Sonic Genetics
Douglass Hanly Moir Pathology

harmony® PRENATAL TEST

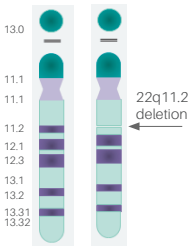
# 22q11.2 deletion screening for your patients

Information for Doctors

**NEW SCREENING OPTION:** 22q11.2 is now part of the Harmony Prenatal Test menu

Sonic Genetics aims to provide clinically relevant NIPT options for clinicians and patients and provides flexibility to order only the tests that are appropriate in a given situation. Assessment of the scientific literature in the field of prenatal diagnosis demonstrated the medical value of NIPT for 22q11.2 deletion.

## 22q11.2 deletion is the most common chromosomal microdeletion[5]



Chromosome 22 shows a microdeletion of the 22q11.2 region. This person would have 22q11.2 deletion syndrome.

- 22q11.2 deletion syndrome is a chromosomal condition that occurs when there is a very small deletion (microdeletion) in a recognised region of chromosome 22.
- This condition may occur in as many as one in 1,000 pregnancies.[6]
- It is the second most common cause of developmental delay with cardiac abnormalities after Down syndrome.[7]
- Conventional screening methods, such as first trimester screening (FTS) or karyotype, do not reliably detect 22q11.2 deletion in the prenatal period.[1]
- Maternal age is not a risk factor for deletions.
- More than 90% of affected individuals have no family history of 22q11.2 deletion.

## Clinically relevant

22q11.2 deletion is the underlying cause of conditions previously described as DiGeorge syndrome. Clinical presentation demonstrates a wide range of severity that cannot be predicted prenatally.

Features are diverse and possible clinical findings may include the following:

| Findings[5,6] | Prevalence |
|---|---|
| Cardiac anomalies | 74% |
| Immune deficiency | 77% |
| Palatal anomalies | 69% |
| Hypocalcaemia | 49% |
| Renal anomalies | 37% |
| Learning difficulties | 66% |
| Growth & developmental delays | >90% |

There is an increased risk of psychiatric illness in later life.

## Request the 22q11.2 test

In order to request the Harmony NIPT test with 22q11.2, it must be indicated on the Harmony Non-invasive Prenatal Request Form (available for download from the Sonic Genetics website or via most Practice Management Software platforms, if installed). We will accept the previous request form, however, we recommend that you use the updated form.

### Can I order the 22q11.2 test as a standalone test?

The 22q11.2 test is an optional add-on to the core Harmony test for trisomy 21, trisomy 18 and trisomy 13. The 22q11.2 test is not available as a stand-alone test.

### Can I add the 22q11.2 test to the patient's previously analysed Harmony specimen?

Yes. It is possible to do so within two weeks of the report date. There is an additional charge of $70 for the 22q11.2 screen, plus $30 re-analysis fee. Please call Sonic Genetics to arrange.

### Do I need to send an additional sample ?

No. The test is carried out on the same sample as the current Harmony Prenatal Test.

## Performance and accuracy

The Harmony Prenatal Test has an overall low cumulative false-positive rate. For trisomies 21, 18, 13 and 22q11.2 deletion, the cumulative false-positive rate is less than 0.6%.[3,4]

### 22q11.2 deletion

| | Detection rate | False-positive rate |
|---|---|---|
| within the 3 Mb region* | 75%[3] | 0.5%[3] |

*including smaller nested deletions

Harmony has performed the largest analytical validation study to date for 22q11.2 deletion (n=1,736), including deletion sizes ranging from 1.96 to 3.25Mb and fetal fraction from 4 to 33%.[3]

Results from analytical validation and clinical verification cohort:

| | Analytical validation | Clinical verification cohort | Combined |
|---|---|---|---|
| Total samples (N) | 1,736 | 217 | 1,953 |
| 22q11.2 (n/N) | 92/122 | 5/7 | 97/129 |
| No evidence of a deletion (n/N) | 1,606/1,614* | 210/210 | 1,816/1,824 |
| Sensitivity %, (95% CI) | 75.4 (67.1–82.2) | 71.4 (35.9–91.8) | 75.2 (67.1–81.8) |
| Specificity %, (95% CI) | 99.5 (99.0–99.7) | 100 (98.2–100) | 99.6 (99.1–99.8) |

*Presumed unaffected - commercial samples without a known diagnosis of 22q11.2 deletion, presumed to be unaffected (may cause underestimation of specificity).[9]

## Importance of early screening

Early screening and diagnosis of 22q11.2 deletion affects management of pregnancy. If a pregnancy is affected with 22q11.2 deletion, the following is recommended.[9]

- Detailed ultrasound with fetal echocardiogram to evaluate for anomalies, such as congenital heart defect, cleft palate, etc.
- Screening for and coordinated management of associated conditions
- Delivery at a tertiary care centre

Genetic counselling is available free of charge to all high-risk patients who are residing in Australia and have prepaid Sonic Genetics for the Harmony Prenatal Test. Instructions on how to access will accompany any high-risk results. We provide all invasive pathology testing at Medicare rebate only, for qualified patients.

**NIPT is a screening test. All high probability results should be confirmed with FISH or microarray testing. If a pregnancy is known to be at increased risk for 22q11.2 deletion based on family history or ultrasound findings, NIPT is not indicated and diagnostic testing (such as CVS or amniocentesis) should be considered.**

## Benefits of the Harmony Prenatal Test

- Flexible testing options and clinically relevant testing
- Reliable timely results regardless of test options ordered
- Minimise unnecessary invasive procedures due to false-positives[2]
- Single blood collection regardless of test options ordered

**Performed in Australia in our NATA-accredited Sullivan Nicolaides Pathology laboratory**


### References

1. McDonald-McGinn et al., *Nature Rev Dis Primer.* 2015 Nov 19;1:15071
2. Wax et al., *J Clin Ultrasound.* 2015 Jan;43(1):1-6
3. Schmid, M et al., *Fetal Diagn.* Ther. 2017; Published online https://doi.org/10.1159/000484317
4. Stokowski et al., *Prenat Diagn.* 2015 Oct; Published online https://doi.org/10.1002/pd.4686
5. McDonald-McGinn et al., GeneReviews(R) [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2018.
6. Grati et al., *Prenat Diagn.* 2015 Aug; 35(8): 801-9
7. Bassett et al., *J Pediatr.* 2011 Aug;159(2):332-9.e1
8. McDonald-McGinn et al. *Genet Couns.* 1999;10(1):11-24
9. Wapneret al., *Am J Obstet Gynecol.* 2015 Mar;212(3):332.e1-9
10. McDonald-McGinn et al. *Genet Med.* 2001 Jan-Feb;3(1):23-9


**For further information, including scientific and peer-reviewed publications, please refer to our website, www.sonicgenetics.com.au/nipt or call us on 1800 010 447**


14 Giffnock Avenue, Macquarie Park, NSW 2113, Australia
**T:** 1800 010 447 | **E:** info@sonicgenetics.com.au
**www.dhm.com.au**





Printed March 2018

DHMSG-22q-Dr-A4-V1-2018-D00047