murdoch children's research institute

The Annual Report on Prenatal Diagnostic Testing in Victoria, 2019

Reproductive Epidemiology group

Genetics theme

Murdoch Children's Research institute

Contents

This report is produced by the **Reproductive Epidemiology group** in the Genetics theme at the MCRI. For more information about us, go to our page at *https://www.mcri.edu.au/reproductiveepidemiology*

How to cite this report: Pynaker C, Loughry L, Hui L, Halliday J. *Annual report on Prenatal Diagnosis in Victoria 2019*, The Victorian Prenatal Diagnosis Database, Murdoch Children's Research Institute 2020. doi: 10.25374/MCRI.14347436.

Contact us

If you wish to be included in our distribution list, contact Cecilia Pynaker at cecilia.pynaker@mcri.edu.au

For other enquiries, please contact A/Prof Lisa Hui at lisa.hui@mcri.edu.au or Prof Jane Halliday at janehalliday.h@mcri.edu.au

About this report

This annual report from the **Victorian Prenatal Diagnosis Database** (VPDD) summarises the results of fetal chromosome testing in Victoria during 2019. Victoria has approximately 76,111 confinements annually, and a median maternal age of 32 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 Medical Centre (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 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.

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

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

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

Technical notes

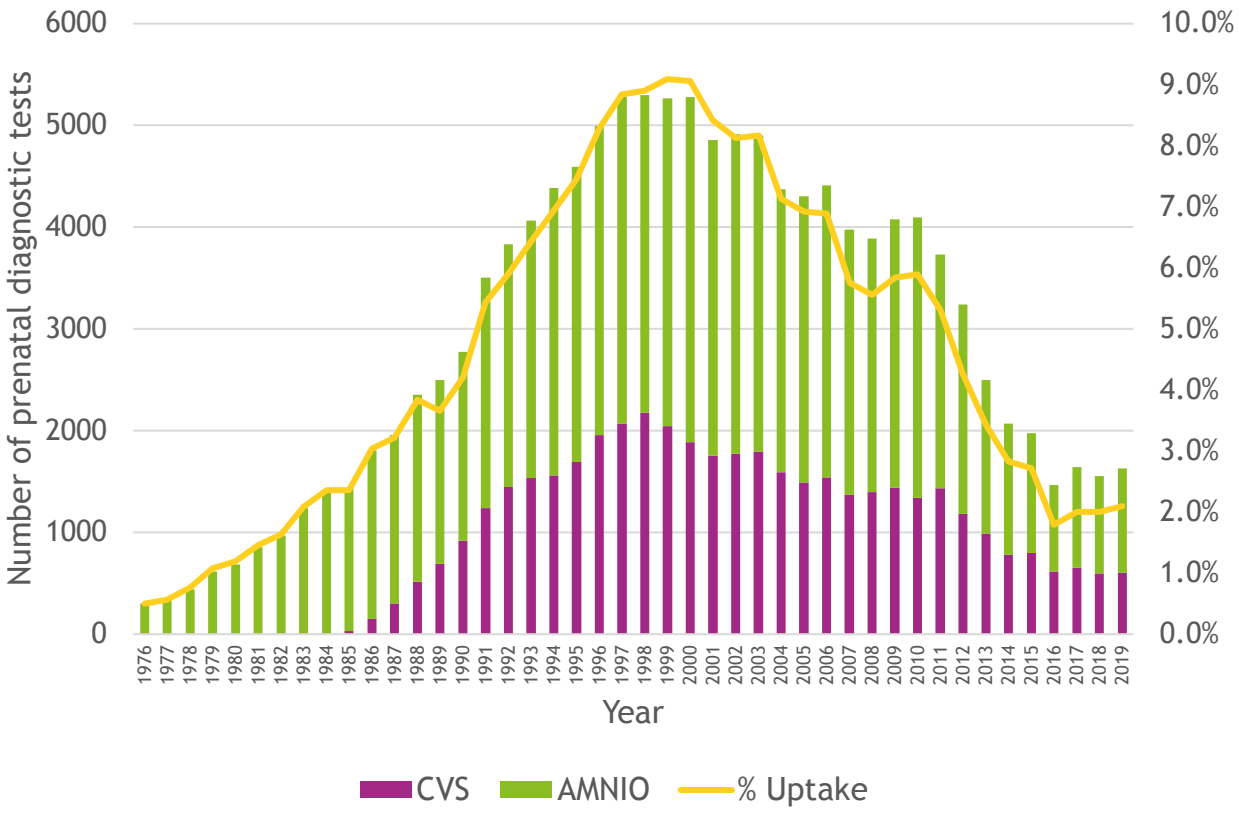
Ethics approval for this study was provided by the Royal Children's Hospital (RCH) Human Research Ethics Committee (HREC) on 17 December 2020 (Ref. No. 31135) and Monash Health local governance authorisation on 17 December 2020 (Ref. No. SSA/42279/RCHM-2020).

Funding: The following institutions have contributed salary support to the work of the VPDD: National Health and Medical Research Council (NHMRC), Medical Research Future Fund (MRFF), Murdoch Children's Research Institute (MCRI) and the Victorian Department of Health.

Trends in the uptake of prenatal diagnostic procedures

In 2019, 1614 women < 25 weeks' gestation underwent a prenatal diagnostic procedure, representing 2.1% 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.

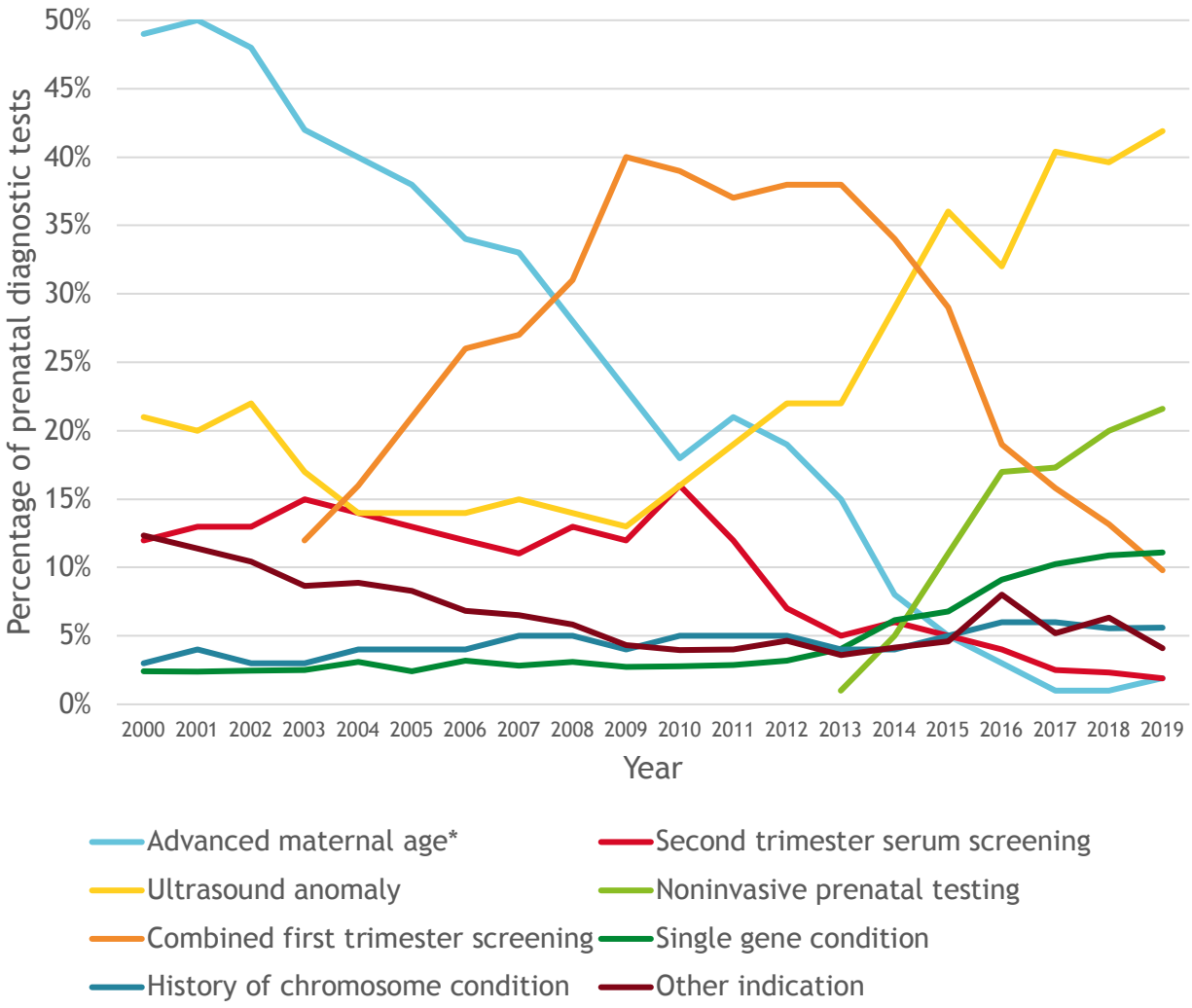
Figure 1. Annual number of prenatal diagnostic tests and uptake as a percentage of total births (1976-2019)



Indications for prenatal diagnostic procedures

Indications for prenatal diagnosis are obtained from the clinical referral information. More than one indication may be recorded. In 2019, 1628 indications were recorded for 1614 diagnostic procedures. The three most common indications for prenatal diagnosis were ultrasound abnormality (41.9%), positive NIPT result (21.6%) and testing for single gene conditions (11.1%).

Figure 2. Indications for prenatal diagnosis as a percentage of total tests



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

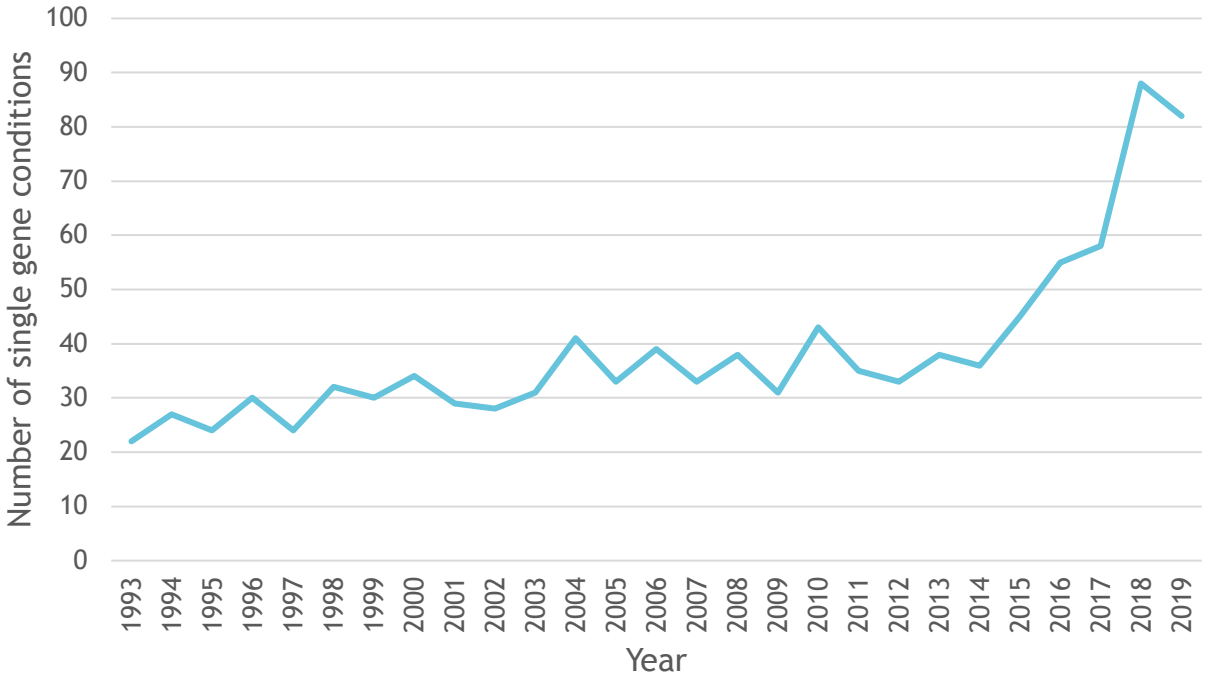
Single gene conditions

Although the number of prenatal diagnostic procedures for the most common single gene conditions has remained relatively consistent over the past 6 years, the number of conditions for which testing is provided has increased from 36 in 2014 to 82 in 2019.

Table 1. Annual tests for the most common single gene conditions

Single gene conditions	2014	2015	2016	2017	2018	2019
Fragile X	22	20	21	22	29	33
Thalassaemia	28	31	23	28	31	18
Cystic fibrosis	18	13	14	23	14	12
Spinal Muscular atrophy	5	6	6	5	5	8

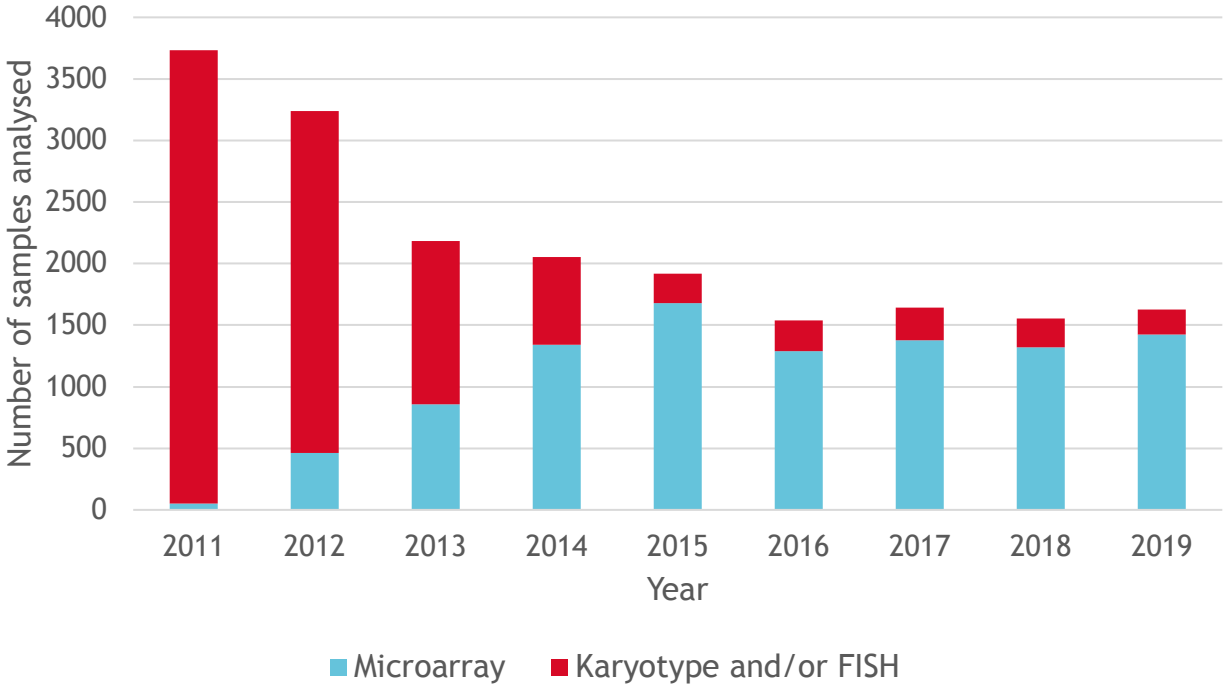
Figure 3. Annual number of single gene conditions for which prenatal diagnosis has been performed



Chromosome analysis

In 2019, the vast majority of samples were analysed with chromosomal microarray (87%), regardless of the indication for testing.

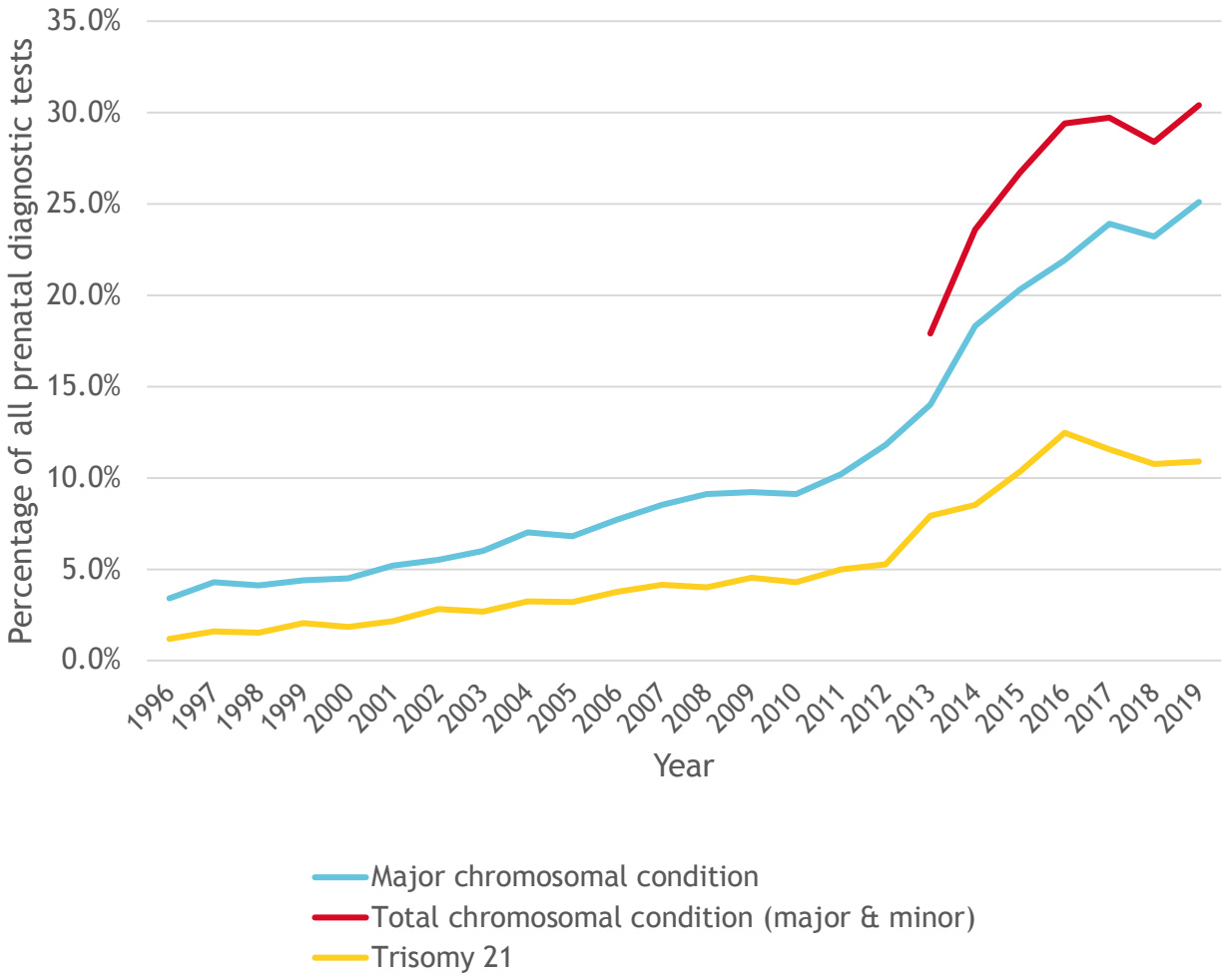
Figure 4. Number of prenatal samples by analysis type, 2011-2019



Overall diagnostic yield

In 2019, 409 (25.1%) of prenatal tests detected a major chromosome condition (aneuploidy, unbalanced rearrangements, polyploidy, uniparental disomy, mosaic aneuploidy, and pathogenic copy number variants (CNVs)). Trisomy 21 remains the most common major chromosome condition detected on prenatal diagnosis. There were 54 pathogenic CNVs, the most common of which was the 22q11.2 deletion syndrome (n=12). In 2019, the number of genomic variants of unknown or uncertain significance detected by CMA was 75 (4.6%). The total diagnostic yield (including major and minor chromosome conditions) was 30.4%.

Figure 5. Diagnostic yield of prenatal diagnostic tests by year

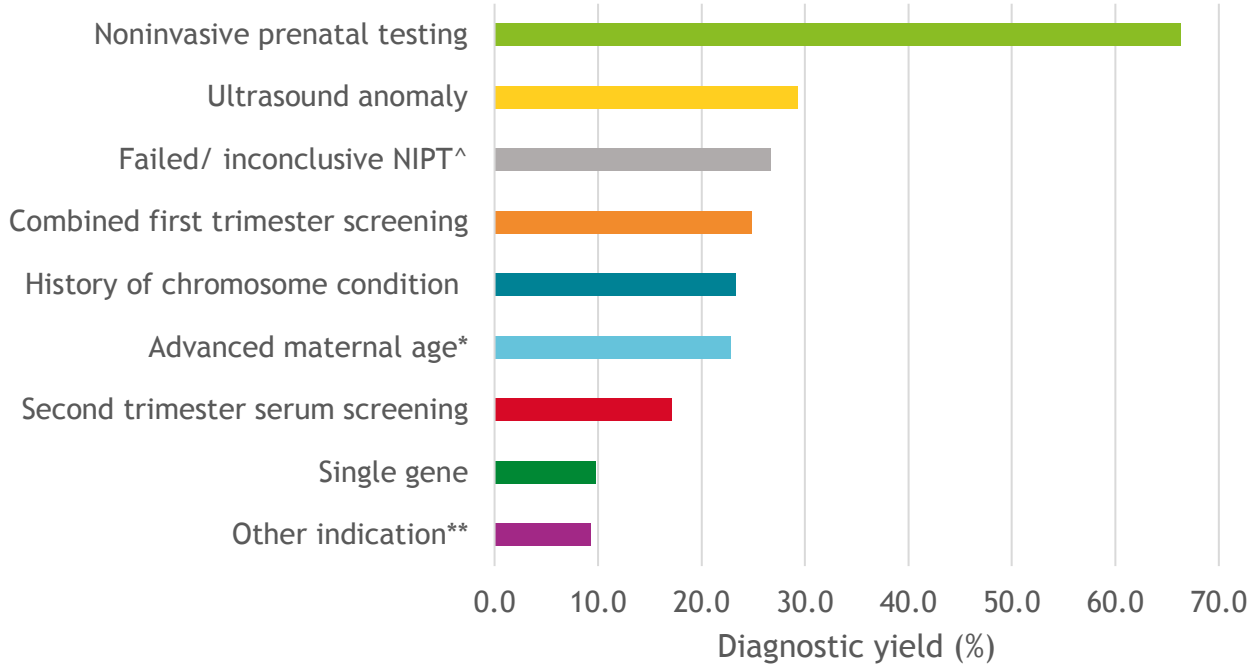


The most common indication for testing among pregnancies with trisomy 21 was a positive NIPT result.

Diagnostic yield by indication

The diagnostic yield is the percentage of women with a major chromosome condition confirmed on diagnostic testing as a proportion of total tests. Diagnostic yield varied according to clinical indication for testing. In 2019, the yield was highest for women undergoing testing for a positive NIPT result (66%), followed by ultrasound abnormality (29%), failed/inconclusive NIPT (27%) and positive first trimester combined screening result (25%).

Figure 6. Diagnostic yield by indication for testing



^8/30 confirmed chromosome conditions from 9 inconclusive NIPT indications and 21 failed NIPT.

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

**Other indication included: testing for diagnostic confirmation following preimplantation genetic diagnosis, maternal request, and opportunistic chromosome testing following amniocentesis for other indications (congenital infection, twin-twin transfusion syndrome, selective reduction, therapeutic amnioreduction).

Prenatal diagnosis of chromosome conditions 2013-2019

Over the past 7 years the annual number of major chromosome conditions has remained relatively consistent, despite the decline in overall prenatal diagnostic testing numbers (table 2). Trisomy 21 remains the most common condition detected, comprising just under half (43%) of all major chromosome conditions.

Table 2. Prenatal diagnosis results 2013-2019

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

*Including unbalanced rearrangements, mosaics, uniparental disomy.

Publications from the Victorian Prenatal Diagnosis Data Collection

- Lindquist A, Hui L, Poulton A, Kluckow E, Hutchinson B, Pertile MD, Bonacquisto L, Gugasyan L, Kulkarni A, Harraway J, Howden A, McCoy R, Da Silva Costa F, Menezes M, Palma-Dias R, Nisbet D, Martin N, Bethune M, Poulakis Z, Halliday J. State-wide utilization and performance of traditional and cell-free DNA-based prenatal testing pathways: the Victorian Perinatal Record Linkage (PeRL) study. Ultrasound Obstet Gynecol. 2020 Aug;56(2):215-224. doi: 10.1002/uog.21899.
- Hui L, Poulton A, Kluckow E, Lindquist A, Hutchinson B, Pertile MD, Bonacquisto L, Gugasyan L, Kulkarni A, Harraway J, Howden A, McCoy R, Costa FDS, Menezes M, Palma-Dias R, Nisbet D, Martin N, Bethune M, Poulakis Z, Halliday J. A minimum estimate of the prevalence of 22q11 deletion syndrome and other chromosome abnormalities in a combined prenatal and postnatal cohort. Hum Reprod. 2020 Mar 27;35(3):694-704. doi: 10.1093/humrep/dez286.
- Kluckow E, Halliday J, Poulton A, Lindquist A, Hutchinson B, Bethune M, Bonacquisto L, Da Silva Costa F, Gugasyan L, Harraway J, Howden A, Kulkarni A, Martin N, McCoy R, Menezes M, Nisbet D, Palma-Dias R, Pertile MD, Poulakis Z, Hui L. Association between timing of diagnosis of trisomy 21, 18, and 13 and maternal socio-economic status in Victoria, Australia: A population-based cohort study from 2015 to 2016. Prenat Diagn. 2019 Dec;39(13):1254-1261. doi: 10.1002/pd.5577.
- Lostchuck E, Hui L. Should second-trimester hypoplastic nasal bone be sole indication for diagnostic testing with chromosomal microarray analysis? Ultrasound Obstet Gynecol. 2019 Jun;53(6):848-850. doi: 10.1002/uog.20141.
- Lostchuck E, Poulton A, Halliday J, Hui L. Population-based trends in invasive prenatal diagnosis for ultrasound-based indications: two decades of change from 1994 to 2016. Ultrasound Obstet Gynecol. 2019 Apr;53(4):503-511. doi: 10.1002/uog.19107.
- Howard-Bath A, Poulton A, Halliday J, Hui L. Population-based trends in the prenatal diagnosis of sex chromosome aneuploidy before and after non-invasive prenatal testing. Prenat Diagn. 2018 Dec;38(13):1062-1068. doi: 10.1002/pd.5363.
- Poulton A, Lewis S, Hui L, Halliday JL. Prenatal and preimplantation genetic diagnosis for single gene disorders: A population-based study from 1977 to 2016. Prenat Diagn. 2018 Nov;38(12):904-910. doi: 10.1002/pd.5352.
- Hui L, Norton M. What is the real "price" of more prenatal screening and fewer diagnostic procedures? Costs and trade-offs in the genomic era. Prenat Diagn. 2018 Mar;38(4):246-249. doi: 10.1002/pd.5228. Epub 2018 Feb 21.
- Hui L, Barclay J, Poulton A, Hutchinson B, Halliday JL. Prenatal diagnosis and socioeconomic status in the non-invasive prenatal testing era: A population-based study. Aust N Z J Obstet Gynaecol. 2018 Aug;58(4):404-410. doi: 10.1111/ajo.12778.
- Lindquist A, Poulton A, Halliday J, Hui L. Prenatal diagnostic testing and atypical chromosome abnormalities following combined first-trimester screening: implications for contingent models of non-invasive prenatal testing. Ultrasound Obstet Gynecol. 2018 Apr;51(4):487-492. doi: 10.1002/uog.18979.
- Hui L, Hutchinson B, Poulton A, Halliday J. Population-based impact of noninvasive prenatal screening on screening and diagnostic testing for fetal aneuploidy. Genet Med. 2017 Dec;19(12):1338-1345. doi: 10.1038/gim.2017.55.

- Hui L, Muggli EE, Halliday JL. Population-based trends in prenatal screening and diagnosis for aneuploidy: a retrospective analysis of 38 years of state-wide data. BJOG. 2016 Jan;123(1):90-7. doi: 10.1111/1471-0528.13488.
- Susman MR, Amor DJ, Muggli E, Jaques AM, Halliday J. Using population-based data to predict the impact of introducing noninvasive prenatal diagnosis for Down syndrome. Genet Med. 2010 May;12(5):298-303. doi: 10.1097/GIM.0b013e3181d5d022.
- Jaques AM, Collins VR, Muggli EE, Amor DJ, Francis I, Sheffield LJ, Halliday JL. Uptake of prenatal diagnostic testing and the effectiveness of prenatal screening for Down syndrome. Prenat Diagn. 2010 Jun;30(6):522-30. doi: 10.1002/pd.2509.
- Muggli EE, Collins VR, Halliday JL. Mapping uptake of prenatal diagnosis for Down syndrome and other chromosome abnormalities across Victoria, Australia. Aust N Z J Obstet Gynaecol. 2006 Dec;46(6):492-500. doi: 10.1111/j.1479-828X.2006.00648.x.
- Muggli EE, McCloskey D, Halliday JL. Health behaviour modelling for prenatal diagnosis in Australia: a geodemographic framework for health service utilisation and policy development. BMC Health Serv Res. 2006 Sep 1;6:109. doi: 10.1186/1472-6963-6-109.
- Muggli EE, Halliday JL. Prenatal diagnostic testing and Down Syndrome in Victoria 1992--2002. Aust N Z J Public Health. 2004 Oct;28(5):465-70. doi: 10.1111/j.1467-842x.2004.tb00029.x.
- Collins VR, Webley C, Sheffield LJ, Halliday JL. Fetal outcome and maternal morbidity after early amniocentesis. Prenat Diagn. 1998 Aug;18(8):767-72.
- Halliday J, Lumley J, Watson L. Comparison of women who do and do not have amniocentesis or chorionic villus sampling. Lancet. 1995 Mar 18;345(8951):704-9. doi: 10.1016/s0140-6736(95)90872-2.
- Halliday JL, Watson LF, Lumley J, Danks DM, Sheffield LJ. New estimates of Down syndrome risks at chorionic villus sampling, amniocentesis, and livebirth in women of advanced maternal age from a uniquely defined population. Prenat Diagn. 1995 May;15(5):455-65. doi: 10.1002/pd.1970150509.
- Halliday JL, Lumley J, Sheffield LJ, Robinson HP, Renou P, Carlin JB. Importance of complete follow-up of spontaneous fetal loss after amniocentesis and chorion villus sampling [published correction appears in Lancet 1992 Nov 14;340(8829):1236]. Lancet. 1992;340(8824):886-890.