

REPORT ON  
PRENATAL DIAGNOSTIC TESTING  
IN VICTORIA 2007

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on Obstetric and Paediatric  
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## 1. KEY FINDINGS

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- 1** The total number of prenatal diagnostic tests done in 2007 was 3978, 430 fewer tests than in the previous year. The number of tests has declined each year since 1998, when we saw the highest number of tests (n=5300). **Pages 9 & 10**
- 2** 5.7% of pregnant women had a prenatal test in 2007. The overall proportion of women having a test has declined by three percent since 1998, this decrease being due to a decline in uptake of testing by older women. **Page 12**
- 3** The proportion of pregnant women 40 years and over who have a prenatal diagnostic test has declined from almost 80% in 1996 to 40% in 2007 and in women aged 37-39 years it has declined from 60% in 1996 to 17% in 2007. Over 2% of pregnant women aged less than 35 years now have a test. **Page 12**
- 4** Reasons for testing in 2007 were similar to those in 2006 and 2005, although tests done for advanced maternal age as the only indication are slightly decreasing in number and proportion each year (38% in 2005, 35% in 2006 and 33% in 2007). At the same time, the proportion of tests done because of an abnormal screening test increases slightly each year (47% in 2005, 51% in 2006 and 53% in 2007). **Pages 13 & 14**
- 5** 614 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 15.4% of all tests in 2007. 75% of these women were under 37 years of age. **Pages 15 & 16**
- 6** 41% of CVS, and 17% of AMN following an abnormal ultrasound were found to have a major chromosomal abnormality. This detection rate is similar to 2006 and 2005. 20% of tests prompted by increased nuchal thickness were found to have a chromosomal abnormality, compared with 24% after another ultrasound abnormality. **Pages 25-27**
- 7** Using information from Genetic Health Services Victoria, we estimate that there were 68.3% of pregnant women (n=47,476) who had maternal serum screening (MSS, either first trimester combined or second trimester serum) **Page 17**

in 2007. The number tested for an increased risk MSS result corresponds to a diagnostic follow-up rate of 3.2%.

- |           |   |                          |
|-----------|---|--------------------------|
| <b>8</b>  | 1541 women had prenatal diagnosis for an increased risk maternal serum screen (MSS) compared with just over 500 in 1999 and 1672 in 2006. There were more diagnostic tests prompted by first trimester combined MSS (n=1104) than by second trimester MSS (n=437)   | <b>Pages 17 &amp; 18</b> |
| <b>9</b>  | Two thirds of women having prenatal diagnosis following second trimester MSS were under 37 years of age (61%) 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.                              | <b>Pages 17 &amp; 18</b> |
| <b>10</b> | A fetal chromosome abnormality was detected in 3.4% of pregnancies tested for an increased risk second trimester MSS, and in 13.0% of tests for increased risk first trimester combined MSS. Trisomies accounted for 80.0% and 75.5% of these abnormalities in the respective tests.  | <b>Pages 28 &amp; 29</b> |
| <b>11</b> | The number of tests done for indications outside the HGSA/RANZCOG recommendations has decreased markedly since 1996, with 243 tests done in 2007 (6.1% 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. | <b>Page 22</b>           |
| <b>12</b> | 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 (2.8% of all tests in 2007). Thalassaemia, cystic fibrosis and Fragile X were the most common conditions tested for.   | <b>Pages 19 &amp; 20</b> |
| <b>13</b> | Of all Victorian women who had CVS or AMN in 2007, 90.2% had a fetus with a normal karyotype and 8.5% of tested pregnancies were found to have a major fetal karyotype abnormality (13.7% of CVS and 5.8% of AMN). The detection rate of abnormalities by both diagnostic tests has more than doubled since prenatal screening became available.                | <b>Page 23</b>           |
| <b>14</b> | Trisomy 21 accounted for just under half of all abnormal fetal karyotypes (49%), with 165 diagnosed prenatally in 2007. For the majority of tests with a diagnosis of Trisomy 21, the major indication was an increased risk  | <b>Pages 33-35</b>       |

screening test result (83.6%). First trimester combined MSS accounted for 51.5% of diagnoses, second trimester MSS for 6.1%, second trimester routine ultrasound for 18.8%, while increased nuchal thickening alone and maternal age alone were associated with 7.3% and 13.9% of diagnoses respectively.

- 15** Fluorescent In Situ Hybridisation (FISH) for aneuploidy was undertaken in over 73% of tests where the indication was abnormal ultrasound or increased nuchal thickness. FISH was also requested in 75% of tests after increased risk first trimester combined screening.

## 2. INTRODUCTION

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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 not 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](http://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.

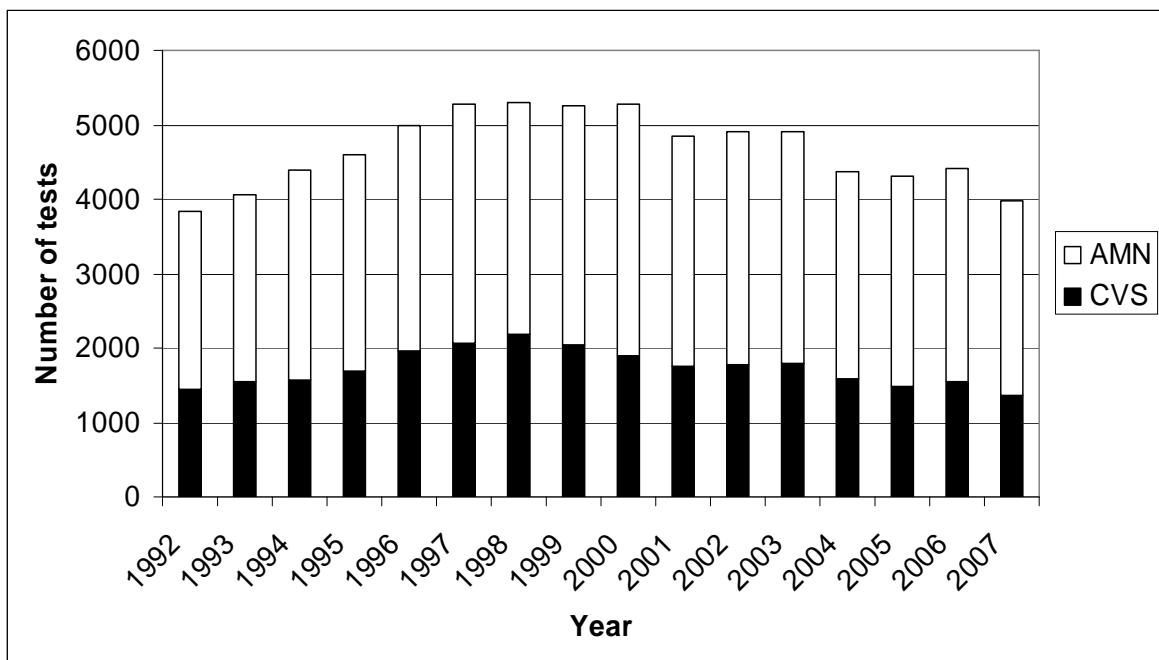
### 3. UTILISATION OF PRENATAL DIAGNOSTIC TESTS

#### 3.1 NUMBER OF TESTS

The total number of prenatal diagnostic tests analysed by Victorian laboratories in 2007 was 4329. This overall number includes some multiple procedures e.g. same day AMN and CVS samples or twin or triplet pregnancies – which have been condensed into one record. In addition, there are six fetal blood samples, 281 samples from women living interstate, 30 repeat samples (including 4 fetal blood repeat samples) and 38 late gestation tests, which are also included in this number.

In 2007, the actual number of pregnant women residing in Victoria having a test before 25 weeks gestation was 3978: 1370 CVS and 2608 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) (Table1) 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. 2007 has seen a further decrease in the number of tests with 430 fewer tests done than in 2006. 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%
2007	3978	1370	34%	2608	66%

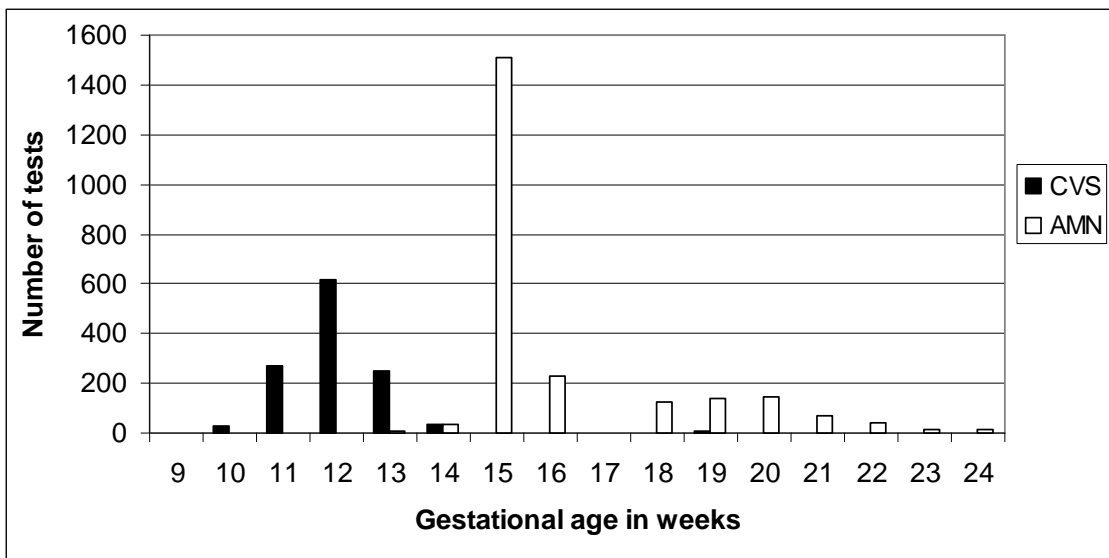
### 3.2 GESTATIONAL AGE < 25 WEEKS

Figure 2 shows the distribution of recorded gestational ages for CVS and AMN for Victorian women under 25 weeks of gestation, excluding 423 records with missing data on gestation (11%).

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 10-24 weeks with a median of 12 weeks when 50% of these tests were performed. For AMN, the reported gestational ages also ranged from 10-24 weeks with a median of 15 weeks when 65% 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 423 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 2007 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 2007 confinements, which is not expected to change much (Table 2).

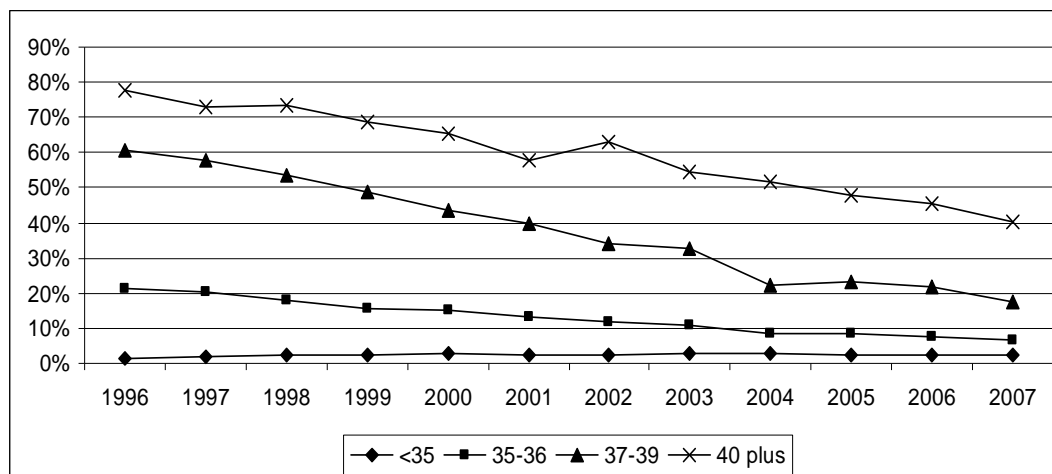
5.7% of pregnant Victorian women had a prenatal diagnostic test in 2007. The overall proportion of women having a test has declined by three percent since 1998. This decline is due to a decrease of tests in older women (Figure 3).

Uptake of prenatal diagnosis by women 35 years and older has declined from 78% in 1996 to 40% in 2007 in the oldest age group, from 60% to 17% in the 37-39 year olds and from 21% to 7% 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, holding steady at 2.2% in 2007 (Figure 3).

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

Age group (years)	Confinements Interim 2007 data (PDCU)	CVS		AMN		Total	
		2007	Uptake	2007	Uptake	2007	Uptake
<35	51672	334	0.6%	781	1.5%	1115	2.2%
35-36	8143	176	2.2%	355	4.4%	531	6.5%
37-39	6827	401	5.9%	786	11.5%	1187	17.4%
≥40	2839	459	16.2%	686	24.2%	1145	40.3%
<b>Total</b>	<b>69481</b>	<b>1370</b>		<b>2608</b>		<b>3978</b>	<b>5.7%</b>

**Figure 3.** Annual uptake rates of prenatal diagnostic testing in Victoria, 1996-2007



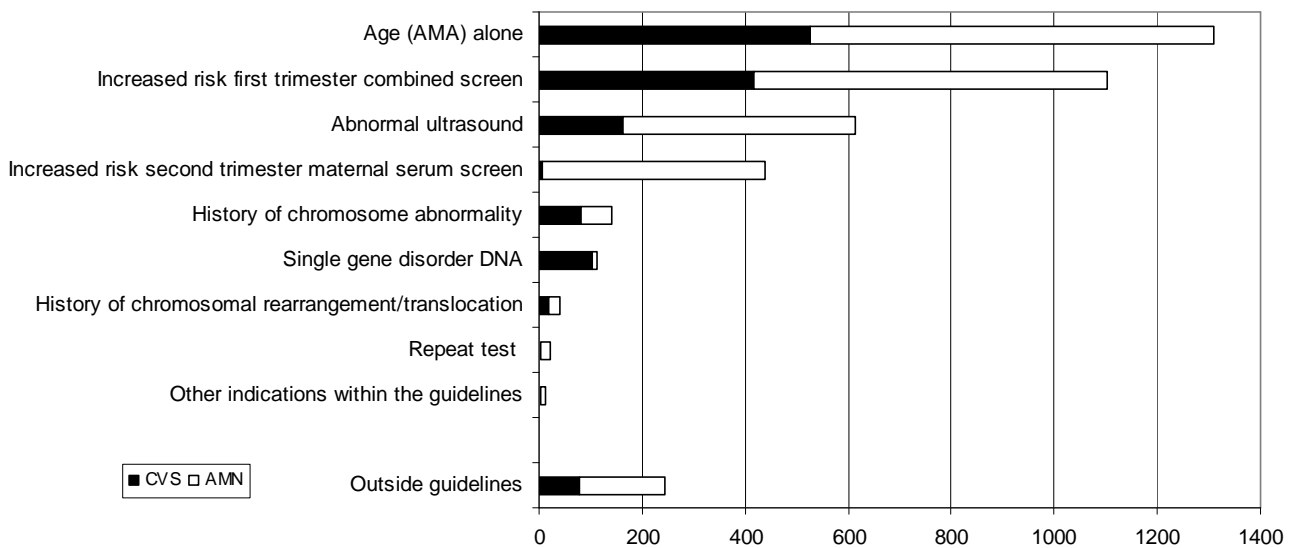
## 4. INDICATIONS FOR PRENATAL DIAGNOSIS

### 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, increased risk second trimester maternal serum screening and indications outside the recommendations of the HGSA/RANZCOG Prenatal Diagnosis Policy. Other indications included previous chromosomal abnormality (142), tests for single

gene disorders (113), history of chromosomal rearrangement/translocation (42) and other within HGSA guidelines (12).

1. 1310 (33.0%) tests were done with advanced maternal age as their only indication for testing. By definition these women were aged 37 and over (*see 4.2, maternal age*).
2. 614 (15.4%) 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. 437 (11.0%) tests were done because of a finding of increased risk second trimester maternal serum screening (*see 4.4, second trimester maternal serum screening*).
4. 1104 (27.8%) tests were done because of a finding of increased risk first trimester combined screening (*see 4.4.2, first trimester combined screening*).
5. 243 (6.1%) 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=1888) from the total (n=3978). Given that a number of tests had more than one indication for testing, in particular when prior screening was specified (n=48) this returned a more conservative estimate of the proportion of tests that were done because the woman had prenatal screening. Using this method, approximately 52.5% 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

1310 women had maternal age as their only indication (i.e. 33.0% of all women having testing). By definition, these women were aged 37 years and over. An additional 1022 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 619 or 15.6% of all tests. 75.3% 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). 31 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.**

21.6% of the tests done for abnormal ultrasound were reported as nuchal translucency screening alone (when not as part of 1st trimester combined screening). Half of abnormal nuchal translucency screens were followed by a CVS (50.3%). This compares with 17.9% 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 19 weeks respectively.

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

	CVS	AMN	Total	% Total
<b>Abnormal nuchal translucency screen</b> (includes 31 pregnancies which <b>also</b> had a suspected fetal abnormality on routine ultrasound)				
<b>Maternal age</b>				
<35 yrs	44	59	103	
35-36 yrs	11	8	19	
37 – 39 yrs	17	10	27	
≥40 yrs	14	8	22	
<i>Sub-total</i>	86	85	171	(27.6%)
<i>% Sub-total</i>	(50.3%)	(49.7%)	(100%)	
<b>Other suspected fetal or pregnancy abnormality on routine ultrasound</b>				
<b>Maternal age</b>				
<35 yrs	48	242	290	
35-36 yrs	8	46	54	
37 – 39 yrs	16	54	70	
≥40 yrs	8	26	34	
<i>Sub-total</i>	80	368	448	(72.4%)
<i>% Sub-total</i>	(17.9%)	(82.1%)	(100%)	
<b>Total</b>	166	453	619	
<b>% Total</b>	(26.8%)	(73.2%)		(100%)

## 4.4 MATERNAL SERUM SCREENING

Increased risk MSS has become a frequent indication for testing since the introduction of second trimester maternal serum screen (2TMSS) in 1996 and first trimester combined screening (1TCS) in 2000.

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.**

In 2007, there were 1541 (38.7%) prenatal diagnostic tests done because of an increased risk in either screening tests. Using information from Genetic Health Services Victoria, we estimate that there were 47476 women who had maternal serum screening (either first trimester combined or second trimester serum) in 2007. The number having prenatal diagnosis for an increased risk screening result corresponds to a diagnostic follow-up rate of 3.2% (which compares to 3.8% in 2006, 3.6% in 2005 and 3.5% in 2004).

### 4.4.1 Second trimester maternal serum screening (2TMSS)

Increased risk 2TMSS as an indication for prenatal diagnostic testing included 48 tests conducted after 14 weeks where the recorded indication was “increased risk on screening test” and the type of test not specified.

After inclusion of these data, 437 or 11.0% of all prenatal diagnostic tests were done following an increased risk 2TMSS. Due to the gestation at which this screening is done, most of the tests are AMN (431, or 98.6%), rather than CVS (6, or 1.4%). Almost two thirds (61.1%) 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	3		194		197	45.1%
35-36			70		70	16.0%
37-39	2		105		107	24.5%
≥40	1		62		63	14.4%
<b>Total</b>	6	1.4%	431	98.6%	437	100.0%

#### 4.4.2 First trimester combined screening (1TCS)

Increased risk 1TCS as an indication for prenatal diagnostic testing included 152 tests before 14 weeks where the recorded indication was “increased risk on screening test” and no further information on the type of test was provided.

After inclusion of these data, 1104 or 27.8% of prenatal diagnostic tests were prompted by an increased risk 1TCS. Of these, 417 (37.8%) were CVS and 687 (62.2%) were AMN (Table 5).

Just under half of (47.2%) 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	128		182		307	27.8%
35-36	84		130		214	19.4%
37-39	124		204		328	29.7%
≥40	84		171		255	23.1%
<b>Total</b>	417	37.8%	687	62.2%	1104	100.0%

## 4.5 HISTORY OF CHROMOSOME ABNORMALITY

Overall, 184 women were tested because of a history of chromosome abnormality, including 42 prenatal tests done because of a history of chromosome translocation or rearrangement (e.g. deletions or inversions) (Table 6).

142 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 63 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	32	31	63
Trisomy 21	32	20	52
Trisomy 18	6	5	11
Trisomy 13	1	1	2
Sex chromosome aneuploidy	1	1	2
Other major chromosome	9	3	12
<b>Total</b>	<b>81</b>	<b>61</b>	<b>142</b>
Translocation	12	13	25
Rearrangements	6	11	17
<b>Total</b>	<b>18</b>	<b>24</b>	<b>42</b>

## 4.6 SINGLE GENE TESTS

113 prenatal diagnostic tests were done because a DNA or biochemical test for a single gene disorder was requested. This number is comparable to the previous six years. The majority of tests for single gene disorders were done following CVS (91.2%, data not shown)

A list of the main conditions tested for in 2007 relative to the previous seven 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=14 for 2007).

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

Single gene test	2007		2006	2005	2004	2004	2003	2002	2001
Thalassaemia	38		27	28	25	25	25	38	23
Cystic fibrosis	26		16	16	15	15	17	11	15
Fragile X	9		19	2	9	9	13	8	10
Duchenne muscular dystrophy	3		4	2	7	7	9	6	5
Neurofibromatosis	3		2	2	3	3			
X-linked mental retardation	3		1	4					1
Spinal muscular atrophy	2		4	9	6	6	4	6	7
Myotonic dystrophy	2		3	3	4	4	3	1	
X-linked myotubular myopathy	2			2					
Carbohydrate deficient glycoprotein type IA	2				1				
Achondroplasia	1		5	1				1	
Adrenoleukodystrophy	1		3		1	1	4	4	
X-linked Hydrocephalus	1		3	2	3	3	2	3	1
Huntington disease	1		3	6	1	1	1	5	1
Haemophilia	1		2	2	3	3	5	5	5
Becker's Muscular Dystrophy	1		2						
Ornithine transcarbamylase deficiency	1		1	1			2	1	1
Gangliosidosis	1		1	2			1		2
Congenital adrenal hypoplasia	1		2	1	2	2	2	3	2
Spondyloepiphyseal dysplasia (SED)			3	1					
X-linked Lissencephaly/Double Cortin			2	2	2	2			
Gaucher Disease			2						
Prader Willi syndrome			1				2		
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	14		16	16	24	24	16	19	24
<b>Total</b>	<b>113</b>		<b>122</b>	<b>105</b>	<b>112</b>	<b>112</b>	<b>108</b>	<b>112</b>	<b>93</b>

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

Aicardi-Goutieres Syndrome	Polycystic kidney disease
Carbonyl phosphatase synthetase 1 deficiency	Pompe disease
Hay-Wells Syndrome	Tay Sachs disease
Incontinentia pigmentosa	TCIRG1 Malignant Osteopetrosis
Metabolic disease not specified	Wolf-Hirschhorn Syndrome
Mucopolysaccharidosis III	X-linked panhypopituitarism
Non-ketotic hyperglycemia	
Noonan Syndrome	

#### 4.7 OTHER WITHIN HGSA/RANZCOG RECOMMENDATIONS

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

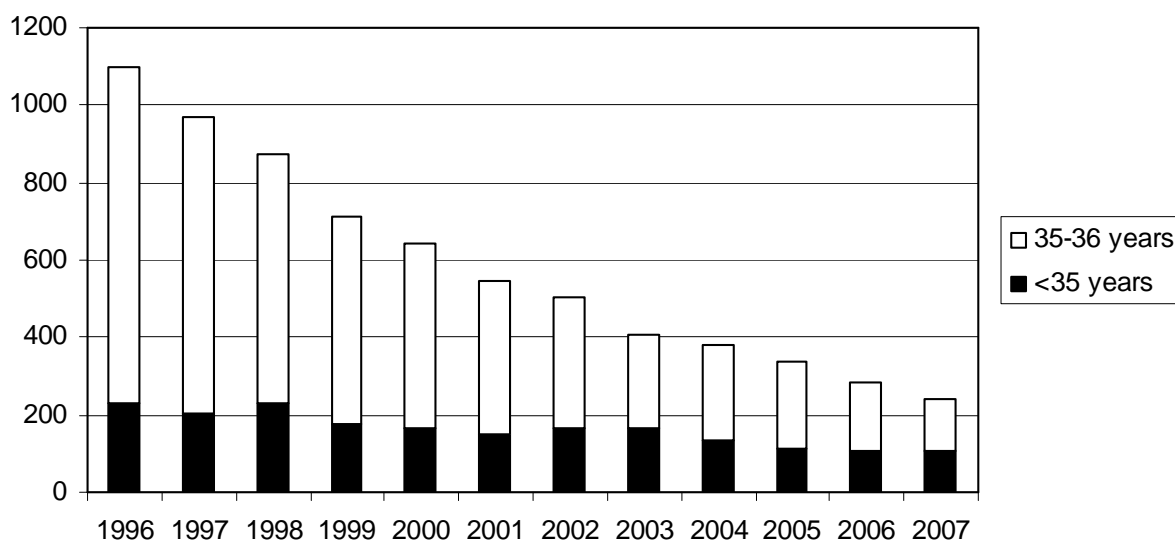
Three tests were done because of a previous neural tube defect and one because the father had Spina Bifida. Others included positive maternal serology for cytomegalovirus (n=4), toxoplasmosis (n=2), fetal anaemia, exomphalos, Kell typing and Rhesus testing. One test was done because of maternal radiation exposure and one because of a previous cystic hygroma.

#### 4.8 OUTSIDE HGSA/RANZCOG RECOMMENDATIONS

Approximately half of the 243 women with an indication outside the HGSA/RANZCOG recommendations were in the 35-36 year age group (55.6%). The indication given was *age* or *anxiety* for 94.8% of this group and for 78.7% 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, previous non-chromosomal abnormalities, twin-twin transfusion syndrome and one advanced paternal age.

The number of tests done for indications outside the HGSA/RANZCOG recommendations has dropped steadily since 1996, when 1099 tests were done for that reason. 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 5.** Indications outside HGSA/RANZCOG recommendations for Victorian women under 37 years and under 25 weeks gestation



## 5. FETAL KARYOTYPES

### 5.1 OVERVIEW

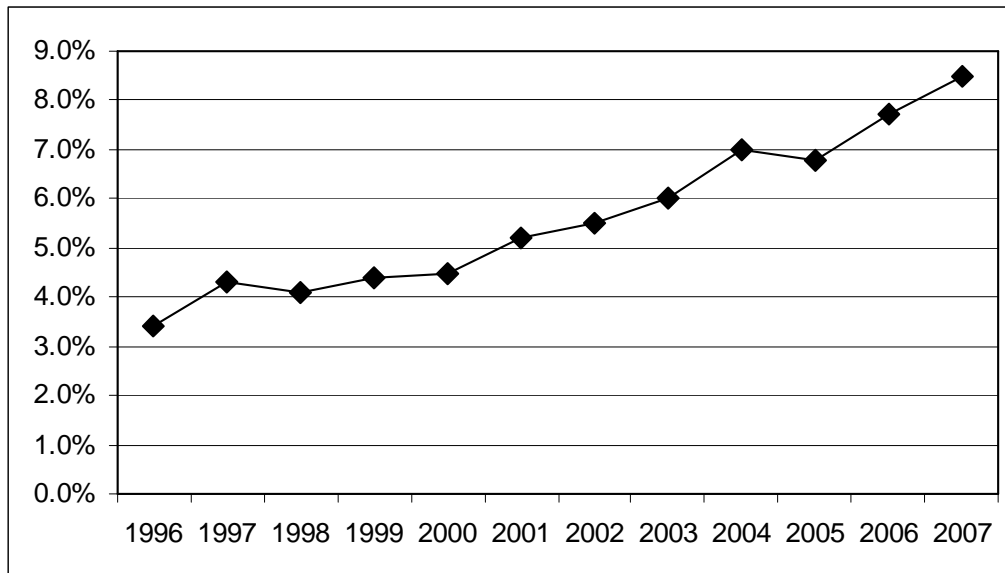
3588 (90.2%) of CVS and AMN had a normal fetal karyotype. An additional 43 (1.1%) showed a minor non-clinically significant variation in fetal karyotype, in that they were not expected to result in an abnormal fetal outcome. 8 CVS or AMN were not karyotyped because a single gene test was the reason for testing, because FISH was the only test performed or because 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	%
<b>Normal</b>				
Normal	1158	2430	3588	<b>90.2%</b>
No growth/not done	6	2	8	<b>0.2%</b>
<b>Non-clinically significant variation</b>				
Confined placental mosaicism (CPM)	8	2	10	0.3%
Balanced rearrangement	3	11	14	0.4%
Balanced translocation	6	12	19	0.5%
<b>Total minor abnormalities</b>	<b>17</b>	<b>25</b>	<b>43</b>	<b>1.1%</b>
<b>Major abnormalities</b>				
Autosomal aneuploidy:				
Trisomy 21	100	65	165	4.1%
Trisomy 18	36	24	60	1.5%
Trisomy 13	8	12	20	0.5%
Other trisomy	1	2	3	0.07%
Polyploidy	6	8	14	0.4%
Sex chromosome aneuploidy:				
45,X	13	1	14	0.4%
47,XXX	1	3	4	0.1%
47,XXY	4	5	9	0.2%
47,XYY	1		1	0.02%
48,XXY		1	1	0.02%
Unbalanced rearrangement	6	16	22	0.6%
Unbalanced translocation		1	1	0.02%
Microdeletion syndrome (22q)		4	4	0.1%
Level III Mosaicism	12	9	21	0.5%
<b>Total major abnormalities</b>	<b>188</b>	<b>151</b>	<b>339</b>	<b>8.5%</b>
<b>% abnormal of procedure</b>	<b>13.7%</b>	<b>5.8%</b>	<b>8.6%</b>	
<b>Total</b>	<b>1370</b>	<b>2608</b>	<b>3978</b>	<b>100.0%</b>

Overall, 339 (8.5%) of pregnancies tested were found to have a major abnormality, a doubling since before MSS was introduced in the mid 1990s (Figure 6). A greater proportion of all CVS were found to have a major abnormality (13.7%) compared with AMN (5.8%).

**Figure 6.** Proportion of prenatal diagnostic tests with a major karyotype abnormality. 1996-2007



Trisomy 21 accounted for 49% of these abnormalities, Trisomy 18 for 18% and Trisomy 13 for 6%. More detailed information on the detection of autosomal trisomies is available in section 6.0 of this report. Other abnormalities included 14 polyploidies, 34 sex chromosome abnormalities, 21 Level III mosaicisms and 27 unbalanced rearrangements (including four 22q deletions and one unbalanced translocation).

## 5.2 ADVANCED MATERNAL AGE AS THE ONLY INDICATION

50 or 3.8% of 1310 diagnostic procedures following a single indication of advanced maternal age only were found to have a chromosomal abnormality, 46% of which were done by CVS (Table 10).

19 of the 595 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 31 of 715 tests done (4.3%).

**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
<b>37-39 years</b>	208	387	595	
Normal/minor variation	200	382	582	97.8%
Trisomy 21	3	4	7	} 1.5%
Trisomy 18	2		2	
Other Trisomy				
Other chromosomal	3	1	4	0.7%
<b>Sub-total major abnormal</b>	<b>8</b>	<b>5</b>	<b>13</b>	<b>2.2%</b>
<b>40+ years</b>	319	396	715	
Normal/minor variation	308	380	688	96.2%
Trisomy 21	6	9	15	} 2.2%
Trisomy 18	1		1	
Other Trisomy				
Other chromosomal	4	7	11	1.5%
<b>Sub-total major abnormal</b>	<b>16</b>	<b>14</b>	<b>30</b>	<b>4.2%</b>
<b>Total major abnormal</b>	<b>24</b>	<b>19</b>	<b>43</b>	
<i>% of all AGE only abnormalities</i>	55.8%	44.2%	100%	
<i>% abnormal of procedure</i>	4.6%	2.4%	3.3%	
<b>Total</b>	<b>527</b>	<b>783</b>	<b>1310</b>	

### 5.3 AFTER ABNORMAL ULTRASOUND

The majority of the 619 pregnancies with an abnormal ultrasound indication had a normal fetal karyotype (76.0%) or a minor non-clinically significant fetal karyotype outcome (0.8%). 22.9% of the tests were found to have a major abnormality, compared to 22.1% in 2006 and 21.9% in 2005. Just under half of the abnormalities detected were by CVS (46.2%) (Table 11) compared to 2006 when 59.4% were detected by CVS.

The majority of abnormalities detected following an abnormal ultrasound were in women 37 years and over (Table 12). Trisomies were diagnosed in 36.0% of women aged 37 years and over, compared to 17.8% for women aged 35-36 years and 9.4% in the youngest age group. This compares to a detection rate in 2006 of 32.5% and 16.5%, and in 2005 when 24.8% and 15.6% 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	%
<b>Normal/minor variation</b>				
Normal	96	371	467	76.1%
Balanced rearrangement or translocation		5	5	0.8%
Not done/no growth		1	1	0.2%
<b>Total normal or minor abnormal</b>	100	377	477	<b>77.1%</b>
<b>Major abnormalities</b>				
Autosomal aneuploidy:				
Trisomy 21	24	20	44	7.2%
Trisomy 18	23	19	42	6.8%
Trisomy 13	5	11	16	2.6%
Other trisomy		2	2	0.3%
Polyploidy	4	6	10	1.6%
Sex chromosome aneuploidy:				
45,X	5		5	0.8%
47,XXX		1	1	0.2%
47,XYY	1	1	2	0.3%
Unbalanced rearrangement or translocation	2	8	10	1.6%
Microdeletion syndrome (22q)		4	4	0.7%
Mosaic Level III	2	3	5	0.8%
<b>Total major abnormal</b>	66	75	141	<b>22.9%</b>
<i>% of all ultrasound abnormalities</i>	46.8%	53.2%	100%	
<i>% abnormal of procedure</i>	40.7%	16.6%	22.7%	
<b>Total</b>	162	452	614	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
<b>≥37 years (AMA)</b>	48	104	152	
Normal/minor variation	27	63	90	59.2%
Trisomy 21	12	10	22	} 35.5%
Trisomy 18	8	19	27	
Trisomy 13		5	5	
Other chromosomal	1	7	8	5.2%
<b>Sub-total major abnormal</b>	<b>21</b>	<b>41</b>	<b>62</b>	<b>40.8%</b>
<b>35 – 36 years</b>	18	54	72	
Normal/minor variation	15	39	54	75.0%
Trisomy 21	3	5	8	} 16.7%
Trisomy 18		4	4	
Trisomy 13				
Other chromosomal		6	6	8.3%
<b>Sub-total major abnormal</b>	<b>4</b>	<b>15</b>	<b>19</b>	<b>25.0%</b>
<b>&lt;35 years</b>	100	290	390	
Normal/minor variation	92	237	329	84.4%
Trisomy 21	3	11	14	} 9.2%
Trisomy 18	1	10	11	
Trisomy 13	1	10	11	
Other chromosomal	3	22	25	6.4%
<b>Sub-total major abnormal</b>	<b>8</b>	<b>53</b>	<b>61</b>	<b>15.6%</b>
<b>Total major abnormal</b>	<b>33</b>	<b>109</b>	<b>142</b>	
<b>% abnormal of ultrasound indication</b>	<b>19.9%</b>	<b>24.3%</b>	<b>23.1%</b>	
<b>Total</b>	<b>166</b>	<b>448</b>	<b>614</b>	

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

4.8% of the 437 procedures done following an increased risk 2TMSS were found to have a chromosomal abnormality, compared to 3.9% of 516 in 2006, 3.8% of 553 in 2005 and 5.0% of 624 in 2004. 12 or 60% of the abnormalities found after an increased risk 2TMSS were trisomies.

**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
<b>≥37 years</b>	3	167	170	
Normal/minor variation	2	163	165	97.1%
Trisomy 21	1	3	4	} 2.9%
Trisomy 18		1	1	
Other Trisomy				
Other chromosomal				
<b>Sub-total major abnormal</b>	<b>1</b>	<b>4</b>	<b>5</b>	<b>2.9%</b>
<b>35 – 36 years</b>		70	70	
Normal/minor variation		69	69	98.6%
Trisomy 21		1	1	} 1.4%
Trisomy 18				
Other Trisomy				
Other chromosomal			1	1.4%
<b>Sub-total major abnormal</b>		<b>1</b>	<b>1</b>	<b>1.4%</b>
<b>&lt;35 years</b>	3	194	197	
Normal/minor variation	1	187	188	95.4%
Trisomy 21	1	4	5	} 3.5%
Trisomy 18		1	1	
Other Trisomy				
Other chromosomal	1	2	3	1.5%
<b>Sub-total major abnormal</b>	<b>2</b>	<b>7</b>	<b>9</b>	<b>4.6%</b>
<b>Total major abnormal</b>	<b>3</b>	<b>12</b>	<b>15</b>	
% of all MSS abnormalities	20.0%	80.0%	100%	
% abnormal of procedure	50.0%	2.8%	<b>3.4%</b>	
<b>Total</b>	<b>6</b>	<b>431</b>	<b>437</b>	

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

143 or 13.0% of the 1104 diagnostic procedures following an increased risk 1TCS were found to have a chromosomal abnormality, 24.9% of CVS and 5.7% of AMN done for an increased risk 1TCS had a chromosomal abnormality (Table 14).

Across all age groups, 108 of the abnormal karyotypes were trisomies (75.5%), 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
<b>≥37 years</b>	208	375	583	
Normal/minor variation	147	353	500	85.8%
Trisomy 21	42	13	55	} 11.3%
Trisomy 18	8	1	9	
Other Trisomy	1	1	2	
Other chromosomal	10	7	17	2.9%
<b>Sub-total major abnormal</b>	<b>61</b>	<b>22</b>	<b>83</b>	<b>14.2%</b>
<b>35 – 36 years</b>	84	130	214	
Normal/minor variation	67	124	191	89.3%
Trisomy 21	8	5	13	} 8.4%
Trisomy 18	3		3	
Other Trisomy	2		2	
Other chromosomal	4	1	5	2.3%
<b>Sub-total major abnormal</b>	<b>17</b>	<b>6</b>	<b>23</b>	<b>10.7%</b>
<b>&lt;35 years</b>	125	182	307	
Normal/minor variation	99	171	270	87.9%
Trisomy 21	14	6	20	} 7.8%
Trisomy 18	1	1	2	
Other Trisomy	2		2	
Other chromosomal	9	4	13	4.3%
<b>Sub-total major abnormal</b>	<b>26</b>	<b>11</b>	<b>37</b>	<b>12.1%</b>
<b>Total major abnormal</b>	<b>104</b>	<b>39</b>	<b>143</b>	
<b>% of all FTC abnormalities</b>	<b>72.7%</b>	<b>27.3%</b>	<b>100%</b>	
<b>% abnormal of procedure</b>	<b>24.9%</b>	<b>5.7%</b>	<b>13.0%</b>	
<b>Total</b>	<b>417</b>	<b>687</b>	<b>1104</b>	

## 5.6 AFTER HISTORY OF CHROMOSOMAL ABNORMALITY

### 5.6.1 History of chromosomal aneuploidy

Of the 142 women tested because of a known history of chromosome aneuploidy, one woman had a second diagnosis of Trisomy 21, one had a second diagnosis of Trisomy 18 and one woman with a previous Trisomy 18 was found to have a fetus with Trisomy 21 (Table 15).

Detailed information on the previous chromosomal abnormality was not available for 44.4% in this category. Therefore we are unable to estimate a Trisomy 21 recurrence rate from this data set.

Previous other major chromosome abnormalities resulting in normal karyotypes included a Trisomy 9, a Trisomy 16, a Trisomy 20 and a Trisomy 13.

**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	30 N 2 CPM	31 N	61 N 2 CPM	44.4%
Trisomy 21	28 N 2 T21 1 CPM 1 47XXX	20 N	48 N <b>2 T21</b> 1 CPM <b>1 47XXX</b>	36.6%
Trisomy 18	5 N 1 T21	4 N 1 T18	9 N <b>1 T21</b> <b>1 T18</b>	7.7%
Trisomy 13	1 N	1 N	2 N	1.4%
Sex chromosome aneuploidy	2 N	3 N	5N	3.5%
Other major chromosome	8 N	1 N	9 N	6.3%
<b>Total</b>	81	61	142	100%

N: Normal karyotype  
CPM: Confined placental mosaicism  
T18: Trisomy 18  
T21: Trisomy 21

### 5.6.2 Previous chromosomal translocation or other rearrangement

42 women were tested because of a family history of chromosome translocation or rearrangement. 11 of these tests showed fetal karyotypes with balanced translocations or rearrangements (26.2%) and two (4.8%) with unbalanced rearrangements (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	7 N	7 N	14 N	
	5 BT	4 BT, 2 UBR	9 BT, 2 UBR	
<i>Sub-total</i>	12	13	25	59.5%
Rearrangements (deletions, inversions, etc)	6 N	9 N	15 N	
		2 BR	2 BR	
<i>Sub-total</i>	6	11	17	40.5%
<b>Total</b>	18	24	42	100%

N: Normal

BR: Balanced rearrangement

BT: Balanced translocation

UBR: Unbalanced rearrangement

### 5.7 OTHER WITHIN HGSA/RANZCOG RECOMMENDATIONS

Of the 12 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 was one unbalanced rearrangement amongst the 136 women aged 35-36 years who were tested for reasons outside the HGSA/RANZCOG and two balanced rearrangements/translocations. One of the 107 tested women under 35 years had a major fetal karyotype abnormality (Trisomy 21) and there were two balanced rearrangements (1.9%) (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		
<b>35-36 years</b>				
Age/anxiety	39 N 1 BR 1BT	86 N 1 UBR	125 N 1 BR, 1BT <b>1 UBR</b>	
Family history of T21	1 N	2 N	3 N	
Other	3 N	2 N	5 N	
<i>Sub-total</i>	<b>45</b>	<b>91</b>	<b>136</b>	<b>56.0%</b>
<b>&lt;35 years</b>				
Age/anxiety	21 N 1 T21	62 N 1 BR	83 N 1BR <b>1 T21</b>	
Family history of T21	4 N	3 N 1 BT	7N 1 BT	
Other	7 N	7N	14 N	
<i>Sub-total</i>	<b>33</b>	<b>74</b>	<b>107</b>	<b>44.0%</b>
<b>Total</b>	<b>78</b>	<b>165</b>	<b>243</b>	<b>100%</b>

N: Normal/not done

BR: Balanced rearrangement/translocation

BT:

T21:

Balanced translocation

Trisomy 21

## 6. AUTOSOMAL TRISOMIES

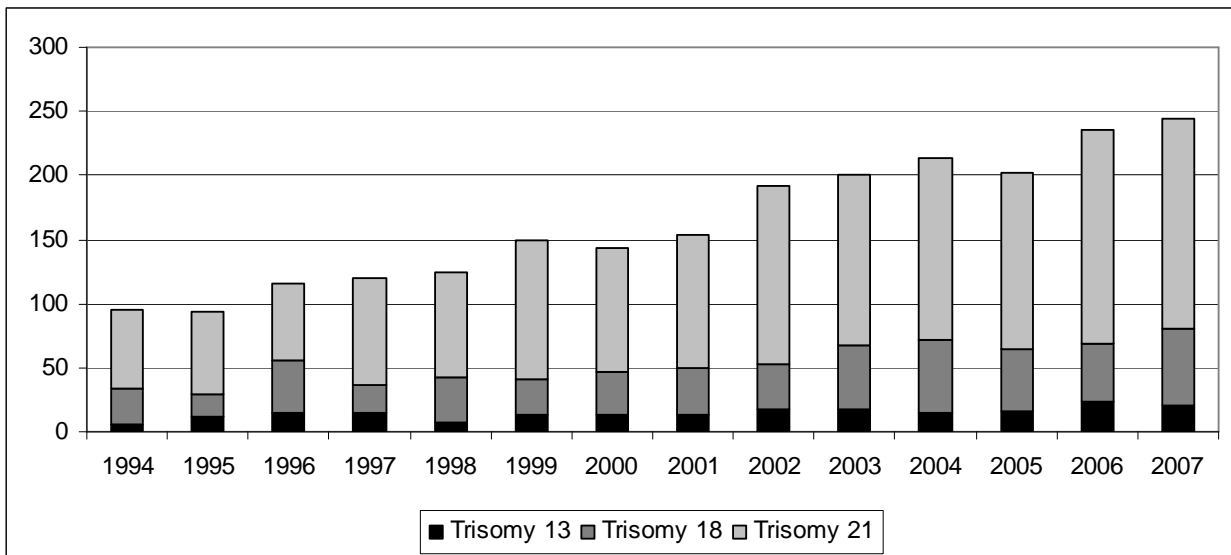
In 2007, prenatal diagnostic tests before 25 weeks of gestation resulted in the diagnosis of 165 Trisomy 21, 60 Trisomy 18, 20 Trisomy 13, two Trisomy 9, and one Trisomy 22. In addition, one Trisomy 21 was diagnosed at 28 weeks and two Trisomy 18 were diagnosed at 27 and 30 weeks (*see 8. Indication 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.

60.6% of Trisomies 21, 60.0% of Trisomies 18 and 40.0% 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. In 2006 prenatal diagnostic tests diagnosed the highest number of Trisomy 21 to date, 166.

**Figure 7.** 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 (83.7%). Only 27 of the 165 Trisomies 21 diagnosed (16.4%) 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 (93.3% and 100% respectively), with a fetal abnormality on ultrasound (other than increased nuchal thickening) accounting for 55.0% and 70.0% (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			2	8		1			1	12	7.3%
First trimester combined screening		14	8	22	18	5	5	8	5	85	51.5%
Second trimester maternal serum screen		1		1		4	1	2	1	10	6.1%
Other ultrasound abnormality		2	3	3	5	10	3	2	3	31	18.8%
No screening test, prompted by age alone		1		3	6			4	9	23	13.9%
Other (previous chromosomal abnormality, outside guidelines)		1		1	1				1	4	2.4%
<b>Total</b>		19	13	38	30	20	9	16	20	165	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		2	5					8	13.3%
First trimester combined screening		1	3	3	4	1			1	13	21.7%
Second trimester maternal serum screen						1			1	2	3.3%
Other ultrasound abnormality		5		5	4	5	4	7	3	33	55.0%
No screening test, prompted by age alone				2	1					3	5.0%
Other (previous chromosomal abnormality, outside guidelines)								1		1	1.7%
<b>Total</b>		7	3	12	14	7	4	8	5	60	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		1								1	5.0%
First trimester combined screening		2	2						1	5	25.0%
Other ultrasound abnormality		2		1		7		3	1	14	70.0%
<b>Total</b>		5	2	1		7		3	2	20	100%

## **7. REPEAT TESTS AND FETAL KARYOTYPES**

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26 (0.7%) prenatal diagnostic tests were repeated.

### **7.1 CLARIFICATION OF MOSAIC OR OTHER FINDINGS OF POTENTIAL PLACENTAL ORIGIN (N=17)**

9 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). One was confirmed as a LIII mosaic and one was found to be a Trisomy 21. A repeat CVS was performed after a normal AMN because there was IUGR and placental insufficiency. The repeat confirmed the normal karyotype. One CVS showing a Trisomy 4 was found to be normal on repeat AMN. One CVS repeat was to exclude placental mosaicism after FDIU. Three repeat tests were fetal blood samples done to clarify a level three mosaic found on AMN. Two of these were confirmed as normal and one as a level III mosaic. One normal twin and one level III mosaic twin (CVS) were confirmed as both normal on repeat AMN. One Trisomy 21 and mosaic twin on AMN were identified as Trisomy 21 and a CPM by repeat AMN.

### **7.2 NO GROWTH, MATERNAL CONTAMINATION, SUSPECTED SAMPLING ERROR (N= 6)**

One fetal sample, two AMN and one CVS where there was no growth in the first sample were found to have normal karyotype on repeat AMN. One AMN that was thought to be contaminated with maternal blood was found to have a normal karyotype on repeat AMN. One test was repeated because one of the two twin fetuses appeared to be female on ultrasound but, like its twin, showed a male karyotype on CVS. The amended karyotype on repeat AMN was female, i.e. they were mixed-sex twins and the discrepancy was due to sampling error.

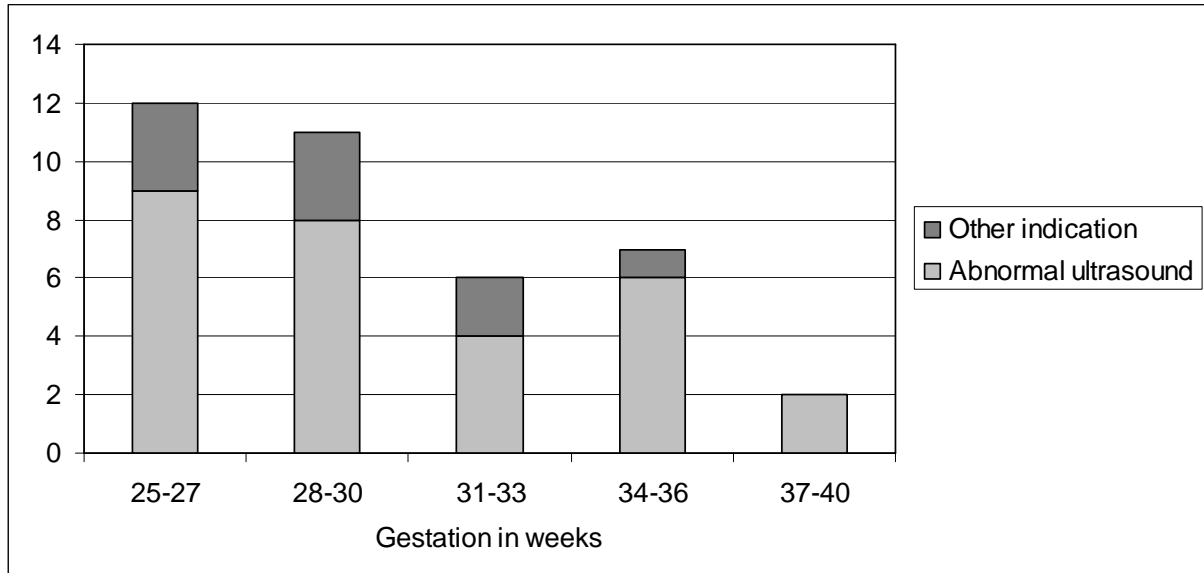
### **7.3 SUSPECTED FETAL ANOMALY (N=3)**

One AMN confirmed a normal CVS, but was repeated for FISH due to a heart anomaly on ultrasound. One CVS was repeated for fragile X testing. Another CVS showing an abnormal chromosome 11 was found to be an unbalanced rearrangement on repeat AMN.

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

38 women had a late (over 24 weeks gestation) prenatal diagnosis compared to 50 women in 2006; 37 were done by AMN and one by CVS.

**Figure 8.** Prenatal diagnosis for Victorian women over 24 weeks gestation by gestational age and indication



29 (76.3%) of these tests were done because of an abnormal ultrasound (Figure 8) and all but 6 were done in women under 37 years. Other indications included one test done for maternal age at 26 weeks, two for single gene tests both at 32 weeks, three for an increased screening risk at 26, 28 and 29 weeks and one due to a previous Trisomy 13. One test was for reasons outside the HGSA/RANZCOG recommendations and one had an unknown indication.

3 tests (7.9%) done after 24 weeks gestation showed a major abnormality (Table 21). Two Trisomy 18 were diagnosed after an abnormal ultrasound at 27 and 30 weeks gestation. One Trisomy 21 was found following an abnormal ultrasound at 28 weeks gestation.

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

Gestation (weeks)	Normal karyotype	Abnormal outcome (All with indication of abnormal ultrasound)	Total
25 - 27	11	1 T18	12
28 - 30	9	1 T21, 1 T18	11
31 - 33	6		6
34 - 36	7		7
37 - 40	2		2
<b>Total</b>	35	3	38
% total	92.1%	7.9%	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 2489 in 2005, 2802 in 2006 and 2611 in 2007. This corresponds to 58% and 64% and 66% 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 (31.5% FISH vs 28.0% 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	241		583		824	31.5%
35-36	129		238		367	14.1%
37-39	284		424		708	27.1%
≥40	341		371		712	27.3%
<b>Total</b>	995	38.1%	1616	61.9%	2611	100.0%

Of the 2611 FISH done, 27.2% 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. 11.4% of tests that included FISH were found to have an abnormal karyotype. 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 2007 (11.4% vs 8.6%). This may be the result of the high proportion of FISH requested following an increased risk screening test result (62.0% vs 51.5% across all tests).

**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	349	360	709	54.1%
First trimester combined screening	316	464	780	75.1%
Second trimester maternal serum screening	46	267	313	64.1%
Abnormal ultrasound	78	323	401	64.8%
Increased nuchal thickness	65	59	124	77.5%
Outside guidelines or unknown indication	54	93	147	51.8%
Previous chromosomal abnormality	59	38	97	68.3%
History rearrangement/translocation	9	6	15	35.7%
Single gene test	18	4	22	19.5%
Other within guidelines	1	0	1	8.3%
Repeat sample		1	1	4.5%
History NTD		1	1	
<b>Total</b>	995	1616	2611	

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

Indication	CVS	AMN	Total	% Total
Normal/minor variation	832	1505	2337	89.5%
Not done/no growth	2	1	3	
Trisomy 21	93	51	144	
Trisomy 18	34	22	56	
Other Trisomy	7	11	19	
Polyploidy	6	7	13	
Sex chromosome abnormality	12	8	20	
Unbalanced rearrangement (incl.22q)	5	10	15	
Level III mosaic	4	1	5	
<b>Total major abnormal</b>	161	110	271	<b>10.4%</b>
<i>% abnormal of procedure</i>	16.9%	6.3%	10.4%	
<b>Total</b>	995	1616	2611	

## 10. INTERSTATE SAMPLES

Victorian cytogenetics laboratories analysed 281 CVS and AMN sent from interstate or overseas in 2007. The majority of samples came from Tasmania (n=222) and New South Wales (n=55) (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	TAS	Total
<35	29			97	126
35-36	8	2	1	28	39
37-39	10			47	57
≥40	8	1		50	59
<b>Total</b>	55	3	1	222	281
<i>%Total</i>	18.2%	1.2%	1.9%	77.1%	100%

Of the 281 interstate samples, most were done for an increased risk screening test result (59.8%) and only 23.1% were for advanced maternal age alone. 6.4% 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	TAS	Total	% Total
Advanced maternal age (alone)	10			55	65	23.1%
First trimester combined screening	7	3		60	70	24.9%
Second trimester maternal serum screening	5			35	40	14.2%
Abnormal ultrasound	10			31	41	14.6%
Increased nuchal thickness	5			12	17	6.1%
Outside guidelines or unknown indication	5		1	12	18	6.4%
Single gene test	8			7	15	5.3%
Previous chromosomal abnormality	1			6	7	2.5%
History translocation/rearrangement	1			1	2	0.7%
Repeat				3	3	1.1%
Other within guidelines	3				3	1.1%
<b>Total</b>	55	3	1	222	281	100.0%

8.9% of tests originating from interstate were found to have an abnormal karyotype. The tests included a further 11 Trisomy 21 diagnoses from Tasmania and 5 from New South Wales (Table 27).

**Table 27.** Interstate samples by state and karyotype outcome

Indication	NSW	NT	QLD	TAS	Total
Normal/minor variation	45	3	1	197	246
Not done/ no growth				1	1
Trisomy 21	5			11	16
Trisomy 18	1			5	6
Trisomy 13				3	3
Polyploidy	1			3	4
Unbalanced rearrangements (incl. 22q)	1			1	2
Sex chromosome abnormality	1			1	2
Level III mosaic	1				1
<b>Total major abnormal</b>			1	24	25
<i>% abnormal</i>	18.2%	0%	0%	10.8%	8.9%
<b>Total</b>	55	3	1	222	281