

The Annual Report on Prenatal Diagnostic Testing in Victoria, 2021

Reproductive Epidemiology group

Genetics theme

Murdoch Children's Research institute



CONTENTS

About this report	3
Trends in the uptake of prenatal diagnostic procedures	4
Indications for prenatal diagnostic procedures	5
Single gene conditions	6
Overall diagnostic yield	8
Prenatal diagnostic yield by indication	9
Trends in prenatal diagnosis of chromosome conditions	10
Publications from the Victorian Prenatal Diagnosis Data Collection	11

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About this report

This annual report from the **Victorian Prenatal Diagnosis Database (VPDD)** summarises the results of fetal chromosome testing in Victoria during 2021. Victoria has approximately 76,000 confinements annually, and a median maternal age of 31.6 years (Australian Bureau of Statistics; <https://www.abs.gov.au/>).

The VPDD has been collecting state-wide data on prenatal diagnostic procedures since 1976. We acknowledge our long-standing collaborators - the Victorian Clinical Genetics Service (VCGS) and Monash Pathology (current contributors), Melbourne Pathology and Australian Clinical Labs (former contributors).

All amniocentesis and chorionic villus sampling (CVS) results performed prior to 25 weeks' gestation on women living in Victoria are included in the annual report. This gestational age limit was chosen to capture diagnostic testing performed after routine screening for chromosome and fetal structural conditions in the first and second trimester.

The data fields collected for each woman include: maternal age and gestation at the time of testing, type of diagnostic test, indication for testing, chromosome results, and pregnancy plurality. A single record is created for twin pregnancies or women who required repeat testing in the same pregnancy.

Definitions

Major chromosome conditions: autosomal trisomies, autosomal monosomies, polyploidy, sex chromosome aneuploidies, pathogenic copy number variants (CNVs), unbalanced rearrangements, gestational trophoblastic disease, and high-level mosaicism.

Minor chromosome conditions: genomic CNVs of uncertain or unknown significance, long continuous stretches of homozygosity (LCSH), uniparental disomy (UPD), confined placental mosaicism (CPM), and balanced rearrangements.

Diagnostic yield: the percentage of women with a major fetal chromosome condition confirmed on diagnostic testing as a proportion of total tests.

Positive non-invasive prenatal testing (NIPT) result: 'increased chance', 'high risk', 'aneuploidy detected' or other result indicating an increased probability of a chromosome condition in the pregnancy.

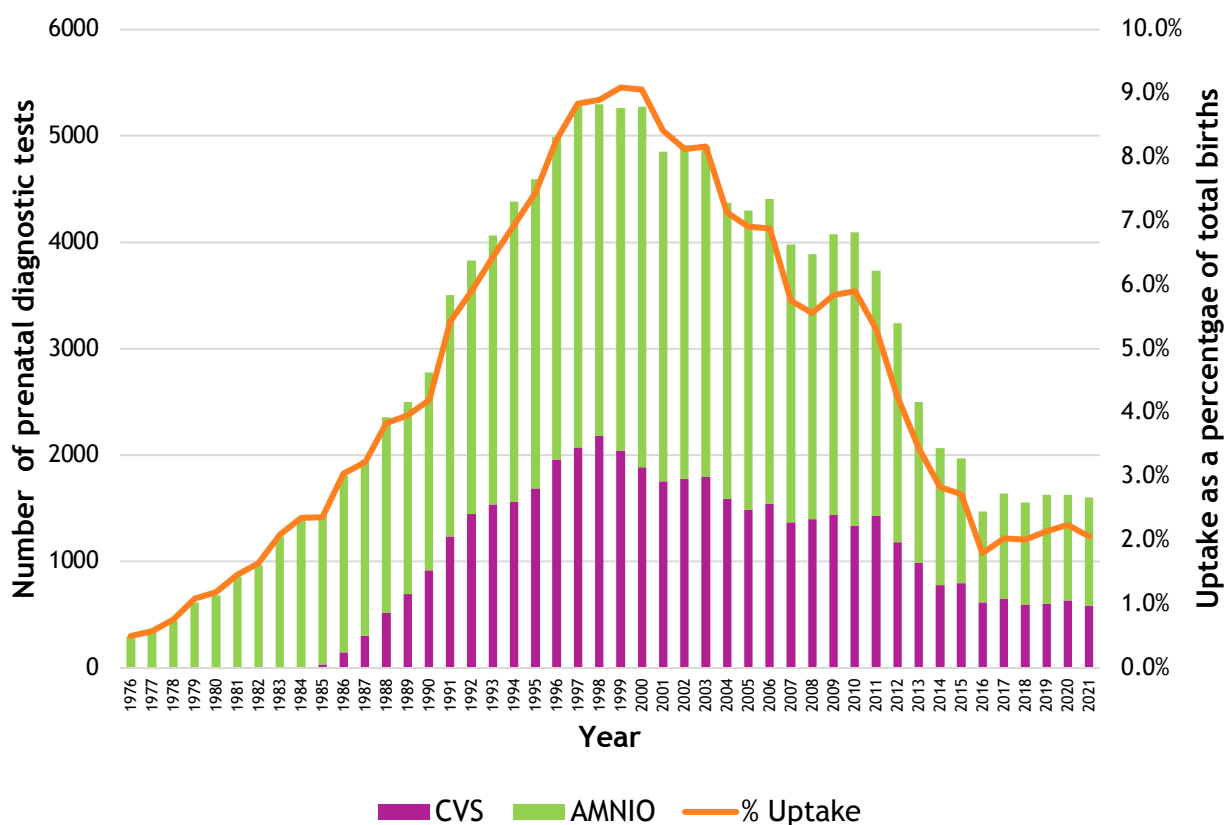
Classification of genomic copy number variants (CNVs): CNVs classified as *pathogenic*, *likely pathogenic*, *uncertain*, or *unknown significance*, *likely benign*, or *benign* according to the clinical laboratory interpretation, which is guided by the American College of Medical Genetics standards and guidelines for interpretation and reporting of copy number variants.^{1, 2}

Trends in the uptake of prenatal diagnostic procedures

The annual uptake of prenatal diagnostic procedures is calculated from the number of women who had prenatal diagnostic testing as a percentage of total registered births in Victoria (Australian Bureau of Statistics; <https://www.abs.gov.au/>).

In 2021, 1603 women underwent a prenatal diagnostic procedure before 25 weeks' gestation, representing 2.06% of total births in Victoria. The steep decline in prenatal diagnostic procedures since the peak in 1998 (n=5300) appears to have plateaued since 2016 (Figure 1).

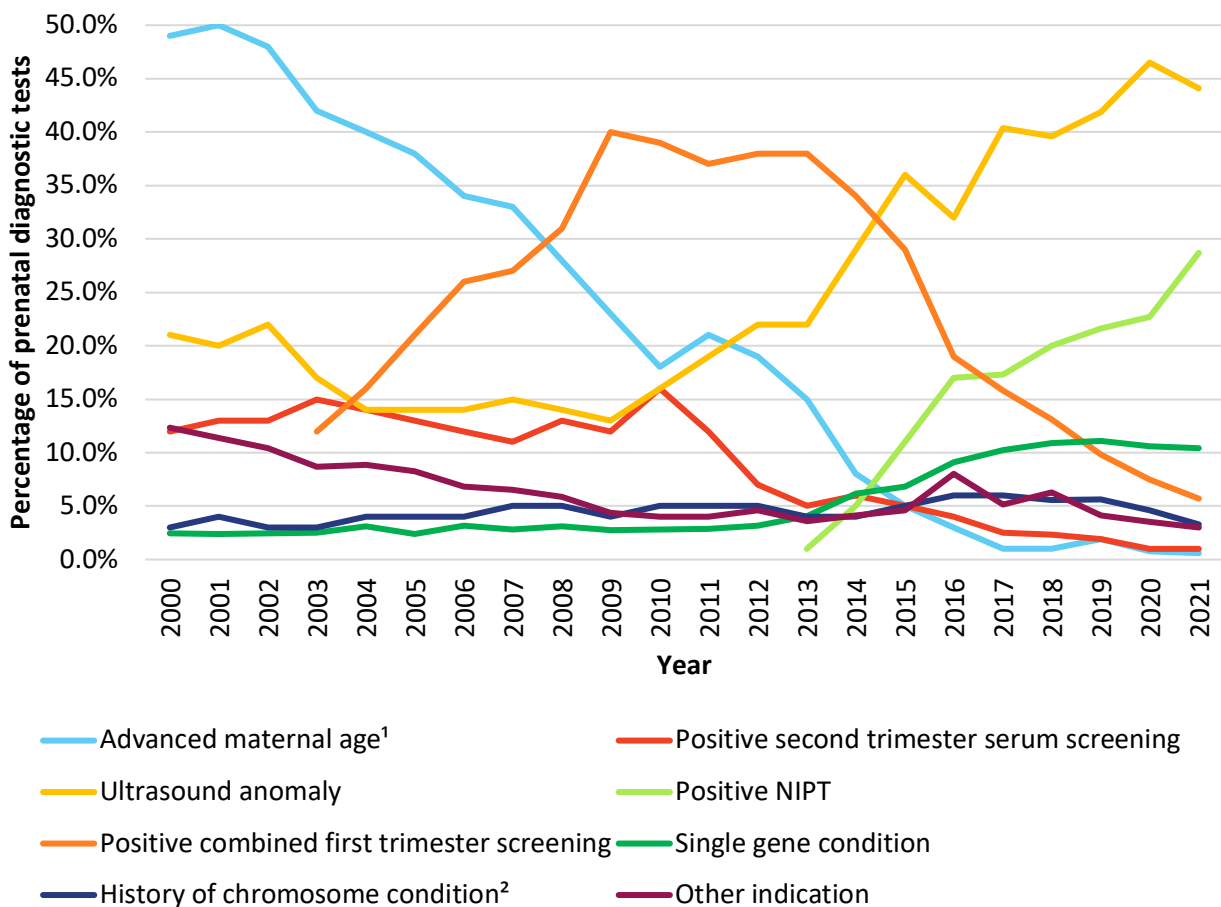
Figure 1. Annual number of prenatal diagnostic tests and uptake as a percentage of total births (1976-2021)



Indications for prenatal diagnostic procedures

Indications for prenatal diagnosis are obtained from the clinical referral information. More than one indication may be recorded. In 2021, 1858 indications were recorded for 1603 diagnostic procedures. The three most common indications for prenatal diagnosis were ultrasound anomaly (44.1%), positive NIPT result (28.7%) and testing for single gene conditions (10.4%) (Figure 2).

Figure 2. Indications for prenatal diagnosis as a percentage of total indications, 2000-2021



¹Maternal age >36 years at estimated due date of delivery.

²History of a chromosomal condition included a parental chromosome condition or previous pregnancy with a chromosomal condition.

Single gene conditions

Prenatal diagnostic testing for a single gene condition has now replaced first trimester combined screening as the third most common indication for a prenatal diagnostic procedure.

In 2021, the five most common conditions for which testing was done were fragile X, thalassaemia, cystic fibrosis, spinal muscular atrophy, and Duchenne muscular dystrophy. Testing for one of these five common single gene conditions has increased from 75 in 2015 to 92 in 2021 (Table 1).

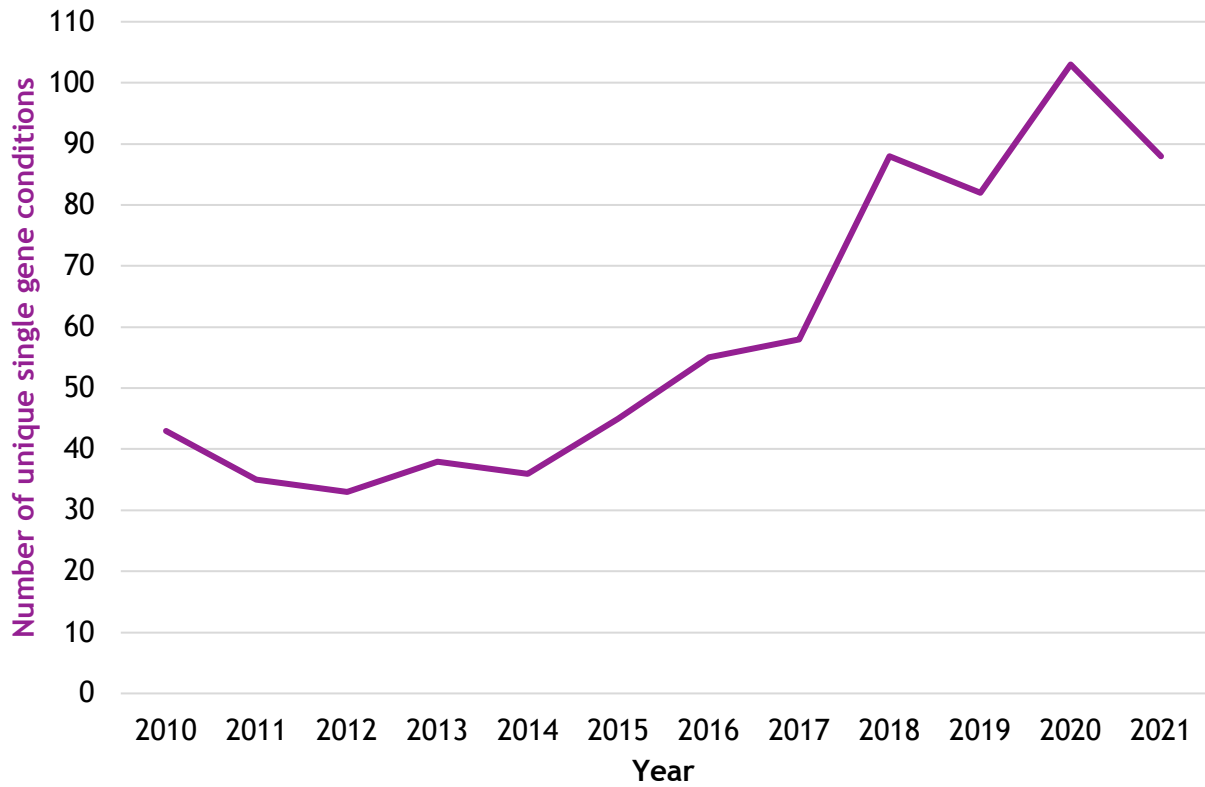
Table 1. Annual frequencies of the top 5 prenatal single gene tests

Single gene conditions	2015	2016	2017	2018	2019	2020	2021
Fragile X	20	21	22	29	33	33	33
Thalassaemia	31	23	28	31	18	28	36
Cystic fibrosis	13	14	23	14	12	21	13
Spinal Muscular atrophy	6	6	5	5	8	3	6
Duchenne Muscular dystrophy	5	4	7	2	5	5	4
Number of unique single gene conditions	45	55	58	88	82	103	88
Total tests for the 5 most common single gene conditions	75	68	85	81	76	90	92
Total number of single gene tests	135	130	165	178	196	207	193

Results from single gene testing are not available from our data collection.

In 2021, 193 prenatal diagnostic procedures were performed to test for 88 different single gene conditions. As a proportion of unique single gene conditions, the group of five most common single gene conditions has declined from 11.6% (5/43) in 2010 to 5.7% (5/88) in 2021 ($p=0.005$) (Figure 3).

Figure 3. Annual number of unique single gene conditions for which prenatal diagnosis was performed



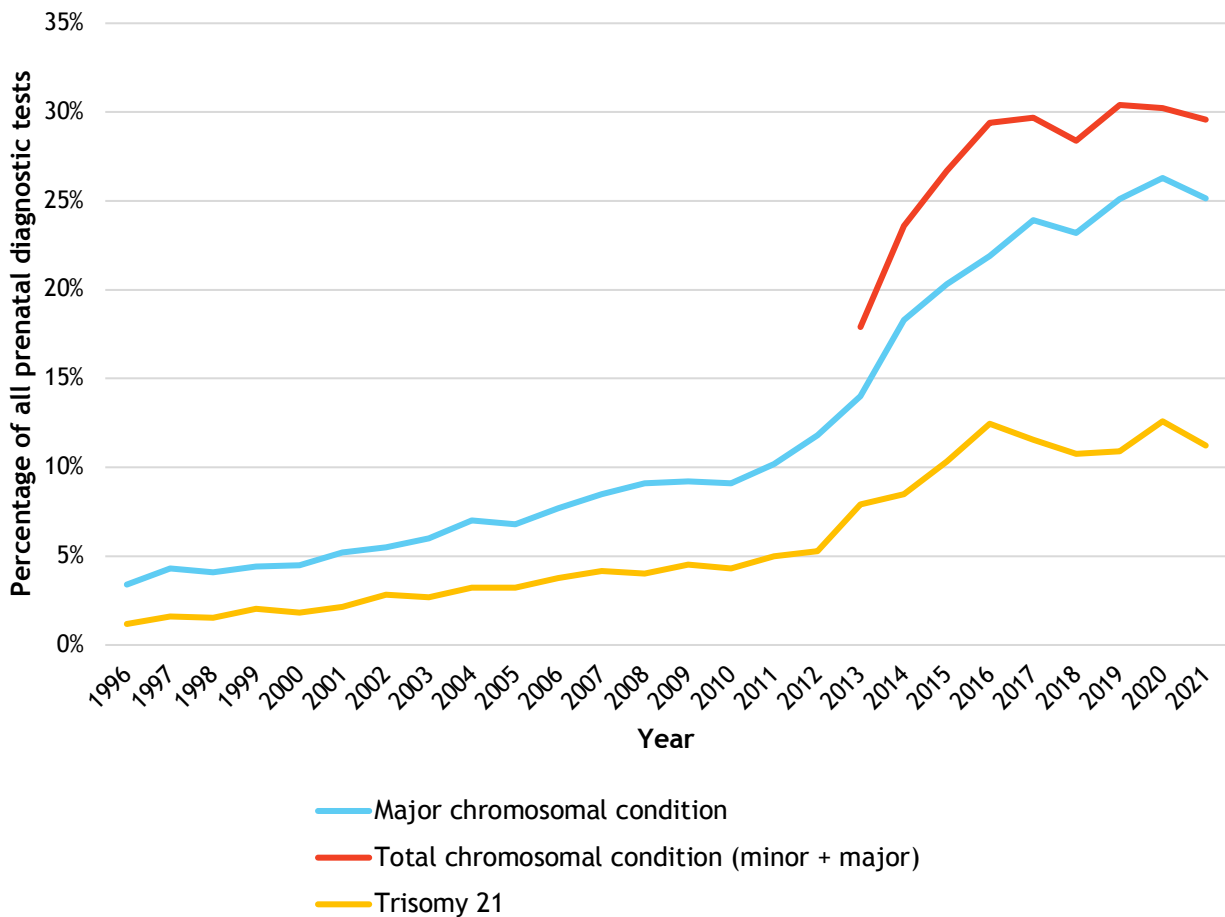
Overall diagnostic yield

Most samples were analysed with chromosomal microarray (93.1%), regardless of the indication for testing.

The diagnostic yield is calculated from the number of major chromosomal conditions confirmed on diagnostic testing as a proportion of total tests. In 2021, 403 (25.1%) prenatal tests detected a major chromosome condition. The total diagnostic yield including major and minor chromosome conditions was 29.6% (Figure 4).

Trisomy 21 remained the most common major chromosome condition detected on prenatal diagnosis in 2021 (n=180). There were 52 pathogenic CNVs, the most common of which was the 22q11.2 deletion syndrome (n=4). The number of genomic variants of unknown or uncertain significance detected by CMA was 43 (2.7%).

Figure 4. Diagnostic yield of prenatal diagnostic tests by year

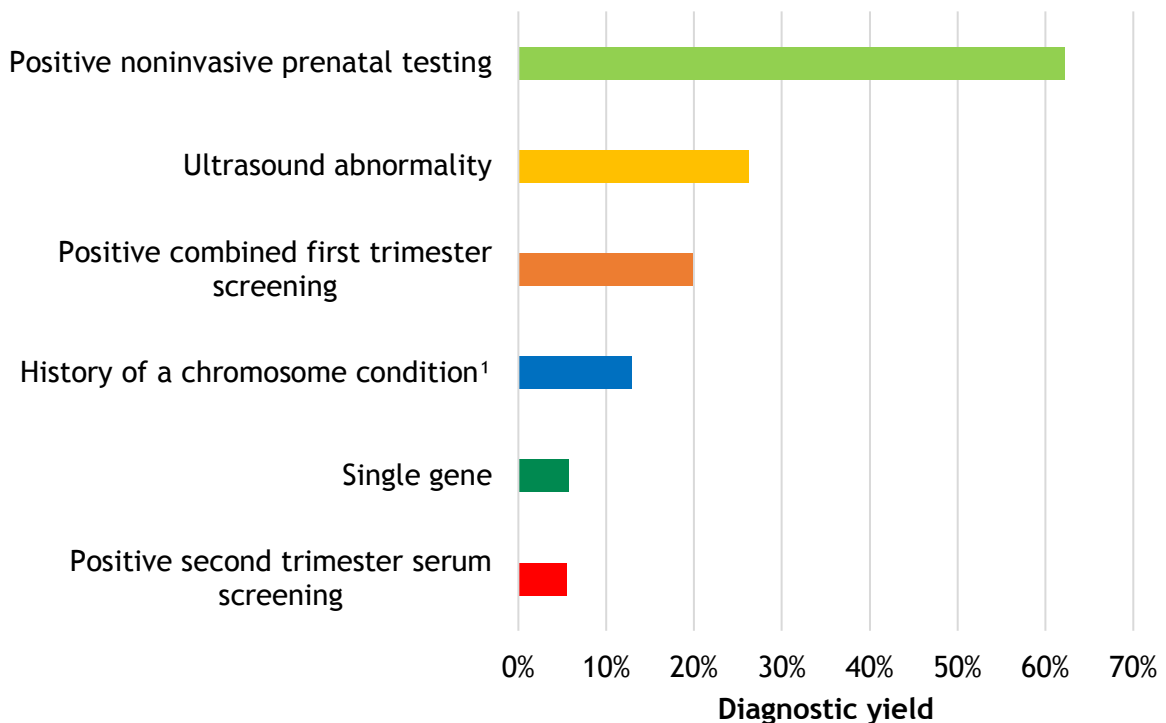


The most common indication for testing among pregnancies with Trisomy 21 in 2021 was a positive NIPT result (65.5%).

Prenatal diagnostic yield by indication

Diagnostic yield for a major or minor chromosome condition varied according to clinical indication for testing. In 2021, the yield was highest for women undergoing testing for a positive NIPT result (62.2%), followed by an ultrasound abnormality (26.2%), combined first trimester screening (19.8%), history of a chromosome condition (12.9%), a single gene condition (5.9%), and second trimester serum screening (5.6%) (Figure 5).

Figure 5. Diagnostic yield by indication for testing



¹History of a chromosomal condition included a parental chromosome condition or previous pregnancy with a chromosomal condition.

Trends in prenatal diagnosis of chromosome conditions

The annual number of major chromosome conditions has not changed markedly for many years, despite the decline in overall prenatal diagnostic testing numbers. Table 2 shows the details of all chromosome result for the last nine years.

Table 2. Prenatal diagnosis results 2013-2021

Result	2013	2014	2015	2016	2017	2018	2019	2020	2021
Normal/benign variant	2014	1548	1427	1037	1152	1104	1130	1138	1129
Total major chromosome conditions	395	369	394	363	394	368	409	428	403
<i>Trisomy 21</i>	198	176	204	183	190	167	177	205	180
<i>Trisomy 18</i>	61	49	42	44	55	60	61	54	41
<i>Trisomy 13</i>	30	21	14	25	18	19	17	20	11
<i>Other autosomal aneuploidy, polyploidy</i>	18	22	22	9	14	5	10	16	12
<i>Sex chromosome aneuploidy</i>	31	33	28	39	52	41	52	61	76
<i>Pathogenic copy number variation</i>	25	39	45	29	44	59	54	38	52
<i>Other conditions¹</i>	32	29	43	34	21	15	38	29	31
Variations of unknown/uncertain significance	97	108	126	68	93	81	75	60	43
Total diagnostic tests	2500	2046	1957	1468	1643	1553	1614	1628	1603

¹Including unbalanced rearrangements and high level mosaics

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