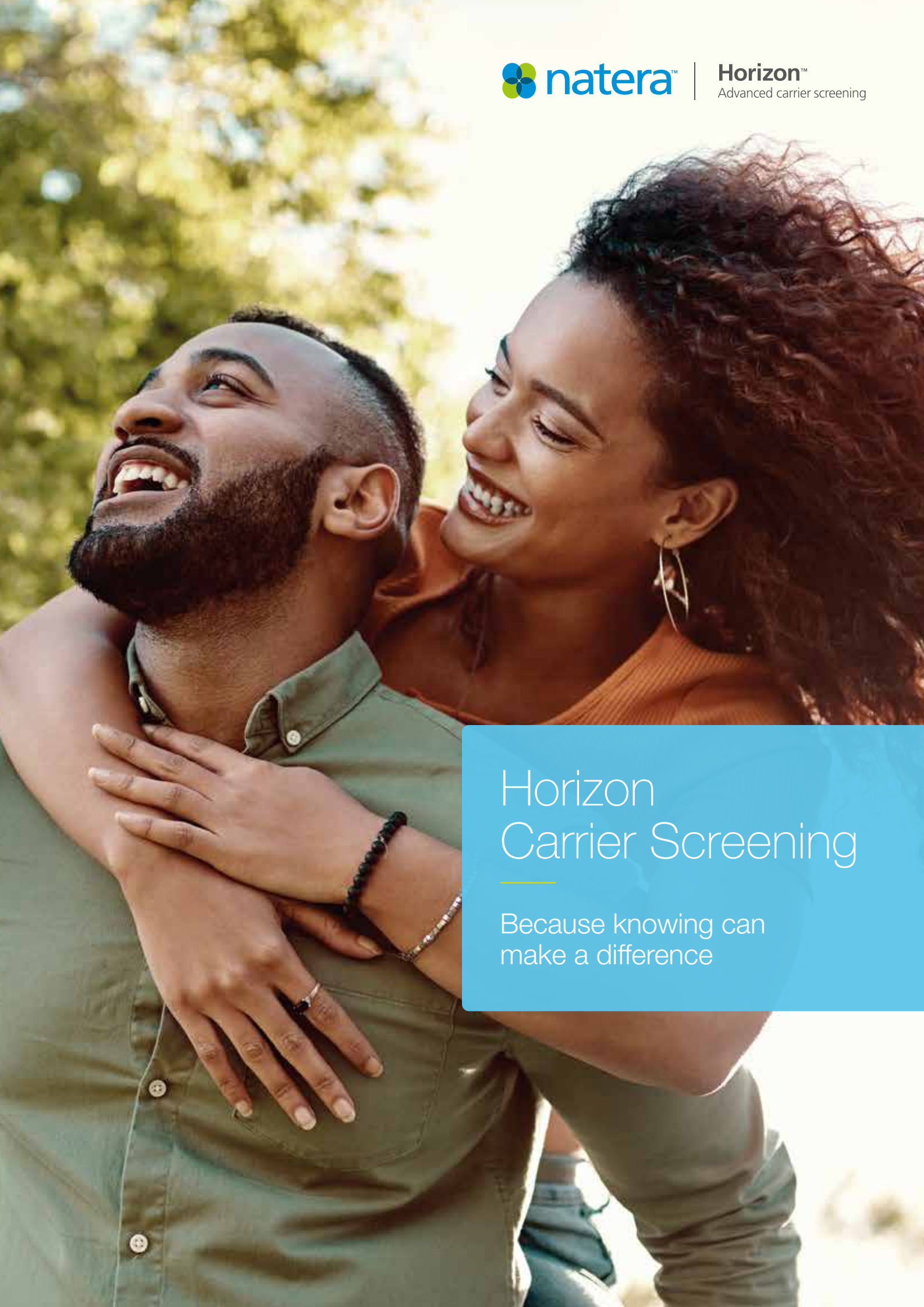
natera™ | Horizon™
Advanced carrier screening



Horizon Carrier Screening

Because knowing can make a difference

natera™ | Horizon™ Advanced carrier screening

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.
- Find out about 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 2020, 3/8 FDA-approved gene therapies target conditions screened by Horizon, with many more in the pipeline.[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 recommended by ACOG for 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 5.5 people are carriers when screened with the Horizon *pan-ethnic medium* panel*

Combined incidence

1 in 620 affected by one of the 27 conditions tested by the Horizon 27 *pan-ethnic medium panel**

* in the US pan-ethnic population[4]

NEWBORN SCREENING ALONE IS NOT SUFFICIENT

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]

ACOG

natera™ | Horizon™
Advanced carrier screening

The #1 ordered carrier screen 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.[7,8]

Horizon 4

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

Horizon 27

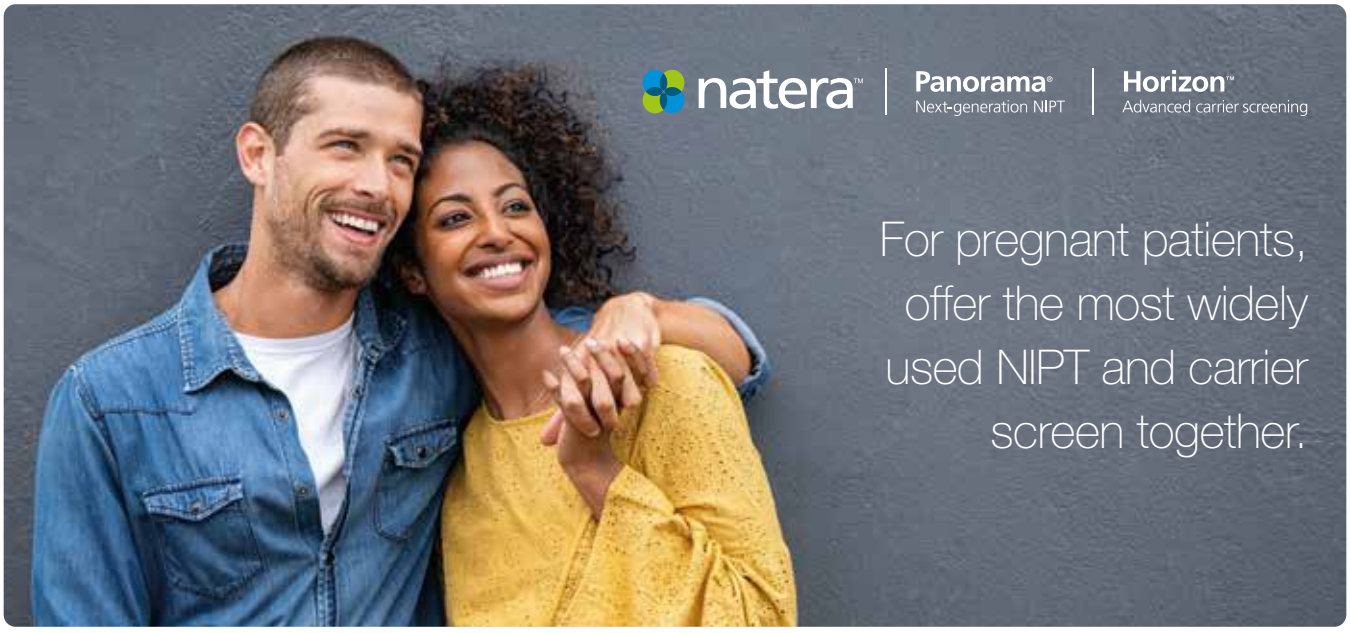
Pan-ethnic medium

Horizon 106

Comprehensive Jewish

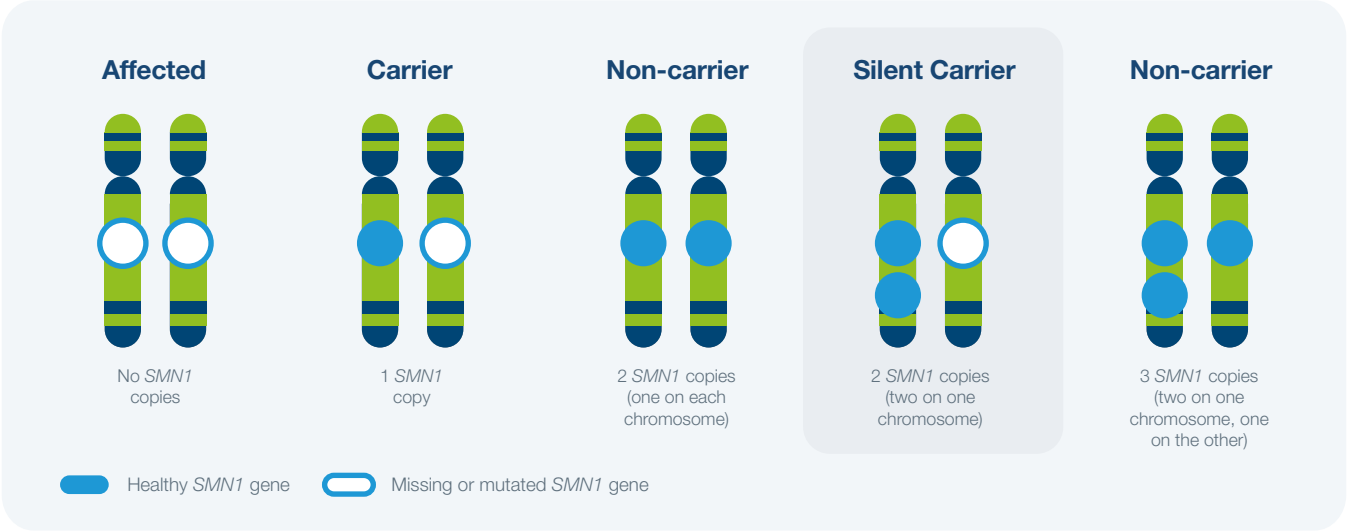
Horizon 274

Pan-ethnic extended



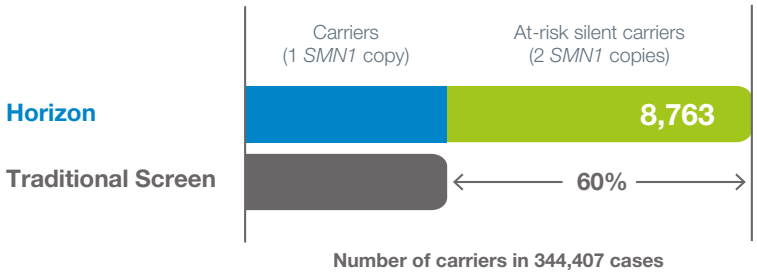
Horizon goes beyond traditional screening to detect at-risk silent SMA carriers

Traditional SMA screens count only the total number of healthy *SMN1* copies.[11] However, as ACOG notes, silent carriers have two healthy *SMN1* copies—but on the same chromosome.[12]



Unlike traditional SMA screening, Horizon looks for a 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 screen for increased risk of being a silent carrier.[4]

Traditional screens miss at-risk silent carriers



> ***"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*

ACOG SAYS

"[A subset] of the general population ... will not be identified as being a carrier ... using [traditional methods]."[12]

ACOG

Traditional tests miss many CF carriers

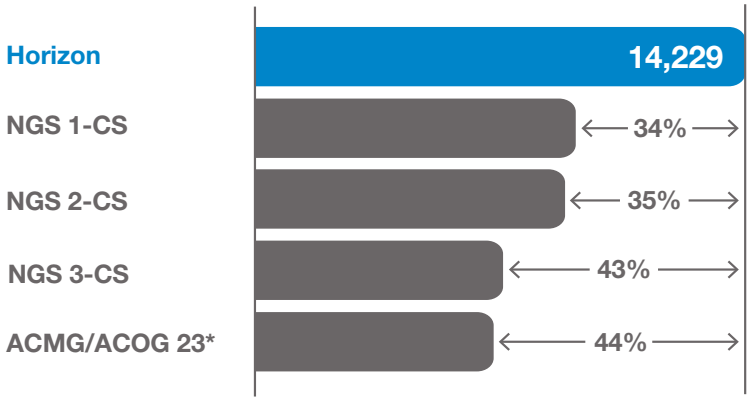
Horizon carrier screening offers full sequencing of the exons in the *CFTR* gene. In contrast, traditional CF screens use a targeted analysis of fewer variants, which means they will miss many of the variants known to cause CF.[4]

ACOG SAYS

"A number of expanded mutation panels ... can be considered to enhance sensitivity for carrier detection, especially in non-Caucasian ethnic groups."[12]

ACOG

Horizon detects more CF carriers



* ACMG/ACOG-recommended 23-mutation panel[13]

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

"A combination of laboratory tests may be required to provide the information necessary to counsel couples who are carriers of one of the thalassemias or sickle cell disease."[12]

ACOG

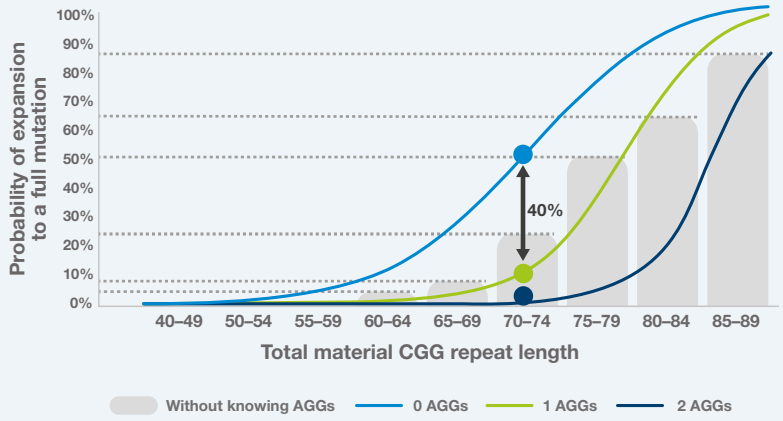
Horizon gives a more accurate fragile X risk assessment than typical screens

Where traditional 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.[14]

FMR1 gene with AGG interruptions

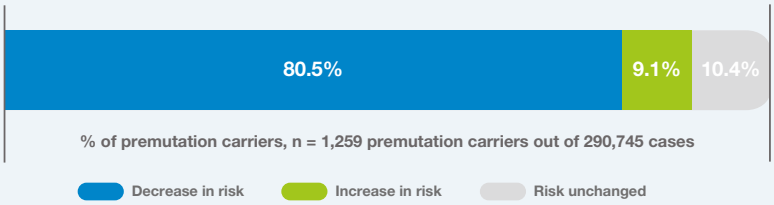
The presence of AGG refines the risk by as much as 40%



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

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

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



Simple, tailored, resources to support you and your patients

Education

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

Ordering

Flexible options based around your needs. For more information contact your local Natera Regional Manager.

Results

Clear, actionable reports, served with a side of expert guidance

Next steps

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

> ***"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 WHO OPTED FOR SPECTRUM ADVANTAGE

References:

1 Bulaklak and Gersbach. *Nat Commun.* 2020:11, 5820.
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 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).
8 Edwards et al. *Obstet Gynecol.* 2015;125(3):653–62.
9 Horizon 14 includes Horizon 4 and the following conditions: alpha-thalassemia, beta-hemoglobinopathies, 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.
10 Spectrum Advantage disclaimer: Spectrum PGT-M and PGT-A must be performed within one year of Horizon screening results. Shipping and batching fees apply. Promotional price good for one test run and not valid if patient chooses to file insurance. Restrictions apply. Both male and female must have completed a Horizon panel with 4 or more conditions. Prior carrier screening/genetic testing identifying positive risk for a disorder voids special pricing.
11 McAndrew et al. *Am J Hum Genet.* 1997;60(6):1411-1422.
12 American College of Obstetricians and Gynecologists, Committee Opinion # 691, March 2017.
13 Watson et al. *Genet Med.* 2004;6:387–391.
14 Nolin et al. *Am J Hum Genet.* 2003;72(2):454-464.

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Horizon has been developed and its performance characteristics determined by the CLIA-certified laboratory performing the test. The test has not been cleared or approved by the US Food and Drug Administration (FDA). CAP accredited, ISO 13485 certified, and CLIA certified. @ 2023 Natera, Inc. All Rights Reserved.

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