Eiira

Report on Hereditary Cancer Risk and Related Measures

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Eiira

Personal data

Name: X
Sex: Kvinna
Birthday: YYYY.MM.DD

Customer ID: X
Test kit ID: X
Report date: YYYY.MM.DD

Ordered product: **Eiira Premium (or classic)**
Genetic test for hereditary cancer based on Whole Genome Sequence (WGS)



Table of content

Executive summary

Purpose of the report

The purpose of our hereditary genetic report is to outline the genetic and familial predispositions to cancer. By analysing genetic variation in your DNA, alongside your family history of cancer, we aim to provide a comprehensive view of your hereditary risks to ten types of cancers. In the case of increased risk, the report will also suggest ways to manage and reduce that risk.

Findings

No pathogenic variants: The analysis did not identify any pathogenic variants (also known as mutations) in the 50 genes that were analysed.

General population risk: Based on the genetic test result and your family history of cancer, your risk of cancer is similar to that of the general population.

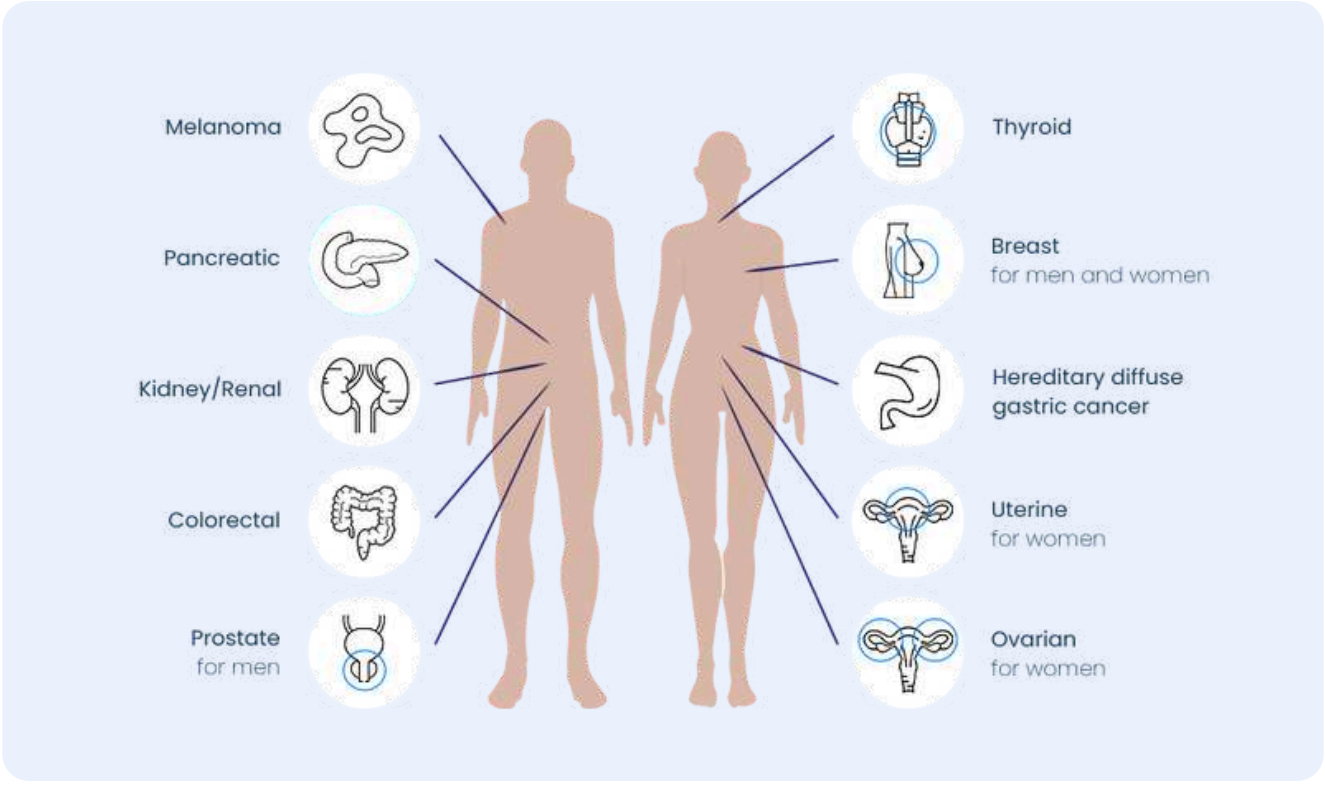
Note

This genetic analysis fully captures all genetic variations in your genome (i.e. all the DNA in a single cell). In the current analysis, we have looked at a subset of your genome, more specifically those genes that are associated with hereditary cancer. Therefore, this analysis does not exclude that you have a pathogenic variant in another place in your genome. However, since your genome has been fully sequenced, it enables updates on genetic findings, as well as new offerings, without a retest.

About the report

Assessment scope

For this report, we have assessed your hereditary risk of developing the cancer types illustrated in the figure below. These cancer types are known to have a hereditary component, which is linked to certain genes (see Table 1). This does not exclude that other cancer types are hereditary. However, to date, there are not any specific genes that have been associated with an increased risk of these other cancer types.



About the report

For this purpose, we have analysed 50 genes in your DNA for the absence or presence of pathogenic variants associated with an increased cancer risk. These genes were selected based on their known association with certain cancer types or cancer syndromes. The table below illustrates ten cancer types and their associated genes (i.e. genes where we know that individuals have an increased risk of developing cancer if they have a pathogenic variant).

Table 1

Cancer type	Genes associated
Breast	BRCA1, BRCA2, PALB2, TP53, PTEN, CDH1, STK11, NF1, ATM, CHEK2, BARD1, RAD51C, RAD51D
Ovarian	BRCA1, BRCA2, PALB2, RAD51C, RAD51D, BRIP1, MLH1, MSH2, EPCAM, MSH6, PMS2
Colon	MLH1, MSH2, MSH6, PMS2, EPCAM, APC, MUTYH, STK11, SMAD4, BMPR1A, PTCH, PTEN, NTHL1, POLD1, POLE, MSH3, TP53
Prostate	BRCA2, HOXB13, BRCA1, MLH1, MSH2, MSH6, EPCAM, PMS2, ATM, CHEK2, PALB2, TP53
Melanoma	CDKN2A, BAP1, CDK4, POT1, TERT, MITF1, MC1R, ASIP, TYR, TYRP1, TP53
Kidney/Renal	VHL, FLCN, FH, MET, PTEN, SDHB, BAP1, SDHA, SDHC, SDHD
Thyroid	RET, APC, PTEN, DICER1, TP53
Uterine	MLH1, MSH2, MSH6, PMS2, PTEN
Pancreatic	BRCA1, BRCA2, ATM, PALB2, MLH1, MSH2, EPCAM, MSH6, PMS2, STK11, CDKN2A
Hereditary diffuse gastric cancer	CDH1, CTNNA1

Germline (i.e. hereditary)

The genetic analysis only examines germline variation, which are the DNA variants that you were born with, specifically those that have their origin in your parents' reproductive cells (sperm and egg cells). These variants are thus inherited from a parent and can be passed on to the next generation. In some cases, a germline variant can occur in an early embryo (de Novo variant). De Novo variants can also give an increased risk of cancer but are not inherited from a parent (but can be passed on to the next generation).

The report doesn't consider somatic variants, which are spontaneous DNA changes that occur in your cells during life.

About the report

Hereditary risk and risk assessment

What is “risk”?

This report only covers **hereditary cancer risks**.

Risk is the likelihood of developing cancer and is based on population studies. It is important to understand the following:

- Risk is not the same as having a cancer diagnosis.
- Having a high risk does not mean you will definitely develop cancer. But you are more likely to develop cancer when compared to the general population.
- Conversely, even those with low risk may still develop cancer (at least one in three in the general population in Sweden will develop cancer during their life).
- An individual's perceived risk of cancer can differ from the actual risk of cancer. Individuals with a family history of cancer often overestimate their risk.

While it cannot predict the future, this profile aims to:

- Give you a better understanding of your risk of cancer.
- Inform you about risk management measures to prevent or detect cancer early.
- Help you discuss with your doctors about what to do next.

About the report

How does the risk assessment work?

A risk assessment is typically based on the result of the genetic test (i.e. absence or presence of a pathogenic variant) and your family history of cancer. In cases of familial risk for breast and ovarian cancers, we also use your personal health profile information in risk computation.

No pathogenic variant doesn't mean no cancer risk. While some genetic risks stem from one gene variant, known as monogenic disorders, others arise from interactions among multiple genes, known as polygenic or complex disorders. Environmental factors also influence cancer risks. Cancers like colorectal, prostate, breast, and pancreatic are particularly influenced by these polygenic elements. A genetic test alone isn't comprehensive; we incorporate family history to improve the risk assessment.

Carrying a pathogenic variant doesn't guarantee a uniform cancer risk for everyone. The estimated risk from a specific gene is based on studies of groups with that variant. Thus, an individual's risk could be higher or lower than the general estimation for that gene. By considering family history, we can provide a more accurate individual risk assessment.

From a clinical perspective, we determine if someone has a significantly increased cancer risk using **Swedish national guidelines**. These guidelines detail who qualifies for preventive actions or specialised screenings. An individual with only a moderate risk increase might just be recommended standard screenings, like mammography for women starting at age 40.

Keep in mind that various factors influence cancer risk. Our assessment focuses solely on genetic factors, so the risk outlined in this report is an estimate, not an exact measure of your actual risk.

Information provided by you

The information you submitted before YYYY.MM.DD has been used in this report's analysis.

Information about you:

- You have no personal history of cancer.
- You had a benign endometrial polyp (non-cancerous) removed at the age of 30.
- You have Swedish ethnicity.

Family tree:

List of relatives with cancer diagnosis:

- Paternal grandfather: colorectal cancer diagnosed at the age of 75.
- Mother: breast cancer diagnosed at the age of 80.

Your results

What did your genetic test show?

We have analysed 50 genes and their pathogenic variants based on your genome data resulted from Whole Genome Sequencing (WGS). Below is the finding.

No pathogenic variants were identified in the analysed genes.

What does this mean?

The genetic analysis did not identify any pathogenic variants in the 50 genes included. Thus, you do not carry a pathogenic variant in any of the analysed genes, and as a result, you do not have an increased risk of cancer based on the genetic result.

Your results

What are your overall risks?

Our analysis has found that:

Your lifetime **hereditary risk of the ten cancer types** appears to be similar to that of the general population.

What does this mean?

- Your genetic result, in combination with the assessment of your family history of cancer, did not identify an increased hereditary risk of cancer.
- This means that your cancer risk is similar to that of the general population. Note that at least one in three in the general population will develop cancer during their lifetime; thus, your risk is not zero.

Note

Your familial risk assessment may change if you can provide more information.

Information about the general population

For your reference, we provide you below the cancer risks, monitoring/screening and prevention information about the general population.

The average cancer risks for women:

To help you understand the below table, here is an example: **Breast, 9.4%** and **<80**, it signifies that among 1000 women, 94 are likely to develop breast cancer before they reach 80 years of age.

Cancer type	< 40 years	< 50 years	< 60 years	< 70 years	< 80 years
Breast	0.43%	1.9%	4.2%	7.5%	9.4%
Colorectal	0.05%	0.16%	0.44%	1.2%	1.9%
Ovarian	0.07%	0.17%	0.42%	0.81%	0.95%
Uterine	0.01%	0.02%	0.06%	0.12%	0.16%
Melanoma of skin	0.29%	0.63%	1%	1.6%	2.2%
Pancreatic	0.01%	0.63%	0.14%	0.44%	0.68%

Sources: Nordcan

The risk management option:

The following options are recommended by national guidelines in Sweden.

1) Screening and monitoring

While screening does not prevent cancer, early detection significantly increases the chances of recovery and survival. In Sweden, the following screening options are automatically offered to women:

- **Breast cancer:** mammography is offered to all women aged 40 - 74 years, at least every two years.
- **Cervical cancer:** cell sampling every five years for women aged 23 - 49 years and every seven years for women aged 50 - 70 years.
- **Colon and rectal cancer:** within a few years, everyone aged 60 - 74 years will be offered screening for this type of cancer every two years.

Source: Cancerfonden (https://www.cancerfonden.se)

Information about the general population

2) Prevention and lifestyle recommendations

According to Cancerfonden, **23.1 % of all cancers** are caused by **preventable factors**.

While there are no guaranteed ways to avoid cancer completely, you have the power to make a positive impact. It may sound cliche, but participating in screening programs and being mindful of your physical activity, diet and lifestyle can play an important role.

Every lifestyle change you make to reduce the risk helps!

Source: Cancerfonden (https://www.cancerfonden.se)

Changes that help to reduce the risk

Avoid smoking

Maintain healthy weight

Reduce or avoid
alcohol consumption

Stay physically active

Try to eat no more than 500g
of cooked red meat per week
and avoid smoked meats

Breastfeeding
(if you have this option) can
help reduce breast cancer risk

Source: RCC (https://cancercentrum.se)

Disclaimers

Eiira is not responsible for any errors made when collecting the saliva sample, during transportation of the saliva sample or other errors made prior to receipt at Eiira's facility.

Diagnostic errors, although rare, may occur due to saliva not being collected according to the instructions, DNA contamination, or other laboratory operational errors. This may consequently limit and/or affect the sensitivity, specificity, and/or accuracy of the Eiira test results. In order to prevent this as much as possible, the quality of the saliva and extracted DNA is monitored during the process.

Classifications of genetic variants are made using an interpretation software that is accredited according to ISO 13485. Note that the classification is based on evidence available at the time of reporting and may, therefore, change as new evidence becomes available.

In the absence of a pathogenic variant, standard risk models, as described in Swedish national guidelines, will be used when appropriate to assess the risk of hereditary cancer due to a family history of cancer. Note that Swedish national guidelines are updated regularly as new evidence becomes available, and thus, this assessment may become inaccurate in a few year's time.

Risk estimation may be inaccurate if a personal or family history is not provided or is not accurate.

It should be noted that the genetic analysis and risk assessments performed via Eiira do not replace a traditional hereditary investigation performed by Swedish health care. Eiira should be regarded as a complementary test and not a substitute for a hereditary assessment.

Test method

Eiira uses Next Generation Sequencing (NGS) to analyse your DNA. First, genomic DNA was extracted from buccal epithelial cells and white blood cells in the saliva provided by the customer. Second, the specific regions of interest (i.e. all coding parts of your genome) were amplified and then sequenced on an Illumina NovaSeq 6000 instrument. Third, The sequencing reads were then mapped to the reference genome, after which different and precise bioinformatic tools are used to identify genetic variants. This was done by using the Illumina DRAGEN platform. Lastly, genetic variants from a selected number of genes (see table below) were interpreted by using an ISO 13485 accredited interpretation software. Results are reported as positive if a pathogenic variant is detected.

Gene table

APC, ASIP, ATM, BAP1, BARD1, BMPR1A, BRCA1, BRCA2, BRIP1, CDH1, CDK4, CDKN2A, CHEK2, CTNNA1, DICER1, EPCAM, FH, FLCN, HOXB13, MC1R, MET, MITF1, MLH1, MSH2, MSH6, MUTYH, NF1, PALB2, PMS2, POT1, PTCH, PTEN, RAD51C, RAD51D, RET, SDHB, SMAD4, STK11, TERT, TP53, TYR, TYRP1, VHL, NTHL1, POLD1, POLE, MSH3, SDHA, SDHC, SDHD