Sonic Genetics
Quality is in our DNA

Harmony® Prenatal Test unable to report on chromosomes examined

Information for patients

Everyone's DNA is packaged into chromosomes. Most people have two copies of the chromosomes that are numbered 1–22. We also have two chromosomes that determine our sex: females have two copies of the X chromosome (XX) and males have an X and a Y chromosome (XY).

A mother's blood contains a mixture of her own DNA from these chromosomes, as well as DNA from the baby's chromosomes. The DNA from the baby's chromosomes comes from the placenta.

The Harmony Prenatal Test

The Harmony Prenatal Test compares the amount of DNA from selected chromosomes in the mother's blood. Most of this DNA comes from the mother, a small proportion comes from baby. The test determines whether the amount of DNA from one chromosome is different to what is expected. For example, if there is more DNA than usual from chromosome 21, the baby may have three copies of that chromosome (causing Down syndrome) rather than the usual two copies.

Non-invasive prenatal testing provides very important information about a woman's pregnancy. The Harmony Prenatal Test will only provide a result when there is very clear evidence regarding the number of different chromosomes. If there is any uncertainty about the result, Harmony will report that a confident result cannot be provided. If there is uncertainty, we would prefer to report, "I'm not sure what the answer is" rather than guess or assume.

If the result is uncertain, this does not necessarily make it more or less likely that there actually is an abnormal number of chromosomes. It simply means that Harmony cannot provide a confident result. This inability for Harmony to provide a confident result is not a technical failure of the test. It is usually due to the complex biology of pregnancy. There are several reasons for this, detailed below.

1. There was not enough of the baby's DNA to report on any chromosome

In about three out of every 100 tests performed, there is insufficient DNA from the baby in the mother's blood sample. This is more likely if the mother is overweight. It may also occur if the mother has an infection or inflammation, or has exercised strenuously just prior to the blood collection.

A low level of baby's DNA can make it difficult to provide a confident result if there are certain benign changes in the mother's or baby's chromosomes (i.e. no alteration in function) which can complicate the analysis. Other complicating factors can include the placenta having a mixture of cells with different numbers of chromosomes (this mix of cells may not be present in the baby); there being a twin pregnancy but one of the twins did not survive; and the sample quality not being adequate.

In these cases, we usually recommended that the test be repeated with a fresh blood sample (at no charge). Most women will get a result on this second blood sample. However, about one in three of these women still do not get a result from the second blood test. Once again, there is not enough of the baby's DNA in the mother's blood for Harmony to provide a confident result.

If the Harmony Prenatal Test cannot provide an answer after two collections, there is a small chance that there is a real problem with the baby's chromosomes. We do not recommend that a third blood collection be performed. You should discuss the situation with your doctor. It may be appropriate for you to have other tests, such as an ultrasound, instead.

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If Harmony is unable to provide a confident result after two blood collections, we will refund the cost of the test (terms and conditions apply); please contact Sonic Genetics on 1800 010 447. This refund is not offered because the test failed or was technically flawed. We offer the refund because we recognise that Harmony may be unable to provide a confident result through no fault of the patient, doctor or laboratory.

2. There was sufficient baby's DNA to report on some chromosomes, but not on the sex chromosomes

In 1–2 in every 200 women tested, Harmony can provide a confident result for chromosomes 13, 18, 21, and (if ordered) 22, but cannot provide a confident result regarding the sex chromosomes.

The baby's sex cannot be determined

If Harmony identifies clear evidence that DNA from a Y chromosome is present, then the baby is predicted to be male. However, sometimes the evidence regarding the Y chromosome is insufficient for Harmony to provide a confident result.

The Y chromosome is much smaller than the X chromosome, and there is less Y chromosome DNA available to test. This can make it challenging to work out if the baby has a Y chromosome. It is also possible that the baby's Y chromosome has a change that is benign (i.e. no alteration in function) but which interferes with the Harmony test. The quality of the sample may also make it difficult to provide a confident result regarding the Y chromosome.

These factors are even more important if there is little DNA from the baby in the mother's blood. There may be just enough of the baby's DNA to provide a confident result for larger chromosomes, such as 13, 18, 21, and 22, but insufficient to be confident of the result for the Y chromosome.

Number of sex chromosomes cannot be reported

Babies can be born with differences in the number of their sex chromosomes. Instead of having XX or XY, some babies are born with only one X (X), an extra X (XXX or XXY), or an extra Y (XYY).
Sometimes it is difficult to provide a confident result regarding the number of X and Y chromosomes. This can be due to:

- Most of the DNA from sex chromosomes coming from the mother's two X chromosomes
- The amount of DNA from the small Y chromosome
- Benign changes in the sex chromosomes of mother or baby (i.e. no alteration in function) which interfere with the Harmony test
- The placenta having a mixture of cells containing different numbers of the sex chromosomes (this mixture of cells may not be present in the baby).

These factors can make it challenging to work out the baby's sex chromosomes, especially if there is little DNA from the baby in the mother's blood. There may be just enough of the baby's DNA to provide a confident result for larger chromosomes, such as 13, 18, and 21, however, insufficient to be confident of the result for the sex chromosomes.

If Harmony is unable to provide a confident result regarding the sex chromosomes, we do not recommend that the test be repeated. In our experience, this is unlikely to provide a useful result. You should discuss with your doctor any other tests that may be suitable.

Checking the baby's sex chromosomes is an optional extra in the Harmony Prenatal Test and is provided at no additional cost. If Harmony provides a confident report regarding chromosomes 13, 18, 21, and 22 (if requested), but not for the sex chromosomes, we do not provide a refund.

Further information and contacts
The Centre for Genetics Education www.genetics.edu.au
Harmony Prenatal Test, Sonic Genetics www.sonicgenetics.com.au/nipt