

REPORT ON
PRENATAL DIAGNOSTIC TESTING
IN VICTORIA 2006

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**The Consultative Council
on Obstetric and Paediatric
Mortality and Morbidity**

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1. KEY FINDINGS

- 1** The total number of prenatal diagnostic tests done in 2006 was 4408. After a substantial decline in the number of all tests done in Victoria since 2000, there was a slight increase in the number of tests in 2006 when compared to the previous year (108 tests more than in 2005).

Pages 9 & 10
- 2** The proportion of older pregnant women who have a prenatal diagnostic test has declined from almost 80% in 1996 to 46% in 2006 (40 years and over) and from 60% in 1996 to 22% in 2006 (37-39 years). Over 2% of pregnant women aged less than 35 years now have a test.

Page 12
- 3** Reasons for testing in 2006 were similar to those in 2005 and 2004, although tests done for advanced maternal age as the only indication for testing are slightly decreasing in number and proportion each year (41% in 2004 and 38% in 2005, compared with 35% in 2006). At the same time, the proportion of tests done because of an abnormal screening test increases slightly each year (44% in 2004, 47% in 2005 and 51% in 2006).

Pages 13 & 14
- 4** 646 women had prenatal diagnosis following an abnormal ultrasound, either suspected fetal anomaly on routine ultrasound or increased nuchal thickening (when not as part of first trimester combined screening). This represents 14.7% of all tests in 2006. 75% of these women were under 37 years of age.

Pages 15 & 16
- 5** 42% of CVS, and 13% of AMN following an abnormal ultrasound were found to have a major chromosomal abnormality. This detection rate is similar to 2005 and 2004. 25% of tests prompted by increased nuchal thickness were found to have a chromosomal abnormality, compared with 21% after another ultrasound abnormality.

Pages 25-27
- 6** Using information from Genetic Health Services Victoria, we estimate that there were 43,811 pregnant women (64.7%) who had maternal serum screening (MSS, either first trimester combined or second trimester serum) in 2006. The number tested for an increased risk MSS result corresponds to a diagnostic follow-up rate of 3.8%.

Page 17

- 7** 1672 women had prenatal diagnosis for an increased risk maternal serum screen (MSS) compared with just over 500 in 1999 and 1443 in 2005. There were more diagnostic tests prompted by first trimester combined MSS (n=1156) than by second trimester MSS (n=516) **Pages 17 & 18**
- 8** Two thirds of women having prenatal diagnosis following second trimester MSS were under 37 years of age (67%) whereas women having prenatal diagnosis following a first trimester combined MSS test were equally distributed across both age groups. The maternal age distribution for these tests has been consistent since 2003. **Pages 17 & 18**
- 9** A fetal chromosome abnormality was detected in 3.9% of pregnancies tested for an increased risk second trimester MSS, and in 10.7% of tests for increased risk first trimester combined MSS. Trisomies accounted for 75.0% and 75.8% of these abnormalities in the respective tests. **Pages 28 & 29**
- 10** The number of tests done for indications outside the HGSA/RANZCOG recommendations has decreased markedly since 1996, with 286 tests done in 2006 (6.5% of all tests). This decline is explained by the increased utilisation of screening tests in women under 37 years of age. Indications outside recommendations decreased mainly in women aged 35-36 years. **Page 22**
- 11** The number of CVS or AMN done to test for single gene disorders has been steady over the last seven years, with around 100-120 procedures done each year for this reason (2.7% of all tests in 2006). Thalassaemia and cystic fibrosis and Fragile X were the most common conditions tested for, and in 2006, Achondroplasia. **Pages 19 & 20**
- 12** Of all Victorian women who had CVS or AMN in 2006, 90.8% had a fetus with a normal karyotype and 7.7% of tested pregnancies were found to have a major fetal karyotype abnormality (13.0% of CVS and 4.8% of AMN). The detection rate of abnormalities by both diagnostic tests has doubled since prenatal screening became available. **Page 23**
- 13** Trisomy 21 accounted for just under half of all abnormal fetal karyotypes (49%), with 166 diagnosed prenatally in 2006. For the majority of tests with a diagnosis of Trisomy 21, the major indication was an increased risk screening test result (82.5%). First trimester combined MSS accounted for **Pages 33-35**

47.0% of diagnoses, second trimester MSS for 7.8%, second trimester routine ultrasound for 10.8%, while increased nuchal thickening alone and maternal age alone were associated with 16.9% and 16.3% of diagnoses respectively.

- 14** Fluorescent In Situ Hybridisation (FISH) for aneuploidy was undertaken in over 80% of tests where the indication was abnormal ultrasound or increased nuchal thickness. FISH was also requested in 77% of tests after increased risk first trimester combined screening.

2. INTRODUCTION

Chorionic villus sampling (CVS) and amniocentesis (AMN) are diagnostic procedures to detect fetal chromosomal abnormalities and are offered in Victoria as an option to pregnant women who are 37 years of age and over. In addition, testing is made available if the indication is other than age but falls within the Prenatal Diagnosis Policy (revised, March, 2004) of the Human Genetics Society of Australasia (HGSA) and the Royal Australian and New Zealand College of Obstetricians and Gynaecologists (RANZCOG) (available at www.hgsa.com.au). For example, an abnormal ultrasound or increased risk maternal serum screen would be such an indication.

There are four Victorian cytogenetics laboratories analysing prenatal diagnostic samples. These are located at the Monash Medical Centre, Genetic Health Services Victoria and at the private laboratories of Melbourne Pathology and Cytogenetic Services.

This report provides information on the uptake and trends of prenatal testing according to the HGSA/RANZCOG recommendations and the numbers and types of chromosomal abnormalities diagnosed.

Prenatal Diagnostic Testing in Victoria is a report compiled annually in collaboration with Public Health Genetics at the Murdoch Childrens Research Institute and the Victorian Perinatal Data Collection Unit, the Department of Human Services. The primary purpose of this document is to report on the utilisation of these tests. The report presents descriptive statistics on the number of tests performed, the indications for testing and the fetal karyotype outcome of tests. Furthermore, by comparing data from the last 17 years, we are able to monitor changes in numbers of tests, reasons given for testing, especially that related to the age of women tested and abnormal fetal karyotype outcomes.

Information on pregnancy outcome for this data set is not routinely collected and would require record linkage to the Victorian Perinatal Data Collection Unit and the Birth Defects Register. This is done for specific projects with appropriate ethics approvals obtained.

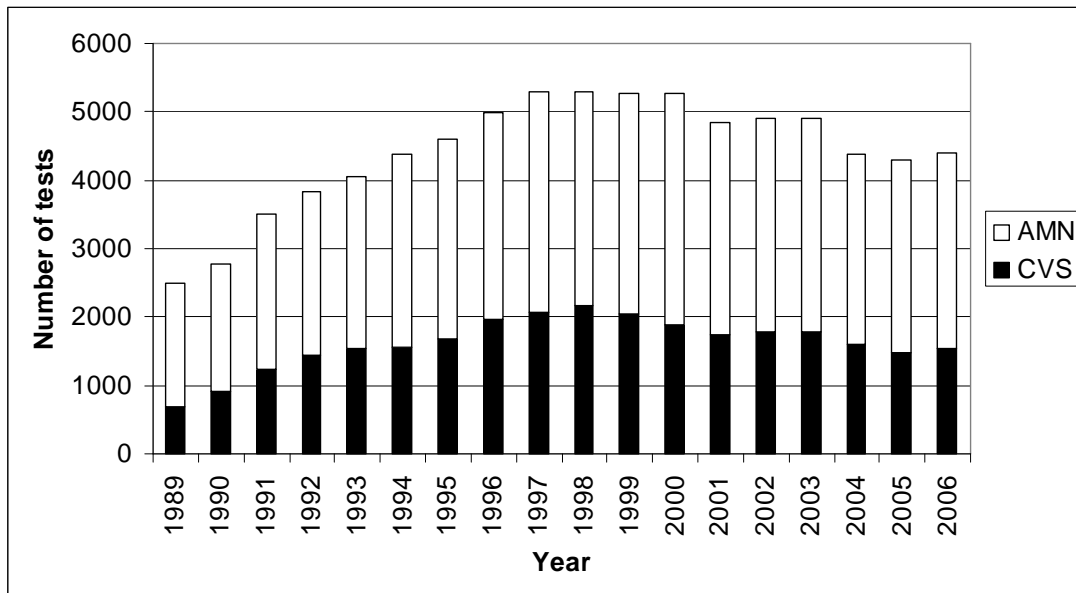
3. UTILISATION OF PRENATAL DIAGNOSTIC TESTS

3.1 NUMBER OF TESTS

The total number of prenatal diagnostic tests analysed by Victorian laboratories in 2006 was 4752. This overall number includes some multiple procedures eg same day AMN and CVS samples, twin or triplet pregnancies – which have been condensed into one record. In addition, there are six fetal blood samples, 263 samples from women living interstate, 25 repeat samples and 52 late gestation tests, which are also included in this number.

In 2006, the actual number of pregnant women residing in Victoria having a test before 25 weeks gestation was 4408: 1542 CVS and 2866 AMN (Figure 1 and Table 1). The body of this report discusses the utilisation, indications and outcomes of these tests on pregnant women residing in Victoria.

Figure 1. Total number of prenatal tests on Victorian women under 25 weeks gestation



The number of prenatal diagnostic tests steadily increased from 1989 to 1998, when the highest number of tests were done (n=5300). After an initial decline in the total number of Victorian women having prenatal diagnosis by CVS or AMN

in 2001, we observed the largest decrease so far in the number of tests in 2004 with 526 fewer samples than the previous year. The number of tests has remained relatively stable since then. Table 1 shows that there has been a fall in both CVS and AMN.

Table 1. Number and proportion of Victorian CVS and amniocenteses under 25 weeks gestation

Year	Total	CVS	% total	AMN	% total
1989	2500	694	28%	1806	72%
1990	2777	916	33%	1861	67%
1991	3505	1239	35%	2266	65%
1992	3831	1449	38%	2383	62%
1993	4061	1537	38%	2524	62%
1994	4382	1559	36%	2823	64%
1995	4592	1689	37%	2903	63%
1996	4993	1957	39%	3036	61%
1997	5283	2072	39%	3211	61%
1998	5300	2179	41%	3121	59%
1999	5263	2043	39%	3220	61%
2000	5276	1887	36%	3389	64%
2001	4854	1753	36%	3101	64%
2002	4914	1776	36%	3138	64%
2003	4898	1793	37%	3105	63%
2004	4372	1593	36%	2779	64%
2005	4300	1489	35%	2811	65%
2006	4408	1542	36%	2866	64%

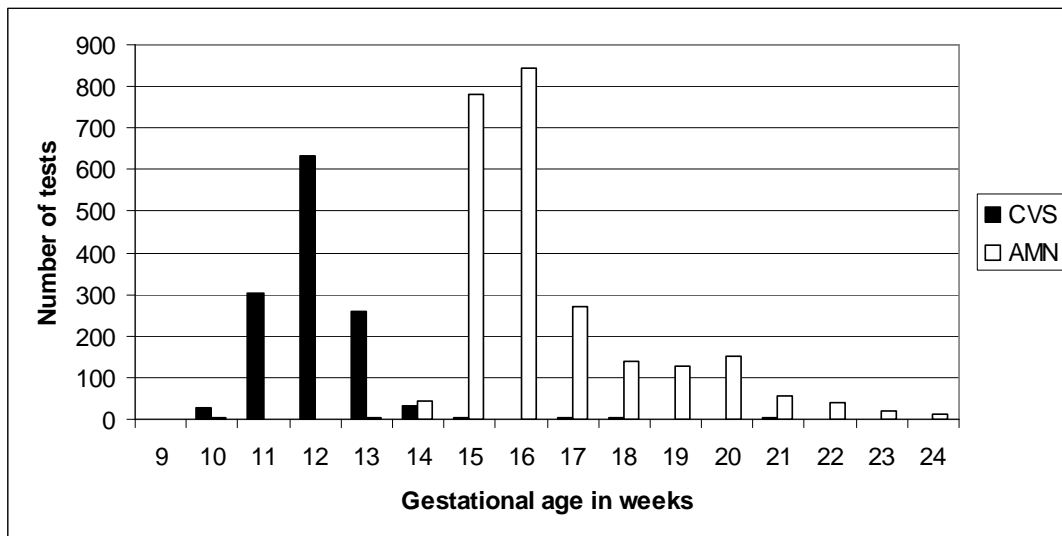
3.2 GESTATIONAL AGE < 25 WEEKS

Figure 2 shows the distribution of recorded gestational ages for CVS and AMN for Victorian women under 25 weeks of gestation, excluding 636 records with missing data on gestation (14%).

The gestational ages used in Figure 2 were those recorded at the time of the procedure, usually estimated by ultrasound.

For CVS the recorded gestational ages ranged from 9-22 weeks with a median of 12 weeks when 50% of these tests were performed. For AMN, the reported gestational ages ranged from 10-24 weeks with a median of 16 weeks when 34% of these tests were performed.

Figure 2. CVS and AMN by recorded gestation in weeks for Victorian women under 25 weeks of gestation



We have included the 636 records with missing gestational ages in the main body of the report, assuming the diagnostic test was done before 25 weeks of gestation.

3.3 ANNUAL UPTAKE RATES BY MATERNAL AGE

At the time of writing, the final 2006 birth file for Victoria from the Perinatal Data Collection Unit (PDCU), the Department of Human Services, was not available. We present annual uptake rates of prenatal diagnostic testing by maternal age group using an **interim** file of Victorian 2006 confinements, which is not expected to change much (Table 2).

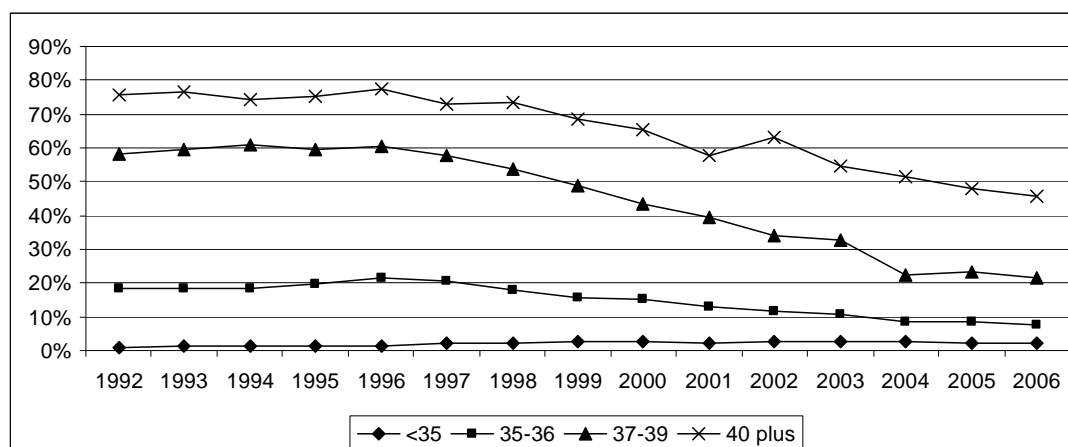
6.5% of pregnant Victorian women had a prenatal test in 2006. The overall proportion of women having a test has declined by one percent since 1998, and a further 1.4% since 2002. This decline is due to older women not having testing anymore.

Uptake of prenatal diagnosis by women 35 years and older continues to decline. It fell from 78% in 1996 to 46% in 2006 in the oldest age group, from 60% to 22% in the 37-39 year olds and from 21% to 8% in women aged 35-36. Meanwhile, the overall proportion of tests in women under 35 years has increased from 1.5% in 1996 to 2.4% in 2006 (Figure 3).

Table 2. Age of Victorian women having a prenatal test under 25 weeks of gestation

Age group (years)	Confinements Interim 2006 data (PDCU)	CVS		AMN		Total	
		2006	Uptake	2006	Uptake	2006	Uptake
<35	51147	381	0.8%	866	1.7%	1247	2.4%
35-36	7679	202	2.6%	397	5.2%	599	7.8%
37-39	6215	487	7.8%	859	13.8%	1346	21.7%
≥40	2668	472	17.7%	744	27.9%	1216	45.6%
Total	67709	1542		2866		4408	6.5%

Figure 3. Annual uptake rates of prenatal diagnostic testing in Victoria, 1992-2006



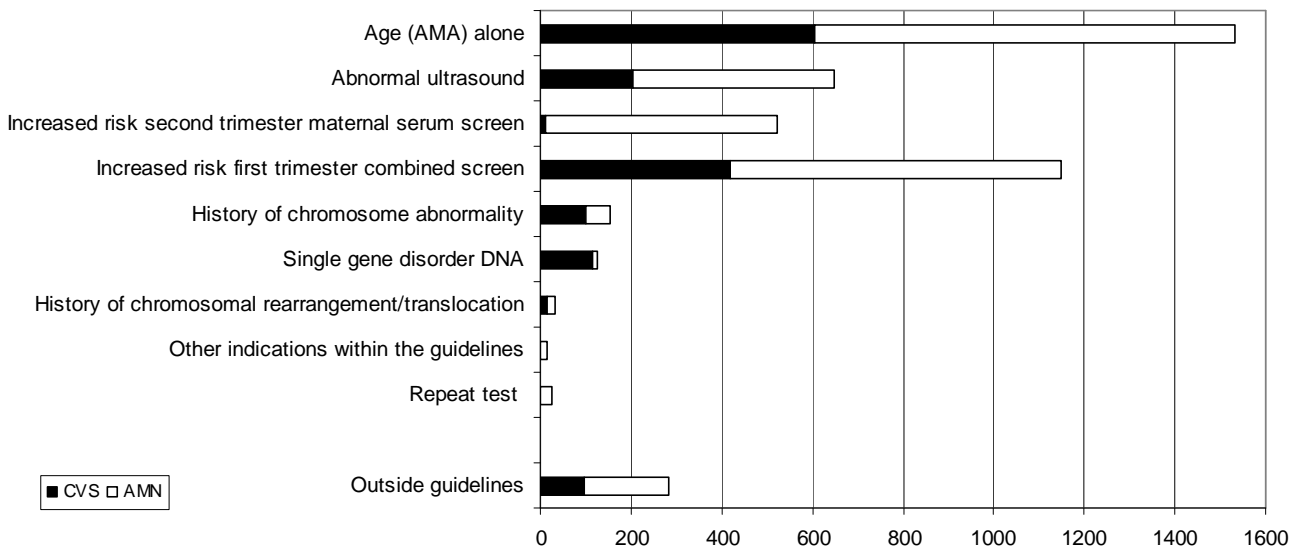
4. INDICATIONS FOR PRENATAL DIAGNOSIS

4.1 OVERVIEW

The indications for testing used in this report are taken from prenatal chromosome and DNA test request slips sent to the cytogenetics laboratories with the sample. The accuracy and completeness of this information has not been confirmed with the referring doctor and *the data must be interpreted within this limitation.*

A number of women had more than one indication for testing and a summary of all indications given as reasons for prenatal diagnosis is presented in Figure 4.

Figure 4. Indications for prenatal diagnosis for Victorian women under 25 weeks gestation



The five most common indications for prenatal diagnostic testing for Victorian women under 25 weeks gestation were maternal age, increased risk first trimester combined screening, abnormal ultrasound, second trimester maternal serum screening and indications outside the recommendations of the HGSA/RANZCOG Prenatal Diagnosis Policy. Other indications included previous chromosomal abnormality (152), tests for single gene disorders (120),

history of chromosomal rearrangement/translocation (38) and other within HGSA guidelines (14).

1. 1531 (34.7%) tests were done because of advanced maternal age as their only indication for testing. By definition these women were aged 37 and over (*see 4.2, maternal age*).
2. 646 (14.7%) tests were done because of an abnormal ultrasound, either raised nuchal translucency screen (excluding those done as part of first trimester combined screening) or a fetal anomaly scan (*see 4.3, abnormal ultrasound*).
3. 516 (11.7%) tests were done because of a finding of increased risk second trimester maternal serum screening (*see 4.4, second trimester maternal serum screening*).
4. 1156 (26.2%) tests were done because of a finding of increased risk first trimester combined screening (*see 4.4.2, first trimester combined screening*).
5. 286 (6.5%) tests were done for indications outside the HGSA/RANZCOG recommendations. These women were under the recommended age of 37 years but requested the service as part of their private health care (*see 4.9, outside recommendations*).

In order to estimate the approximate number of diagnostic tests prompted by prenatal screening we deducted the number of tests with an indication other than screening (n=2167) from the total (n=4408). Given that a number of tests had more than one indication for testing, in particular when prior screening was specified (n=74), this returned a more conservative estimate of the proportion of tests that were done because the woman had prenatal screening. Using this method, approximately 51% of all prenatal diagnostic tests were done following an increased risk screening test result (ie. nuchal translucency, first trimester combined screening, second trimester maternal serum screening and/or second trimester routine ultrasound).

4.2 MATERNAL AGE

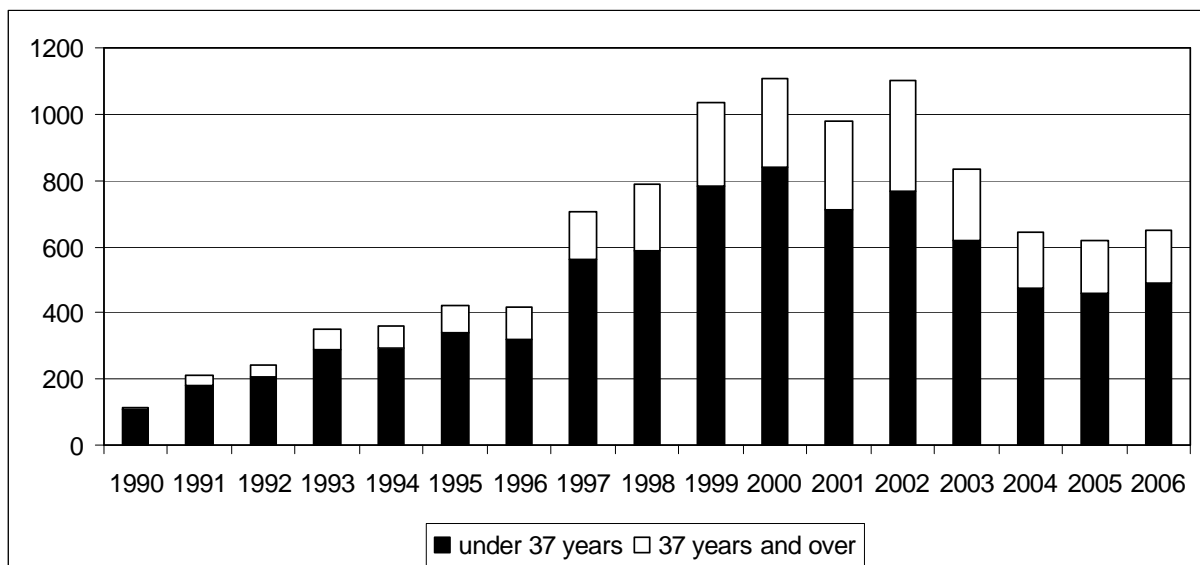
1531 women had maternal age as their only indication (ie 34.7% of all women having testing). By definition, these women were aged 37 years and over. An additional 1031 women in this age group had a prenatal diagnostic test following other indications for testing, such as an increased risk screening test result.

4.3 ABNORMAL ULTRASOUND

The number of women undergoing prenatal diagnosis following an abnormal ultrasound was 646 or 14.7% of all tests. 75% of these women were under 37 years of age.

Abnormal ultrasound was defined as suspected fetal or other pregnancy anomaly on routine ultrasound, or increased nuchal thickening (nuchal translucency screen). 16 tests had a double indication of fetal abnormality and increased nuchal translucency. **Nuchal translucency screens done as part of first trimester combined screening are no longer included here, which accounts for an apparent drop in the number of tests following abnormal ultrasound since 2002.**

Figure 5. Number of Victorian women under 25 weeks gestation having prenatal diagnosis following abnormal ultrasound by age group



One third (33.7%) of the tests done for abnormal ultrasound were reported as nuchal translucency screening alone (when not as part of 1st trimester combined screening). Over half of abnormal nuchal translucency screens were followed by a CVS (60.1%). This compares with 17.2% of women having a CVS following a suspected fetal abnormality on routine ultrasound (Table 3). The median gestational ages for a CVS or AMN for tests prompted by an ultrasound indication were 12 weeks and 18 weeks respectively.

Table 3. Abnormal ultrasound as indication for Victorian women under 25 weeks gestation, by maternal age and procedure

	CVS	AMN	Total	% Total
Abnormal nuchal translucency screen (includes 16 pregnancies which also had a suspected fetal abnormality on routine ultrasound)				
Maternal age				
<35 yrs	63	61	124	
35-36 yrs	17	8	25	
37 – 39 yrs	29	6	35	
≥40 yrs	21	12	33	
<i>Sub-total</i>	130	87	217	(33.7%)
	(60.1%)	(39.9%)	(100%)	
Other suspected fetal or pregnancy abnormality on routine ultrasound				
Maternal age				
<35 yrs	40	243	283	
35-36 yrs	10	44	54	
37 – 39 yrs	21	43	64	
≥40 yrs	3	25	28	
<i>Sub-total</i>	74	355	429	(66.3%)
	(17.2%)	(82.8%)	(100%)	
Total	204	442	646	
	(31.7%)	(68.3%)		(100%)

4.4 MATERNAL SERUM SCREENING

Increased risk MSS is becoming increasingly frequent as an indication for testing since the introduction of second trimester maternal serum screen (2TMSS) in 1996 and first trimester combined screening (1TCS) in 2000. In 2006, there were 1672 prenatal diagnostic tests done because of an increased risk in either screening tests.

2003 was the first year this report distinguished between first trimester combined screening and second trimester maternal serum screening. **However, the accuracy and completeness of this information has not been confirmed with the referring doctor and the data must be interpreted within this limitation.**

Using information from Genetic Health Services Victoria, we estimate that there were 43811 women who had maternal serum screening (either first trimester combined or second trimester serum) in 2006. The number having prenatal diagnosis for an increased risk screening result corresponds to a diagnostic follow-up rate of 3.8% (which compares to 3.6% in 2005 and 3.5% in 2004).

4.4.1 Second trimester maternal serum screening (2TMSS)

516 or 11.7% of all prenatal diagnostic tests are done following an increased risk 2TMSS. By necessity, due to the gestation at which this screening is done, most of the tests are AMN (514, or 99.6%), rather than CVS (2, or 0.4%). Two thirds (66.7%) of tests prompted by increased risk 2TMSS were in women under the age of 37 (Table 4). This maternal age distribution has been consistent since 2003.

Table 4. Increased risk 2TMSS as indication for Victorian women under 25 weeks gestation, by maternal age and procedure

Age group (years)	CVS	% total	AMN	% total	Total	% Total
<35	1		258		259	50.2%
35-36			85		85	16.5%
37-39	1		107		108	20.9%
≥40	0		64		64	12.4%
Total	2	0.4%	514	99.6%	516	100.0%

4.4.2 First trimester combined screening (1TCS)

Increased risk 1TCS as an indication for prenatal diagnostic testing included 24 tests where the recorded indication was “increased risk first trimester *serum* screening”. Additionally, 42 tests were done before 14 weeks gestation because of “increased risk MSS”, “Down syndrome risk” or “elevated risk Trisomy 18 and/or 21”.

After inclusion of these data, 1156 or 26.2% of prenatal diagnostic tests were prompted by an increased risk 1TCS. Of these, 427(36.9%) were CVS and 729 (63.1%) were AMN (Table 5).

Approximately half of (49.0%) of tests prompted by increased risk 1TCS were in women under the age of 37 (Table 5). As with tests prompted by 2TMSS this maternal age distribution has been consistent since 2003.

Table 5. Increased risk 1TCS as indication for Victorian women under 25 weeks gestation, by maternal age and procedure

Age group (years)	CVS	% total	AMN	% total	Total	% Total
<35	154		208		362	31.3%
35-36	72		132		204	17.7%
37-39	1122		203		325	28.1%
≥40	79		186		265	22.9%
Total	427	36.9%	729	63.1%	1156	100.0%

4.5 HISTORY OF CHROMOSOME ABNORMALITY

Overall, 190 women were tested because of a history of chromosome abnormality, including 38 prenatal tests done because of a history of chromosome translocation or rearrangement (eg deletions or inversions) (Table 6).

152 of these tests were performed because of a previous pregnancy with a chromosomal abnormality but information on the type of abnormality was not available for 69 of these indications.

Table 6. History of chromosome abnormality as indication for testing in Victorian women under 25 weeks gestation

Previous abnormality	CVS	AMN	Total
Unspecified	38	31	69
Trisomy 21	41	13	54
Trisomy 18	10	1	11
Trisomy 13	3	3	6
Sex chromosome aneuploidy	2	2	4
Other major chromosome	5	3	8
Total	99	53	152
Translocation	14	14	28
Rearrangements	5	5	10
Total	19	19	38

4.6 SINGLE GENE TESTS

120 prenatal diagnostic tests were done because a DNA or biochemical test for a single gene disorder was requested, two procedures requiring two gene tests, giving a total of 122 prenatal single gene tests for 2006. This number is comparable to the previous six years. The majority of tests for single gene disorders were done following CVS (91.7%, data not shown)

A list of the main conditions tested for in 2006 relative to the previous five years is provided in Table 7. Table 8 expands the category *other* where there was never more than one test for a condition in any given year (n=16 for 2006).

Table 7. Single gene tests in Victorian women under 25 weeks gestation

Single gene test	2006	2005	2004	2004	2003	2002	2001
Thalassaemia	27	28	25	25	25	38	23
Fragile X	19	2	9	9	13	8	10
Cystic fibrosis	16	16	15	15	17	11	15
Achondroplasia	5	1				1	
Duchenne muscular dystrophy	4	2	7	7	9	6	5
Spinal muscular atrophy	4	9	6	6	4	6	7
Myotonic dystrophy	3	3	4	4	3	1	
Huntington disease	3	6	1	1	1	5	1
Adrenoleukodystrophy	3		1	1	4	4	
X-linked Hydrocephalus	3	2	3	3	2	3	1
Spondyloepiphyseal dysplasia (SED)	3	1					
Haemophilia	2	2	3	3	5	5	5
Neurofibromatosis	2	2	3	3			
Congenital adrenal hypoplasia	2	1	2	2	2	3	2
X-linked Lissencephaly/Double Cortin	2	2	2	2			
Becker's Muscular Dystrophy	2						
Gaucher Disease	2						
X-linked mental retardation	1	4					1
Ornithine transcarbamylase deficiency	1	1			2	1	1
Gangliosidosis	1	2			1		2
Prader Willi syndrome	1				2		
X-linked myotubular myopathy		2					
X-linked Hydrocephalus		2	3	3	2	3	1
Glycogen storage disease		2			1	1	
Nieman Pick disease		2					
Connexin 26		1			3	1	
Mucopolysaccharidosis I			2	2		2	
Sialidosis			2	2			
Epidermolysis Bullosa			3	3			
BRCA 1					1	2	
Other	16	16	24	24	16	19	24
Total	122	105	112	112	108	112	93

Table 8. 'Other' single gene tests in Victorian women under 25 weeks gestation

Allagille syndrome	Menkes syndrome
Androgen Insensitivity syndrome	Mucopolysaccharidosis Type III
Chronic Granulomatous Disease	Non-ketotic Hyperglycaemia
Fanconi's Anaemia	Polycystic Kidney Disease
HADDAD syndrome	Retinoblastoma
Hereditary Sensory Neuropathy	Severe Combined Immunodeficiency
Infantile Polycystic Kidney Disease	Smith Lemli Opitz syndrome
Marfan Syndrome	X-linked Stapes-Gusher syndrome

4.7 OTHER WITHIN HGSA/RANZCOG RECOMMENDATIONS

15 prenatal diagnostic tests were performed for other indications within the HGSA/RANZCOG recommendations.

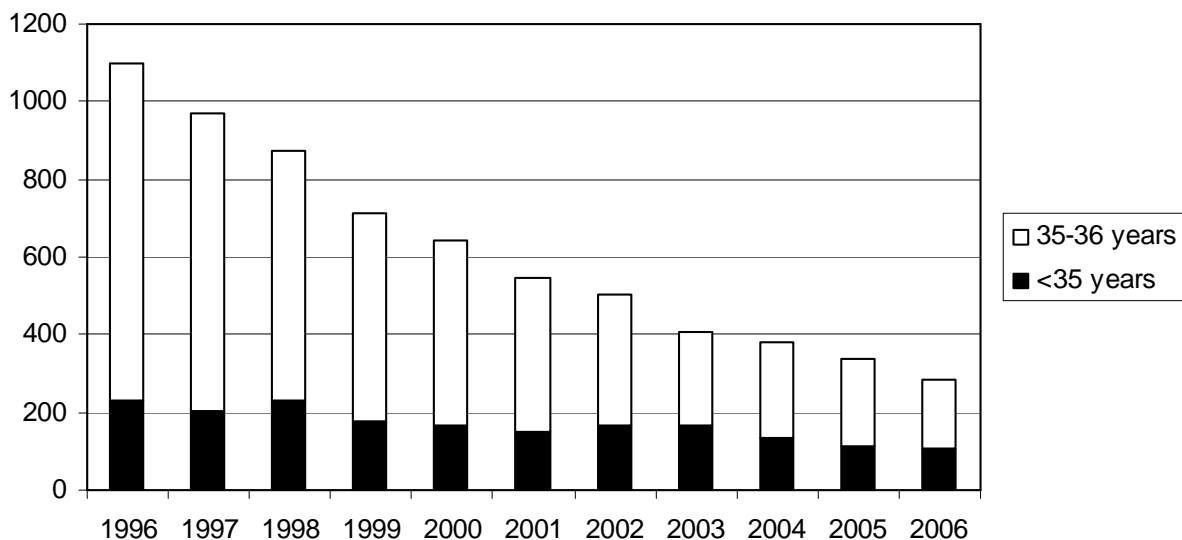
Two tests were done because of a previous neural tube defect. Others included positive maternal serology for Cytomegalovirus (n=5), Toxoplasmosis or Hepatitis, human platelet antigen (HPA) genotyping, Rhesus, Duffy, D or E immunisation. One test was done because of paternal uniparental disomy (UPD) risk.

4.8 OUTSIDE HGSA/RANZCOG RECOMMENDATIONS

Almost two thirds of the 286 women with an indication outside the HGSA/RANZCOG recommendations were in the 35-36 year age group (61.9%). The indication given was *age* or *anxiety* for 98% of this group and for 83% of women under 35 years. The remaining indications related to paternity testing, family history of Trisomy 21 or family history of chromosomal abnormalities other than trisomy 21 and previous non-chromosomal abnormalities.

The number of tests done for indications outside the HGSA/RANZCOG recommendations has dropped steadily since 1996, with 1099 tests done for that reason in 1996 and 286 tests done in 2006. Figure 6 shows that indications outside HGSA/RANZCOG recommendations decreased mainly in women aged 35-36 years. This decline may be explained by the increased utilisation of prenatal screening in women under 37 years.

Figure 6. Indications outside HGSA/RANZCOG recommendations for Victorian women under 37 years and under 25 weeks gestation



5. FETAL KARYOTYPES

5.1 OVERVIEW

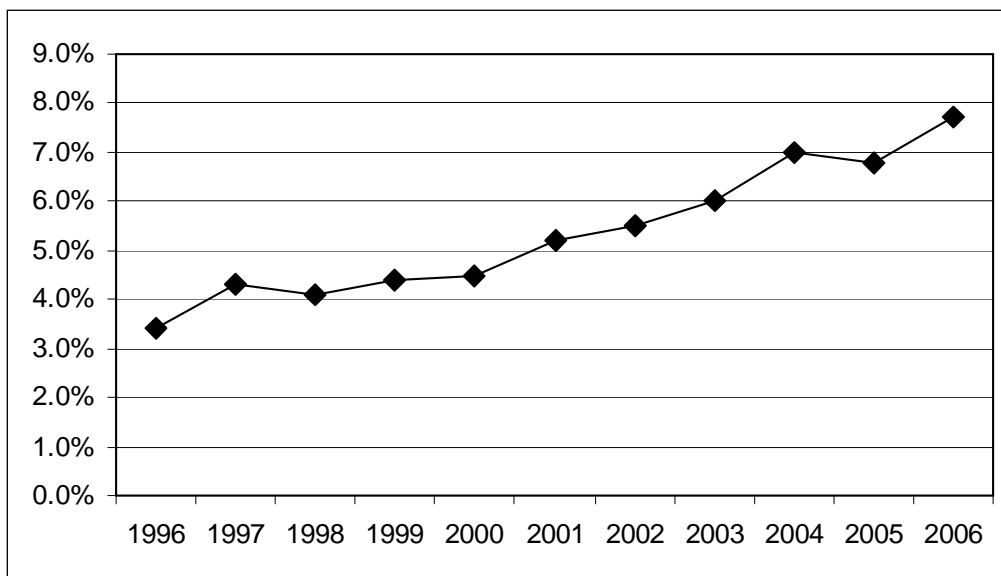
4004 (90.8%) of CVS and AMN had a normal fetal karyotype. An additional 52 (1.2%) showed a minor non-clinically significant variation in fetal karyotype, in that they were not expected to result in an abnormal fetal outcome. 15 CVS or AMN were not karyotyped because a single gene test was the reason for testing, because FISH was the only test performed or there was no cell growth (and the test was not repeated) (Table 9).

Table 9. Summary data on all fetal karyotypes for Victorian women tested at under 25 weeks gestation

Fetal karyotype	CVS	AMN	Total	%
Normal				
Normal	1308	2696	4004	90.8%
No growth/not done	12	3	15	0.3%
Non-clinically significant variation				
Confined placental mosaicism (CPM)	5		5	0.2%
Balanced rearrangement	6	10	16	0.3%
Balanced translocation	10	21	31	0.7%
Total minor abnormalities	21	31	52	1.2%
Major abnormalities				
Autosomal aneuploidy:				
Trisomy 21	98	68	166	3.8%
Trisomy 18	26	19	45	1.0%
Trisomy 13	14	10	24	0.6%
Other trisomy	2	2	4	0.1%
Polyploidy	12	2	14	0.3%
Sex chromosome aneuploidy:				
45,X	23	8	31	0.7%
47,XXX	2	1	3	0.07%
47,XXY	2	4	6	0.1%
47,XYY		1	1	0.02%
48,XXXX				
Unbalanced rearrangement	9	9	18	0.4%
Unbalanced translocation				
Microdeletion syndrome (22q)	1	1	2	0.04%
Level III Mosaicism	12	11	23	0.5%
Total major abnormalities	201	136	337	7.7%
% abnormal of procedure	13.0%	4.8%	7.7%	
Total	1542	2866	4408	100.0%

Overall, 337 (7.7%) of pregnancies tested were found to have a major abnormality, a doubling since before MSS was introduced in the mid 1990s (Figure 7). A greater proportion of all CVS were found to have a major abnormality (13.4%), compared with the proportion of all AMN (4.8%).

Figure 7. Proportion of diagnostic tests with a major karyotype abnormality.
1996-2006



Trisomy 21 accounted for 49% of these abnormalities, Trisomy 18 for 13% and Trisomy 13 for 7%. More detailed information on the detection of autosomal trisomies is available in section 6.0 of this report. Other abnormalities included 14 polyploidies, 41 sex chromosome abnormalities, 23 Level III mosaicisms and 20 unbalanced rearrangements (including two 22q deletions).

5.2 ADVANCED MATERNAL AGE AS THE ONLY INDICATION

54 or 3.5% of 1532 diagnostic procedures following an indication of advanced maternal age only were found to have a chromosomal abnormality, 53.7% of which were done by CVS (Table 10).

24 of the 758 tests (3.2%) done for advanced maternal age in women aged 37-39 years were found to have an abnormal karyotype. In women aged 40 and over an abnormality was detected in 30 of 774 tests done (3.9%).

Table 10. Maternal age as only indication and fetal karyotype outcome by maternal age group and procedure for Victorian women under 25 weeks gestation

	CVS	AMN	Total	% in age group
37-39 years	277	481	758	
Normal/minor variation	264	470	734	96.8%
Trisomy 21	8	7	15	} 2.6%
Trisomy 18	2	2	4	
Other Trisomy				
Other chromosomal	3	2	5	0.6%
Sub-total major abnormal	13	11	24	3.2%
40+ years	329	445	774	
Normal/minor variation	313	431	744	96.1%
Trisomy 21	4	6	10	} 2.2%
Trisomy 18	6	1	7	
Other Trisomy				
Other chromosomal	6	7	13	1.7%
Sub-total major abnormal	16	14	30	3.9%
Total major abnormal	29	25	54	
<i>% of all AGE only abnormalities</i>	53.7%	46.3%	100%	
<i>% abnormal of procedure</i>	4.8%	2.7%	3.5%	
Total	606	926	1532	

5.3 AFTER ABNORMAL ULTRASOUND

The majority of the 646 pregnancies with an abnormal ultrasound indication had a normal fetal karyotype (76.8%) or a minor non-clinically significant fetal karyotype outcome (0.9%). 22.1% of the tests were found to have a major abnormality, compared to 21.9% in 2005 and 22.5% in 2004. A greater proportion of the abnormalities detected were by CVS (59.4%) (Table 11).

The majority of abnormalities detected following an abnormal ultrasound were in women 37 years and over (Table 12). Trisomies were diagnosed in 32.5% of women aged 37 years and over, compared to 16.5% for women aged 35-36

years and 7.9% in the youngest age group. This compares to a detection rate in 2005 of 24.8% and 15.6%, and in 2004 when 32.2% and 25.3% of tests diagnosed a trisomy in the two older age groups following an ultrasound indication.

Table 11. Abnormal ultrasound and fetal karyotype outcome by procedure for Victorian women under 25 weeks gestation

Fetal karyotype	CVS	AMN	Total	%
Normal/minor variation				
Normal	116	380	496	76.8%
Balanced rearrangement or translocation	2	4	6	0.9%
Not done/no growth	1		1	0.2%
Total normal or minor abnormal	119	384	503	77.9%
Major abnormalities				
Autosomal aneuploidy:				
Trisomy 21	35	19	54	8.4%
Trisomy 18	14	11	25	3.9%
Trisomy 13	9	9	18	2.8%
Other trisomy	1	2	3	0.5%
Polyploidy	4	2	6	0.9%
Sex chromosome aneuploidy:				
45,X	14	5	19	2.9%
47,XXX	1		1	0.2%
47,XYY		1	1	0.2%
Unbalanced rearrangement or translocation	4	5	9	1.4%
Microdeletion syndrome (22q)		1	1	0.2%
Mosaic Level III	3	3	6	0.9%
Total major abnormal	85	58	143	22.1%
% of all ultrasound abnormalities	59.4%	40.6%	100%	
% abnormal of procedure	41.7%	13.2%	22.1	
Total	204	442	646	100.0%

Table 12. Abnormal ultrasound and fetal karyotype outcome by maternal age group for Victorian women under 25 weeks gestation

	Increased nuchal thickness	Other abnormal ultrasound	Total	% in age group
≥37 years (AMA)	68	92	160	
Normal/minor variation	36	63	99	61.9%
Trisomy 21	18	13	31	} 32.5%
Trisomy 18	6	10	16	
Trisomy 13	4	1	5	
Other chromosomal	4	5	9	5.6%
Sub-total major abnormal	32	29	61	38.1%
35 – 36 years	25	54	79	
Normal/minor variation	18	42	60	75.9%
Trisomy 21	5	2	7	} 16.5%
Trisomy 18	1	1	2	
Trisomy 13		4	4	
Other chromosomal	1	5	6	7.6%
Sub-total major abnormal	7	12	19	24.1%
<35 years	124	283	407	
Normal/minor variation	112	232	344	84.5%
Trisomy 21	5	11	16	} 7.9%
Trisomy 18	1	6	7	
Trisomy 13		9	9	
Other chromosomal	6	25	31	7.6%
Sub-total major abnormal	12	51	63	15.5%
Total major abnormal	51	92	143	
% abnormal of ultrasound indication	25.0%	20.8%	22.1%	
Total	204	442	646	

5.4 AFTER INCREASED RISK SECOND TRIMESTER MATERNAL SERUM SCREEN (2TMSS)

3.9% of the 516 procedures done following an increased risk 2TMSS were found to have a chromosomal abnormality, compared to 3.8% of 553 in 2005, 5.0% of 624 in 2004 and 3.2% of 759 in 2003.

15 or 75% of the abnormalities found after an increased risk 2TMSS were trisomies. The highest proportion of trisomies was found in women aged 37 and over, with six diagnoses (3.5%) in the 172 women tested.

Table 13. Increased risk second trimester maternal serum screen and karyotype outcome by maternal age and procedure for VIC women under 25 weeks gestation

	CVS	AMN	Total	% in age group
≥37 years	1	171	172	
Normal/minor variation		164	164	95.3%
Trisomy 21	1	4	5	} 3.5%
Trisomy 18		1	1	
Trisomy 13				
Other chromosomal		2	2	
Sub-total major abnormal	1	7	8	4.7%
35 – 36 years		85	85	
Normal/minor variation		81	81	95.2%
Trisomy 21		2	2	} 2.4%
Trisomy 18				
Other Trisomy				
Other chromosomal		2	2	2.4%
Sub-total major abnormal		4	4	4.8%
<35 years	1	258	259	
Normal/minor variation	1	250	251	96.9%
Trisomy 21		6	6	} 2.7%
Trisomy 18		1	1	
Other Trisomy				
Other chromosomal		1	1	0.4%
Sub-total major abnormal		8	8	3.1%
Total major abnormal	1	19	20	
<i>% of all MSS abnormalities</i>		100%	100%	
<i>% abnormal of procedure</i>	50%	3.7%	3.9%	
Total	2	514	516	

5.5 AFTER INCREASED RISK FIRST TRIMESTER COMBINED SCREEN (1TCS)

124 or 10.7% of the 1156 diagnostic procedures following an increased risk 1TCS were found to have a chromosomal abnormality, 21.3% of CVS and 4.5% of AMN done for an increased risk 1TCS had a chromosomal abnormality (Table 14).

Across all age groups, 94 of the abnormal karyotypes were trisomies (75.8%), the highest proportion of which was in women aged 37 and over.

Table 14. Increased risk first trimester combined screen and fetal karyotype outcome by maternal age group and procedure for Victorian women under 25 weeks gestation

	CVS	AMN	Total	% in age group
≥37 years	201	245	590	
Normal/minor variation	154	374	528	89.5%
Trisomy 21	35	13	48	} 9.3%
Trisomy 18	4	1	5	
Trisomy 13	1	1	2	
Other chromosomal	7		7	1.2%
Sub-total major abnormal	47	15	62	10.5%
35 – 36 years	72	132	204	
Normal/minor variation	58	127	185	90.7%
Trisomy 21	10	3	13	} 7.8%
Trisomy 18		1	1	
Trisomy 13	1	1	2	
Other chromosomal	3		3	1.5%
Sub-total major abnormal	14	5	19	9.3%
<35 years	154	208	362	
Normal/minor variation	124	195	319	88.1%
Trisomy 21	9	8	17	} 6.4%
Trisomy 18	2	1	3	
Trisomy 13	3		3	
Other chromosomal	16	4	20	5.5%
Sub-total major abnormal	30	13	43	11.9%
Total major abnormal	91	33	124	
% of all FTC abnormalities	73.4%	26.6%	100%	
% abnormal of procedure	21.3%	4.5%	10.7%	
Total	427	729	1156	

5.6 AFTER HISTORY OF CHROMOSOMAL ABNORMALITY

5.6.1 History of chromosomal aneuploidy

Of the 152 women tested because of a known history of chromosome aneuploidy, one woman with an unspecified previous chromosomal abnormality was found to have a fetus with Trisomy 18, one woman had a second diagnosis of Trisomy 21 and one woman with a previous Trisomy 18 was found to have a fetus with Trisomy 13. (Table 15).

Detailed information on the previous chromosomal abnormality was not available for 45% in this category. Therefore we are unable to estimate a Trisomy 21 recurrence rate from this data set.

Table 15. Fetal karyotype outcome for Victorian women under 25 weeks gestation when there is a history of chromosome aneuploidy

Previous abnormality	Outcome		Total	%
	CVS	AMN		
Unspecified	35 N 1 BR, 1BT 1 CPM	30 N 1 T21	65 N 1 BR, 1BT 1 CPM, 1 T18	45.4%
Trisomy 21	40 N 1 T21	12 N 1 BR	52 N 1 BR, 1 T21	35.5%
Trisomy 18	9 N 1 T13	1 N	10 N 1 T13	7.2%
Trisomy 13	3 N	3 N	6 N	4.0%
Sex chromosome aneuploidy	2 N	2 N	4 N	2.6%
Other major chromosome	5 N	3 N	8 N	5.3%
Total	99	53	152	100%

N: Normal karyotype
 CPM: Confined placental mosaicism
 BR: Balanced rearrangement
 T18: Trisomy 18
 BT: Balanced translocation
 PP: Polyplody
 T21: Trisomy 21

5.6.2 Previous chromosomal translocation or other rearrangement

38 women were tested because of a family history of chromosome translocation or rearrangement. 17 of these tests showed fetal karyotypes with balanced translocations or rearrangements (44.7%) and four (10.5%) with a major abnormality (Table 16).

Table 16. Fetal karyotype outcome for Victorian women under 25 weeks gestation when there was a previous chromosomal translocation or other rearrangement, and/or parents are carriers

Previous fetal karyotype or parental carrier	Outcome		Total	%
	CVS	AMN		
Translocation	6 N 7 BT, 1 UBR	4 N 9 BT, 1 UBR	10 N 16 BT, 2 UBR	
<i>Sub-total</i>	14	14	28	73.7%
Rearrangements (deletions, inversions, etc)	2 N 2 UBR, 1 22Q	4 N 1 BR	6 N 1 BR, 1 UBR 1 22Q	
<i>Sub-total</i>	5	5	10	26.3%
Total	19	19	38	100%

N: Normal
BR: Balanced rearrangement
BT: Balanced translocation
22Q: 22q Microdeletion
UBR: Unbalanced rearrangement

5.7 OTHER WITHIN HGSA/RANZCOG RECOMMENDATIONS

Of the 15 prenatal diagnostic tests done for other indications within the HGSA/RANZCOG recommendations, all had a normal fetal karyotype.

5.8 OUTSIDE HGSA/RANZCOG RECOMMENDATIONS

There were three (1.7%) abnormal outcomes amongst the 177 women aged 35-36 years who were tested for reasons outside the HGSA/RANZCOG recommendations. None of the 109 tested women under 35 years had a major fetal karyotype abnormality, but there were 2 balanced rearrangements (1.8%) (Table 17).

Table 17. Fetal karyotype outcome for Victorian women under 25 weeks gestation if indication outside HGSA/RANZCOG recommendations

Outside HGSA/RANZCOG recommendations	Outcome		Total	%
	CVS	AMN		
35-36 years				
Age/anxiety	54 N 1 CPM 1 T9	115N 1 T21 1 UBR	169 N 1 CPM, 1 T21 1 UBR, 1 T9	
Family history of T21				
Other	3 N	1 N	4 N	
<i>Sub-total</i>	59	118	177	61.9%
<35 years				
Age/anxiety	25 N 2 BR	62 N	87 N 2 BR	
Family history of T21	1 N	1 N	2 N	
Other	10 N	8 N	18 N	
<i>Sub-total</i>	38	71	109	38.1%
Total	97	189	286	100%

N: Normal/not done
 BT: Balanced translocation
 BR: Balanced rearrangement/translocation
 CPM: Confined placental mosaicism
 LIII: Level III mosaicism
 SA: Sex chromosome aneuploidy
 T21: Trisomy 21
 T9: Trisomy 9

6. AUTOSOMAL TRISOMIES

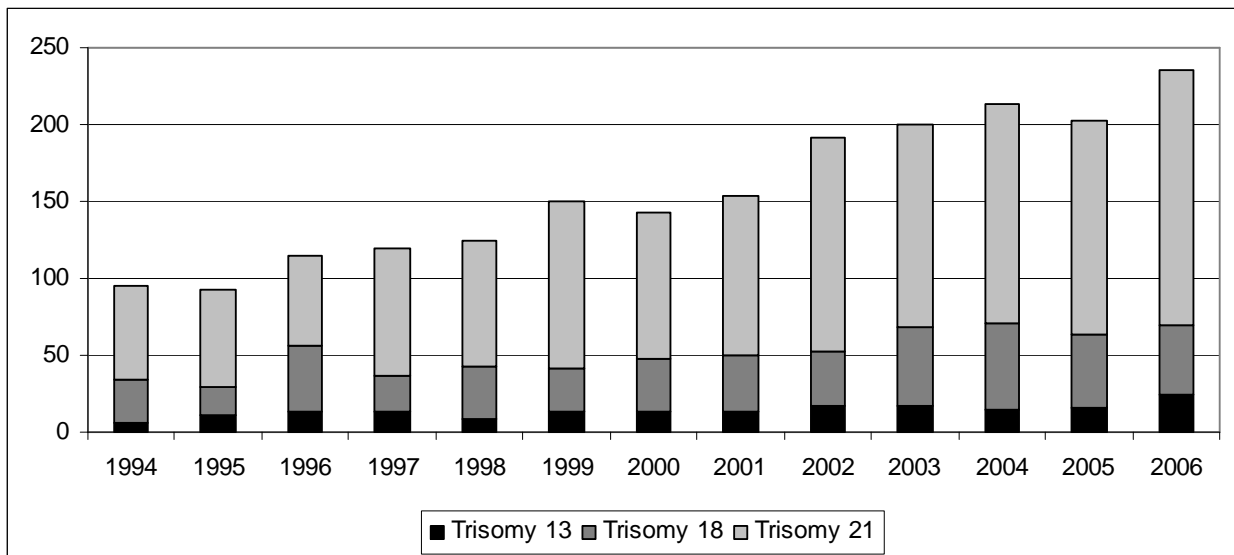
In 2006, prenatal diagnostic tests before 25 weeks of gestation resulted in the diagnosis of 166 Trisomy 21, 45 Trisomy 18, 24 Trisomy 13, three Trisomy 9, and one Trisomy 22. In addition, four Trisomy 21 were diagnosed at 25, 28, 30 and 33 weeks and five Trisomy 18 were diagnosed at 25, 26, 31, 33 and 34 weeks. (see 8. *Indication and fetal karyotype outcome for Victorian women over 24 weeks of gestation*).

In this section we present detailed information on the more common Trisomies 21, 18 and 13, diagnosed before 25 weeks of gestation.

59.0% of Trisomies 21, 57.8% of Trisomies 18 and 58.3% of Trisomies 13 were diagnosed following CVS.

Figure 8 shows that the number of trisomies diagnosed prenatally has more than doubled since 1994, mainly due to an increasing number of Trisomy 21 diagnoses until 2003. However, in 2006 prenatal diagnostic tests diagnosed the highest number of Trisomy 21 to date.

Figure 8. Autosomal trisomies diagnosed in Victorian women under 25 weeks gestation



Tables 18, 19 and 20 present Trisomies 21, 18 and 13 respectively, by indication.

The majority of Trisomy 21 were detected by prenatal diagnosis following an increased risk prenatal screening test result (82.5%). Only 29 of the 166 Trisomies 21 diagnosed (17.5%) had no prior increased risk screening test result reported (Table 18).

Similarly, in the diagnosis of Trisomy 18 and Trisomy 13, the most common indication was an increased risk screening test result (75.5% and 95.8% respectively), with fetal abnormality on ultrasound (other than increased nuchal thickening) accounting for 33.3% and 50.0% (Tables 19 and 20 respectively).

Table 18. Trisomy 21 detected by prenatal diagnosis in Victorian women under 25 weeks gestation, grouped by age and indication

Indication	Age	CVS				AMN				Total	%
		<35	35-36	37-39	≥40	<35	35-36	37-39	≥40		
Increased nuchal thickness		4	4	8	9	1	1		1	28	16.9%
First trimester combined screening		9	10	20	15	8	3	7	6	78	47.0%
Second trimester maternal serum screen				1		6	2	1	3	13	7.8%
Other ultrasound abnormality		3		1		7		3	4	18	10.8%
No screening test, prompted by age alone				8	4		1	8	6	27	16.3%
No screening test, prompted by DNA test				1	1					2	1.2%
Total		16	14	39	29	22	7	19	20	166	100%

Table 19. Trisomy 18 detected by prenatal diagnosis in Victorian women under 25 weeks gestation, grouped by age and indication

Indication	Age	CVS				AMN				Total	%
		<35	35-36	37-39	≥40	<35	35-36	37-39	≥40		
Increased nuchal thickness		1	1	2	3				1	8	17.8%
First trimester combined screening		2		2	2	1	1		1	9	20.0%
Second trimester maternal serum screen						1		1		2	4.4%
Other ultrasound abnormality		2		2	1	3	1	1	5	15	33.3%
No screening test, prompted by age alone				2	6			2	1	11	24.5%
Total		5	1	8	12	5	2	4	8	45	100%

Table 20. Trisomy 13 detected by prenatal diagnosis in Victorian women under 25 weeks gestation, grouped by age and indication

Indication	Age	CVS				AMN				Total	%
		<35	35-36	37-39	≥40	<35	35-36	37-39	≥40		
Increased nuchal thickness				2	2					4	16.7%
First trimester combined screening		3	1	1			1		1	7	29.1%
Second trimester maternal serum screen											NIL
Other ultrasound abnormality		3	1			5	2	1		12	50.0%
No screening test, prompted by previous chromosomal abnormality				1						1	4.2%
Total		6	2	4	2	5	3	1	1	24	100%

7. REPEAT TESTS AND FETAL KARYOTYPES

25 (0.6%) prenatal diagnostic tests were repeated.

10 of the repeat tests were AMN done to clarify a level three mosaic found on CVS. For 7 of these, the mosaicism was confined to the placenta (CPM). Two were confirmed as LIII mosaic and one was found to be an unbalanced rearrangement.

One Trisomy of chromosome 16 and was found to be normal on repeat AMN. One Trisomy of chromosome 16 and one Trisomy 20 were identified as a Level III mosaicism on repeat.

One Trisomy 21 and two unbalanced rearrangements were confirmed on repeat AMN.

One apparently normal karyotype and one normal FISH test result on CVS were confirmed as normal. Three CVS and one AMN samples where there was no cell growth in the first sample, were found to have a normal karyotype on repeat AMN.

One CVS without a reported karyotype was repeated and was found to be a Trisomy 21 on AMN.

One CVS with a Trisomy 21 on FISH but with a normal karyotype was confirmed as normal on AMN.

One test was repeated because one of two fetuses appeared to be female on ultrasound but, like its twin, showed a male karyotype on AMN. The amended karyotype on repeat AMN was female, ie they were mixed-sex twins and the discrepancy was due to a sampling error.

8. INDICATION AND FETAL KARYOTYPES FOR WOMEN OVER 24 WEEKS OF GESTATION

50 women had a late (over 24 weeks gestation) prenatal diagnosis, 45 were done by AMN and five by CVS.

Figure 9. Prenatal diagnosis for Victorian women over 24 weeks gestation by gestational age and indication



43 (86.0%) of these tests were done because of an abnormal ultrasound (Figure 9) and all but 11 were done in women under 37 years. Other indications included one test done for maternal age at 26 weeks, one test for maternal toxoplasmosis serology, two for CMV infection and one test for rhesus genotyping at 25 and 26 weeks gestation. One test was done for maternal anxiety at 27 weeks and one test was done for twin-to-twin transfusion syndrome at 26 weeks.

18% of tests done after 24 weeks gestation showed a major abnormality (Table 21). Four Trisomy 21 were diagnosed after an abnormal ultrasound at 25, 28, 30 and 33 weeks gestation. Five Trisomy 18 were found following an abnormal ultrasound at 25, 26, 31, 33 and 34 weeks gestation.

Table 21. Fetal karyotype outcome for Victorian women over 24 weeks gestation

Gestation (weeks)	Normal outcome or minor variation	Abnormal outcome (All with indication of abnormal ultrasound)	Total
25 - 27	15	2 T18, 1 T21	18
28 - 30	14	1 T21	15
31 - 33	6	2 T18, 2 T21	10
34 - 36	4	1 T18	5
37 - 40	2		2
Total	41	9	50
% total	82.0%	18.0%	100%

T18: Trisomy 18
T21: Trisomy 21

9. FLUORESCENT IN SITU HYBRIDISATION (FISH) FOR ANEUPLOIDY

FISH analysis is a molecular test, which uses fluorescence-labelled DNA probes to detect the presence or absence of specific chromosomes or chromosome regions. Currently, FISH analysis is mainly performed to detect autosomal trisomies and sex chromosome aneuploidies. Although all samples are also karyotyped in the traditional manner, the advantage of this test is that a result is usually available within one or two days.

Since its introduction in 1999, there has been a marked increase in use of FISH for chromosome analysis from 427 in 2000 to 2331 tests in the year 2004, 2489 in 2005 and 2802 in 2006. This corresponds to 53%, 58% and 64% of all CVS or AMN in the three most recent years.

The percentage of FISH done in each age group (Table 22) is similar to the overall distribution of diagnostic tests across all ages, with a slightly higher use of FISH for tests done on women under the age of 35 (32.1% FISH vs 27.3% of all tests).

Table 22. FISH for Victorian women under 25 weeks gestation, by maternal age and procedure

Age group (years)	CVS	% total	AMN	% total	Total	% Total FISH
<35	280		619		899	32.1%
35-36	140		247		387	13.8%
37-39	340		479		819	29.2%
≥40	337		360		697	24.9%
Total	1097	39.2%	1705	60.8%	2802	100.0%

Of the 2802 FISH done, 27.1% followed an indication of advanced maternal age and 62.0% had a prior increased risk screening test as indication for testing. 5.6% of FISH were requested in women under the age of 37 years for reasons outside the HGSA/RANZCOG guidelines or an unknown indication (Table 23).

Results of FISH are not collected in our database, however Table 24 provides karyotype outcomes for all tests that included FISH. 9.2% of tests that included FISH were found to have an abnormal karyotype.

Table 23. FISH for Victorian women under 25 weeks gestation, by indication for testing and procedure

Indication	CVS	AMN	Total	% of indication
Advanced maternal age	367	393	760	49.6%
First trimester combined screening	394	493	887	76.7%
Second trimester maternal serum screening	2	307	309	59.9%
Abnormal ultrasound	46	306	352	82.1%
Increased nuchal thickness	118	70	188	86.7%
Outside guidelines or unknown indication	57	100	157	54.9%
Previous chromosomal abnormality	72	26	98	64.5%
History rearrangement/translocation	7	3	10	26.3%
Single gene test	32	5	37	30.8%
Other within guidelines	2	1	3	21.4%
Repeat sample		1	1	4.0%
Total	1097	1705	2802	

This proportion of karyotype abnormalities in samples where FISH was requested is higher than the overall proportion of abnormal karyotypes in all tests done in 2006 (10.4% vs 7.7%). This may be the result of the high proportion of FISH requested following an increased risk screening test result (62.0% vs 51.0% across all tests).

Table 24. FISH for Victorian women under 25 weeks gestation, by karyotype outcome and procedure

Indication	CVS	AMN	Total	% Total
Normal/minor variation	909	1595	2504	89.4%
Not done/no growth	3	3	6	0.2%
Trisomy 21	94	52	146	
Trisomy 18	26	17	43	
Other Trisomy	12	10	22	
Polyploidy	10	2	12	
Sex chromosome abnormality	24	10	34	
Unbalanced rearrangement (incl.22q)	8	7	15	
Level III mosaic	11	9	20	
Total major abnormal	185	107	292	10.4%
<i>% abnormal of procedure</i>	16.9%	6.3%	10.4%	
Total	1097	1705	2802	

10.0 INTERSTATE SAMPLES

Victorian cytogenetics laboratories analysed 262 CVS and AMN sent in from interstate or overseas in 2006. The majority of samples came from Tasmania (n=202) and New South Wales (n=48) (Table 25). The majority of NSW samples came from women residing on the Victorian border who may have given birth in Victoria.

Table 25. Interstate samples by state and maternal age group

Age group (years)	NSW	NT	QLD	SA	TAS	WA	Total
<35	16	1	1		77		95
35-36	5				22		27
37-39	14	1	3	1	56	2	77
≥40	13	1	1		47		63
Unknown						1	1
Total	48	3	5	1	202	3	262
<i>%Total</i>	<i>18.2%</i>	<i>1.2%</i>	<i>1.9%</i>	<i>0.4%</i>	<i>77.1%</i>	<i>1.2%</i>	<i>100%</i>

Of the 262 interstate samples done, most were done for an increased risk screening test result (58.7%) and only 28.2% were for advanced maternal age alone. 6.2% of interstate samples were on women under the age of 37 years for reasons outside the HGSA/RANZCOG guidelines or an unknown indication (Table 26).

Table 26. Interstate samples by state and indication for testing

Indication	NSW	NT	QLD	SA	TAS	WA	Total	<i>% Total</i>
Advanced maternal age (alone)	19	1	1		52	1	74	28.2%
First trimester combined screening	6	1	1		55		63	24.0%
Second trimester maternal serum screening	5				37	2	44	16.8%
Abnormal ultrasound	5		1		20		26	9.9%
Increased nuchal thickness	1		1		19		21	8.0%
Outside guidelines or unknown indication	4	1			11		16	6.2%
Single gene test	6				4		10	3.8%
Previous chromosomal abnormality			1	1	3		5	1.9%
History translocation/rearrangement	2						2	0.8%
Repeat					1		1	0.4%
Total	48	3	5	1	202	3	262	100.0%

8.8% of tests originating from interstate were found to have an abnormal karyotype. The tests included a further nine Trisomy 21 diagnoses from Tasmania (Table 27).

Table 27. Interstate samples by state and karyotype outcome

Indication	NSW	NT	QLD	SA	TAS	WA	Total
Normal/minor variation	48	3	4	1	180	3	239
Trisomy 21					9		9
Trisomy 18					4		4
Trisomy 13					4		4
Polyploidy			1		1		2
Unbalanced rearrangements					2		2
Level III mosaic					2		2
Total major abnormal			1	0	22		23
<i>% abnormal</i>	0%	0%	20.0%	0%	10.9%	0%	8.8%
Total	48	3	5	1	202	3	262