2007

Annual Report

of

The South Australian

Birth Defects Register

Children born from 1986 to 2007 with birth defects

notified to the Register by 31st March 2008

and incorporating the

Annual Report of Prenatal Diagnosis

in South Australia, 2007

The South Australian Birth Defects Register

Location

Public Health Research Unit
Women's and Children's Hospital Campus
Children, Youth and Women's Health Service
Ground Floor, Angas Building
72 King William Road
North Adelaide, South Australia 5006
Telephone: (08) 8161 7368
Email: sabdr@health.sa.gov.au

SABDR Website (to access online version of SABDR Annual Report):
http://www.wch.sa.gov.au/services/az/other/phru/birthdefect.html

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Contents

Annual Report of the South Australian Birth Defects Register

Annual Report of Prenatal Diagnosis

Tables

Figures and Appendices

South Australian Birth Defects Register Staff

Left to Right

Left to Right: Associate Professor Peter Baghurst, Associate Professor Annabelle Chan, Mrs Phillipa van Essen, Ms Heather Scott, Mrs Rosie Rice and Dr Catherine Gibson

Thanks to Notifiers and Acknowledgments

We wish to thank all the notifiers who supplied the information on which this report is based. We greatly appreciate their support and advice, the time and effort they spend on completing the forms and their cooperation in supplying extra information when requested.

In particular, we would like to express our thanks to the staff of the particular departments who have data collections or registers with which the Birth Defects Register interfaces:

Children, Youth and Women's Health Service:

- The Department of Cardiology for data on congenital heart defects,
- The Division of Medical Imaging for radiology and ultrasound information,
- The Medical Records Department.

SA Pathology:

- Genetics and Molecular Pathology for cytogenetics reports, Down Syndrome data, information on maternal serum screening, inborn errors of metabolism, abnormal neonatal screening results and data on prenatal diagnostic tests such as amniocentesis and chorionic villus sampling,
- Surgical Pathology for autopsy reports,
- Haematology.

We also express thanks to the Medical Records Departments of South Australian metropolitan and regional hospitals, in particular Flinders Medical Centre, Lyell McEwin Health Service, Modbury Hospital and The Queen Elizabeth Hospital.

We would like to thank all those people who have contributed to the South Australian Birth Defects Register since its inception. Their ongoing support and practical contribution is much appreciated.

Special thanks are due to Joan Scott and the staff of the Pregnancy Outcome Unit for providing the important perinatal data and to Kevin Priest and Anh-Minh Nguyen, the staff of the Health Statistics Unit of the Epidemiology Branch, SA Health for assistance with data linkage and statistical support.

The Birth Defects Register Advisory Committee was established in June 1989 to advise the Register on issues of confidentiality and to review the activities of the Register. We thank its members for their time, expertise and valuable advice.

Dr Judy Jaensch, Paediatrician
Dr Geoffrey Martin, General Practitioner
Dr Wendy Scheil, representing the Epidemiology Branch of SA Health
Professor Eric Haan, Clinical Geneticist
Dr Karen Shand, Obstetrician
Dr Brian Peat, Obstetrician

The advice of many clinicians has been sought on the classification and coding of defects in specialised areas, eg. orthopaedics, craniofacial malformations, urology, neurosurgery and cardiology. We would like to express our gratitude to these consultants for their ongoing guidance.

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A very special thank you goes to both Associate Professor Annabelle Chan and Mrs Phillipa van Essen, for their hard work and dedication over many years working with the SA Birth Defects Register. We are very sorry to see them leave, and wish them all the best with their future endeavours.

Executive Summary 2007

Annual Birth Defects Report

- The Register received 898 notifications of children born with one or more birth defects in 2007. This represents 4.5% of the total births in that year. The proportion of total births with birth defects for the period 1986-2007 was 5.9%. The difference represents the additional notifications, around 30%, received over the Register's further four year ascertainment period for each birth year cohort.
- There were 23 births or terminations with neural tube defects in 2007. The Register has documented a significant decreasing trend in the prevalence of neural tube defects between 1986 and 2007. The percentage of livebirths among cases of neural tube defects in 2007 was 8.7%.
- There were 56 Down syndrome births or terminations in 2007. There was an increasing trend in the total prevalence of Down syndrome between 1986 and 2007 due to increasing maternal age. The percentage of livebirths among cases of Down syndrome in 2007 was 26.8%.
- In 2007, the Central Western CURB region recorded the highest proportions of births with birth defects, with 5.2% of total births, compared to the lowest proportion of 3.6% seen in the Northern CURB region. These differences are not statistically significant and reflect year to year variation in prevalence of birth defects and in ascertainment between regions. The prevalence of sentinel birth defects is similar across all regions when assessed over longer time periods.
- As seen in previous years, male sex and multiple births were associated with an increased risk of birth defects in 2007.
- In 2007, births to Caucasian mothers had a higher proportion of birth defects (4.8%) compared with births to Asian mothers (2.4%) and Aboriginal mothers (2.5%).
- The most commonly reported birth defects in 2007 were: Musculoskeletal abnormalities (eg developmental dysplasia of the hip) and Urogenital abnormalities (eg vesico-ureteric reflux), with 14.6 and 9.6 cases per 1,000 total births respectively. Chromosomal abnormalities (eg Down syndrome) had a prevalence of 5.1 per 1,000 total births.
- In 2007, 13.6% of spontaneous stillbirths and 27.3% of neonatal deaths in South Australia were associated with birth defects.
- 28.5% of gastrointestinal and 27.7% of cardiovascular birth defects were identified after discharge from the birth hospital in 2007.

Executive Summary 2007

Annual Prenatal Diagnosis Report

In 2007:

- 952 amniocenteses and 219 chorionic villus samplings were performed on South Australian women, representing 4.8% and 1.1% of all women who gave birth, respectively.
- Maternal age was a factor in 61.2% of amniocenteses and 66.7% of chorionic villus samplings.
- 8 fetal blood samplings in 4 fetuses were performed for Rh or other isoimmunisation. There were 7 fetal transfusions (3 fetuses).
- The Women's and Children's Hospital and Gribbles Pathology screened 4,415 pregnancies (22.7% of all pregnancies) at 15-20 weeks gestation for a fetal neural tube defect by estimation of maternal serum alpha-fetoprotein. This can be compared to a peak of around 83% in the early-mid 1990s, reflecting increasing reliance on ultrasound as the main screening method for neural tube defects.
- All 20 cases of neural tube defect that had screening by maternal serum screening, ultrasound screening or both, were detected prenatally.
- The Women's and Children's Hospital and Gribbles Pathology used first trimester combined or second trimester maternal serum screening to detect Down syndrome in 14,598 pregnancies (75.0% of all pregnancies in SA).
- Of the 46 Down syndrome cases prenatally screened or tested by one or more screening or testing method, 39 (85%) were detected. The screening or diagnostic methods used were:
  - First trimester combined screen (nuchal translucency and maternal serum screen),
  - Second trimester maternal serum screen,
  - Chorionic villus sampling,
  - Amniocentesis,
  - Ultrasound alone as the first indication of Down syndrome.
- There have been significant changes over time in the proportion of pregnancies in which prenatal diagnosis by amniocentesis or chorionic villus sampling is performed; from 5% in 1986 to a peak of 12% in 1996, followed by a gradual fall to 6% in 2007. A contributing factor to the fall in recent years has been a decrease in the proportion of women 35 years and older using amniocentesis and chorionic villus sampling, following the introduction of first trimester Down syndrome screening.

Introduction

The South Australian Birth Defects Register is a population-based collection of information on birth defects, including cerebral palsy, from a population with an average of 18,424 births per year over the past five years. The Register collects information on all children born in South Australia on or after 1st January 1986 who have a significant birth defect detected in the first five years of life. It thus complements and extends the collection of congenital abnormalities detected in the perinatal period and notified by doctors to the Pregnancy Outcome Unit of SA Health.

The Register defines a birth defect as "any abnormality, structural or functional, identified up to five years of age, provided that the condition had its origin before birth."

The Register includes:

- Terminations of pregnancy at any gestation performed because of a diagnosis of a birth defect,
- Stillbirths and newborn babies with birth defects,
- Children diagnosed with a birth defect after the neonatal period and prior to their fifth birthday.

The Register is located in the Women's and Children's Hospital in the Public Health Research Unit. This is an ideal location for the following reasons:

- The majority of children with birth defects requiring medical or surgical care are referred to the Women's and Children's Hospital for assessment or further management at some stage.
- The major paediatric diagnostic services and perinatal/paediatric pathology services are located at the Women's and Children's Hospital.

Notifications of birth defects come from various sources including:

- Doctors and other health professionals involved with;
  - the care of children with birth defects in hospital
  - special paediatric assessment
  - treatment and rehabilitation centres
  - private practices
- The Pregnancy Outcome Unit of SA Health,
- The State Perinatal Autopsy Service
- Diagnostic services including laboratories diagnosing cytogenetic or biochemical abnormalities, and organ imaging departments.

This annual report presents information for the years 1986-2007, including birth defects notified up to March 2008 for children born in 2007. It also updates numbers and rates for the years 2002 to 2006. Notifications for the cohorts of children born between 1986 and 2002 are now complete. All children in the 2002 cohort reached their fifth birthday by the end of 2007 and notifications of defects received by 31st March 2008 have been accepted for inclusion. After this date the 2002 cohort is considered complete and no further notifications are added. Similarly, the 2008 report will record complete numbers for the 2003 birth cohort.

This report also describes prenatal diagnosis in South Australia for the year 2007, combining information from the Children, Youth and Women's Health Service, SA Pathology and Gribbles Pathology.

For further information regarding the SA Birth Defects Register, Confidentiality Guidelines, Inclusion and Exclusion Lists, and a copy of the Notification Form, please refer to the Appendices at the end of this report.

Recent Register Activities

The South Australian Birth Defects Register (incorporating the South Australian Cerebral Palsy Register) is involved with many research activities, including the following:

Audit of pregnancy outcome following use of assisted reproductive technology
Birth defects and cerebral palsy are some of the pregnancy outcomes being examined in this study in relation to the use of assisted reproductive technologies. A paper was submitted in 2010 for publication.

Down syndrome screening and invasive prenatal testing
Trends in Down syndrome screening and invasive prenatal testing following the introduction of first trimester combined Down syndrome screening were reported in this study. This was published in the American Journal of Obstetrics and Gynecology in 2007.

Different epidemiology of late diagnosed developmental dysplasia of the hip (DDH)
The aim of this study was to evaluate the epidemiological differences between early and late diagnosed DDH. This study was published in the Journal of Pediatric Orthopaedics B in January 2011.

Congenital abnormalities of the spine and ribcage
In conjunction with the Orthopaedic Department at the Women's and Children's Hospital, the Register is investigating the incidence and prevalence of congenital abnormalities of the spine and ribcage to determine if there is any relationship between these defects and plurality, gender and mother's race. Data collection is currently underway.

A genomic basis for cerebral palsy – national study
This is a case-control study across Australia with the aim of investigating the role of maternal and fetal genetic variations in the development of cerebral palsy. The study is currently undertaking analysis and interpretation, and the Register's involvement is ongoing.

Controlled trial of upper limb Botulinum toxin A injection in children with hemiplegic cerebral palsy
Children with hemiplegic cerebral palsy were recruited for a study to assess the effect of botulinum toxin A and occupational therapy compared with occupational therapy alone on body structure, activities participation, and self perception in children with hemiplegic cerebral palsy. This study was published in Pediatrics in 2007.

Cerebral palsy or not cerebral palsy? A review of diagnoses from a population-based cerebral palsy register
The diagnosis of cerebral palsy is not always easy. Occasionally children may present with symptoms indicative of CP, which resolve over time or are ultimately determined to be associated with some other condition (eg. chromosomal or metabolic). With this in mind, we audited the level of misdiagnosis seen in the SA Cerebral Palsy Register. This study was published in Pediatric Neurology in 2010.

The impact of day-to-day childcare tasks on the lives of mothers of children with cerebral palsy
This study aimed to examine the relationship between the amount of time mothers spend caring for children with chronic disability and maternal psychological adjustment and health-related quality of life. Data analysis is currently being undertaken, and the Register's involvement is ongoing.

Requests for information
The Register answers many requests for information from government departments, health professionals in the community, other birth defect registers and students who require statistics on the prevalence of birth defects occurring in South Australia. The Register regularly contributes data for the National Perinatal Statistics Unit Congenital Anomalies Reports as well as the Australian Cerebral Palsy Register, and also provides data to the ongoing South Australian Burden of Disease Study, undertaken by SA Health.

Prevalence of Birth Defects

This report includes all notifications of birth defects for births (and terminations of pregnancy) occurring in South Australia in the years 1986-2007 and received by 31st March, 2008. The percentages of births with birth defects for the years 1986-2007 are provided in Table 1. As birth defects continue to be diagnosed and notified to the Register up to the age of 5 years, the percentage of births with birth defects is higher in cohorts with 5 completed years of ascertainment than in more recent cohorts (see Table 1). This is particularly true for defects such as congenital heart disease and urogenital malformations, which often are not diagnosed at birth.

It is interesting to note that the percentage of total births with birth defects has not changed significantly since the Register began to collect data in 1986.

Table 1: Birth defects in children born in South Australia, 1986-2007

Year of Birth	Total Births	Cases of Birth Defects	Percentage of Births With Birth Defects
1986-2002	326,185	19,445	6.0%
2003	17,844	1,058	5.9%
2004	17,522	1,055	6.0%
2005	18,196	1,115	6.1%
2006	18,803	1,005	5.3%
2007	19,757	898	4.5%
Total	**418,307**	**24,576**	**5.9%**

The numerator used in calculating the percentage is all South Australian births and terminations with birth defects. These consist of livebirths and stillbirths of at least 400g birthweight or 20 weeks gestation, and terminations of pregnancies of fetuses with birth defects. The denominator used is the total number of livebirths and stillbirths only, and excludes terminations of pregnancy before 20 weeks gestation. This makes our statistics comparable with those of other registers, but slightly overestimates the percentage of births with defects. This denominator has been selected also because accurate statistics on terminations may not be available elsewhere (as they are in South Australia), and fetuses from terminations in early pregnancy may not be examined for birth defects. Spontaneous fetal deaths, where weight is less than 400g and gestation is less than 20 weeks, are not included among the Register cases as accurate statistics on them are also not available.

Notifications of children with birth defects who were born outside South Australia in the years 1986-2007 but who are currently resident in South Australia are not included in the statistics.

Demographic Information

Residence of Mother

Table 2 shows the distribution of cases by residence of mother at time of birth (see Figure 1). Births to mothers resident interstate had the highest prevalence of birth defects due to the referral of high risk pregnancies from interstate to Adelaide tertiary hospitals. For the period 1986-2007, the Central Northern Region had the highest overall percentage of birth defects with 6.3%; the lowest percentage of birth defects was seen in the South East region with 4.8%. Over this period there was significant ($\chi^2 = 162.00$, $p<0.0001$) variation in the prevalence of total birth defects between CURB regions. However, there was no significant difference between CURB regions ($\chi^2 = 3.16$, $p=0.08$) for sentinel defects, which are more reliably identified (Table 7). This suggests that the variation seen for total birth defects is due to differences in ascertainment between CURB regions.

Table 2: Cases with birth defects by residence of mother at time of birth, SA 1986-2007

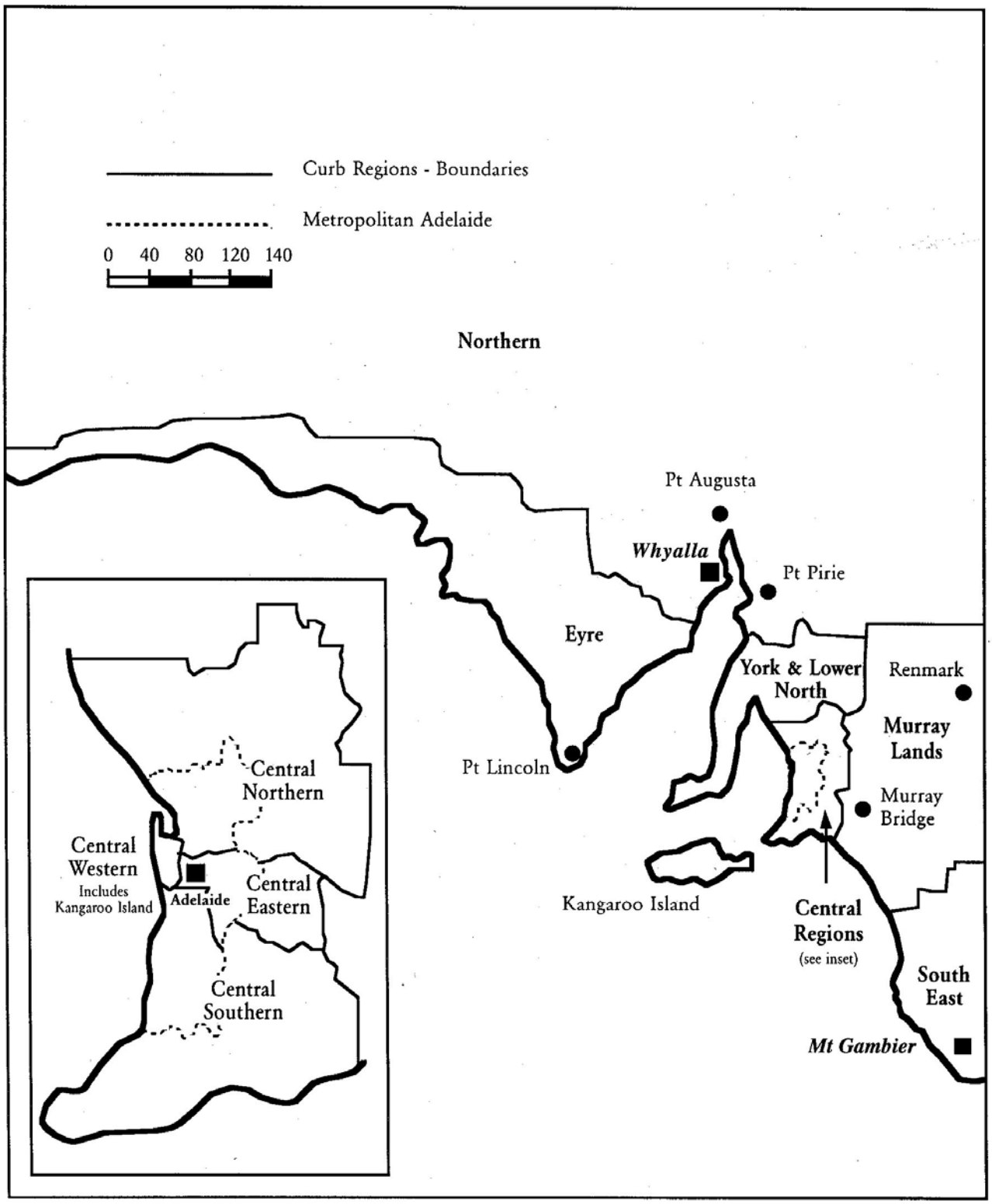
	Year of Birth						Total
	1986-2002	**2003**	**2004**	**2005**	**2006**	**2007**	**1986-2007**
CURB^ Region	No. (%*)	No. (%*)	No. (%*)	No. (%*)	No. (%*)	No. (%*)	**No. (%*)**
Central Northern	5968 (6.5)	307 (5.9)	295 (5.8)	339 (6.3)	283 (5.1)	285 (4.7)	**7477 (6.3)**
Central Western	2673 (6.3)	137 (6.0)	136 (6.3)	150 (6.5)	114 (5.0)	125 (5.2)	**3335 (6.2)**
Central Eastern	3020 (6.4)	178 (6.3)	171 (6.0)	161 (5.6)	163 (5.4)	135 (4.4)	**3828 (6.2)**
Central Southern	3833 (5.4)	253 (6.4)	280 (7.3)	249 (6.3)	265 (6.2)	192 (4.3)	**5072 (5.6)**
Yorke & Lower North	529 (5.7)	26 (6.2)	18 (4.1)	25 (5.4)	22 (4.7)	24 (4.8)	**644 (5.6)**
Murraylands	882 (5.5)	29 (3.6)	42 (5.1)	46 (5.6)	29 (3.5)	34 (4.1)	**1062 (5.3)**
South East	754 (4.9)	40 (4.8)	34 (4.3)	43 (5.1)	36 (4.2)	32 (3.7)	**939 (4.8)**
Northern	1113 (5.0)	49 (5.0)	53 (5.3)	57 (5.7)	50 (4.9)	39 (3.6)	**1361 (5.0)**
Eyre	448 (5.1)	26 (6.3)	17 (3.6)	25 (5.9)	25 (5.4)	17 (3.9)	**558 (5.1)**
Residence – Interstate** or Unknown	225 (9.5)	13 (10.7)	9 (9.2)	20 (14.8)	18 (16.7)	15 (12.9)	**300 (10.1)**
Total	**19445** (6.0)	**1058** (5.9)	**1055** (6.0)	**1115** (6.1)	**1005** (5.3)	**898** (4.5)	**24576 (5.9)**

*Number of children with birth defects in the region divided by the total number of births in the region x 100

** Usual residence interstate but born in South Australia

^Committee on Uniform Regional Boundaries (CURB)

Figure 1: South Australian
CURB^ Regions



^Committee on Uniform Regional Boundaries (CURB)

Demographic Information

Sex of Child

The sex distribution of children born between 1986 and 2007 in South Australia with notified birth defects is shown in Table 3. For 1986-2007 the ratio of males to females for birth defects was 1.37:1, i.e., 37% more male than female births being notified with a birth defect. This contrasts with a male to female ratio of 1.06:1 for all births. The percentage of male births with notified defects for the period 1986-2007 was 6.5%; this was significantly higher (relative risk (RR) = 1.29 (95% CI 1.26-1.33), p<0.0001), than for female births (5.0%).

There are a number of birth defects that are specific to each sex (eg. undescended testis). Taking into account these gender-specific defects, there is still a greater prevalence of certain defects in males, for example pyloric stenosis, short segment Hirschsprung's disease and congenital talipes equinovarus. These defects are consistently found more often in males than in females.

Table 3: Cases with birth defects by sex of child, SA 1986-2007

	Year of Birth						Total
	1986-2002	**2003**	**2004**	**2005**	**2006**	**2007**	**1986-2007**
Sex	No. (%*)	No. (%*)	No. (%*)	No. (%*)	No. (%*)	No. (%*)	**No.** **(%*)**
Male	11091 (6.6)	601 (6.5)	597 (6.6)	607 (6.5)	530 (5.5)	491 (4.9)	**13917** **(6.5)**
Female	8055 (5.1)	425 (4.9)	417 (4.9)	451 (5.1)	428 (4.6)	374 (3.9)	**10150** **(5.0)**
Indeterminate	14 -	2 -	0 -	0 -	0 -	1 -	**17** -
Not Specified[#]	285 -	30 -	41 -	57 -	47 -	32 -	**492** -
Total	**19445** **(6.0)**	**1058** **(5.9)**	**1055** **(6.0)**	**1115** **(6.1)**	**1005** **(5.3)**	**898** **(4.5)**	**24576** **(5.9)**

* Percentage of births of that category in that year
# These were all terminations of pregnancy

Demographic Information

Race of Mother

The percentage of births with birth defects by mother's race is shown in Table 4. There were significant differences between the prevalences of birth defects according to mother's race for 2007 ($\chi^2 = 14.98$, $p<0.0001$), which were also seen for the period 1986-2007 ($\chi^2 = 74.98$, $p<0.0001$). For 1986-2007, there was a significantly higher prevalence of birth defects for Caucasian mothers compared with Asian (RR = 1.27, 95% CI 1.19-1.37), Aboriginal (RR = 1.16, 95% CI 1.06-1.26) and Other race (RR = 1.35, 95% CI 1.19-1.53) mothers.

Table 4: Cases with birth defects by mother's race, SA 1986-2007

	Year of Birth						Total
	1986-2002	**2003**	**2004**	**2005**	**2006**	**2007**	**1986-2007**
Mother's Race	No. (%*)	No. (%*)	No. (%*)	No. (%*)	No. (%*)	No. (%*)	**No. (%*)**
Caucasian	18284 (6.0)	992 (6.1)	975 (6.1)	1027 (6.3)	922 (5.5)	831 (4.8)	**23031 (5.9)**
Aboriginal	389 (5.6)	24 (5.1)	16 (3.3)	20 (4.1)	24 (4.3)	15 (2.5)	**488 (5.1)**
Asian	572 (4.9)	25 (3.0)	51 (6.1)	47 (4.9)	44 (4.6)	29 (2.4)	**768 (4.7)**
Other	141 (4.7)	17 (5.0)	13 (3.9)	21 (5.1)	15 (2.9)	23 (3.7)	**230 (4.4)**
Unspecified	59 -	0 -	0 -	0 -	0 -	0 -	**59 -**
Total	**19445 (6.0)**	**1058 (5.9)**	**1055 (6.0)**	**1115 (6.1)**	**1005 (5.3)**	**898 (4.5)**	**24576 (5.9)**

* Percentage of births of that category in that year

Plurality

The distribution of cases of birth defects by plurality is shown in Table 5. The percentage of cases among multiple births was 7.6% for the 22 year period 1986-2007; this was significantly higher (RR = 1.31, 95% CI 1.23-1.39, $p<0.0001$) than among singleton births, with 5.8%. Certain birth defects are associated with twin pregnancies, in particular monozygotic twins. Examples of defects that occur more often in monozygotic twins are sirenomelia, VATER association, holoprosencephaly and anencephaly.

Table 5: Cases with birth defects by plurality, SA 1986-2007

	Year of Birth						Total
	1986-2002	**2003**	**2004**	**2005**	**2006**	**2007**	**1986-2007**
Plurality	No. (%*)	No. (%*)	No. (%*)	No. (%*)	No. (%*)	No. (%*)	**No. (%*)**
Single	18698 (5.9)	1019 (5.9)	1002 (5.9)	1080 (6.1)	952 (5.2)	864 (4.5)	**23615 (5.8)**
Multiple	747 (7.7)	39 (6.0)	53 (9.1)	35 (5.9)	53 (9.4)	34 (6.0)	**961 (7.6)**
Total	**19445 (6.0)**	**1058 (5.9)**	**1055 (6.0)**	**1115 (6.1)**	**1005 (5.3)**	**898 (4.5)**	**24576 (5.9)**

* Percentage of births of that category in that year

Types of Birth Defects Notified

The diagnostic categories used by the Register for coding are those of the British Paediatric Association (BPA) Classification of Diseases, 1979, a 5-digit system compatible at the 4-digit level with the ninth revision of the International Classification of Diseases (ICD9). Its Congenital Anomaly codes are those in the range 74000-75999. The BPA also provides codes outside this range for some disorders which are included in the Register's collection. For disorders without a BPA code the Register uses the ICD9 classification.

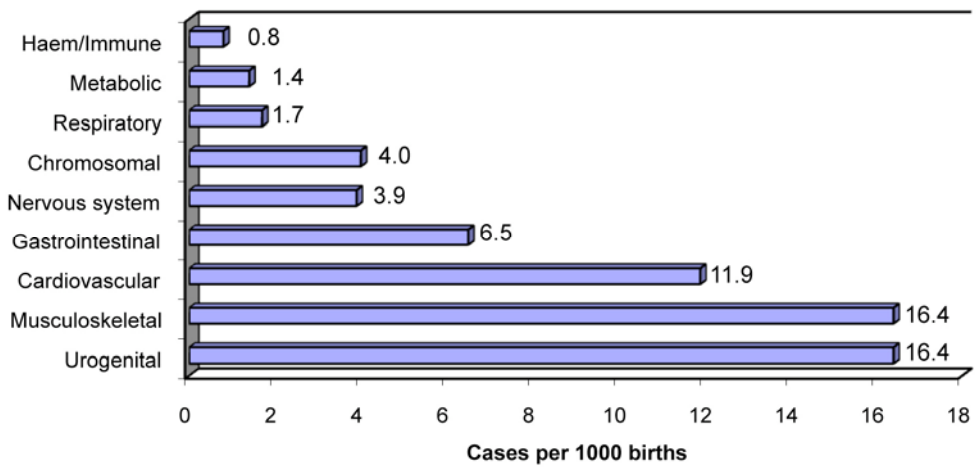
We anticipate a change in coding to the tenth revision of the International Classification of Diseases after a BPA-ICD10AM system has been established nationally.

The prevalence of birth defects per 1,000 total births for major diagnostic groupings (ie. not all birth defects) are provided in Figure 2. The most commonly reported birth defects between 1986 and 2007 were: Urogenital abnormalities (eg. Vesico-ureteric reflux) and Musculoskeletal abnormalities (eg. Developmental dysplasia of the hip), both with 16.4 per 1,000 births.

In Table 6 we present the number of cases with specified birth defects by diagnostic category. Children with multiple defects will appear in more than one category. For example, a child with trisomy 18 who has spina bifida will appear in Chromosome defects and also under Nervous system defects and hence the number of cases in each body system total does not necessarily equal the sum of the individual defects listed under it. Within a specific category, e.g. Nervous system, the total may be smaller than the number obtained by adding together cases with anencephaly, spina bifida and encephalocele. This is because some cases of neural tube defects have more than one lesion, for example the combination of spina bifida and anencephaly.

Figures 3.1 to 3.11 provide trends in selected birth defects 1986 to 2007.

Figure 2: Cases with birth defects by major diagnostic category 1986-2007 (prevalence per 1,000 births)



Types of Birth Defects Notified

Table 6: Cases with specified birth defects by diagnostic category, SA 1986-2007

	Year of Birth						Total	
	1986-2002	2003	2004	2005	2006	2007	1986-2007	
Diagnostic Category (BPA Code)	**No.** (per 1000*)	**No.** (per 1000*)	**No.** (per 1000*)	**No.** (per 1000*)	**No.** (per 1000*)	**No.** (per 1000*)	**No.**	**per 1000***
Nervous System (74000-74299)	1283 (3.9)	62 (3.5)	76 (4.3)	67 (3.7)	69 (3.7)	64 (3.2)	**1621**	**3.9**
Neural Tube Defects	571	21	21	23	25	23	**684**	**1.6**
Anencephaly	232	7	9	12	10	9	**279**	**0.7**
Spina Bifida	295	12	12	9	14	9	**351**	**0.8**
Encephalocele	52	2	0	2	1	7	**64**	**0.2**
Microcephaly	166	8	12	5	4	5	**200**	**0.5**
Congenital Hydrocephalus	270	13	17	15	16	16	**347**	**0.8**
Cardiovascular (74500-74799)	3993 (12.2)	196 (11.0)	189 (10.8)	232 (12.8)	186 (9.9)	173 (8.8)	**4969**	**11.9**
Transposition of Great Vessels	215	9	8	18	8	10	**268**	**0.6**
Tetralogy of Fallot	112	5	6	8	8	7	**146**	**0.3**
Ventricular Septal Defect	2026	98	93	119	91	86	**2513**	**6.0**
Atrial Septal Defect	961	31	33	43	26	27	**1121**	**2.7**
Hypoplastic Left Heart Syndrome	99	1	3	6	8	7	**124**	**0.3**
Patent Ductus Arteriosus	601	33	33	19	26	36	**748**	**1.8**
Coarctation of Aorta	200	12	7	15	10	9	**253**	**0.6**
Respiratory (74800-74899)	530 (1.6)	42 (2.4)	42 (2.4)	44 (2.4)	24 (1.3)	30 (1.5)	**712**	**1.7**
Pulmonary Hypoplasia/Dysplasia	284	21	26	23	12	18	**384**	**0.9**
Gastrointestinal (74900-75199)	2128 (6.5)	114 (6.4)	108 (6.2)	130 (7.1)	122 (6.5)	123 (6.2)	**2725**	**6.5**
Cleft Palate	329	17	15	21	17	15	**414**	**1.0**
Cleft Lip	135	6	5	5	4	9	**164**	**0.4**
Cleft Lip with Cleft Palate	241	11	13	11	17	20	**313**	**0.7**
Tracheo-Oesophageal Fistula, Oesophageal Atresia & Stenosis	141	3	3	8	6	12	**173**	**0.4**
Pyloric Stenosis	619	25	31	36	36	22	**769**	**1.8**
Rectal/Anal Atresia & Stenosis	171	8	8	20	8	10	**225**	**0.5**
Hirschsprung Disease	61	5	3	2	4	2	**77**	**0.2**
Urogenital (75200-75399)	5592 (17.1)	289 (16.2)	292 (16.7)	279 (15.3)	236 (12.6)	190 (9.6)	**6878**	**16.4**
Undescended Testicle	1621	73	69	56	59	13	**1891**	**4.5**
Hypospadias	1233	82	87	89	56	57	**1604**	**3.8**
Renal Agenesis & Dysgenesis	185	13	5	14	12	12	**241**	**0.6**
Vesico-ureteric Reflux	1061	29	31	29	21	21	**1192**	**2.8**

* Prevalence per 1,000 total births

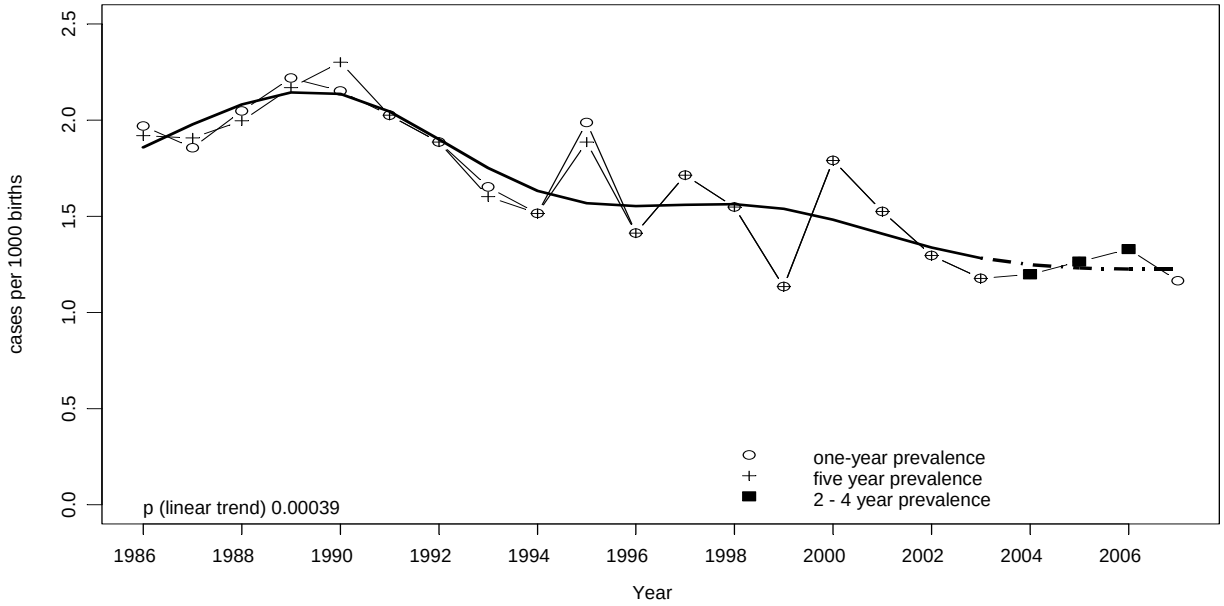
Types of Birth Defects Notified

Table 6: Cases with specified birth defects by diagnostic category, SA 1986-2007

	Year of Birth						Total	
	1986-2002	2003	2004	2005	2006	2007	1986-2007	
Diagnostic Category (BPA Code)	**No.** (per 1000*)	**No.** (per 1000*)	**No.** (per 1000*)	**No.** (per 1000*)	**No.** (per 1000*)	**No.** (per 1000*)	**No.**	**per 1000***
Musculoskeletal (75400-75699)	5380 (16.5)	287 (16.1)	290 (16.6)	322 (17.7)	290 (15.4)	288 (14.6)	**6857**	**16.4**
Developmental Dysplasia of Hip	2270	116	135	131	132	116	**2900**	**7.0**
Talipes Equinovarus	706	45	44	42	43	46	**926**	**2.2**
Polydactyly	349	17	21	24	20	23	**454**	**1.1**
Syndactyly	250	9	14	14	13	11	**311**	**0.7**
Reduction Deformity of Limbs	260	9	16	19	21	23	**348**	**0.8**
Diaphragmatic Hernia	126	4	4	11	13	10	**168**	**0.4**
Exomphalos	138	8	13	7	5	6	**177**	**0.4**
Gastroschisis	70	7	5	6	6	5	**99**	**0.2**
Achondroplasia	17	1	1	1	1	0	**21**	**0.1**
Osteogenesis Imperfecta	41	1	1	0	1	6	**50**	**0.1**
Chromosome (75800-75899)	1183 (3.6)	84 (4.7)	71 (4.1)	110 (6.0)	109 (5.8)	99 (5.1)	**1656**	**4.0**
Down Syndrome	563	43	34	50	55	56	**801**	**1.9**
Trisomy 13	53	2	3	3	3	6	**70**	**0.2**
Trisomy 18	134	9	10	13	16	10	**192**	**0.5**
Turner Syndrome	89	2	5	10	13	7	**126**	**0.3**
Metabolic (24390-27790)	426 (1.3)	34 (1.9)	25 (1.4)	36 (2.0)	32 (1.7)	24 (1.2)	**577**	**1.4**
Congenital Hypothyroidism	116	8	6	13	6	11	**160**	**0.4**
Phenylketonuria	22	0	1	0	4	1	**28**	**0.1**
Galactosaemia	12	0	0	0	0	2	**14**	**0.0**
Albinism	19	2	0	0	1	1	**23**	**0.1**
Cystic Fibrosis	133	12	3	9	8	5	**170**	**0.4**
Other Metabolic	123	11	14	15	13	5	**181**	**0.4**
Haematological/Immune (28200-28699)	319 (1.0)	6 (0.3)	10 (0.6)	9 (0.5)	8 (0.4)	3 (0.2)	**355**	**0.8**
Haemolytic Anaemias	163	3	3	3	3	1	**176**	**0.4**
Thalassaemias	35	1	1	1	2	0	**40**	**0.1**
Coagulation Defects	56	0	3	3	1	0	**63**	**0.2**
Other Selected								
Congenital Syphilis Syndrome	7	0	1	0	0	0	**8**	**0.0**
Congenital Rubella Syndrome	2	0	0	0	0	0	**2**	**0.0**
Fetal Alcohol Syndrome	10	2	0	1	0	0	**13**	**0.0**
Non-immune Fetal Hydrops	145	7	12	10	13	16	**203**	**0.5**
Haemangioma	192	17	23	20	18	14	**284**	**0.7**
Lymphangioma	141	9	13	16	11	16	**206**	**0.5**
Anotia / Microtia	51	3	4	2	1	1	**62**	**0.1**

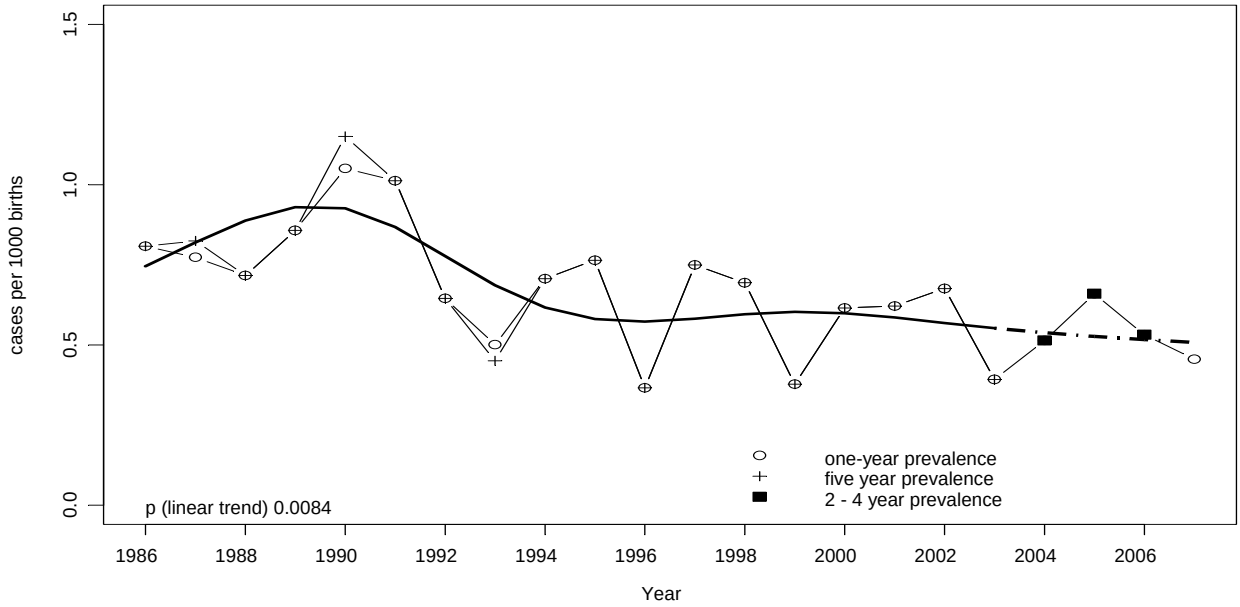
* Prevalence per 1,000 total births

Figure 3.1: Prevalence of Neural Tube Defects, SA 1986-2007



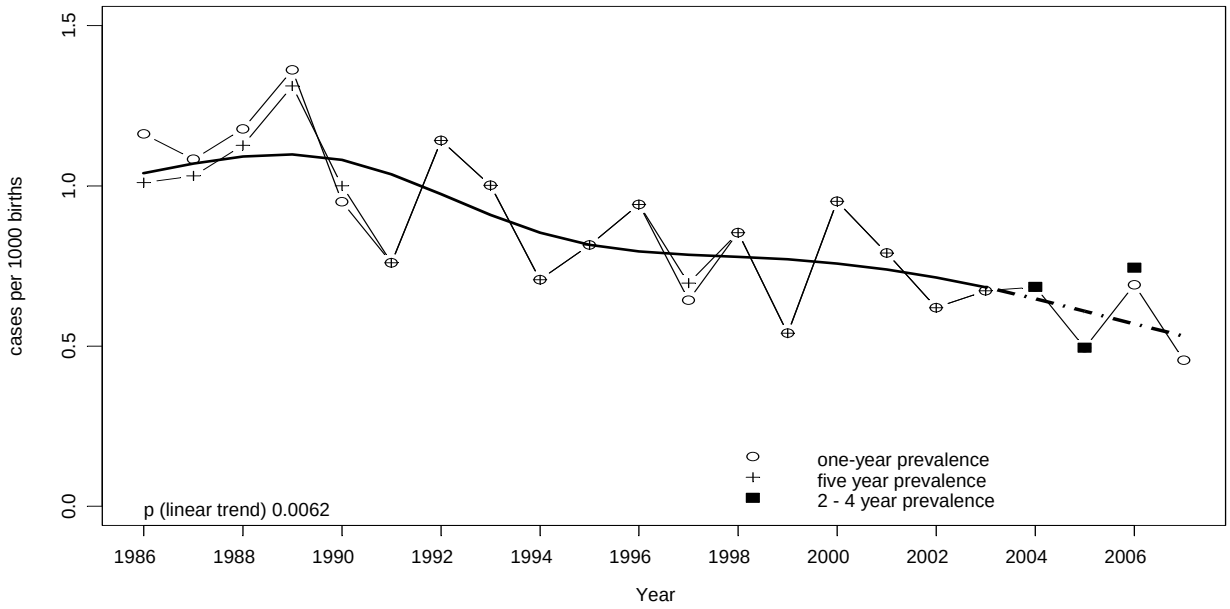
There was a significant downward trend in the prevalence of all Neural Tube Defects for the period 1986-2007 (Poisson regression, p=0.00039). This downward trend may be due to the increased use of periconceptional folic acid.

Figure 3.2: Prevalence of Anencephaly, SA 1986-2007



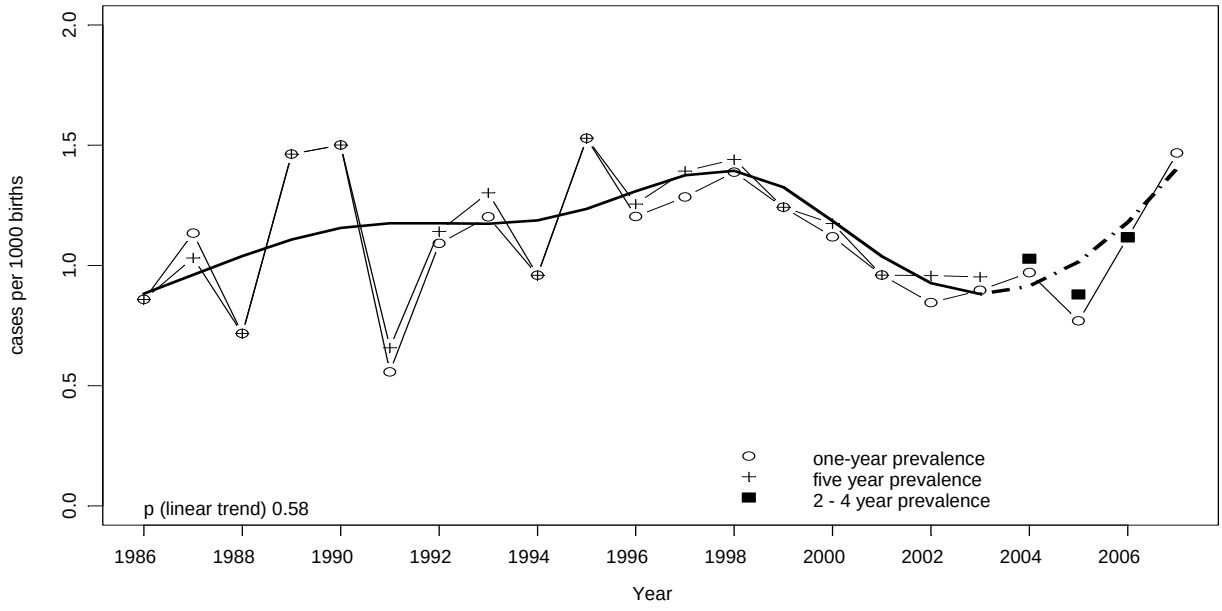
There was a significant downward trend in the prevalence of Anencephaly for the period 1986-2007 (Poisson regression, p=0.0084). This downward trend may be due to the increased use of periconceptional folic acid.

Figure 3.3: Prevalence of Spina Bifida, SA 1986-2007



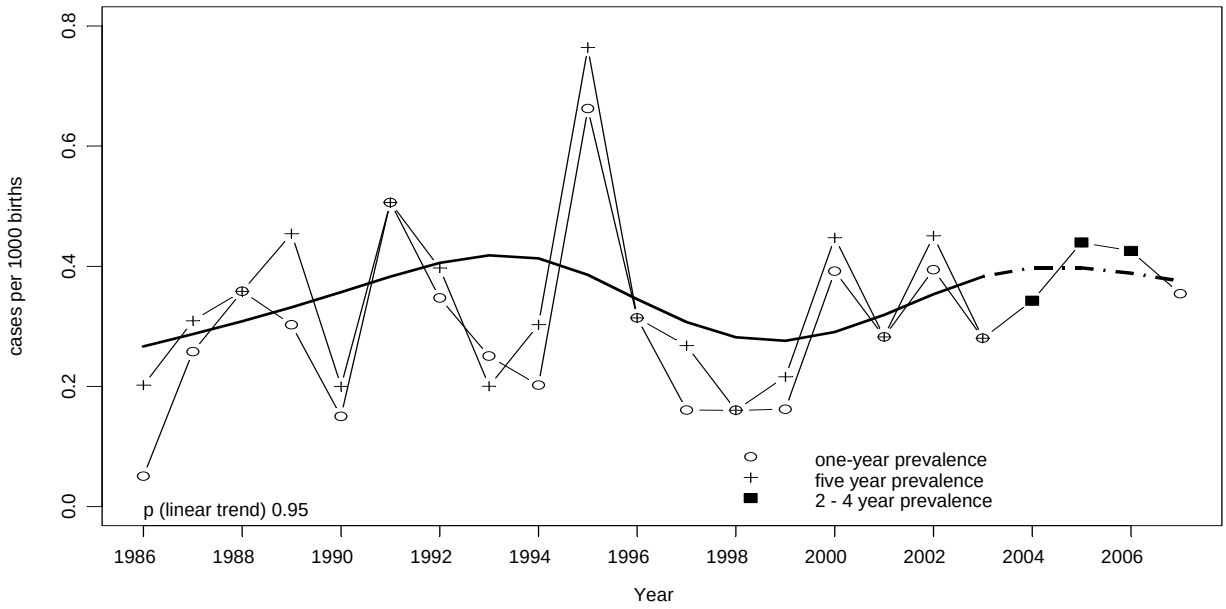
There was a significant downward trend in the prevalence of all Spina Bifida for the period 1986-2007 (Poisson regression, p=0.0062). This downward trend may be due to the increased use of periconceptional folic acid.

Figure 3.4: Prevalence of Total Cleft Lip, SA 1986-2007



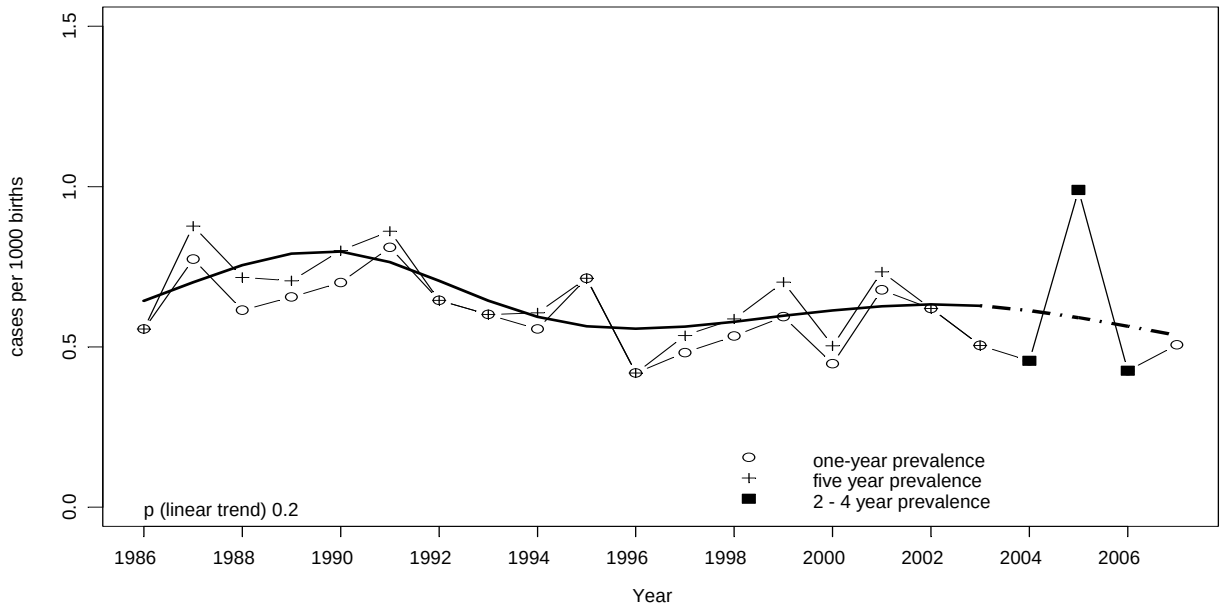
No significant trend was seen in the prevalence of Total Cleft Lip (cleft lip alone and cleft lip with cleft palate) for the years 1986-2007 (Poisson regression, p=0.58). However, a downward trend is apparent for the period 1995-2007 although it is not supported by the most recent data (2007).

Figure 3.5: Prevalence of Tetralogy of Fallot, SA 1986-2007



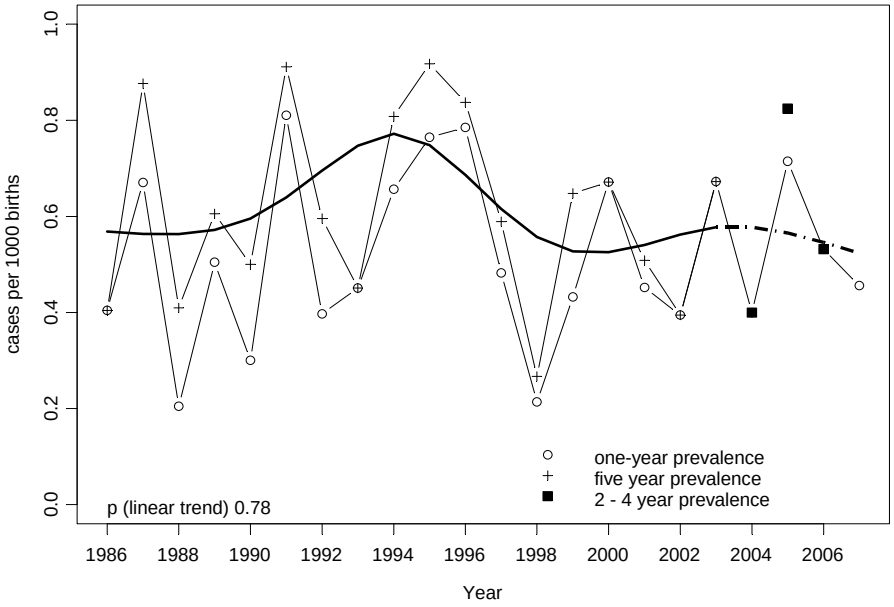
No significant trend was seen in the prevalence of Tetralogy of Fallot for the years 1986-2007, (Poisson regression, p=0.95).

Figure 3.6: Prevalence of Transposition of the Great Vessels, SA 1986-2007



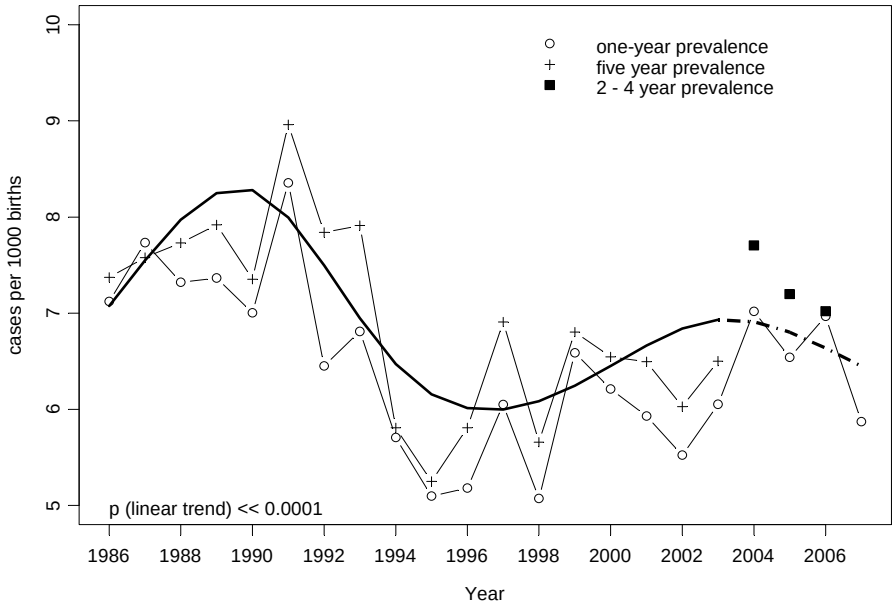
There was no significant trend in the prevalence of Transposition of Great Vessels over the period 1986-2007 (Poisson regression, p=0.20). In 2005 the number of cases was higher than in previous years (18 compared with 8 in 2004). No reason for this increase has been identified. This increase was not seen again in 2006 or 2007.

Figure 3.7: Prevalence of Coarctation of the Aorta, SA 1986-2007



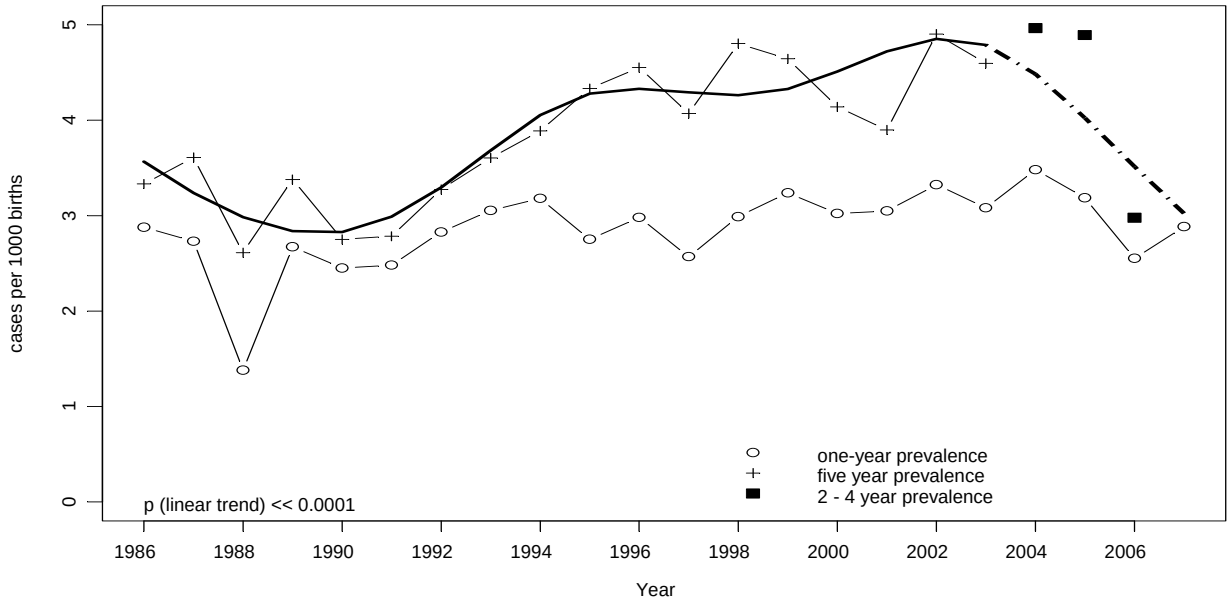
No significant trend was seen in the prevalence of Coarctation of the Aorta for the years 1986-2007, (Poisson regression, p=0.78).

Figure 3.8: Prevalence of Developmental Dysplasia of the Hip, SA 1986-2007



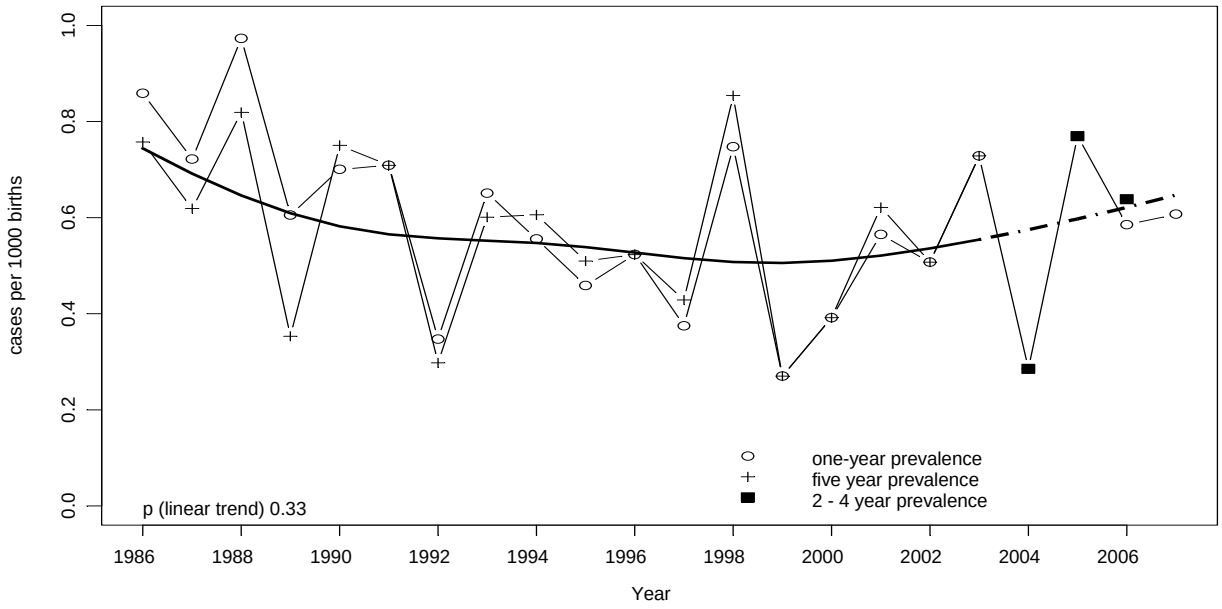
There was a significant downward trend in the prevalence of Developmental Dysplasia of the Hip over the period 1986-2007 (Poisson regression, p<0.0001) but the prevalence appears to be relatively stable from 1995 onwards.

Figure 3.9: Prevalence of Hypospadias, SA 1986-2007



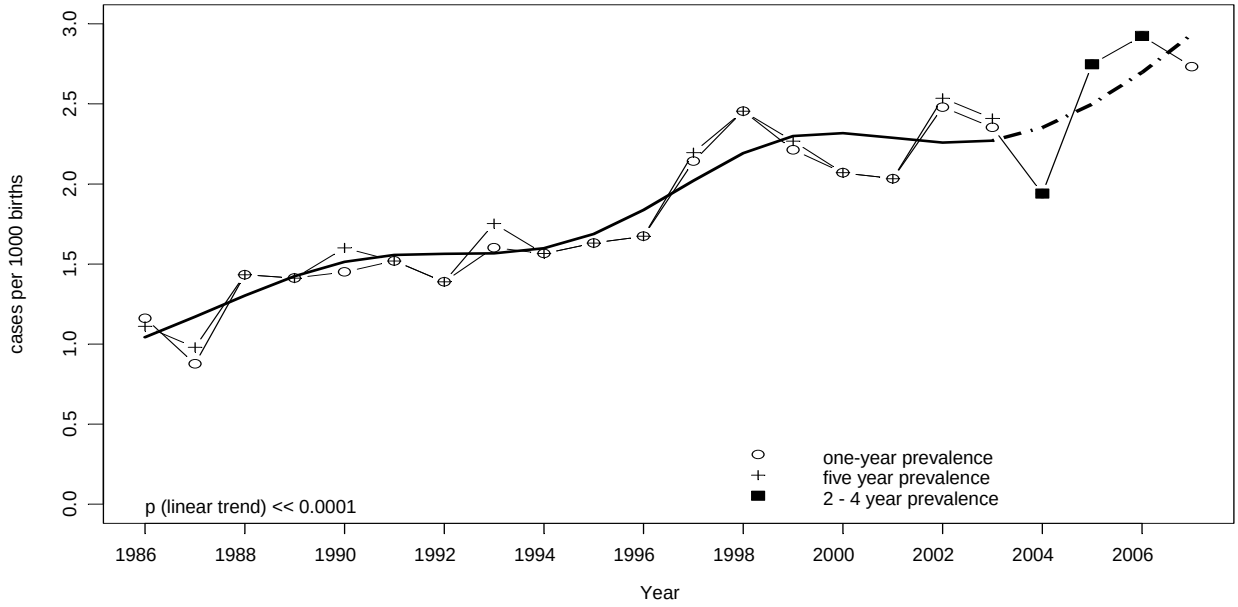
There was a significant upward trend in the five year prevalence of Hypospadias for the years 1986-2007 (Poisson regression, $p<0.0001$). Hospital records defined cases more specifically following validation reviews between the SABDR and hospital data. This commenced in 1995 and has led to improved ascertainment of cases not diagnosed at birth and undergoing surgery at a later date. There was no significant trend for the one year prevalence of Hypospadias, most likely due to the delays in notification to the Register.

Figure 3.10: Prevalence of Renal Agenesis/Dysgenesis SA 1986-2007



No significant trend was seen in the prevalence of Renal Agenesis/Dysgenesis for the years 1986-2007, (Poisson regression, $p=0.33$).

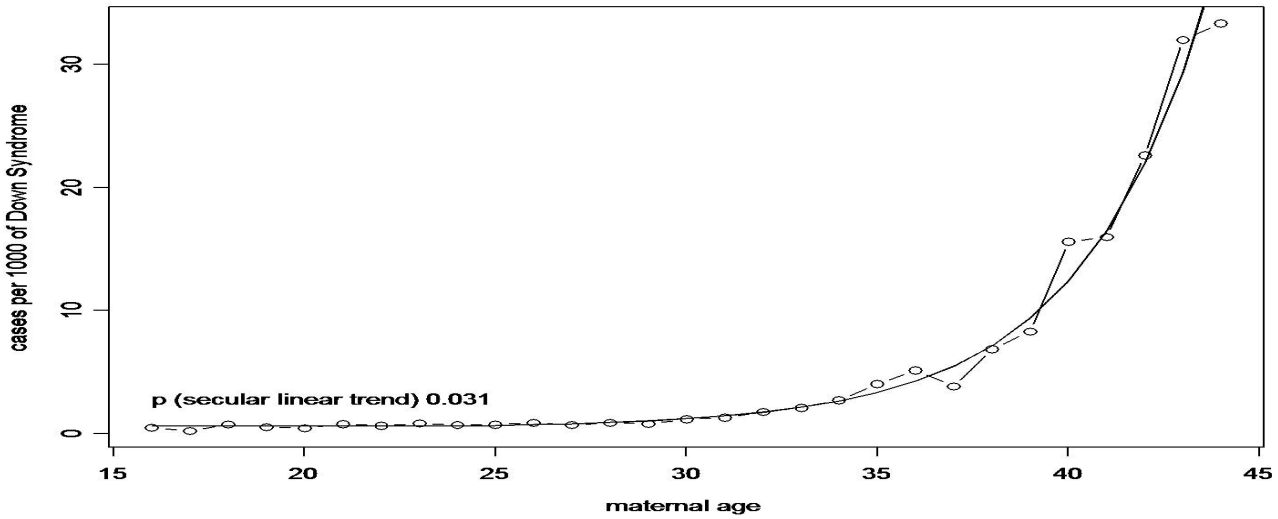
Figure 3.11: Prevalence of Down Syndrome, SA 1986-2007



Over the period 1986-2007, there was a significant increasing trend in the prevalence of Down Syndrome (Poisson regression, $p<0.0001$). In the past, this increase has been attributed to increasing maternal age. However, with the additional data for 2007, the adjustment for maternal age (in Poisson regression, using single year age-bands), shows that the prevalence appears to be increasing by a factor of 1.26% per year (95% CI 0.11% to 2.42%). This indicates that other factors, in addition to maternal age, may be influencing the prevalence of Down Syndrome. The risk of a future pregnancy being affected by Down Syndrome is known to be increased for women who have already had a Down Syndrome pregnancy*, and this could be an influencing factor.

*De Souza, E, Halliday J, Chan A, Bower C, Morris J. Recurrence risks for Trisomies 13, 18 and 21. Am J Med Genetics. In Press (Accepted Aug. 2009)

Figure 3.12: Incidence of Down Syndrome by maternal age, SA 1986-2007



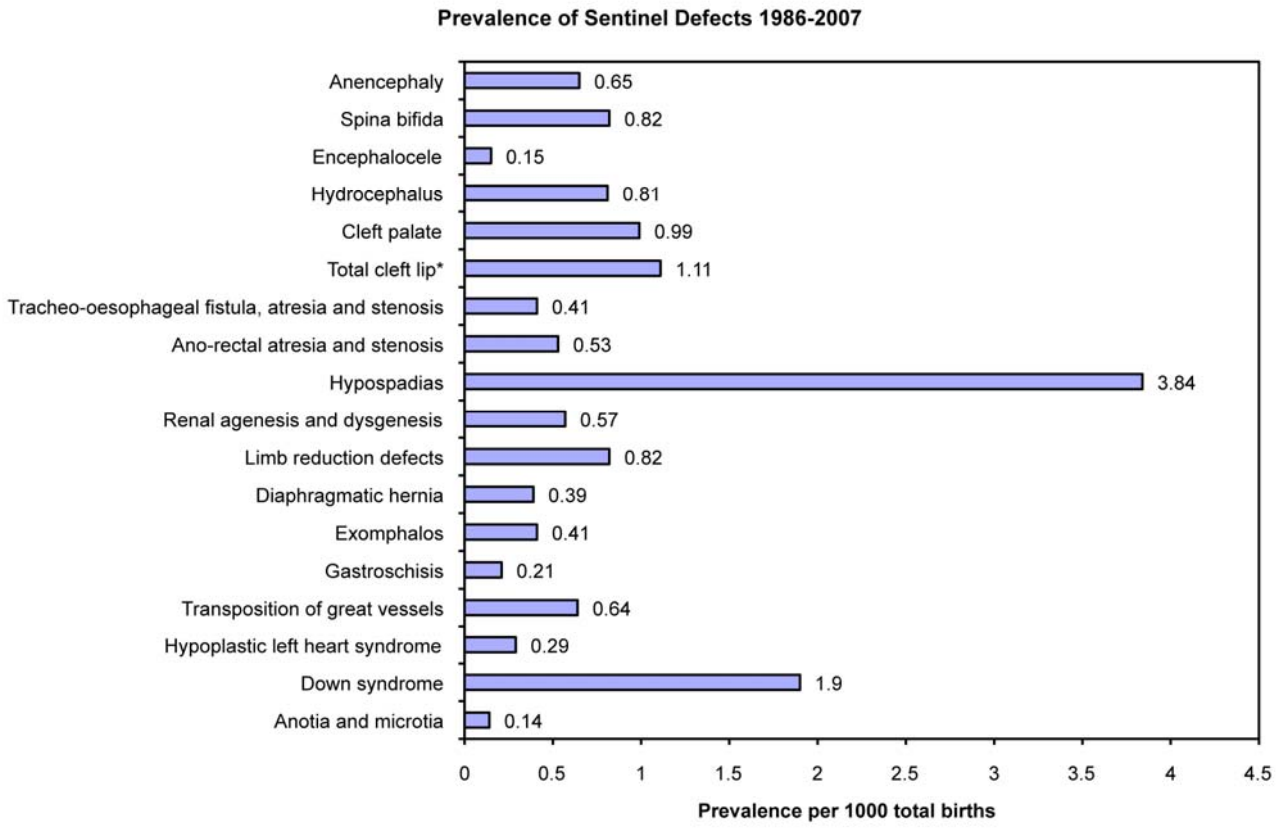
As demonstrated by this figure, there is an exponential increase in the risk of Down Syndrome with increasing maternal age.

Sentinel Defects

A number of readily identifiable defects have been chosen as 'sentinel' defects for monitoring purposes by the International Clearinghouse for Birth Defects Monitoring Systems. Figure 4 and Table 7 present sentinel defects by CURB region for the period 1986-2007. The totals for individual defects may be less than those shown in Table 6 as births to women who are interstate residents have been excluded from this table. This tabulation is an important tool for detecting regional and temporal clusters of birth defects. The SABDR monitors the occurrence of defects over time and by geographical area in this way. The Register assesses the significance of variations in prevalence by comparing the observed and expected numbers for each region using the Poisson distribution.

The prevalence of Down syndrome in the Central Eastern Region between 1986 and 2007 was again significantly greater than in the rest of South Australia (RR = 1.44, 95% CI 1.21-1.72, $p<0.001$). This was shown to be related to the older age of mothers in that region. After adjustment for maternal age, no significant difference was seen (Mantel-Haenszel RR = 1.04, 95% CI 0.87-1.23, $p=0.73$). There were no other significant regional increases in prevalence ($p<0.01$) between 1986 and 2007.

Figure 4: Prevalence of Sentinel Defects, SA 1986-2007



* Total cleft lip includes cleft lip with or without cleft palate

Sentinel Defects

Table 7: Cases of sentinel defects by CURB region, SA 1986-2007

	CURB Region									
	Central North	**Central West**	**Central East**	**Central South**	**Yorke & Low Nth**	**Murray Lands**	**South East**	**North**	**Eyre**	**Total**
% State Births	**28.6%** No. (per 1000*)	**13.0%** No. (per 1000*)	**14.9%** No. (per 1000*)	**21.9%** No. (per 1000*)	**2.8%** No. (per 1000*)	**4.9%** No. (per 1000*)	**4.8%** No. (per 1000*)	**6.5%** No. (per 1000*)	**2.7%** No. (per 1000*)	**100%** No. (per 1000*)
Anencephaly	72 (0.61)	36 (0.72)	39 (0.63)	61 (0.67)	8 (0.69)	14 (0.69)	7 (0.35)	21 (0.77)	7 (0.63)	**268 (0.65)**
Spina Bifida	93 (0.78)	57 (1.06)	45 (0.73)	69 (0.76)	8 (0.69)	19 (0.94)	16 (0.81)	24 (0.88)	8 (0.73)	**339 (0.82)**
Encephalocele	22 (0.19)	8 (0.15)	9 (0.15)	10 (0.11)	3 (0.26)	1 (0.05)	3 (0.15)	4 (0.15)	2 (0.18)	**62 (0.15)**
Hydrocephalus	95 (0.80)	44 (0.82)	52 (0.84)	88 (0.97)	7 (0.61)	11 (0.55)	12 (0.61)	22 (0.81)	6 (0.54)	**337 (0.81)**
Cleft Palate	132 (1.11)	53 (0.98)	57 (0.92)	85 (0.93)	8 (0.69)	17 (0.84)	20 (1.01)	23 (0.85)	16 (1.45)	**411 (0.99)**
Total Cleft Lip#	148 (1.25)	46 (0.85)	64 (1.03)	102 (1.12)	16 (1.39)	22 (1.09)	21 (1.06)	30 (1.11)	14 (1.27)	**463 (1.11)**
Tracheo-Oesophageal Fistula, Atresia & Stenosis	52 (0.44)	21 (0.39)	34 (0.55)	30 (0.33)	5 (0.43)	8 (0.40)	5 (0.25)	13 (0.48)	4 (0.36)	**172 (0.41)**
Ano-Rectal Atresia & Stenosis	65 (0.55)	28 (0.52)	37 (0.60)	46 (0.51)	4 (0.35)	10 (0.50)	9 (0.46)	16 (0.59)	4 (0.36)	**219 (0.53)**
Hypospadias	497 (4.18)	196 (3.63)	223 (3.60)	326 (3.58)	49 (4.25)	87 (4.31)	62 (3.14)	105 (3.87)	48 (4.35)	**1593 (3.84)**
Renal Agenesis & Dysgenesis	59 (0.50)	37 (0.69)	40 (0.65)	50 (0.55)	8 (0.69)	10 (0.50)	7 (0.35)	24 (0.88)	2 (0.18)	**237 (0.57)**
Limb Reduction Defects	95 (0.80)	42 (0.78)	52 (0.84)	65 (0.71)	14 (1.21)	22 (1.09)	16 (0.81)	28 (1.03)	7 (0.63)	**341 (0.82)**
Diaphragmatic Hernia	41 (0.35)	21 (0.39)	22 (0.35)	29 (0.32)	7 (0.61)	10 (0.50)	9 (0.46)	17 (0.63)	6 (0.54)	**162 (0.39)**
Exomphalos	44 (0.37)	21 (0.39)	28 (0.45)	37 (0.41)	6 (0.52)	6 (0.30)	8 (0.41)	16 (0.59)	3 (0.27)	**169 (0.41)**
Gastroschisis	33 (0.28)	15 (0.28)	6 (0.10)	11 (0.12)	1 (0.09)	7 (0.35)	5 (0.25)	10 (0.37)	1 (0.09)	**89 (0.21)**
Transposition of Great Vessels	70 (0.59)	41 (0.76)	33 (0.53)	75 (0.82)	6 (0.52)	12 (0.60)	10 (0.51)	11 (0.41)	6 (0.54)	**264 (0.64)**
Hypoplastic Left Heart	32 (0.27)	17 (0.31)	18 (0.29)	29 (0.32)	2 (0.17)	2 (0.10)	8 (0.41)	7 (0.26)	4 (0.36)	**119 (0.29)**
Down Syndrome	197 (1.66)	105 (1.95)	161 (2.60)	199 (2.19)	26 (2.25)	35 (1.74)	28 (1.42)	24 (0.88)	15 (1.36)	**790 (1.90)**
Anotia & Microtia	14 (0.12)	13 (0.24)	8 (0.13)	16 (0.18)	1 (0.09)	0 (0.00)	3 (0.15)	2 (0.07)	2 (0.18)	**59 (0.14)**
Total	**1636** (13.8)	**749** (13.9)	**854** (13.8)	**1229** (13.5)	**157** (13.6)	**272** (13.5)	**231** (11.7)	**358** (13.2)	**144** (13.1)	**5630 (13.6)**

* Prevalence per 1,000 total births in region; # cleft lip with or without cleft palate

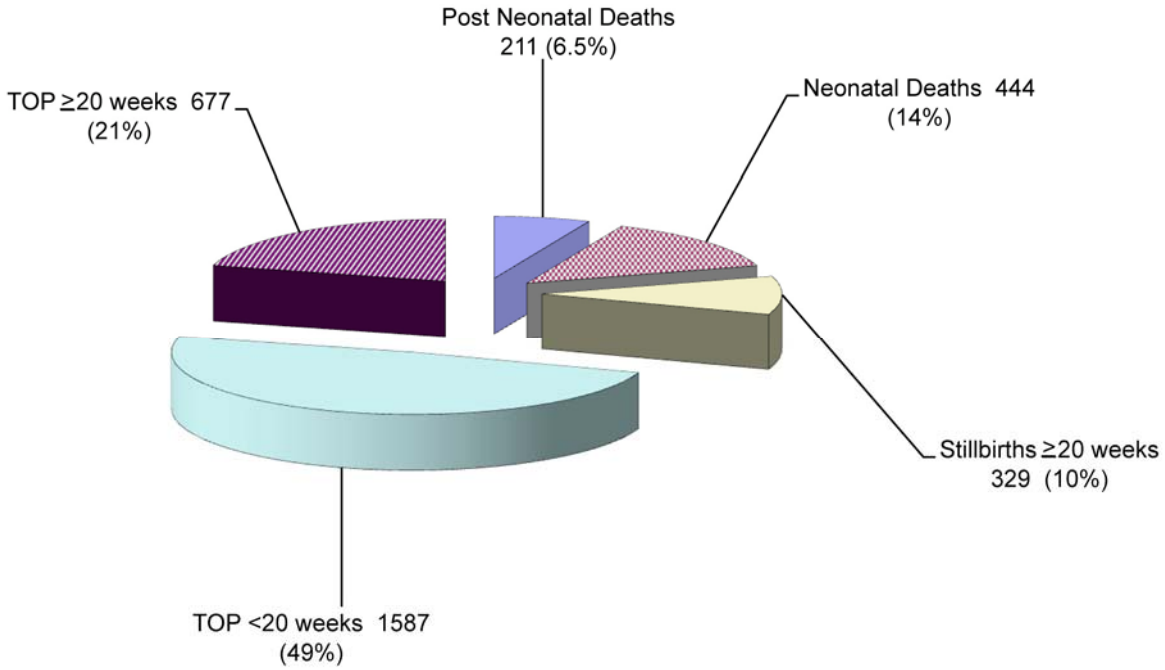
Deaths Associated with Birth Defects

In Table 8, the number of deaths associated with birth defects is listed by death category. Note that the birth defect is not necessarily the cause of death. Spontaneous stillbirths with birth defects represented 13.6% of all spontaneous stillbirths in South Australia in 2007; neonatal deaths with birth defects represented 27.3% of all neonatal deaths in the same period. Overall, for the period 1986-2007, spontaneous stillbirths with birth defects represented 11.8% of all spontaneous stillbirths, whilst neonatal deaths with birth defects represented 31.0% of all neonatal deaths. Figure 5 shows deaths associated with birth defects for the years 1986-2007 by category of death.

The different death categories are mutually exclusive. For example, the stillbirth category does not include terminations of pregnancy ≥ 20 weeks gestation.

In the category "TOP (termination of pregnancy) <20 weeks gestation", the Register distinguishes between first and second trimester diagnoses. Some notifications specify whether testing has been by chorionic villus sampling or amniocentesis. Otherwise, classification into these two groups is based on gestation. At a gestation of ≤ 14 weeks, diagnosis is assumed to be via chorionic villus sampling or ultrasound. At a gestation of > 14 weeks, diagnosis is assumed to be via amniocentesis or ultrasound.

Figure 5: Deaths associated with birth defects by death category, SA 1986-2007



Deaths Associated with Birth Defects

Table 8: Deaths associated with birth defects, SA 1986-2007

Death Category	Year of Birth 1986-2002	2003	2004	2005	2006	2007	Total 1986-2007
	No. (%*)	No. (%*)	No. (%*)	No. (%*)	No. (%*)	No. (%*)	**No. (%*)**
Post Neonatal Death (death of a liveborn infant between 28 days of age and the first birthday)	172 (7.2)	13 (8.9)	5 (3.5)	6 (3.2)	9 (4.7)	6 (3.1)	**211 (6.5)**
Neonatal Death (death of a liveborn infant before 28 days of age)	378 (15.8)	10 (6.8)	11 (7.8)	14 (7.6)	16 (8.4)	15 (7.7)	**444 (13.7)**
Stillbirth (spontaneous fetal death ≥ 20 weeks)	248 (10.4)	7 (4.8)	6 (4.3)	25 (13.5)	25 (13.2)	18 (9.3)	**329 (10.1)**
Termination of Pregnancy (≥ 20 weeks)	454 (19.0)	33 (22.6)	50 (35.5)	38 (20.5)	47 (24.7)	55 (28.4)	**677 (20.8)**
Termination of Pregnancy (< 20 weeks)							
• Diagnosis by chorionic villus sampling and/or ultrasound in first trimester	176 (7.4)	16 (11.0)	30 (21.3)	31 (16.8)	25 (13.2)	39 (20.1)	**317 (9.8)**
• Diagnosis by amniocentesis, cordocentesis and/or ultrasound after first trimester	963 (40.3)	67 (45.9)	39 (27.7)	71 (38.4)	68 (35.8)	62 (32.0)	**1270 (39.1)**
All Termination of Pregnancy (any gestation)	1593 (66.6)	116 (79.5)	119 (84.4)	140 (75.7)	140 (73.7)	156 (80.4)	**2264 (69.7)**
Total	**2391**	**146**	**141**	**185**	**190**	**195**	**3248**

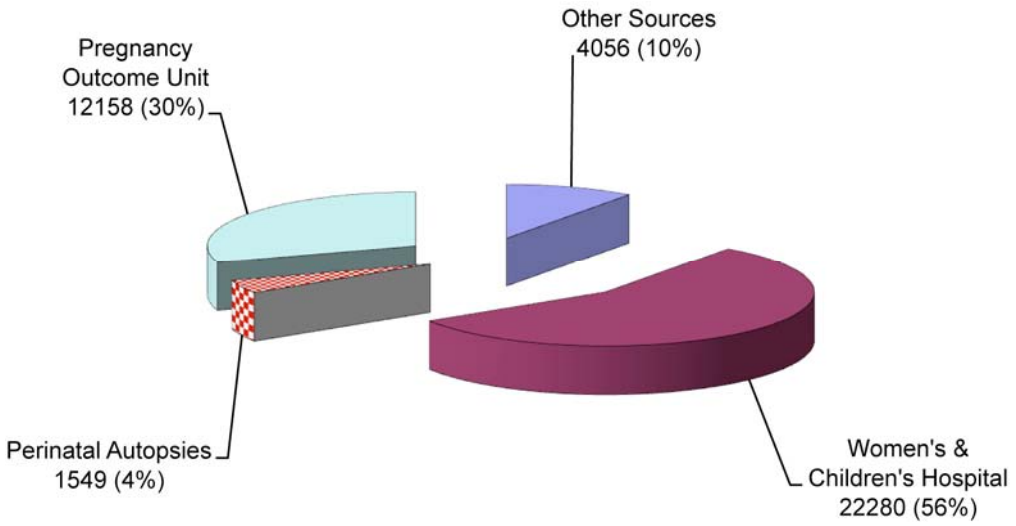
* Percentage of total deaths associated with birth defects in that year

Sources of Notification

The sources of notification for cases born in 1986-2007 are provided in Figure 6. As outlined earlier, each case may be notified by more than one source and considerable checking is required by the Register to validate the information.

Notifications from the Pregnancy Outcome Statistics Unit are obtained from all obstetric units as well as homebirth midwives in South Australia.

Figure 6: Sources of notification, SA 1986-2007: Total notifications received*



*Each case may have multiple notifications

Birth Defects Detected/Notified after Discharge from the Birth Hospital

Table 9 and Figure 7 use diagnostic categories to show the number and proportion of cases of birth defects in 1986-2007 which were detected and notified after discharge from the birth hospital. Over 50% of cardiovascular, urogenital, metabolic and haematological/immune defects were notified after discharge from the birth hospital.

The value of the Register in collecting later diagnosed defects is clearly illustrated by the proportions of cases in these latter categories, especially for earlier birth cohorts where collection has been of longer duration. The use of the Integrated South Australian Activity Collection (ISAAC), which is an admitted patient morbidity data collection, largely contributes to the validation of cases by SABDR staff, and this is reflected in the majority of cases being notified from the WCH as shown in Figure 6.

Examples of birth defects that are commonly notified after discharge form the birth hospital are ventricular septal defects, vesico-ureteric reflux, craniosynostosis and pyloric stenosis.

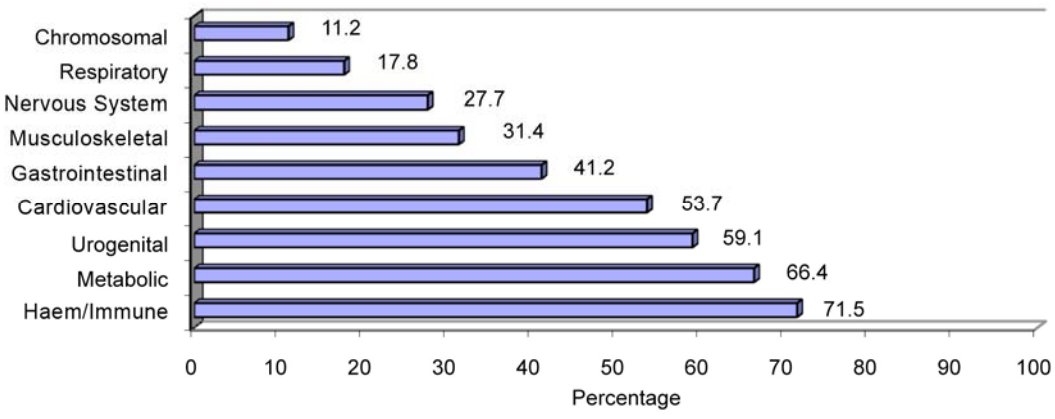
Birth Defects Detected/Notified after Discharge from the Birth Hospital

Table 9: Cases with birth defects notified after discharge from the birth hospital by major diagnostic category, SA 1986-2007

	Year of Birth						Total
	1986-2002	2003	2004	2004	2006	2007	1986-2007
Diagnostic Category	No. (%*)	No. (%*)	No. (%*)	No. (%*)	No. (%*)	No. (%*)	**No. (%*)**
Nervous System	364 (28.4)	20 (32.3)	26 (34.2)	18 (26.9)	13 (18.8)	8 (12.5)	**449 (27.7)**
Cardiovascular	2231 (55.9)	98 (50.0)	98 (51.9)	109 (47.0)	85 (45.7)	48 (27.7)	**2669 (53.7)**
Respiratory	90 (17.0)	14 (33.3)	7 (16.7)	9 (20.5)	3 (12.5)	4 (13.3)	**127 (17.8)**
Gastrointestinal	882 (41.4)	46 (40.4)	50 (46.3)	62 (47.7)	49 (40.2)	35 (28.5)	**1124 (41.2)**
Urogenital	3373 (60.3)	179 (61.9)	171 (58.6)	155 (55.6)	136 (57.6)	51 (26.8)	**4065 (59.1)**
Musculoskeletal	1678 (31.2)	100 (34.8)	105 (36.2)	108 (33.5)	84 (29.0)	80 (27.8)	**2155 (31.4)**
Chromosomal	155 (13.1)	5 (6.0)	3 (4.2)	8 (7.3)	8 (7.3)	6 (6.1)	**185 (11.2)**
Metabolic	292 (68.5)	14 (41.2)	13 (52.0)	29 (80.6)	22 (68.8)	13 (54.2)	**383 (66.4)**
Haematological/ Immune Disorders	232 (72.7)	4 (66.7)	5 (50.0)	8 (88.9)	4 (50.0)	1 (33.3)	**254 (71.5)**

* Percentage of total cases per category, per year

Figure 7: Percentage of cases with birth defects notified after discharge from the birth hospital by diagnostic category, SA 1986-2007



Prenatal Diagnosis in South Australia, 2007
Introduction

The Annual Report of Prenatal Diagnosis in South Australia records the 2007 experience based on the techniques of amniocentesis, chorionic villus sampling (CVS), fetal blood sampling, first trimester combined screening by nuchal translucency and maternal serum screening, and second trimester maternal serum screening for neural tube defects and Down syndrome.

No attempt has been made to compile information on pregnancies where ultrasound was the sole diagnostic technique used to detect birth defects. Its role in the detection of neural tube defects is recorded in the review of the maternal serum alpha-fetoprotein screening programme.

It should be noted that this report includes cases *screened* in each calendar year. This contrasts with the SA Birth Defects Register report which includes cases *born or terminated* in each calendar year.

We are grateful to the following groups for providing data for this report:

- Genetics and Molecular Pathology Directorate, SA Pathology
- Gribbles Pathology
- Pregnancy Outcome Statistics Unit, Department of Health
- Clinical Information Services, Women's and Babies Division, Women's and Children's Hospital
- Ashford Ultrasound Specialists for Women

Table 10: Screening and diagnostic tools used to detect Down Syndrome and Neural Tube Defects, SA 2007

Screen / Test	First Trimester	Second Trimester
Screening for Down syndrome	Nuchal Translucency (NT) plus Maternal Serum Screening (βHCG/PAPPA)	Maternal Serum Screening (βHCG/uE_3/AFP)
	10^{+0} to 13^{+6} weeks	14^{+0} to 20^{+6} weeks
Screening for neural tube defects	N/A	Maternal Serum Screening (AFP) 14^{+0} to 20^{+6} weeks
Screening for congenital malformations	Not routinely performed	Ultrasound 19 to 20 weeks
Diagnostic testing tools for chromosome abnormalities and genetic disorders	Chorionic Villus Sampling (CVS) 10 to 12 weeks	Amniocentesis After 15 weeks

Abbreviations:

βHCG, Beta human chorionic gonadotropin; **PAPPA**, Pregnancy-associated plasma protein A; **uE_3**, Unconjugated estriol; **AFP**, Alpha-fetoprotein.

Amniocentesis and Chorionic Villus Sampling

The number of amniocenteses performed in 2007 on South Australian women was 952, a decrease from 2006. Maternal age was a factor in 583 (61%) of all amniocenteses for that year.

The number of chorionic villus samplings performed in 2007 was 219, an increase compared with 2006. Maternal age was a factor in 146 (67%) of all CVS for that year.

Table 11: Amniocentesis and chorionic villus sampling, SA 2007: Indications

Indication	**Amniocentesis**			**CVS**			**Total**
	< 35 years	≥ 35 years	Unk	< 35 years	≥ 35 years	Unk	
Maternal age ≥ 35 years	-	257	-	-	59	-	**316**
Maternal anxiety/maternal age <35 years	30	-	0	1	-	0	**31**
Following abnormal CVS result	0	3	0	-	-	0	**3**
Previous child with							
1. Down syndrome	0	3	0	2	12	0	**17**
2. Other chromosomal abnormality (not Down)	3	4	0	2	7	0	**16**
3. Neural tube defect	0	0	0	0	0	0	**0**
Family history of							
1. Down syndrome	1	3	0	0	0	0	**4**
2. Other chromosomal abnormality including translocation carrier parent	4	2	0	6	6	0	**18**
3. Neural tube defect	0	0	0	0	0	0	**0**
At increased risk of chromosomal abnormality following screening by MSS* or NT#							
1. 1st trimester combined screen	135	173	0	24	36	0	**368**
2. 1st trimester NT alone	0	3	0	0	2	0	**5**
3. 1st trimester MSS alone	1	0	0	0	0	0	**1**
4. 2nd trimester MSS alone	88	63	0	-	-	-	**151**
At increased risk of NTD^ following MSS*	0	1	0	-	-	-	**1**
Abnormality found on ultrasound	83	58	0	0	3	0	**144**
At increased risk of a disorder diagnosed by molecular or biochemical techniques	4	2	0	24	11	0	**41**
Other (eg failed cordocentesis)	6	2	0	0	2	0	**10**
Multiple reasons	11	8	0	6	6	0	**31**
Blood Group/Antibodies	1	0	0	0	0	0	**1**
Paternity	2	1	0	8	2	0	**13**
Unknown indication	0	0	0	0	0	0	**0**
Total	**369**	**583**	**0**	**73**	**146**	**0**	**1171**

* MSS = Maternal Serum Screening; # NT = Nuchal Translucency
^ Neural tube defect;

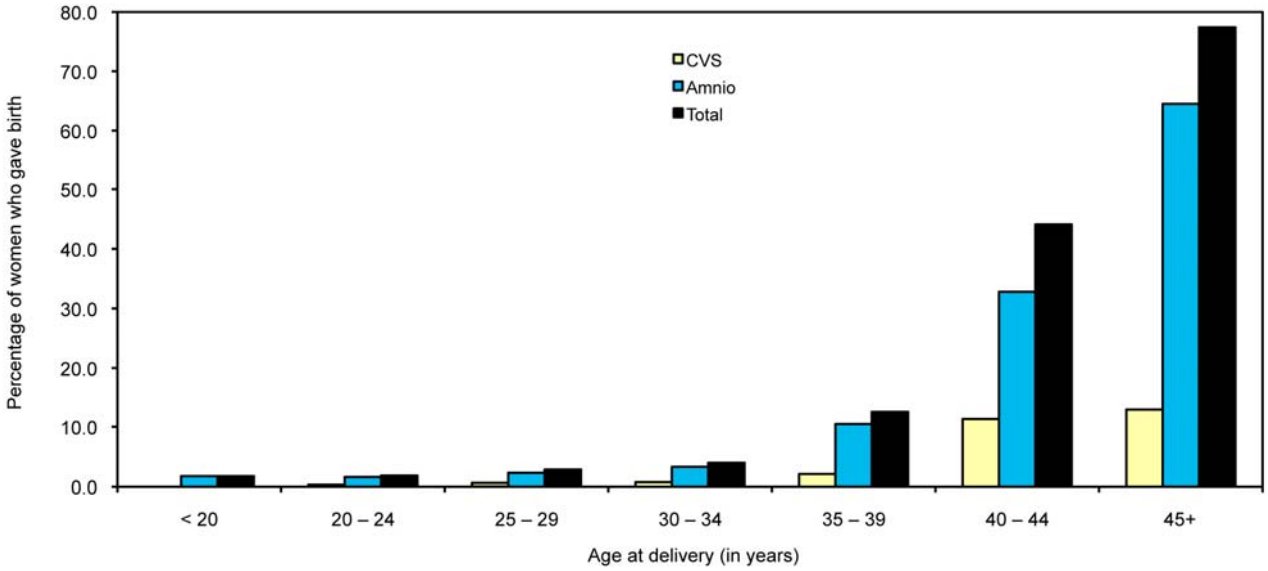
Amniocentesis and Chorionic Villus Sampling

Table 12: Amniocentesis and chorionic villus sampling, SA 2007: Utilisation by maternal age

Age*	Amniocentesis	CVS	Total	No. of women who gave birth	Percentage^
<20	15	0	15	897	1.7
20-24	46	7	53	3001	1.8
25-29	121	29	150	5392	2.8
30-34	203	42	245	6243	3.9
35-39	344	67	411	3287	12.5
40-44	203	70	273	619	44.1
45+	20	4	24	31	77.4
Total	**952**	**219**	**1171**	**19741**	**5.9**

* Age in years at expected delivery date. ^ Percentage of women who gave birth in that age range

Figure 8: Amniocentesis and chorionic villus sampling, SA 2007: Utilisation by maternal age



Amniocentesis and Chorionic Villus Sampling

Table 13: Disorders diagnosed by molecular or biochemical techniques, SA 2007

	Amniocentesis		Chorionic Villus Sampling	
Indication	Tested	Affected	Tested	Affected
Adrenoleukodystrophy	0	0	1	1
Apert syndrome	1	0	0	0
Arginosuccinic aciduria	0	0	1	0
Autosomal recessive polycystic kidney disease	0	0	1	1
Batten disease	0	0	1	0
Central core disease	0	0	1	0
Cystic fibrosis	0	0	8	1
Duchenne muscular dystrophy	0	0	2	0
Facioscapulohumeral dystrophy	0	0	1	0
Familial adenomatous polyposis	0	0	1	0
Fragile X syndrome	1	0	2	1
Haemophilia	0	0	1	0
Hypohidrotic ectodermal dysplasia – x-linked	0	0	1	0
Incontinentia pigmenti	0	0	1	1
IPEX syndrome	1	0	0	0
Leigh disease	0	0	1	1
Lissencephaly – x-linked	1	1	0	0
Lymphoproliferative disorder – x-linked	0	0	1	0
Myotonic dystrophy	1	1	1	0
Myotubular myopathy – x-linked	0	0	1	0
Osteogenesis imperfecta type III	1	1	0	0
Pelizaeus-Merzbacher disease – x-linked	0	0	1	1
Pfeiffer syndrome	0	0	1	0
Spinal muscular atrophy type I	0	0	1	0
Spinal muscular atrophy type II	0	0	1	0
Tuberous sclerosis	0	0	1	0
Zellweger syndrome	0	0	2	1
Thalassaemia	0	0	1	1
Blood group testing (including Rhesus)		N/A		N/A
Huntington disease	0	0	2	2

Fetal Blood Sampling

Fetal blood is obtained from the umbilical cord or a blood vessel in the fetal liver by an ultrasound guided needle technique. In 2007, 8 fetal blood samplings were performed. Fetal transfusions were performed in 3 out of 4 fetuses sampled.

Table 14: Fetal blood sampling, SA 2007: Indications

Indication	**No. of procedures**	**No. of fetuses**	**Outcome**
Rhesus or other isoimmunisation	8	4	7 fetal transfusions (3 fetuses)
Total	**8**	**4**	

Maternal Serum Screening for Neural Tube Defects in the Second Trimester

In 2007, 4,415 pregnancies were screened by estimation of maternal serum alpha-fetoprotein by the South Australian Maternal Serum Antenatal Screening (SAMSAS) Programme or Gribbles Pathology at 15-20 weeks gestation for a fetal neural tube defect. This represents 22.7% of all pregnancies.

There were 20 cases of neural tube defect in SA births whose mothers reached 14 weeks of pregnancy on or after 01.01.2007 or were no more than 20^{+6} weeks by the 31.12.2007 and hence would have been eligible for maternal serum alpha-fetoprotein screening during the 2007 screening year. This figure includes all neural tube defects confirmed in terminations of pregnancy or in births (≥ 400g or ≥ 20 weeks gestation).

100% of fetuses with a neural tube defect that had screening by either maternal serum alpha-fetoprotein screening or ultrasound screening or both were detected prenatally.

Table 15.1 Maternal serum screening for neural tube defects, SA 2007: SAMSAS and Gribbles Pathology

Number of pregnancies screened 2007	4,415
Total women who gave birth in SA in 2007	19,471
Percentage of pregnancies screened	22.7%

Table 15.2 Detection of neural tube defects by screening, SA 2007

Method of detection	Spina bifida	Anencephaly	Encephalocele	Total
1. AFP screen abnormal, as first indication of neural tube defect	0	1	0	1
2. Ultrasound abnormal, as first indication of neural tube defect				
(a) No serum AFP	5	1	1	7
(b) Serum AFP normal	1	0	0	1
(c) Too early for AFP	1	8	2	11
(d) Serum (or amniotic fluid) AFP abnormal	0	0	0	0
3. Screened by AFP &/or ultrasound Not detected	0	0	0	0
Total#	**7**	**10**	**3**	**20**

AFP = alpha-fetoprotein, # Neural tube defects detected as a result of serum AFP and/or ultrasound screening or elective testing because of previous affected child, or from examination of child at delivery.

Table 15.3 Outcome of neural tube defect pregnancies screened, SA 2007

Outcome	Spina bifida	Anencephaly	Encephalocele	Total
Livebirth	0	0	1	1
Livebirth, neonatal death	0	0	0	0
Termination of pregnancy	7	10	2	19
Total#	**7**	**10**	**3**	**20**

Neural tube defects detected as a result of serum AFP and/or ultrasound screening or elective testing because of previous affected child, or from examination of child at delivery.

Screening for Down Syndrome

There are both screening and diagnostic tests for Down syndrome during pregnancy. The screening tests include nuchal translucency (NT) screening, 1st trimester maternal serum screening (MSS), and the most commonly used first trimester test, combined NT and first trimester MSS. Second trimester MSS is also available if 1st trimester screening has not been performed.

Diagnostic tests are invasive and carry a small risk to the pregnancy; they are chorionic villus sampling (CVS) performed in the 1st trimester, and amniocentesis performed in the 2nd trimester, and are generally performed after a high risk screen. Patients will choose the most appropriate test for them after counselling. Some choose to proceed to diagnostic testing without screening tests.

Pregnancies are screened in the 1st trimester by the combination of nuchal translucency screening and maternal serum screening (free βHCG and PAPP-A). Software developed by SAMSAS or the Fetal Medicine Foundation (FMF) is used to estimate the risk for each pregnancy, based on blood analyte and nuchal translucency results and maternal age. Pregnancies are screened in the 2nd trimester by maternal serum screening. In 2007, for both SAMSAS and FMF, a risk of 1 in 300 or greater at term was used as the cut-off point for recommending consideration of CVS or amniocentesis. At Gribbles Pathology, the cut-off risk used in 2007 was 1 in 405 at term.

NT thickness for each fetus in multiple pregnancies parallels that of singleton pregnancies. A Down syndrome risk for each fetus is issued using the combination of NT thickness and maternal age. Monochorionic twins have an identical maternal age-related Down syndrome risk but may show different NT thickness; the greater risk is taken to recommend counselling. A 75% detection of affected multiple pregnancies is achievable according to published data using 1:300 as the cut-off. The use of serum markers for multiple pregnancies is currently not offered in SA but marker levels are measured for future studies to assess their possible utility.

There were 50 cases of Down syndrome that reached 10 weeks gestation on or after 01.01.2007 or were not greater than 13^{+6} weeks by 31.12.2007. This figure includes all Down syndrome cases confirmed in terminations of pregnancy or in births (≥ 400g or ≥ 20 weeks gestation). Of the 46 Down syndrome cases prenatally screened or tested by one or more screening or testing method, 39 (85%) were detected.

Table 16.1 Screening for Down syndrome, SA 2007: All testing laboratories

	Pregnancies Screened *
First trimester screening	11,363 (58%)
Second trimester screening only	3,235 (17%)
Total number of pregnancies screened †	14,598 (75%)

* numbers are expressed as a percentage of the total livebirths in SA in 2007 (19,471)

†A further 1.3% of women who gave birth (246 cases) did not have screening, and instead had a diagnostic amniocentesis or CVS for Down syndrome (maternal age indication, maternal anxiety, previous child with or family history of Down syndrome), resulting in a total of 76.3% of pregnancies having some form of investigation to screen for or identify Down syndrome.

Table 16.2 Down syndrome cases, SA 2007 screening year: Detected / Not detected

1. Cases detected	
First trimester screening (Nuchal translucency plus MSS+)	26
Second trimester screening (MSS+)	4
Amniocentesis (without prior screening)	3
CVS (without prior screening)	2
Ultrasound	4
Amniocentesis (missed by 1st trimester screening)	0
	39
2. Not detected	
First trimester screening (Nuchal translucency plus MSS+)	5
Second trimester screening (MSS+)	2
Not screened	4
	11
Total	**50**

+ MSS = Maternal serum screening. One case, detected later by ultrasound, had been missed by first trimester screening.

Table 16.3 Down syndrome cases, SA 2007 screening year: Pregnancy outcome

Termination of pregnancy	36
Livebirth	14
Total	**50**

Table 16.4 First trimester combined biochemical and nuchal translucency screening by maternal age: SAMSAS and FMF, SA 2007

Maternal Age	**< 35 years**		**≥ 35 years**		**Total**	
	SAMSAS	**FMF**	**SAMSAS**	**FMF**	**SAMSAS**	**FMF**
Number of pregnancies screened with valid risks reported* (% of pregnancies screened)	7409 (77.8%)	1198 (65.0%)	2111 (22.2%)	645 (35.0%)	**9520 (100%)**	**1843 (100%)**
Identified as "increased risk" after correction of gestational age (% of pregnancies screened)	196 (2.6%)	28 (2.3%)	211 (10.0%)	41 (6.4%)	**407 (4.3%)**	**69 (3.7%)**
Total CVS/Amniocentesis performed on pregnancies identified as "increased risk" (%)	168 (85.7%)	24 (85.7%)	156 (73.9%)	31 (%)	**324 (79.6%)**	**55 (79.7%)**
Affected pregnancies in screened population	11	1	18	7	**29**	**8**
Affected pregnancies among those screened at "increased risk"	8	1	15	6	**24**	**7**
Affected pregnancies among those who proceeded to CVS/Amniocentesis	7	1	15	5	**22**	**6**
Sensitivity (%)	72.7	100	88.9	85.7	**82.8**	**87.5**
Risk of an affected pregnancy in those at "increased risk" (risk ≥ 1:300) on screening (positive predictive value, PPV)	1:25	1:28	1:13	1:7	1:17	**1:10**

* "Pregnancies screened with valid risks reported" exclude pregnancies which are <10 weeks and >14 weeks gestation and duplicate samples.

Screening for Down Syndrome

Table 16.5 First trimester combined biochemical and nuchal translucency screening by maternal age: SAMSAS and FMF, SA 2001 - 2007

Maternal Age	< 35 years		≥ 35 years		Total	
	SAMSAS	FMF	SAMSAS	FMF	SAMSAS	FMF
Number of pregnancies screened with valid risks reported* (% of pregnancies screened)	30294 (79.3%)	7475 (69.0%)	7914 (20.7%)	3361 (31.0%)	**38208 (100%)**	**10836 (100%)**
Identified as "increased risk" after correction of gestational age (% of pregnancies screened)	968 (3.2%)	219 (2.9%)	871 (11.0%)	339 (10.1%)	**1839 (4.8%)**	**558 (5.1%)**
Total CVS/Amniocentesis performed on pregnancies identified as "increased risk" (%)	798 (82.4%)	176 (80.4%)	643 (73.8%)	263 (77.6%)	**1441 (78.4%)**	**439 (78.7%)**
Affected pregnancies in screened population	44	12	67	26	**111**	**38**
Affected pregnancies among those screened at "increased risk"	36	9	61	24	**97**	**33**
Affected pregnancies among those who proceeded to CVS/Amniocentesis	32	9	54	21	**86**	**30**
Sensitivity (%)	81.8	75.0	91.0	92.3	**87.4**	**86.8**
Risk of an affected pregnancy in those at "increased risk" (risk ≥ 1:300) on screening (positive predictive value, PPV)	1:27	1:24	1:14	1:14	**1:19**	**1:17**

* "Pregnancies screened with valid risks reported" exclude pregnancies which are <10 weeks and >14 weeks gestation and duplicate samples.

Table 16.6 Second trimester maternal serum screening by maternal age: SAMSAS only, SA 2007

Maternal Age	< 35 years	≥ 35 years	Total
Number of pregnancies screened with valid risks reported*	2474	406	**3153**
Identified as "increased risk" after correction of gestational age (% of pregnancies screened)	124 (4.5%)	70 (17.2%)	**194 (6.2%)**
Amniocentesis performed on pregnancies identified as "increased risk" (%)	93 (75%)	50 (71.4%)	**143 (73.7%)**
Affected pregnancies in screened population	2	4	**6**
Affected pregnancies among those screened as "increased risk"	1	3	**4**
Affected pregnancies among those who proceeded to amniocentesis	1	3	**4**
Sensitivity (%)	50	75	**66.7**
Risk of an affected pregnancy in those at "increased risk" (risk ≥ 1:300) on MSS (positive predictive value or PPV)	1:124	1:23	**1:49**

* "Pregnancies screened with valid risks reported" exclude pregnancies which are multiple, <14 weeks and >20 weeks and duplicate samples and those requested for neural tube defect risk only

Trends in Utilisation of Amniocentesis and CVS

Since 1986 there has been an overall increase in the percentage of all women undertaking prenatal diagnostic amniocentesis and CVS (Figure 9). In 2007, the proportion was 6% of all women who gave birth, slightly less than 2006. This is still a higher percentage than those undertaken in 1986 (5%). In comparison, Figure 10 shows the proportion of amniocentesis or CVS undertaken by women ≥ 35 years of age which has decreased between 1986 and 2007.

Although the number of women who gave birth in women 35 years and over has risen from 1285 in 1986 to 3937 in 2007, the proportion of women in this age group having a test has decreased over time (Figure 10). This is most evident from 1996 onwards. In the last few years, this decrease can only partly be explained by an increasing proportion of women having first trimester combined screening and therefore less women directly requesting amniocentesis or CVS (see figures 11 and 12).

Figure 9: Percentage of Amniocentesis and CVS by year for all women, SA 1986-2007: all indications

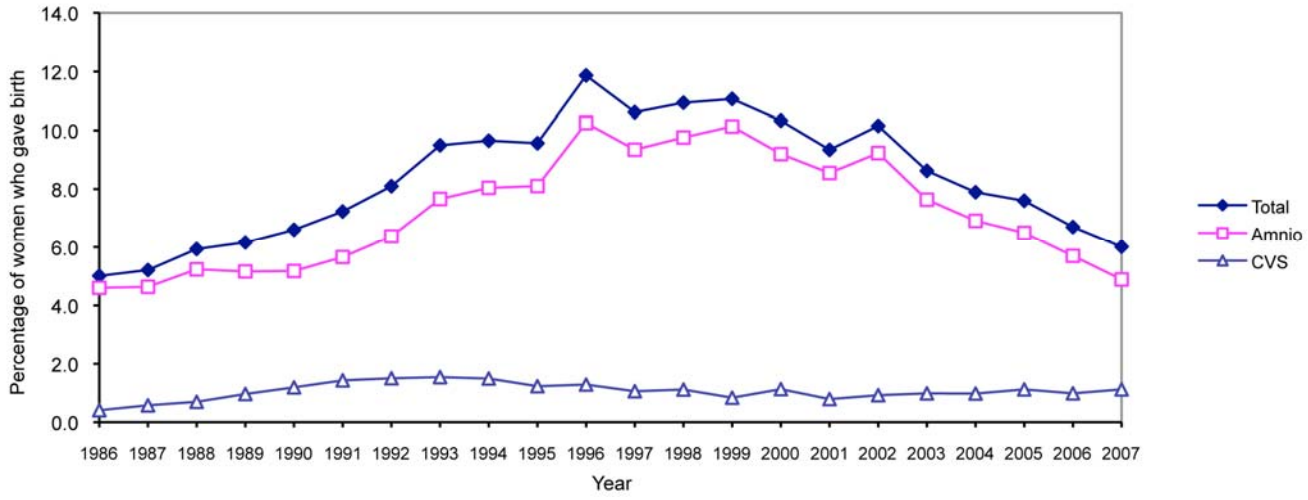
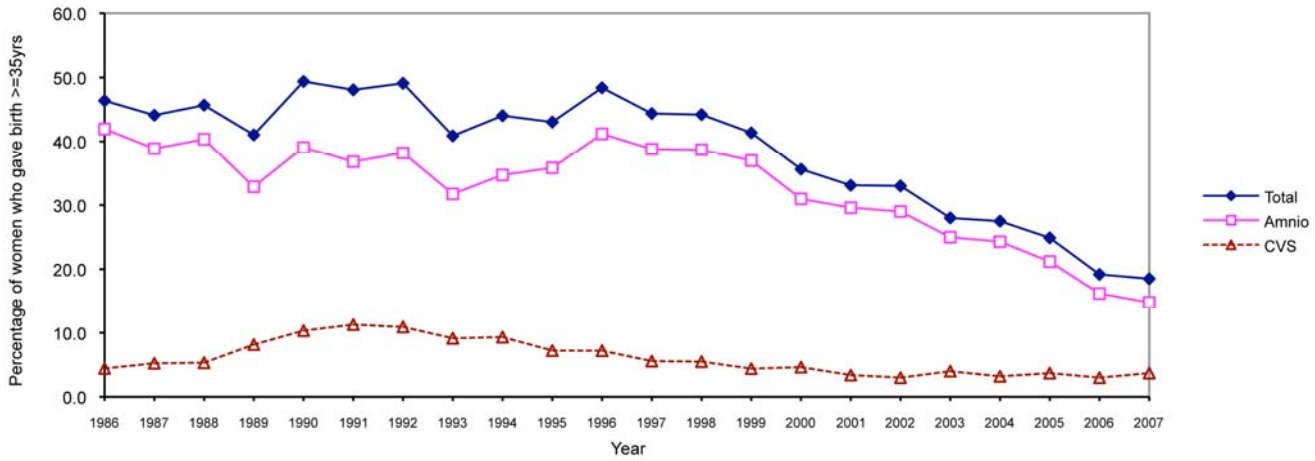
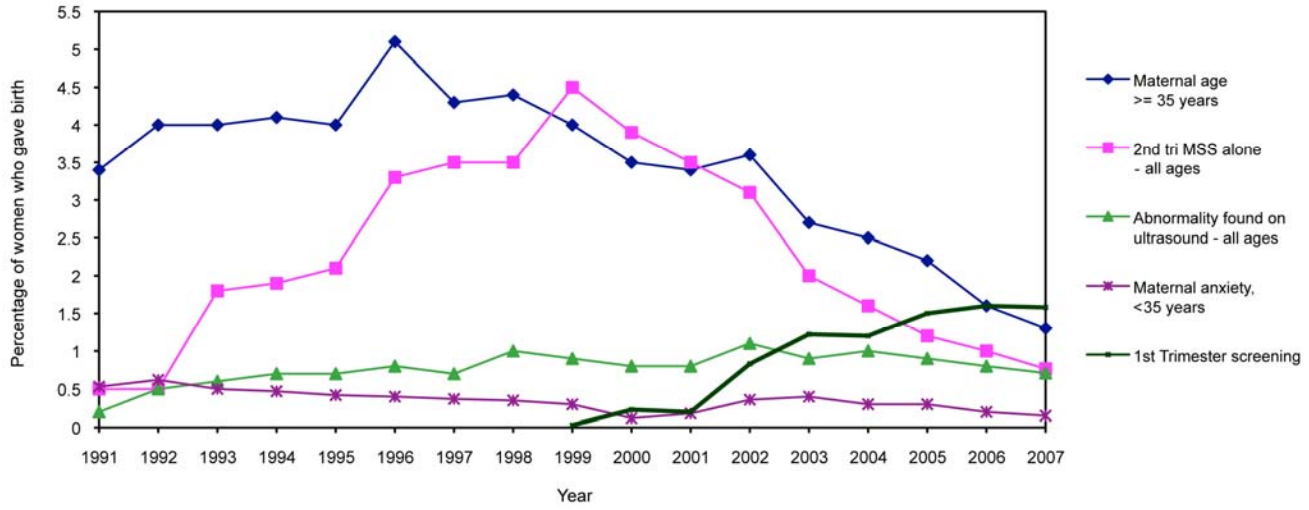


Figure 10: Percentage of Amniocentesis and CVS by year for maternal age ≥35 years, SA 1986-2007: all indications



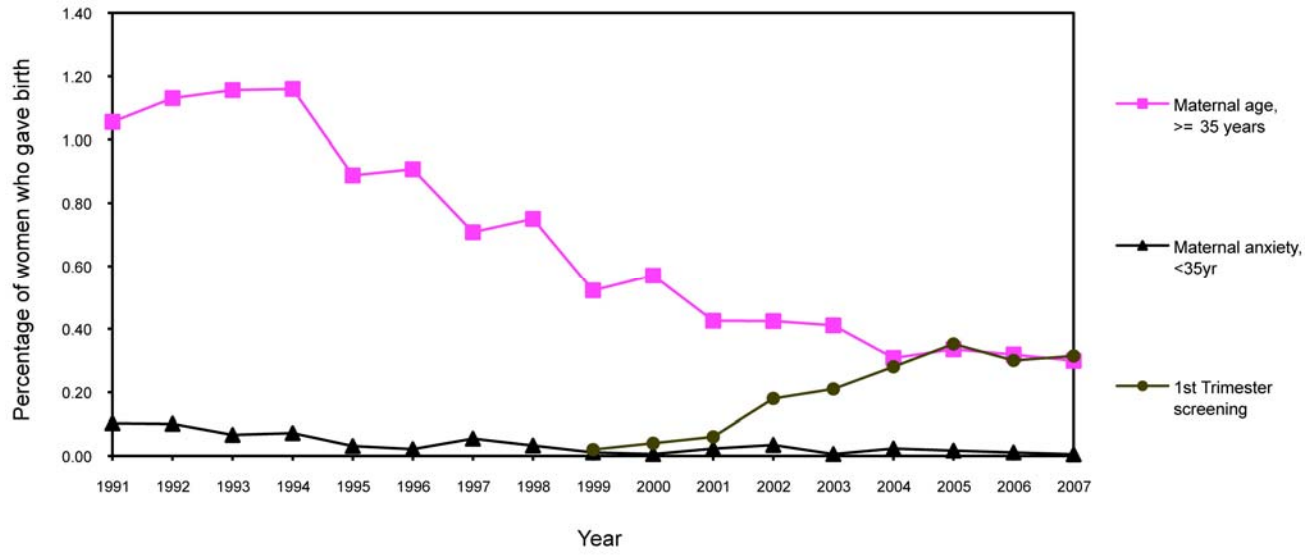
Trends in Utilisation of Amniocentesis and CVS

Figure 11: Indications for Amniocentesis by year, SA 1991*-2007
Percentage of all women who gave birth



*No routine screening prior to 1991

Figure 12: Indications for Chorionic Villus Sampling by year, SA 1991*-2007
Percentage of all women who gave birth



*No routine screening prior to 1991

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"Mannose binding lectin haplotypes are associated with cerebral palsy." Perinatal Society of Australia and New Zealand Conference, 2007, Melbourne, Australia. (CS Gibson)

"The association between inherited cytokine polymorphisms and cerebral palsy." Society for Maternal Fetal Medicine Conference, 2006, Miami, USA. (CS Gibson)

"The role of fetal inherited thrombophilia in the development of adverse pregnancy outcomes." Society for Maternal Fetal Medicine Conference, 2006, Miami, USA. (CS Gibson)

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"Folate awareness in South Australia: Results from the South Australian Computer Assisted Telephone Interview surveys 1994-2004." South Australian Department of Health. Australian Birth Defects Society Annual Meeting, 2005, Melbourne, Australia. (P Sharpe)

"Maternal diabetes and congenital anomalies in South Australia 1986-2000: a population based cohort study." Australian Birth Defects Society Annual Meeting, 2005, Melbourne, Australia. (P Sharpe)

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"Late diagnosis of developmental dysplasia of the hip: risk factors and outcomes in South Australia." Australian Birth Defects Society Annual Meeting, 2002, Sydney, Australia. (P Sharpe)

"Folate before pregnancy: impact of a South Australian health promotion campaign on women and health professionals." The Royal Australasian College of Physicians Annual Scientific Meeting 2000, Adelaide, South Australia. (A Chan)

"Prevalence and prenatal diagnosis of neural tube defects." National meeting of Perinatal Statistics Units, 1998, Sydney, Australia. (R Keane)

"A comparison of selected birth defects in Aboriginal and non-Aboriginal births in South Australia." Australian Birth Defects Society Annual Meeting 1998, Sydney, Australia. (R Byron-Scott)

"A validation study of congenital heart defects in South Australia." Australian Birth Defects Society Annual Meeting 1998, Sydney, Australia. (R Byron-Scott)

"Down syndrome screening in South Australia." Australasian Faculty of Public Heatlh Medicine, South Australian Branch General Meeting, 1998, Adelaide, Australia. (T Cheffins and A Chan)

"A validation study of congenital heart defects in South Australia." The Australian Society for Medical Research, South Australian Division Annual Scientific Meeting, 1998, Adelaide, Australia. (R Byron-Scott)

"Effect of rubella immunisation in South Australia." Public Health Association of SA Inc Annual Conference, 1997, Melbourne, Australia. (T Cheffins)

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"Gastroschisis and Exomphalos." Human Genetics Society of Australasia Annual Conference, 1997, Perth, Australia. (R Byron-Scott)

"Update on folate." Women's and Children's Hospital Grand Rounds, 1997, Adelaide, Australia. (A Chan)

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Approximately 24 presentations on the prevention of neural tube defects, as part of the "Folate before pregnancy health prevention programme" were made by Jane Dounton in 1994 and 1995 to hospital staff (in particular midwives and paediatric nurses), women's health professionals, midwifery students, childbirth educators and community groups. These included the Health Department Foundation, the Family Planning Association, the Pharmaceutical Society, the Child, Adolescent and Family Health Service and the South Australian Health Commission Public and Environmental Health Service.

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"Folate before Pregnancy Programme." Public Health Association of Australia Annual Conference, 1994, Adelaide, Australia. (J Dounton, A Chan, M, Netting)

"How effective is prenatal screening for neural tube defects in South Australia?" Seminars in Genetics, Women's and Children's Hospital, 1994, Adelaide, Australia. (A Chan)

"Can ultrasound replace serum alpha-fetoprotein in population based antenatal screening for neural tube defects?" First International Congress on Teratology, 1994, Chengdu, China. (A Chan)

Appendix 1

Background Information on the SA Birth Defects Register

1. Aims

The Birth Defects Register aims to provide complete, accurate and up-to-date information for the following purposes:

- Establishing local prevalence rates for birth defects
- Monitoring the occurrence of defects over time and by geographical area to allow investigation of suspected teratogens
- Increasing community knowledge about birth defects through education and by acting as a source of information
- Utilisation of local prevalence rates to plan health care facilities
- Epidemiological studies on the causation of birth defects
- As an accurate diagnostic index for clinical research

2. Sources of Notification

Cases notified to the Register include those with birth defects detected in a variety of circumstances:

- Pregnancies terminated because of a diagnosis of a birth defect in the fetus
- Late fetal deaths (stillbirths)
- Newborn babies
- Children diagnosed after the neonatal period and prior to their fifth birthday

The sources of notification include:

- Doctors and other health professionals involved with the care of children with birth defects in hospitals, special paediatric assessment, treatment and rehabilitation centres and private practices
- The Pregnancy Outcome Statistics Unit of SA Health
- The State Perinatal Autopsy Service and other pathology services
- Diagnostic services including laboratories diagnosing cytogenetic or biochemical abnormalities, and organ imaging departments.

While notifications of defects detected prenatally are made by doctors to the Pregnancy Outcome Statistics Unit, it is recognised that many defects, for example some congenital heart defects or malformations of the urinary tract, may not be detected at the time of birth. Moreover, diagnoses made in the neonatal period may change with time. The Register, by extending the period of time for receiving notifications, and receiving them from multiple sources, achieves more complete ascertainment of birth defects in South Australian children (The notification form is included in Appendix 4).

3. Definition of a Birth Defect

A birth defect is defined within the Register as any abnormality, structural or functional, identified up to five years of age, provided that the condition had its origin before birth. Thus, structural (eg. Spina bifida), chromosomal (eg. Down syndrome) and biochemical (eg. Phenylketonuria) defects are included. For Register purposes, single gene defects, eg. Neurofibromatosis, cystic fibrosis and muscular dystrophy, are also considered to be birth defects, although clinical manifestations may not appear until well after birth, and some may not cause malformations. Most minor malformations are excluded unless they are disfiguring, require treatment, or accompany another defect. (A list of inclusions and exclusions is provided in Appendix 3).

4. Ascertainment and Accuracy of Diagnoses

Ascertainment of birth defects will be incomplete in the first few years of life of each birth cohort. Data collection to five years of age, the use of multiple notification sources, and confirmation of diagnoses by clinicians and pathologists increases the accuracy of final diagnoses, and with it the value of the Register.

5. Confidentiality of Data

The Register has detailed and comprehensive confidentiality guidelines (Appendix 2). The guidelines ensure the confidentiality of the Register's data, while allowing research to be carried out in accordance with the National Health and Medical Research Council Guidelines for Epidemiological Research.

Confidentiality of Register data is overseen by the Birth Defects Register Advisory Committee. This Committee reviews the operation of the Register and comments on research proposals involving Register data.

Appendix 2

Confidentiality Guidelines

The South Australian Birth Defects Register has been receiving notifications of children with birth defects under the provisions of Section 64d of the South Australian Health Commission Act, 1976. Although notification does not require parental consent, provisions are made to inform public and parents about the Register. Section 64d requires the Register to maintain the confidentiality of notified information, whilst allowing the release of data to certain persons for specified purposes. The Register has developed guidelines to enable the confidential management of personal information in accordance with the provisions of Section 64d. Since September 1999, notification of children with birth defects identified later, ie after discharge from the hospital of birth but before the child's fifth birthday, has been required under legislation (South Australian Health Commission (Pregnancy Outcome Statistics) Regulations, 1999). This notification is required to be made to the Pregnancy Outcome Statistics Unit of the Department of Health, which also receives notification of birth defects detected at birth under the same legislation. The Pregnancy Outcome Statistics Unit has asked the SA Birth Defects Register to assist it in the collection of late notifications of children with birth defects. The historical data collected under the South Australian Health Commission Act continue to be subject to the privacy provisions of that Act. More recent data collected under the new Health Care Act 2008 are subject to slightly modified privacy provisions. This legislation does not alter the confidentiality guidelines under which the Register functions.

Purpose of Confidentiality Guidelines

The purpose of confidentiality guidelines is:

- To protect the privacy of children and women notified to the Register and the confidentiality of the information received;
- To ensure confidentiality by documenting procedures for managing personal information in a confidential manner;
- To ensure a balance between individual privacy and the confidentiality of information held by the Register, and the public benefit arising from knowledge of the frequency, cause, prevention and treatment of birth defects through the use of the Register;
- To ensure that the Register data are of the best quality possible. Data quality is dependent on the use of identified personal information in a confidential manner in accordance with these guidelines;
- To ensure that the Register retains the support of notifying health professionals by managing the information they notify in a confidential manner;
- To facilitate the best possible use of Register data for the benefit of the community and promotion of best practice medicine.

Responsibility for Confidentiality

Responsibility for the confidentiality of the Birth Defects Register's data lies with the Head, Public Health Research Unit and ultimately with the Board of Management of the Women's and Children's Hospital through the hospital's line management structure. The SA Birth Defects Advisory Committee advises the Register on the preservation of confidentiality of data collected by the Register. Membership of the Advisory Committee is:

Professor Eric Haan, *Clinical Geneticist*
Associate Professor Annabelle Chan, *Public Health Physician*
Dr Judy Jaensch, *Paediatrician*
Dr Geoff Martin, *General Practitioner*
Dr Karen Shand, *Obstetrician*
Dr Brian Peat, *Obstetrician*

Ethical Principles Governing Research Conducted by the Register

The Register uses the National Health and Medical Research Council's National Statement on Ethical Conduct in Research Involving Humans (1999) when considering research proposals. Section 14, "Epidemiological Research" describes the conditions under which research can be undertaken.

Principles and Procedures for Ensuring Confidentiality While Managing Personal Information

1 Release of Information

1.1 Routine Reports

All routine reports from the Register, such as the Annual Report, are in statistical form without the identification of individual patients, doctors or hospitals. Unnamed statistical information that may be identifiable to particular recipients is not released.

1.2 Non-routine Statistical Reports

Ad hoc requests for grouped statistical information on birth defects will, in general, be provided freely. Information which may be of concern to the public will be released at the discretion of the SA Birth Defects Register Advisory Committee. Unnamed statistical information that may be identifiable to particular recipients is not released to the person or agency making the request.

1.3 Release of Identifying Data

No information about identified individuals is provided to non-Register staff unless that person was the original notifier or that person is assisting the Register in its work.

1.3.1 Release of identifying data for purposes other than research

The Register does not provide personal information for individual patient management, insurance, sick fund, child disability allowance or other administrative purposes. The Health Care Act, 2008, protects staff from any legal obligation to divulge information.

The Register does not provide any information directly to parents or children about notified birth defects. The parent or child is referred to their doctor as information provided by their doctor is more clinically relevant, up to date, clinically accurate and accompanied by appropriate counselling. Because the information collected by the Register was not given by the family in the first instance, the Register would risk harm to the doctor-patient relationship by divulging information gained from medical notes without consultation with that doctor. In some circumstances, notified information may be provided to the doctor for release to parents and children as part of the broader information available to the doctor, and with relevant counselling.

Identifying data will not be released for clinical audit or another clinical purpose unless the clinician or agency requiring the information was the original source of all cases required for that purpose.

1.3.2 Release of identifying information for research purposes

No information about identified individuals is provided to people for research projects unless that person was the original notifier or that person is assisting the Register in its work. The following section provides guidelines for facilitating research with Register data while maintaining the Register's ethical and legal obligations for confidentiality.

2. Research Projects

The Register encourages and facilitates research, using personal information where necessary, and in accordance with these guidelines. In particular, access to personal information is provided for research projects that promote the understanding, prevention or alleviation of health problems associated with pregnancy, delivery, infancy and birth defects and result in no harm to notified individuals in any way.

2.1 Research conducted by Register staff

Research projects performed by Register staff or other people/agencies authorised under The Health Care Act, 2008, are considered internal research projects. The Register defines "research" as a project designed to generate new knowledge, with the aim of publishing the results in a peer reviewed journal. Approval from the Department of Health Research Ethics Committee is required for internal research projects, in compliance with the NHMRC Statement on the Ethical Conduct in Research involving Humans (1999).

The Register conducts internal research projects in accordance with the section 2.4, "Procedures for ensuring confidentiality while conducting research projects".

2.2 Co-opted researchers

From time to time the Register co-opts researchers to perform a research project in collaboration with its staff. The Register retains control over the conduct of the research and the output from the research group.

Access to personal information on the Register is granted to co-opted outside people/agencies for epidemiological or other research purposes only if:

- It is considered that the proposed use of the data would promote the understanding, prevention or alleviation of health problems associated with pregnancy, delivery, infancy and birth defects;
- It is considered unlikely to harm notified individuals in any way;
- Any costs incurred for the research are borne by the relevant body;
- A copy of final reports or papers for publication is provided, prior to publication, to the Register.

The minimum data set needed for the research project is provided to the co-opted researcher. This data set may include identifying information.

The co-opted researcher must undertake to comply with the confidentiality procedures of the Register, in particular section 2.4, "Procedures for ensuring confidentiality while conducting research projects".

Approval from the Department of Health Research Ethics Committee must be sought before identified data can be released.

2.3 Other researchers

Identified information will not be provided to researchers from outside the Register who are not co-opted by the Register. However, unidentified information on individuals may be sufficient to achieve the aims of the research. The Register makes every effort to encourage and facilitate research and will try to provide information for research projects within the constraints of these confidentiality guidelines.

2.4 Procedures for ensuring confidentiality while conducting research projects

The need for confidentiality must be balanced with the benefits of research and the need to facilitate participation of notifiers in research projects. The following procedures are considered within the interpretation of "not divulging confidential information".

2.4.1 When additional clinical information is required for a research project but no contact with patients is needed.

- The Register will review the medical records which it is authorised to access.
- If further information is required, the original notifier will be approached first.
- If the original notifier does not have the required information, permission will be sought from him/her to contact the appropriate health professional. It may also be necessary to identify the patient's most appropriate health professional from the original notifier.
- The appropriate health professional can then be approached for their assistance with the research project.
- If the Pregnancy Outcome Statistics Unit (POSU) of the South Australian Health Commission is the only notifier, it will approach its original notifier to obtain the information.

2.4.2 When contact with patients is required for the research project.

- Permission in writing will be sought from the original notifier to contact a family for the purposes of gathering data for a research study.
- If the original notifier does not consider himself/herself to be the child's managing clinician then permission will be sought from the managing clinician.
- The family will be contacted through the managing clinician.
- Subsequently, the procedures for obtaining consent from families to enter their child into a research study will be followed.

3. Other Specific Aspects of Confidentiality

3.1 Staff aspects

All Register staff are instructed regarding the need for, and maintenance of, confidentiality. On appointment to the Register, staff are required to sign a declaration, as part of their contract of service, that no information on data in the Register will be disclosed, except under the conditions stated in the above section "Release of Information". This also applies to any other information of a confidential nature they might hear or see in respect to subjects notified or their families, and apply even after employment ceases. The terms of employment make it clear that a deliberate breach of confidentiality may lead to severe disciplinary action.

3.2 Storage of Data

Keys giving access to files are held by members of the Register staff only. Files are locked when not in use or when the rooms are unattended. Data are kept on a stand alone computing system within the Register and are not accessible from outside the Register.

Appendix 3

Birth Defect Inclusions and Exclusions

Diagnostic Information

A birth defect is defined by the Register as any abnormality of prenatal origin. Thus, structural (eg. Spina bifida), genetic and chromosomal (eg. Down syndrome) and biochemical (eg. Phenylketonuria) defects are included. Excluded are most minor malformations unless they are disfiguring or require treatment.

THE FOLLOWING LIST OF BIRTH DEFECTS IS NOT COMPLETE, BUT MANY OF THE COMMON DEFECTS INCLUDED IN THE REGISTER ARE MENTIONED. THIS LIST CONTAINS EXAMPLES ONLY. IF A BIRTH DEFECT IS NOT LISTED HERE OR IF IN DOUBT, PLEASE NOTIFY THE DEFECT, UNLESS IT IS ON THE EXCLUSION LIST

INCLUSIONS (examples only)

Nervous System
Anencephaly
Spina bifida
Encephalocele
Congenital hydrocephalus
Microcephaly
Dandy Walker syndrome
Craniosynostosis
Cerebral palsy

Genital System
Undescended testis
(requiring treatment)
Hypospadias
Indeterminate Sex

Urinary System
Cystic kidney
Absent kidney
Ectopic kidney
Double ureter
Ectopic ureter ± ureterocoele
Vesico-ureteric reflux

Cardiovascular System
Congenital heart defects
Coarctation of the aorta
Patent ductus Arteriosus*
Dextrocardia

Blood
Thalassaemia major
Sickle cell anaemia
Haemophilia

Teratogens
Fetal alcohol syndrome
Fetal hydantoin syndrome

Musculo-Skeletal System
Developmental dysplasia of hip
Congenital talipes equinovarus
Polydactyly
Syndactyly
Absence (complete or partial) of limbs
Osteogenesis imperfecta
Congenital spinal anomalies
Congenital torticollis
Congenital scoliosis
Bone dysplasias
Muscular dystrophy

Chromosomal Anomalies
Down syndrome
Trisomy 13
Trisomy 18
Turner syndrome
Chri-du-chat syndrome
Fragile X

Respiratory System
Pulmonary hypoplasia
Diaphragmatic hernia
Choanal atresia
Congenital lung cyst

Congenital Infection
Toxoplasmosis
Rubella
Cytomegalovirus
Herpes simplex
Syphilis

Gastro-Intestinal System
Cleft lip, palate
Tracheo-oesophageal fistula
Pyloric stenosis
Intestinal atresia
Hirschsprung disease
Ectopic anus
Imperforate anus
Exomphalos
Gastroschisis

Metabolic Disorders
Phenylketonuria
Cystic fibrosis
Congenital hypothyroidism
Adreno-genital syndrome
Glycogen storage disorders
Lipid storage disorders
Mucopolysaccharidoses
Albinism

Eye
Microphthalmia/Anophthalmia
Congenital glaucoma
Congenital cataract
Coloboma

Skin
Cystic hygroma
Birthmarks) if >4cm^2
Haemangiomas)multiple or
Naevi)requiring surgery
Ichthyosis congenita
Epidermolysis bullosa

*CRITERIA FOR INCLUSION OF PATENT DUCTUS ARTERIOSUS (PDA)

1. All term babies (37 weeks and beyond) where the duct remains open after 72 hours
2. All preterm babies where the duct remains open past the expected date of delivery

NB If PDA exists in the presence of other congenital heart disease it is always notified

Appendix 3 (continued)

Birth Defect Inclusions and Exclusions

Exclusion List

Excluded from the Register are the following, ***when occurring in isolation:***

THIS IS NOT A COMPLETE LIST OF EXCLUSIONS. IF IN DOUBT, PLEASE NOTIFY

- Balanced translocation in normal individual
- Blocked tear duct
- Broncho-pulmonary dysplasia
- Calcaneovalgus deformity
- Clicky hips
- Congenital pneumonia
- Delayed milestones
- Deviated nasal septum
- Ear anomalies – minor
- Epigastric hernia
- Epilepsy
- Failure to thrive
- Foot deformities – minor positional not requiring treatment
- Gastro-oesophageal reflux
- Hydrocoele testis
- Hydrops – immune. Include non-immune hydrops
- Hypoglycaemia
- Imperforate hymen
- Infection *in utero* if no associated birth defect
- Inguinal hernia
- Intrauterine growth retardation
- Intussusception
- Labial adhesion or fusion
- Large fontanelles
- Laryngeal stridor unless treated
- Laryngomalacia
- Low birth weight
- Lymphangioma, haemangioma, naevus or other birthmark under $4cm^2$
  Include if $>4cm^2$ or multiple
- Meconium ileus (unless the result of cystic fibrosis)
- Mental retardation in isolation
- Metatarsus adductus even if treated
- Mongolian blue spot
- Patent foramen ovale
- Persistent fetal circulation
- Pilonidal sinus
- Sacral dimple
- Sacral sinus unrelated to occult Spinal dysraphism
- Single palmar crease
- Skin tag
- Single umbilical artery
- Strabismus
- Submucous retention cyst
- Supraventricular tachychardia
- Thalassaemia minor
- Toe anomalies – minor
- Tongue tie, even if surgery
- Trigger finger/thumb
- Umbilical hernia
- Undescended testis (unless treated)
- Wide suture lines
- Webbing of 2^{nd} and 3^{rd} toes (minor degrees)

Revised December 1990

Appendix 4

Notification Form

SA Birth Defects Register

NOTIFICATION FORM

(Please return to Women's and Children's Hospital, 72 King William Rd, North Adelaide, S.A. 5006)

CHILD'S SURNAME.....

GIVEN NAMES.....

ADDRESS.....

.....

POSTCODE ☐☐☐☐

MOTHER'S SURNAME.....

GIVEN NAMES.....

PREVIOUS NAME.....

MOTHER'S DATE OF BIRTH ☐☐☐☐☐☐

CHILD'S DATE OF BIRTH ☐☐☐☐☐☐

HOSPITAL OF BIRTH.....

CASE RECORD No. ☐☐☐☐☐☐☐

STATE OF BIRTH (if not SA).....

SEX: M ☐ F ☐ Indeterminate ☐ Unk ☐

PLURALITY: Single ☐ Twin ☐ Other.....

RACE OF MOTHER: Caucasian ☐ Asian ☐ Aboriginal ☐ Other ☐

FAMILY HISTORY OF BIRTH DEFECTS IN:

PARENTS: Yes ☐ No ☐ Unk ☐

SIBLINGS: (inc. stillbirths, and 2nd trimester TOP)

Yes ☐ No ☐ Unk ☐

RELATIVES: Yes ☐ No ☐ Unk ☐

DETAILS.....

.....

GESTATION: ☐☐ weeks

IF DECEASED: DATE OF DEATH ☐☐☐☐☐☐

AUTOPSY DONE: Yes ☐ No ☐ Unk ☐ If Yes, where.....

BIRTH DEFECTS PRESENT: (please list all defects)	Code	Date of Diagnosis
1.	☐☐☐☐☐	___/___/___
2.	☐☐☐☐☐	___/___/___
3.	☐☐☐☐☐	___/___/___
4.	☐☐☐☐☐	___/___/___
5.	☐☐☐☐☐	___/___/___
6.	☐☐☐☐☐	___/___/___
7.	☐☐☐☐☐	___/___/___
8.	☐☐☐☐☐	___/___/___
9.	☐☐☐☐☐	___/___/___
10.	☐☐☐☐☐	___/___/___
.....	☐☐☐☐☐	___/___/___
.....	☐☐☐☐☐	___/___/___
SYNDROME: (if known).....	☐☐☐☐☐	___/___/___
.....	☐☐☐☐☐	___/___/___

COMMENTS: (eg. possible aetiology of defects, such as parental exposure to toxic chemicals, medications, drugs, maternal infections, etc)

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DOCTOR(S) CARING FOR CHILD: (if other than notifier).....

NOTIFIER:..... SOURCE:.....

..... DATE ___/___/___