CENTOGENE
THE RARE DISEASE COMPANY

CentoScreen

The earliest step to responsible family planning

Working together ...

What is Carrier Screening?

Carrier screening is a genetic test used to determine if a healthy person is a carrier of a recessive genetic disease. The goal of carrier screening is to help individuals understand their risks of having a child with a genetic disorder and review the range of options available to guide pregnancy and family planning.

Previous studies have demonstrated that:

- An individual is a carrier of ~ 2.8 pathogenic variants on average [1]
- Approximately 1 in 4 (24.0%) individuals were carriers for at least 1 disorder and 1 in 20 (5.2%) were carriers for multiple disorders (of ~ 24000 individuals screened for 108 disorders)[2]
- 1 in 20 (5.0%) individuals (of 12,000 individuals screened for 3 disorders) were carriers, 88.0% had no previous family history and 1 in 240 were carrier couples with increased risk of having a child with a disorder [3]

Recent Committee Opinions from the American College of Obstetricians and Gynecology recommend carrier screening to be offered to all individuals considering pregnancy or during early pregnancy. Pan-ethnic and expanded carrier screening in addition to just ethnicity-based carrier screening is also recommended.[1,4]

What is Carrier Screening at CENTOGENE?

CENTOGENE offers CentoScreen, covering 330 genes, to help couples understand their risk of having a child with a recessive genetic disorder. The 330 genes were selected based on the following criteria:

1. a high carrier frequency
2. a well-defined phenotype
3. an early onset of disease
4. a highly severe phenotype
5. a severe effect on quality of life
6. the availability of surgical or medical intervention

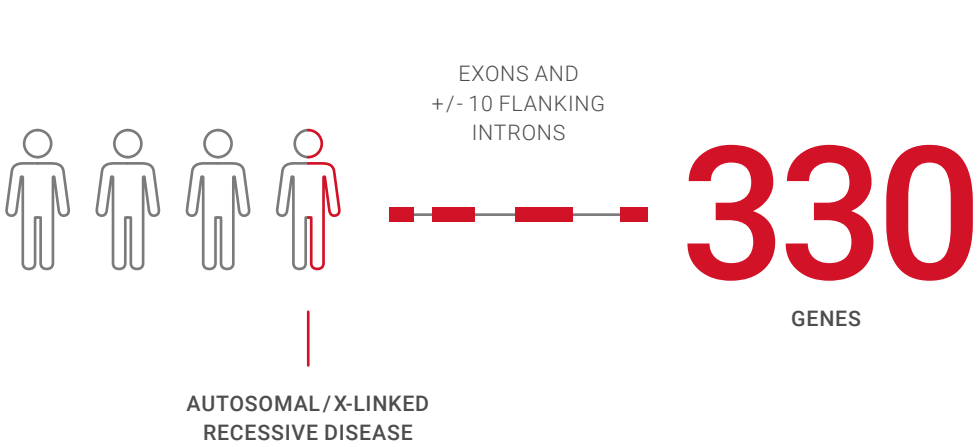
Who Can Be Offered Carrier Screening With CentoScreen?

CentoScreen can be offered to individuals considering pregnancy or during early pregnancy. It is appropriate for:

- Couples without any family history of genetic disease to understand their genetic risks
- Couples with a family history of or previous child with genetic disease
- Couples from regions with high consanguinity
- Couples from ethnicities with high incidence of certain genetic diseases

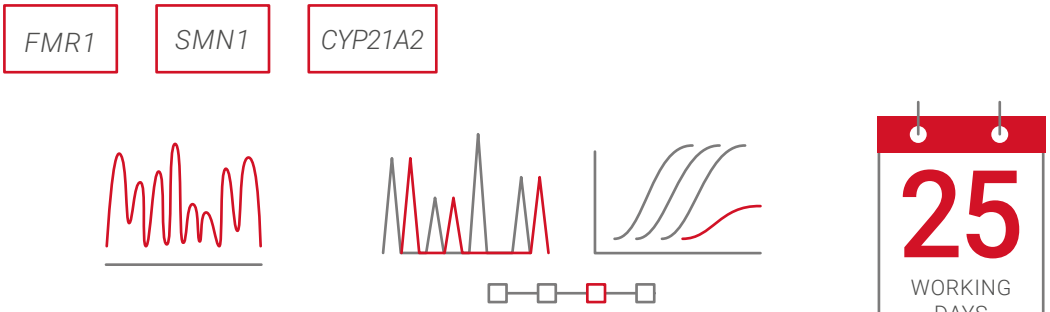
Carrier screening performed before pregnancy will allow you to provide your patients with a broader range of options consistent with their values and offer them more time to make an informed decision.

Scan the QR code to gain insights on the complete, up-to-date list of genetic diseases covered by CentoScreen or visit the Reproductive Health section on our NGS Panel webpage.



Why Choose CentoScreen for Your Patients?

- Comprehensive carrier screening panel targeting most relevant autosomal and X-linked recessive diseases
- Full gene sequencing of coding regions +/-10 flanking intronic bases of 330 genes
- Integrated copy number variation (CNV) reporting for 34 genes where high frequency of structural variants have been reported
- Covers most relevant disease-causing variants from HGMD®, including deep intronic variants, and proprietary Bio / Databank variants



CONFIRMATION SNP BY SANGER

CNVS BY MLPA OR QPCR

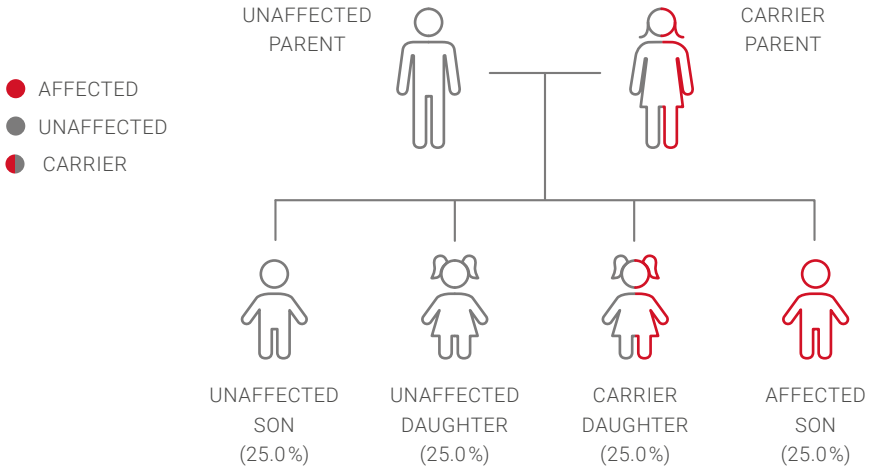
TAT

- Additional analyses for fragile X syndrome, spinal muscular atrophy, and congenital adrenal hyperplasia (*FMR1*, *SMN1* and *CYP21A2* genes respectively)
- ≥ 99.0 % of targeted genes covered at ≥ 20 x sequenced by next generation sequencing
- Low quality single nucleotide variants (SNVs) and all relevant deletion / insertion variants are confirmed by sanger sequencing or MLPA / qPCR prior to reporting
- CentoScreen Solo: 25 days, CentoScreen Duo: 25 days, CentoScreen Paired: 30 days
- Sample required: 1ml EDTA blood or 1 CentoCard® (10 drops of blood)

Risk Counseling for Couples / Patients Who Test Positives

X-linked Recessive Disorder

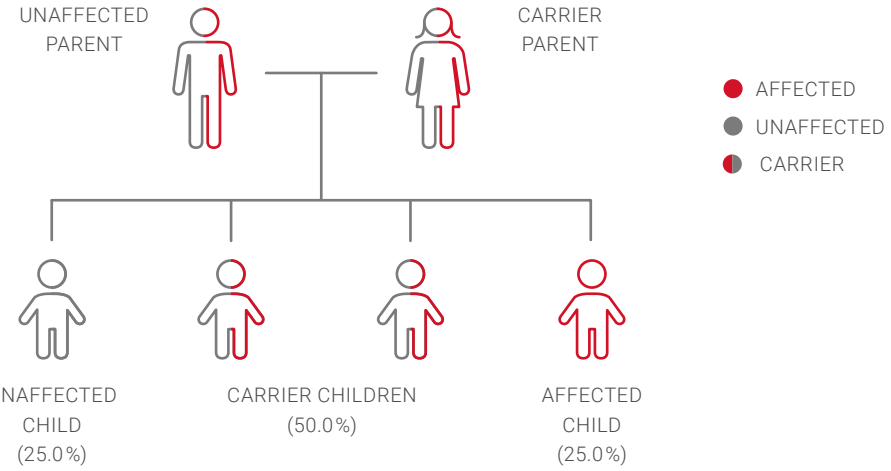
In an X-linked recessive disorder, if the mother is a carrier, there is a 25% chance that she will have an affected male child in each pregnancy:



- There is a 1/2 (50.0%) chance that the child is a male or female who is healthy with a normal copy of a particular gene
- There is a 1/4 (25.0%) chance that it is a healthy carrier female child or a mildly affected female child
- There is a 1/4 (25.0%) chance that it is an affected male with only one mutated copy of the gene

Autosomal Recessive Disorder

In an X-linked recessive disorder, if the mother is a carrier, there is a 25% chance that she will have an affected male child in each pregnancy:



- There is 1/4 (25.0%) chance that the child will be born with an autosomal recessive disorder. The child will have inherited two changed mutated genes, one from each parent
- There is 1/2 (50.0%) chance that the child will be a carrier like the parents, but will not have any symptoms
- The child will have inherited one normal gene and one mutated gene
- There is a 1/2 (50.0%) chance that the child will not inherit the defected gene with a change (mutation) from either parent. This child will not be a carrier and will not be affected by the disorder

How Do I Order Centoscreen and Receive the Results?

Depending on your patients' needs, different CentoScreen ordering options are available.

	CENTOGENE products	DESCRIPTION
INITIAL ANALYSIS	**CentoScreen Solo**	Complete Panel Evaluation for 1 Patient
	CentoScreen Paired Pack	Complete Panel Evaluation + risk gene analysis partner
	CentoScreen Duo	Complete Panel Evaluation for 2 Patients

1.

Order CentoScreen via CentoPortal

2.

Spot blood on our easy-to-use CentoCard or draw and ship blood sample

3.

Sample arrives at the lab and DNA is extracted and analyzed

4.

Test report is created and shared as a download via CentoPortal

*CentoNIPT is unavailable in the US.

What Types of Results Are Reported?

Genetic counseling, both before and after CentoScreen, is essential to help couples understand the results of the test, its implications and the options available. CENTOGENE will report pathogenic (class 1) and likely pathogenic (class 2) variants with strong evidence supporting pathogenicity.

If your patient is identified as a carrier of one or more genetic diseases, then testing is recommended for the partner. If the partner is also identified as a carrier for the same genetic disease, then this couple is at risk to have a child with the disease and will need genetic counseling about the disease and their options.

If the couple opts for prenatal testing in the future for the particular genetic disease, this can be performed at CENTOGENE with a short turnaround time of 15 business days. This will help you and your patients plan further steps together for the management of the pregnancy.

It is important to note that couples can be carriers for diseases other than those tested by CentoScreen as the list of genes and diseases tested is not exhaustive.

This test may also inform you and your patients of a genetic condition they have and may require medical follow-up. This includes testing of late-onset autosomal dominant inherited conditions.

The CENTOGENE Advantage

OUR DIAGNOSTIC SERVICES ARE MORE THAN LABORATORY AND BIOINFORMATICS.

CentoCard®

Our quick, cost-effective, and hassle-free solution for shipment of clinical blood samples for genetic testing. CentoCard provides a single sample for complete patient diagnostics: enzyme assay, biomarker analysis, and genetic testing.

Extended Phenotyping

Structuring your patient's symptoms into Human Phenotype Ontology (HPO) terms ensures the best quality of clinical information for data interpretation.

Data Safety and Research Use

With transparent and easy-to-understand consent forms, your patients can make educated decisions without worrying about data protection. By consenting to the research and storage option, you and your patients will advance research, the understanding of rare diseases, and the quality of future diagnoses and therapies.

Multiomics Testing

We have pioneered a multiomic testing strategy – combining panel technology with biochemical testing. By starting out with a complete clinical picture, you can now direct patients to the most precise diagnosis and potential treatment options.

CentoPortal®

Our user-friendly and fully-secure online service www.centoportal.com is designed to assist in ordering tests, transferring patient data, administering patient's samples, and accessing your diagnostic reports 24/7.

Bio/Databank

Our rare disease-centric Bio/Databank with over half a million patients and more than 31 million unique variants enable world-class medical interpretation.

Clinical Studies and Pharma Partnerships

By participating in clinical studies, your patients benefit as they foster the development of new therapies and improved monitoring. Through pharmaceutical partnerships, we also leverage our expertise to speed up drug development in rare diseases.

World-Class Expertise

At CENTOGENE, we connect patients around the world to empower innovative solutions for the global rare disease community. With our unique expertise in rare disease diagnostics and insights from over half a million patients, we provide answers today so that your patients can have a better tomorrow.

REFERENCES

1 Bell CJ, et al. (2011) Sci Transl Med.3(65):65ra4
2 Lazarin et al. (2013) Genet Med.15(3):178-86
3 Archibald et al. (2017) Genet Med. doi:10.1038/gim.2017.134
4 Committee Opinion No. 691. American College of Obstetricians and Gynecologists. (2017) Obstet Gynecol.129:e41–55 Cancer Network (NCCN)

... for a patients' better tomorrow.

FOR ORDERING

www.centoportal.com

FOR MORE INFORMATION

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V3eng_April2022