

AnteCRC test report

A polygenic risk score test for colorectal cancer

Name	POTTER, LILY	Sample Id	TS00150511
Id	12345678910	Sample material	Buccal swab
Age	43	Analysis method	Illumina Global Screening Array-24
Date of birth	13.02.1985	Report Id	176552-2023-07-17
Ethnic descent	European	Time of result	07.10.2023
Country	United Kingdom		

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

Result		Explanation
Polygenic risk score (z-score)	1.3 SD	Your polygenic risk score is higher than the population average. The result shows that the colorectal cancer polygenic risk score is 1.3 standard deviation units higher than the population average.
Percentile	91	More than 90% of women have lower and more than 9% of women have higher polygenic risk score.
Absolute risk (10 years)	0.34% (0.35-0.32%)	Your personal risk of developing colorectal cancer in the next 10 years is 0.34% (0.35-0.32%). The general population risk of colorectal cancer among 43-year-old women in United Kingdom is 0.20% (0.20-0.20%).
Relative risk	1.70	This means that the risk of developing colorectal cancer in the next 10 years is 1.70 times higher than the 10-year genetic risk among 43-year-old women.

Time of evaluation of the result: 07.10.2023
The results were confirmed: Dr. Neeme Tõnisson, D07099.
Healthcare professional speciality: E190 Laboratory medicine.
Name of test manufacturer: OÜ Antegenes.





AnteCRC test general information

AnteCRC is a genetic test that estimates a patient's risk of developing colorectal cancer. AnteCRC test is based on the methodology of polygenic risk scores, which enables early detection and prevention of colorectal 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 AnteCRC test are distributed throughout the genome. The AnteCRC test includes a total of 91 genetic variants that can increase or decrease the risk of colorectal cancer.

The result of the AnteCRC 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.

AnteCRC test limitations

- AnteCRC cannot be used to diagnose colorectal cancer.
- The risks identified by the AnteCRC test take into account the polygenic risk, but do not consider other risk factors (see section Health behavior).
- An elevated risk estimated by the AnteCRC test does not mean that the patient will develop colorectal cancer during their lifetime. Also, a moderate or low-risk score does not mean that the patient will not develop colorectal cancer.
- AnteCRC 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.
- AnteCRC test does not analyze rare risk increasing mutations in single genes, e.g., *APC*, *KRAS*, *TP53*, *MLH1*, *MSH2*, *MSH6*, *PMS2*, *STK11*, *MUTYH*, 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 genes heavily predisposing to colorectal cancer (*APC*, *KRAS*, *TP53*, *MLH1*, *MSH2*, *MSH6*, *PMS2*, *STK11*, *MUTYH*);
 2. Several first-, second- or third-degree biological relatives have been diagnosed with colorectal cancer;
 3. A first- or second-degree biological relative has been diagnosed with three or more cancers.
- The AnteCRC 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 colorectal cancer.

AnteCRC Test Clinical Recommendations

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

- Selection A:
 - Colonoscopy at ages 45, 55, 65 and 75
 - Annual fecal immunochemical test starting from the age 85
- Selection B:
 - Annual fecal immunochemical test starting from the age 45

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, gastroenterologist, colorectal surgeon, 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 AnteCRC test, there are also other colorectal cancer risk factors to be considered.

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

For the doctor and the medical team

The clinical recommendations accompanying the AnteCRC 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.

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Health behaviour and other diseases

The following factors increase the risk of colorectal cancer:

- A diet low in fiber and high in saturated animal fat;
- Overweight and lack of exercise;
- Smoking and drinking alcohol;
- Inflammatory bowel disease (ulcerative colitis, Crohn's disease);
- History of polyps in the gastrointestinal tract;
- Previous bowel cancer;
- Close relatives (parents, siblings) have had colorectal cancer.

To reduce the risk of colorectal cancer, we recommend:

- Consume more high-fiber foods and reduce or avoid foods containing animal fats and red meat;
- Avoid being overweight and ensure adequate physical activity (minimum 150 minutes per week);
- Avoid alcohol and smoking.

Rationale for Current Clinical Recommendations

We recommend starting colorectal cancer screening at age 50 in case of average or low risk level. We recommend colonoscopy as the preferred method for screening. Colonoscopy intervals are proposed according to individual polygenic risk score levels. As an alternative to colonoscopy, we recommend annual fecal immunochemical testing, with individualized starting from the age at which the patient attains the 10-year risk of the average 50-year-old person. The choice of screening method also depends on specific opportunities for service and personal preferences.

Body awareness

We recommend you to be aware of possible changes and the condition of your body (including gastrointestinal tract).

If you notice any of the symptoms listed below, we recommend that you seek medical attention. These may indicate the development of colorectal cancer:

- A change in the bowel movements i.e., diarrhea or constipation for a prolonged period, or alternation of the two;
- Feeling that the colon is not completely emptied when defecating;
- Blood in or on the stool;
- Persistent stomach or rectal pain;
- Unexplained weight loss, fatigue, weakness.

People who have long-term (more than 1 month) unexplained digestive complaints should consult their family doctor who will decide on further examination and referral to a specialist.

AnteCRC explanatory information and post-test counselling

The AnteCRC test includes a total of 91 positions. By analyzing all risk positions in the patient's genome, we estimated that the patient's risk score for developing colorectal cancer is 1.3 SD units. The risk score is higher than in 90% and lower than in 9% of 43-year-old women. In other words, the patient's colorectal cancer risk score is placed in the 91st percentile of 43-year-old women.

Patient and the general population



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

AnteCRC test considers the patient's nationality, gender, age, and the demographic background of colorectal cancer. The patient's risk of developing colorectal cancer within the next 10 years is 0.34% (0.35–0.32%). About 34 women out of 10,000 will develop the disease.

At the same time, the risk of colorectal cancer among 43-year-old women in United Kingdom is 0.20% (0.20–0.20%) meaning that the expected rate of developing the disease is 20 women out of 10 000.

10-year risk of developing the disease

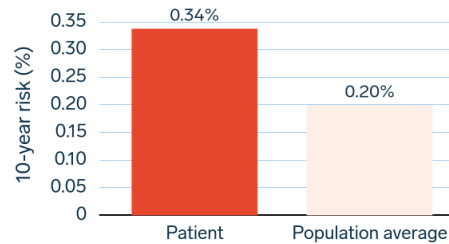


Figure 2: The patient's breast cancer polygenic risk over next 10 years compared to the population average

Population risk levels

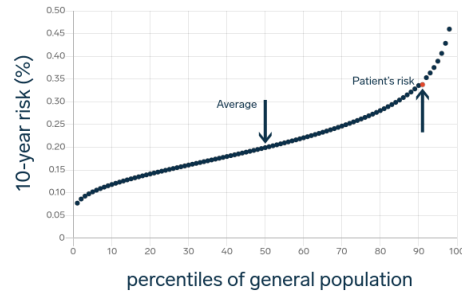


Figure 3: Location of the patient's 10-year polygenic risk on the population risk distribution curve

Contact

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