Short human genetics opinion for a health insurer

Risk-reducing mastectomy in a BRCA2 carrier

Human genetics opinion on variant classification, cancer risk and professional justifiability of bilateral risk-reducing mastectomy in a healthy insured woman

Fictitious sample case – case, persons, events and instruction are simulated, not a real expert opinion. Cited sources are real.

Instructed by	Private health insurer (private Krankenversicherung) [fictitious], Inpatient Benefits Review	Reference	KV-2026-11802 [fictitious]
Insured person	A. W. [fictitious], born 1990	Date	8 November 2026

Result in brief

On the assumption made in this sample case that a pathogenic *BRCA2* variant is present, the insured woman's breast cancer risk is increased several-fold compared with the general population. According to the German S3 guideline, bilateral risk-reducing mastectomy is a recognised option after comprehensive counselling. Intensified early detection is a further recognised strategy. The two pursue different aims: surgery reduces the incidence of disease, early detection finds tumours earlier. A survival benefit of surgery has not been demonstrated for *BRCA2*. The choice is a preference-based decision after counselling.

1. Instruction and question

The insurer requests a human genetics opinion on an application for cost approval for bilateral risk-reducing mastectomy with immediate reconstruction. It asks whether the genetic finding has been correctly classified, how high the risk of disease is and whether the procedure is professionally justifiable. Whether an increased risk of disease constitutes an insured event under the tariff is a legal question and not the subject of this opinion. The surgical indication in the individual case remains a matter for the treating breast centre.

2. Records

The following applies to this fictitious sample case: the 36-year-old insured woman is healthy. Her mother developed breast cancer at the age of 41, and a maternal aunt developed ovarian cancer at the age of 58. In a specialised centre [fictitious], a heterozygous *BRCA2* frameshift variant was detected first in the mother and subsequently in the insured woman and classified as pathogenic (class 5). The exact variant designation is not given in the fictitious files. The insured woman has been taking part in intensified early detection with annual MRI for two years. After two interdisciplinary counselling sessions she wishes to undergo surgery. A psycho-oncological assessment is available.

3. Assessment

Variant classification. Without the complete variant designation, the classification cannot be independently verified and is taken as an assumption of the sample case. Under the ACMG/AMP standard, a frameshift with a premature stop codon in *BRCA2*, where loss of function is the established disease mechanism, is very strong evidence of pathogenicity. Exceptions, for example at the extreme end of the gene, would have to be examined once the variant is known. The complete report with HGVS designation and reference transcript should be requested.

Risk of disease. In an international prospective cohort of carriers, recruited predominantly from family cancer clinics and followed for a median of five years, the cumulative breast cancer risk up to the age of 80 in *BRCA2* carriers was 69% (95% confidence interval 61 to 77%). The cumulative risk of ovarian cancer was 17% (11 to 25%) [1]. By comparison, about one in eight women in Germany develops breast cancer in the course of her life [2]. Cohort figures are not an individual prediction, and the risk may differ depending on family history and location of the variant [1].

Effect of surgery. In a multicentre study, bilateral prophylactic mastectomy reduced the breast cancer risk in *BRCA1* and *BRCA2* carriers by about 90% [3]. In a Dutch cohort, surgery was associated with lower mortality in *BRCA1* carriers. In *BRCA2* carriers, breast cancer-specific survival was similarly high after surgery and under surveillance, and no survival benefit could be demonstrated. The authors recommend gene-specific counselling [4].

Professional assessment. The S3 guideline Breast Cancer (S3-Leitlinie Mammakarzinom, version 5.1, June 2026, recommendation 3.37, grade of recommendation B, level of evidence 2) names prophylactic bilateral mastectomy as a risk-reducing operation for healthy carriers of pathogenic *BRCA1* or *BRCA2* variants. It reduces breast cancer incidence. According to the guideline, a reduction in breast cancer-specific or overall mortality is not sufficiently established. The decision therefore requires comprehensive information and multidisciplinary counselling that takes the alternatives into account [5]. As an alternative for *BRCA1* and *BRCA2*, the guideline recommends intensified early detection with MRI and ultrasound within the framework of knowledge-generating care (recommendation 3.35). According to the guideline, there is no direct evidence that intensified early detection reduces mortality, but it can detect tumours at early stages [5]. The consensus recommendations of the German Consortium for Hereditary Breast and Ovarian Cancer likewise state that, unlike for *BRCA1*, a survival benefit of mastectomy could not be shown for *BRCA2* [6]. The decision therefore depends substantially on the informed preference of the insured woman. The required counselling is documented here.

4. Answers to the questions

Question 1: Has the genetic finding been correctly classified?

> **Answer:** A pathogenic frameshift in *BRCA2* is professionally plausible as class 5. Without the complete variant designation this cannot be independently verified. The complete report should be submitted.

Question 2: How high is the risk of disease?

> **Answer:** According to prospective cohort data, the cumulative breast cancer risk up to the age of 80 is about 69%, compared with about one in eight women in the general population.

Question 3: Is the operation professionally justifiable?

> **Answer:** Yes. According to the S3 guideline, it is a recognised option for reducing the incidence of disease that requires comprehensive counselling. Continuing intensified early detection would also be justifiable. A survival benefit of surgery has not been demonstrated for *BRCA2*.

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