Calculating Future 10-Year Breast Cancer Risks in Risk-Adapted Surveillance: A Method Comparison and Application in Clinical Practice

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ABSTRACT

The German Consortium for Hereditary Breast and Ovarian Cancer (GC-HBOC) has successfully implemented risk-adapted breast cancer surveillance for women at high breast cancer risk in Germany. Women with a family history of breast and ovarian cancer but without pathogenic germline variants in recognized breast cancer risk genes are recommended annual breast imaging if their predicted 10-year breast cancer risk is 5% or higher, using the Breast and Ovarian Analysis of Disease Incidence and Carrier Estimation Algorithm (BOADICEA) breast cancer risk model, as outlined in the current GC-HBOC guideline. However, women who initially do not meet this risk threshold may do so later, even if there is no new cancer in their family. To determine when this threshold is crossed, one could annually repeat BOADICEA calculations using an aging pedigree: the "prediction by aging pedigree" (AP) approach. Alternatively, we propose a simplified and more practical "'conditional probability" (CP) approach, which calculates future risks based on the initial BOADICEA assessment. Using data from 6,661 women registered with GC-HBOC, both methods were compared. Initially, 74% of women, ages 30 to 48 years, had a 10-year breast cancer risk below 5%, but 53% exceeded this threshold at an older age based on the AP approach. Among the women with an initial risk below the threshold, the CP approach revealed that 99% of women exceeded the 5% threshold at the same or an earlier age compared with the AP approach (88% of cases were within the same year or 1 year earlier). The CP approach has been implemented as a user-friendly web application.

Prevention Relevance: The German Consortium for Hereditary Breast Cancer recommends annual breast imaging for women if their 10-year breast cancer risk is 5% or higher. Women who initially do not meet this risk threshold may do so later. We propose a simple method to determine future risks based on initial risk assessments.

Introduction

Breast cancer is the most common cancer among women in Germany (1, 2). Notably, about 30% of patients with breast cancer report a family history of breast and ovarian cancer (3). In approximately 22% of these families, pathogenic or likely pathogenic germline variants in *BRCA1/2* or

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other well-known genes can be identified, which are associated with an increased risk of breast cancer (4).

However, in approximately 78% of these families, no pathogenic variants can be detected in the known genes (5, 6). Nevertheless, women from these families have an increased risk of breast cancer compared with the general population (7).

For this specific risk group, risk-adapted intensified breast cancer surveillance has been successfully implemented by the German Consortium for Hereditary Breast and Ovarian Cancer (GC-HBOC; refs. 8, 9). Women ages 30 years and older are offered annual MRI and ultrasound until the age of 50 years if their predicted 10-year breast cancer risk is ≥5% using BOADICEA model, as outlined in the current GC-HBOC guideline (10). Mammography is offered every 1 to 2 years starting at age 40 (8).

In this study, breast cancer risks were calculated using the BOADICEA model 6.2.1, version 0.6.0, considering only family history and genetic test results (11). Although some women may not initially meet the 10-year breast cancer risk threshold of 5% at their first risk assessment, the likelihood of exceeding this threshold increases with age (12). Consequently, women may become eligible for intensified surveillance later, even without new cancer cases in the family. Thus, there is a clinical need to anticipate if and when a woman may exceed the decision threshold after the initial risk calculation (13).

An obvious method to determine if and when a woman crosses the decision threshold would be to construct an aging pedigree and calculate the expected future 10-year risk repeatedly over time using BOADICEA: the "prediction by aging pedigree" (AP) approach. However, this would require many repeated individual calculations, which would be too inconvenient in clinical practice.

Therefore, one aim of this study was to determine the number of women who do not initially exceed a 10-year breast cancer risk of 5% at their initial assessment but who do so later before reaching the age of 50 years. Another aim was to develop a simplified and more practical method, the "conditional probability" (CP) approach, using only a single BOADICEA calculation at the time of the initial risk assessment instead of repeated risk calculations. We compared the two approaches based on data from 6,661 healthy women enrolled in the GC-HBOC registry. We also developed and implemented an easy-to-use web application to enable genetic counsellors to conveniently perform these simplified calculations.

Materials and Methods

Study sample

The study sample comprised 6,661 women, ages 30 to 48 years, without breast cancer who received genetic counseling at one of the GC-HBOC clinical centers. All patients met the inclusion criteria of the GC-HBOC for germ line testing (3). All women were from families that met at least one of the following inclusion criteria: (i) three or more women with breast cancer, regardless of age at diagnosis; (ii) two or more women with breast cancer, one of whom was diagnosed before the age of 51; (iii) one or more women with breast cancer and one or more (same or different) women with ovarian cancer; (iv) two or more women with ovarian cancer; (v) one or more men with breast cancer and one or more women with breast cancer and/or ovarian cancer; (vi) one or more women with breast cancer diagnosed before the age of 36; and (vii) at least one woman with bilateral breast cancer with first diagnosis before the age of 51 (5, 14). The inclusion criteria of the GC-HBOC started off as study-specific criteria (5). The criteria are now implemented into clinical guidelines (15).

All patients were counseled at a participating GC-HBOC center. In all families, an index patient was screened for pathogenic germline variants in the *BRCA1/2* genes, but no pathogenic or likely pathogenic variants were found (6). Additionally, physicians who were qualified in genetic counseling recorded a comprehensive three-generation pedigree of each family, compiled with information on cancer (type and age at diagnosis and tumor receptor status) and vital status of each family member. Medical reports were requested where possible. The family history was usually taken from the index patient. If other family members came to the consultation, the family history was updated accordingly.

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Written informed consent was obtained from all participants. The study was approved by the relevant ethics committees of each participating center. The study was conducted in accordance with the ethical standards of the involved institutional ethics committees and with the Declaration of Helsinki.

Risk calculation

Breast cancer risk was calculated using the BOADICEA breast cancer model 6.2.1, version 0.6.0 (11). BOADICEA calculates a woman's risk of developing breast or ovarian cancer based on family cancer history and genetic test results for moderate and high-risk breast/ovarian cancer susceptibility genes. The model is continually updated; the current version includes risk factors such as lifestyle and hormonal factors, common genetic susceptibility variants (polygenic risk scores), and mammographic density. Breast cancer risks were calculated considering only family history and genetic test results. Other risk factors were not included. We used the default settings of the BOADICEA model (11). UK prevalences were used as German prevalences are not currently implemented.

We compared two approaches for calculating the expected future time course of 10-year breast cancer risks. In the AP approach, the risks were calculated using repeated BOADICEA calculations, performed by "aging" the pedigree annually, assuming no new cancer cases in the family. Aging involved incrementing the current age of each living family member yearly (up to a maximum age of 110, as per BOADICEA limits). To do this, one has to create a BOADICEA input for each year and perform separate risk calculations for each year. This is very time consuming and too inconvenient for clinical practice.

In the CP approach, the time course of 10-year breast cancer risk was determined using only the initial BOADICEA risk assessment at the current age of the counselee. For this, we used age-dependent cumulative risks provided by BOADICEA up to ages divisible by 5 up to 80 years. For ages not specified, we employed linear interpolation between adjacent time points. We then calculated the conditional future 10-year breast cancer risk at each age x after the initial risk assessment, assuming no breast cancer development in the interim:

$$10Year\ breast\ cancer\ risk\ at\ age\ x = \frac{[Breast\ cancer\ risk\ at\ age\ (x+10)] - [Breast\ cancer\ risk\ at\ age\ x]}{1 - [Breast\ cancer\ risk\ at\ age\ x]},$$

where x ranges from the initial age at risk assessment to age 49.

For both methods, we calculated individual time courses of 10-year breast cancer risks annually from the age at first risk assessment to age 49. We also determined the age at which the 10-year risk exceeded the defined 5% threshold.

Statistical analysis

Both methods were applied to all women in our study sample, and the results were compared using descriptive methods such as absolute numbers and percentages. The analysis of future 10-year breast cancer risk was limited to women whose 10-year breast cancer risk was below 5% at the time of their first assessment. We compared the frequency of exceeding the 5% threshold before the age of 50 years between the two methods. Additionally, we analyzed differences in the ages at which the risk threshold exceeded for both methods.

All data preparation and statistical analyses were performed using R version 4.3.1 (R Core Team. R: a language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. URL: https://www.R-project.org).

Data availability

Data are available on request.

Results

The study sample comprised 6,661 women, ages 30 to 48 years, without breast cancer, representing 5,996 families, all registered in the central database of the GC-HBOC (**Table 1**). At the time of initial counseling, 1,743 (26%) women had a 10-year breast cancer risk of 5% or greater, qualifying them for the intensified surveillance program of the GC-HBOC. Conversely, 4,918 women (74%) ages 30 to 48 years had a breast cancer risk below 5% and were, on average, younger and had less extensive familial breast cancer histories than counselees with an initial 10-year breast cancer risk of 5% or higher (**Table 1**). Among those initially below the threshold, 2,613 of 4,918 women (53%) reached the 5% risk threshold at a later time before the age of 50 years (**Table 2**).

Comparison of the AP and CP calculation methods for expected future 10-year risks

For the 4,918 counselees with an initial 10-year breast cancer risk below 5%, we compared the two methods of calculating the future 10-year risks. **Figure 1** illustrates the time course of the mean 10-year breast cancer risks for each age up to 49 years, categorized by age group at initial risk assessment and averaged within those groups.

Table 1. Patient characteristics.

Characteristic	Initial 10-year breast cancer risk at first counseling	
	<5% (*n* = 4,918, 74%)	**≥5% (*n* = 1,743, 26%)**
Age at counseling[a]	37 (30–48)	44 (30–48)
Year of birth[a]	1974 (1950–1989)	1967 (1948–1986)
Relatives with breast cancer or ovarian cancer, *n* (%)		
0	0 (0.0%)	0 (0.0%)
1	241 (4.9%)	43 (2.5%)
2+	4,677 (95.1%)	1,700 (97.5%)
Relatives with breast cancer, *n* (%)		
0	135 (2.7%)	0 (0.0%)
1	667 (13.6%)	64 (3.7%)
2+	4,116 (83.7%)	1,679 (96.3%)

[a]Median (minimum–maximum).

Table 2. Number and percentages of patients exceeding the 5% risk threshold before the age of 50 using the CP versus the AP method (for patients below the threshold at initial risk calculation).

Counselees exceeding the breast cancer risk limit before the age of 50 years	Using the AP method		
Using the CP method	**No**	**Yes**	**Total**
No	1,908 (38.8%)	3 (0.1%)	1,911 (38.9%)
Yes	397 (8.1%)	2,610 (53.1%)	3,007 (61.1%)
Total	2,305 (46.9%)	2,613 (53.1%)	4,918 (100.0%)

AP prediction by aging pedigree
CP prediction by conditional probability calculation

The average risks calculated using the CP method are higher than those obtained using the AP method, indicating that the 5% threshold is reached at an earlier age with the CP method. The mean differences between the CP and the AP risks increased over time but remained small, with a maximum of 0.5%. To assess whether counselees would exceed the breast cancer risk threshold before the age of 50 years, we compared the results of the two methods (**Table 2**). In 92% of cases, the two methods agreed. However, 397 counselees (8.1%) exceeded the risk threshold only using the CP method, whereas only three counselees (0.1%) did so using the AP approach (**Table 2**).

Table 3 indicates that in 99% of cases, the CP method leads to the same or an earlier age for crossing the 5% threshold compared with the AP method. Specifically, in 88% of cases, the CP method resulted in the threshold being exceeded within the same year or 1 year earlier than with the AP method.

Use of the CP method in clinical practice

Table 4 presents the age distribution for exceeding the 5% breast cancer risk threshold using the CP method, categorized by age at initial risk assessment. The likelihood of reaching the threshold is notably higher among younger counselees and decreases as age increases. For instance, 75% of counselees who were 30 years old at initial risk assessment and 60% of those who were 40 years old reached the threshold before the age of 50. Some counselees exceeded the threshold just a few years after the initial assessment. Overall,

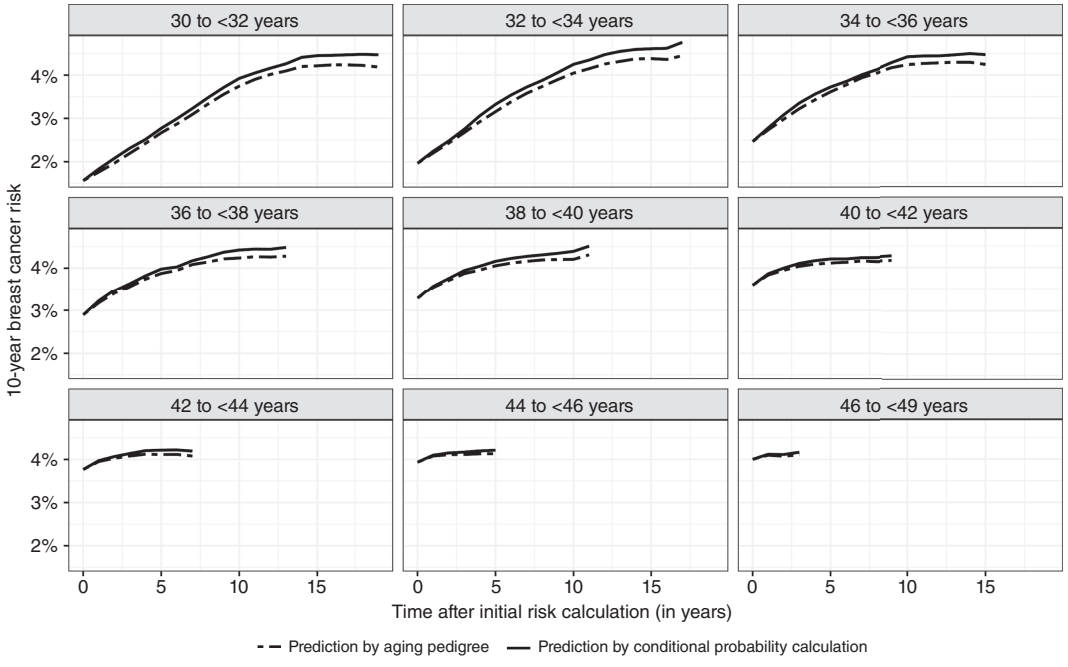

Figure 1.
10-Year breast cancer risk for the AP and CP methods, grouped by the age at first counseling. Curves are shown for the AP method (dashed line) and the CP method (solid line) from the age of initial risk calculation until the age when the risk limit is exceeded by the AP method, grouped by age at initial risk calculation (panels).

Table 3. Distribution of the differences in predicted ages when the 5% risk threshold is exceeded between the AP and CP approaches (for patients exceeding the threshold before the age of 50 after initial risk assessment with both methods).

	***N* = 2,610**
Using the CP method, breast cancer risk limit is exceeded	
1 Year later than using the AP method	25 (1%)
In the same year as using the AP method	1,273 (48.8%)
1 Year earlier than using the AP method	1,024 (39.2%)
2 Years earlier than using the AP method	210 (8.0%)
3 Years earlier than using the AP method	65 (2.5%)
4 Years earlier than using the AP method	9 (0.3%)
5 Years earlier than using the AP method	4 (0.2%)

AP prediction by aging pedigree
CP prediction by conditional probability calculation

39% of counselees did not reach the threshold before the age of 50.

Software tool: a *future 10-year risk calculator*

To implement the CP method into clinical practice, we developed a web-based application for calculating expected future 10-year breast cancer risks over time, known as the "*Future 10-year risk calculator*." This tool is accessible to registered users at https://www.health-atlas.de/models/29/. We will demonstrate its use with an example case:

A 30-year-old woman is concerned about her cancer risk, given her mother's diagnosis of bilateral breast cancer at age 43 and her maternal grandmother's diagnosis at age 45. Although genetic testing did not identify any (likely) pathogenic variants in *BRCA1*, *BRCA2*, and other breast cancer–associated genes in her mother, she is interested in whether she qualifies for intensified breast cancer screening. Using the BOADICEA model, as implemented in the certified CanRisk Tool, her 10-year breast cancer risk is calculated at 2.3%. To determine the age at which the counselee might reach the 5% risk threshold, we utilized the *Future 10-year risk calculator*. By copying and pasting the cumulative breast cancer risk distribution of the BOADICEA output based on the initial pedigree assessment into the calculator, we generated the projections. As depicted in **Fig. 2**, the result indicates that the counselee is likely to exceed the 10-year breast cancer risk threshold of 5% by the age of 38 and could be recommended to take part in intensified breast cancer screening starting at this age.

Discussion

This study highlights the importance of monitoring changes in 10-year breast cancer risks over time within risk-adapted breast cancer surveillance programs in clinical settings. Initially, 1,773 women (26%) were identified with a 10-year risk of 5% or higher, leading to recommendations for intensified screening. Conversely, 4,918 women (74%) ages 30 to 48 years presented with a risk below this threshold. Notably, 53% of these initially lower-risk women eventually exceeded the 5% threshold before reaching the age of 50. This crucial finding highlights the need for a continuous risk assessment strategy in clinical practice, rather than relying on a single time assessment.

In this study, we evaluated two different methods for calculating future 10-year breast cancer risks: the AP method, which involves annual BOADICEA recalculations using an aging pedigree, and the CP method, which relies solely on the initial BOADICEA risk assessment. The AP method, although comprehensive, proves impractical for clinical use due to the necessity for repeated annual risk recalculations—an approach not currently supported by BOADICEA v6 (11) or any other existing models to our knowledge. Our analysis demonstrated that the CP method aligned with the AP method in 99% of cases, accurately predicting the age when the 5% risk threshold would be reached at an earlier or the same age. Therefore, the CP method emerged as an almost equivalent yet significantly more convenient alternative for clinical application. With the CP approach, clinicians tend to recommend re-assessement earlier, just to be on the safe side.

This study led us to develop a user-friendly web application called the *Future 10-year risk calculator* (https://www.health-atlas.de/models/29). This tool is designed for daily use by clinicians and consultants. For example, using this tool, a 30-year-old woman initially assessed with a 10-year breast cancer risk of 2.3% was projected to reach the 5% risk threshold by the age of 38. Consultants can use this information to decide when to recommend a risk re-assessment. Operating solely based on the result of the initial risk assessment, this tool has proven to be user-friendly and efficient. It serves as a valuable decision aid in counseling and strategizing risk-adapted screening, enhancing the capability to tailor preventive measures to individual risk profiles over time.

A strength of this study is its large sample size. However, a limitation is that the methods for calculating future 10-year risk have only been compared using family history and the results of genetic testing of *BRCA1* and *BRCA2* genes, which are non-modifiable risk factors (16, 17). BOADICEA is a comprehensive statistical model that calculates breast and ovarian cancer risks using individual information on family history, lifestyle, hormonal risk factors, rare and common variants in cancer susceptibility genes, and mammographic density (11, 18, 19). One limitation of the BOADICEA model is that there are other risk factors such as personal history of atypical hyperplasia and Lobular carcinoma in situ that are not included in the BOADICEA model.

The BOADICEA model v6 has been incorporated into a user-friendly interface called "CanRisk" (https://canrisk.org/), which enables healthcare professionals to calculate an individual's future risks of developing breast and ovarian cancer (20). It has yet to be determined whether the two methods will yield similar results when additional risk factors and results of genetic testing of further known risk genes are included.

Table 4. Distribution of age when the 5% risk threshold is exceeded using the CP method, depending on age at initial risk calculation.

Age at initial risk calculation	Age when the 5% risk threshold is exceeded before the age of 50 using the CP method																			Total
	31	32	33	34	35	36	37	38	39	40	41	42	43	44	45	46	47	48	49	<50	
30	0	2	3	5	4	6	7	11	20	12	22	14	20	32	28	20	17	7	10	240 (75%)	320
31		2	1	3	4	12	4	7	11	12	23	15	19	29	31	7	19	10	17	226 (72%)	312
32			3	2	0	9	11	13	10	13	22	18	19	31	28	17	18	19	23	256 (76%)	338
33				3	4	8	11	10	18	20	22	18	19	21	27	17	16	18	14	246 (72%)	340
34					3	5	15	15	16	15	12	22	31	33	12	15	17	13	15	239 (76%)	316
35						6	14	14	20	21	17	20	12	34	31	17	20	21	13	260 (73%)	356
36							11	16	20	17	25	9	24	28	26	20	8	16	15	235 (68%)	348
37								13	20	18	29	22	17	20	16	27	18	15	9	224 (69%)	323
38									19	16	25	22	27	17	18	22	17	19	17	219 (69%)	318
39										20	21	26	25	21	18	16	19	11	16	193 (61%)	314
40											17	24	27	22	16	11	19	15	16	167 (60%)	277
41												26	20	26	20	13	14	10	11	140 (58%)	240
42													11	17	17	16	5	9	5	80 (41%)	197
43														22	13	20	18	22	7	102 (46%)	221
44															13	15	14	14	10	66 (36%)	183
45																24	12	5	11	52 (35%)	149
46																	16	10	9	35 (24%)	144
47																		9	9	18 (15%)	120
48																			9	9 (8.8%)	102
Total	0	4	7	13	15	46	73	99	154	164	235	236	271	353	314	277	267	243	236	3,007 (61%)	4,918

CP prediction by conditional probability calculation

It is important to emphasize that the proposed simplified approach for calculating expected future 10-year breast cancer risks should not serve as the basis for intensified surveillance, nor should it replace calculations performed with the certified BOADICEA model. Instead, the goal is to assist in determining the optimal time for a person at risk to receive follow-up counseling, at which point a new risk assessment can be conducted using BOADICEA based on the latest anamnestic information. This approach will support informed clinical decision-making. Moreover, the estimated timing for recalculating the risk assumes that the individual's and family's risk profile remains unchanged. Should there be significant changes in these risk factors, it is advisable to perform recalculations earlier than initially planned, if necessary.

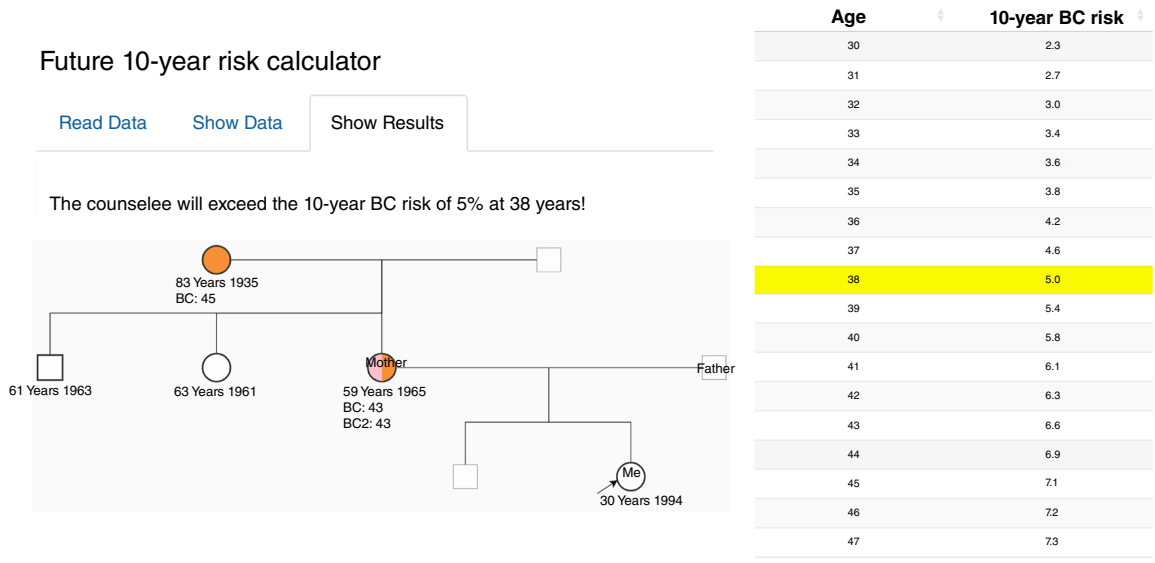

Figure 2.
Future 10-year risk calculator. The 10-year breast cancer (BC) risk course for a healthy counselee with early-onset BC cases in the family calculated using the web application.

Conclusion

This study revealed that 74% of the women, ages 30 to 48 years, had a 10-year breast cancer risk lower than 5% at the initial risk assessment. However, 53% of these women eventually exceeded this threshold before reaching the age of 50. This underscores the need for a valid yet simple and convenient method to calculate expected future 10-year risks. Our findings demonstrate that a calculation method based solely on the results of the initial BOADICEA risk assessment is nearly as effective as the more time-consuming and inconvenient repeated annual BOADICEA calculations. The simplified approach has been developed into a user-friendly web application, accessible to registered users.

Authors' Disclosures

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Authors' Contributions

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References

1. Krebs in Deutschland für 2019/2020. Berlin: Robert Koch Institute, Association of Population-based Cancer Registries in Germany; 2023. p. 78.
2. Quante AS, Ming C, Rottmann M, Engel J, Boeck S, Heinemann V, et al. Projections of cancer incidence and cancer-related deaths in Germany by 2020 and 2030. Cancer Med 2016;5:2649–56.
3. Rhiem K, Bücker-Nott HJ, Hellmich M, Fischer H, Ataseven B, Dittmer-Grabowski C, et al. Benchmarking of a checklist for the identification of familial risk for breast and ovarian cancers in a prospective cohort. Breast J 2019;25:455–60.
4. Schmutzler R. Konsensusempfehlung des Deutschen Konsortiums Familiärer Brust- und Eierstockkrebs zum Umgang mit Ergebnissen der Multigenanalyse. Geburtshilfe und Frauenheilkunde 2017;77:733–9.
5. Kast K, Rhiem K, Wappenschmidt B, Hahnen E, Hauke J, Bluemcke B, et al. Prevalence of BRCA1/2 germline mutations in 21 401 families with breast and ovarian cancer. J Med Genet 2016;53:465–71.
6. Hauke J, Horvath J, Groß E, Gehrig A, Honisch E, Hackmann K, et al. Gene panel testing of 5589 BRCA1/2-negative index patients with breast cancer in a routine diagnostic setting: results of the German Consortium for Hereditary Breast and Ovarian Cancer. Cancer Med 2018;7:1349–58.
7. Engel C, Fischer C, Zachariae S, Bucksch K, Rhiem K, Giesecke J, et al. Breast cancer risk in BRCA1/2 mutation carriers and non-carriers under prospective intensified surveillance. Int J Cancer 2020;146:999–1009.
8. Bick U, Engel C, Krug B, Heindel W, Fallenberg EM, Rhiem K, et al. High-risk breast cancer surveillance with MRI: 10-year experience from the German Consortium for Hereditary Breast and Ovarian Cancer. Breast Cancer Res Treat 2019;175:217–28.
9. Herold N, Bredow K, Ernst C, Tüchler A, Blümcke B, Waha A, et al. Implementing mainstream genetic counseling within the area-wide network of the German Consortium Hereditary Breast and Ovarian Cancer (GC-HBOC): satisfaction of primary care providers with the provided state-of-the-art training by the cologne center. J Genet Couns 2024;33:206–15.
10. Quante AS, Engel C, Kiechle M, Schmutzler R, Fischer C. Umstrukturierung der Risikoberechnung für die intensivierte

Früherkennung im Deutschen Konsortium für Brust und Eierstockkrebs. Der Gynäkologe 2020;53:259–264.
11. Lee A, Mavaddat N, Wilcox AN, Cunningham AP, Carver T, Hartley S, et al. BOADICEA: a comprehensive breast cancer risk prediction model incorporating genetic and nongenetic risk factors. Genet Med 2019;21:1708–18.
12. Quante AS, Strahwald B, Fischer C, Kiechle M. Individualisiertes Brustkrebsrisiko - wie berechnen, wie bewerten und wie besprechen? Gynäkologe 2018;51:397–402.
13. Fürst N, Kiechle M, Strahwald B, Quante AS. Mammography screening 2.0 - how can risk-adapted screening be implemented in clinical practice?: results of a focus group discussion with experts in the RISIKOLOTSE.DE project. Geburtshilfe Frauenheilkd 2018;78:506–11.
14. Fischer C, Kuchenbäcker K, Engel C, Zachariae S, Rhiem K, Meindl A, et al. Evaluating the performance of the breast cancer genetic risk models BOADICEA, IBIS, BRCAPRO and Claus for predicting BRCA1/2 mutation carrier probabilities: a study based on 7352 families from the German Hereditary Breast and Ovarian Cancer Consortium. J Med Genet 2013;50:360–7.
15. Leitlinienprogramm Onkologie (Deutsche Krebsgesellschaft, Deutsche Krebshilfe, AWMF). Interdisziplinäre S3-Leitlinie für die Früherkennung, Diagnostik, Therapie und Nachsorge des Mammakarzinoms, Version 4.4. AWMF Registernummer: 032-045OL. 2021 [cited 2024 Nov 18]. Available from: http://www.leitlinienprogramm-onkologie.de/leitlinien/mammakarzinom/
16. Quante AS, Herz J, Whittemore AS, Fischer C, Strauch K, Terry MB. Assessing absolute changes in breast cancer risk due to modifiable risk factors. Breast Cancer Res Treat 2015;152:193–7.
17. Tüchler A, De Pauw A, Ernst C, Anota A, Lakeman IMM, Dick J, et al. Clinical implications of incorporating genetic and non-genetic risk factors in CanRisk-based breast cancer risk prediction. Breast 2024;73:103615.
18. Mavaddat N, Ficorella L, Carver T, Lee A, Cunningham AP, Lush M, et al. Incorporating alternative polygenic risk scores into the BOADICEA breast cancer risk prediction model. Cancer Epidemiol Biomarkers Prev 2023;32:422–7.
19. Lee AJ, Cunningham AP, Tischkowitz M, Simard J, Pharoah PD, Easton DF, et al. Incorporating truncating variants in PALB2, CHEK2, and ATM into the BOADICEA breast cancer risk model. Genet Med 2016;18:1190–8.
20. Carver T, Hartley S, Lee A, Cunningham AP, Archer S, Babb de Villiers C, et al. CanRisk tool-a web interface for the prediction of breast and ovarian cancer risk and the likelihood of carrying genetic pathogenic variants. Cancer Epidemiol Biomarkers Prev 2021;30:469–73.