AntePC test report A polygenic risk score test for prostate cancer

Name	JOHN, POTTER		
ld	12345678910	Sample Id	BC66545345
Age	43	Sample material	Buccal swab
Date of birth	13.02.1985	Analysis method	Illumina Global Screening Array-24
Ethnic descent European		Report Id	176554-2023-07-17
Country	United Kingdom	Time of result	09.04.2024

Genotyping: University of Tartu Core Facility of Genomics Processing and interpretation of analysis results: Antegenes

Result		Explanation
Polygenic risk score (z-score)	1.64 SD	Your polygenic risk score is higher than the population average. The result shows that the prostate cancer polygenic risk score is 1.64 standard deviation units higher than the population average.
Percentile	95	More than 94% of men have lower and more than 5% of men have higher polygenic risk score.
Absolute risk (10 years)	2.48% (2.73-2.23%)	Your personal risk of developing prostate cancer in the next 10 years is 2.48% (2.73–2.23%). The general population risk of prostate cancer among 43-year-old men in United Kingdom is 1.09% (1.04–1.14%).
Relative risk	2.27	This means that the risk of developing prostate cancer in the next 10 years is 2.27 times higher than the 10-year genetic risk among 43-year-old men.

Time of evaluation of the result: 09.04.2024 The results were confirmed: Dr. Neeme Tõnisson, D07099. Healthcare professional speciality: E190 Laboratory medicine. Name of test manufacturer: OÜ Antegenes.



 \heartsuit

AntePC test general information

AntePC is a genetic test that estimates a patient's risk of developing prostate cancer. AntePC test is based on the methodology of polygenic risk scores, which enables early detection and prevention of prostate 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 AntePC test are distributed throughout the genome. The AntePC test includes a total of 121 genetic variants that can increase or decrease the risk of prostate cancer.

The result of the AntePC 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.

AntePC test limitations

- AntePC cannot be used to diagnose prostate cancer.
- The risks identified by the AntePC test take into account the polygenic risk, but do not consider other risk factors (see section Health behavior).
- An elevated risk estimated by the AntePC test does not mean that the patient will develop prostate cancer during their lifetime. Also, a moderate or low-risk score does not mean that the patient will not develop prostate cancer.
- AntePC 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.
- AntePC test does not analyze rare risk increasing mutations in single genes, e.g., *BRCA1* and *BRCA2*. Therefore, we recommend testing of rare risk increasing mutations in single genes if the following criteria are met:
 - 1. A close (biological) relative has a mutation in single genes predisposed to breast and ovarian cancer (*BRCA1*, *BRCA2*, etc.).
 - 2. A first- or second-degree biological relative has been diagnosed with breast cancer below 45 years of age, male breast cancer, pancreatic cancer, ovarian cancer, metastatic prostate cancer, or two or more cases of breast cancer in one person.
 - 3. Biological relatives have had three or more tumors associated with hereditary cancer syndromes.
 - 4. Patient is of Ashkenazi Jewish origin.
- The AntePC 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 prostate cancer.

AntePC Test Clinical Recommendations

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

• Prostate cancer screening with two-year intervals starting at the age of 48. Prostate-specific antigen (PSA) testing and digital rectal palpation are recommended in prostate cancer screening.

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, urologist, andrologist, 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 AntePC test, there are also other prostate cancer risk factors to be considered.

We recommend further medical consultation if several of your biological first or second degree relatives have had prostate, breast or ovarian cancer.

For the doctor and the medical team

The clinical recommendations accompanying the AntePC 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.

AntePC test does not analyse rare risk increasing mutations in single genes, e.g., *BRCA1*, *BRCA2*, etc. Therefore, we recommend testing of rare risk increasing mutations in single genes if the following criteria are met:

- 1. A close (biological) relative has a mutation in single genes predisposed to breast and ovarian cancer (*BRCA1*, *BRCA2*, etc.).
- 2. A first- or second-degree biological relative has been diagnosed with breast cancer below 45 years of age, male breast cancer, pancreatic cancer, ovarian cancer, metastatic prostate cancer, or two or more cases of breast cancer in one person.
- 3. Biological relatives have had three or more tumors associated with hereditary cancer syndromes.
- 4. Patient is of Ashkenazi Jewish origin.

Health behaviour

• Do not smoke!

Rationale for Current Clinical Recommendations

Based on the polygenic risk score (PRS), it is possible to divide the patient's relative risk of developing prostate cancer into different levels compared to the average in the given age, while accurately assessing the risk of a particular percentile.

Low risk (<0.5)

Average risk (0.50-1.49)

High risk (>1.5-3.0)

Very high risk (>3.0)

The cut-off value of 1.5 is determined benchmarked to the prostate cancer risk conferred by positive family history. Positive family history is associated with a 1.5-fold increased risk for prostate cancer from multiple prospective studies.

Our recommendations combine polygenic risk score information and recommendations by the European Association of Urologists.

Body awareness

You should also see your doctor if you notice any of the following signs that point to a prostate disease (signs that indicate urinary obstruction or irritation):

- Symptoms pointing to urinary tract obstruction:
 - difficulty passing urine;
 - weak urine flow;
 - urinary flow interruption and dripping;
 - feeling that your bladder isn't empty;
- Symptoms pointing to urinary irritation:
 a strong persistent urge to urinate;
 - more frequent urge to urinate, especially at night;
- The prostate disease causes pain or discomfort in the following organs:
 - the area between the anus and scrotum (the perineum);
 - testicles;
 - penis;
 - lower abdomen, groin and lower back;
- Urination and ejaculation may also be painful

AntePC explanatory information and post-test counselling

The AntePC test includes a total of 121 positions. By analyzing all risk positions in the patient's genome, we estimated that the patient's risk score for developing prostate cancer is 1.64 SD units. The risk score is higher than in 94% and lower than in 5% of 43-year-old men. In other words, the patient's prostate cancer risk score is placed in the 95th percentile of 43-year-old men.

Patient and the general population

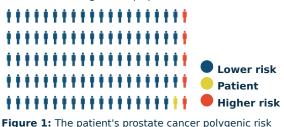


Figure 1: The patient's prostate cancer polygenic risk position compared to other men of the same age.

AntePC test considers the patient's nationality, gender, age, and the demographic background of prostate cancer. The patient's risk of developing prostate cancer within the next 10 years is 2.48% (2.73–2.23%). About 248 men out of 10,000 will develop the disease.

At the same time, the risk of prostate cancer among 43-year-old men in United Kingdom is 1.09% (1.04–1.14%) meaning that the expected rate of developing the disease is 109 men out of 10 000.

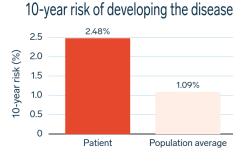


Figure 2: The patient's breast cancer polygenic risk over next 10 years compared to the population average

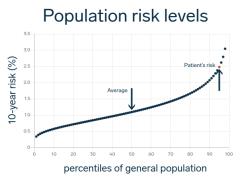


Figure 3: Location of the patient's 10-year polygenic risk on the population risk distribution curve

Contact

OÜ Antegenes (Licence L05386) Registry code: 14489312 <u>info@antegenes.com</u> Phone: +372 53 778 141 (Mon-Fri 9.00-17.00) <u>www.antegenes.com</u>