

## ORIGINAL STUDY

# Menopausal hormone therapy for *BRCA*-mutation carriers: attitudes of Israeli healthcare providers before and after a brief educational intervention

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### Abstract

**Objective:** *BRCA*-mutation carriers are offered risk-reducing bilateral salpingo-oophorectomy (RRBSO) at age 35 to 40 years, leading to major life-quality and health-related issues associated with early menopause. Hormone therapy (HT) may significantly alleviate menopausal symptoms without increasing breast or ovarian cancer risk in *BRCA* carriers. We investigated attitudes of Israeli healthcare providers to HT post-RRBSO in *BRCA* carriers, before and after a brief educational intervention.

**Methods:** In this pre-post survey of gynecologic departments in Israel, healthcare providers were given questionnaires (based on scores of 1-4) assessing attitudes to prescribing HT in different clinical scenarios, before and after an educational intervention on current knowledge about HT in *BRCA*-mutation carriers. Higher scores indicated higher tendency to prescribe HT. Mean and median scores were calculated for each scenario, and the association between scores and various healthcare providers' characteristics were assessed. The change in attitude pre versus postintervention was evaluated, and the Cohen's *d* effect size was calculated.

**Results:** Of the 200 healthcare providers who were offered participation, 162 responded. Of them, 25.3% were obstetricians, 13.6% gynecologists, 5.55% gynecologic-oncologists, 8% medical oncologists, 38.9% obstetrics-gynecology residents, and 8.6% were nurses. Median age was 44 (interquartile range 36-58); 42.6% were males. Higher score correlated weakly with older age, but did not correlate with gender or personal HT/menopause experience. Significantly higher mean and median preintervention scores were obtained by gynecologists (3.2±0.96; 4 [2.25-4]) and gynecologic-oncologists (3.6±0.78; 4 [3.6-4.0]) than by medical oncologists (2.6±1.06; 2.13 [1.88-3.81]), obstetricians (2.7±1.09; 2.25 [1.88-4.0]), residents (2.48±0.99; 2 [1.69-3.56]) or nurses (2.2±0.92; 2 [1.5-2.69]). Overall scores were higher postintervention ( $P < 0.001$ , effect size  $d = 0.901$ ). The change in scores postintervention was most prominent among younger participants and nurses.

**Conclusions:** In Israel, it is acceptable to offer HT post-RRBSO to healthy *BRCA*-mutation carriers. Younger healthcare workers and nurses tend to be more hesitant, yet they are more likely to adopt a pro-HT attitude after an educational intervention. Such intervention is likely to improve overall care for *BRCA*-mutation carriers.

**Key Words:** *BRCA* – Education – Hormone therapy – Risk-reducing salpingo-oophorectomy.

Germline mutations in the *BRCA1* and *BRCA2* genes confer a substantially increased risk of developing breast and ovarian cancer. The cumulative lifetime risk of breast and ovarian cancers is 72% and 44% in *BRCA1* mutation carriers, and 69% and 17% in *BRCA2* mutation carriers, respectively.<sup>1</sup> The substantially increased risk for

developing ovarian cancer conferred by *BRCA* mutations leads to the recommendation to undergo risk-reducing bilateral salpingo-oophorectomy (RRBSO) after completion of childbearing, usually at the age of 35 to 40 years.<sup>2,3</sup> However, the fear of premature menopause with all its consequences is a deterrent to complying with this recommendation. In some populations these rates may be as low as 52.4%.<sup>4,5</sup> Menopausal hormone therapy (HT) after RRBSO in premenopausal women has proved to be beneficial in minimizing both endocrine and sexual symptoms<sup>6-8</sup>; however, only 21% of *BRCA*-mutation carriers are actually treated with HT after RRBSO.<sup>9</sup> A main concern of both physicians and patients in this situation is the possibility of increased risk of breast cancer with HT use, though there are no clear data to suggest that short-term use of HT indeed increases that risk in *BRCA*-mutation carriers.<sup>10</sup> Indeed, for *BRCA*-mutation carriers with

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no history of breast cancer, current international guidelines adopted in many countries recommend systemic HT from the time of RRBSO until the age of natural menopause, after a discussion of risks and benefits, including controversies in the literature regarding the combination of estrogen and progesterone, and the differences that might exist in breast cancer risk of patients with a *BRCA2* versus *BRCA1* mutations.<sup>11-13</sup>

The aim of the present research was to determine the attitudes of Israeli healthcare professionals concerning HT treatment to average-risk and high-risk populations including post-RRBSO carriers of *BRCA* mutations, and to evaluate the effect of a brief educational intervention on these attitudes.

## METHODS

The study was approved by the Ethics Committee of the Sheba medical center. Between April, and August, 2018, we surveyed a pre-post cohort of multidisciplinary teams of healthcare providers in gynecologic departments of public hospitals in Israel. During eight staff meetings, healthcare providers who attended these meetings were asked to fill in an anonymous questionnaire that was administered twice, that is, immediately before and immediately after their attendance at an educational intervention on the subject of current knowledge about prescribing HT for carriers of *BRCA* mutations. The intervention consisted of a 30-minute lecture delivered by a resident (Y.F.), followed by a 15-minute discussion led by a specialist in gynecologic oncology (T.P.). The questionnaire related to demographic and occupational information including age and sex, professional group details, seniority, years of practice, type of workplace in addition to the public hospital, frequency of encountering questions about HT from patients, and whether they or their partners use HT, if they were age-relevant.

The questionnaires considered nine scenarios, listed alphabetically from A to I. Questionnaire respondents were required to indicate whether they would advise HT in the case of each clinical setup. Their responses were rated on a 4-point scale, as follows: "I will not advise HT," 1 point; "I will refer to another specialist," 2 points; "I will advise HT if the patient requests it," 3 points; "I will actively suggest HT," 4 points. The score of each case was calculated as following: the sum of all the points given by all participants was divided by the number of participants, yielding a mean score for that case. The higher the score, the greater the tendency to recommend/prescribe HT. This exercise was done both before and after the intervention.

Results were analyzed using IBM SPSS Statistics for Windows, Version 23.0 (IBM Corp., Armonk, NY). Categorical variables were presented as number and percentage, and continuous variables were evaluated from the normal distribution curve using histograms and Q-Q plots, and were reported as means and standard deviation (SD), or median and interquartile ranges (IQRs). Factor analysis was used to identify groups of questions with similar patterns of answers, using the principal components method with varimax rotation.

Cronbach's alpha was used to evaluate internal consistency in the group of questions with similar patterns identified by the factor analysis. Spearman's coefficient was used to evaluate association between ordinal or continuous variables and the answers, and a Mann-Whitney test was used to compare categorical variables. Wilcoxon signed-ranks test was used to compare mean and median scores pre and postintervention. Generalized estimating equations were used to compare the change between scores pre and postintervention between categories (*P* for interaction). Effect size *d* was calculated using the method described by Jacob Cohen.<sup>14</sup> Small, medium, and large effect sizes were considered as 0.2, 0.5, and 0.8, respectively. All tests were two-sided, and the significance threshold was set at 0.05.

## RESULTS

Of the 200 healthcare providers who attended the staff meetings, 162 (81%) participated in the survey by filling in both pre and postintervention questionnaires. The pertinent descriptive characteristics of all participants are shown in Table 1.

Table 2 displays the numbers and percentages of respondents who marked scores for each of the nine presented scenarios preintervention. The responses for cases B and E (healthy yet has menopausal symptoms, non-*BRCA*-mutation carriers), and also for scenarios F, G, H, and I (*BRCA*-mutation carriers) showed high internal consistency before

**TABLE 1.** Descriptive characteristics of the survey participants (*N* = 162)

Variables	Survey participants
Age in y, median (IQR)	44 (36–58)
Sex, n (%)	
Male	69 (42.6)
Work place <sup>a</sup> , n (%)	
Hospital	153 (95.6)
Private clinic	35 (21.9)
Public clinic	36 (22.5)
Other	3 (1.9)
NA	3 (1.9)
Professional group, n (%)	
Nurses	14 (8.6)
Obstetricians	41 (25.3)
Gynecologists	22 (13.6)
Gynecologic-oncologists	9 (5.55)
Medical oncologists	13 (8)
Residents	63 (38.9)
Frequency of encounters with patients' questions, n (%)	
Often	47 (29)
Sometimes	42 (26)
Rarely	50 (30.8)
Never	19 (11.7)
NA	4 (2.5)
Have you/your partner ever suffered from menopausal symptoms? n (%)	
Yes	36 (22.2)
No	119 (73.5)
NA	7 (4.3)
Have you/your partner ever used HT? n (%)	
Yes	30 (18.5)
No	122 (75.3)
NA	10 (6.2)

HT, hormone therapy; NA, no answer.

<sup>a</sup>Some responders indicated more than one response.

**TABLE 2.** Description statistics for answers in each scenario preintervention

Case	Mean (SD), median (IQR)	I will not prescribe HT (1), n (%)	I will refer to a specialist (2), n (%)	I will prescribe on patient request (3), n (%)	I will suggest HT (4), n (%)	NA, n (%)
A Healthy, age 50, no FHC, no BRCA-M, menopausal, asymptomatic	2.24 (1.2), 2 (1-3)	71 (43.82)	10 (6.17)	48 (29.62)	31 (19.1)	2 (1.2)
B Healthy, age 50, no FHC, no BRCA-M, menopausal, symptomatic	3.66 (0.7), 4 (4-4)	3 (1.9)	11 (6.9)	24 (15)	122 (76.3)	2 (1.2)
C Breast cancer survivor, age 50, no BRCA-M, menopausal, asymptomatic	2.07 (1.01), 2 (1-3)	53 (32.9)	66 (41)	19 (11.8)	23 (14.2)	1 (0.6)
D Healthy, age 50, positive FHC, no BRCA-M, menopausal, symptomatic	2.48 (1.03), 2 (2-3)	26 (16.3)	71 (44.4)	24 (15)	39 (24.4)	2 (1.2)
E Healthy, age 35, no FHC, no BRCA-M, BSO for benign reason, symptomatic	3.68 (0.73), 4 (4-4)	4 (2.5)	13 (8.1)	14 (8.8)	129 (80.6)	2 (1.2)
F Healthy, age 35, BRCA-M, had both RRBSO and RRM, asymptomatic	2.55 (1.25), 2 (1-4)	46 (28.4)	42 (25.9)	13 (8)	61 (37.7)	0
G Healthy, age 35, positive FHC, BRCA-M, had both RRBSO and RRM, symptomatic	2.93 (1.13), 3 (2-4)	18 (11.1)	56 (34.6)	8 (4.9)	80 (49.4)	0
H Healthy, age 35, BRCA-M, had RRBSO asymptomatic	2.46 (1.23), 2 (1-4)	48 (30)	45 (28.1)	13 (8.1)	54 (33.8)	2 (1.2)
I Healthy, age 35, BRCA-M, had RRBSO symptomatic	2.88 (1.08), 3 (2-4)	15 (9.3)	60 (46.6)	15 (9.3)	71 (44.1)	1 (0.6)

BRCA-M, breast cancer mutation carrier; BSO, bilateral salpingo-oophorectomy; FHC, family history of breast/ovarian cancer; HT, hormone therapy; NA, no answer; RRBSO, risk-reducing bilateral salpingo-oophorectomy; RRM, risk-reducing mastectomy.

the educational intervention ( $\alpha = 0.72$  and  $0.92$ , respectively). For each of these two groups, therefore, the respondents' scores were combined, and a mean score was calculated for the grouped set at a whole. Responses for cases A, C, and D had low internal consistencies, and each was therefore scored separately.

The overall mean score for the responses of all 162 respondents at baseline was  $2.7 \pm 1.05$ . When asked about the average-risk population (cases A-E), almost 50% of respondents were in favor of treating healthy asymptomatic patients with HT (case A), either actively or at the patients' request (20% and 30%, respectively), and 88% to 91% would prescribe HT for healthy noncarriers of *BRCA*-mutation patients with no family history of cancer who suffer menopausal symptoms (cases B and E), of whom 76.3% to 80.6% would actively suggest HT. For asymptomatic non-*BRCA*-mutation carriers with personal history of breast cancer (case C), HT would be prescribed for symptomatic patients by only 26% of respondents, and for symptomatic healthy noncarriers with familial breast cancer (case D) HT would be prescribed by 40%. In *BRCA*-mutation carriers (cases F, G, H, and I), HT would be actively suggested by 37.7% of respondents if an asymptomatic patient had both RRBSO and RRM (33.8% if no RRM), and by 49.4% if the same patient was symptomatic (44.1% if no RRM).

Correlations between mean and median scores of responses and respondent characteristics are presented in Table 3. Sex was not a significant factor in determining score. Older respondents showed a higher tendency than younger ones to prescribe

HT for all patients, and tendency was significantly correlated with age of responses in scenarios C and D (non-*BRCA*-mutation carriers with personal or family history of breast cancer, respectively) and cases F, G, H, and I (*BRCA*-mutation carriers). Medical oncologists had lower mean scores compared with gynaecologic-oncologists, gynecologists and obstetricians, with statistically significant differences in scenarios A, B + E, D, and F to I (Table 3).

The scores obtained by respondents who had personal experience with suffering from menopausal symptoms or with the use of HT, were significantly higher than the scores of the other respondents in case C only (a symptomatic patient who survived breast cancer) (Table 3).

Table 4 presents mean and median scores of prescribing HT for *BRCA*-mutation carriers by respondent characteristics before and after the educational intervention. For all scenarios involving *BRCA*-mutation carriers (F, G, H, and I), the mean and median scores obtained by all respondents for prescribing HT were significantly higher after the intervention than before it ( $P < 0.01$ , effect size  $d > 0.8$ ), except gynecologic oncologists who had a high score preintervention, and also post-intervention. Male and female responders were as likely to have higher scores post compared with preintervention, as were respondents with or without personal experience with menopausal symptoms or HT use. There was a weak negative correlation ( $r = -0.23$ ) between age and change in score (not shown). Nurse changes to higher scores after the intervention were significant compared with other professional group change ( $P$  for interaction = 0.002).

TABLE 3. Preintervention association between mean scores (1-4) (SD<sup>a</sup>) and responders' characteristics in each case

Variables	Case A			Case C			Case D			Cases B, E			Cases F, G, H, I			
	Mean (SD)	Median (IQR)	P <sup>b</sup>	Effect size d	Mean (SD)	Median (IQR)	P	Effect size d	Mean (SD)	Median (IQR)	P	Effect size d	Mean (SD)	Median (IQR)	P	Effect size d
Sex																
Male	2.38 (1.28)	3 (1-4)	0.28	0.173	3.71 (0.99)	2 (1-3)	0.51	0.1	2.5 (1.03)	2 (2-3)	0.91	0.019	2.75 (1.03)	2.5 (2-4)	0.58	0.085
Female	2.17 (1.14)	2 (1-3)			3.61 (0.98)	2 (1-3)			2.47 (1.0)	2 (2-3)			2.66 (1.07)	2.25 (1.75-4)		
Professional group																
Nurses	1.86 (0.86)	2 (1-3)	0.238	0.347	2.64 (1.2)	2.5 (1.75-4)	0.056	0.621	2.43 (1.16)	2 (1.75-4)	0.79	0.048	2.2 (0.92)	2 (1.5-2.68)	0.075	0.528
Obstetricians	2.51 (1.26)	3 (1-4)	0.137	0.316	2.12 (0.94)	2 (1-3)	0.88	0.059	2.55 (1.08)	2 (2-4)	0.003 <sup>c</sup>	0.106	3.8 (0.55)	2.25 (1.87-4)	>0.001 <sup>d</sup>	0.006
Gynecologists	2.33 (1.3)	3 (1-3.75)	0.71	0.082	2.04 (0.95)	2 (1-2)	0.96	0.039	3.00 (1.06)	3 (2-4)	0.009 <sup>e</sup>	0.106	3.9 (0.24)	4 (2.25-4)	0.006 <sup>f</sup>	0.591
Gyn-oncologists <sup>g</sup>	2.62 (1.26)	3 (1-4)	0.23	0.34	2.0 (1.15)	2 (1-3)	0.61	0.089	2.92 (1.04)	3 (2-4)	0.11	0.464	3.96 (0.14)	4 (3.62-4)	0.001 <sup>h</sup>	1.019
Medical-oncologists	1.65 (0.93)	1 (1-2)	0.041 <sup>i</sup>	0.551	2.06 (1.16)	2 (1-3)	0.74	0.019	1.94 (0.94)	2 (1-3)	0.021 <sup>j</sup>	0.588	3.03 (0.72)	2.12 (1.9-3.8)	0.61	0.111
Residents	2.09 (1.2)	1 (1-3)	0.28	0.173	1.9 (0.87)	2 (1-2)	0.19	0.267	2.33 (0.9)	2 (2-3)	0.28	0.202	2.48 (0.99)	2 (1.68-3.56)	0.094	0.286
Responder or partner ever suffer from menopausal symptoms	0.33		0.33	0.172			0.028 <sup>k</sup>	0.340			0.17	0.234			0.39	0.186
Yes	2.43 (1.3)	3 (1-4)			2.34 (0.9)	2 (2-3)			2.66 (0.9)	2 (2-3)			3.75 (0.53)	4 (4-4)		
No	2.22 (1.19)	2 (1-3)			2.0 (1.02)	2 (1-2)			2.24 (1.06)	2 (2-3)			3.63 (0.66)	4 (3.5-4)		
Responder or partner ever used HT																
Yes	2.6 (1.35)	3 (1-4)	0.104	0.329	2.34 (0.86)	2 (2-3)	0.024 <sup>l</sup>	0.365	2.66 (0.93)	2 (2-3.5)	0.21	0.233	2.8 (1.08)	2.75 (2-4)	0.9	0.113
No	2.2 (1.18)	2 (1-3)			1.98 (1.0)	2 (1-2)			2.24 (1.04)	2 (2-3)			2.7 (1.07)	2.25 (2-4)		
Age <sup>e</sup> , r	0.116		0.15		0.188		0.018 <sup>m</sup>		0.193		0.016 <sup>n</sup>		2.8 (1.06)	2.875 (2-4)	0.009 <sup>o</sup>	
													2.7 (1.075)	2.25 (1.93-4)		
													0.207			

<sup>a</sup>Statistically significant.  
<sup>b</sup>P indicates statistical significance across subgroup levels.  
<sup>c</sup>r, Spearman's correlation coefficient.

DISCUSSION

The findings of this research indicate that the majority of Israeli gynecologic healthcare providers who participated in this study are prescribing HT for symptomatic population-risk menopausal patients, but to a lesser extent for symptomatic high-risk population, which includes patients with personal or familial history of breast cancer, and also patients with BRCA-mutations. In addition, the study indicates that a short educational intervention might positively affect the rate of prescribing/suggesting HT to BRCA-mutation carriers by Israeli healthcare providers.

In the absence of any reliable method for early detection of EOC, RRBSO is actively recommended for BRCA-mutation carriers as the most effective method of significantly lowering ovarian cancer risk.<sup>15-17</sup> However, the early menopause induced by RRBSO in young women is likely to be associated with vasomotor symptoms (hot flashes, night sweats, and sweating), a decline in sexual functioning,<sup>8</sup> and also long-term sequelae such as osteopenia and osteoporosis, impaired cardiovascular health, and a possible decrease in cognitive function.<sup>18</sup>

Many of these symptoms and possibly clinical complications can be alleviated by HT. Yet, the recommendation and use of HT are not widespread, primarily fueled by the fear from an increased risk of breast cancer in HT users by both patients and physicians alike.<sup>15,19</sup> This concept is presumably supported by data from both the Women's Health Initiative and the Million Women Study, indicating an increase of 1.24 and 2.00, respectively, in the relative risk of breast cancer in users of combined HT (estrogen and progesterone).<sup>20-22</sup> Yet, in healthy BRCA-mutation carriers both retrospective and prospective observational studies have shown that HT after RRBSO, at least until the age of natural menopause, does not increase the risk of either breast or ovarian cancer.<sup>23,24</sup> Current guidelines indeed support the routine use of HT in healthy BRCA-mutation carriers after RRBSO.<sup>11-13</sup>

Our findings show that in Israel, where the prevalence of BRCA-mutation carriers is high, HT after RRBSO was actively recommended by 33% to 49% of participating health-worker respondents, depending upon whether the patient was symptomatic and whether she had undergone RRM. This recommendation rate is higher than the rate usually found for patients with a personal or familial history of breast cancer,<sup>15,19</sup> but much lower than that for the average-risk population. Older professionals were more likely to have a positive attitude towards HT, possibly because of their more advanced knowledge of the subject and greater familiarity with current guidelines. Nurses and residents displayed more hesitant attitudes toward HT prescription for BRCA-mutation carriers, possibly for the opposite reason. The medical oncologists in our survey were less likely than the other professional groups to recommend HT for high-risk and general-risk asymptomatic populations or for healthy BRCA-mutation carriers. This attitude probably reflects concerns regarding the use of HT and risk of breast cancer in high-risk women, especially given the current paucity of relevant large-scale

**TABLE 4.** Pre and postintervention mean and median scores of prescribing HT for BRCA-mutation carriers, by responder characteristics

Variables	Preintervention		Postintervention		P pre vs postintervention	Effect size	P for interaction <sup>a</sup>
	Mean (SD)	Median (IQR)	Mean (SD)	Median (IQR)			
Sex							0.085
Male	2.75 (1.03)	2.5 (2-4)	3.54 (0.78)	4 (3.5-4)	<0.001 <sup>b</sup>	0.766	
Female	2.66 (1.07)	2.25 (1.75-4)	3.73 (0.49)	4 (3.75-4)	<0.001 <sup>b</sup>	1.07	
Responder or partner ever suffer from menopausal symptoms							0.662
Yes	2.80 (1.08)	2.75 (2-4)	3.64 (0.73)	4 (3.75-4)	<0.001 <sup>b</sup>	0.821	
No	2.71 (1.07)	2.25 (2-4)	3.64 (0.64)	4 (3.5-4)	<0.001 <sup>b</sup>	0.88	
Responder or partner ever used HT							0.977
Yes	2.82 (1.06)	2.875 (2-4)	3.72 (0.61)	4 (3.75-4)	<0.001 <sup>b</sup>	0.993	
No	2.70 (1.075)	2.25 (1.93-4)	3.61 (0.68)	4 (3.5-4)	<0.001 <sup>b</sup>	0.841	
Professional group							
Nurses	2.20 (0.92)	2 (1.5-2.68)	3.85 (0.30)	4 (3.75-4)	0.003 <sup>b</sup>	1.71	0.002 <sup>b</sup>
Obstetricians	2.70 (1.08)	2.25 (1.87-4)	3.55 (0.80)	4 (3.5-4)	<0.0001 <sup>b</sup>	0.834	0.490
Gynecologists	3.33 (0.93)	4 (2.25-4)	3.77 (0.58)	4 (4-4)	0.004 <sup>b</sup>	0.74	0.085
Gyn-oncologists <sup>b</sup>	3.65 (0.76)	4 (3.62-4)	3.62 (0.85)	4 (3.5-4)	0.492	0.101	
Medical oncologists	2.59 (1.06)	2.12 (1.9-3.8)	3.52 (0.80)	4 (3.43-4)	0.003 <sup>b</sup>	0.956	0.993
Residents	2.48 (0.99)	2 (1.68-3.56)	3.64 (0.53)	4 (3.5-4)	<0.0001 <sup>b</sup>	1.082	0.081

IQR, interquartile range; SD, standard deviation.

<sup>a</sup>P for interaction, statistical significance across subgroup levels.

<sup>b</sup>Statistically significant.

randomized studies on the subject. Nevertheless, current guidelines imply that despite those limitations, it is important to discuss the HT option with the patient, sharing present concerns while mentioning that as yet there seems to be no contraindication for HT, especially if menopausal considerations are the main factors affecting her decision of whether or not to undergo RRBSO.<sup>25</sup>

As our present survey demonstrated, a short educational intervention can serve to change attitudes of healthcare workers toward prescribing HT for BRCA-mutation carriers after RRBSO. Using educational interventions to translate research results into routine clinical practice is a challenging prospect.<sup>26</sup> Nevertheless, previous survey-based research has shown that educational experiences as part of professional meetings, either unaccompanied by or combined with other interventions, might lead to improved professional practice,<sup>27</sup> increase the knowledge, and hence the comfort levels of clinicians who must relate to arguable recommendations concerning medications or interventions.<sup>28-31</sup> In the framework of Continuing Medical Education (CME) activities, a meta-analysis of 13 articles examining audience characteristics that influence educational interventions found that the roles of age and sex of the audience were not significant, and subspecialty was a minor contributor to the effectiveness of an educational intervention.<sup>32</sup> A change in attitude towards HT prescription in the present study was likewise unrelated to sex. However, after the short intervention, the younger healthcare providers, who were mainly nurses and residents, were more likely than their elder counterparts to change their attitudes in favor of prescribing HT. Younger participants and nonphysicians have been found more likely to be affected and to change their attitudes after an educational intervention in other studies as well. Berenson et al,<sup>33</sup> in a study aimed at assessing changes in knowledge levels of physicians, nonphysician healthcare workers, and medical students before and after attending a 30-minute lecture on human

papillomavirus (HPV), found that knowledge scores of younger participants and nonphysician healthcare workers were the most improved of all groups tested. This might be explained by their lower baseline knowledge, but might also represent higher flexibility and greater willingness to change their attitudes when presented with new compelling evidence.

There are some inherent limitations to this study that must be acknowledged. The relatively small number of respondents is one of the main limitations of our survey. In addition, the “before” and “after” surveys were conducted on the same day, and there was no follow-up about possible longer-term changes in attitude, nor any real-life confirmation of that change in practice. Another limitation is that the cases were generalized, and did not differ, for example, between patients with mutations in BRCA1 and in BRCA2, or between different HT protocols. For example, attitude toward prescribing estrogen-only for hysterectomized patients, which is beyond the scope of the current study. Despite these limitations, however, this survey summarized attitudes toward HT in general and particularly in high-risk populations in Israel.

## CONCLUSIONS

Our study results imply that a brief educational intervention in the form of a lecture and discussion might increase the knowledge of healthcare providers about HT after RRBSO in BRCA-mutation carriers, and hence might encourage evidence-based attitudes towards this controversial issue.

## REFERENCES

1. Kuchenbaecker KB, Hopper JL, Barnes DR, et al. Risks of breast, ovarian, and contralateral breast cancer for BRCA1 and BRCA2 mutation carriers. *JAMA* 2017;317:2402-2416.
2. Kauff ND, Domchek SM, Friebel TM, et al. Risk-reducing salpingo-oophorectomy for the prevention of BRCA1- and BRCA2-associated breast and gynecologic cancer: a multicenter, prospective study. *J Clin Oncol* 2008;26:1331-1337.

3. Eleje GU, Eke AC, Ezebialu IU, Ikechebeli JI, Ugwu EO, Okonkwo OO. Risk-reducing bilateral salpingo-oophorectomy in women with BRCA1 or BRCA2 mutations. *Cochrane Database Syst Rev* 2018;8:CD012464.
4. Kim SI, Lim MC, Lee DO, et al. Uptake of risk-reducing salpingo-oophorectomy among female BRCA mutation carriers: experience at the National Cancer Center of Korea. *J Cancer Res Clin Oncol* 2016;142:333-340.
5. Kim D, Kang E, Hwang E, et al. Factors affecting the decision to undergo risk-reducing salpingo-oophorectomy among women with BRCA gene mutation. *Fam Cancer* 2013;12:621-628.
6. Vermeulen RFM, Beurden Mvan, Kieffer JM, et al. Hormone replacement therapy after risk-reducing salpingo-oophorectomy minimises endocrine and sexual problems: a prospective study. *Eur J Cancer* 2017;84:159-167.
7. Madalinska JB, van Beurden M, Bleiker EMA, et al. The impact of hormone replacement therapy on menopausal symptoms and sexual function in younger high-risk women after prophylactic salpingo-oophorectomy. *J Clin Oncol* 2006;24:3576-3582.
8. Finch A, Metcalfe KA, Chiang JK, et al. The impact of prophylactic salpingo-oophorectomy on menopausal symptoms and sexual function in women who carry a BRCA mutation. *Gynecol Oncol* 2011;121:163-168.
9. D'Alonzo M, Piva E, Pecchio S, et al. Satisfaction and impact on quality of life of clinical and instrumental surveillance and prophylactic surgery in BRCA-mutation carriers. *Clin Breast Cancer* 2018;18:1361-1366.
10. Marchetti C, De Felice F, Boccia S, et al. Hormone replacement therapy after prophylactic risk-reducing salpingo-oophorectomy and breast cancer risk in BRCA1 and BRCA2 mutation carriers: a meta-analysis. *Crit Rev Oncol/Hematol* 2018;132:111-115.
11. The 2017 hormone therapy position statement of The North American Menopause Society. *Menopause* 2017;24:728-753.
12. Familial breast cancer: classification, care and managing breast cancer and related risks in people with a family history of breast cancer | Guidance and guidelines | NICE. Available at: <https://www.nice.org.uk/guidance/cg164>. Accessed November 13, 2018.
13. Menopause Management—Australasian Menopause Society. Available at: <https://www.menopause.org.au/hp/management>. Accessed November 13, 2018.
14. Cohen J. *Statistical Power Analysis for the Behavioral Sciences*, second Edition. Hillsdale, New York, NJ: Lawrence Erlbaum Associates; 1988.
15. Johansen N, Liavaag AH, Iversen O-E, Dørum A, Braaten T, Michelsen TM. Use of hormone replacement therapy after risk-reducing salpingo-oophorectomy. *Acta Obstet Gynecol Scand* 2017;96:547-555.
16. Daly MB, Pilarski R, Berry M, et al. NCCN guidelines insights: genetic/familial high-risk assessment: breast and ovarian, version 2.2017. *J Natl Compr Canc Netw* 2017;15:9-20.
17. Paluch-Shimon S, Cardoso F, Sessa C, et al. Prevention and screening in BRCA mutation carriers and other breast/ovarian hereditary cancer syndromes: ESMO Clinical Practice Guidelines for cancer prevention and screening. *Ann Oncol* 2016;27 (Suppl 5):v103-v110.
18. Gordhandas S, Norquist BM, Pennington KP, Yung RL, Laya MB, Swisher EM. Hormone replacement therapy after risk reducing salpingo-oophorectomy in patients with BRCA1 or BRCA2 mutations; a systematic review of risks and benefits. *Gynecol Oncol* 2019;153:192-200.
19. Challberg J, Ashcroft L, Lalloo F, et al. Menopausal symptoms and bone health in women undertaking risk reducing bilateral salpingo-oophorectomy: significant bone health issues in those not taking HRT. *Br J Cancer* 2011;105:22-27.
20. Anderson GL, Limacher M, Assaf AR, et al. Effects of conjugated equine estrogen in postmenopausal women with hysterectomy: the Women's Health Initiative randomized controlled trial. *JAMA* 2004;291:1701-1712.
21. Chlebowski RT, Hendrix SL, Langer RD, et al. Influence of estrogen plus progestin on breast cancer and mammography in healthy postmenopausal women: the Women's Health Initiative Randomized Trial. *JAMA* 2003;289:3243-3253.
22. Beral V; Million Women Study Collaborators. Breast cancer and hormone-replacement therapy in the Million Women Study. *Lancet* 2003;362:419-427.
23. Eisen A, Lubinski J, Gronwald J, et al. Hormone therapy and the risk of breast cancer in BRCA1 mutation carriers. *J Natl Cancer Inst* 2008;100:1361-1367.
24. Rebbeck TR, Friebel T, Wagner T, et al. Effect of short-term hormone replacement therapy on breast cancer risk reduction after bilateral prophylactic oophorectomy in BRCA1 and BRCA2 mutation carriers: the PROSE Study Group. *J Clin Oncol* 2005;23:7804-7810.
25. Dombchek S, Kaunitz AM. Use of systemic hormone therapy in BRCA mutation carriers. *Menopause* 2016;23:1026-1027.
26. Johnson MJ, May CR. Promoting professional behaviour change in healthcare: what interventions work, and why? A theory-led overview of systematic reviews. *BMJ Open* 2015;5:e008592.
27. Forsetlund L, Bjørndal A, Rashidian A, et al. Continuing education meetings and workshops: effects on professional practice and health care outcomes. *Cochrane Database Syst Rev* 2009;CD003030.
28. Mendoza KS, McPherson ML. Knowledge skills, and attitudes regarding the use of medical cannabis in the hospice population: an educational intervention. *Am J Hosp Palliat Care* 2018;35:759-766.
29. Sachdeva R, Kelleman MS, McCracken CE, et al. Physician attitudes toward the first pediatric appropriate use criteria and engagement with educational intervention to improve the appropriateness of outpatient echocardiography. *J Am Soc Echocardiogr* 2017;30:926.e2-931.e2.
30. AlZoubi F, Mannocci F, Newton T, Manoharan A, Djemal S. What do dental students know about trauma? *Dent Traumatol* 2015;31:482-486.
31. Kaya Z, Gültekin KE, Demirtaş OK, Karadeniz D, Çalapkulu Y, Tap Ö. Effects of targeted education for first-year university students on knowledge and attitudes about stem cell transplantation and donation. *Exp Clin Transplant* 2015;13:76-81.
32. Lowe MM, Bennett N, Aparicio A. American College of Chest Physicians Health and Science Policy Committee. The role of audience characteristics and external factors in continuing medical education and physician change: effectiveness of continuing medical education: American College of Chest Physicians Evidence-Based Educational Guidelines. *Chest* 2009;135 (3 Suppl):56S-61S.
33. Berenson AB, Rahman M, Hirth JM, Rupp RE, Sarpong KO. A brief educational intervention increases providers' human papillomavirus vaccine knowledge. *Hum Vaccin Immunother* 2015;11:1331-1336.