Polygenic Risk Score Tests for Common Cancers

Antegenes offers innovative genetic tests for **breast cancer** (AnteBC), **prostate cancer** (AntePC), **colorectal cancer** (AnteCRC), and **skin melanoma** (AnteMEL). **The tests assess an individual's genetic risk of developing these cancers using a polygenic risk score (PRS) technology.** Their aim is to reduce cancer morbidity and mortality.

Antegenes' tests are recommended:

- AnteBC test: for women between the ages of 30-75.
- AntePC test: for men between the ages of 40-70.
- AnteCRC test: for men and women between the ages of 40-75.
- AnteMEL test: for men and women between the ages of 18-70.

All tests are clinical tests registered as CE-marked medical devices (in vitro diagnostics, IVD) in the EUDAMED database, in the Estonian Medical Devices Database, and in the UK MHRA Registry (GMDN code: 59918). Antegenes' tests are used and are available for use in accordance with regulations within healthcare services across the all European Union, the United Kingdom, Norway, and Switzerland.

The test results provide information about the individual's polygenic risk level for specific cancer. This includes a cancer specific PRS value, the absolute risk for specific cancer in the next 10 years, and the relative risk in comparison to other individuals in the same age group and population on average.

Depending on the application, the test report may include individual clinical recommendations to reduce the risk of developing these specific cancers such as:

- What age the individual should start specific cancer screening and how
- Whether the individual should take additional measures to prevent cancer
- What possible changes and symptoms the individual should look out for concerning these cancers.

Altogether, Antegenes' tests provide polygenic risk stratifications for personalized recommendations and follow-up actions to prevent or detect specific cancer at an early stage when it is efficiently curable.

Tests' Development and Methodology

The polygenic risk scores and their risk differentiation estimations were validated using anonymous data from the Estonian Biobank and UK Biobank. Based on large-scale genetic data, various risk prediction models published in the international scientific literature were compared. The prediction accuracy of the best-performing models was evaluated on independent data and developed further for the test (1-4). The polygenic risk scores underlying the risk score tests (5-8) are tailored for practical use and independently validated (1-4, 9). After validation, the risk score tests use 2803 breast cancer-related SNPs, 121 prostate cancer-related SNPs, 91 colorectal cancer-related SNPs, and 28 melanoma-related SNPs to calculate personalized risk scores.
The tests are based on genome-wide association studies of patients and study participants of primarily European ancestry. However, the tests are adapted to other ethnicities based on the analyses of risk performance in the ethnically diverse UK Biobank data.

Limitations of Polygenic Risk Score Tests

- PRS tests cannot be used to diagnose breast, prostate, colorectal cancer, and skin melanoma.
- High risk does not necessarily mean that the patient will develop specific cancer during his/her lifetime.
- Moderate or lower risk does not necessarily mean that the patient will never develop specific cancer during his/her lifetime.
- PRS tests results are individual and patient specific. The tests do not assess the risk for the patient's family members or relatives. The inheritance pattern of PRS is complex and each person has to be tested separately.

- PRS tests do not analyse rare monogenic pathogenic variants in genes that significantly increase the risk of specific cancers.
- PRS tests are based on the most recent scientific data, which may be supplemented and/or changed in the future if additional information becomes available. The field of genetics is constantly evolving, which may lead to changes in risk assessments over time, changes in test selection, and clinical recommendations.
- Different polygenic risk scores predicting risks of the same trait may give different estimates of the individual's risks due to differences in the genetic variants included in these models and their weights.
- The results of PRS tests should be applied in combination with other relevant clinical data. In addition to genetic predisposition, other risk factors influence the risk of developing cancers.

Getting started with Antegenes' Tests

To perform the test, a DNA sample must be taken using a buccal swab or saliva kit. This is an easy and safe procedure. The buccal swab or saliva collection kit is convenient to use independently at home or at a medical facility. Detailed instructions are included in each kit. The sample is sent to the Antegenes laboratory via organized delivery.

Based on patient data, individual test reports are generated. Reports are available only for an individual or for his/her doctor if a test is ordered by a healthcare professional.

Genetic data is managed, stored, and protected safely within Antegenes' server according to GDPR and healthcare data regulations.

Antegenes' polygenic risk score tests can also be used in healthcare facilities only as CE-marked software as medical device if genotyping or sequencing is performed by an on-site laboratory.

Additional Information:

OÜ Antegenes
Address: Raatuse 21, 50603 Tartu, Estonia
E-mail: info@antegenes.com
Phone number: + 372 5377 8141
www.antegenes.com

References

1. Padrik P, Puustusmaa M, Tonisson 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. Tasa T, Puustusmaa M, Tõnisson N, Kolk B, Padrik P. Precision Prostate Cancer Screening with a Polygenic Risk Score. medRxiv. 2020:2020.08.23.20180570.
3. Tasa T, Puustusmaa M, Tõnisson N, Kolk B, Padrik P. Precision Colorectal Cancer Screening with Polygenic Risk Score. medRxiv. 2020:2020.08.19.20177931.
4. Tasa T, Puustusmaa M, Tõnisson N, Kolk B, Padrik P. Recommendations for Primary Prevention of Skin Melanoma. medRxiv. 2020:2020.08.25.20181610.
5. 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.
6. Schumacher FR, Al Olama AA, Berndt SI, Benlloch S, Ahmed M, Saunders EJ, et al. Association analyses of more than 140,000 men identify 63 new prostate cancer susceptibility loci. Nature genetics. 2018;50(7):928-36.
7. Huyghe JR, Bien SA, Harrison TA, Kang HM, Chen S, Schmit SL, et al. Discovery of common and rare genetic risk variants for colorectal cancer. Nature genetics. 2019;51(1):76-87.
8. Fritsche LG, Beesley LJ, VandeHaar P, Peng RB, Salvatore M, Zawistowski M, et al. Exploring various polygenic risk scores for skin cancer in the phenomes of the Michigan genomics initiative and the UK Biobank with a visual catalog: PRSWeb. PLoS Genet. 2019;15(6):e1008202.
9. Tasa T, Puustusmaa M, Tõnisson N, Kolk B, Padrik P. Precision Breast Cancer Screening with a Polygenic Risk Score. medRxiv. 2020:2020.08.17.20176263.