



Customized breast cancer risk assessment in an ambulatory clinic: a portal for identifying women at risk

Anna Weiss^{1,2,3} · Samantha Grossmith^{1,2} · Danielle Cutts^{1,2} · Sage A. Mikami^{1,2} · Johanna A. Suskin^{1,2} · Mary Knust Graichen¹ · Negui Arilis Rojas^{1,2} · Lydia E. Pace^{1,4} · Eileen Joyce^{1,2} · Esther Rhei^{1,2,3} · Rochelle Scheib^{1,3,5} · Brittany Bychkovsky^{1,3,5} · Judy E. Garber^{1,3,5} · Daniel Morganstern^{1,4,5,6} · Tari A. King^{1,2,3} 

Received: 18 December 2018 / Accepted: 20 December 2018 / Published online: 21 January 2019
© Springer Science+Business Media, LLC, part of Springer Nature 2019

Abstract

Purpose Existing high-risk clinic models focus on patients with known risk factors, potentially missing many high-risk patients. Here we describe our experience implementing universal risk assessment in an ambulatory breast center.

Methods Since May 2017, all breast center patients completed a customized intake survey addressing known breast cancer risk factors and lifestyle choices. Patient characteristics, family history, risk scores, and lifestyle factors were examined; patients with high-risk breast lesions were excluded. Patients were considered at increased risk by model thresholds Gail 5-year risk > 1.7% (35–59 years), Gail 5-year risk > 5.5% (≥ 60 years), or Tyrer–Cuzick (T–C) v7 lifetime risk > 20% (any age).

Results From May 2017–April 2018, there were 874 eligible patients—420 (48%) referred for risk assessment (RA) and 454 (52%) for non-specific breast complaints (NSBC). Overall, 389 (45%) were at increased risk of breast cancer. Gail 5-year risks were similar between RA and NSBC patients. However, RA patients more frequently met criteria by T–C score ($P=0.02$). Of all patients at increased risk, 149 (39%) were overweight (BMI > 25) or obese (BMI > 30) and only 159 (41%) met recommended exercise standards. NSBC patients who met criteria were more frequently smokers (8% vs 1%, $P < 0.01$); all other demographic/lifestyle factors were similar among high-risk patients regardless of referral reason.

Conclusions Universal risk assessment in a comprehensive breast health center identified 45% of our population to be at increased risk of breast cancer. This clinical care model provides a unique opportunity to identify and address modifiable risk factors among women at risk.

Keywords Breast cancer · Risk assessment · High-risk program · Modifiable risk factors · Prevention

Electronic supplementary material The online version of this article (<https://doi.org/10.1007/s10549-018-05116-5>) contains supplementary material, which is available to authorized users.

✉ Tari A. King
Tking7@bwh.harvard.edu

¹ Comprehensive Breast Health Center, Brigham and Women's Hospital, Boston, MA, USA

² Division of Breast Surgery, Department of Surgery, Brigham and Women's Hospital, Boston, MA, USA

³ Breast Oncology Program, Dana-Farber/Brigham and Women's Cancer Center, Boston, MA, USA

Introduction

Nearly one-third of postmenopausal breast cancers are thought to be potentially preventable by modifying lifestyle risk factors [1–5]. These factors include but are not limited to excess alcohol intake [6, 7], obesity [8, 9], and a sedentary lifestyle [10]. Pharmacologic prevention strategies have

⁴ Division of Women's Health, Brigham and Women's Hospital, Boston, MA, USA

⁵ Division of Cancer Genetics and Prevention, Dana-Farber Cancer Institute, Boston, MA, USA

⁶ Starling Physicians Group, Hartford Healthcare Cancer Institute, Plainville, CT, USA

also proven effective for patients at increased breast cancer risk due to family history or high-risk benign breast lesions, but uptake of these strategies remains limited. Importantly, breast cancer risk conferred by these non-modifiable risk factors can also be impacted by healthy lifestyle practices including maintaining a healthy weight, abstaining from alcohol and smoking, and avoiding hormone replacement therapy [5].

Despite the value of preventive strategies for reducing risk of breast cancer, identifying women at elevated risk of breast cancer poses an implementation challenge for healthcare systems. Studies suggest that anywhere from 30 to 75% of women are unaware of their risk [11–13]. Further, healthcare providers may not be identifying patients at increased risk who lack typical triggers for risk assessment such as significant family histories or prior high-risk breast lesions, limiting opportunities to intervene with preventive strategies [14]. Previously described models for high-risk breast clinics have predominantly included patients with known high-risk breast lesions, atypical hyperplasias and lobular carcinoma in situ, or significant family histories of breast cancer [15–17], and it is likely that these efforts are also missing a large number of women who are at elevated risk due to combinations of other factors including lifestyle. The American College of Radiology has suggested that all women are assessed for breast cancer risk by the age of 30 [18], but implementation of this recommendation in healthcare settings poses several challenges and has not been widely accepted.

Ideally, universal risk assessment would allow for identification of a broader population of women at increased breast cancer risk and would increase the opportunity for engagement of both patients and healthcare providers in a dialogue about risk reduction strategies. Here we describe our experience in the first year of implementation of a customized universal risk assessment program in an ambulatory breast center, highlighting modifiable risk factors and opportunities for focused behavioral changes in this population of women at increased risk.

Methods

The Comprehensive Breast Health Center at Brigham and Women's Hospital is an ambulatory clinic in an urban academic hospital that provides care for patients with a range of breast complaints. These include patients referred for breast lumps, pain, infections, imaging abnormalities, nipple discharge, or high-risk breast lesions. Referrals are from primary care physicians and other healthcare providers, including radiologists and emergency room physicians. Patients can also self-refer to our clinic. In May 2017, we launched a universal breast cancer risk assessment tool across this

population. All patients, regardless of reason for referral, were asked to complete a customized, electronic tablet-based intake survey upon checking in for their appointment. Our customized survey was adapted from Hughes RiskApps [19] and addresses known hereditary and reproductive breast cancer risk factors, personal history of breast biopsies and subsequent pathology, as well as lifestyle and behavior questions which were derived from validated questions used in the Nurses' Health Study [20]. Following program implementation the Breast Health Center also began receiving direct referrals for risk assessment. In collaboration with our clinical cancer genetics colleagues at Dana-Farber Cancer Institute, we triage patients with a family history strongly suggestive of an inherited predisposition to breast cancer directly to the clinical cancer genetics program for consultation.

For the purposes of this study, patients presenting to The Comprehensive Breast Health Center from May 2017 to April 2018 were analyzed. Our goal was to describe our experience with universal risk assessment among patients seen at our comprehensive breast center, many of whom presented for non-specific breast complaints, without prior knowledge of their breast cancer risk. We excluded patients with a personal history of breast cancer, prior mantle radiation for lymphoma, known genetic mutations or known high-risk breast lesions (including atypical ductal hyperplasia, atypical lobular hyperplasia, and lobular carcinoma in situ) from this analysis.

Patient-reported survey data included demographics (age, race, ethnicity, education status, and relationship status), breast density, family history of breast and other cancers, and lifestyle questions related to alcohol use, smoking status, exercise and weight. At-risk alcohol intake was defined as more than one alcoholic beverage on average per day [7]. Body mass index (BMI) was calculated from patient-reported height and weight. Patients were considered overweight if their BMI was between 25 and 29.9, and obese if BMI was greater than or equal to 30, according to the World Health Organization (WHO) definitions of obesity [21]. Benchmarks for exercise goals were adopted from the American Cancer Society (ACS) Guidelines on Nutrition and Physical activity, defined as more than 75 min of vigorous exercise or more than 150 min of moderate exercise per week [10]. "At-risk weight gain" thresholds were adopted from Eliassen et al. and defined as gaining more than 55 pounds between age 18 and 50; gaining more than 22 pounds from age 50 to the present; or a greater than 10% increase in weight over the past year [9].

Survey data were used to calculate 5-year and lifetime risks of breast cancer, as well as the risk of having a germline mutation predisposing to breast cancer. Patients were considered to be at increased risk if they met the following standardized risk assessment thresholds: a Gail 5-year breast

cancer risk higher than 1.7% for patients 35–59 years old; a Gail 5-year risk higher than 5.5% for patients older than 60 [22]; or a Tyrer–Cuzick v.7 lifetime risk over 20% at any age [23]. Patients were considered for referral to Dana-Farber Cancer Institute’s Cancer Genetics and Prevention clinic for counseling and germline testing if their BRCAPRO or Myriad scores were greater than 10%. Patient characteristics, lifestyle factors, and family history were compared between patients referred for risk assessment and patients referred for non-specific breast complaints both in the overall cohort and among those meeting criteria for increased risk. In addition, among those meeting high-risk criteria, median Gail and Tyrer–Cuzick v7 breast cancer risk scores, as well as BRCAPRO and Myriad risk scores were compared by reason for referral using Chi square and Mann–Whitney tests as appropriate. A *P*-value less than 0.05 was considered statistically significant.

Results

From May 2017 to April 2018, 1624 patients were evaluated in the comprehensive breast health center and completed the customized risk assessment survey. Of these, 400 (25%) reported a personal history of breast cancer, 15 had prior

mantle radiation, 2 had a known genetic mutation, and 303 (19%) reported having a high-risk breast lesion and were thus excluded from this analysis. Among the remaining 904 patients, 427 (47%) were referred specifically for risk assessment and 477 (53%) for non-specific breast complaints. Of these, 30 were discovered to have a high-risk lesion following further work-up in our breast center (7 in the risk assessment group and 23 in the non-specific breast complaint group) and these patients were also excluded from further analyses. The remaining 874 patients formed our study cohort.

Median age of the cohort was 48 years (range 15–88); 668 (76%) self-reported as Caucasian and 112 (13%) reported Ashkenazi Jewish ancestry. Thirty-nine percent of patients had an advanced degree and 56% were married (Table 1). Among all patients, 494 (56%) reported less than 1 alcoholic beverage per week, 222 (25%) were former smokers and 30 (3%) were current smokers. Current weight distribution included: 215 (25%) with a BMI > 25 and 173 (20%) with a BMI > 30. Lastly, 493 (56%) reported they had been told they had dense breasts (Table 2).

Patients referred for risk assessment were younger (median age 47 vs 49 years), less likely to be Hispanic or Latina (8% vs 16%) and reported higher degrees of education as compared to patients referred for non-specific breast

Table 1 Patient demographics for overall cohort and by reason for clinic referral

Patient reported demographics	All patients <i>N</i> = 874	Risk assessment <i>N</i> = 420	Non-specific breast complaint <i>N</i> = 454	<i>P</i> value
Median age at visit, years (range)	48 (15–88)	47 (16–84)	49 (15–88)	0.04
Race				0.05
White	668 (76%)	336 (80%)	332 (73%)	
Black or African American	51 (6%)	24 (6%)	27 (6%)	
Asian or Pacific Islander	32 (4%)	13 (3%)	19 (4%)	
Caribbean/West Indian	28 (3%)	7 (2%)	21 (5%)	
Other ^a /unknown/missing	95 (11%)	40 (9%)	55 (12%)	
Ashkenazi Jewish heritage	112 (13%)	63 (15%)	49 (11%)	0.06
Hispanic or Latino	107 (12%)	35 (8%)	72 (16%)	<0.01
Highest degree obtained				<0.01
Middle school	32 (3%)	8 (2%)	24 (5%)	
High school	185 (21%)	67 (16%)	118 (26%)	
College	277 (32%)	147 (35%)	130 (29%)	
Advanced degree	339 (39%)	180 (43%)	159 (35%)	
Missing	41 (5%)	18 (4%)	23 (5%)	
Relationship status				0.25
Married	496 (56%)	258 (61%)	258 (57%)	
In a steady relationship	118 (14%)	54 (13%)	64 (14%)	
Single, never married	99 (11%)	40 (10%)	59 (13%)	
Separated/divorced/widowed	84 (10%)	34 (8%)	50 (11%)	
Other/missing	77 (9%)	34 (8%)	43 (9%)	

^aIncludes American Indian/Aleutian/Eskimo

Table 2 Patient reported lifestyle factors for overall cohort and by reason for clinic referral

Risk factors	All patients N=874	Risk assessment N=420	Non-specific breast complaint N=454	P value
Alcohol use: number of alcoholic drinks per week				0.03*
Never/<1	494 (56%)	219 (52%)	275 (61%)	
1–9	350 (40%)	185 (44%)	165 (36%)	
10–19 drinks/week	16 (2%)	10 (2%)	6 (1%)	
≥ More than 19/week	1 (<1%)	0 (0%)	1 (<1%)	
Unknown	13 (1%)	6 (1%)	7 (2%)	
Smoking status				0.02#
Never	622 (72%)	313 (74%)	309 (68%)	
Former smoker	222 (25%)	99 (24%)	123 (27%)	
Current smoker (cigarettes/day)	30 (3%)	8 (2%)	22 (5%)	
1–4	11 (37%)	3 (38%)	8 (36%)	
5–14	13 (43%)	4 (50%)	9 (41%)	
15–24	3 (10%)	0 (0%)	3 (14%)	
Missing	3 (10%)	1 (<1%)	2 (10%)	
Has tried to quit	25 (83%)	6 (75%)	19 (86%)	
Body mass index				<0.01
Underweight (<18.5)	20 (2%)	11 (3%)	9 (2%)	
Normal weight (18.5–24.9)	446 (51%)	240 (57%)	206 (45%)	
Overweight (25.0–29.9)	215 (25%)	88 (21%)	127 (28%)	
Obese (≥30.0)	173 (20%)	74 (18%)	99 (22%)	
Unknown	20 (2%)	7 (2%)	13 (3%)	
Dense breasts	493 (56%)	274 (65%)	219 (48%)	<0.01

*P value compares never drinker, 1–9 drinks per week, and 10–19 drinks per week categories only

#P value compares never smoker, former smoker, and current smoker categories only

complaints (Table 1). Patients referred for risk assessment also reported higher rates of alcohol intake were less likely to be smokers, less likely to be overweight or obese and more likely to have been told they had dense breasts (Table 2). Patients referred for risk assessment were more likely to meet exercise guidelines than those referred for non-specific breast complaints (Table 3). Not surprisingly patients referred for risk assessment also had stronger family histories of breast cancer (Table 4).

Overall 389/874 patients (45%) were found to be at increased risk per our criteria as outlined above. Of these patients at risk, 168/389 (43%) met criteria based on their Gail score and 318/389 (82%) met criteria based on their Tyrer–Cuzick score. Tyrer–Cuzick lifetime risk scores ranged from 0.5 to 65.4% for the entire study cohort (Fig. 1). Of the 318 patients who met criteria by their Tyrer–Cuzick score, 292 (92%) had lifetime risk scores between 20 and 40%.

Of the 420 patients referred specifically for risk assessment, 274 (65%) were at increased risk (Table 5). Of the 35–59 year olds referred for risk assessment, 57% (112/195) met increased risk criteria by Gail 5-year risk cutoff (median risk 2.4%, range 1.8–6.4), 41% of patients older than 60

(9/22) met increased risk criteria by Gail 5-year risk cutoff (median risk 7.6%, range 5.6–11.5) and 86% (237/274) met increased risk criteria by Tyrer–Cuzick >20% lifetime risk (median risk 27.4%, range 20.2–65.4). In addition, 47 (17%) and 27 (10%) of patients met criteria for referral to genetic counseling by the BRCAPRO and Myriad models, respectively.

Among the 454 patients referred for non-specific breast complaints, 115 (25%) were at increased risk. Of the 35–59 year olds referred for non-specific breast complaints, 59% (44/75) met increased risk criteria by Gail 5-year risk cutoff (median risk 2.3%, range 1.8–4.1), 33% of patients older than 60 years (3/9) met increased risk criteria by Gail 5-year cutoff (median risk 8.8%, range 5.6–10.4), and 70% (81/115) met increased risk criteria by Tyrer–Cuzick >20% lifetime risk (median risk 24.5%, range 20–47.5). Similarly, 14 (12%) of patients met criteria for referral to genetic counseling by both the BRCAPRO and Myriad models. When examined by reason for referral, there were no significant differences in the number of patients who met criteria by the Gail model ($P=0.67$ for 35–59 year olds, $P=0.69$ for those over 60), nor in the number of patients who qualified for genetic counseling ($P=0.22$ BRCAPRO, $P=0.5$ Myriad).

Table 3 Self-reported weight change and exercise habits among all patients by reason for clinic referral

Weight/exercise factor	All patients N=874	Risk assessment N=420	Non-specific breast complaint N=454	P value
Patients that met exercise standards	308 (35%)	167 (40%)	141 (31%)	0.03
Met by vigorous activity	202 (23%)	112 (27%)	90 (20%)	
Met by moderate activity	106 (12%)	55 (13%)	51 (11%)	
Did not meet exercise standards	328 (38%)	146 (35%)	182 (40%)	
Unknown exercise activity	238 (27%)	107 (25%)	131 (29%)	
Patients who had at risk weight gain^a	90/874 (10%)	38/420 (9%)	52/454 (11%)	0.24
> 55 pounds gained between age 18–50 ^c	33/383 (9%)	17/166 (10%)	16/217 (7%)	
Not at risk	223/383 (58%)	99/166 (60%)	124/217 (57%)	
Unknown ^b	127/383 (33%)	50/166 (30%)	77/217 (35%)	
> 22 pounds gained between age 50–present ^d	30/367 (8%)	9/156 (6%)	21/211 (10%)	
Not at risk	255/367 (69%)	115/156 (74%)	140/211 (66%)	
Unknown ^b	82/367 (22%)	32/156 (21%)	50/211 (24%)	
> 10% weight gain in last year	34/874 (4%)	16/420 (4%)	18/454 (4%)	
Not at risk	766/874 (88%)	370/420 (88%)	396/454 (87%)	
Unknown ^b	74/874 (8%)	34/420 (8%)	40/454 (9%)	
Trying to lose weight	407 (47%)	200 (48%)	207 (46%)	0.55

^aPatients may be in more than one at-risk weight gain category at a time, so the sum of at risk patients in the 3 categories may be greater than the at risk total patients in this row

^bUnable to calculate due to blanks or obvious outlier

^cFiltered for patients 50 and over

^dFiltered for patients 51 and over

Table 4 Family history of breast cancer for overall cohort and by reason for clinic referral

Relative	All patients N=874	Risk assessment N=420	Non-specific breast complaint N=454	P value [#]
Total with family history ^a	612 (70%)	381 (91%)	231 (51%)	<0.01
Single 1st degree relative	279 (32%)	203 (48%)	76 (17%)	
Multiple 1st degree relatives	44 (5%)	38 (9%)	6 (1%)	
Single 2nd degree relative	177 (20%)	74 (18%)	103 (23%)	
Multiple 2nd degree relatives	84 (10%)	51 (12%)	33 (7%)	
Single 3rd degree relative	20 (2%)	10 (2%)	10 (2%)	
Multiple 3rd degree relatives	8 (1%)	5 (1%)	3 (<1%)	

[#]P value calculated for the percentage of patients with any-degree family history

^aIncludes only 1 count per patient per category in the following hierarchical order: multiple relatives > single; 1st degree > 2nd degree > 3rd degree

Patients referred for risk assessment were more likely to meet increased risk criteria by Tyer–Cuzick ($P=0.02$).

Despite the differences in patient characteristics and lifestyle factors noted above by reason for referral for the entire cohort, the only difference among those meeting high-risk criteria was higher rates of current smoking in the group of women referred for non-specific breast complaints (Supplemental Tables 1–3). All other demographics and lifestyle factors were similar among those identified to be at increased risk. Among patients meeting criteria for increased risk, only

159/389 (41%) met recommended exercise standards and 38/389 (10%) reported at risk weight gain; neither of which differed by reason for referral (Supplemental Table 3).

Discussion

Strategies to enhance patient education and awareness of breast cancer risk coupled with interventions to encourage healthy behaviors are needed to reduce the incidence of and

Fig. 1 Distribution of Tyrer–Cuzick lifetime breast cancer risk scores among the study cohort

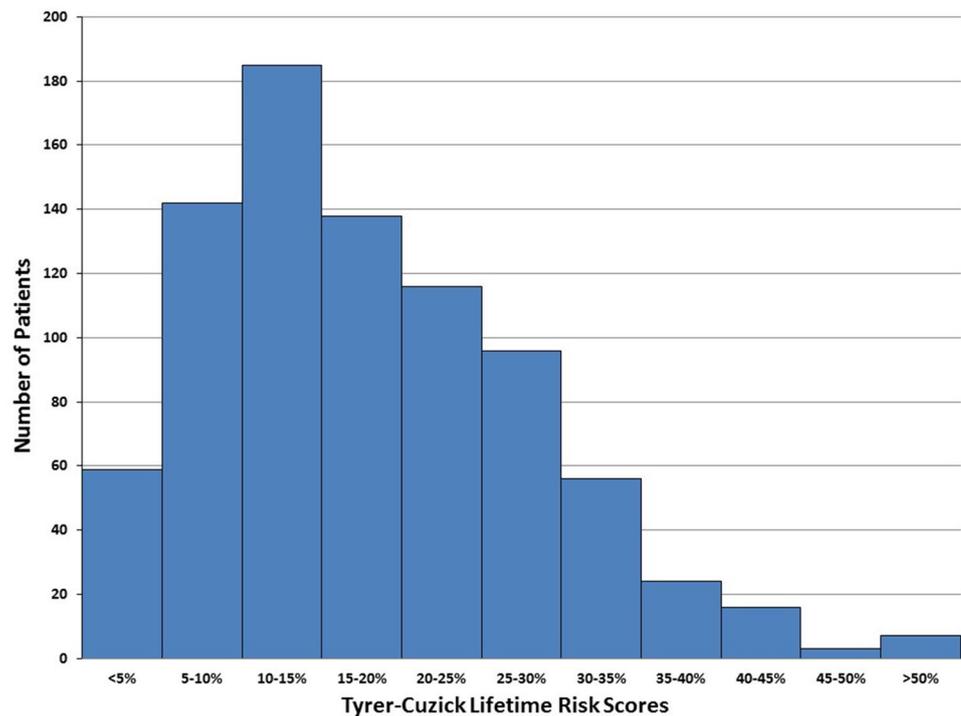


Table 5 Median 5-year Gail risk, median lifetime Tyrer–Cuzick v7 risk, and risk of a genetic mutation for patients meeting criteria for increased risk by reason for clinic referral

Risk model ^a	Risk assessment <i>N</i> = 274		Non-specific breast complaint <i>N</i> = 115		<i>P</i> value [@]
	<i>N</i> ^c	Median risk (range) ^b	<i>N</i> ^c	Median risk (range) ^b	
Gail 5-year risk; > 1.7%	112/195 (57%)	2.4% (1.8–6.4)	44/75 (59%)	2.3% (1.8–4.1)	0.67
Gail 5-year risk; > 5.5%	9/22 (41%)	7.6% (5.6–11.5)	3/9 (33%)	8.8% (5.6–10.4)	0.69
T–C v.7 lifetime risk > 20%	237/274 (86%)	27.4% (20.16–65.35)	81/115 (70%)	24.5% (20.01–47.5)	0.02
BRCAPRO > 10%	47/274 (17%)	19.3% (10.13–47.77)	14/115 (12%)	18.8% (12.98–50.66)	0.22
Myriad > 10%	27/274 (10%)	13% (12.7–22.9)	14/115 (12%)	13% (12.7–16.4)	0.50

[@]*P* value compares the percentage of patients who met high-risk criteria in each group

^aPatients may be in more than one category

^bMedian risk and range for those who met high-risk criteria

^cNumber of patients who met high-risk criteria/the number of patients who were eligible by age group

mortality from breast cancer among US women. In our first year of implementing universal risk assessment in our comprehensive breast health clinic, we screened 874 patients referred either for non-specific breast complaints or for formal risk assessment and identified 389 women, 45% of this population, to be at increased risk. Patients referred for breast concerns were at equally high risk compared to those referred specifically for risk assessment. Among patients with elevated risk in our cohort, 92% had Tyrer–Cuzick lifetime risk scores between 20 and 40%, representing a heterogeneous cohort that largely includes women whose family history is not necessarily triggering referral to a genetic

high-risk clinic. Across the country, this likely represents the largest group of patients at elevated risk and potentially those that may benefit most from efforts to address modifiable lifestyle factors and/or efforts to improve uptake of chemoprevention, as well as implementation of risk-tailored screening protocols.

Notably, the population of women referred to our clinic for non-specific breast complaints were more likely to be Hispanic or Latino and to have achieved lesser degrees of education than those referred specifically for risk assessment. From the non-specific breast complaint group, we identified 115 (25%) women at increased risk, suggesting

that universal screening has the potential to identify a previously unrecognized or underserved population at risk. Further, among all patients found to be at increased risk, the only difference between those referred for risk assessment and those referred for a non-specific breast complaint was a higher likelihood of family history in the risk assessment group. While family history remains an important component of risk assessment, the myriad of factors that influence breast cancer risk extend well beyond family history and lack of family history should not be considered absence of risk.

Our approach to breast cancer risk assessment represents a collaborative effort with specialists in our cancer genetics program. Our efforts to screen patients with a family history strongly suggestive of an inherited predisposition to breast cancer and directly triage them to the clinical cancer genetics program are reflected in the relatively low rate of patients in our population (10–17%) meeting the criteria for genetic risk assessment by either the Myriad or BRCAPRO models. Interesting, however, was again the lack of difference among patients meeting these criteria by reason for referral to our breast center. Patients referred for non-specific breast complaints were as likely to meet these thresholds as patients referred for risk assessment. Identification of significant family history and appropriate referrals for genetic counseling has been highlighted by the United States Preventive Services Task Force as an area for improvement among primary care providers [17]; yet with increasing workloads and decreasing resources, programs like ours have the potential to fill this void.

Increased awareness and focus on obesity-related cancers in the USA provides the optimal background to educate women about modifiable lifestyle factors. Among all women screened in our first year, 173 (20%) met the WHO criteria for obesity and 215 (25%) met criteria for overweight [21]. Further, among those identified to be at increased risk, 38 (10%) met criteria for at risk weight gained as outlined by Eliassen et al. [9] Related to this, only 35% of our screened population and 41% of our elevated risk population met ACS exercise guidelines for cancer prevention [10]. Failure to maintain a healthy weight or meet national exercise standards may be contributed to by a lack of awareness about health behaviors and their role in breast cancer prevention. Work by Hartman et al. has shown there is a perception that mammographic screening is effective against breast cancer, yet lifestyle factors are not perceived the same way [24]. Health behaviors have also been reported to be similar between patients with and without family history of breast cancer, despite one group being at an allegedly higher perceived risk [24–27]. In our population, self-reported lifestyle factors also did not differ by reason for referral, risk assessment versus non-specific breast complaint, among the overall cohort nor among those found to be at increased risk.

Recognizing the need for education and counseling about modifiable risk factors, we have developed several interventions in our comprehensive breast health center to understand optimal ways to educate and engage patients in breast cancer risk reduction. We have developed patient-facing literature discussing relative risk and absolute risk, and we are piloting a post-clinic survey to measure patient's knowledge of their risk and to capture their perception of the risk reducing options presented to them at their visit including exercise, weight loss, and chemoprevention. For those with at-risk weight gain or meeting standards for obesity, we are collaborating with our colleagues in weight management and triaging directly to their program for evaluation.

Implementation of a universal risk assessment strategy in a comprehensive breast clinic also provides a multi-faceted platform to advance breast cancer prevention research. We are participating in two clinical trials for women with dense breasts, one assessing the impact of physical exercise on proliferation and immune markers in benign breast tissue (DFCI IRB #18–168) and the second, a randomized, double-blind, placebo-controlled study of 4-hydroxytamoxifen gel (<https://clinicaltrials.gov/ct2/show/NCT03063619>) assessing the efficacy of the topical gel to reduce breast density as a surrogate marker of reduced breast cancer risk. Although we excluded patients with high-risk lesions from the analysis reported here, we are also collecting and banking biopsy specimens from these lesions for future translational research opportunities (DFCI IRB #13–325). And lastly, while we are focusing this report on modifiable risk factors, we did classify increased risk by validated models including the Gail five-year risk scores used in the landmark prevention trials [28, 29]. As such, we do provide counseling on the risks and benefits of selective estrogen receptor modulators and aromatase inhibitors for prevention [30, 31] and uptake of these strategies will be the focus of future reports.

Limitations of this study include design characteristics of our survey including that answers to each question are not required to continue the survey; as such we may be underestimating the number of patients at elevated risk. For example, the questions about exercise are multi-part which led to incomplete or outlier answers for 91 (23%) high-risk patients. Also, patients who reported obvious outlier numbers (e.g., a weight greater than 1000 pounds) or left weight blank were excluded from the at-risk calculations for weight gain, depending on the at-risk weight category, this represented 5–37% of possible patients. In general, education and health literacy may also bias our results as patients may simply answer some questions incorrectly. Lastly, although we saw a high number of Hispanic patients, other minorities are underrepresented in our clinic population, which may limit the generalizability of our findings.

Despite these limitations, our findings support implementation of universal breast cancer risk screening in

comprehensive breast health centers. Evolving data on lifestyle factors and breast density [32, 33], conflicting recommendations about when to begin and frequency of mammographic screening [34–36], emergence of “new” risk factors including single nucleotide polymorphisms [5], and updated data on risks conferred by the classic high-risk breast lesions [37] contribute to the increasingly complicated landscape of breast cancer risk assessment and prevention. The lack of differentiation among patients referred for risk assessment versus non-specific breast complaints in our population illustrates the challenges for providers in identifying those at increased risk. In the era of personalized medicine, there is also the opportunity for personalized risk assessment and prevention.

In conclusion, implementation of a universal breast cancer risk assessment survey in a comprehensive breast health center identified 45% of our population to be at increased risk and highlighted opportunities to address modifiable risk factors. This model represents an opportunity for identifying women at risk and provides a framework for a personalized approach to breast cancer screening and prevention.

Funding This research is funded by a grant from the Susan G. Komen foundation.

Data Availability The datasets during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Compliance with ethical standards

Conflict of interest JA Suskin reports stock ownership in Pfizer, Thermo Fisher, and Danaher (owned by immediate family members). JE Garber reports a consultant/advisory role for Helix Genetics. TA King reports a consultant/advisory role for Genomic Health. None of these affiliations influenced this work. All other authors report no conflicts.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Informed consent The study was approved by the Brigham and Women’s Hospital Institutional Review Board as a low risk study and approved with waiver of consent.

References

- Sprague BL, Trentham-Dietz A, Egan KM, Titus-Ernstoff L, Hampton JM, Newcomb PA (2008) Proportion of invasive breast cancer attributable to risk factors modifiable after menopause. *Am J Epidemiol* 168(4):404–411. <https://doi.org/10.1093/aje/kwn143>
- Tamimi RM, Spiegelman D, Smith-Warner SA, Wang M, Pazaris M, Willett WC, Eliassen AH, Hunter DJ (2016) Population attributable risk of modifiable and nonmodifiable breast cancer risk factors in postmenopausal breast cancer. *Am J Epidemiol* 184(12):884–893. <https://doi.org/10.1093/aje/kww145>
- Azevedo ESG, de Moura L, Curado MP, Gomes Fda S, Otero U, Rezende LF, Daumas RP, Guimaraes RM, Meira KC, Leite Ida C, Valente JG, Moreira RI, Koifman R, Malta DC, Mello MS, Guedes TW, Boffetta P (2016) The Fraction of cancer attributable to ways of life, infections, occupation, and environmental agents in Brazil in 2020. *PLoS ONE* 11(2):e0148761. <https://doi.org/10.1371/journal.pone.0148761>
- Wilson LF, Page AN, Dunn NA, Pandeya N, Protani MM, Taylor RJ (2013) Population attributable risk of modifiable risk factors associated with invasive breast cancer in women aged 45–69 years in Queensland, Australia. *Maturitas* 76(4):370–376. <https://doi.org/10.1016/j.maturitas.2013.09.002>
- Maas P, Barrdahl M, Joshi AD, Auer PL, Gaudet MM, Milne RL, Schumacher FR, Anderson WF, Check D, Chattopadhyay S, Baglietto L, Berg CD, Chanock SJ, Cox DG, Figueroa JD, Gail MH, Graubard BI, Haiman CA, Hankinson SE, Hoover RN, Isaacs C, Kolonel LN, Le Marchand L, Lee IM, Lindstrom S, Overvad K, Romieu I, Sanchez MJ, Southey MC, Stram DO, Tumino R, VanderWeele TJ, Willett WC, Zhang S, Buring JE, Canzian F, Gapstur SM, Henderson BE, Hunter DJ, Giles GG, Prentice RL, Ziegler RG, Kraft P, Garcia-Closas M, Chatterjee N (2016) breast cancer risk from modifiable and nonmodifiable risk factors among white women in the United States. *JAMA Oncol* 2(10):1295–1302. <https://doi.org/10.1001/jamaoncol.2016.1025>
- Strumylaite L, Sharp SJ, Kregzdyte R, Poskiene L, Bogusevicius A, Pranys D (2015) The association of low-to-moderate alcohol consumption with breast cancer subtypes defined by hormone receptor status. *PLoS ONE* 10(12):e0144680. <https://doi.org/10.1371/journal.pone.0144680>
- Baan R, Straif K, Grosse Y, Secretan B, El Ghissassi F, Bouvard V, Altieri A, Coglian V (2007) Carcinogenicity of alcoholic beverages. *Lancet Oncol* 8(4):292–293
- Amadou A, Hainaut P, Romieu I (2013) Role of obesity in the risk of breast cancer: lessons from anthropometry. *J Oncol*. <https://doi.org/10.1155/2013/906495>
- Eliassen AH, Colditz GA, Rosner B, Willett WC, Hankinson SE (2006) Adult weight change and risk of postmenopausal breast cancer. *JAMA* 296(2):193–201. <https://doi.org/10.1001/jama.296.2.193>
- Kushi LH, Doyle C, McCullough M, Rock CL, Demark-Wahnefried W, Bandera EV, Gapstur S, Patel AV, Andrews K, Gansler T (2012) American Cancer Society Guidelines on nutrition and physical activity for cancer prevention: reducing the risk of cancer with healthy food choices and physical activity. *CA Cancer J Clin* 62(1):30–67. <https://doi.org/10.3322/caac.20140>
- Andersen MR, Thorpe J, Buist DS, Beatty JD, Watabayashi K, Hanson N, Resta R, Chubak J, Urban N (2016) Cancer risk awareness and concern among women with a family history of breast or ovarian cancer. *Behav Med* 42(1):18–28. <https://doi.org/10.1080/08964289.2014.947234>
- Hannan E, Peter O’Leary D, Cheung C, Buhamad F, O’Donoghue G, Manning A, Oliver Murphy J, Hill A, Power C (2018) Knowledge of breast cancer risk factors, screening, and treatment methods in patients attending the breast clinic: a survey of 1,018 women. *Breast J* 24(6):1094–1096. <https://doi.org/10.1111/tbj.13082>
- Livaudais-Toman J, Karliner LS, Tice JA, Kerlikowske K, Gregorich S, Perez-Stable EJ, Pasick RJ, Chen A, Quinn J, Kaplan CP (2015) Impact of a primary care based intervention on breast cancer knowledge, risk perception and concern: a randomized, controlled trial. *Breast* 24(6):758–766. <https://doi.org/10.1016/j.breast.2015.09.009>
- Haas JS, Kaplan CP, Gregorich SE, Perez-Stable EJ, Des Jarlais G (2004) Do physicians tailor their recommendations for breast cancer risk reduction based on patient’s risk? *J Gen Intern Med*

- 19(4):302–309. <https://doi.org/10.1111/j.1525-1497.2004.30280.x>
15. Rosenberger LH, Weber R, Sjöberg D, Vickers AJ, Mangino DA, Morrow M, Pilewskie ML (2017) Impact of self-reported data on the acquisition of multi-generational family history and lifestyle factors among women seen in a high-risk breast screening program: a focus on modifiable risk factors and genetic referral. *Breast Cancer Res Treat* 162(2):275–282. <https://doi.org/10.1007/s10549-017-4115-x>
 16. Ormseth SR, Wellisch DK, Arechiga AE, Draper TL (2015) Predicting reattendance at a high-risk breast cancer clinic. *Palliat Support Care* 13(5):1441–1448. <https://doi.org/10.1017/s1478951515000164>
 17. Engel NJ, Gordon P, Thull DL, Dudley B, Herstine J, Jankowitz RC, Zorn KK (2012) A multidisciplinary clinic for individualizing management of patients at increased risk for breast and gynecologic cancer. *Fam Cancer* 11(3):419–427. <https://doi.org/10.1007/s10689-012-9530-x>
 18. Monticciolo DL, Newell MS, Moy L, Niell B, Monsees B, Sickles EA (2018) Breast cancer screening in women at higher-than-average risk: recommendations from the ACR. *J Am Coll Radiol* 15(3 Pt A):408–414. <https://doi.org/10.1016/j.jacr.2017.11.034>
 19. Ozanne EM, Loberg A, Hughes S, Lawrence C, Drohan B, Semine A, Jellinek M, Cronin C, Milham F, Dowd D, Block C, Lockhart D, Sharko J, Grinstein G, Hughes KS (2009) Identification and management of women at high risk for hereditary breast/ovarian cancer syndrome. *Breast J* 15(2):155–162. <https://doi.org/10.1111/j.1524-4741.2009.00690.x>
 20. Colditz GA, Hankinson SE (2005) The Nurses' Health Study: lifestyle and health among women. *Nat Rev Cancer* 5(5):388–396. <https://doi.org/10.1038/nrc1608>
 21. Obesity: Preventing and managing the global epidemic. Report of a WHO consultation (2000) WHO Technical Report Series, vol 894. Geneva
 22. Gail MH, Brinton LA, Byar DP, Corle DK, Green SB, Schairer C, Mulvihill JJ (1989) Projecting individualized probabilities of developing breast cancer for white females who are being examined annually. *J Natl Cancer Inst* 81(24):1879–1886
 23. Tyrer J, Duffy SW, Cuzick J (2004) A breast cancer prediction model incorporating familial and personal risk factors. *Stat Med* 23(7):1111–1130. <https://doi.org/10.1002/sim.1668>
 24. Hartman SJ, Dunsiger SI, Jacobsen PB (2011) The relationship of psychosocial factors to mammograms, physical activity, and fruit and vegetable consumption among sisters of breast cancer patients. *Int J Womens Health* 3:257–263. <https://doi.org/10.2147/ijwh.s23246>
 25. Bertoni N, de Souza MC, Crocarno S, Szklo M, de Almeida LM (2018) Is a family history of the breast cancer related to women's cancer prevention behaviors? *Int J Behav Med Aug*. <https://doi.org/10.1007/s12529-018-9737-9>
 26. Spector D, Deroo LA, Sandler DP (2011) Lifestyle behaviors in black and white women with a family history of breast cancer. *Prev Med* 52(5):394–397. <https://doi.org/10.1016/j.ypmed.2011.03.001>
 27. Bostean G, Crespi CM, McCarthy WJ (2013) Associations among family history of cancer, cancer screening and lifestyle behaviors: a population-based study. *Cancer Causes Control* 24(8):1491–1503. <https://doi.org/10.1007/s10552-013-0226-9>
 28. Cuzick J, Forbes J, Edwards R, Baum M, Cawthorn S, Coates A, Hamed A, Howell A, Powles T, investigators I (2002) First results from the International Breast Cancer Intervention Study (IBIS-I): a randomised prevention trial. *Lancet* 360(9336):817–824
 29. Fisher B, Costantino JP, Wickerham DL, Cecchini RS, Cronin WM, Robidoux A, Bevers TB, Kavanah MT, Atkins JN, Margolese RG, Runowicz CD, James JM, Ford LG, Wolmark N (2005) Tamoxifen for the prevention of breast cancer: current status of the National Surgical Adjuvant Breast and Bowel Project P-1 study. *J Natl Cancer Inst* 97(22):1652–1662. <https://doi.org/10.1093/jnci/dji372>
 30. Vogel VG, Costantino JP, Wickerham DL, Cronin WM, Cecchini RS, Atkins JN, Bevers TB, Fehrenbacher L, Pajon ER Jr, Wade JL III, Robidoux A, Margolese RG, James J, Lippman SM, Runowicz CD, Ganz PA, Reis SE, McCaskill-Stevens W, Ford LG, Jordan VC, Wolmark N, National Surgical Adjuvant B, Bowel P (2006) Effects of tamoxifen vs raloxifene on the risk of developing invasive breast cancer and other disease outcomes: the NSABP Study of Tamoxifen and Raloxifene (STAR) P-2 trial. *JAMA* 295(23):2727–2741. <https://doi.org/10.1001/jama.295.23.joc60074>
 31. Goss PE, Ingle JN, Ales-Martinez JE, Cheung AM, Chlebowski RT, Wactawski-Wende J, McTiernan A, Robbins J, Johnson KC, Martin LW, Winquist E, Sarto GE, Garber JE, Fabian CJ, Pujol P, Maunsell E, Farmer P, Gelmon KA, Tu D, Richardson H, Investigators NCMS (2011) Exemestane for breast-cancer prevention in postmenopausal women. *N Engl J Med* 364(25):2381–2391. <https://doi.org/10.1056/NEJMoa1103507>
 32. Tice JA, Miglioretti DL, Li CS, Vachon CM, Gard CC, Kerlikowske K (2015) Breast density and benign breast disease: risk assessment to identify women at high risk of breast cancer. *J Clin Oncol* 33(28):3137–3143. <https://doi.org/10.1200/JCO.2015.60.8869>
 33. Brentnall AR, Harkness EF, Astley SM, Donnelly LS, Stavrinou P, Sampson S, Fox L, Sergeant JC, Harvie MN, Wilson M, Beetles U, Gadde S, Lim Y, Jain A, Bundred S, Barr N, Reece V, Howell A, Cuzick J, Evans DG (2015) Mammographic density adds accuracy to both the Tyrer–Cuzick and Gail breast cancer risk models in a prospective UK screening cohort. *Breast Cancer Res* 17(1):147. <https://doi.org/10.1186/s13058-015-0653-5>
 34. Siu AL (2016) Screening for breast cancer: U.S. preventive services task force recommendation statement. *Ann Intern Med* 164(4):279–296. <https://doi.org/10.7326/m15-2886>
 35. Lee CH, Dershaw DD, Kopans D, Evans P, Monsees B, Monticciolo D, Brenner RJ, Bassett L, Berg W, Feig S, Hendrick E, Mendelson E, D'Orsi C, Sickles E, Burhenne LW (2010) Breast cancer screening with imaging: recommendations from the Society of Breast Imaging and the ACR on the use of mammography, breast MRI, breast ultrasound, and other technologies for the detection of clinically occult breast cancer. *J Am Coll Radiol* 7(1):18–27. <https://doi.org/10.1016/j.jacr.2009.09.022>
 36. Oeffinger KC, Fontham ET, Etzioni R, Herzog A, Michaelson JS, Shih YC, Walter LC, Church TR, Flowers CR, LaMonte SJ, Wolf AM, DeSantis C, Lortet-Tieulent J, Andrews K, Manassaram-Baptiste D, Saslow D, Smith RA, Brawley OW, Wender R (2015) Breast cancer screening for women at average risk: 2015 guideline update From the American Cancer Society. *JAMA* 314(15):1599–1614. <https://doi.org/10.1001/jama.2015.12783>
 37. Degnim AC, Winham SJ, Frank RD, Pankratz VS, Dupont WD, Vierkant RA, Frost MH, Hoskin TL, Vachon CM, Ghosh K, Hieken TJ, Carter JM, Denison LA, Broderick B, Hartmann LC, Visscher DW, Radisky DC (2018) Model for predicting breast cancer risk in women with atypical hyperplasia. *J Clin Oncol* 36(18):1840–1846. <https://doi.org/10.1200/jco.2017.75.9480>