natera™ | Horizon™
Advanced carrier screening

Horizon Carrier Screening

Because knowing can make a difference

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The earlier your patients know, the better they can make decisions and prepare

Horizon carrier screening gives your patients and their partners actionable insight into their risk of passing on serious genetic conditions, no matter where they are in their reproductive journey.

Preconception

- Get genetic counseling.
- Seek evaluation for carrier symptoms, if needed.
- Discuss implications with family.
- Pursue alternatives, like IVF (in vitro fertilization) with PGT (preimplantation genetic testing).

Pregnancy

- Undergo diagnostic testing.
- Identify care team and, if needed, specialist facility for delivery.
- Plan financially (e.g., supplemental insurance).
- Prepare emotionally.

Post-delivery

- Access early interventions including FDA-approved treatment and clinical trials.

As of June 2023, 7 gene therapies approved by the FDA address conditions screened by Horizon.[1]

LOLA'S STORY

"Had we gotten carrier screening and known before Lola was born, they probably would have given her treatment within the first couple days after birth, and she could have missed no milestones."

BRADY CAMP,
FATHER OF LOLA (BORN WITH SMA)

Hear Lola's story and learn how carrier screening can help your patients:
natera.com/sma-screening

Carrier screening is no longer "nice-to-have"; it's standard of care

ACOG recommends offering carrier screening to all, either preconception or during pregnancy.[2]

THREE CONDITIONS ARE RECOMMENDED FOR ALL PATIENTS

- Cystic fibrosis (CF): **1 in 45 are carriers**
- Spinal muscular atrophy (SMA): **1 in 50 are carriers**
- Hemoglobinopathies: **1 in 49 are carriers**[2]

CARRIERS ARE COMMON, AND FAMILY HISTORY IS NOT A PREDICTOR

Family history

Not a predictor: **88%** of carriers of cystic fibrosis, SMA, and fragile X syndrome have no known family history[3]

Carrier frequency

1 in 7* people are carriers when screened with the Horizon *pan-ethnic standard* panel (our most popular panel)[4]

Combined incidence

1 in 634 babies born are affected by one of the 14 conditions tested by the Horizon 14 *pan-ethnic standard* panel[4]

* Excludes at-risk silent SMA carriers and fragile X carriers with intermediate CGG repeat size.

NEWBORN SCREENING ALONE IS NOT SUFFICIENT

- It screens for fewer conditions.[5]
- Results can return too late, delaying diagnosis and treatment.[5,6]

Waiting to screen until after delivery does not allow new parents adequate time for planning.

ACOG SAYS

"Prenatal carrier screening does not replace newborn screening, nor does newborn screening replace the potential value of prenatal carrier screening."[2]

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The #1 ordered carrier screen[7] delivers comprehensive, actionable insights

SCREEN FOR UP TO 274 CONDITIONS WITH OUR THOUGHTFULLY DESIGNED PANELS

All panels are conscientiously designed to include serious and clinically actionable conditions, and align with the 2015 ACMG/ACOG/NSGC/PQF/SMFM Joint Statement on expanded carrier screening.[8,9]

Horizon 4
Pan ethnic-basic: CF, SMA, fragile X syndrome, Duchenne muscular dystrophy (DMD)

Horizon 14
Pan-ethnic standard: includes hemoglobinopathies[10]
All 14 conditions have FDA-approved treatments / ongoing clinical trials[1]

Horizon 27
Pan-ethnic medium

Horizon 106
Comprehensive Jewish

Horizon 274
Pan-ethnic extended

CF, SMA, DMD, and Tay-Sachs enzyme can be ordered individually. Panel customization and additional genes are available upon clinic request.

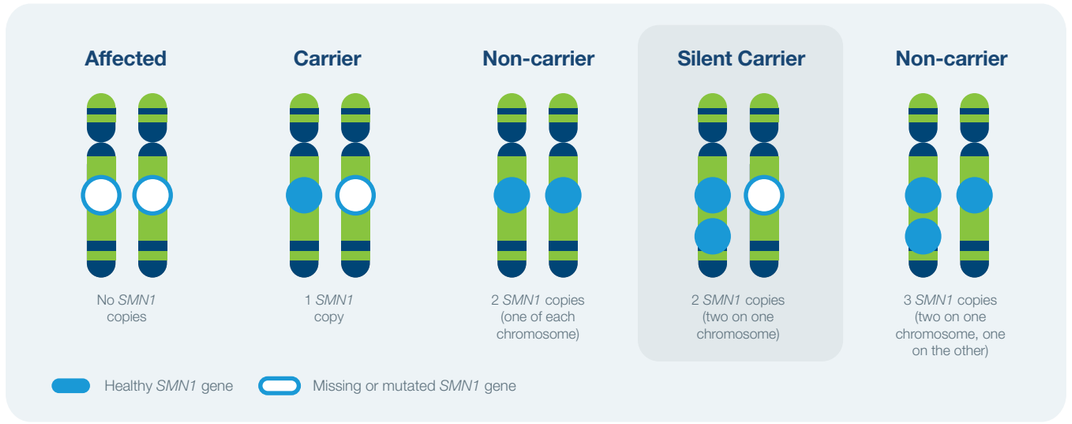
Better together
The #1 ordered NIPT and carrier screen in the Panorama™ + Horizon™ combo kit.[7]

One kit. One requisition. One blood draw.

Complete ACOG-aligned screening in a single workflow.[2,11]

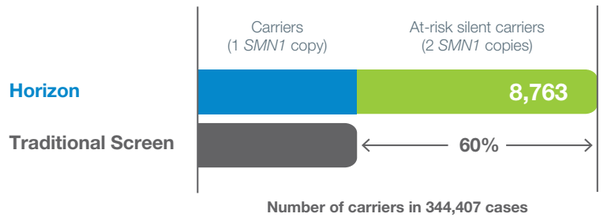
Horizon goes beyond traditional screening to detect at-risk silent SMA carriers

Traditional SMA screens[12] count only the total number of healthy *SMN1* copies.[13] However, as ACOG notes, silent carriers have two healthy *SMN1* copies—but on the same chromosome.[14]



Unlike traditional SMA screening, Horizon looks for a specific single nucleotide polymorphism (SNP) associated with having two healthy *SMN1* copies on one chromosome. By looking for the number of copies plus the identifying SNP, Horizon has the ability to detect silent carriers.[4]

Traditional screens miss at-risk silent carriers



ACOG SAYS

"[A subset] of the general population ... will not be identified as being a carrier ... using [traditional methods]."[14]

> ***"Prenatal carrier screening is so important; we can completely change the course of [spinal muscular atrophy] with treatment. The earlier the diagnosis is made and treatment is initiated, the better."***
>
> *Shadé Moody M.D., Pediatric Neurologist, University of Texas, Houston*

Targeted analysis misses many CF carriers

Horizon carrier screening offers full sequencing of the exons in the *CFTR* gene. In contrast, some CF screens use a targeted analysis of fewer variants, which means they will miss many of the variants known to cause CF.[4]

CORRINE'S STORY

"At 8 weeks I thought I was in the clear, but after doing Horizon at 12 weeks I found out I was a carrier of one of the less common cystic fibrosis mutations."

CORRINE, WHO FOUND OUT SHE IS A CARRIER OF CF DESPITE INITIALLY SCREENING NEGATIVE BASED ON A TARGETED ANALYSIS

ACOG SAYS

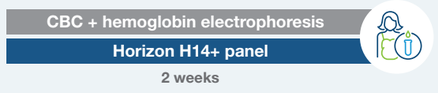
"A number of expanded mutation panels ... can be considered to enhance sensitivity for carrier detection, especially in non-Caucasian ethnic groups."[14]

Horizon complements blood tests for hemoglobinopathies

CBC and electrophoresis testing alone could miss **90%** of alpha- and **6%** of beta-hemoglobinopathy silent carriers detected by Horizon. Adding a DNA-based screen like Horizon identifies the exact variant, providing fast and comprehensive hemoglobinopathy results. Horizon results support confirmatory prenatal diagnosis or PGT.[4]

Concurrent CBC and Horizon Screening

Offer Horizon and CBC + hemoglobin electrophoresis together on the first OB visit. All results are available in 2 weeks.



ACOG SAYS

"Hemoglobinopathy testing may be performed using hemoglobin electrophoresis or molecular genetic testing (e.g., expanded carrier screening that includes sickle cell disease and other hemoglobinopathies)."[15]

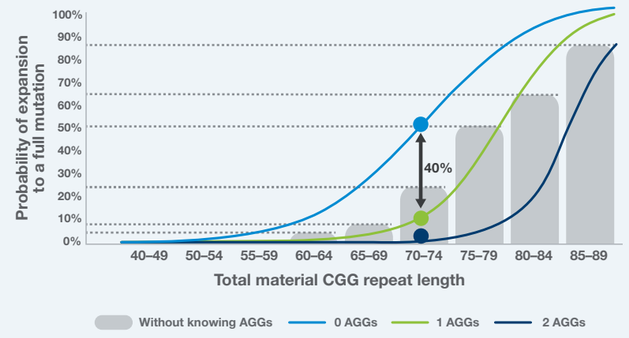
Horizon provides an accurate fragile X risk assessment

Where some screens only report the number of CGG repeats, Horizon also analyzes AGG interruptions within CGG repeats.

Fragile X carriers have 55-200 CGG repeats in the *FMR1* gene while individuals with a full mutation have >200 CGG repeats. AGG interruptions among CGG repeats slow down CGG expansion.[16]

FMR1 gene with AGG interruptions

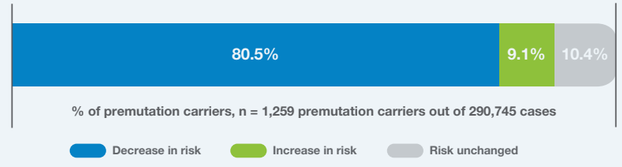
The presence of AGG refines the risk by as much as 40%



Without AGG interruption analysis, fragile X carrier screening can over-or underestimate the risk of expansion to a full mutation.[4]

Horizon automatically includes AGG reflex testing for female patients with 55-90 CGG repeats.

Horizon's AGG reflex refines risk in ~90% of fragile X CGG carriers



NateraCore—simple, tailored resources to support you and your patients every step of the way

Education
Patient-friendly materials and information sessions, covering basic genetics to specific tests

Access
Programs and price transparency – rooted in our commitment to provide affordable testing for all who can benefit

Ordering
Flexible options based around your needs, including intuitive remote ordering and comprehensive EMR solutions

Results
Clear, actionable reports, served with time-saving tools and a side of expert guidance

Next steps
Value-add services that go beyond the test to address what's next

Streamline your carrier screening workflow with our tools and services

Price Transparency Program (PTP) provides personalized cost estimates and a self-pay cash alternative.

Joint Reports provide reproductive risk for couples in which at least one individual is a carrier.

The Patient Call-Out Program (PCOP) delivers results and provides interactive genetic education via **NEVA** (Natera's Educational Virtual Assistant), available 24/7.

Partner Auto-Enroll streamlines your workflow for testing the partners of patients with positive Horizon results.

> *"Natera was there for us every step of the way, and they really were a bright spot in the process. Natera's genetic counselor was very kind and always available for questions."*
>
> A PRECONCEPTION HORIZON CARRIER SCREENING PATIENT

References:

1. https://www.fda.gov/vaccines-blood-biologics/cellular-gene-therapy-products/approved-cellular-and-gene-therapy-products. Accessed July 2023.
2. American College of Obstetricians and Gynecologists, Committee Opinion # 690, March 2017.
3. Archibald et al. *Genet Med.* 2018;20:513-523.
4. Westemeyer et al. *Genet Med.* 2020;22(8):1320-28.
5. https://www.babysfirsttest.org/. Accessed April 2020.
6. Wilcken. *N Engl J Med.* 2008;358(6):647.
7. Internal market research and claims data analysis using Definitive Healthcare data set. Dec 2023.
8. Joint statement was a collaboration with the American College of Medical Genetics (ACMG), the American College of Obstetricians and Gynecologists (ACOG), the National Society of Genetic Counselors (NSGC), the Perinatal Quality Foundation (PQF), and the Society for Maternal-Fetal Medicine (SMFM).
9. Edwards et al. *Obstet Gynecol*. 2015;125(3):653–62.
10. Horizon 14 includes Horizon 4 and the following conditions: alpha-thalassemia, betahemoglobinopathies, Canavan disease, familial dysautonomia, galactosemia, Gaucher disease, medium chain acyl-CoA dehydrogenase deficiency (MCAD), autosomal recessive polycystic kidney disease (PKD), Smith-Lemli-Opitz syndrome, and Tay-Sachs.
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12. Prior and Professional Practice Guidelines Committee. *Genet Med.* 2008;10:840–842.
13. McAndrew et al. *Am J Hum Genet.* 1997;60(6):1411-1422.
14. ACOG Committee Opinion # 691, March 2017.
15. Hemoglobinopathies in Pregnancy. ACOG Practice Advisory. Aug 2022.
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