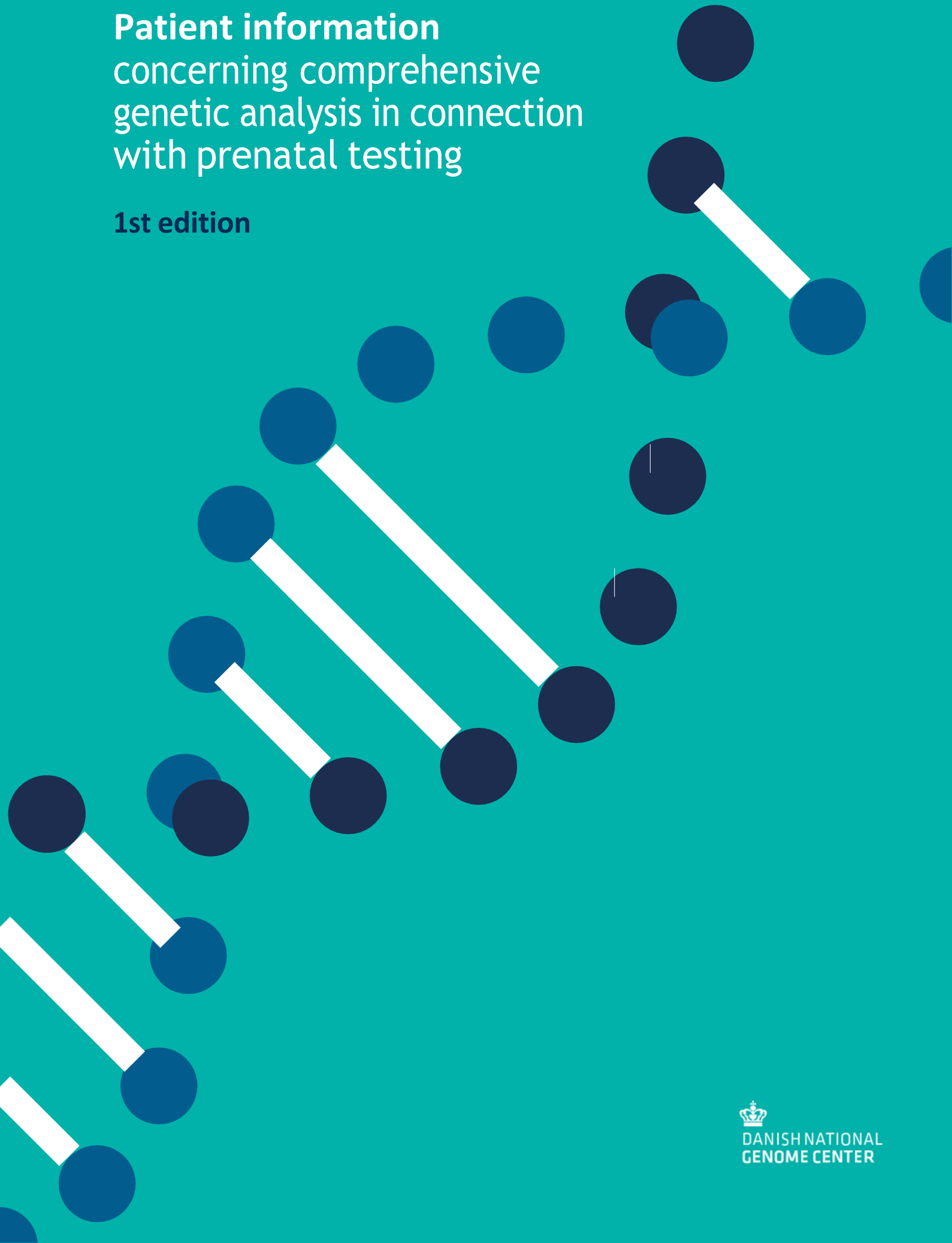
Patient information concerning comprehensive genetic analysis in connection with prenatal testing

1st edition



DANISH NATIONAL
GENOME CENTER

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1st edition

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Patient information regarding comprehensive genetic analysis in connection with prenatal testing

For pregnancies with an increased risk of chromosomal abnormalities in the fetus, genetic testing of the fetus is offered. It is your choice whether you want to have this treatment, which involves comprehensive genetic analysis. If you do, you must give written consent and at the same time make some choices regarding the feedback you receive.

Below, you will read information about genes and genetic changes, what is going to happen and then information about some of the choices you need to make in connection with giving informed consent for treatment that involves comprehensive genetic analysis (consent form). You will be given the opportunity to ask questions. You may also find detailed information on the Danish National Genome Center's website: www.ngc.dk/patient.

What are genes?

All cells in the body contain genetic material. The genetic material is also called DNA. The DNA contains the code for the structure of our body, our physical appearance and the functioning of our body. A gene is a piece of our DNA. Each cell contains approximately 20,000 genes. All genes have specific functions, but there are many of these functions that we still do not know. Genes most often exist in pairs - one gene from each parent. There are genetic changes (mutations/variants) in the genes of all people, and sometimes these changes lead to disease.

A disease with genetic cause can occur if one or more genes do not function properly. This may be because part of the gene is missing or the information in the gene has changed. A genetic change that causes disease may also occur if areas of the genetic material with many genes are either missing or present in too many copies. A genetic change can either be new in a fetus or be inherited from one or both parents.

In connection with pregnancy, the identification of a genetic change in the fetus and the physician's knowledge of it may form the basis of the advice given to you.

The overall purposes of prenatal testing are:

- To prepare parents for a child who may have special needs.
- To prepare the healthcare professionals for a child who may have special needs immediately after delivery.
- To give parents the opportunity to request permission to terminate the pregnancy in the event of a serious illness of their future child.

What is a comprehensive genetic analysis?

A comprehensive genetic analysis involves the examination of many genes at once (gene panel), all genes at once (exome or whole genome sequencing), or examining how many copies of genes there are (microarray).

How is the test carried out?

A sample (blood or tissue sample) from you is required. From this sample, DNA from the fetus is extracted. In some cases, we will also need to examine your own DNA and that of the father of the fetus (blood sample) as in some cases a better basis for examining the fetus can be obtained. The DNA is examined, and after the analysis the physician who ordered the test receives the result and contacts you.

What results may you receive?

There are several possible outcomes of comprehensive genetic analysis in connection with prenatal testing:

A. Normal
B. One or more gene changes are identified, which confirms a possible prior suspicion of chromosomal abnormalities in the fetus.

More rarely, the following may be identified:

C. One or more genetic changes the implication of which cannot be assessed with certainty. It is thus unclear whether the genetic change confirms a possible prior suspicion of a chromosomal abnormality in the fetus.
D. A so-called incidental finding, i.e. genetic changes that are found to increase the risk of diseases, which are not related to the possible suspicion of chromosomal abnormality for which your fetus is being examined. Below, you can read more about important health-related incidental findings and about the option to refuse feedback on any incidental findings.

You will be offered the opportunity to ask questions before making a decision.

Your choices

You decide for yourself whether you want to receive treatment in the healthcare system. No treatment may be initiated or continued without your informed consent. This also applies to treatment that involves comprehensive genetic analysis of your fetus, and in this connection you must also make some choices regarding the feedback on important health-related incidental findings that you may then receive. You can therefore ask to have the test stopped by contacting your treating physician.

You will be given time to think before making any decisions on this matter. If you do not want prenatal testing that involves a comprehensive genetic analysis of your fetus, your physician will inform you of any other examination and treatment options and the possible consequences of not having a comprehensive genetic analysis.

Important health-related incidental findings

When examining many or all genes, there is a possibility that genetic changes are detected that are assessed to increase the risk of disease, but are unrelated to the suspicion of chromosomal abnormalities which was the reason for the examination. This is called incidental findings. If, for example, you examine a fetus after detection of a malformation, a gene search may in rare cases reveal a gene variant that is assessed to involve a high risk of a completely different and possibly serious illness, including illnesses that occur later in life, such as breast cancer.

When you sign the consent form, you must decide whether you want to be informed of any important health-related incidental findings in your fetus and, if so, what type of incidental findings you want to be informed of. These will only be findings that the physician deems to have significant health implications. Some people only prefer feedback if the condition can subsequently be prevented or treated. Others prefer feedback on important health-related incidental findings regardless of whether they can be prevented or treated. Others still prefer not to receive feedback at all on important health-related incidental findings. However, you should be aware that in very rare cases, there may be incidental findings with such significant health implications for you and your family that your physician may be under an obligation to inform you even if you have chosen not to receive information about important health-related incidental findings.

The implication of the test for the father of the fetus and other close relatives

A finding of hereditary disease in the fetus may in some cases have consequences for you, the child's father or others in the family who may have inherited the same genetic change from previous generations. In that case, you may be offered a referral for genetic counselling.

New knowledge

In the future, our knowledge of genes and gene changes as well as their implication will increase. This means that there may be new knowledge which may be significant for the disease or any malformation for which your fetus is being examined. However, you should know that a yes to being contacted about new knowledge does not mean that the DNA of your fetus is re-examined at regular intervals. See also appendix 2 on your right to decide in relation to research.

Your right to decide over your genetic data

You have a statutory right to decide over the genetic data derived from the analysis and stored with the Danish National Genome Center, which is mentioned at the bottom of the consent form. If you do not want the researchers to include the genetic data from your fetus in health research, you must register with the National Database of Non-Consent to the Use of Tissue Samples for Scientific Purposes (Vævsanvendelsesregister). Read more about your right to decide in relation to research in appendix 2.

Storage of genetic data and data security

The genetic data from your fetus are stored in the Danish National Genome Center under your civil registration number. Data are stored and used under the highest level of security. You can read more about data security and the Danish National Genome Center at www.ngc.dk.

The Danish National Genome Center is an institution under the Danish Ministry of Health and is located at Ørestads Boulevard 5, 2300 Copenhagen S. The Danish National Genome Center may be contacted by email: kontakt@ngc.dk, or by telephone: 24 97 17 65.

See also appendix 1 for information on storing your genetic data and data security.

Contact information

If you have questions or want to change your consent, you are very welcome to contact your place of treatment.

DANISH NATIONAL
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Appendix 1: Storing your data with the Danish National Genome Center

in connection with
comprehensive genetic analyses

1st edition

DANISH NATIONAL
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Colophon

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Data from comprehensive genetic analyses is stored with the Danish National Genome Center

What is the Danish National Genome Center?

The Danish National Genome Center is an agency under the Ministry of Health. If you have a comprehensive genetic analysis in the healthcare system, your data will be stored with the Danish National Genome Center.

At the Danish National Genome Center, we work to help physicians and researchers develop tailored treatment, also called precision medicine, through knowledge of the patients' genes and other knowledge. Precision medicine comprises diagnostics, treatment and prevention that are tailored to the individual patient to a much greater extent. The center is responsible for developing a national infrastructure providing physicians and researchers throughout Denmark access to advanced whole genome sequencing (comprehensive genetic analyses) and to analysis of large data sets for the purpose of making it better for current and future patients.

Your genetic data and civil registration number are stored separately in the national supercomputer system. Your data are well protected with the Danish National Genome Center. Protecting data about you and other patients is a top priority for the Danish National Genome Center, and we have developed a strict security model.

You can read more about data security and the Danish National Genome Center at www.ngc.dk.

Data Protection Officer

The Danish Ministry of Health has a joint data protection officer who is charged with providing advice on and monitoring the protection of personal data at, for example, the Danish National Genome Center. You can contact our data protection officer by email: databeskyttelse@sum.dk.

Which types of data do we receive about you?

The Danish National Genome Center receives health data about you from the regions. We will therefore inform you how we store and handle your data at the Danish National Genome Center.

Which types of data do we receive about you?

We receive your

- genetic data
- health data
- meta data
- Civil registration number

What do your genetic data consist of?

Your genetic data consist of data generated from your genetic material, or data which contains information about your genes and/or genetic variants in relation to other people. The data are compared against a human reference genome to map your genome and determine the variants in your genome in relation to the reference genome.

Data about your genetic variants are stored in a variant database. The data also consist of your choices regarding incidental findings and whether you may be contacted if we gain new knowledge about your genetic test. We do not carry out a new interpretation of your data.

What do your health data consist of?

When we receive your genetic data and they are transferred to the Danish National Genome Center, we also receive health data about your suspected diagnosis. For example, we use your health data to ensure knowledge of the characteristics of your genetic data, that data are used correctly and to ensure that data can be found (retrieved).

What does metadata consist of?

When your genetic and health data are transferred to the Danish National Genome Center, we also receive so-called metadata. Metadata are a multitude of practical/technical data such as data about the department in the healthcare system from which we receive your genetic data. Metadata also consist of the date of your sampling as well as the manufacturer and model of the machine used for your analysis. For example, we use metadata to ensure knowledge of the characteristics of the transferred data, that data are used correctly and to ensure that data can be found (retrieved).

What do we use your civil registration number for and why?

We use your civil registration number to be able to identify your genetic data, if necessary. We use your civil registration number in a so-called pseudonymised form. This means that we use some form of encryption to translate your identifiable civil registration number into a unique, artificial identifier. In this way, we remove the "personal" aspect of your civil registration number.

What is a reference genome?

The reference genome acts as a reference book. When physicians or researchers have to find out whether a disease is caused by a specific gene variant in a patient, they look up the reference genome to see if the gene variant is normal among an average of healthy Danes, or whether it stands out.

How do we store and handle your data?

How long do we store your data?

As part of your patient treatment, we store your data for 30 years as a main rule. We will then erase your data.

What is the purpose of processing your data?

We only process your data if it is necessary for the purpose of

- prevention of disease
- medical diagnosis
- nursing care
- patient treatment
- management of medical and health services

We may also process your data if the processing is solely for the purpose of performing statistical or scientific studies of significant importance for society, and if the processing is necessary for the conduct of the studies.

The Danish National Genome Center is subject to a statutory purpose limitation. This means that it is stated in the Danish Health Act that we may only use your data for the purposes and within the framework described above.

What does it mean that your data may be processed for the purpose of patient treatment?

When your data are processed for the purpose of patient treatment, it means that the data can also be processed for purposes that are directly related to the patient treatment. This could be, for example, quality assurance, method development, training of healthcare professionals at the place of treatment and similar routine functions that are directly related to and connected with the treatment.

In some cases, your data may be used to treat patients other than you, and your data may be passed on to healthcare professionals for that purpose.

Genetic diagnostics

Genetic data about an examined person may also show an increased risk of disease in close relatives if they have the same genetic variant. In some cases, there is a 50% probability that first-degree relatives have the same predisposition for the disease as the person examined. You should therefore be aware that your data with the Danish National Genome Center may indirectly contain health data about close relatives.

How do we store and handle your data?

What does it mean that your information must be processed in order to perform statistical or scientific studies?

Processing of data for the purpose of conducting statistical or scientific studies of significant importance for society means that your data may be used for research. However, this presupposes that your data are necessary for the research, and that the research has been approved by a health research ethics committee (videnskabsetisk komité). The research contributes to knowledge in the healthcare system on how genes can help ensure better and more accurate treatment of patients.

You can read more about general rules related to research in genomes on the website of the National Committee on Health Research Ethics ("National Videnskabsetisk Komité") www.en.nvk.dk

You can read more about research projects that use data from the Danish National Genome Center on our website www.ngc.dk/forskning

The National Database of Non-Consent to the Use of Tissue Samples for Scientific Purposes (Vævsanvendelsesregister)

If you do not want your data to be used for research, you must register with the National Database of Non-Consent to the Use of Tissue Samples for Scientific Purposes (Vævsanvendelsesregister). You contact the National Database of Non-Consent to the Use of Tissue Samples for Scientific Purposes (Vævsanvendelsesregister) by sending a letter to the Danish Health Data Authority or via www.borger.dk.

You will find instructions on how to register in the National Database of Non-Consent to the Use of Tissue Samples for Scientific Purposes (Vævsanvendelsesregister) on our website www.ngc.dk/blanketter-og-vejledninger

Who do we share your data with?

Healthcare professionals

We share genetic data with healthcare professionals as part of your patient treatment.

Researchers

If you have not registered with the National Database of Non-Consent to the Use of Tissue Samples for Scientific Purposes (Vævsanvendelsesregister), we may also pass on your data for the use of research into precision medicine.

Boards of appeal, the legal system and the Danish Patient Safety Authority

If your data are to be used in a complaint case, we share your data for the purpose of processing the complaint and compensation case under the Danish Act on the Right to Complain and Receive Compensation within the Health Service.
We share your data with the Danish Patient Safety Authority if your data are to be used for the Agency's handling of supervisory tasks under the Authorization Act or the Danish Health Act.

A judge may in special cases decide that your data may be passed on to the police, but only if this takes place as part of an investigation of terrorism and terrorist-like acts.

Who do we work with?

The Danish National Genome Center has a close collaboration with the Technical University of Denmark (DTU) and Rook IT via Peak Consulting Group on the supercomputer on which your genetic data are stored. However, DTU does not have access to view your data.

The Danish National Genome Center has IT systems operated or supported by The Agency for Governmental IT Services, The Danish Ministry of Health, KMD and The Danish Health Data Authority on behalf of the Danish National Genome Center, where your data - except your genetic data - are processed.

We have entered into data processing agreements with our data processors, and we monitor their compliance with the data processing agreements in accordance with the applicable rules.

What are your rights?

As data controller, we at the Danish National Genome Center must fulfill your rights under the General Data Protection Regulation (GDPR).

If you want to exercise your rights in relation to the Danish National Genome Center, we may be contacted at
Email: kontakt@ngc.dk
Telephone: 24 97 17 65.

Below is a brief review of your rights.

You can read more about your rights on the Danish Data Protection Agency's website https://www.datatilsynet.dk/generelt-om-databeskyttelse/hvad-er-dine-rettigheder

Here you will also find the guidelines from the Danish Data Protection Agency on the rights of data subjects.

The right to see your data

You have the right to receive a copy of the data that we process about you, as well as some additional information on the processing of your data.

Article 15 of the Regulation on the right of access.

The right to have your data rectified or erased

In certain cases, you have the right to have incorrect personal information about yourself rectified or information erased by the data controller without undue delay.

Articles 16 and 17 of the Regulation.

However, it is not always possible to have data erased at the Danish National Genome Center as we are obliged to store the data, for example to document your physician's rationale for your treatment. We will normally only be able to erase or rectify your data if we have legal authority to do so. The reason is that the authorities must be able to document what has happened to your data, for example in connection with complaints.

It follows from the general administrative law rules, legislation relating to archives and records management etc. that apply to authorities such as the Danish National Genome Center.

The right to have the processing of your data restricted

In certain cases, you have the right to have the processing of your data restricted. Remember that you also have the right to have the processing of your data restricted by registering with the National Database of Non-Consent to the Use of Tissue Samples for Scientific Purposes (Vævsanvendelsesregister).

Article 18 of the Regulation.

The right to object

In special situations, you also have the right to object to the processing of your personal data.

Article 21 of the Regulation.

The right to complain

You have the right to complain to the Danish Data Protection Agency if you are dissatisfied with the way we process your personal data at the Danish National Genome Center. You will find the contact information of the Danish Data Protection Agency on www.datatilsynet.dk/kontakt.

Do you want to read more about the legal basis for the processing of your personal data?

The rules on the Danish National Genome Center may be found in sections 223-223 b of part 68 of the Danish Health Act. Pursuant to section 223 a (1) and (2), the Minister of Health has issued Executive Order no. 360 of 4 April 2019 on the Danish National Genome Center's collection of genetic data, which regulates the extent to which genetic data must be reported to the Danish National Genome Center.

Within the framework of the purpose limitation in section 223 b of the Danish Health Act, the Danish National Genome Center may collect data for use in patient treatment and research as well as combine data, including genetic data and health data, received by the Danish National Genome Center from various sources, including patient records. registers, databases and biobanks etc.

In addition, the statutory comments stipulate that the Danish National Genome Center may process personal data for a few ancillary purposes related to the Danish National Genome Center's task execution, including passing on data for use in processing complaints and compensation cases pursuant to the Danish Act on the Right to Complain and Receive Compensation within the Health Service or for use by the Danish Patient Safety Authority in carrying out supervisory tasks in accordance with the Authorization Act or the Danish Health Act.

The Danish Data Protection Act and the General Data Protection Regulation - Regulation (EU) 2016/679 of the European Parliament and of the Council of 27 April 2016 - also regulate the processing by the Danish National Genome Center of personal data.

The Danish National Genome Center collects and processes personal data, including metadata, for use in patient treatment and research pursuant to Article 6(1), point e) of the General Data Protection Regulation, cf. section 6 of the Danish Data Protection Act.

The Danish National Genome Center collects and processes health data for use in patient treatment specifically under Article 9(2), point h) of the General Data Protection Regulation, cf. section 7(3) of the Danish Data Protection Act.

The Danish National Genome Center collects and processes genetic data for use in patient treatment specifically under Article 9(2), point h) of the General Data Protection Regulation, cf. section 7(3) of the Danish Data Protection Act.

The National Genome Center collects and processes health data and genetic data for use in research specifically pursuant to the section 10(1) of the Danish Data Protection Act.

It appears from section 32(2) of the Danish Health Act that genetic data derived from biological material in connection with patient treatment and stored with the Danish National Genome Center may be passed on to a researcher for use in a specific research project if the conditions in section 46(1) or (2), are fulfilled unless the patient has had a decision registered under section 29(1) second sentence, in the National Database of Non-Consent to the Use of Tissue Samples for Scientific Purposes (Vævsanvendelsesregisteret).

The Danish National Genome Center processes data on civil registration number on the basis of section 11(1) of the Danish Data Protection Act.

The Danish National Genome Center will also be able to disclose personal data on the basis of an order on disclosure pursuant to section 804 of the Danish Administration of Justice Act, in the case of an investigation of a violation of section 114 or section 114 a of the Danish Penal Code, cf. section 223 b(2) of the Danish Health Act.

Appendix 2: Your right to decide in relation to research

The genetic data from your fetus are used in connection with diagnostic workup and/or treatment, but can also be included in research projects after approval by relevant authorities, for example the research ethics committee system.

When the genetic data are used in research, it contributes to the generation of new knowledge for the benefit of future patients and pregnant women.

You decide for yourself whether the results from the analysis may be used for purposes that go beyond your own treatment (including your fetus) and purposes that are directly related thereto. Purposes that are directly related to your treatment could be, for example, quality assurance, method development or training of healthcare professionals at the place of treatment.

You therefore decide for yourself whether the data from your fetus may be used for health research, for example. If you do not want the data from your fetus to be used for research, you must register with the National Database of Non-Consent to the Use of Tissue Samples for Scientific Purposes (Vævsanvendelsesregister). You can do this via borger.dk with your NemID or on a form that you will receive or can download from the Danish National Genome Centre's website www.ngc.dk. Here, you can also read more about the National Database of Non-Consent to the Use of Tissue Samples for Scientific Purposes (Vævsanvendelsesregister). It is not possible to register or de-register yourself and your fetus separately with/from the National Database of Non-Consent to the Use of Tissue Samples for Scientific Purposes (Vævsanvendelsesregister).

You must be aware that the use of the genetic data from your fetus in connection with research takes place in accordance with the rules that apply to research. This means that the choices you have made about feedback on incidental findings on the consent form do not apply to any findings that are identified in connection with research. In practice, you will only be able to receive feedback on any incidental findings identified in connection with research projects if they have significant health implications for you, your fetus or your family, and feedback provides an opportunity to prevent or treat the disease.

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Regional appendix to 'Patient information concerning comprehensive genetic analysis in connection with prenatal testing, 1st version'

Explanatory text for the following phrase in '*Informed consent to comprehensive genetic analysis in connection with prenatal testing*':

I hereby confirm that any findings can be shared in international databases, in anonymized form, for the purpose of obtaining further knowledge about the significance of these findings in relation to my treatment.

Explanatory text*:*

Our knowledge about diseases, and the influence of gene alterations on diseases, is constantly changing and increasing. Sharing information across borders through international databases, is a central tool for increasing our knowledge on the association between a specific gene alteration and disease. If you consent to the sharing of findings in these databases, it is only information about the individual findings which will be shared, and hence the complete genome will not be shared. Sharing of findings in international databases will always take place in anonymized form.