

# Mosaicism Ratio: Personalized NIPT insights when you need them most

Refine each patient’s risk for aneuploidy using personalized data specific to their NIPT results.

The final result is the most important aspect of a non-invasive prenatal test (NIPT), and while most NIPT laboratories work hard to deliver the best possible results, experience, sequencing technology, and capability varies from lab to lab, along with result reliability and the risk for false positive results.

After nearly a decade of experience with NIPT, one insight that has emerged is the tendency for NIPT samples with ‘mosaic’ data to have lower positive predictive values (PPV).<sup>1</sup> **MaterniT 21 PLUS with Mosaicism Ratio** helps to *refine your patient’s risk for aneuploidy using personalized data specific to their results*, building upon the current generic PPV calculation using maternal age and gestational age.

Now there is a way to identify which NIPT results are more likely to be true positive results, offering providers greater reliability and confidence as they counsel their patients.

## What is Mosaicism Ratio?

- A metric calculated in the event of a positive NIPT result for trisomy 21, 18, or 13
- Requires two data points:
  - **Affected fraction** – the percentage of cell-free DNA that is impacted by aneuploidy
  - **Fetal fraction** – the percentage of cell-free DNA contributed by the pregnancy

$$\text{Mosaicism Ratio} = \frac{\text{Affected fraction}}{\text{Fetal fraction}}$$

## How is Mosaicism Ratio interpreted?

Positive results are classified into one of three Mosaicism Ratio groups:

Groups	Likelihood of POSITIVE result being a TRUE POSITIVE
High mosaic	Positive NIPT result is more likely to be a true positive, associated with a higher PPV (see report below)
Low mosaic	Positive NIPT result is more likely to be a false positive, associated with a lower PPV (see report below)
Non-mosaic	Positive NIPT result that is very likely to be a true positive, associated with the highest PPV. No ‘mosaic’ language will display on the report.

In general, as Mosaicism Ratio increases, so does the positive predictive value (PPV) of the result. The PPV associated with an individual patient result depends on the trisomy involved and the Mosaicism Ratio group associated with the results (i.e. non-mosaic, high mosaic, or low mosaic).

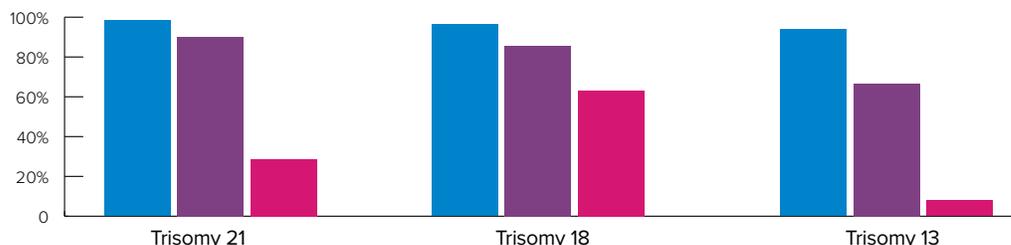
## How is Mosaicism Ratio reported? (Singleton pregnancies only)

For patients with a positive result for trisomies 21, 18, and 13, a Mosaicism Ratio comment will feature in the **Lab Director Comments** box on the MaterniT 21 PLUS lab report.

Test Result	Positive Trisomy 13
<p><b>Lab Director Comments</b></p> <p>This specimen showed an increased representation of chromosome 13, suggestive of high mosaic trisomy 13, which may affect the reported PPV (Rafalko et al, 2020). In placental testing, trisomy 13 is a common finding that is often confined to the placenta (CPM). Grafi et al, 2014. However, true fetal involvement is associated with phenotypic abnormality. Genetic counseling, confirmatory diagnostic testing, and clinical correlation are recommended.</p>	

Test Result	Positive Trisomy 18
<p><b>Lab Director Comments</b></p> <p>This specimen showed an increased representation of chromosome 18, suggestive of low mosaic trisomy 18, which may affect the reported PPV (Rafalko et al, 2020). In placental testing, trisomy 18 is a common finding that is often confined to the placenta (CPM). Grafi et al, 2014. However, true fetal involvement is associated with phenotypic abnormality. Genetic counseling, confirmatory diagnostic testing, and clinical correlation are recommended.</p>	

## Positive Predictive Value (PPV) by trisomy and Mosaicism Ratio group<sup>1</sup>



Mosaicism Ratio Group (MR value)	Trisomy 21	Trisomy 18	Trisomy 13
Non-mosaic (0.7 and above)	<b>98.4%</b> [95% CI: 96.6-99.3%]	<b>96.3%</b> [95% CI: 91.2-98.6%]	<b>93.9%</b> [95% CI: 82.1-98.4%]
High mosaic (0.5-0.69)	<b>90.0%</b> [95% CI: 66.9-98.2%]	<b>85.7%</b> [95% CI: 70.8-94.1%]	<b>66.7%</b> [95% CI: 46.0-82.8%]
Low mosaic (0.2-0.49)	<b>28.6%</b> [95% CI: 5.1-69.7%]	<b>63.2%</b> [95% CI: 38.6-82.8%]	<b>7.9%</b> [95% CI: 2.1-22.5%]

## What are the potential causes of a low Mosaicism Ratio?

Though it may be difficult to pinpoint the exact cause of a low Mosaicism Ratio in any particular case, in general a depressed Mosaicism Ratio may be the result of placental mosaicism, prior co-twin demise, or other biological phenomenon.

## Summary

- Mosaicism Ratio allows clinicians to provide customized counseling for patients with positive results for trisomy 21, 18, and 13 in singleton pregnancies
- The lower the Mosaicism Ratio, the greater the chance for a discordant result from diagnostic testing
- MaterniT 21 PLUS with Mosaicism Ratio identifies when a positive result is more likely to be a true positive
- Regardless of Mosaicism Ratio, diagnostic testing and genetic counseling are recommended for all positive NIPT results according to ACOG, Practice Bulletin 226<sup>2</sup>

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Test name	Test no.	Fetal sex opt-out
MaterniT 21 PLUS Core (Trisomy 21, 18, 13, fetal sex)	451927	451951
MaterniT 21 PLUS Core + SCA* (Singletons only)	451934	452112
MaterniT 21 PLUS Core + ESS**	451931	452136
MaterniT 21 PLUS Core + ESS + SCA* (Singletons only)	451937	452122
GENOME-Flex (Add On)	452104	n/a
GENOME-Flex (Add On) Redraw	452114	n/a
MaterniT GENOME (Singletons only)	451941	452106

\* Sex chromosome aneuploidies \*\* Enhanced sequencing series (microdeletions, trisomies 16 & 20)

## REFERENCES

1. Rafalko et al. Impact of Mosaicism Ratio on positive predictive value of cfDNA screening. *Prenatal Diagnosis*, 2020.
2. American College of Obstetricians and Gynecologists. Screening for Fetal Chromosomal Abnormalities. Practice bulletin no. 226. *Obstet Gynecol*. 2020;136(4):859-867



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