GENOMICS OCCASIONAL PAPER 5

Statewide evaluation of first trimester screening for Down syndrome and other fetal anomalies in Western Australia

September 2005

Department of Health
Government of Western Australia

Genomics Occasional Paper 5

Statewide evaluation of first trimester screening for Down syndrome and other fetal anomalies in Western Australia

September 2005

Department of Health
Western Australia

Acknowledgments

The authors wish to acknowledge the support and assistance with data collection of all those clinicians below:

Mr Konrad Pscheidl, GE Medical, Germany

Professor Caroline Bower and, Births Defects Registry, Women's and Children's Health Service, Subiaco

Dr Ashleigh Murch, Pathology Support Unit, Women's and Children's Health Service

Assc Prof Jan Dickinson, Ultrasound Department, Women's and Children's Health Service

Ms Eleanor Snell, Imaging the South, Mandurah

Mr Neville Phillips, Obstetric and Gynaecological Ultrasound, Wembley

Dr Chelsea Hunter, Dr Susan Lamp and Mr Glen Payne, Perth Radiology Clinic, Parmelia and Joondalup

Mr Paul Steffanetti and Mr Wally Harmer, Quinns Medical Imaging, Quinns Rocks

Dr Anthony Murphy, Western Ultrasound for Women, Subiaco

Dr Peter Hugo, St John of God Medical Clinic, Murdoch

Dr Leila Dekker, Pilbara Radiology, Karratha

Dr Bev Hewitt, Park Ultrasound, West Perth

Dr Sue Ulreich, SKG Radiology, West Perth

Dr John Phillips, Perth Ultrasound, Subiaco

The laboratories below also provided summary data:

Mayne Health Western Diagnostic Pathology, Dr Narelle Hadlow, Myaree

Western Australian Institute for Medical Research, Professor Nigel Laing, Nedlands

Molecular Genetics Unit, Women's and Children's Health Service, Dr Ted Edkins, Subiaco

PathCentre, Dr John Beilby, Nedlands

Clinipath, Dr Wayne Smit, West Perth

General Pathology Laboratories, Dr Graham McLellan, Fremantle

Citation

Breheny N, O'Leary P, Dickinson J, Bower C, Goldblatt J, Hewitt B, Murch A and Stock R (2005). *Statewide evaluation of first trimester screening for Down syndrome and other fetal anomalies in Western Australia.* Genomics Occasional Paper 5. Prenatal Diagnosis Committee, Department of Health Western Australia.

Executive Summary

In Western Australia, Down syndrome has a birth prevalence of 1:445[1]. It is the most common form of mental retardation and many affected infants have major structural abnormalities. Since the late 1980s, screening programs have been used to determine whether a fetus is at 'increased risk' for a chromosomal disorder such as Down syndrome (Trisomy 21). Ultrasound and biochemical markers in early pregnancy indicate a woman's risk status, with 'increased risk' being greater than a 1 in 300 chance of a Down syndrome pregnancy. Subsequent diagnostic tests, amniocentesis or chorionic villus sampling, can clarify whether a fetus has the disorder.

Diagnostic test results and pregnancy outcome information show the effectiveness of screening tests. First trimester screening provides an 83% detection rate with a false positive rate of 3.7%. It uses a combination of ultrasound and biochemistry at 10-13 weeks gestation. Second trimester maternal serum screening has a detection rate of 70-80% with a false positive rate of 5%. It relies on biochemistry only at 15-18 weeks gestation.

Population screening programs across public and private sectors are difficult to monitor at a state-wide level. The only way to evaluate the screening program performance has involved the voluntary submission of data. This is resource intensive and some laboratories see the data in their systems as 'commercial-in-confidence'.

The aim of this study was to evaluate the performance of screening service providers through the benchmarking of data against other states[2] and large international screening programs. Rates of detection, false negatives, false positives and median values for each measurement were collected as recommended by the Human Genetics Society of Australia and the Royal Australia and New Zealand College of Obstetricians and Gynaecologists.

Under S95A of the Privacy Act 1988 patient-identified, health information can be collected for surveillance of population health screening programs. On this basis the Institutional Ethics Committee at King Edward Memorial Hospital and Confidentiality of Health Information Committee, Department of Health Western Australia endorsed the evaluation. All data linkage was completed under established security protocols and no intervention or alteration occurred in the management of women as a result of this study.

Linking screening data with pregnancy outcomes has provided a unique opportunity to determine the effectiveness of the maternal prenatal screening program, the health care costs and the impact on families and individuals in Western Australia.

Table of Contents

1. Background 5

2. Ethics 5

3. Budget 6

4. Data Collection 6

6. Data Cleaning and Composition into a Single Final Dataset 7

7. Missing Data 8

8. Data Analysis 8

8.1 Performance of the first trimester screening program 8
8.2 Trends in maternal age 10
8.3 Specifics of the first trimester screening group 10
8.2 Diagnostic test data 12
8.3 Adverse outcome data 13
8.4 Single gene disorder tests 14

9. Future Research 15

Appendix A: Prenatal Diagnosis Committee 16

Appendix B: Statewide Audit of Prenatal Screening and Diagnosis in WA 17

Appendix C: SQL Script for Sybase Anywhere 18

Appendix D: Data Sought from the Data Linkage Unit, DOHWA 19

Appendix C: Structure for Final database 20

References 23

1. BACKGROUND

The prenatal screening program for Downs syndrome and fetal anomalies involves close coordination between: ultrasound, biochemistry, genetic, cytogenetic, obstetric and primary health care providers.

The Human Genetics Society of Australasia and the Health Technology Assessment Program in the United Kingdom recommend service providers:

- maintain comprehensive records and follow-up cases;
- continuously monitor their screening practice;
- provide accurate information on the number of pregnancies screened, detection and screen positive rates to consumers; and
- contribute data to a central body for external evaluation.

In his *Review of state-wide delivery of genetic services in Western Australia*[3], Associate Professor Eric Haan (2000) recommended the department establish an audit process for prenatal screening in Western Australia. Accordingly the Prenatal Diagnosis Committee (of the Western Australian Genetics Council see listed in Appendix A) identified ongoing prenatal screening evaluation as a key activity within its terms of reference.

In keeping with international standards for quality assurance and prenatal data collection in other states, the Genomics Directorate took on the collection and evaluation prenatal screening and diagnostic test data initiated by an earlier pilot study[4].

2. ETHICS

When maternal serum screening tests began in the early 1990s screening data were shared on a voluntary basis to determine state-wide performance. Emerging privacy concerns have made it increasingly difficult to collect screening, diagnosis and outcome data. However, exemption from Section 95A of the 1988 Privacy Act was sought for the evaluation for several reasons:

- No intervention in the management of women would occur;
- The composite database would contain no personal identifying information;
- The logistics of collecting thousands of consent forms and cross checking these with the databases of ultrasound and pathology practices would preclude the research being performed properly. Further, annual Downs' births are so few, that non-cooperation of one or two persons could skew the statistics.
- All Department of Health prenatal pamphlets contain the statement; '*To improve the accuracy of the screening program, results and outcomes will be monitored. Your personal information will remain confidential*'.

For these reasons the Institutional Ethics Committee at King Edward Memorial approved the evaluation in July 2003.

The original study proposed linking identified data from the laboratories with non-identified data from ultrasound clinics using mother's date of birth, nuchal translucency measurements and biochemistry results. A more efficient means of data collection was devised in which, the Fetal Medicine Foundation (FMF) patient database was copied from each ultrasound clinic and identified data extracted using a customised query and software from the FMF program developers. The Ethics Committee approved the modified study design in September 2003.

Ethical approval for data linkage was also granted by the departmental Confidentiality of Health Information Committee (CHIC) in February 2003 subject to the following conditions:

- The Genomics Directorate undertakes to allow access to (de-identified) data only in accordance with the Department of Health (CHIC) protocol; and
- The Genomics Directorate undertakes to obtain signed statements from each laboratory and ultrasound clinic provider, in which they accept full responsibility for providing data to the Data Linkage Unit.

Each of the ultrasound clinics signed a statement of authorisation (see Appendix B) and first trimester screening data and cytogenetic data from the Women's and Children's Health Service were collected.

Second trimester screening and cytogenetic data were sought from private laboratories but they expressed concern at the wording of the signed statement requested by CHIC. This issue was resolved in August 2004 when CHIC approved a revised statement in which the Genomics Directorate accepted responsibility for data in transit from the laboratory to the Data Linkage Unit (DLU). However, support for the evaluation was not forthcoming so the study was confined to the evaluation of first trimester screening data only.

3. BUDGET

Expenses for the collection, linkage and compilation of a single dataset included:

• Sybase SQL Anywhere 5.5 Single User software	May 2003	$250
• Data Linkage Unit services	Sep 2004	$3,200
• Consultant biostatistician: 45 hours	Jan 2005	$3,000

4. DATA COLLECTION

All registered nuchal translucency ultrasound providers in Australia are provided software from the Fetal Medicine Foundation through the Nuchal Translucency Program[5]. The software, known as the '*PIA - Fetal Database*', (since superseded by FMF '*The 11-13[6] Week Scan*' software) was developed by Viewpoint (GE Healthcare) in close cooperation with Professor Nicolaides of the Fetal Medicine Foundation in the United Kingdom to estimate the risk of a fetus having Downs Syndrome.

Standard database files from 13 ultrasound clinics were collected on floppy disk, cd-rom or memory stick between November 2003 and January 2004. At this stage first trimester screening data were encrypted.

Software (Sybase SQL Anywhere 5.5 Single User) was purchased from the screening program developers, Viewpoint in Germany. Customised syntax (see Appendix C) extracted identified first trimester screening data from the 27-month period 1 August 2001 until 31 October 2003 to coincide with an earlier pilot's end of data collection.

Data were collated into a single excel spreadsheet (N=26,641 records) and stored on a secure non-networked laptop in the Genomics Directorate.

Diagnostic test (karyotype) information was provided by the Cytogenetic Laboratory at Women's and Children's Health Service (N=2,103 records) for the same collection period.

5. DATA LINKAGE

In accordance with CHIC protocols, first trimester screening and karyotype datasets containing key linkage fields only (no clinical details) were provided to the DLU at the Department of Health WA in April 2004. Data were linked with pregnancy outcome information from the Births Defects Registry, the Midwives Notification System, the WA Mortality Register and the WA Morbidity Database. See Appendix D for the list of linked data fields.

In November 2004 the DLU provided Genomics Directorate with excel, data, text and layout files containing over 140,000 linked records. Each of the linked files had 'key fields' (12-digit alphanumeric encrypted codes) to link one dataset to another. A mapping file containing only the necessary 'key fields' from the various files enabled the construction of a composite dataset.

6. DATA CLEANING AND COMPOSITION INTO A SINGLE FINAL DATASET

Richard Parsons, a consultant biostatistician to the Data Linkage Unit was contracted to provide on-site assistance with complex data linkage composition into a single 'final' dataset.

The contractor signed a confidentiality clause and all linkage was completed on a password protected non-networked computer in a secure office within the department. During linkage, no identified data were taken off-site or made accessible to other parties.

The first trimester screening dataset was reviewed before linkage with pregnancy outcome information. Records removed from the dataset included cases where:

- no adjusted Trisomy 21 risk was recorded;
- NT data were absent;
- data entry error was apparent (NT of 65mm, and persons named 'Test Patient');
- the patient was less than 10 years old;
- more than one fetus was recorded;
- the patient had a second scan within 34 days; or
- the risk of a Down syndrome pregnancy was calculated using biochemistry or ultrasound data alone, instead of the combined risk.

Over the data collection period, multiple principal diagnoses and procedures were recorded for some hospital patients. The matched morbidity data for the first trimester patients contained up to 21 diagnosis and 11 procedure codes. When separated out, these corresponded to 176,691 diagnosis records and 145,586 procedure records (one code on each record).

Likewise, the matched morbidity data for the karyotype data were separated into 20,085 diagnosis and 13,929 procedure code records.

For this reason a single composite file was assembled, containing data from each of these files, only for the 22,695 records present in the cleaned first trimester screening file. Karyotype records which did not link to one of these first trimester screening records were ignored.

New variables were derived which report the date of conception, date of the ultrasound scan and the estimated date of delivery for each record plus a variety of the other dates, depending on the pregnancy outcome.

When linking to the morbidity data, only terminations that occurred between the period, date of conception and the estimated date of delivery for each scan, were considered. There were often cases of terminations or miscarriages that occurred outside these dates, presumably for a different fetus (single or plural). These were recorded in the field 'other abortion'. A list of fields in the 'Final' composite dataset is recorded in Appendix E.

7. MISSING DATA

Of all the first trimester pregnancies screened in the composite dataset (N=22,695), 420 cases had no outcome information at all. Follow-up forms from one clinic revealed five of these women had normal births.

The remaining 415 patients (of whom 20 were high-risk) may have miscarried, terminated and, or relocated overseas or interstate. Data from the WA Electoral Roll confirmed at least three patients had relocated overseas and one patient had died. These cases (1.8% of total screened) were removed from the composite dataset before analysis.

8. DATA ANALYSIS

Analysis was undertaken in SPSS version 12.

8.1 Performance of the first trimester screening program

Between August 2001 and 31 October 2003, there were 55,867 still and live births in WA. Over half of these women were screened for a fetal anomaly in their first (73%) or second trimester (27%).

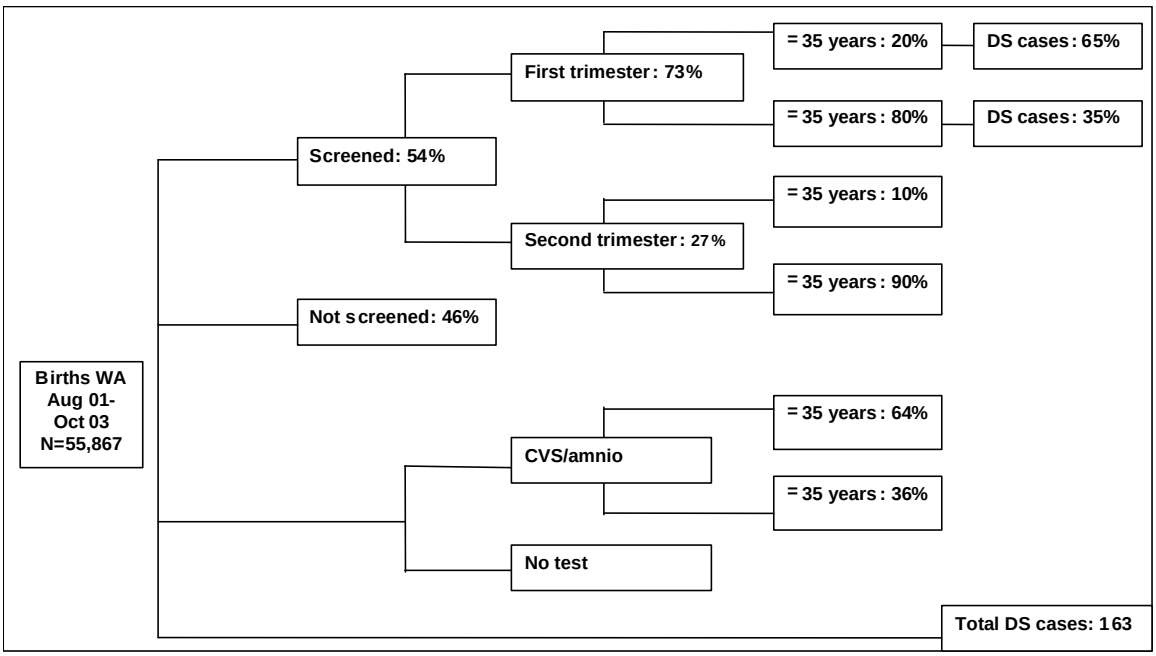

Figure 1: Flow chart of screening and diagnosis between August 2001 and October 2003

Among women that had first trimester screening (N=22,280), 3.9% (N=877) were found to be at 'increased risk' of having a Down syndrome pregnancy. A woman was considered at 'increased risk' if her combined biochemistry and ultrasound risk was greater than or equal to 1 in 300.

Of all the Down syndrome pregnancies (N=60), 83% (N=50) were predicted through first trimester screening with a false positive rate of 3.7%. See Table 1. This translates to 1 in 17.5 chance of detecting Down syndrome in women identified to be at increased risk.

Table 1: First trimester screening test performance

	Ultrasound only	Biochemistry only	Combined
Detection rate	73% (44 / 60)	85% (51 / 60)	83% (50 / 60)
Recall rate (high-risk cases)	8.75% (1,949 / 22,280)	11.7% (2,611 / 22,280)	3.9% (877 / 22,280)
False positive rate	8.5% (1,949-44 / 22,280)	11.5% (2,611-51 / 22,280)	3.7% (877-50 / 22,280)
Down syndrome cases missed	16	9	10

If the false positive rate was fixed at 5%, the detection rate for Down syndrome would increase from 83% to 85%.

Of women considered at 'population risk' only, ten Down syndrome pregnancies were later detected. This translates to a 1 in 2,227 chance of a Down syndrome pregnancy being missed by first trimester screening.

Though biochemistry alone would have detected 85% (51 out of 60 cases) of women at high risk of having a Down syndrome pregnancy the false positive rate of 11.5% makes it less viable. In acceptable comparison, ultrasound alone would have detected 73% (44 out of 60) of Down syndrome pregnancies with a false positive rate of 5.9%[6]. The combination of biochemistry with ultrasound screening however lifts the overall detection rate from 73 to 83%.

Details of the ten Down syndrome pregnancies missed by first trimester screening are reported in Table 2. The NT measurement appears to decrease with maternal age.

Table 2: Down syndrome pregnancies missed through screening

Age (yrs)	Weight (kg)	Gestation (wks)	Background risk of Tr21	BhCG MoM	PAPP-A MoM	Biochemistry only risk Tr21	CRL (mm)	NT (mm)	Combined risk Tr21
22	67	Wk11	1012	3.21	1.04	2496	59	2.7	887
28	67	Wk12	710	1.17	1.43	5043	60	2.8	1468
32	74	Wk12	441	1.57	0.61	290	61	2.2	445
32	61	Wk12	454	1.04	0.41	3235	62	2.1	4528
32	49	Wk13	434	0.96	0.44	726	75	2.6	657
33	59	Wk13	340	0.87	0.54	137	76	2.0	584
34	67	Wk12	277	0.58	0.45	550	65	2.1	1343
35	70	Wk12	218	0.65	0.85	203	60	1.8	807
36	80	Wk13	182	0.71	0.44	140	72	1.5	1159
36	67	Wk11	179	1.37	0.37	49	52	1.2	401

8.2 Trends in maternal age

Of total births in WA only 6% of mothers were aged 35 and over in 1983; by 1993 this figure was 11% and by 2003, 18%. See Figure 2.

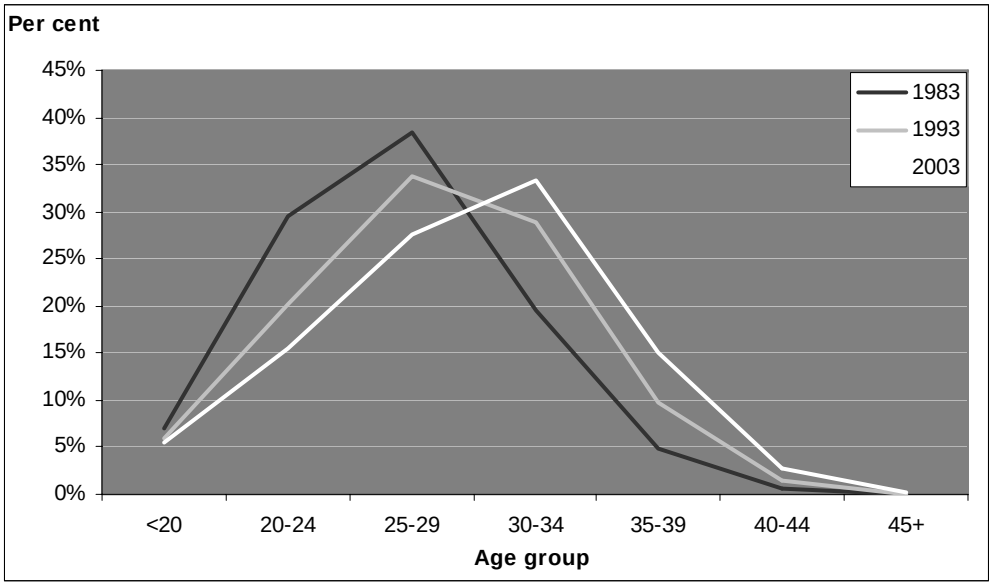

Figure 2: Maternal age group by year of birth in 1983, 1993 and 2003

Older women were more likely to have screening than younger women. The median maternal age was 29 years[7] for all women that gave birth in WA between 2001 and 2003 compared to the median maternal age for women that had first trimester screening in WA in a similar period, which was 31 years (range 14-47yrs). Of those that had first trimester screening, 20% of women were aged 35 or older.

Among women that elected second trimester screening, 10% were aged 35 or older and 64% of women that had a diagnostic test (CVS or amniocenteses).

8.3 Specifics of the first trimester screening group

The median gestation at screening was 12 weeks 4 days (range 70-101 days). In summary 16% of women were screened in the 11-11^{6} week of gestation, 61% in the 12-12^{6} week and 23% in the13-13^{6} week. See Figure 3.

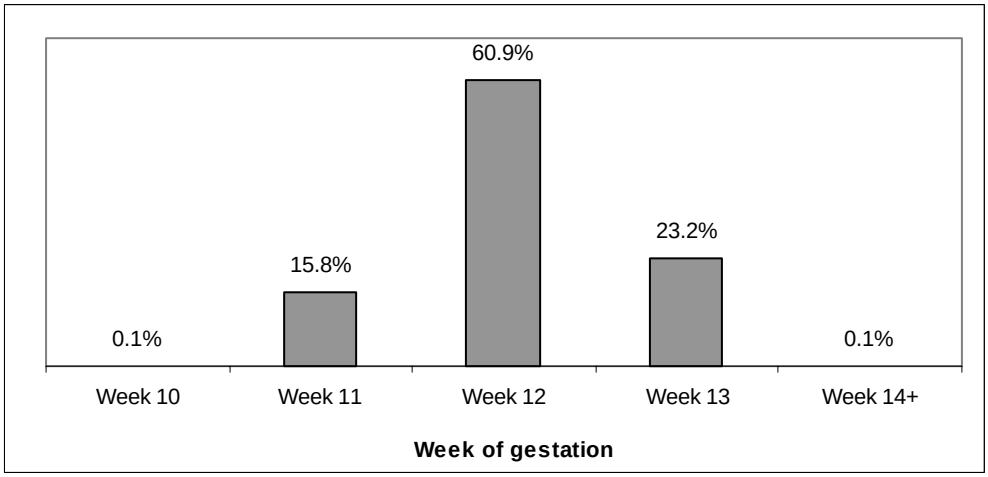

Figure 3: Women screened by week of gestation

The weight of patients was available for 90% of cases, with a median of 65 kilograms (range 33-160kgs). More than one in ten women recorded weights of 100 kilograms and over. See Figure 4.

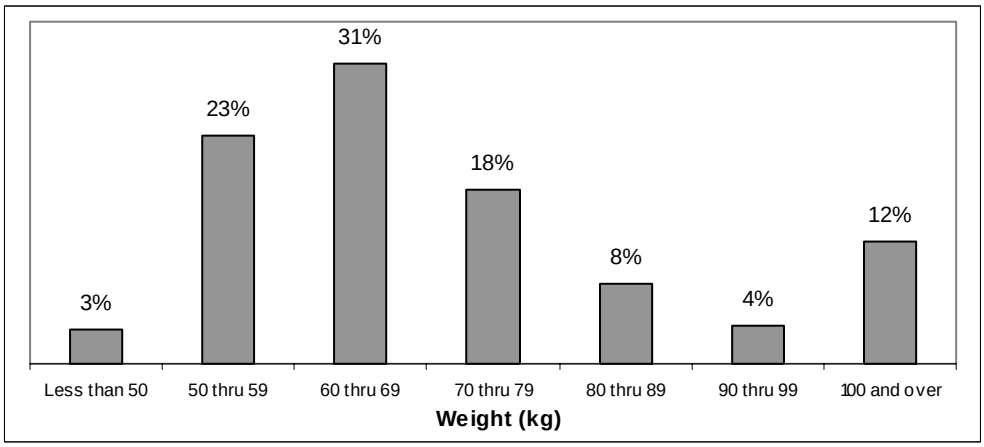

Figure 4: Women screened by weight (kgs)

Though medians for BhCG and PAPP-A were 0.94 and 1.01 MoMs respectively, the relationship was inverse since the PAPP-A median increased while the median BhCG decreased with each additional week of gestation. See Figure 5.

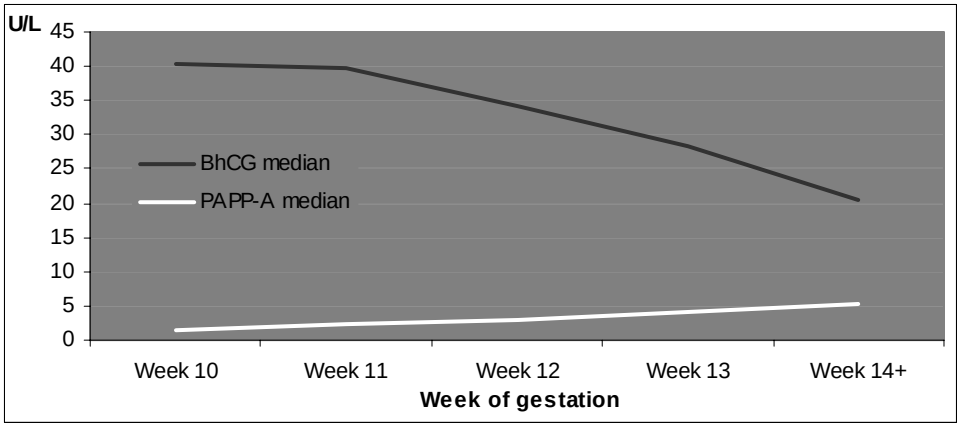

Figure 5: Median biochemistry (BhCG and PAPP-A) by week of gestation for all women screened

The median fetal crown rump length was 62.5mm (range 33-92mm) and nuchal translucency 1.5mm (range 0.1-12mm). See Table 3.

Table 3: Median NT and CRL by week of gestation

Week of gestation	N	Median NT	Median CRL
Week 10	25	1	40
Week 11	3511	1.2	52
Week 12	13561	1.5	62
Week 13	5162	1.6	72
Week 14+	21	1.8	83
Total	22280	1.5	62.5

Of the 54 women that reported a previous Trisomy 21 pregnancy, ten were identified to be at 'increased risk' and one Down syndrome pregnancy was confirmed.

The false positive rate (number of false positives amongst all women screened in the relevant age group) is examined in Figure 6. The rate escalates from 3% in women aged less than 40 years, to 36% of women aged 42 and 100% by age 44 indicating since their risk status is invariably 'increased' because of their age.

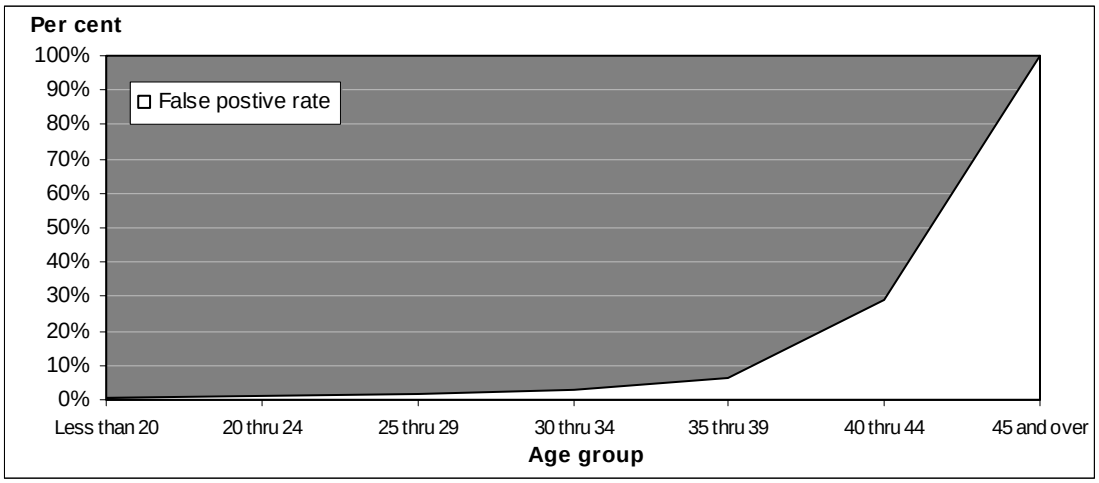

Figure 6: False positive rate for women by age group

8.2 Diagnostic test data

Around two-thirds of all amniocenteses for Down syndrome in the last ten years were in women aged 35 years and over. The proportion of women aged 35 and over having a CVS decreased from 89% to 48%. The slightly higher rate of spontaneous fetal loss associated with CVS may explain this. See Figure 7.

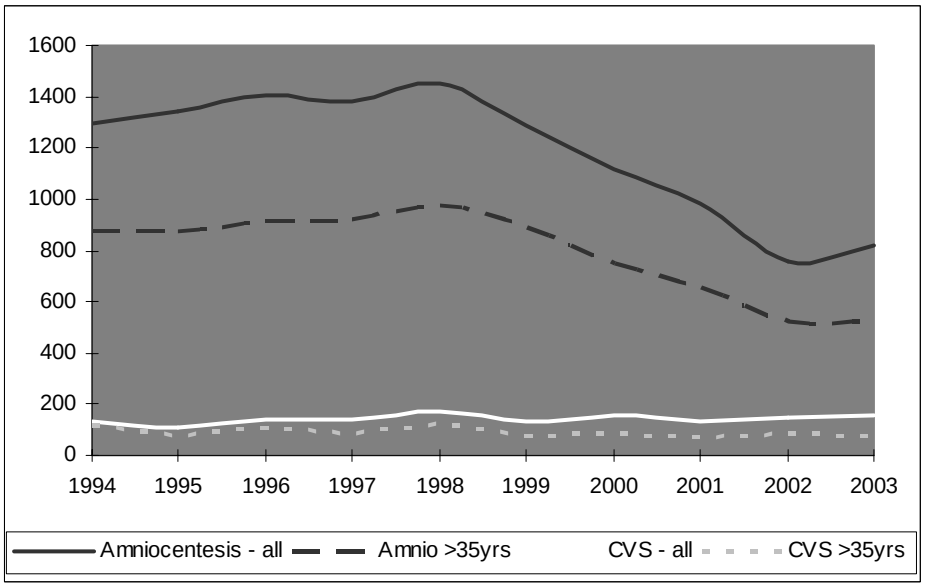

Figure 7: Prenatal diagnostic tests for Down syndrome in WA, 1994-2003[8]

8.3 Adverse outcome data

Defects reported by the Births Defects Registry are defined as 'a structural or functional abnormality that is present at conception or occurs before the end of the pregnancy, and is diagnosed by six years of age'. Most minor malformations are excluded unless they are disfiguring or require treatment.

A quarter of all fetal defects were detected prenatally through first or second trimester screening, CVS, amniocentesis or routine ultrasound. Another 64% were notified to the Births Defects Registry after the birth and 11% post-mortem. Of all defects reported, 15% were chromosomal, 21% cardiovascular, 26% uro-genital and 24% musculo-skeletal. See Figure 8.

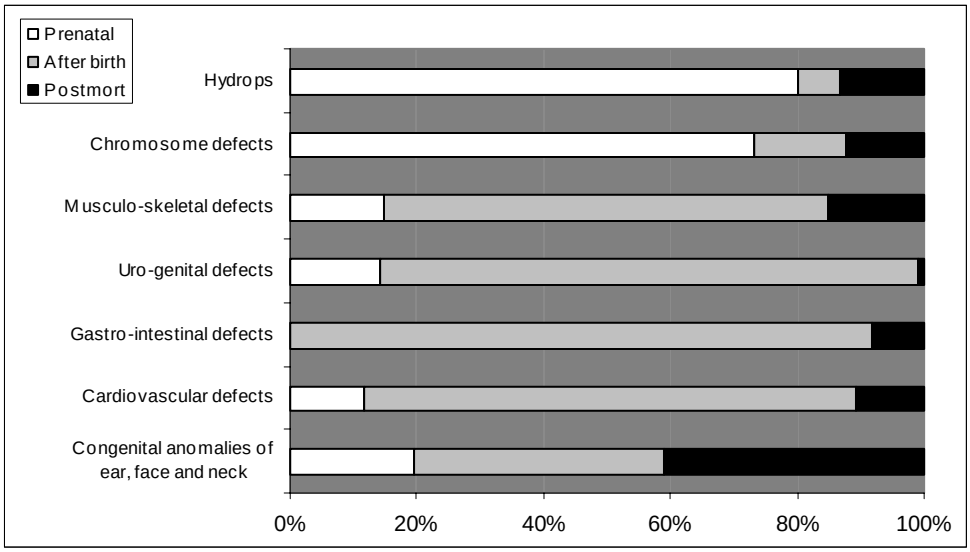

Figure 8: Defects by time of diagnosis

Though women at 'increased risk' represented less than 4% of all women screened, a quarter of all defects (N=233) were diagnosed in this group. The rate of pregnancies with one or more defects (1 in 6) was almost seven times greater in women with a high-risk status compared to women in the 'low risk' group (1 in 41). . See Table 4.

Down syndrome pregnancies excluded, women with a high-risk status still had a greater number of affected pregnancies. One in nine high-risk women had pregnancies with one or more defects compared with 1 in 42 women from the low risk group, a five-fold increase.

Table 4: Adverse outcomes by risk status

	High risk	Low risk	All women
Women	4% (877)	96% (21,403)	100% (22,280)
Defects	26% (233)	3% (684)	4% (917)
Pregnancies with one or more defects	1 in 6 (151)	1 in 41 (516)	1 in 33 (666)
Pregnancies with one or more defects excluding Down syndrome	1 in 9 (101)	1 in 42 (506)	1 in 37 (607)

Note the number of defects may increase since defects can be reported up until children are six years old.

Although only 20% of musculo-skeletal defects were found in the high-risk group, the rate of musculo-skeletal defects per 100 women was 5.1 in the high risk group but only 0.8 in the low risk group, see Figure 9. Musculo-skeletal defects included developmental dysplasia of the hip and clubfoot.

Rates of congenital anomalies of ear, face and neck, hydrops and cardiovascular defects were also greater in the high risk group of women, see Figure 10.

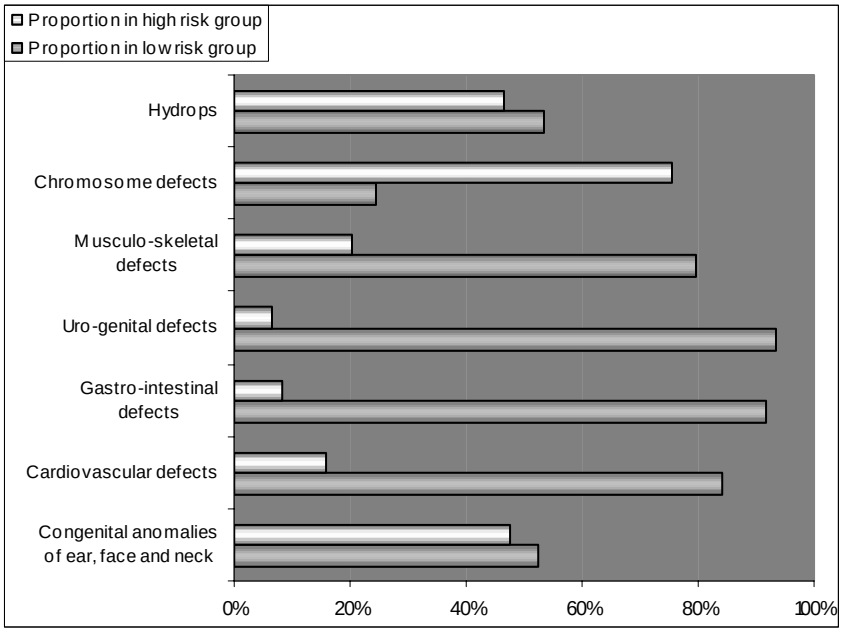

Figure 9: Proportion of defects by risk status

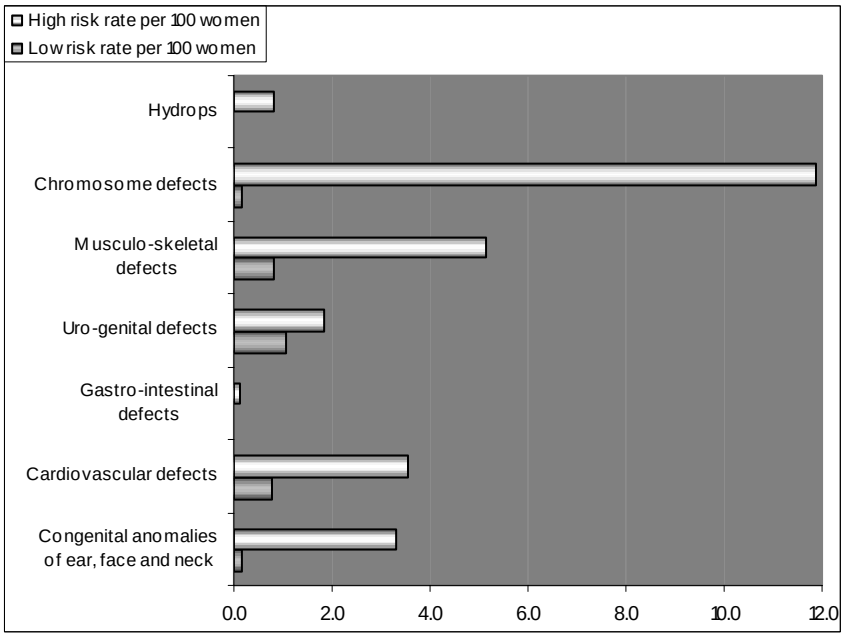

Figure 10: Rate of defects per 100 women by risk status

8.4 Single gene disorder tests

Almost half of all single gene disorder tests undertaken in WA women at less than 25 weeks gestation were to diagnose Cystic Fibrosis, Becker-Duchenne muscular dystrophy or spinal muscular atrophy. See Table 5.

Table 5: Single gene tests in all WA women at less than 25 weeks gestation, 2002–2004

Single gene test	2002	2003	2004	Total
Alpha -1 anti trypsin	-	1	-	**1**
Becker / Duchenne MD	6	3	5	**14**
Beta thalassaemia	-	2	1	**3**
Central core disease	1	-	1	**2**
Congenital Adrenal Hyperplasia	1	-	2	**3**
Connexin 26	-	1	-	**1**
Cystic Fibrosis	1	8	8	**17**
Fragile X	2	2	4	**8**
Familial Adenomatous Polyposis	-	-	1	**1**
Haemophilia	-	2	2	**4**
Huntingtons	2	2	1	**5**
Hypophosphatasia	-	-	1	**1**
MEN 2A	-	1	-	**1**
Micro Y deletion	-	-	1	**1**
Myotonia congenita	1	-	-	**1**
Myotonic dystrophy	1	1	-	**2**
Nemaline myopathy	1	-	3	**4**
Neurofibromatosis type 1	-	-	1	**1**
Non ketotic hyperglycinaemia	-	1	1	**2**
Noonan syndrome	-	1	-	**1**
Rett syndrome	1	-	1	**2**
Skeletal dysplasia	-	1	-	**1**
Spinal muscular atrophy	4	2	6	**12**
Spinocerebellar ataxia type 7	-	-	2	**2**
Uniparental disomy chromosome 7	-	2	1	**3**
Uniparental disomy chromosome 14	-	2	1	**3**
X-linked agammaglobulinaemia - BTK	-	-	1	**1**
X-linked lymphoproliferative disorder	-	-	1	**1**
X-linked lissencephaly	-	-	1	**1**
Total	**21**	**32**	**46**	**99**

9. FUTURE RESEARCH

The Prenatal Diagnosis Committee, established by the Department of Health WA in 2002, will review research applications for prenatal screening data and oversee the preparation of a bi-annual report.

APPENDIX A: PRENATAL DIAGNOSIS COMMITTEE

Membership

The Prenatal Diagnosis Committee reports to the Western Australian Genetics Council, which reports to the Department of Health of Western Australia.

Assc Professor Jan Dickinson (Chair)	Fetal Medicine Specialist, Women's and Children's Health Service
Professor Carol Bower	Medical Specialist and Head, Birth Defects Registry, Women's and Children's Health Service
Clin Professor Jack Goldblatt	Clinical Geneticist, Director, Genetic Services of Western Australia
Dr Beverley Hewitt	Specialist Obstetric Ultrasonologist, Park Ultrasound
Dr Ashleigh Murch	Cytogeneticist, Director Pathology Support Unit, Women's and Children's Health Service
Dr Peter O'Leary	Director, Genomics Directorate, Department of Health, and Biochemist, Women's and Children's Health Service
Ms Rosanne Stock	Genetic Counsellor, Genetic Services of Western Australia
Dr Steve Wilson	General Practitioner and Representative, WA Divisions of General Practice
Dr Narelle Hadlow (Ex-officio)	Pathologist, Mayne Health Western Diagnostic Pathology
Ms Nikki Breheny (Secretariat)	Senior Project Officer, Genomics Directorate, Department of Health Western Australia

Terms of Reference

- To advise the Western Australian Genetics Council (WAGC) on the implementation, development, review and modification of prenatal screening programs and diagnostic procedures.
- To monitor and evaluate prenatal screening programs including the problems and research needs and, where appropriate, advise on standards and monitoring arrangements in Western Australia.
- To advise the Western Australian Genetics Council (WAGC) on the need for research reviews, for research in relation to prenatal diagnostic procedures and screening and the implementation of research findings.
- To advise on the continuing education of consumers, GPs and other clinical providers in prenatal screening and diagnosis in Western Australia.
- To utilise collaborative channels to assess prenatal screening and diagnosis requirements in Western Australia through local and national networks.

APPENDIX B: STATEWIDE AUDIT OF PRENATAL SCREENING AND DIAGNOSIS IN WA

Statement of Authorisation

The Prenatal Diagnosis Committee of the Western Australia Genetics Council aims to conduct an ongoing review of the performance of first and second trimester screening and diagnostic tests in Western Australia. Ongoing evaluation of such prenatal screening programs is important to determine their efficacy in the community.

Recently we obtained a standard database file containing de-identified first trimester screening data from your organisation. The data extract was successful and we now a have a composite dataset containing 26,641 records. As a custodian of this data, could you please sign and date the below statement allowing for provision dataset to the Data Linkage Unit, Department of Health WA for linkage with second trimester screening, diagnostic and outcome data.

I hereby agree to accept responsibility for the provision of data to the Data Linkage Unit, Department of Health WA for the state-wide audit of prenatal screening and diagnosis in Western Australia.

Data Custodian _____ **Date** _____

Please note, permission to conduct the annual audit has been provided by Confidentiality of Health Information Committee and the Institutional Ethics Committee of King Edward Memorial and Princess Margaret Hospital (Registration No.746/EW). The conduct of this audit is within the specifications of the National Privacy Act for research and audit. No information regarding individual practices will be released (except to the specific practice at their request).

Thank you for your participation,

Dr Peter O'Leary
Director, Genomics
Department of Health Western Australia

Member, Prenatal Diagnosis Committee
Genetics Council of Western Australia

APPENDIX C: SQL SCRIPT FOR SYBASE ANYWHERE

Logon details as follows: User ‘dba’ and the password ‘sql’.

```
select
exam."date",
exam.us_operator,
exam.us_gestation,
coalesce (exam.us_gestation, exam.msb_ga_w*7 + exam.msb_ga_d)
exam.weight,
exam.age,
exam.background_risk_tr13_18,
exam.background_risk_tr21,
exam.bhcg,
exam.pappa,
exam.BhCG_MoM,
exam.PAPPA_MoM,
exam.msb_analysed,
exam.msb_assay,
exam.risk_biochemistry,
exam.risk_nt,
exam.sb_date,
exam.sb_risk_downs,
exam.@no_fetus,
episode.cigarettes,
episode.edd_us,
patient.@ID,
patient.name,
patient.other_names,
patient.hospital_number,
patient.dob,
patient.previous_trisomy13,
patient.previous_trisomy18,
patient.previous_trisomy21,
fetus.crl,
fetus.nt,
fetus.bpd,
fetus.adjusted_risk_tr21
from exam key join episode key join patient key join fetus
WHERE exam."date" between  '2001-08-01'
and '2003-10-31';
output to C:\PRENATAL_AUDIT_03\Export_Standard_Files_03.csv;
```

APPENDIX D: DATA SOUGHT FROM THE DATA LINKAGE UNIT, DOHWA

Dataset	Field
Births Defects Registry	Encrypted Births Defects Registry ID Babies sex Babies date of birth Date of babies death Pregnancy outcome Gestational age Diagnosis Codes (up to 9) Diagnosis Description (up to 9) Whether it is major or not (up to 9) Time of diagnosis (up to 9)
Midwives Notification System	Expected due date Procedures or treatments Birth date Plurality Status of baby at birth Birth defects specified
WA Mortality Register	Description of date of death Age at date of death The type of age Maiden surname of the mother of the deceased Given names of the mother of the deceased
WA Morbidity Database	Mother's Identifier (URN) Principal diagnosis (mothers) Principal procedure (mothers)

APPENDIX C: STRUCTURE FOR FINAL DATABASE

Field	Fieldname	Type	Width	Definition	Source
1	FTSID	Character	6	FTS ID assigned by Nikki	GENOMICS
2	KARYOID	Character	11	Karyotype ID assigned by Nikki	GENOMICS
3	BDRID	Character	13	Births Defects Registry ID	BDR
4	MOTHROOT	Character	13	Mothers identifier	DLU
5	ROOT	Character	13	Fetus identifier	DLU
6	MWLPNO	Character	13	DLU lpno	DLU
7	KARYO	Character	1	Karyotype Record	CONSULTANT - PMH
8	BDR	Character	1	Births Defects Registry Record	CONSULTANT - BDR
9	MAP	Character	1	Mapped Record	CONSULTANT - DLU
10	MNS	Character	1	Midwives Newborn Screening Record	CONSULTANT - MNS
11	DEATH	Character	1	Mortality Record	CONSULTANT - MORT
12	CONCEPD	Date	8	Estimated date of conception	CONSULTANT – FMF
13	SCAND	Date	8	Date of ultrasound scan	CONSULTANT - FMF
14	ABORTD	Date	8	Date of termination or miscarriage	CONSULTANT - MORB
15	EDDELD	Date	8	Estimated day of delivery by ultrasound	CONSULTANT - FMF
16	BDOBD	Date	8	Babies date of birth - MNS	CONSULTANT – MNS
17	BDTHD	Date	8	Babies date of death - BDR	CONSULTANT - BDR
18	DODD	Date	8	Babies date of death - Mort	CONSULTANT - MORT
19	BAGE	Character	5	Babies age at death	CONSULTANT - MORT
20	BAGETXT	Character	3	Babies age at death code	CONSULTANT - MORT
21	OCHROM	Numeric	2	Other chromosomal defect	CONSULTANT - MORB
22	OABORT	Numeric	2	Other termination or miscarriage	CONSULTANT - MORB
23	CHROMAB	Character	2	Chromosomal abnormality	CONSULTANT - MORB
24	CHROMABD	Date	8	Date chromosomal abnormality reported	CONSULTANT - MORB
25	ABORTION	Character	1	Termination or miscarriage	CONSULTANT - MORB
26	DOBD	Date	8	Mothers date of birth	CONSULTANT - MORB
27	MORBDOB	String	1	Available date of birth from morb data	CONSULTANT - MORB
28	MBDOBD	Date	11	Babies date of birth - morb data	CONSULTANT - MORB
29	OBIRTH	Numeric	2	Other birth	CONSULTANT - MORB
30	PRV_NO	Numeric	2	Provider Code	GENOMICS
31	COALESCE	Numeric	4	Gestation in days	FMF
32	WEIGHT	Numeric	5	Mothers weight	FMF
33	AGE	Numeric	2	Mothers age	FMF
34	BGD13_18	Numeric	4	Background risk of Trisomy 13-18	FMF
35	BGDTR21	Numeric	4	Background risk of Trisomy 21	FMF
36	BHCG	Numeric	7	BhCG	FMF
37	PAPPA	Numeric	6	PAPP-A	FMF
38	BHCG_MOM	Numeric	7	BhCG MoM	FMF
39	PAPP_MOM	Numeric	7	PAPP-A MoM	FMF
40	MSBD	Date	8	Date blood analysed	FMF
41	MSBASSAY	Numeric	1	Type of assay	FMF
42	RISKBIO	Numeric	1	Risk using biochemistry	FMF
43	RISKNT	Numeric	1	Risk using NT	FMF
44	SBD	Date	8	Date blood collected	FMF
45	SBRISK21	Numeric	4	Risk of Tr21 on biochem alone	FMF
46	PRV_TR13	Numeric	1	Previous Trisomy13	FMF
47	PRV_TR18	Numeric	1	Previous Trisomy18	FMF
48	PRV_TR21	Numeric	1	Previous Trisomy21	FMF

49	CRL	Numeric	4	Crown Rump Length	FMF
50	NT	Numeric	4	Nuchal Transulcency	FMF
51	BPD	Numeric	5	Biparietal diameter	FMF
52	ADJRSK21	Numeric	5	Adjusted risk of Trisomy21	FMF
53	DIAG	Character	6	Reason for karytype diagnosis	PMH
54	TISSUE	Character	3	CVS or amniocentesis	PMH
55	RESULT	Character	106	Karyotype result	PMH
56	NORESULT	Character	73	No karyotype result available	PMH
57	ABNORM	Character	250	Karyotype abnormal	PMH
58	TRI21	Numeric	1	Trisomy21 detected	CONSULTANT - PMH
59	TRI18	Numeric	1	Trisomy18 detected	CONSULTANT - PMH
60	TRI13	Numeric	1	Trisomy13 detected	CONSULTANT - PMH
61	OTHER	Numeric	1	Other chromosomal abnomality detected	CONSULTANT - PMH
62	RECD	Date	8	Date karyotype received	PMH
63	EXPECTD	Date	8	Date of birth expected	MNS
64	PROC_01	Character	1	Fertility treatment	MNS
65	PROC_02	Character	1	Cervical suture	MNS
66	PROC_03	Character	1	CVS or placental biopsy	MNS
67	PROC_04	Character	1	Amniocentesis	MNS
68	PROC_05	Character	1	Ultrasound	MNS
69	PROC_06	Character	1	CTG antepartum	MNS
70	PROC_07	Character	1	CTG intrapartum	MNS
71	PLURAL	Numeric	1	Plurality	MNS
72	BSTATUS	Numeric	1	Babies status at birth	MNS
73	BDEFECT	Character	100	Babies defect detected at birth	MNS
74	BSEX	Character	1	Babies sex	BDR
75	OUTCOME	Character	1	Pregnancy outcome	BDR
76	GA	Numeric	2	Week of gestation	BDR
77	D74100	Character	1	SPBIF OPEN WITH HYDROCEPH	BDR
78	D74101	Character	1	SPBIF CL WI AC &HYDROCEPH	BDR
79	D74194	Character	1	SBBIF CL SACR WOUT HYDRO	BDR
80	D74195	Character	1	SPBIF SACROLUMBAR	BDR
81	D74424	Character	1	MISPLACED EARS	BDR
82	D74491	Character	1	DYSMORPHIC/UNUSUAL FACIES	BDR
83	D74519	Character	1	TGV UNSPECIFIED	BDR
84	D74548	Character	1	VSD SMALL MUSC	BDR
85	D74549	Character	1	UNSPECIFIED VSD	BDR
86	D74551	Character	1	OSTIUM SECUNDUM DEFECT	BDR
87	D74700	Character	1	PDA	BDR
88	D74719	Character	1	COARCTATION OF AORTA NOS	BDR
89	D74907	Character	1	CL SOFT PALATE NOS	BDR
90	D75250	Character	1	UNILATERAL UDT	BDR
91	D75262	Character	1	CONGENITAL CHORDEE	BDR
92	D75263	Character	1	GLANULAR HYPOSPADIAS	BDR
93	D75286	Character	1	PENOSCROATL FUSION	BDR
94	D75320	Character	1	HYDRONEPHROSIS	BDR
95	D75344	Character	1	VESICO-URETERIC REFLUX	BDR
96	D75409	Character	1	MICROGNATHIA	BDR
97	D75430	Character	1	DDH BILATERAL	BDR
98	D75431	Character	1	DDH LEFT	BDR
99	D75432	Character	1	DDH RIGHT	BDR
100	D75450	Character	1	TALIPES EQUINOVARUS	BDR

101	D75550	Character	1	FINGER ANOMALIES	BDR
102	D75670	Character	1	EXOMPHALOS	BDR
103	D75738	Character	1	NAEVUS/HAEMANGIOMA	BDR
104	D75800	Character	1	TRISOMY 21	BDR
105	D75810	Character	1	TRISOMY 13	BDR
106	D75820	Character	1	TRISOMY 18	BDR
107	D75835	Character	1	DELTION SHORT ARM 18	BDR
108	D75838	Character	1	OTHER LOSS OF CHROMOSOMAL MATERIAL	BDR
109	D75850	Character	1	TRISOMY 8	BDR
110	D75851	Character	1	HYPOPLASIA OF LUNGS	BDR
111	D75852	Character	1	TRISOMY 16	BDR
112	D75854	Character	1	OTHER TRANSLOCATIONS	BDR
113	D75857	Character	1	TRIPLOIDY 69,XXX/XXY	BDR
114	D75858	Character	1	OTHER CHROMSOMAL ANOMALY	BDR
115	D75860	Character	1	TURNERS SYNDROME	BDR
116	D75861	Character	1	TURNERS MOSAIC	BDR
117	D75870	Character	1	KLINEFELTERS SYND 47XXY	BDR
118	D75882	Character	1	MOSAIC ANOMALY	BDR
119	D75884	Character	1	KLINEFELTERS SYND 47XYY	BDR
120	D75885	Character	1	KLINEFELTERS SYND 47XXX	BDR
121	D75888	Character	1	FRAGILE X	BDR
122	D75893	Character	1	DUPLICATION OF CHROMOSOME	BDR
123	D75800	Character	1	HYDROPS FOETALIS EXTENSIV	BDR
124	P90461	Character	1	INTRA-AMNIOTIC INJECTION FOR ABORTION	MORB
125	P90462	Character	1	INSERTION OF PROSTAGLANDIN SUPPOSITORY FOR INDUCTION OF ABORTION	MORB
126	P16600	Character	1	DIAGNOSTIC AMNIOCENTESIS	MORB
127	P16603	Character	1	CHORIONIC VILLUS SAMPLING	MORB

Key

FMF	Fetal Medicine Foundation
MORB	WA Morbidity Database
MORT	WA Mortality Register
BDR	Births Defects Registry
MNS	Midwives Notification System
CONSULTANT	Derived from core datasets by consultant biostatistician
GENOMICS	Assigned by the Genomics Directorate

REFERENCES

[1] Bower C, Ryan A, Rudy E, and Cosgrove P. Report of the Births Defects Registry of Western Australia 1980-2002. King Edward Memorial Hospital, No. 10, 2003 (1 in 445 prevalence is derived from1995-2002 data).

[2] Muggli EE and Halliday JL (2004): Report on prenatal diagnostic testing in Victoria 2003. Murdoch Children's Research Institute Report, Melbourne.

[3] Haan E (2000): Review of state-wide delivery of genetic services in Western Australia. Department of Health Western Australia Report, Perth.

[4] Hadlow N, Dickinson J, Bower C et al (2004): A regional screening program for Down syndrome in the first trimester using ultrasound and maternal serum biochemistry. British Journal of Obstetrics and Gynaecology (in press).

[5] See online at: http://www.fetalmedicine.com/

[6] Data collected from the FMF software did not include the risk of a Down syndrome pregnancy based on ultrasound alone. The detection rate is based on data from the South Australian program which reported a recall rate of 6.1% using NT alone.

[7] WA Midwives Notification System, maternal age 1980-2003

[8] Data sourced from the King Edward Memorial Hospital and Health Insurance Commission, Medical Benefits Schedule Items 66750 and 67743

Department of **Health**
Government of **Western Australia**

Produced by Genomics Branch
© Department of Health 2005

HP 3129 OCT'05 20752