice guidelines recommend that trained cancer genetic professionals provide comprehensive cancer genetics risk assessment to women who meet testing criteria. However, it is estimated that less than one-third of these women receive genetic counseling.^{29,30,66} During our recruitment process, we observed low rates of prior counseling and testing utilization by women with a personal history of cancer (30%), providing additional evidence for low rates of accessing genetic counseling and

Table 4. Noninferiority of Telephone Counseling to In-Person Counseling on Psychosocial, Quality-of-Life, and Informed Decision-Making Outcomes Per-Protocol Analysis

Outcome	Mean Difference	97.5% CI	Noninferiority Margin*
Anxiety	0.08	-0.52 to 0.45	5
Cancer-specific distress	0.66	-1.75 to 2.28	4
Quality of life: physical health	-0.39	-1.35 to 1.06	-2.5
Quality of life: mental health	0.30	-0.83 to 2.26	-2.5
Decisional conflict	-0.12	-3.69 to 2.03	4
Decisional regret	-0.31	-4.25 to 2.29	5
Perceived personal control	-0.01	-0.06 to 0.06	-0.2

*A noninferiority test tests that the telephone counseling mean is not worse than the in-person counseling mean (as the reference mean) by more than the prespecified noninferiority margin.

Table 5. Breast and Ovarian Cancer Risk Management* by *BRCA1/2* Testing Status and Intervention Arm at 1-Year Follow-Up

Cancer Case/Relative	Test Status	Screening by Guideline Recommended Age	No. of Participants†	Overall	In Person	Telephone
Previous cancer diagnosis						
	<i>BRCA1/2</i> positive (n = 16)				(n = 6)	(n = 8)
		CBE (> 25 years old)	14	11 (78.6%)	6 (100%)	5 (62.5%)
		Mammogram (> 25 years old)	14	10 (71.4%)	6 (100%)	4 (50.0%)
		Breast MRI (> 25 years old)	14	7 (50.0%)	3 (50.0%)	4 (50.0%)
		PM	14	1 (7.1%)	0 (0%)	1 (12.5%)
	(n = 7)	PO (≥ 35 years old)	7	5 (71.4%)	3 of 3 (100%)	2 of 4 (50.0%)
	(n = 0)	PO (< 35 years old)	0	0 (0%)	0 (0%)	0 (0%)
	<i>BRCA1/2</i> negative‡ (n = 2)				(n = 1)	(n = 1)
		CBE	2	1 (50.0%)	1 (100%)	0 (0%)
		Mammogram	2	1 (50.0%)	1 (100%)	0 (0%)
		Breast MRI	2	0 (0%)	0 (0%)	0 (0%)
	Uninformative§ (n = 191)				(n = 82)	(n = 74)
		CBE	156	132 (84.6%)	70 (85.4%)	62 (83.8%)
		Mammogram	156	133 (85.3%)	71 (86.6%)	62 (83.8%)
		Breast MRI	156	10 (6.4%)	5 (6.1%)	5 (6.8%)
	Nontester (n = 492)				(n = 198)	(n = 226)
		CBE	424	375 (88.4%)	178 (89.9%)	197 (87.2%)
		Mammogram	424	377 (88.9%)	177 (89.4%)	200 (88.5%)
		Breast MRI	424	15 (3.5%)	4 (2.0%)	11 (4.9%)
Unaffected at-risk relative						
	<i>BRCA1/2</i> positive (n = 6)				(n = 4)	(n = 2)
		CBE (> 25 years old)	6	3 (50.0%)	2 (50.0%)	1 (50.0%)
		Mammogram (> 25 years old)	6	2 (33.3%)	1 (25.0%)	1 (50.0%)
		Breast MRI (> 25 years old)	6	1 (16.7%)	1 (25.0%)	0 (0%)
		PM	6	2 (33.3%)	2 (50.0%)	0 (0%)
		Chemoprevention	6	0 (0%)	0 (0%)	0 (0%)
	(n = 4)	PO (≥ 35 years old)	3	1 (33.3%)	1 of 3 (33.3%)	0 of 0 (0%)
	(n = 3)	PO (< 35 years old)	2	0 (0%)	0 of 0 (0%)	0 of 2 (0%)
	<i>BRCA1/2</i> negative				(n = 4)	(n = 3)
	(n = 9)	CBE (≥ 40 years old)	7	7 (100%)	4 (100%)	3 (100%)
		Mammogram (≥ 40 years old)	7	7 (100%)	4 (100%)	3 (100%)
					(n = 2)	(n = 1)
	(n = 4)	CBE (< 40 years old)	3	2 (66.7%)	2 (100%)	0 (0%)
		Mammogram (< 40 years old)	3	1 (33.3%)	1 (50.0%)	0 (0%)
	Nontester (n = 2)				(n = 1)	(n = 1)
		CBE (> 25 years old)	2	1 (50.0%)	0 (0%)	1 (100%)
		Mammogram (> 25 years old)	2	0 (0%)	0 (0%)	0 (0%)
		Breast MRI (> 25 years old)	2	0 (0%)	0 (0%)	0 (0%)
		PM	2	0 (0%)	0 (0%)	0 (0%)
		Chemoprevention	2	0 (0%)	0 (0%)	0 (0%)
	(n = 0)	PO (≥ 35 years old)	0	0 (0%)	0 of 0 (0%)	0 of 0 (0%)
	(n = 2)	PO (< 35 years old)	2	0 (0%)	0 of 1 (0%)	0 of 1 (0%)

NOTE. Percent of participants younger than 40 years of age are as follows: cancer case, seven of 701 participants (1%); at-risk relative, 12 of 21 participants (57%). Abbreviations: CBE, clinical breast examination; MRI, magnetic resonance imaging; PM, prophylactic mastectomy; PO, prophylactic oophorectomy.

*Those included in the analysis reported that at least one breast or ovary was present at baseline; age-eligible women were considered for specific screening and prophylactic surgery outcomes.

†These numbers include only those who responded to the baseline and the 6- and/or 12-month surveys.

‡Test result negative is defined as a person who tested negative for a known mutation.

§Test result uninformative is defined as no pathogenic mutation identified in the family, and the cause of the cancer risk remains unknown.

testing. To our knowledge, our population-based recruitment approach to deliver remote cancer genetic services is unprecedented. It is noteworthy that the Utah Cancer Registry was able to contact 91.5% of potentially eligible cancer survivors, and 89.8% of eligible survivors who were invited to participate in the study accepted genetic counseling. Cancer registries have primarily focused on collecting epidemiologic data. Our study exemplifies how cancer registries can help implement health promotion interventions with survivors and their at-risk family members. Furthermore, patient contact through registries may be an effective public health strategy for expanding access to telephone counseling at a lower cost than in-person counseling^{27,28} to large numbers of

people who may benefit from such services.⁷⁰⁻⁷³ Involving patients' providers, especially in follow-up of test results and recommendations, is likely to maximize program effectiveness.

Recent discussions about population-wide *BRCA* testing have been spurred by new findings that it is not uncommon for *BRCA1* and *BRCA2* mutations to be identified in individuals without a clear indication for testing. Recent estimates suggest that population screening would identify a mutation in approximately one in 300 women.^{74,75} Evidence-based alternative counseling models, such as telephone counseling, could be implemented as part of comprehensive precision cancer prevention approaches that involve genetic testing.

Our study had several limitations. Because our sample was from a single state, was largely non-Hispanic white, and had a personal history of cancer, our study may have limited generalizability. Furthermore, our findings may be generalizable only to settings where patients are counseled by board-certified genetic counselors because adherence to best practices differs by provider type.^{17,76} The small number of women who obtained genetic testing limits our ability to draw meaningful conclusions about the noninferiority of telephone counseling for risk management outcomes. Our sample may not be representative of patients who are physician- or self-referred for genetic counseling/testing, or who are referred for urgent testing to help make immediate treatment decisions. The small number of mutation carriers limited our ability to draw meaningful conclusions about uptake of prophylactic surgeries. We did not assess behavioral intent to undergo surveillance or prophylactic surgery. Finally, our results may not be generalizable to rapidly evolving multigene panel testing, which poses challenges for risk communication, especially given uncertainties about cancer risks and medical management.⁷⁷

In conclusion, this study provides strong long-term evidence that telephone counseling for women at risk of HBOC is not inferior to in-person counseling with regard to fostering informed decision making, minimizing adverse psychologic and quality-of-life outcomes, and promoting perceived personal control 1 year

after counseling. Alternative care delivery approaches, such as telephone communication, can make cancer genetic services more widely accessible without sacrificing safety.

AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

Disclosures provided by the authors are available with this article at www.jco.org.

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AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

Randomized Noninferiority Trial of Telephone Delivery of *BRCA1/2* Genetic Counseling Compared With In-Person Counseling: 1-Year Follow-Up

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Appendix

Table A1. National Comprehensive Cancer Network Risk Management Recommendations^{41,43}

Risk Category	Breast and Ovarian Cancer Risk Management
Previous cancer diagnosis*	
Test status	
BRCA1/2 positive	<ul style="list-style-type: none"> • Follow-up of cancer as recommended by physician • Annual clinical breast examination starting at 25 years of age • Annual mammogram starting at 25 years of age • Annual breast MRI starting at 25 years of age • Consideration of prophylactic mastectomy • Recommend prophylactic salpingo-oophorectomy between 35 and 40 years of age or after childbearing is complete
Negative for familial BRCA1/2 mutation	<ul style="list-style-type: none"> • Follow-up of cancer as recommended by physician • Annual clinical breast examination • Annual mammogram • Imaging with breast MRI may be considered based on personal and family history
Uninformative† or VUS	<ul style="list-style-type: none"> • Follow-up of cancer as recommended by physician • Annual clinical breast examination • Annual mammogram • Imaging with breast MRI may be considered based on personal and family history
No testing done	<ul style="list-style-type: none"> • Follow-up of cancer as recommended by physician • Annual clinical breast examination • Annual mammogram • Imaging with breast MRI may be considered based on personal and family history
Unaffected relative at risk of a familial mutation	
Test status	
BRCA1/2 positive	<ul style="list-style-type: none"> • Annual clinical breast examination starting at 25 years of age • Annual mammogram starting at 25 years of age • Annual breast MRI starting at 25 years of age • Consideration of prophylactic mastectomy • Recommend prophylactic salpingo-oophorectomy between 35 and 40 years of age or after childbearing is complete • Consider chemoprevention (eg, tamoxifen)‡
BRCA1/2 negative with known familial mutation§	<ul style="list-style-type: none"> • Clinical breast examination every 3 years until 40 years of age; then annually • Annual mammogram starting at 40 years of age • Annual clinical breast examination starting at 25 years of age • Annual mammogram starting at 25 years of age • Annual breast MRI starting at 25 years of age • Consideration of prophylactic mastectomy • Consideration of prophylactic salpingo-oophorectomy between 35 and 40 years of age or after childbearing is complete • Consider chemoprevention (eg, tamoxifen)‡
No testing done	

Abbreviations: MRI, magnetic resonance imaging; VUS, variant of uncertain significance.

*There are less specific guidelines for patients with cancer. Recommendations depend on the individual's cancer history and are made in consultation with their oncologist. For example, patients with cancer may take estrogen inhibitors (ie, tamoxifen) as treatment rather than chemoprevention, as is the case for unaffected relatives.

†Test result uninformative is defined as no pathogenic mutation identified in the family, and the cause of the cancer risk remains unknown.

‡The survey assessed chemoprevention only in the at-risk family member group because these drugs are often used for treatment in people with a cancer diagnosis.

§For those in this category, it is important to consider cancer history from the other side of the family.

Table A2. Noninferiority of Telephone to In Person Counseling for Psychosocial, Quality-of-Life, and Informed Decision-Making Outcomes by Intervention Arm and Previous Cancer Diagnosis Versus At-Risk Relative

Outcome	Cancer Case						Relative					
	Telephone			In Person			Telephone			In Person		
	n	Mean (95% CI)	n	Mean (95% CI)	Mean (95% CI)	Mean (95% CI)	n	Mean (95% CI)	n	Mean (95% CI)	Mean (95% CI)	Difference, (TEL - IP)
Anxiety*	395	-0.05 (-0.28 to 0.19)	370	-0.08 (-0.34 to 0.22)	0.04 (-0.86 to 0.36)	0.04 (-0.86 to 0.36)	8	1.63 (0.13 to 4)	12	-0.25 (-0.89 to 0.57)	1.88 (-0.66 to 3.89)	
Cancer-specific distress*	387	-3.85 (-5.03 to -2.78)	357	-4.32 (-5.54 to -3.06)	0.47 (-2.67 to 1.83)	0.47 (-2.67 to 1.83)	8	-0.13 (-3.63 to 6.4)	12	-7.67 (-12.32 to -1.55)	7.54 (-2 to 14.68)	
Quality of life: physical health*	390	-0.45 (-1.2 to 0.2)	368	0.01 (-0.65 to 0.66)	-0.46 (-1.34 to 1.04)	-0.46 (-1.34 to 1.04)	7	2.96 (0.74 to 4.44)	11	-0.31 (-3.28 to 2.68)	3.27 (-0.18 to 9.55)	
Quality of life: mental health *	390	-0.78 (-1.58 to 0.08)	368	-1.03 (-1.91 to -0.2)	0.26 (-0.725 to 2.19)	0.26 (-0.725 to 2.19)	7	-1.36 (-5.76 to 3.64)	11	-2.95 (-7.41 to -0.45)	1.59 (-3.02 to 11.48)	
Decisional conflict	371	27.02 (25.38 to 28.62)	343	27.15 (25.55 to 28.7)	-0.13 (-4.09 to 1.75)	-0.13 (-4.09 to 1.75)	8	14.84 (8.75 to 19.53)	12	19.11 (9.24 to 34.38)	-4.26 (-41.96 to 5.44)	
Decisional regret	369	21.27 (19.39 to 23.02)	342	22 (20.06 to 23.77)	-0.72 (-4.48 to 1.375)	-0.72 (-4.48 to 1.375)	8	11.88 (4 to 16.11)	12	3.75 (0.22 to 8.75)	8.13 (-7.92 to 12.98)	
Perceived personal control	397	1.52 (1.48 to 1.55)	368	1.52 (1.49 to 1.56)	-0.01 (-0.05 to 0.08)	-0.01 (-0.05 to 0.08)	8	1.81 (1.73 to 1.93)	13	1.79 (1.63 to 1.95)	0.01 (-0.15 to 0.41)	

Abbreviations: IP, in person; TEL, telephone.

*Values indicate change from baseline.

Abbreviations: IP, in person; TEL, telephone.
*Values indicate change from baseline.

	Negative						Positive						Uninformative						Nonsterile								
	Telephone			In Person			Difference (TEL - IP)			Telephone			In Person			Difference (TEL - IP)			Telephone			In Person			Difference (TEL - IP)		
	n	Mean, 95% CI	n	Mean, 95% CI	n	Mean, 95% CI	n	Mean, 95% CI	n	Mean, 95% CI	n	Mean, 95% CI	n	Mean, 95% CI	n	Mean, 95% CI	n	Mean, 95% CI	n	Mean, 95% CI	n	Mean, 95% CI	n	Mean, 95% CI	n	Mean, 95% CI	
Anxiety*	4	0.75 (-1.0 to 1.3)	9	-0.33 (-0.92 to 0.4)	12	1.08 (-1.67 to 1.93)	12	0.33 (-0.87 to 1.35)	12	-0.25 (-2 to 1.82)	109	0.11 (-0.32 to 0.52)	89	0.11 (-0.32 to 0.52)	109	-0.48 (-0.95 to -0.02)	291	-0.12 (-0.41 to 0.18)	247	0.08 (-0.27 to 0.41)	291	-0.12 (-0.41 to 0.18)	247	0.08 (-0.27 to 0.41)	291	-0.12 (-0.41 to 0.18)	
Cancer-specific distress*	4	-3.0 (-7.0 to -1.67)	9	-6.89 (-12.8 to 4.79)	11	3.89 (-18.67 to 9.58)	12	-2.09 (-9.01 to 5.54)	12	-2.25 (-8 to 1.79)	103	-5.23 (-7.27 to -3.36)	87	-5.23 (-7.27 to -3.36)	103	-4.55 (-6.8 to -2.46)	286	-3.59 (-5.0 to -2.31)	240	-4.63 (-6.15 to -3.14)	286	-3.59 (-5.0 to -2.31)	240	-4.63 (-6.15 to -3.14)	286	-3.59 (-5.0 to -2.31)	
Quality of life-physical health*	4	3.48 (-0.3 to 4.73)	9	-0.76 (-3.45 to 1.43)	11	4.24 (-0.6 to 10.35)	12	2.19 (-1.49 to 5.76)	12	-0.86 (-4.57 to 2.32)	109	-1.21 (-2.78 to 0.39)	89	-1.21 (-2.78 to 0.39)	109	-0.51 (-1.94 to 0.93)	286	-0.24 (-1.03 to 0.53)	245	0.27 (-0.51 to 1.04)	286	-0.24 (-1.03 to 0.53)	245	0.27 (-0.51 to 1.04)	286	-0.24 (-1.03 to 0.53)	
Quality of life-mental health*	4	-3.49 (-6.74 to 6.25)	9	-1.65 (-5.76 to 0.55)	11	-1.84 (-6.29 to 14.41)	12	-2.74 (-9.87 to 3.2)	12	-0.07 (-1.72 to 1.9)	109	0.19 (-1.43 to 1.72)	89	0.19 (-1.43 to 1.72)	109	-0.09 (-1.68 to 1.59)	286	-0.89 (-1.84 to 0.13)	245	-1.45 (-2.5 to -0.49)	286	-0.89 (-1.84 to 0.13)	245	-1.45 (-2.5 to -0.49)	286	-0.89 (-1.84 to 0.13)	
Decisional conflict	5	13.44 (0 to 21.88)	8	22.27 (6.88 to 43.75)	12	-8.83 (-45.38 to 1.57)	12	23.44 (15.0 to 31.1)	13	21.96 (15.27 to 31.67)	1682	13.64 (10.46 to 20.46)	86	16.82 (13.64 to 20.46)	99	22.74 (19.96 to 25.75)	270	30.37 (28.5 to 32.26)	231	29.16 (27.37 to 30.94)	270	30.37 (28.5 to 32.26)	231	29.16 (27.37 to 30.94)	270	30.37 (28.5 to 32.26)	
Decisional regret	5	9 (0 to 15.0)	8	7.5 (1.43 to 15)	12	1.5 (-17.86 to 8.97)	12	20 (12.21 to 28.33)	13	8.08 (2.26 to 17.5)	953	6.91 (12.5 to 15.5)	86	9.53 (6.91 to 12.5)	99	13.59 (10.8 to 16.77)	268	25.2 (23.09 to 27.43)	230	25.95 (23.83 to 28.25)	268	25.2 (23.09 to 27.43)	230	25.95 (23.83 to 28.25)	268	25.2 (23.09 to 27.43)	
Perceived personal control	5	1.73 (1.44 to 2.0)	9	1.8 (1.62 to 1.99)	12	-0.07 (-0.34 to 0.32)	12	1.55 (1.28 to 1.77)	13	1.73 (1.48 to 1.99)	1631	1.55 (1.28 to 1.77)	90	1.63 (1.55 to 1.7)	109	1.61 (1.54 to 1.67)	291	1.48 (1.41 to 1.53)	245	1.48 (1.41 to 1.53)	291	1.48 (1.41 to 1.53)	245	1.48 (1.41 to 1.53)	291	1.48 (1.41 to 1.53)	