Guidelines Breast
Version 2024.1D

Brustkrebsrisiko, Genetik und Prävention

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Version 2024.1D

Brustkrebsrisiko und Prävention

- **Versionen 2003–2023:**
  Albert / Bischoff / Blohmer / Dall / Ditsch / Fasching / Fehm / Gerber / Kiechle / Maass / Müller-Schimpfle / Mundhenke / Park-Simon / Rhiem / Rody / Schmidt / Schmutzler / Schütz / Stickeler / Thomssen / Witzel

- **Version 2024:**
  Gluz / Untch

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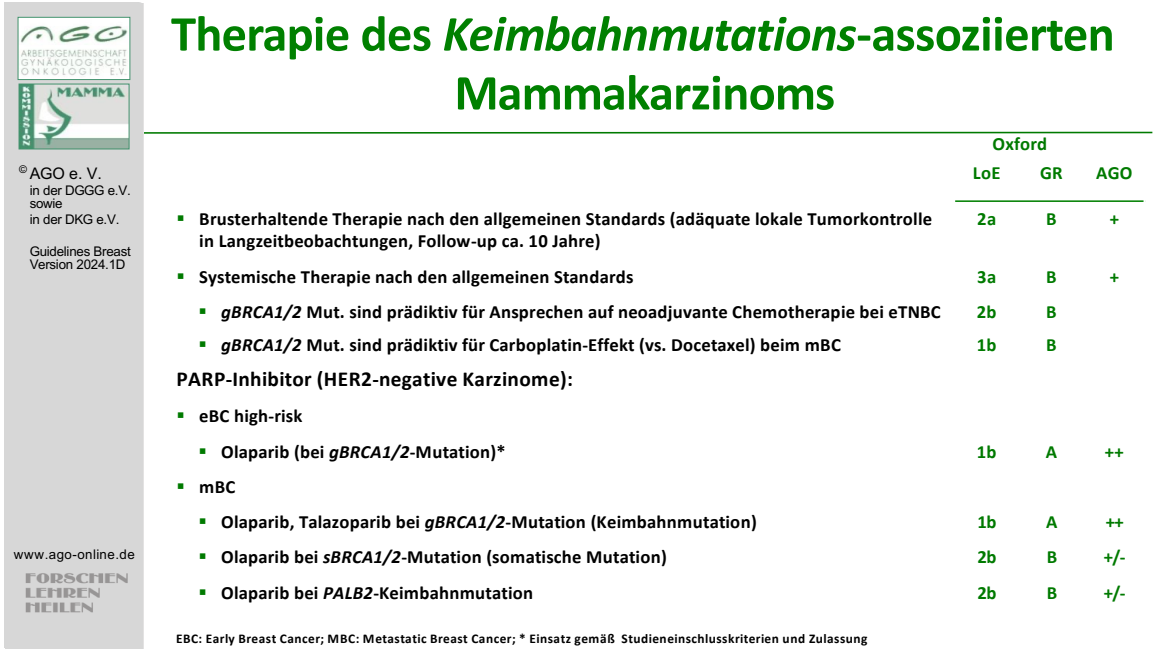
gBRCA-Diagnostik mit therapeutischer Konsequenz

Oxford LoE: 1b GR: A AGO: ++

gBRCA-Testung bei therapeutischer Konsequenz (unabh. von der familiären Risikokonstellation)



Therapie des *Keimbahnmutations*-assoziierten Mammakarzinoms

	Oxford LoE	Oxford GR	AGO
▪ **Brusterhaltende Therapie nach den allgemeinen Standards (adäquate lokale Tumorkontrolle in Langzeitbeobachtungen, Follow-up ca. 10 Jahre)**	2a	B	+
▪ **Systemische Therapie nach den allgemeinen Standards**	3a	B	+
▪ ***gBRCA1/2* Mut. sind prädiktiv für Ansprechen auf neoadjuvante Chemotherapie bei eTNBC**	2b	B	
▪ ***gBRCA1/2* Mut. sind prädiktiv für Carboplatin-Effekt (vs. Docetaxel) beim mBC**	1b	B	
PARP-Inhibitor (HER2-negative Karzinome):			
▪ **eBC high-risk**			
▪ **Olaparib (bei *gBRCA1/2*-Mutation)***	1b	A	++
▪ **mBC**			
▪ **Olaparib, Talazoparib bei *gBRCA1/2*-Mutation (Keimbahnmutation)**	1b	A	++
▪ **Olaparib bei *sBRCA1/2*-Mutation (somatische Mutation)**	2b	B	+/-
▪ **Olaparib bei *PALB2*-Keimbahnmutation**	2b	B	+/-

EBC: Early Breast Cancer; MBC: Metastatic Breast Cancer; * Einsatz gemäß Studieneinschlusskriterien und Zulassung

<u>BCS bei BRCA 1/2 Mutationsträgern</u>

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PARP-inhibitors eBC high-risk

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PARP-inhibitors mBC

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PARP-inhibitors mBC gPALB2mut

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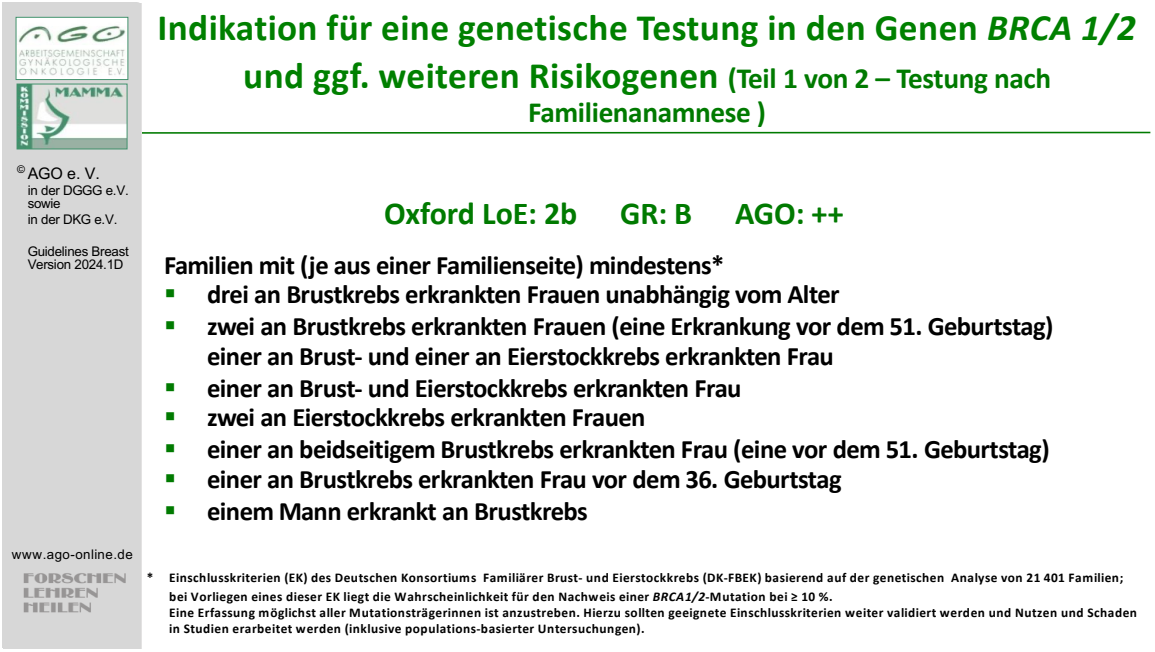

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Indikation für eine genetische Testung in den Genen *BRCA 1/2* und ggf. weiteren Risikogenen
(Teil 2 von 2 – Testung nach Familienanamnese)

Oxford LoE: 2b GR: B AGO: ++

- **Weitere empfohlene Kriterien**
  - **Eigene Erkrankung mit triple-negativem Brustkrebs mit Erkrankungsalter vor dem 60. Geburtstag**
  - **Eigene Erkrankung mit Eierstockkrebs vor dem 80. Geburtstag**
  - **Bei therapeutischer Relevanz (z. B. PARPi; nur *gBRCA1* und *gBRCA2*; ggf. *gPALB2*)**

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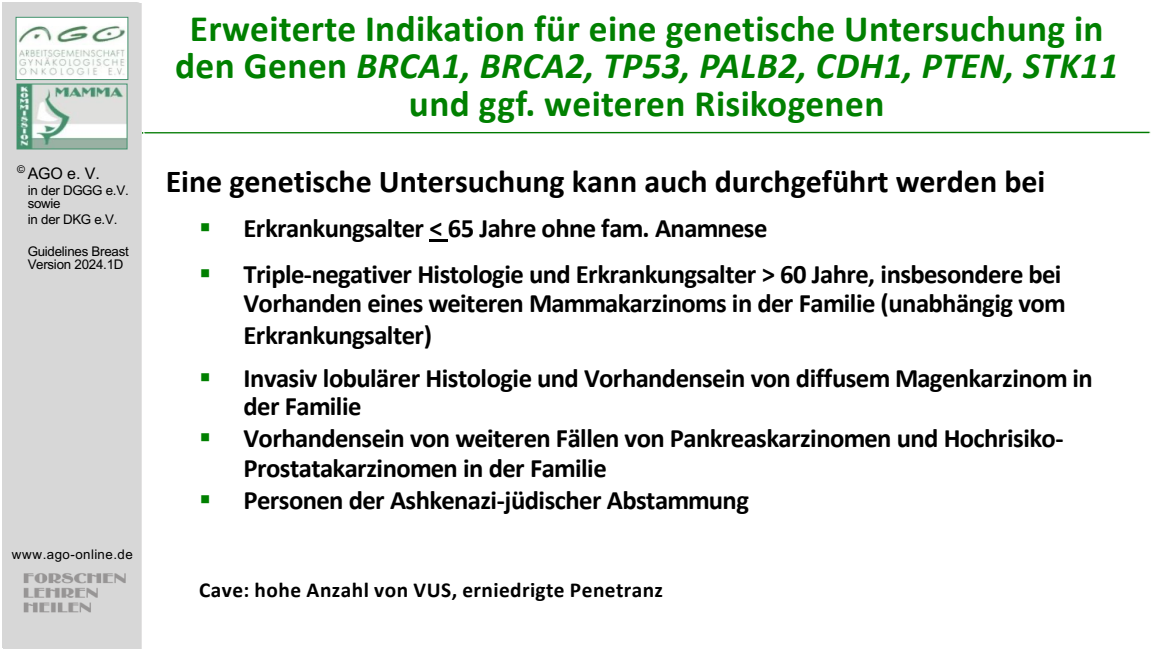

Literatur:

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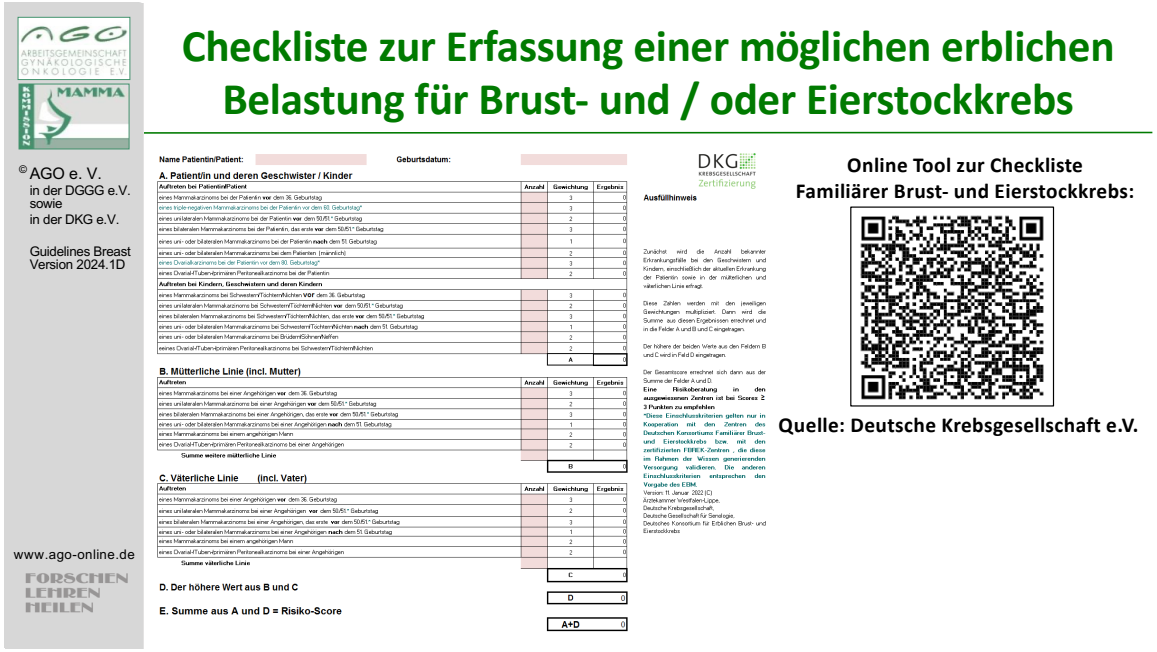
Checkliste zur Erfassung einer möglichen erblichen Belastung für Brust- und / oder Eierstockkrebs



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Name Patientin/Patient: **Geburtsdatum:**

A. Patientin und deren Geschwister / Kinder

Auftreten bei Patientin/Patient	Anzahl	Gewichtung	Ergebnis
eines Mammakarzinoms bei der Patientin **vor** dem 36. Geburtstag		3	0
eines triple-negativen Mammakarzinoms bei der Patientin vor dem 66. Geburtstag*		3	0
eines unilateralen Mammakarzinoms bei der Patientin **vor** dem 50/51.* Geburtstag		2	0
eines bilateralen Mammakarzinoms bei der Patientin, das erste **vor** dem 50/51.* Geburtstag		3	0
eines uni- oder bilateralen Mammakarzinoms bei der Patientin **nach** dem 51. Geburtstag		1	0
eines uni- oder bilateralen Mammakarzinoms bei dem Patienten (männlich)		2	0
eines Ovarial-/Tuben-/primären Peritonealkarzinoms bei der Patientin vor dem 80. Geburtstag*		3	0
eines Ovarial-/Tuben-/primären Peritonealkarzinoms bei der Patientin		2	0
Auftreten bei Kindern, Geschwistern und deren Kindern			
eines Mammakarzinoms bei Schwestern/Töchtern/Nichten **VOR** dem 36. Geburtstag		3	0
eines unilateralen Mammakarzinoms bei Schwestern/Töchtern/Nichten **vor** dem 50/51.* Geburtstag		2	0
eines bilateralen Mammakarzinoms bei Schwestern/Töchtern/Nichten, das erste **vor** dem 50/51.* Geburtstag		3	0
eines uni- oder bilateralen Mammakarzinoms bei Schwestern/Töchtern/Nichten **nach** dem 51. Geburtstag		1	0
eines uni- oder bilateralen Mammakarzinoms bei Brüdern/Söhnen/Neffen		2	0
eines Ovarial-/Tuben-/primären Peritonealkarzinoms bei Schwestern/Töchtern/Nichten		2	0
		A	0

B. Mütterliche Linie (incl. Mutter)

Auftreten	Anzahl	Gewichtung	Ergebnis
eines Mammakarzinoms bei einer Angehörigen **vor** dem 36. Geburtstag		3	0
eines unilateralen Mammakarzinoms bei einer Angehörigen **vor** dem 50/51.* Geburtstag		2	0
eines bilateralen Mammakarzinoms bei einer Angehörigen, das erste **vor** dem 50/51.* Geburtstag		3	0
eines uni- oder bilateralen Mammakarzinoms bei einer Angehörigen **nach** dem 51. Geburtstag		1	0
eines Mammakarzinoms bei einem angehörigen Mann		2	0
eines Ovarial-/Tuben-/primären Peritonealkarzinoms bei einer Angehörigen		2	0
Summe weitere mütterliche Linie			
		B	0

C. Väterliche Linie (incl. Vater)

Auftreten	Anzahl	Gewichtung	Ergebnis
eines Mammakarzinoms bei einer Angehörigen **vor** dem 36. Geburtstag		3	0
eines unilateralen Mammakarzinoms bei einer Angehörigen **vor** dem 50/51.* Geburtstag		2	0
eines bilateralen Mammakarzinoms bei einer Angehörigen, das erste **vor** dem 50/51.* Geburtstag		3	0
eines uni- oder bilateralen Mammakarzinoms bei einer Angehörigen **nach** dem 51. Geburtstag		1	0
eines Mammakarzinoms bei einem angehörigen Mann		2	0
eines Ovarial-/Tuben-/primären Peritonealkarzinoms bei einer Angehörigen		2	0
Summe väterliche Linie			
		C	0

D. Der höhere Wert aus B und C D 0

E. Summe aus A und D = Risiko-Score A+D 0

DKG KREBSGESELLSCHAFT Zertifizierung

Ausfüllhinweis

Zunächst wird die Anzahl bekannter Erkrankungsfälle bei den Geschwistern und Kindern, einschließlich der aktuellen Erkrankung der Patientin sowie in der mütterlichen und väterlichen Linie erfragt.

Diese Zahlen werden mit den jeweiligen Gewichtungen multipliziert. Dann wird die Summe aus diesen Ergebnissen errechnet und in die Felder A und B und C eingetragen.

Der höhere der beiden Werte aus den Feldern B und C wird in Feld D eingetragen.

Der Gesamtscore errechnet sich dann aus der Summe der Felder A und D.

Eine Risikoberatung in den ausgewiesenen Zentren ist bei Scores ≥ 3 Punkten zu empfehlen.

*Diese Einschlusskriterien gelten nur in Kooperation mit den Zentren des Deutschen Konsortiums Familiärer Brust- und Eierstockkrebs bzw. mit den zertifizierten FBREK-Zentren, die diese im Rahmen der Wissen generierenden Versorgung validieren. Die anderen Einschlusskriterien entsprechen den Vorgabe des EBM.

Version: 11. Januar 2022 (C)
Ärztekammer Westfalen-Lippe,
Deutsche Krebsgesellschaft,
Deutsche Gesellschaft für Senologie,
Deutsches Konsortium für Erblichen Brust- und Eierstockkrebs

Online Tool zur Checkliste Familiärer Brust- und Eierstockkrebs:

Quelle: Deutsche Krebsgesellschaft e.V.

Hier ist das Online Tool zur Checkliste „Familiärer Brust- und Eierstockkrebs“ hinterlegt:
https://www.krebsgesellschaft.de/zertdokumente.html?file=files/dkg/deutsche-krebsgesellschaft/content/pdf/Zertifizierung/Checklisten-und-Algorithmen/checkliste_erbliche_belastung_brust_gyn-220118.xlsx&cid=98969

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Risikoabschätzung für syndromassoziierte Mammakarzinome (non-BRCA)

	Oxford		
	LoE	GR	AGO
Eigen- und Familienanamnese über mindestens drei Generationen (mit Angabe des Ersterkrankungsalters)	**2b**	**B**	**++**

- **Typische Erkrankungen:**
  - **Mamma- und Ovarialkarzinom**
- **Weitere Erkrankungen, insbesondere:**
  - **Pankreas-, Schilddrüsen-, Kolorektal-, Magenkarzinom, hepato-biliäres und urogenitales Karzinom, Melanom, Osteosarkom, Leukämie, Lymphom, Lungenkarzinom**
  - **Nierenzellkarzinom**
  - **Hodenkarzinom**
  - **Endometriumkarzinom**
  - **Prostatakarzinom**

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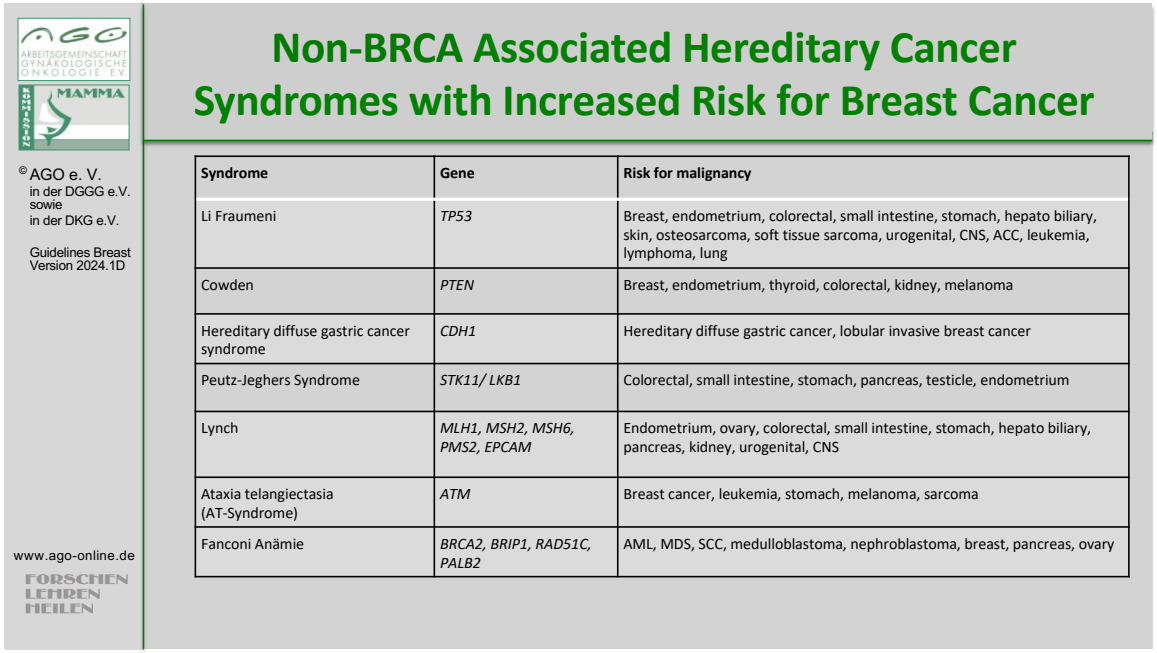

Non-BRCA Associated Hereditary Cancer Syndromes with Increased Risk for Breast Cancer

Syndrome	Gene	Risk for malignancy
Li Fraumeni	*TP53*	Breast, endometrium, colorectal, small intestine, stomach, hepato biliary, skin, osteosarcoma, soft tissue sarcoma, urogenital, CNS, ACC, leukemia, lymphoma, lung
Cowden	*PTEN*	Breast, endometrium, thyroid, colorectal, kidney, melanoma
Hereditary diffuse gastric cancer syndrome	*CDH1*	Hereditary diffuse gastric cancer, lobular invasive breast cancer
Peutz-Jeghers Syndrome	*STK11/ LKB1*	Colorectal, small intestine, stomach, pancreas, testicle, endometrium
Lynch	*MLH1, MSH2, MSH6, PMS2, EPCAM*	Endometrium, ovary, colorectal, small intestine, stomach, hepato biliary, pancreas, kidney, urogenital, CNS
Ataxia telangiectasia (AT-Syndrome)	*ATM*	Breast cancer, leukemia, stomach, melanoma, sarcoma
Fanconi Anämie	*BRCA2, BRIP1, RAD51C, PALB2*	AML, MDS, SCC, medulloblastoma, nephroblastoma, breast, pancreas, ovary

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Nicht-direktive Beratung vor der Durchführung präventiver Maßnahmen

AGO ++

Berücksichtigung des:

- **Gendiagnostikgesetzes**
- **Medizinproduktegesetzes (z. B. Risikokalkulation)**

Anwendung von Software zur Risikokalkulation erfordert ein professionelles Training und Erfahrung

Kommunikation von:

- **absoluten Erkrankungsrisiken in einem überschaubaren Zeitraum**
- **Risiken und Nutzen der intensivierten Früherkennung**
- **Risiken und Nutzen präventiver Maßnahmen**
- **konkurrierenden Risiken, z. B. Rezidiv- / Metastasierungsrisiko im Vergleich zum Zweitkarzinomrisiko bei bereits erkrankten Frauen**

Angemessene Bedenkzeit vor prophylaktischen Operationen

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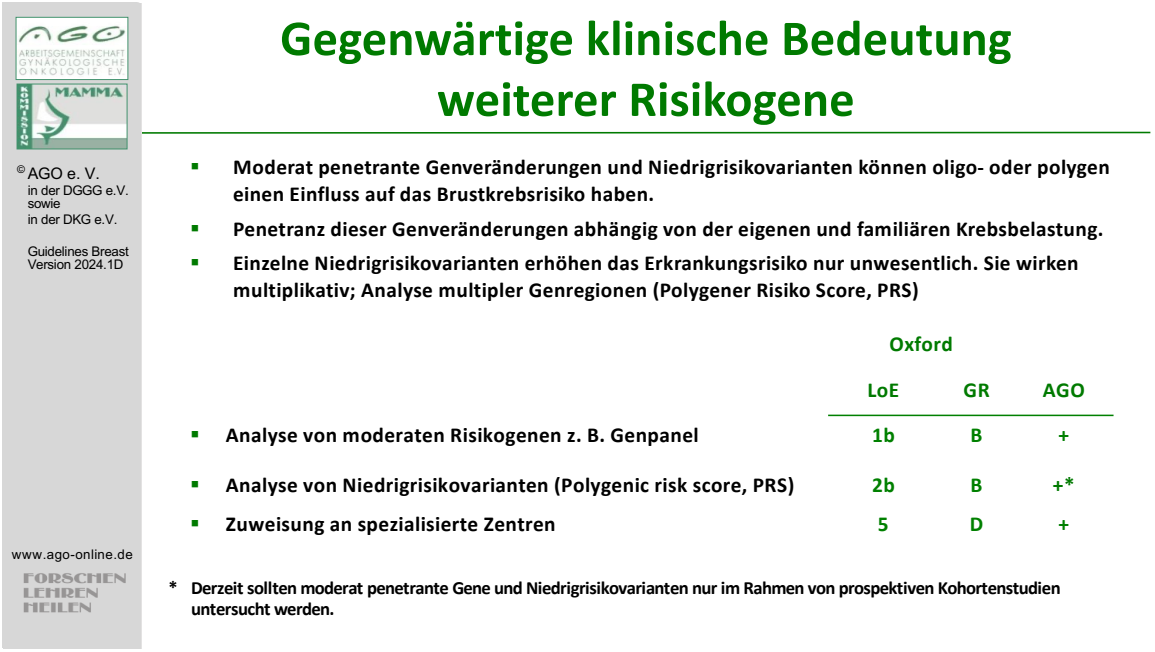

Gegenwärtige klinische Bedeutung weiterer Risikogene

- **Moderat penetrante Genveränderungen und Niedrigrisikovarianten können oligo- oder polygen einen Einfluss auf das Brustkrebsrisiko haben.**
- **Penetranz dieser Genveränderungen abhängig von der eigenen und familiären Krebsbelastung.**
- **Einzelne Niedrigrisikovarianten erhöhen das Erkrankungsrisiko nur unwesentlich. Sie wirken multiplikativ; Analyse multipler Genregionen (Polygener Risiko Score, PRS)**

	Oxford		
	LoE	GR	AGO
▪ Analyse von moderaten Risikogenen z. B. Genpanel	1b	B	+
▪ Analyse von Niedrigrisikovarianten (Polygenic risk score, PRS)	2b	B	+*
▪ Zuweisung an spezialisierte Zentren	5	D	+

* **Derzeit sollten moderat penetrante Gene und Niedrigrisikovarianten nur im Rahmen von prospektiven Kohortenstudien untersucht werden.**

Analyse von moderaten Risikogenen e.g. Genpanel

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Analyse von Niedrigrisikovarianten (Polygenic risk score, PRS)

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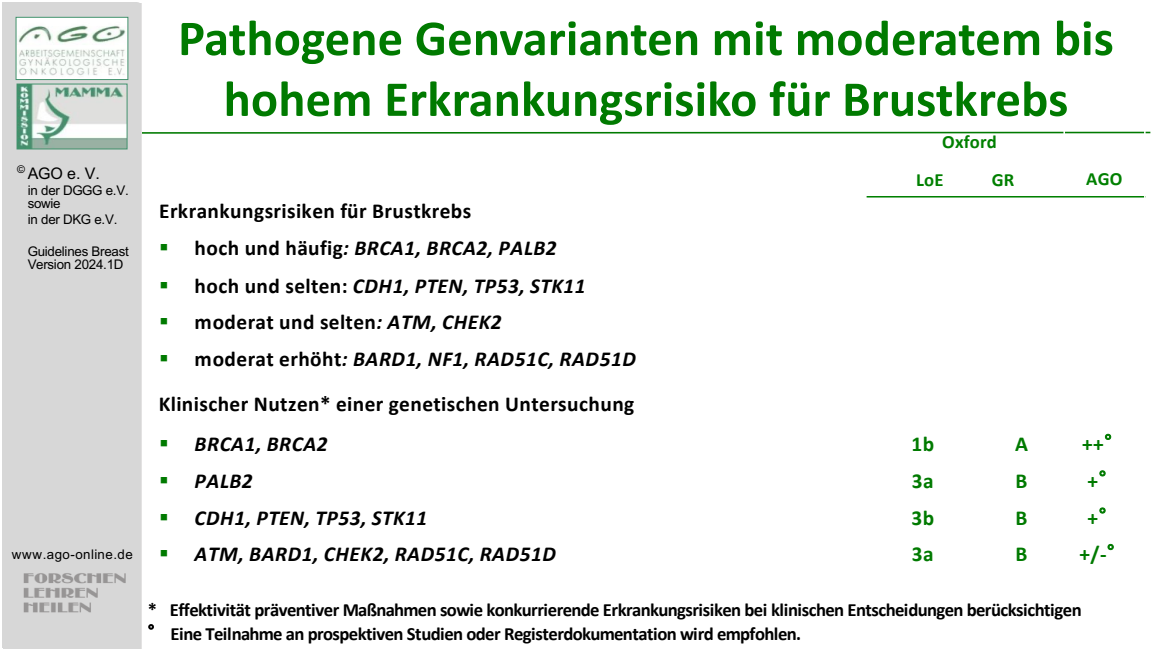

Pathogene Genvarianten mit moderatem bis hohem Erkrankungsrisiko für Brustkrebs

	Oxford		
	LoE	GR	AGO
Erkrankungsrisiken für Brustkrebs			
▪ **hoch und häufig*: BRCA1, BRCA2, PALB2***			
▪ **hoch und selten: *CDH1, PTEN, TP53, STK11***			
▪ **moderat und selten*: ATM, CHEK2***			
▪ **moderat erhöht*: BARD1, NF1, RAD51C, RAD51D***			
Klinischer Nutzen* einer genetischen Untersuchung			
▪ ***BRCA1, BRCA2***	1b	A	++°
▪ ***PALB2***	3a	B	+°
▪ ***CDH1, PTEN, TP53, STK11***	3b	B	+°
▪ ***ATM, BARD1, CHEK2, RAD51C, RAD51D***	3a	B	+/-°

* Effektivität präventiver Maßnahmen sowie konkurrierende Erkrankungsrisiken bei klinischen Entscheidungen berücksichtigen
° Eine Teilnahme an prospektiven Studien oder Registerdokumentation wird empfohlen.

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PALB2:

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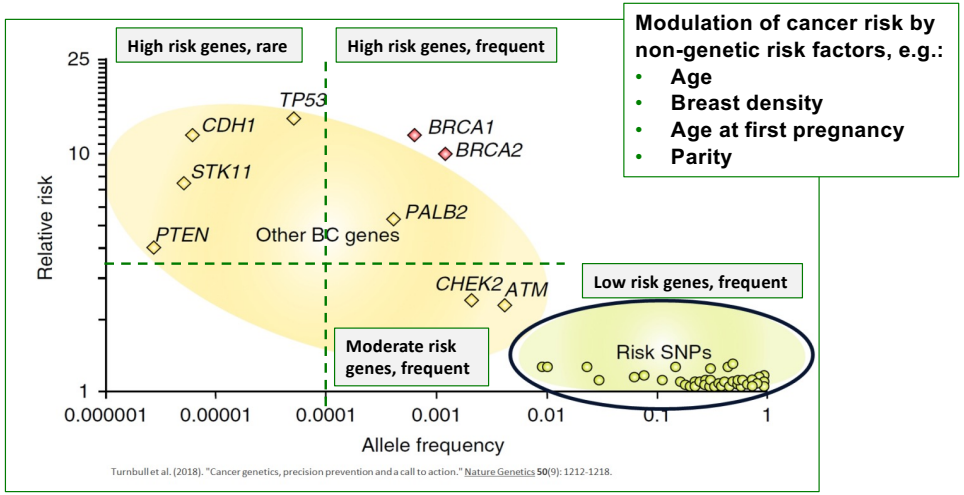
State of research: Relevance of Genetic and non-Genetic Risk Factors



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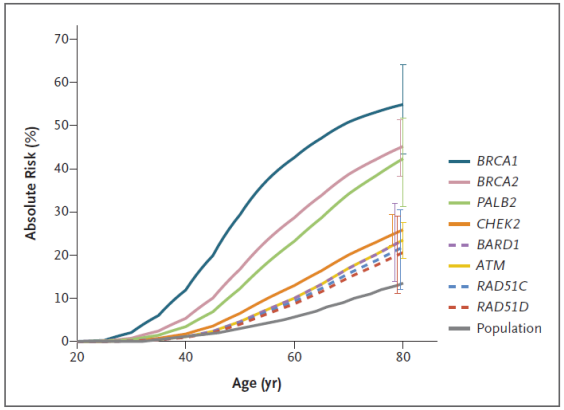
Estimated Cumulative Risk of Breast Cancer with Protein-Truncating Variants in 8 Genes



Shown are cumulative risks of breast cancer through 80 years of age for protein-truncating variants in 8 genes that had significant evidence of an association with breast cancer overall, on the basis of estimated odds ratios from population-based studies. Baseline absolute risks were derived from population incidences in the United Kingdom in 2016. The I bars indicate 95 % confidence intervals.
Dorling L, Carvalho S, Allen J et al. Breast-Cancer Risk Genes — Association Analysis in More than 113,000 Women. January 20, 2021 DOI: 10.1056/NEJMoa1913948

1. Dorling L, Carvalho S, Allen J et al. Breast-Cancer Risk Genes — Association Analysis in More than 113,000 Women. January 20, 2021 DOI: 10.1056/NEJMoa1913948
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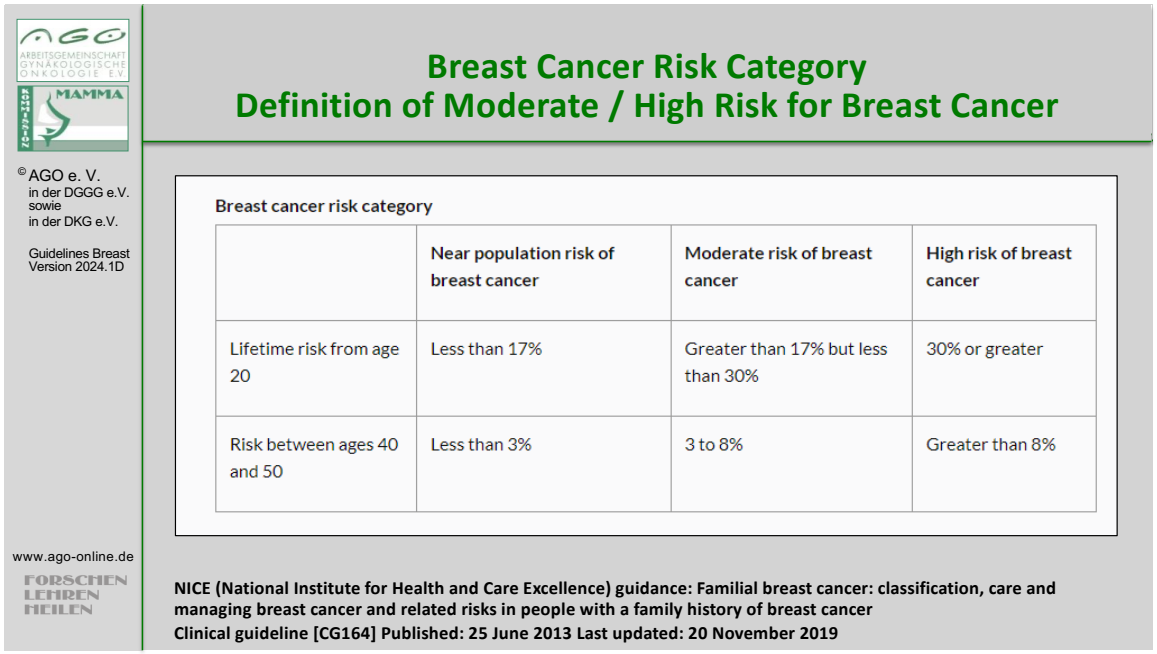


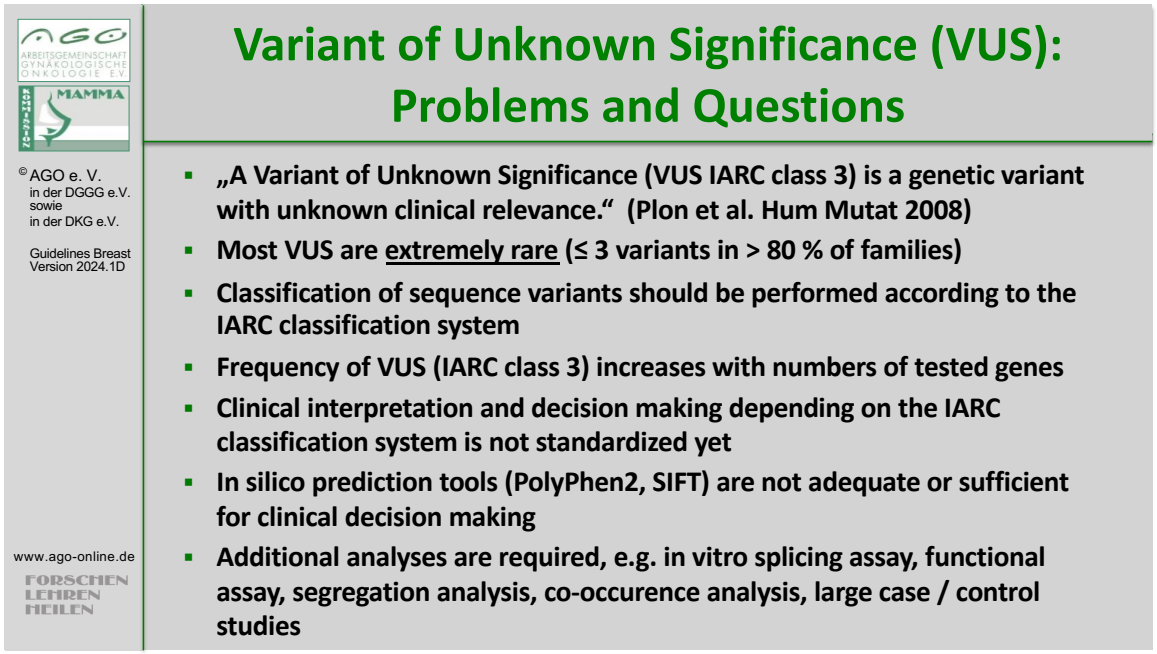
1. NICE (National Institute for Health and Care Excellence) guidance: Familial breast cancer: classification, care and managing breast cancer and related risks in people with a family history of breast cancer. Clinical guideline [CG164] Published: 25 June 2013 Last updated: 20 November 2019
2. NCCN Guidelines. Genetic/Familial High-Risk Assessment: Breast, Ovarian, and Pancreatic. Version 1.2023. https://www.nccn.org/login?ReturnURL=https://www.nccn.org/professionals/physician_gls/pdf/genetics_bop.pdf

IARC - Classification of Sequence Variants (Plon et al., Human Mutation, 2008)

Proposed Classification System for Sequence Variants Identified by Genetic Testing		
Class	**Description**	**Probability of being pathogenic**
5	Definitely pathogenic	> 0,99
4	Likely pathogenic	0,95-0,99
3	Uncertain	0,05-0,949
2	Likely not pathogenic or of little clinical significance	0,001-0,049
1	Not pathogenic or no of clinical significance	< 0,001

Only class 4 and class 5 variants are considered clinically relevant.
Class 3 are considered as Variants of Unknown Significance (VUS).

1. Plon SE, Eccles DM, Easton D, et al. Sequence variant classification and reporting: recommendations for improving the interpretation of cancer susceptibility genetic test results. Human mutation. 2008;29(11):1282-91.
2. Fanale D, Pivetti A, Cancelliere D et al. BRCA1/2 variants of unknown significance in hereditary breast and ovarian cancer (HBOC) syndrome: Looking for the hidden meaning. Crit Rev Oncol Hematol. 2022 Apr;172:103626.



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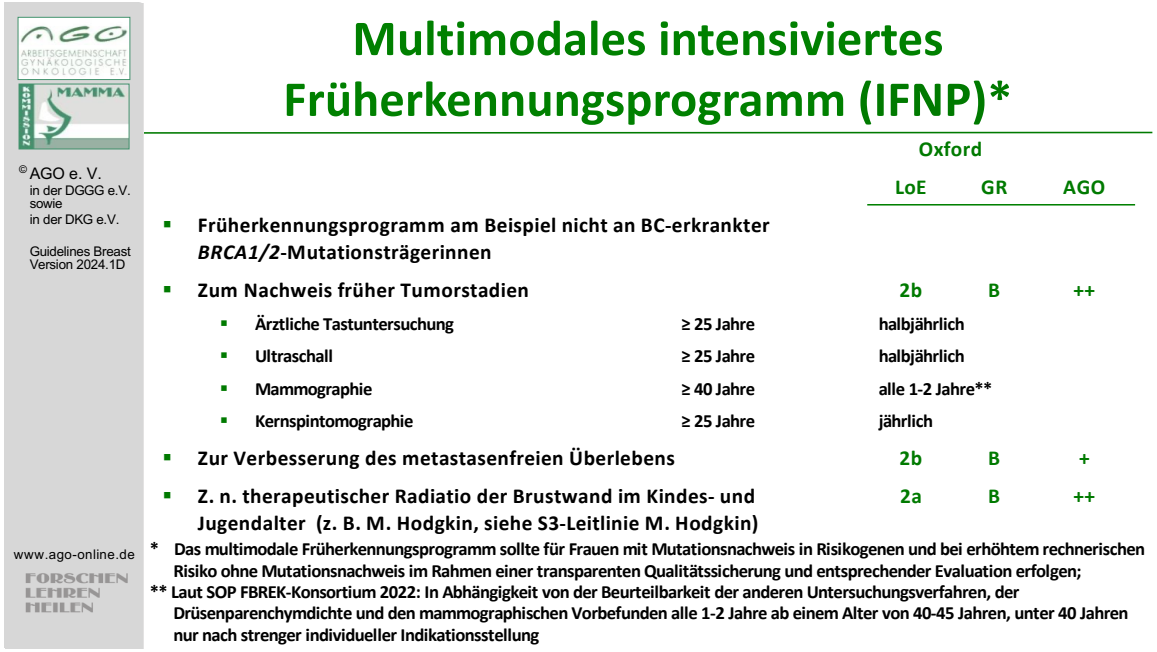

Multimodales intensiviertes Früherkennungsprogramm (IFNP)*

		Oxford LoE	GR	AGO
▪ Früherkennungsprogramm am Beispiel nicht an BC-erkrankter *BRCA1/2*-Mutationsträgerinnen				
▪ Zum Nachweis früher Tumorstadien		2b	B	++
▪ Ärztliche Tastuntersuchung	≥ 25 Jahre	halbjährlich		
▪ Ultraschall	≥ 25 Jahre	halbjährlich		
▪ Mammographie	≥ 40 Jahre	alle 1-2 Jahre**		
▪ Kernspintomographie	≥ 25 Jahre	jährlich		
▪ Zur Verbesserung des metastasenfreien Überlebens		2b	B	+
▪ Z. n. therapeutischer Radiatio der Brustwand im Kindes- und Jugendalter (z. B. M. Hodgkin, siehe S3-Leitlinie M. Hodgkin)		2a	B	++

* Das multimodale Früherkennungsprogramm sollte für Frauen mit Mutationsnachweis in Risikogenen und bei erhöhtem rechnerischen Risiko ohne Mutationsnachweis im Rahmen einer transparenten Qualitätssicherung und entsprechender Evaluation erfolgen;
** Laut SOP FBREK-Konsortium 2022: In Abhängigkeit von der Beurteilbarkeit der anderen Untersuchungsverfahren, der Drüsenparenchymdichte und den mammographischen Vorbefunden alle 1-2 Jahre ab einem Alter von 40-45 Jahren, unter 40 Jahren nur nach strenger individueller Indikationsstellung

1. E-Learning DKG/FBREK, 2022
2. Leitlinienprogramm Onkologie (Deutsche Krebsgesellschaft, Deutsche Krebshilfe, AWMF): S3-Leitlinie Früherkennung, Diagnose, Therapie und Nachsorge des Mammakarzinoms, Version 4.4, 2021, AWMF Registernummer: 032-045OL, http://www.leitlinienprogramm-onkologie.de/leitlinien/mammakarzinom/ (abgerufen am: 24.1.2022) Bick U, Engel C, Krug B, 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(1):217–228.
3. Ellen Warner: Screening BRCA1 and BRCA2 Mutation Carriers for Breast Cancer. Review. Cancers 2018, 10, 477;
4. Evans, D.G.; Kesavan, N.; Lim, Y. et al.: MRI breast screening in high-risk women: Cancer detection and survival analysis. Breast Cancer Res. Treat. 2014, 145: 663–672
5. Leach MO, Boggis CR, Dixon AK, et al. Screening with magnetic resonance imaging and mammography of a UK population at high familial risk of breast cancer: a prospective multicentre cohort study (MARIBS). Lancet. 2005;365(9473):1769-78.
6. Meindl A, Ditsch N, Kast K, et al. Hereditary breast and ovarian cancer: new genes, new treatments, new concepts. Dtsch Arztebl Int. 2011;108(19):323-30.
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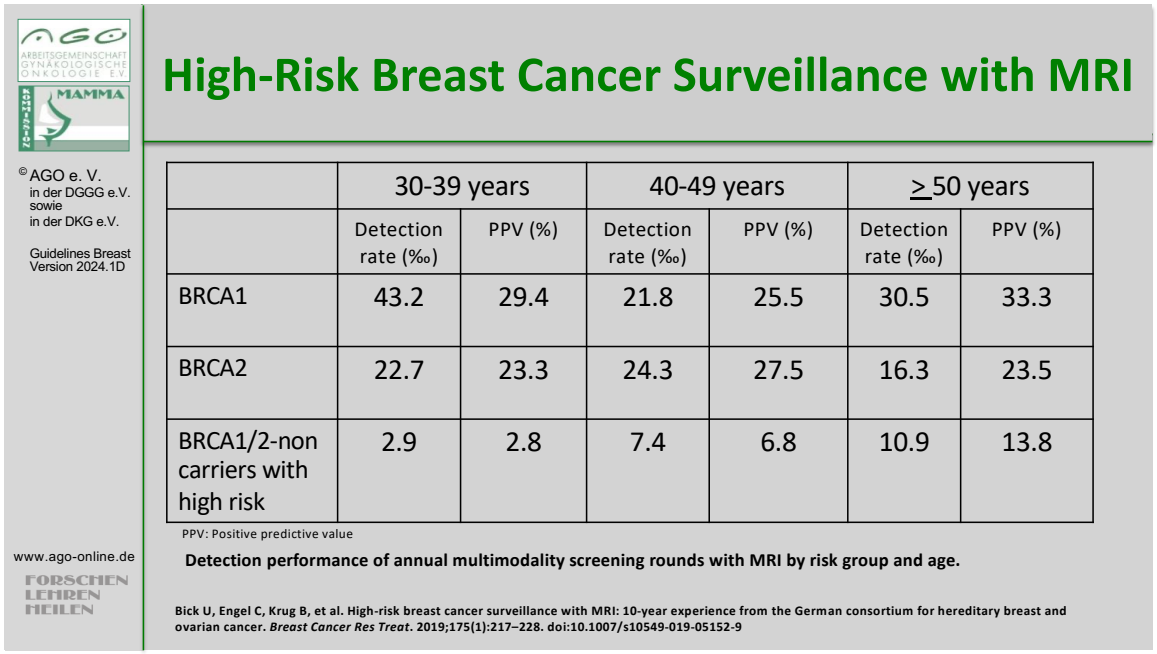
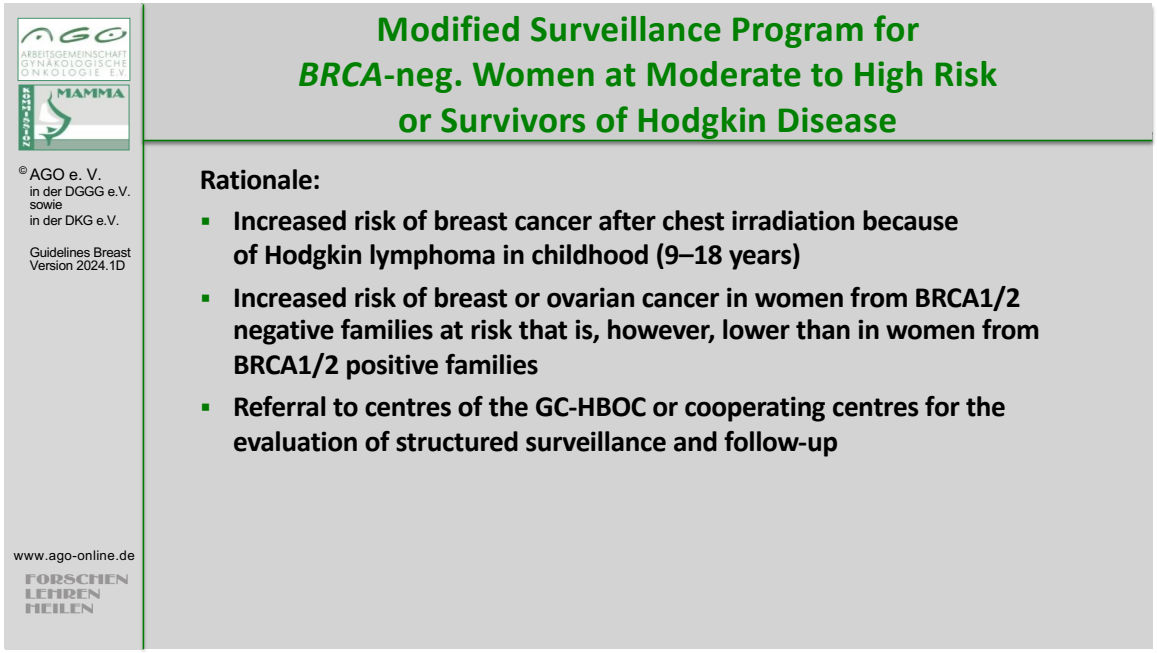


	30-39 years		40-49 years		≥ 50 years	
	Detection rate (‰)	PPV (%)	Detection rate (‰)	PPV (%)	Detection rate (‰)	PPV (%)
BRCA1	43.2	29.4	21.8	25.5	30.5	33.3
BRCA2	22.7	23.3	24.3	27.5	16.3	23.5
BRCA1/2-non carriers with high risk	2.9	2.8	7.4	6.8	10.9	13.8

1. Bick U, Engel C, Krug B 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 May;175(1):217-228. doi: 10.1007/s10549-019-05152-9. Epub 2019 Feb 6. PMID: 30725383.



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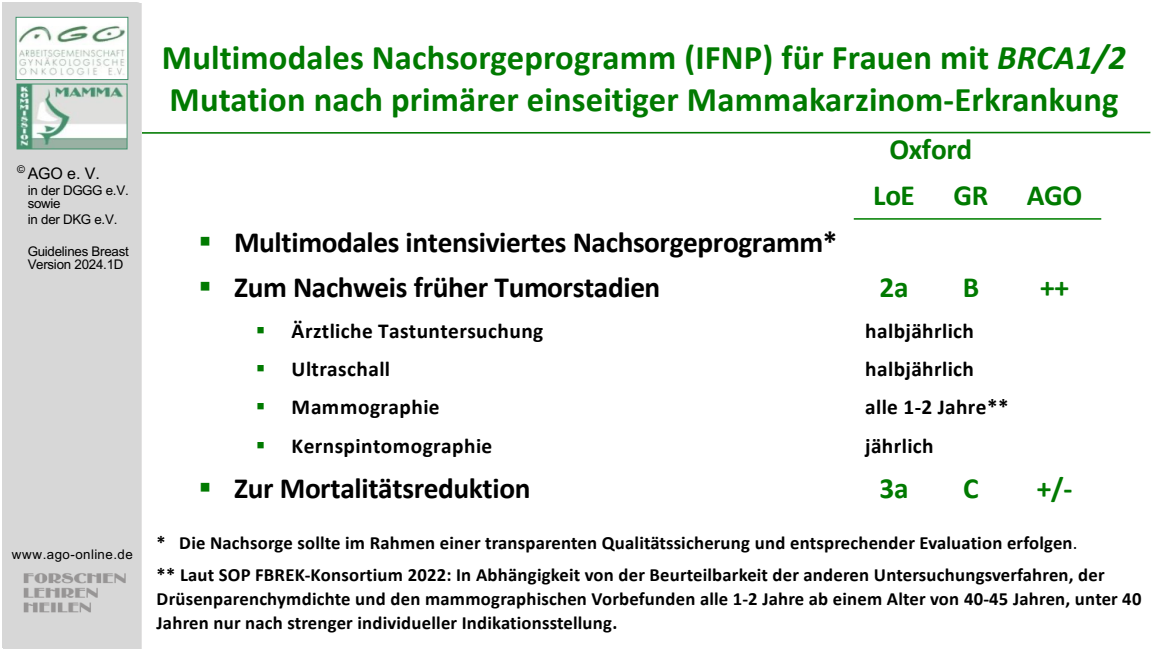

Multimodales Nachsorgeprogramm (IFNP) für Frauen mit *BRCA1/2* Mutation nach primärer einseitiger Mammakarzinom-Erkrankung

	Oxford LoE	GR	AGO
▪ **Multimodales intensiviertes Nachsorgeprogramm***			
▪ **Zum Nachweis früher Tumorstadien**	**2a**	**B**	**++**
▪ **Ärztliche Tastuntersuchung**	**halbjährlich**		
▪ **Ultraschall**	**halbjährlich**		
▪ **Mammographie**	**alle 1-2 Jahre****		
▪ **Kernspintomographie**	**jährlich**		
▪ **Zur Mortalitätsreduktion**	**3a**	**C**	**+/-**

*** Die Nachsorge sollte im Rahmen einer transparenten Qualitätssicherung und entsprechender Evaluation erfolgen.**

**** Laut SOP FBREK-Konsortium 2022: In Abhängigkeit von der Beurteilbarkeit der anderen Untersuchungsverfahren, der Drüsenparenchymdichte und den mammographischen Vorbefunden alle 1-2 Jahre ab einem Alter von 40-45 Jahren, unter 40 Jahren nur nach strenger individueller Indikationsstellung.**

1. Leitlinienprogramm Onkologie (Deutsche Krebsgesellschaft, Deutsche Krebshilfe, AWMF): S3-Leitlinie Früherkennung, Diagnose, Therapie und Nachsorge des Mammakarzinoms, Version 4.4, 2021, AWMF Registernummer: 032-045OL, http://www.leitlinienprogramm-onkologie.de/leitlinien/mammakarzinom/ (abgerufen am: 24.1.2022) Bick U, Engel C, Krug B, 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(1):217–228. doi:10.1007/s10549-019-05152-9
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7. Carbine NE, Lostumbo L, Wallace J et al.: Risk-reducing mastectomy for the prevention of primary breast cancer. Cochrane Database Syst Rev. 2018 Apr 5;4:CD002748. Review
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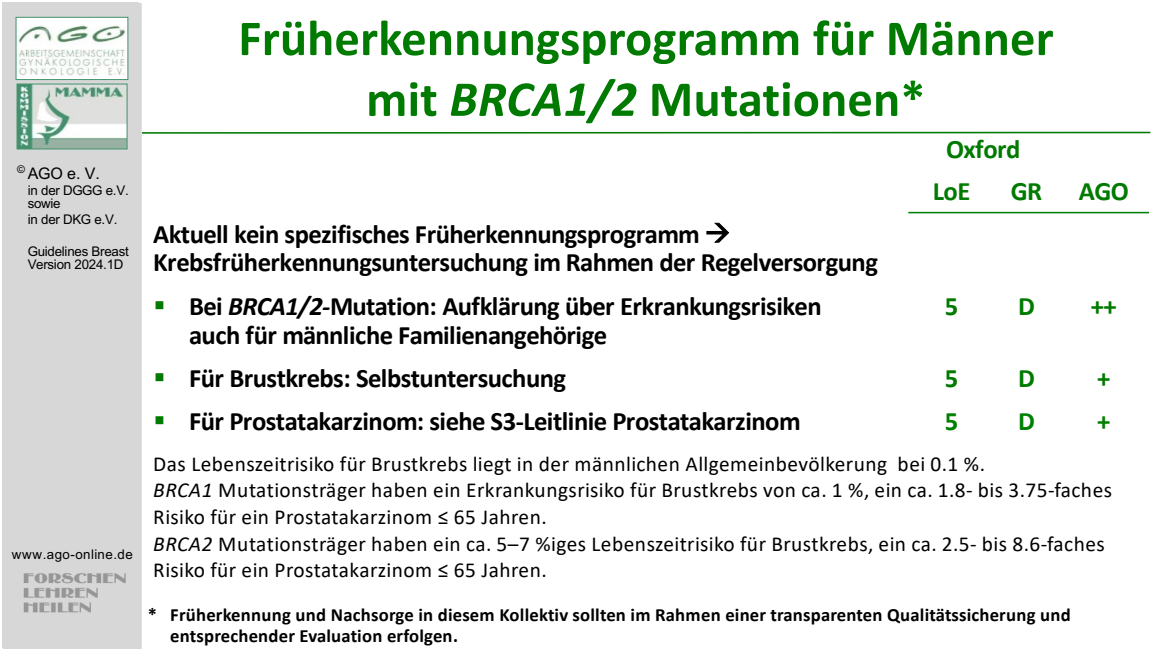

Früherkennungsprogramm für Männer mit *BRCA1/2* Mutationen*

	Oxford LoE	Oxford GR	Oxford AGO
Aktuell kein spezifisches Früherkennungsprogramm → Krebsfrüherkennungsuntersuchung im Rahmen der Regelversorgung			
▪ **Bei *BRCA1/2*-Mutation: Aufklärung über Erkrankungsrisiken auch für männliche Familienangehörige**	5	D	++
▪ **Für Brustkrebs: Selbstuntersuchung**	5	D	+
▪ **Für Prostatakarzinom: siehe S3-Leitlinie Prostatakarzinom**	5	D	+

Das Lebenszeitrisiko für Brustkrebs liegt in der männlichen Allgemeinbevölkerung bei 0.1 %.
BRCA1 Mutationsträger haben ein Erkrankungsrisiko für Brustkrebs von ca. 1 %, ein ca. 1.8- bis 3.75-faches Risiko für ein Prostatakarzinom ≤ 65 Jahren.
BRCA2 Mutationsträger haben ein ca. 5–7 %iges Lebenszeitrisiko für Brustkrebs, ein ca. 2.5- bis 8.6-faches Risiko für ein Prostatakarzinom ≤ 65 Jahren.

* **Früherkennung und Nachsorge in diesem Kollektiv sollten im Rahmen einer transparenten Qualitätssicherung und entsprechender Evaluation erfolgen.**

1. Albert US, Schreer I; Arbeitsgruppe der Stufe-3-Leitlinie Mammakarzinom. S3 guideline breast cancer: update on early detection, and mammography screening. Radiologe. 2019 Jan;59(1):13-18.
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13. Barnes DR, Silvestri V, Leslie G, et al: Breast and Prostate Cancer Risks for Male BRCA1 and BRCA2 Pathogenic Variant Carriers Using Polygenic Risk Scores. J Natl Cancer Inst 2022 Jan 11;114(1):109-122.
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Chirurgische Prävention

	Oxford		
	LoE	GR	AGO
▪ **Risiko-reduzierende, unilaterale oder bilaterale Mastektomie (RRME) ohne Vorliegen von genetischen Risikofaktoren (führt nicht zu einer Mortalitätsreduktion)**	2a	B	-*
▪ **Axilladissektion oder Sentinel-Lymphknoten Exzision bei RRME**	2a	B	--

* **Studienteilnahme empfohlen**

RRME ohne gentisches Risiko

1. Kurian AW, Lichtensztajn DY, Keegan TH, et al. Use of and mortality after bilateral mastectomy compared with other surgical treatments for breast cancer in California, 1998-2011. JAMA. 2014;312(9):902-14.
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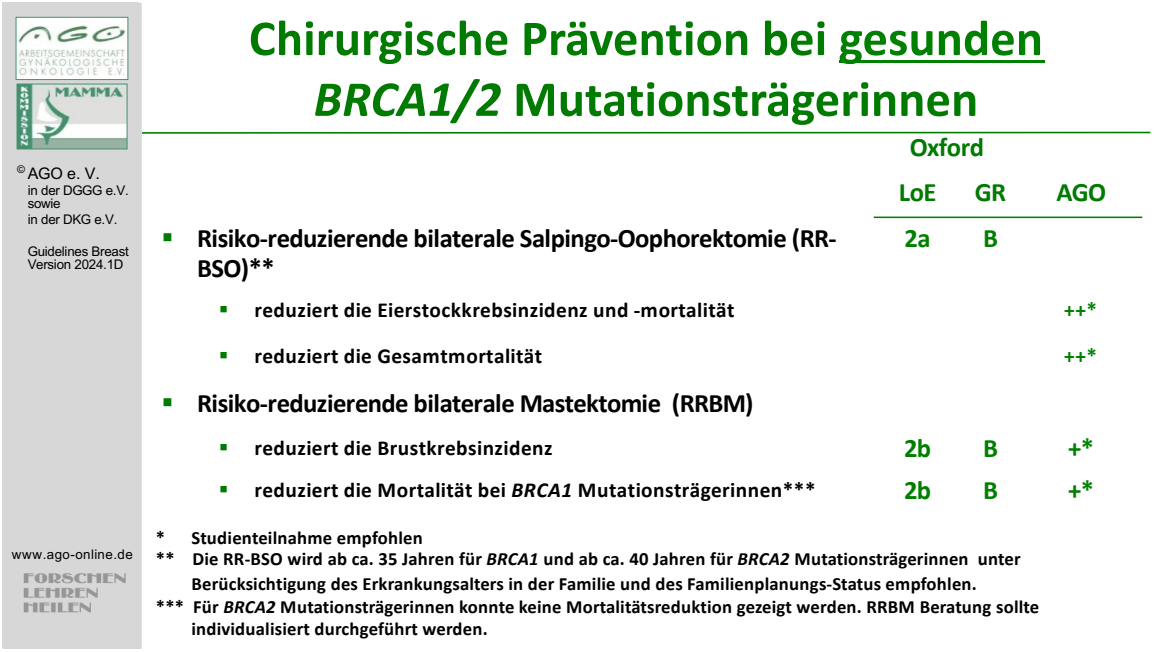
Sentinel-Lymphknoten Exzision bei RRME

1. Wong SM, Ferroum A, Apostolova C et al. Incidence of Occult Breast Cancer in Carriers of BRCA1/2 or Other High-Penetrance Pathogenic Variants Undergoing Prophylactic Mastectomy: When is Sentinel Lymph Node Biopsy Indicated? Ann Surg Oncol. 2022 Oct;29(11):6660-6668.



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8. Lostumbo L, Carbine NE, Wallace J. Prophylactic mastectomy for the prevention of breast cancer. Cochrane Database Syst Rev.

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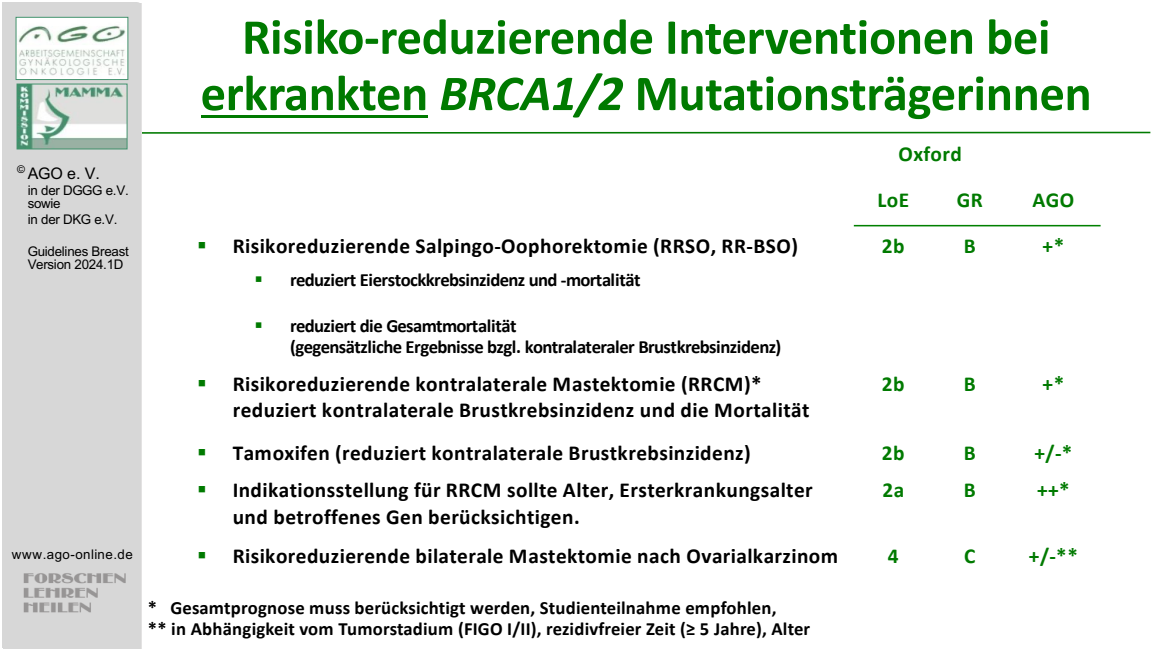

Risiko-reduzierende Interventionen bei erkrankten *BRCA1/2* Mutationsträgerinnen

	Oxford		
	LoE	GR	AGO
▪ Risikoreduzierende Salpingo-Oophorektomie (RRSO, RR-BSO)	2b	B	+*
▪ reduziert Eierstockkrebsinzidenz und -mortalität			
▪ reduziert die Gesamtmortalität (gegensätzliche Ergebnisse bzgl. kontralateraler Brustkrebsinzidenz)			
▪ Risikoreduzierende kontralaterale Mastektomie (RRCM)* reduziert kontralaterale Brustkrebsinzidenz und die Mortalität	2b	B	+*
▪ Tamoxifen (reduziert kontralaterale Brustkrebsinzidenz)	2b	B	+/-*
▪ Indikationsstellung für RRCM sollte Alter, Ersterkrankungsalter und betroffenes Gen berücksichtigen.	2a	B	++*
▪ Risikoreduzierende bilaterale Mastektomie nach Ovarialkarzinom	4	C	+/-**

* Gesamtprognose muss berücksichtigt werden, Studienteilnahme empfohlen,
** in Abhängigkeit vom Tumorstadium (FIGO I/II), rezidivfreier Zeit (≥ 5 Jahre), Alter

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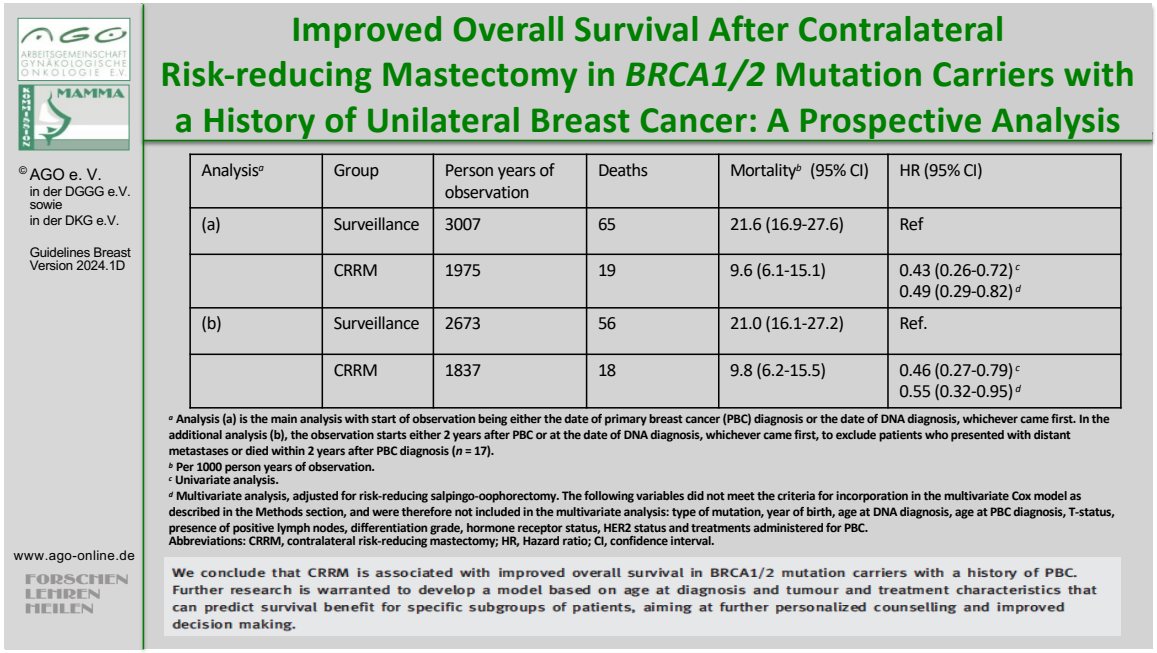

Improved Overall Survival After Contralateral Risk-reducing Mastectomy in *BRCA1/2* Mutation Carriers with a History of Unilateral Breast Cancer: A Prospective Analysis

Analysis[a]	Group	Person years of observation	Deaths	Mortality[b] (95% CI)	HR (95% CI)
(a)	Surveillance	3007	65	21.6 (16.9-27.6)	Ref
	CRRM	1975	19	9.6 (6.1-15.1)	0.43 (0.26-0.72)[c] 0.49 (0.29-0.82)[d]
(b)	Surveillance	2673	56	21.0 (16.1-27.2)	Ref.
	CRRM	1837	18	9.8 (6.2-15.5)	0.46 (0.27-0.79)[c] 0.55 (0.32-0.95)[d]

[a] Analysis (a) is the main analysis with start of observation being either the date of primary breast cancer (PBC) diagnosis or the date of DNA diagnosis, whichever came first. In the additional analysis (b), the observation starts either 2 years after PBC or at the date of DNA diagnosis, whichever came first, to exclude patients who presented with distant metastases or died within 2 years after PBC diagnosis (n = 17).
[b] Per 1000 person years of observation.
[c] Univariate analysis.
[d] Multivariate analysis, adjusted for risk-reducing salpingo-oophorectomy. The following variables did not meet the criteria for incorporation in the multivariate Cox model as described in the Methods section, and were therefore not included in the multivariate analysis: type of mutation, year of birth, age at DNA diagnosis, age at PBC diagnosis, T-status, presence of positive lymph nodes, differentiation grade, hormone receptor status, HER2 status and treatments administered for PBC.
Abbreviations: CRRM, contralateral risk-reducing mastectomy; HR, Hazard ratio; CI, confidence interval.

We conclude that CRRM is associated with improved overall survival in BRCA1/2 mutation carriers with a history of PBC. Further research is warranted to develop a model based on age at diagnosis and tumour and treatment characteristics that can predict survival benefit for specific subgroups of patients, aiming at further personalized counselling and improved decision making.

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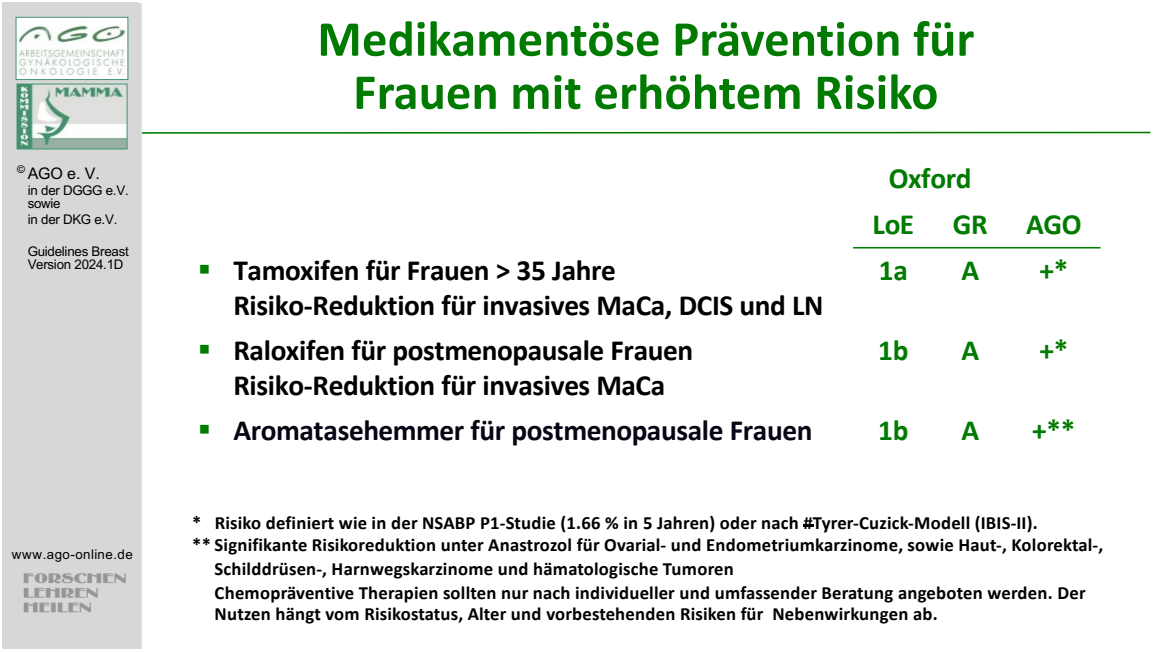

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