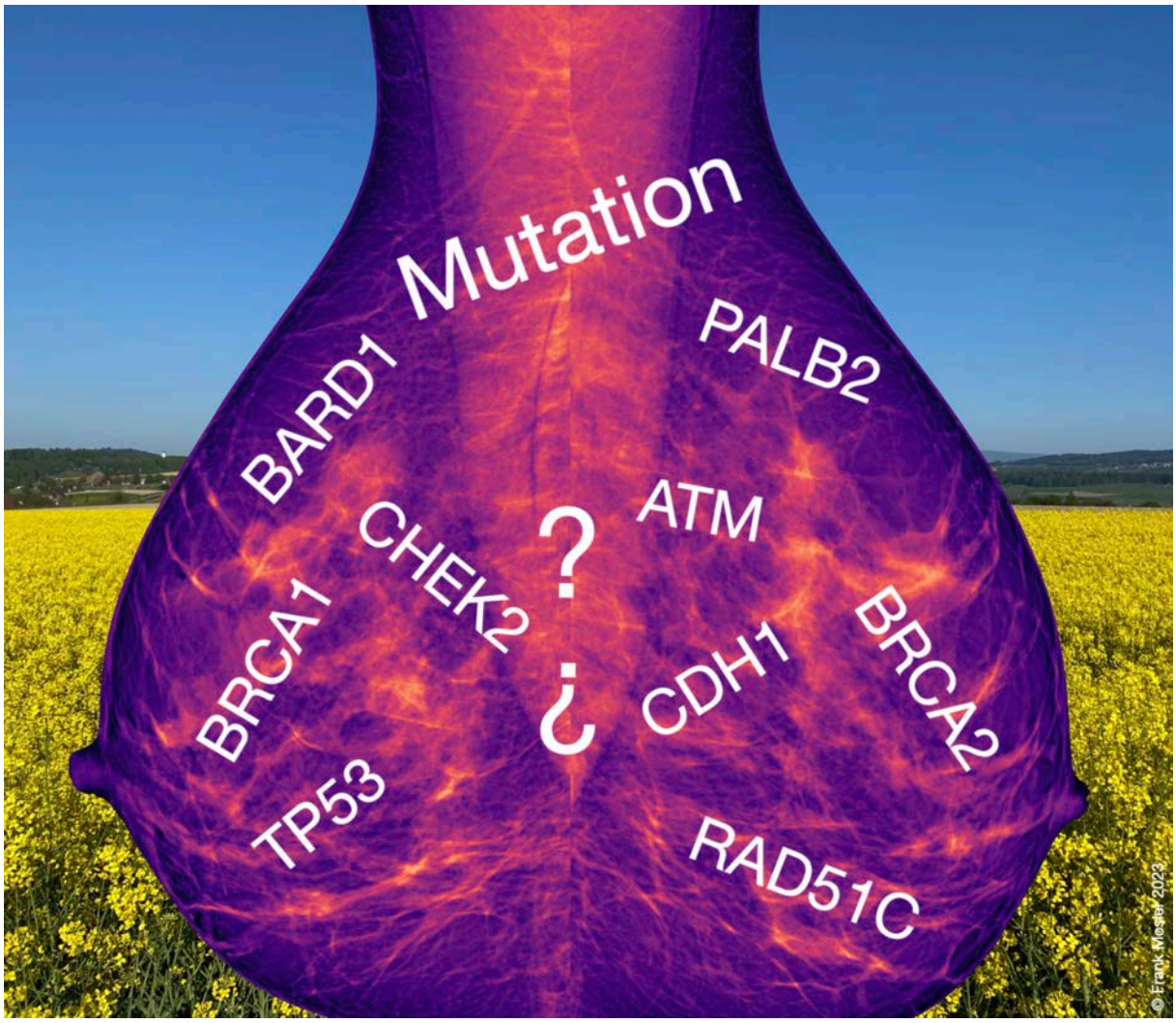
Early detection in cases of familial breast cancer predisposition: What is appropriate and beneficial for the individual seeking advice?

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Asymptomatic women with a family history of breast cancer should first receive comprehensive and detailed counselling with a risk-benefit assessment of diagnostic or preventive measures. The medical counselling should enable individuals seeking advice to make a participatory decision.

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Abstract

A "high-risk situation" is present when the lifetime risk of developing breast cancer is ≥ 30%. The Tyrer-Cuzick (IBIS) model is an established approach to individual risk assessment. Its estimates depend on the model version and the available family history, genetic and personal risk information; mammographic density can also be incorporated. In addition to BRCA1 and BRCA2 several other risk genes are known that can be tested using gene panels. However specific familial risk constellations are prerequisites for indicating a genetic test. Prior to conducting a genetic test comprehensive counselling should take place and the individual seeking advice should be given time to consider. The individual seeking advice faces a series of questions regarding the potential implications of a genetic test which not only affect herself but also her environment.

In high-risk situations prophylactic mastectomy is an established surgical measure and intensified surveillance is a conservative approach. The latter includes semi-annual clinical breast examination with ultrasound starting from age 25 as well as an annual MRI mammography which exhibits the highest reliability compared to other imaging methods.

Medical consultation aims to enable a participatory decision-making process for the individual seeking advice. This requires comprehensive information for the individual seeking advice and incorporation of her preferences. Evidence-based decision aids from professional societies can improve the decisions of the individual seeking advice.

Keywords: breast cancer – high risk – intensified surveillance – genetic testing - psychological aspects of patient management - participatory decision-making

Despite now having good chances of cure and significantly improved survival rates a diagnosis of breast cancer is perceived as potentially life-threatening and affects the entire family and friends. Fears of disease-specific and psychosocial limitations take center stage along with the fear of a much too early end of life. This is particularly true when there is a suspected hereditary predisposition which substantially increases the risk of developing breast cancer especially at a young age.

This article explains how individual risk can be determined and what to consider in risk counselling. In particular it presents the option of intensified surveillance and possible alternatives.

Assessment of the Risk Situation

To assess the risk situation it is first necessary to examine the environment of the individual seeking advice. Concrete methodological guidelines for this are provided by the S3 Guideline for Breast Cancer from the Association of Scientific Medical Societies in Germany (AWMF) [1], the guidelines/recommendations of the Gynecological Oncology Working Group (AGO) of the German Society of Gynecology and Obstetrics (DGGG) and the German Cancer Society (DKG) [2], as well as the German Consortium for Hereditary Breast and Ovarian Cancer [3]. The information and recommendations derived from these three organizations largely coincide for practical use.

What Risk Groups exist?

The risk of developing breast cancer over the course of one's life, referred to as "lifetime risk" can be categorized into three classes: based on the epidemiological understanding that approximately one in eight women will develop breast cancer in their lifetime [4], the normal lifetime risk is 10-13%. High risk is classified at a lifetime risk of

30% for breast cancer or at a 20% probability of carrying a pathogenic variant in a breast cancer susceptibility gene based on pedigree analysis [1;3]. An intermediate risk is present when the lifetime risk falls between the two aforementioned risk groups.

When is there a "Family History" of Breast Cancer?

Approximately 30% of all women with breast cancer have a family history of the disease. A family history is considered to be present when multiple women (and possibly men) in the biological relatives of the individual seeking advice have been diagnosed with breast cancer and/or ovarian cancer in specific constellations (Tab. 1).

Recommendations/Statements	
Genetic testing should be offered when there is a familial or individual history that is associated with at least a 10% probability of detecting a mutation. This is true if in one line of the family: • At least three women have been diagnosed with breast cancer. • At least two women have been diagnosed with breast cancer, one of them before the age of 51. • At least one woman has breast cancer and one woman has ovarian cancer. • At least two women have ovarian cancer. • At least one woman has breast and ovarian cancer. • At least one woman aged 35 or younger has been diagnosed with breast cancer. • At least one woman aged 50 or younger has bilateral breast cancer. • At least one man has breast cancer and one woman has breast and ovarian cancer. An appropriate time to think things over should be observed before carrying out the diagnostic procedure.	**Level of recommendation: Grade B** **Level of Evidence 5/2a (LoE2a = for mutation probability)**

Tab. 1: Inclusion criteria for a genetic investigation due to "family history" of breast cancer.

In these constellations a detection rate of at least 10% for genetic mutations can be expected. Thus the inclusion criteria for a genetic investigation would be met. Therefore before undergoing genetic testing it is essential to have a risk counselling session to determine the individual's lifetime risk.

Furthermore it is important to ensure that the individual seeking advice is given sufficient time for consideration before undergoing genetic testing: is she truly ready to handle knowing that she carries a pathogenic variant associated with increased breast cancer risk and thus a potentially existential threat along with the associated consequences?

Genetic Factors

The currently most well-known risk genes are the BReast CAncer (BRCA) genes, BRCA1 and BRCA2. These were the first breast cancer genes discovered in the 1990s. Since that time, it has been understood that women carrying pathogenic variants in BRCA1 or BRCA2 develop breast cancer approximately 20 years earlier, have a lifetime risk of 50-80% for breast cancer, a contralateral breast cancer risk of 60% and a lifetime risk of 10-40% for ovarian cancer [5-7].

In recent years numerous variants of other gene regions that could be associated with breast cancer risk have been identified [8]. To more accurately assess the significance of individual gene defects two research groups from the USA and Europe have compiled data from case-control studies. The Breast Cancer Association Consortium analysed variants in 34 genes for their association with breast cancer risk [9]. The analysis involved 44 studies with 113’927 women (60’466 with

breast cancer and 53'461 healthy women as a control group) from 25 countries [9].

The CARRIERS analysis evaluated germline pathogenic variants in 28 cancer-predisposition genes across 12 population-based studies involving 64'791 women (32'247 with breast cancer and 32'544 without breast cancer) [10].

Both studies found a significant association between breast cancer risk and genetic alterations in the following eight genes: BRCA1, BRCA2, PALB2, BARD1, RAD51C, RAD51D, ATM, and CHEK2 [9]. The European study also identified a significant association with changes in the TP53 gene while the US study associated pathogenic variants of the CDH1 gene. For alterations in most of the other tested genes a significant correlation with an elevated breast cancer risk could not be described [9].

BRCA1 & BRCA2: Tip of the Iceberg

In the population-based CARRIERS analysis, pathogenic BRCA1 variants were associated with a breast cancer odds ratio of 7.62 (95% CI 5.33–11.27), and pathogenic BRCA2 variants with an odds ratio of 5.23 (95% CI 4.09–6.77), compared with non-carriers of pathogenic variants in the respective gene. These estimates were adjusted for study, age, first-degree family history of breast cancer, and race or ethnic group [10]. Odds ratios from this case-control analysis should not be interpreted as direct multipliers of lifetime absolute risk.

Dorling et al. reported odds ratios of 10.57 for BRCA1 and 5.85 for BRCA2 protein-truncating variants in their population-based analysis [9]. PALB2 is also considered a high-risk gene [2]. Moreover pathogenic variants in the ATM and CHEK2 genes were associated with a lifetime risk of over 20% [9]. Other moderately penetrant risk genes identified include BARD1, RAD51C, and RAD51D [11]. Additionally, it was observed that different breast cancer subtypes are influenced by these gene variants in distinct ways: While alterations in BRCA1, BRCA2, and PALB2 were more frequently discovered in triple-negative breast cancer, women with mutations in the ATM or CHEK2 genes were more likely to have estrogen receptor-positive tumors [9]

Increased Risk in Other Cancer Types

Pathogenic variants of breast cancer genes not only elevate the risk of developing breast cancer. Alterations in BRCA1 and BRCA2 also raise the risk of ovarian cancer in women and prostate cancer in men. Carriers of BRCA1 mutations have an elevated risk of colorectal cancer while carriers of BRCA2 mutations are more susceptible to other cancer types than the average population. Mutations in the CHEK2 gene increase the risk of colorectal cancer. ATM mutations are possibly linked to an increased risk of pancreatic cancer. Other associations such as between hereditary non-polyposis colo-rectal cancer and breast cancer could not be confirmed [9]. However several other cancer syndromes are recognized to come with an elevated risk of breast cancer such as Li-Fraumeni syndrome [2]. Since some years now, commercially available gene panels have the capability to detect pathogenic variants in cancer-predisposition genes [3]. Some of these provide a polygenetic risk score (PRS) as a single value to estimate an individual's genetic susceptibility to developing cancer.

Non-Genetic Risks

A specific risk situation arises following radiation therapy in the thoracic region. A typical scenario is radiation exposure to the thorax during childhood or adolescence such as in cases of Hodgkin's lymphoma leading to an increased risk of developing breast cancer [12-14].

How Lifetime Risk is determined

The individual's lifetime risk of developing breast cancer is influenced not only by genetic factors but also by a variety of other variables. Over the past years several models have been introduced aiming to achieve both high pre-

dictive accuracy and user-friendly applicability.

The Tyrer-Cuzick (IBIS) model is an established tool for breast cancer risk assessment [15,16]. Model performance should be considered separately in terms of calibration and discrimination and depends on the model version, included predictors, prediction horizon and population. A prospective comparison of BOADICEA v5 and Tyrer-Cuzick v8, both incorporating a 313-variant polygenic risk score, found better calibration of the extended BOADICEA model in the highest risk categories among women of European ancestry [25]. These findings do not establish a universally superior model. The version and inputs used for an individual assessment should be documented.

substantially reduces the risk of breast cancer [19]. Bilateral prophylactic mastectomy gained public attention a few years ago when Angelina Jolie a prominent individual facing a high-risk situation openly discussed her experience. However such a procedure can have significant psychological and psycho-sexual impacts on the individuals, an area that remains insufficiently explored [20; 21]. For carriers of BRCA1 or BRCA2 mutations, due to the increased risk of ovarian cancer consideration should also be given to risk-reducing salpingo-oophorectomy [2].

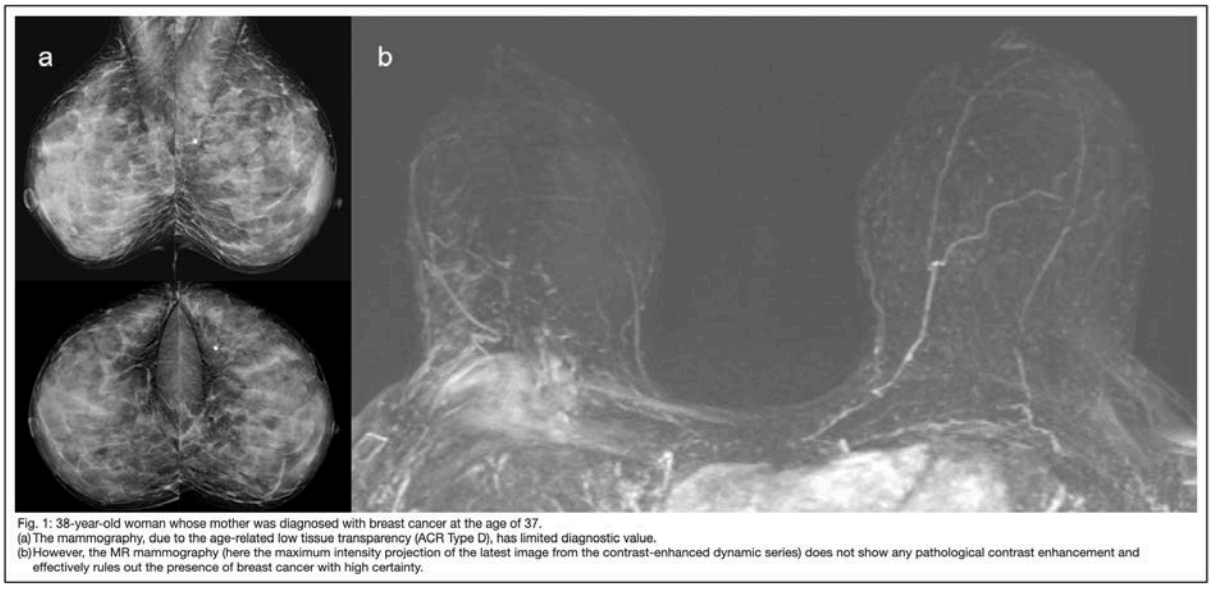


Fig. 1: 38-year-old woman whose mother was diagnosed with breast cancer at the age of 37.
(a) The mammography, due to the age-related low tissue transparency (ACR Type D), has limited diagnostic value.
(b) However, the MR mammography (here the maximum intensity projection of the latest image from the contrast-enhanced dynamic series) does not show any pathological contrast enhancement and effectively rules out the presence of breast cancer with high certainty.

What Preventive Measures for which Level of Risk?

For individuals with a "normal" lifetime risk of breast cancer participation in a systematic breast screening program is recommended. The basis of this approach is a mammography at 2-year intervals between the ages of 50 and 70 or 75 [17].

For a "moderate" risk situation there are no standardized recommendations. In cases of a "high-risk" constellation conservative methods of care are summarized under the term "intensified surveillance" [18]. As a surgical measure mastectomy is an option which involves removing the mammary gland and

What is Intensified Surveillance?

The goal of intensified surveillance is twofold: to detect newly occurring breast cancer as early as possible while minimizing the potential harmful effects of diagnostic procedures. These harmful effects include not only physical damage from ionizing radiation exposure or biopsy-related effects but also emotional distress reactions. The key aspects of intensified surveillance are therefore the choice of intervals and diagnostic methods. Regarding diagnostic methods all known breast examination techniques are applicable for intensified surveillance: clinical examination involving physical inspection, palpation, ultra-sound, mammo-

graphy, and magnetic resonance imaging (MRI) with potential image-guided biopsies. Breast self-examination does not play a role within intensified surveillance.

Compared to systematic breast cancer screening intensified surveillance faces distinct challenges. These challenges include higher proliferation rates and faster growth of breast cancers specific tumor biology as seen in BRCA1-associated malignancies often presenting with a "benign" morphology and the relatively younger age at first manifestation resulting in reduced breast tissue transparency in young women and consequently reduced mammography sensitivity for early detection. These characteristics are not accounted for in systematic breast cancer screening programs.

of detecting breast cancers at an early stage. The impact of new genetic diagnostics on the other hand is still uncertain [1].

Therefore the AWMF recommends intensified surveillance with MR mammography within a quality-assured program for women with pathogenic BRCA1/2 mutations and for women with a lifetime risk of ≥ 30% due to other reasons [1].

Bick et al. reported a sensitivity of 89.6% (95% CI 84.9–93.0) for the MRI-based surveillance programme as a whole [22]. The AGO 2020 summary of this study reports MRI-only detection in 15/71 cancers among BRCA1 carriers, 17/47 among BRCA2 carriers and 29/80 among high-risk BRCA1/2 non-carriers (Figs. 1 and 2).

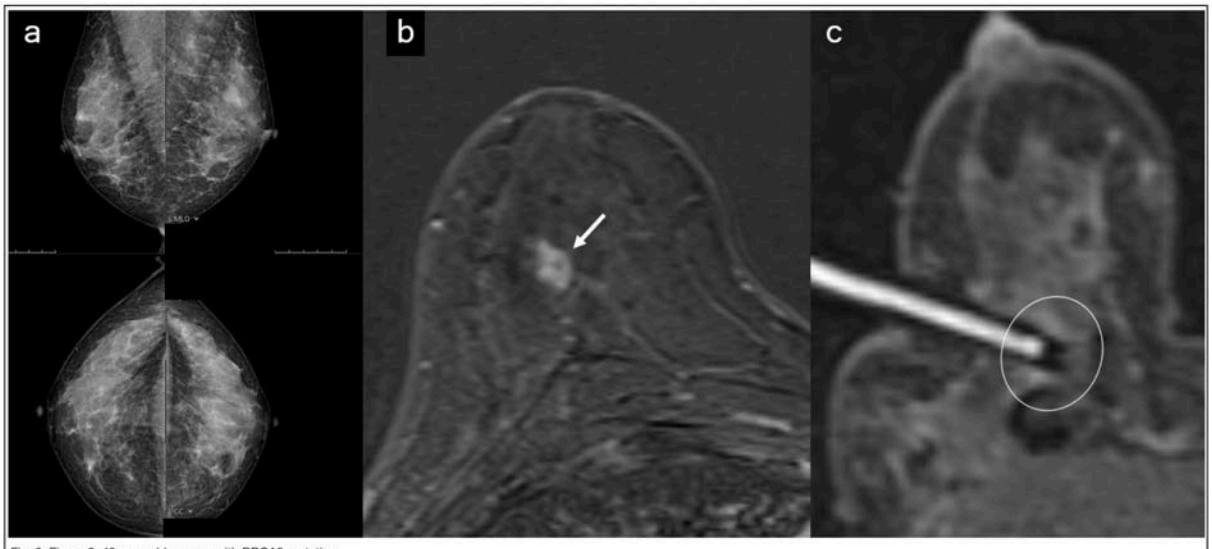


Fig. 2: Figure 2: 43-year-old woman with BRCA2 mutation.
(a) Mammography does not reveal any significant findings, but due to low tissue transparency (ACR Type C), it has limited diagnostic value. An ultrasound-guided core biopsy of an complex echo area in the upper outer quadrant of the right breast did not show evidence of malignancy.
(b) MR mammography exhibited a non-mass enhancement in the right breast (arrow).
(c) MR-guided vacuum biopsy of the area (circle) confirmed the diagnosis of ductal cancer in situ (DCIS).

For these reasons recommendations from medical societies are based on the specific benefit-risk ratio of available methods in high-risk situations. The guideline from the AWMF notes that the diagnostic accuracy of mammography and MRI is published but a reduction in mortality through these methods in high-risk situations has not yet been proven. However it is clear that intensified surveillance with MRI is capable

Mammography-only and ultrasound-only detection accounted for 7/198 (3.5%) and 2/198 (1.0%) cancers, respectively [26]. These detection proportions should be distinguished from modality-specific sensitivity.

The AGO recommends a multimodal approach to intensified surveillance starting at the age of 25, including semi-annual clinical breast examination, and ultrasound, as well as annual MR mammography [2].

Case Presentation

The following vignette is a hypothetical teaching example. Julia, a 36-year-old woman and mother of two daughters has a 3 year younger sister who recently discovered a lump in her breast. Subsequent diagnosis confirmed breast cancer. Since then Julia has been gripped by a strong fear that she might also be afflicted with breast cancer.

Though she hasn't detected any lumps in her own breasts Julia has been experiencing a sensation of pressure and occasional discomfort in both breasts lately. She is deeply concerned about whether these sensations could potentially be indicative of breast cancer. Seeking guidance, she schedules an appointment with her gynecologist and asks for advice on what steps she should take next.

Fear

Experiencing fear is principally normal and healthy. Fear arises when we find ourselves in situations we are not yet equipped to handle or understand. The fear response has evolved over time to ensure human survival. Therefore fear is not an illness in itself; it triggers actions for personal protection and self-care such as seeking advice undergoing genetic testing, and participating in an intensified surveillance program when facing a suspected or confirmed high-risk situation for breast cancer.

The trigger for fear is not a specific perception but rather how we evaluate that perception. When fear takes up increasing space and becomes an energy drain it can reach a pathological level. Particularly when fear significantly impacts quality of life or daily functioning, psychological support might be necessary.

What do the guidelines say?

As a physician in the consultation room we acknowledge and address Julia's fears and concerns. In the first step it is important to recognize that we are not facing a patient, but an individual seeking advice. Therefore our response is guided by the principle of "primum nil nocere" which means "first do no harm" [2]. This principle encompasses both potential physical and psychological harm. Therefore before offering any preventive measures a comprehensive and thorough consultation with a balanced consideration of benefits and risks should take place [2]. The evidence-based decision aids provided by professional societies can enhance the decisions made by those seeking advice [1].

How can we advise the individual seeking guidance?

It is important to conduct the consultation in a way that enables participatory decision-making for the individual seeking advice. This requires comprehensive information provision, addressing their questions, and taking their preferences into account. This applies not only to the decision regarding the extent of risk assessment such as whether to explore "only" familial or individual burdens but also extends to the consideration of predictive diagnostics, including genetic testing. It is crucial that the individuals have sufficient time to absorb the information and make their own decisions.

During the consultation it is essential that the options presented are not seen as obligations by the individual seeking advice. Particularly the decision-making process regarding genetic testing is open-ended. Several questions need to be clarified for the individual seeking advice (Tab. 2).

In addition to the responsibility for oneself family responsibilities also play a role in the decision-making process. For instance, mothers might contemplate

their children's future, women in partnerships may consider the impact on their relationship, and young women might ponder the implications for their desire to have children.

analyses not only assess predispositions, but also have psychological and social consequences for those being tested and their relatives directly influencing their life and family planning.

Questions to be answered
What is the aim of the examination for me?
What risks are associated with the examination?
What does the disease under investigation mean for me and my family?
What are the consequences of an abnormal test result for us?
What options are available when a disease/genetic condition is identified ? Are they suitable for me?
What are the alternatives if I decide not to undergo the examination?
Who will support my decision?

Tab. 2: Questions that the individuals seeking advice should be able to answer for themselves after a consultation on genetic diagnostics [23].

Engaging with the options is a process of becoming that orients itself toward the future. Experiences of the family and others who have faced or are facing the same life challenge are taken into consideration. Satisfaction with the decision can arise when the individual seeking advice can be certain that they are only asked or required to undertake what they believe they are capable of handling.

Auxiliary Communication

The collaboration between the physician and the individual seeking advice within the context of genetic counselling in high-risk situations is a significant challenge for both communication partners. The diversity of diagnostic, therapeutic, and preventive options requires a high degree of orientation not only from medical professionals but also from those affected and their families. Genetic

Experience shows that inadequate communication and misunderstanding between the physician and the individual seeking advice is a major and burdensome problem that often leads to hurt feelings, frustration, or anger. What is routine for the physician is an entirely new life situation for the individual seeking advice. What is professional work for the physician is personal fate for the individual seeking advice. The most important instrument for guidance is the guides themselves. In a consultation conversation it is not only the medical expertise of the counsellor that is needed but also their communicative competence as a significant qualitative determinant. Appropriate communication requires mastery of situation-appropriate conversation techniques as well as interpersonal skills. In recent years the concept of patient-centered communication has gained prominence, emphasizing understanding and considering the

patient's perspective at its core [24]. Patient-centered communication includes providing understandable information to the individual seeking advice regarding examination techniques such as genetic analysis in cases of possible familial disposition, diagnosis, and treatment options, as well as patient-centered, empathetic communication even for unfavorable news. The concept of patient-centered communication does not only incorporate the individual experiences, expectations, and fears of the patient or individual seeking advice into the physician-patient interaction but also aims to perceive and understand patients/individuals seeking advice within their own psychosocial reference frames. Patient-oriented dialogue necessitates mutual listening and sharing. The concept of auxiliary (help-related) communication implements these basic assumptions by not only providing factual information but also attempting to comprehend the individual's reference system and experience, including its impact on their life. The guiding attitude is patient-oriented rather than centered on the perspective of the advisor or expert. The advising physician does not need to agree with or find everything the individual seeking advice expresses to be good or right. What is crucial is that the advisor "does not find" it at all – neither positively nor negatively. This non-evaluative stance is a prerequisite for the individual seeking advice to open up without fearing rejection. Furthermore, neutrality ensures a neutral stance of the advisor towards the individual seeking advice. If the advisor manages to accept the individuals seeking advice with all their pain and fear and withstand it; it will also be easier for the individuals seeking advice to accept themselves. The advising physician is a companion who presents alternatives or suggestions for solutions. However the final decision always remains with the patient.

Resolution of the Case Presentation

For this teaching example, the illustrative 10-year and lifetime breast cancer risks are 3% and 24%, respectively, when the sister's BRCA status is unknown. In the alternative hypothetical scenario in which the sister carries a pathogenic BRCA1 variant, the illustrative figures are approximately 18% and 48%. No calculation record specifying the model version and complete inputs is available; these figures are retained solely for illustration and should not be interpreted as reproducible individual risk estimates. The example demonstrates how additional family information may affect risk counselling.

Due to her sister's breast cancer diagnosis at the age of 33 Julia meets the criteria for undergoing genetic testing herself.

Consequently Julia is confronted with the questions formulated in Tab. 2 which we as the advising physician can help her address by providing factual information and appropriate communication techniques. It is ultimately her decision whether she wants to proceed with genetic testing, opt for intensified surveillance, consider prophylactic mastectomy, or choose not to undergo any of these measures.

Conclusion for Clinical Practice

Asymptomatic women who are concerned about an increased risk of breast cancer due to family history should first receive comprehensive and detailed counselling including a discussion of the benefits and risks of diagnostic and preventive measures. Since these individuals are not "patients" but healthy women seeking guidance the principle of non-maleficence takes precedence.

In cases of high-risk situations besides prophylactic mastectomy, intensified

surveillance, following clearly structured recommendations of the relevant professional societies is an established approach. These measures should be carried out at specialized centers within the frame of quality-assured programs. The focus should be on considering the individual preferences of the women seeking advice.

Conflict of interest:

The authors declare that there were no conflicts of interest within the meaning of the recommendations of the International Committee of Medical Journal Editors when the article was written.

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References

1. S3-Leitlinie Früherkennung, Diagnose, Therapie und Nachsorge des Mammakarzinoms. Version 4.3. 2020. AWMF-Registernummer: 032-045OL. Online source search from 03.11.2022
2. Arbeitsgemeinschaft Gynäkologische Onkologie e. V. Früherkennung und Diagnostik. Online source search from 03.11.2022
3. Deutsches Konsortium Familiärer Brust- und Eierstockkrebs. Konsensusempfehlungen des Konsortiums (Stand 2022). Online source search from 03.11.2022
4. Robert Koch-Institut, Zentrum für Registerdaten. Brustkrebs (Mammakarzinom). Online source search from 03.11.2022
5. Antoniou A et al. Average risks of breast and ovarian cancer associated with BRCA1 or BRCA2 mutations detected in case Series unselected for family history: a combined analysis of 22 studies. Am J Hum Genet 2003; 72: 1117–30. DOI: 10.1086/375033
6. Goldberg JI & Borgen PI. Breast cancer susceptibility testing: past, present and future. Expert Rev Anticancer Ther 2006; 6: 1205–14. DOI: 10.1586/14737140.6.8.1205
7. Engel C et al. Breast cancer risk in BRCA1/2 mutation carriers and noncarriers under prospective intensified surveillance. Int J Cancer 2020; 146: 999–1009. DOI: 10.1002/ijc.32396
8. Fachal L et al. Fine-mapping of 150 breast cancer risk regions identifies 191 likely target genes. Nat Genet 2020; 52: 56–73. DOI: 10.1038/s41588-019-0537-1
9. Dorling L et al. Breast Cancer Association Consortium. Breast Cancer Risk Genes - Association Analysis in More than 113,000 Women. N Engl J Med 2021; 384: 428–39. DOI: 10.1056/NEJMoa1913948
10. Hu C et al. A Population-Based Study of Genes Previously Implicated in Breast Cancer. N Engl J Med 2021; 384: 440–51. DOI: 10.1056/NEJMoa2005936
11. Yang X et al. Ovarian and Breast Cancer Risks Associated With Pathogenic Variants in RAD51C and RAD51D. J Natl Cancer Inst 2020; 112: 1242–50. DOI: 10.1093/jnci/djaa030
12. Alm El-Din MA et al. Breast cancer after treatment of Hodgkin‘s lymphoma: risk factors that really matter. Int J Radiat Oncol Biol Phys 2009; 73: 69–74. DOI: 10.1016/j.ijrobp.2008.03.066
13. Preston DL et al. Radiation effects on breast cancer risk: a pooled analysis of eight cohorts. Radiat Res 2002; 158: 220–35. DOI: 10.1667/0033-7587(2002)158[0220:REOBCR]2.0.CO;2
14. Travis LB et al. Cumulative absolute breast cancer risk for young women treated for Hodgkin lymphoma. J Natl Cancer Inst 2005; 97: 1428–1437. DOI: 10.1093/jnci/dji290
15. Tyrer J, Duffy SW, Cuzick J. A breast cancer prediction model incorporating familial and personal risk factors. Stat Med 2004; 23: 1111–30. DOI: 10.1002/sim.1668
16. Ikonopedia. IBIS (International Breast Cancer Intervention Study). Online Tyrer-Cuzick model breast cancer risk evaluation tool – IBIS risk assessment tool v8.0b. Online source search from 03.11.2022
17. Bundesministerium für Gesundheit. Krebsfrüherkennungsuntersuchung in der gesetzlichen Krankenversicherung (§ 25 Abs. 2 SGB V) /Mammographie. Informationsblatt Nr. 315-02. Online source search from 03.11.2022
18. Deutsches Konsortium Familiärer Brust- und Eierstockkrebs. Intensivierte Früherkennung. Früherkennung durch moderne Bildgebung. Online source search from 03.11.2022
19. Jakub JW et al. Oncologic Safety of Prophylactic Nipple-Sparing Mastectomy in a Population With BRCA Mutations: A Multi-institutional Study. JAMA Surg 2018; 153: 123–9. DOI: 10.1001/jamasurg.2017.3422
20. Jeffers L et al. Interventions to improve psychosocial well-being in female BRCA-mutation carriers following risk-reducing surgery. Cochrane Database Syst Rev 2019; 10: CD012894. DOI: 10.1002/14651858.CD012894.pub2
21. Scheepens JCC et al. Contralateral prophylactic mastectomy: A narrative review of the evidence and acceptability. Breast 2021; 56: 61–9. DOI: 10.1016/j.breast.2021.02.003
22. Bick U et al. German Consortium for Hereditary Breast and Ovarian Cancer (GC-HBOC). 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. DOI: 10.1007/s10549-019-05152-9
23. Gödde E. Erbliche Krebsdisposition: Familienplanung zwischen Angst und Verantwortung. EHK 2010; 59: 189–98. DOI: 10.1055/s-0030-1257735
24. Langewitz W. Patientenzentrierte Kommunikation. In: Adler RH, Herzog W, Joraschky P, Köhle K, Langewitz W, Söllner W, Wesiak W, Hrsg. Uexküll, Psychosomatische Medizin. Theoretische Modelle und klinische Praxis. München: Urban & Fischer; 2011. S. 338–47. DOI of chapter 28 (Arzt-Patient-Gespräch): 10.1016/B978-3-437-21831-6.10028-0
25. Pal Choudhury P, Brook MN, Hurson AN, et al. Comparative validation of the BOADICEA and Tyrer-Cuzick breast cancer risk models incorporating classical risk factors and polygenic risk in a population-based prospective cohort of women of European ancestry. Breast Cancer Res. 2021;23:22. DOI: 10.1186/s13058-021-01399-7
26. AGO Breast Committee. Diagnosis and Treatment of Patients with Primary and Metastatic Breast Cancer. Guidelines Breast, Version 2020.1. High risk screening including MRI, PDF p. 71. Online source