AnteBC Personalised Breast Cancer Prevention Plan

Name	**POTTER, LILY**		
Id	1234567890	**Sample Id**	CP000002
Age	42	**Sample material**	Buccal swab
Date of birth	13.02.1983	**Analysis method**	Illumina Global Screening Array-24
Ethnic descent	European	**Report Id**	176550-2024-07-17
Country	United Kingdom	**Time of result**	2025-02-07T17:26:04+0200

Based on the breast cancer polygenic risk score test results, Antegenes' Clinic recommends:

- Mammography screening every two years starting at the age of 42.
- Follow general guidelines to reduce the risk of breast cancer (see our recommendations).

For the patient - what should be done next?

In order to implement our clinical recommendations, you can contact a doctor that suits you (GP, family doctor, breast specialist, gynaecologist, medical geneticist, etc.).

Polygenic risk score assessment as an innovation in healthcare may not be yet in use in all medical practices, but doctors can use clinical recommendations and rationales provided in this report.

In addition to the polygenic component used by the AnteBC test, there are also other breast cancer risk factors to be considered.

We recommend further medical consultation if your biological first or second degree relative has had breast cancer.

Health behaviour

To reduce the risk of breast cancer, we recommend considering the following factors.

- A body mass index greater than 30 increases the risk of breast cancer by a factor of 1.5 to 2. Thus, it is recommended for adults to maintain a body mass index between 18.5 and 24.9 or at least below 30.
- Physical activity is risk-reducing. At least 30 minutes of moderate-to-vigorous intensity physical activity is recommended on most days, a total of 1.5 to 4 hours per week.
- Consuming just one alcoholic drink a day increases breast cancer risk by 5%. Regular alcohol consumption should be avoided to reduce the risk of breast cancer.
- Women who have never given birth and women who give birth to their first child at the age of 35 or older have a slightly higher risk of developing breast cancer.
- Smoking increases the risk of breast cancer.

Body awareness

We recommend you to be aware of your body, including the condition and possible changes in your breasts. If you notice any of the symptoms listed below, we recommend that you seek medical attention. These may indicate the development of breast cancer:

- Abnormal changes in breast shape, size or color;
- New lump or mass in breast tissue;
- Pain or discomfort in one breast;
- Changes in the surface of the breast skin (looking like an orange peel), skin retraction, "wrinkling" or ulcer;
- Change of shape or position of a nipple or retraction;
- Bleeding or flushing around the nipple, discharge from the nipple;
- Enlargement of the axillary lymph nodes.

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For the doctor and the medical team

The clinical recommendations accompanying the AnteBC test are based only on the patient's age and polygenic risk results and do not consider other possible risk factors. Therefore, taking into account other risk factors, it is possible to modify the current recommendations if necessary.

The results of the AnteBC test can be used in the CanRisk combined breast cancer risk assessment model by entering the z-score in the AnteBC test report and the alpha value of 0.437.

The UK National Institute for Health and Care Excellence (NICE) Clinical Guideline CG164 provides guidance for women with a family history of breast cancer, as well as recommendactions for women with elevated risk levels. Increased risk is defined as a 10-year breast cancer risk of over 3% between the ages of 40 and 50.

Based on the AnteBC test, the patient's corresponding polygenic risk of breast cancer between the ages 40 and 50 is 2.16%.

The AnteBC test provides information based solely on polygenic risk. The overall risk may differ when other risk factors are taken into account. The above recommendations are based on the interpretation of polygenic risk alone, which is not currently considered in NICE Guideline CG164.

AnteBC test does not analyse rare risk increasing mutations in single genes, e.g., *BRCA1*, *BRCA2*, *CHEK2*, *PALB2*, *ATM*, *TP53*, *CDH1*, *STK11*, etc. Therefore, we recommend testing of rare risk increasing mutations in single genes if the following criteria are met:

1. The patient has a history of breast, ovarian, fallopian tube or peritoneal cancer.
2. A biological relative has a mutation in a single gene predisposed to breast cancer (*BRCA1*, *BRCA2*, etc.).
3. A first- or second-degree biological relative has been diagnosed with breast cancer (under the age of 45 years), pancreatic cancer, ovarian cancer, metastatic prostate cancer; two or more cases of breast cancer in one person or a first/second-degree male biological relative has a history of breast cancer.
4. Biological relatives have had three or more tumors associated with hereditary cancer syndromes.
5. Patient is of Ashkenazi Jewish origin.

Rationale for Current Clinical Recommendations

The World Health Organization (WHO) recommends mammography screening for women between the ages of 50 and 69. Independent research has shown that high-quality mammography screening reduces the risk of breast cancer mortality by an average of 20% in this age group. But the individual risks of breast cancer in women are very different and this must be taken into account when conducting screening. The polygenic risk score is one of the strongest risk factors for breast cancer that must be considered in risk assessment.

Our recommendations are currently based on the following:

- In cases of elevated polygenic risk, we recommend that a woman starts mammographic screening at the same age as her individual risk reaches the same level as the average risk at the start of the current standard screening.
- If the polygenic risk level is average or low, we recommend starting screening at the age of the current standard screening.
- If the risk level exceeds twice the average risk, we recommend performing mammography every year.
- If the risk level exceeds three times the average risk, we recommend, in addition to mammography, the use of Magnetic Resonance Imaging (MRI).

In the UK, breast cancer screening is conducted through mammography every three years for women aged between 50 and 70, as part of the NHS Breast Screening Programme. The clinical recommendations based on the AnteBC test suggest that, in cases of elevated polygenic risk, screening should start earlier for women under age 50 and be conducted also more frequently for women over age 50.

UK National Institute for Health and Care Excellence (NICE) Clinical Guidelines CG164 provide guidance for women with a family history of breast cancer, as well as recommendation for women with elevated risk levels. If any of your immediate biological relatives have had breast cancer, we recommend that you see your primary care physician to determine your next course of action. The AnteBC polygenic risk score report is important information for planning further breast cancer prevention, also in case of a family history of breast cancer.

The NICE Guideline CG164 also provides recommendations on surveillance for high- and moderate-risk groups across different ages, including annual mammography from age 40 for increased-risk groups. Increased risk is defined as a 10-year breast cancer risk of over 3% between the ages of 40 and 50.

AnteBC explanatory information and post-test counselling

The AnteBC test includes a total of 2803 positions. By analyzing all risk positions in the patient's genome, we estimated that the patient's risk score for developing breast cancer is 0.88 SD units. The risk score is higher than in 80% and lower than in 19% of 42-year-old women. In other words, the patient's breast cancer risk score is placed in the 81st percentile of 42-year-old women.

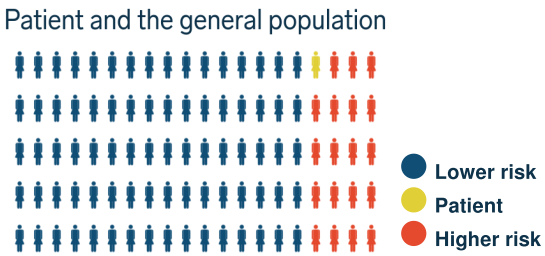

Figure 1: The patient's breast cancer polygenic risk position compared to other women of the same age.

AnteBC test considers the patient's nationality, gender, age, and the demographic background of breast cancer. The patient's risk of developing breast cancer within the next 10 years is 2.45% (2.47–2.42%). About 245 women out of 10,000 will develop the disease.

At the same time, the breast cancer risk of an average 42-year-old woman in United Kingdom is 1.66% (1.65–1.68%) meaning that the expected rate of developing the disease is 166 women out of 10 000.

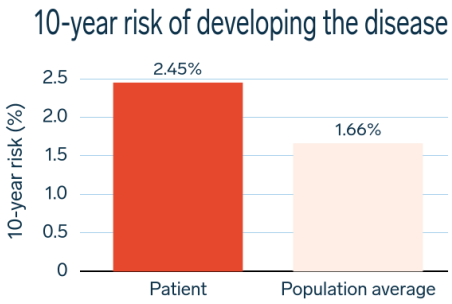

Figure 2: The patient's breast cancer polygenic risk over next 10 years compared to the population average

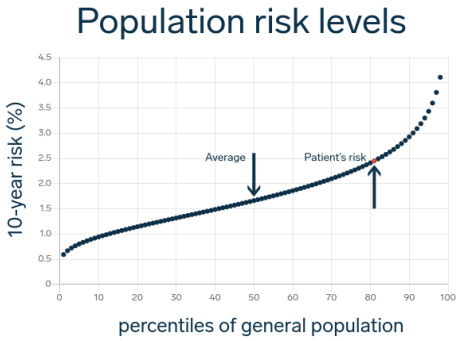

Figure 3: Location of the patient's 10-year polygenic risk on the population risk distribution curve

References

1. Padrik P, Puustusmaa M, Tõnisson N, Kolk B, Saar R, Padrik A, et al. Implementation of Risk-Stratified Breast Cancer Prevention With a Polygenic Risk Score Test in Clinical Practice. Breast Cancer (Auckl). 2023;17:11782234231205700.
2. Mavaddat N, Michailidou K, Dennis J, Lush M, Fachal L, Lee A, et al. Polygenic Risk Scores for Prediction of Breast Cancer and Breast Cancer Subtypes. Am J Hum Genet. 2019;104(1):21-34.

Contact

Antegenes Ltd.
info@antegenes.co.uk
Phone: 07351868794 (Mon-Fri 7.00-15.00)
www.preventcancer.co.uk

AnteBC test report

A polygenic risk score test for breast cancer

Name	**POTTER, LILY**		
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Genotyping: Eurofins Genomics Denmark A/S
Processing and interpretation of analysis results: Antegenes

Result		Explanation
Polygenic risk score (z-score)	0.88 SD	**Your polygenic risk score is higher than the population average.** The result shows that the breast cancer polygenic risk score is 0.88 standard deviation units higher than the population average.
Percentile	81	More than 80% of women have lower and more than 19% of women have higher polygenic risk score.
Absolute risk (10 years)	2.45% (2.47–2.42%)	Your personal risk of developing breast cancer in the next 10 years is **2.45%** (2.47–2.42%). The breast cancer risk of an average 42-year-old woman in United Kingdom is **1.66%** (1.65–1.68%).
Relative risk	1.47	This means that the risk of developing breast cancer in the next 10 years is 1.47 times higher than the 10-year genetic risk among 42-year-old women.

Time of evaluation of the result: 2025-02-07T17:26:04+0200
The results were confirmed: Dr. Neeme Tõnisson, D07099.
Healthcare professional speciality: E190 Laboratory medicine.
Name of test manufacturer: OÜ Antegenes.

AnteBC test general information

AnteBC is a genetic test that estimates a patient's risk of developing breast cancer. AnteBC test is based on the methodology of polygenic risk scores, which enables early detection and prevention of breast cancer.

In addition to the patient's genetics, age, gender and ancestry, risk calculations also take into account the United Kingdom population average morbidity and mortality rates. As the risk of cancer increases with age, each patient is compared with people of the same age when evaluating the test results.

Genetic variants used in the AnteBC test are distributed throughout the genome. The AnteBC test includes a total of 2803 genetic variants that can increase or decrease the risk of breast cancer.

The result of the AnteBC is given as units of standard deviation (SD) that characterizes the patient's genetic risk compared to the population average taking into account patient's ancestry (European, African, East Asian, South Asian or Mixed ancestry). For example, an outcome that exceeds 2.326 SD units corresponds to the highest level of risk in the 99th percentile. A result lower than -2.326 SD units corresponds to the lowest level of risk in the 1st percentile.

In case the patient's age exceeds the actual recommended starting age for screening or any other procedures, the report will state the patient's age for the start time.

AnteBC test limitations

- AnteBC cannot be used to diagnose breast cancer.
- The risks identified by the AnteBC test take into account the polygenic risk, but do not consider other risk factors (see section Health behavior).
- An elevated risk estimated by the AnteBC test does not mean that the patient will develop breast cancer during their lifetime. Also, a moderate or low-risk score does not mean that the patient will not develop breast cancer.
- AnteBC test is patient-specific, it does not give any information about the risk of developing a disease in the patient's family or close relatives, i.e. polygenic risk score-based disease risks may not be transmitted directly from parents to children.
- AnteBC test does not analyze rare risk increasing mutations in single genes, e.g., *BRCA1*, *BRCA2*, *CHEK2*, *PALB2*, *ATM*, *TP53*, *CDH1*, *STK11*, etc. Therefore, we recommend testing of rare risk increasing mutations in single genes if the following criteria are met:
    1. The patient has a history of breast, ovarian, fallopian tube or peritoneal cancer.
    2. A biological relative has a mutation in a single gene predisposed to breast cancer (*BRCA1*, *BRCA2*, etc.).
    3. A first- or second-degree biological relative has been diagnosed with breast cancer (under the age of 45 years), pancreatic cancer, ovarian cancer, metastatic prostate cancer; two or more cases of breast cancer in one person or a first/second-degree male biological relative has a history of breast cancer.
    4. Biological relatives have had three or more tumors associated with hereditary cancer syndromes.
    5. Patient is of Ashkenazi Jewish origin.
- The AnteBC test is based on up-to-date scientific data. However, the field of genetics is constantly evolving which may lead to changes in the risk assessments in the future as additional information becomes available. Therefore, also the clinical recommendations based on the test results may change.
- Different polygenic risk score models of the same trait may give different estimates to the individual's risks due to differences in the genetic variants included in the model and their weights.
- The result of this test should be applied in context with other relevant clinical data. In addition to the possible genetic predisposition, other risk factors also affect the risk of developing breast cancer.