

# General information about positive NIPT results: XYY syndrome (Jacobs syndrome)

## My patient's NIPT is positive for XYY syndrome (Jacobs syndrome). What does this mean?

Your patient's noninvasive prenatal testing (NIPT) result suggests the presence of an extra copy of the Y chromosome. NIPT is a screening test; false positives can occur. The actual chance for the pregnancy to have XYY syndrome depends on many factors, including the patient's clinical and family history.

**Next steps to consider:** You should discuss the results and the potential clinical implications with your patient. Globally, professional medical societies recommend that all women with a positive screening result should have genetic counseling and a comprehensive ultrasound evaluation with an opportunity for diagnostic testing to confirm the results.<sup>1,2</sup> Confirmation prior to birth can also help with pregnancy and neonatal management.

See below for more information about XYY syndrome.

## What is XYY syndrome?

XYY syndrome is a condition that is caused by a male having an extra copy of the Y sex chromosome (one copy of the X chromosome and two copies of the Y chromosome rather than the usual one copy of each).

## What are the features of XYY syndrome?

XYY syndrome is likely to result in live birth. Males with XYY syndrome have variable phenotypes. Some of the common features of XYY syndrome include delayed speech and language development and taller stature. Prenatal ultrasounds are usually normal. There is a slightly increased risk for males with XYY syndrome to have an autism spectrum disorder or learning disability. Fertility is usually normal.

## What is the prevalence of this condition?

Approximately 1 in 1000 males are born with XYY syndrome. This condition usually happens by chance and is not associated with advanced parental age.

## What testing could be considered?

Specialized genetic tests such as karyotyping, fluorescence *in situ* hybridization (FISH), quantitative polymerase chain reaction (qPCR), and microarray are available to confirm the presence of XYY syndrome.

These confirmatory tests are generally performed on cells from chorionic villus sampling (CVS) or amniocentesis during pregnancy, on cord blood or peripheral blood sample after the baby is born, or on products of conception (POC) in the case of a miscarriage. The type of invasive procedure and diagnostic testing should take into account the underlying chromosome anomaly.<sup>3,4</sup>

Ultrasound evaluation is not expected to be useful in aiding with a prenatal diagnosis of XYY syndrome, as ultrasound is usually normal. Normal ultrasound cannot exclude this condition.

## Resources for XYY syndrome

MedlinePlus Genetics  
[medlineplus.gov/genetics/condition/47xyy-syndrome](https://medlineplus.gov/genetics/condition/47xyy-syndrome)

National Organization for Rare Disorders  
[rarediseases.org/rare-diseases/xyy-syndrome](https://rarediseases.org/rare-diseases/xyy-syndrome)

## References

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2. Benn P, Borrell A, Chiu RW, et al. Position statement from the Chromosome Abnormality Screening Committee on behalf of the Board of the International Society for Prenatal Diagnosis. *Prenat Diagn.* 2015;35(8):725-734.
3. Cherry AM, Akkari YM, Barr KM, et al. Diagnostic cytogenetic testing following positive noninvasive prenatal screening results: a clinical laboratory practice resource of the American College of Medical Genetics and Genomics (ACMG). *Genet Med.* 2017;19(8):845-850.
4. Van Opstal D, Srebniak MI. Cytogenetic confirmation of a positive NIPT result: evidence-based choice between chorionic villus sampling and amniocentesis depending on chromosome aberration. *Expert Rev Mol Diagn.* 2016;16(5):513-520.

## Additional resources

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Gardner RJM, Amor DJ. *Gardner and Sutherland's Chromosome Abnormalities and Genetic Counseling.* 5th ed. Oxford University Press; 2018.

Jones KL, Jones MC, del Campo M. *Smith's Recognizable Patterns of Human Malformation.* 7th ed. W.B. Saunders Company; 2013.

Gruchy N, Blondeel E, Le Meur N, et al. Pregnancy outcomes in prenatally diagnosed 47, XXX and 47, XYY syndromes: a 30-year French, retrospective, multicentre study. *Prenat Diagn.* 2016;36(6):523-529.

Urbanus E, van Rijn S, Swaab H. A review of neurocognitive functioning of children with sex chromosome trisomies: Identifying targets for early intervention. *Clin Genet.* 2020;97(1):156-167.