Congenital Anomaly Register for
Oxfordshire, Berkshire & Buckinghamshire

First report of the Congenital Anomaly Register for Oxfordshire, Berkshire and Buckinghamshire (CAROBB)

CAROBB births 2005-2006

and

Oxford births 1991-2006

April 2008

National Perinatal Epidemiology Unit

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Congenital Anomaly Register for Oxfordshire, Berkshire and Buckinghamshire
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Births in 2005-2006
with Oxford births 1991-2006

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The report can be accessed at website: www.npeu.ox.ac.uk/carobb/

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Confidentiality and policy on non-disclosure of small numbers

As a member of BINOCAR (British Isles Network of Congenital Anomaly Registers), CAROBB has the approval of PIAG (Patient Information Advisory Group) and the Trent MREC to collect identifiable information without explicit consent from individuals registered. See documentation in Appendix 5.

We have followed the advice of the Office for National Statistics concerning the disclosure of small numbers (www.statistics.gov.uk/about/Consultations/disclosure.asp).

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Part 1 - Introduction and Summary

Introduction

In April 2003 the Department of Health awarded funding for the expansion and development of the Oxford Congenital Anomaly Register (OXCAR), for research purposes. A new population-based register, covering the three counties which make up the former Thames Valley Strategic Health Authority and now are the northern half of the South Central Strategic Health Authority was formed, called the Congenital Anomaly Register for Oxfordshire, Berkshire and Buckinghamshire (CAROBB). CAROBB is based at the National Perinatal Epidemiology Unit, University of Oxford. This is the first full report from CAROBB and provides population based information on congenital anomalies affecting births in 2005 and 2006 to mothers resident in the three counties.

The principal objectives of CAROBB are to

- Provide data for research on the aetiology and natural history of congenital anomalies to enable better advice based on accurate information to be given to parents.
- Enable the evaluation and monitoring of new invasive and non invasive prenatal diagnostic tests and screening programmes.
- Provide data for health care policies and planning.
- Provide data to investigate clusters of abnormalities and putative teratogens by the monitoring of rates over time and of population trends such as maternal age, ethnicity, and health inequalities.
- Improve ascertainment to the National Congenital Anomaly System (NCAS) and to European Congenital Anomaly Surveillance (EUROCAT, www.eurocat.ulster.ac.uk).

The population studied for this report

- This report has information on congenital anomalies suspected and/or confirmed in fetuses / babies born to mothers resident in the three counties of Thames Valley (Oxfordshire, Berkshire and Buckinghamshire), the geographical area of CAROBB.
- Data are provided on cases notified to CAROBB by November 2007 and with a date of birth 2005-2006 inclusive. For this report a “case” is a birth with a suspected and / or confirmed congenital anomaly notified to CAROBB. The term “birth” (unless otherwise stated) is used to cover all pregnancies (from 10 weeks gestation) ending in live birth, stillbirth, miscarriage/intrauterine death and termination of pregnancy for fetal anomaly (TOPFA).
- Denominator data are provided by the Office for National Statistics and include only live births and stillbirths of 24 weeks gestation or more. There were 55,993 births in Thames Valley in 2005 and 2006.
- The proportion of births with congenital anomalies are given as a percentage of total births or as a rate per 1,000 total births.

The report gives data on anomalies, their rate and, where appropriate their prenatal detection, in Thames Valley. Information on cases by hospital at which the mother booked for delivery can be provided and will be presented at the individual hospitals.

Information on cases with an OX postcode and booked for delivery at the John Radcliffe Hospital is available from 1991 and is provided in Appendix 1.

Definition and coding of congenital anomalies

The definition of congenital anomaly, used by CAROBB is “a structural or functional anomaly, presumed to be of prenatal origin”. All anomalies present at birth or diagnosed after birth are recorded. Prenatally suspected anomalies including ultrasound “soft markers” are also recorded including those occurring in cases subsequently confirmed to be structurally normal babies. In line with other British and European registries each anomaly is coded using the ICD10 classification with the BPA extensions where appropriate.

Summary

- In 2005 and 2006 there were 1,027 births with a confirmed congenital anomaly, that is 1.8% of all births, to mothers resident in Thames Valley, notified to CAROBB.
- In 53% of these births there was prenatal suspicion of congenital anomaly.
- Three hundred and thirty-three births (32% of all births with a congenital anomaly) were terminations of pregnancy for fetal anomaly.
- More male than female births were affected by a congenital anomaly, M:F = 1.4:1
- We recognise that there is underascertainment of postnatally diagnosed anomalies to CAROBB, particularly cardiac anomalies diagnosed after the mother has been discharged from the maternity hospital and also some other specific groups of anomalies (e.g. eye and musculo-skeletal anomalies). Births to mothers resident in Thames Valley but delivering outside the CAROBB area (e.g. in London) may not at present be notified.
- There were 155 births with Down's syndrome of which 84 (54%) were prenatally diagnosed. Screen positive first trimester nuchal scanning (with or without biochemical screening) was the most common reason for prenatal diagnosis. Taking into account those cases with a positive Down's syndrome screening test where karyotyping was declined, the potential prenatal detection rate was 69%.
- Research using CAROBB (and previously OXCAR) data is reported in Appendices 3 and 4.

Main Aim for 2008/9

- To improve ascertainment of specific congenital anomalies, particularly cardiac anomalies, orthopaedic anomalies and eye anomalies.

Table 1 Prenatal detection of specific congenital anomalies in Thames Valley, 2005 - 2006

Anomaly	Test performed	Number of pregnancies notified with prenatal suspicion of anomaly (not incl. false positive diagnoses)	Number of cases notified with anomaly confirmed at birth	Rate at birth / 1,000 total births	Prenatal detection rate
Isolated neural tube defects	Ultrasound Scanning +/- MS AFP[1]	52	53	0.9	98%
Isolated cardiac anomaly	Ultrasound scanning	46	104	1.9[2]	44%
Isolated cleft lip +/- palate	Ultrasound scanning	25	34	0.6	74%
Down's Syndrome	Karyotyping[3]	84	155	2.8	54%
Isolated diaphragmatic hernia	Ultrasound scanning	8	11	0.2	73%
Isolated exomphalos	Ultrasound scanning +/- MS AFP	8	8	0.1	100%
Isolated gastroschisis	Ultrasound scanning +/- MS AFP	15	15	0.3	100%

1 MS AFP Maternal Serum Alpha Feto Protein screening.
2 Low prevalence because of low ascertainment of cases diagnosed after birth.
3 For details of reasons for karyotyping and prenatal screening tests for Down's syndrome see page 18.

Part 2 - Routine statistics, area covered by CAROBB and outcome of pregnancies

Population and area covered

There were over two million people resident in Thames Valley in 2005 and 2006, with Berkshire having the highest and Oxfordshire the lowest population. The numbers in Table 2 are supplied by the Office for National Statistics and are mid 2005 and mid 2006 population estimates.

Table 2 Total population covered

	Oxfordshire	Berkshire	Buckinghamshire	Thames Valley
2005	629,100	808,300	706,200	**2,143,600**
2006	632,000	815,900	712,200	**2,160,100**

Table 3 Total births (live and stillbirths), by county and year

	Oxfordshire	Berkshire	Buckinghamshire	Thames Valley
2005	7616	10920	8762	**27,298**
2006	8028	11391	9276	**28,695**
Total	**15,644**	**22,311**	**18,038**	**55,993**

Figure 1 Map of the CAROBB area, Oxfordshire, Berkshire and Buckinghamshire, forming Thames Valley and the northern half of South Central Strategic Health Authority

Total births with congenital anomalies, pre and postnatal diagnosis

Table 4 Number (% of all births) of cases (all births including termination of pregnancy for fetal anomaly) with congenital anomaly, by year

	Oxfordshire n (%)	Berkshire n (%)	Buckinghamshire n (%)	Thames Valley n (%)
2005	172 (2.3)	150 (1.4)	166 (1.9)	**488 (1.8)**
2006	205 (2.6)	167 (1.5)	167 (1.8)	**539 (1.9)**
Total	**377 (2.4%)**	**317 (1.4%)**	**333 (1.9%)**	**1,027 (1.8%)**

There appears to be a lower rate of congenital anomalies in Berkshire. This almost certainly does not reflect a true reduction in incidence but is due to lower ascertainment, partly because more babies with congenital anomalies born to mothers resident in Berkshire are delivered in London (i.e. outside the Thames Valley area). We plan, during the next year, to establish mechanisms to ascertain these cases. The rate in Oxfordshire appears higher and this is due to the fact that there are well established mechanisms in place for ascertaining cases because a congenital anomaly register (OXCAR) was established in 1991, whereas in Berkshire and Buckinghamshire mechanisms are still being set up.

Table 5 illustrates the number and percentage of cases prenatally and postnatally diagnosed. Twenty nine percent of cases with a prenatal suspicion of anomaly were apparently normal at birth. Most of these cases were associated with ultrasound "soft markers" such as echogenic bowel and nuchal thickening.

The percentage of births with a congenital anomaly (1.8%) in Table 5 differs from that using the data transferred to EUROCAT (1.7%, see Table 7) because some anomalies are excluded from analysis by EUROCAT (e.g. those cases resulting in miscarriages before 20 weeks gestation).

Table 5 Total births and notifications; number prenatally suspected with and without congenital anomaly at birth and total births with anomalies, by year

Year	2005	2006	Total
Total births	27,298	28,695	55,993
Total cases notified to CAROBB	616	704	1320
Number of cases notified but with incomplete data			73
Number of cases notified prenatally (including "soft markers")	452	540	992
(% of total notified)	(73%)	(77%)	(75%)
Number of cases notified prenatally with anomaly confirmed at birth	324	375	699
(% of total notified)	(53%)	(53%)	(53%)
Number of cases notified prenatally & considered normal at birth	128	165	293
(% of total notified prenatally)	(28%)	(31%)	(29%)
Total cases with anomaly at birth, miscarriage or TOPFA (excludes those notified prenatally and lost to follow up)	**486**	**536**	**1027**
(% of total births)	**(1.8%)**	**(1.9%)**	**(1.8%)**

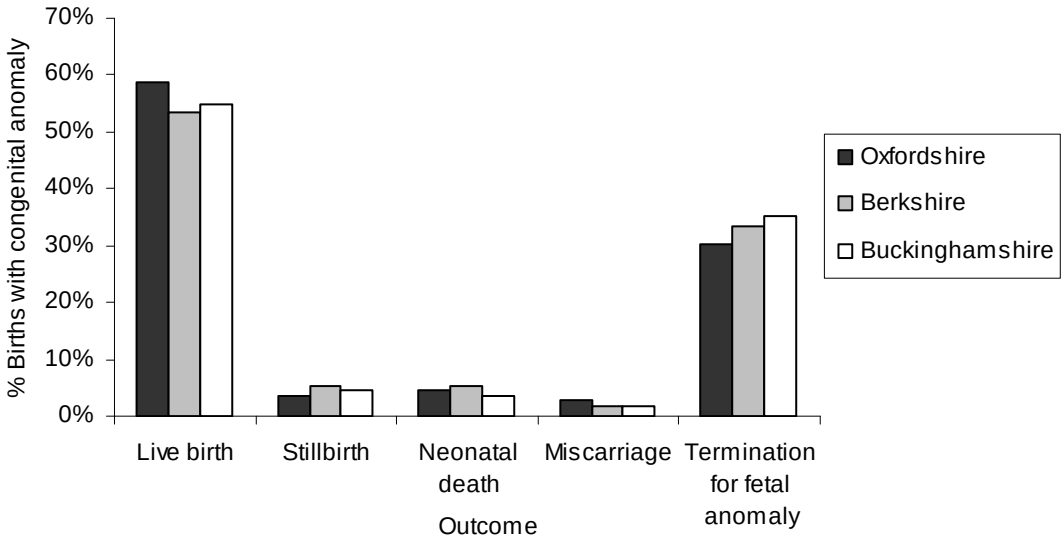
Outcome of pregnancy

Table 6 Outcome of pregnancy of cases notified with congenital anomaly confirmed at birth in 2005 and 2006, by county (n = 1,027)

	Oxfordshire n (%)	Berkshire n (%)	Buckinghamshire n (%)	Thames Valley n (%)
Live birth	222 (59%)	169 (53%)	183 (55%)	**574 (56%)**
Neonatal death	17 (5%)	17 (5%)	12 (4%)	**46 (4%)**
Stillbirth	13 (3%)	17 (5%)	15 (5%)	**45 (4%)**
Miscarriage	11 (3%)	6 (2%)	6 (2%)	**23 (2%)**
Termination for fetal anomaly	114 (30%)	106 (33%)	117 (35%)	**337 (33%)**
Total	**377**	**317***	**333**	**1,027***

***includes two where the diagnosis was known but the outcome was not known**

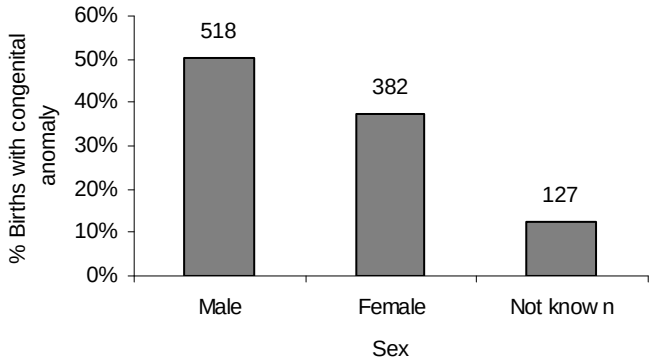
Figure 2 Outcome of pregnancy (percentage of live births, stillbirths, neonatal deaths, miscarriages or terminations of pregnancy) of births with congenital anomaly, by county, n = 1,025



Sex ratio of births with congenital anomalies

Figure 3 Percentage and number of male and female births with congenital anomaly

Sex ratio of cases with anomaly at birth M:F 1.4:1
(Background rate for all births in England & Wales: M:F 1.05:1.0)



Termination of pregnancy for fetal anomaly (TOPFA)

Figure 4a Percentage and number of cases resulting in TOPFA by type of anomaly, n = 337

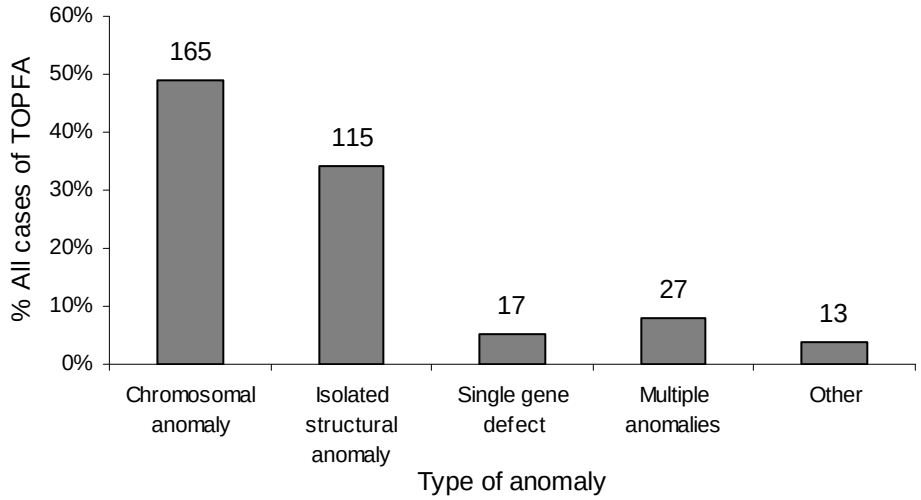


Figure 4b:
TOPFA, chromosome anomalies by type, n = 165

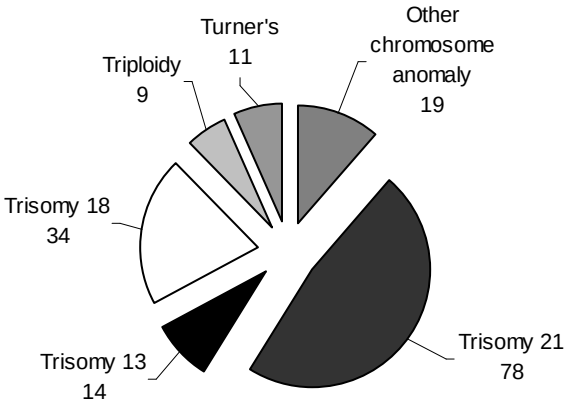


Figure 4c:
TOPFA, isolated anomalies by type, n = 115

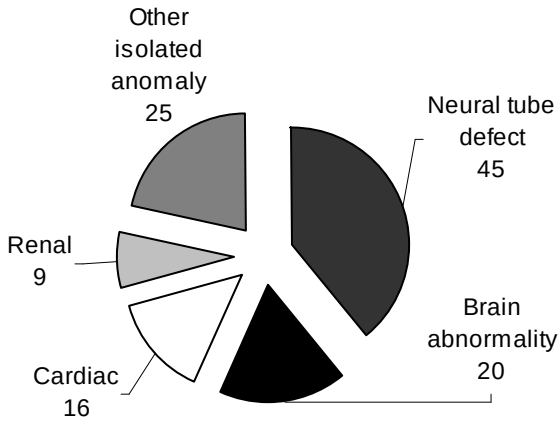
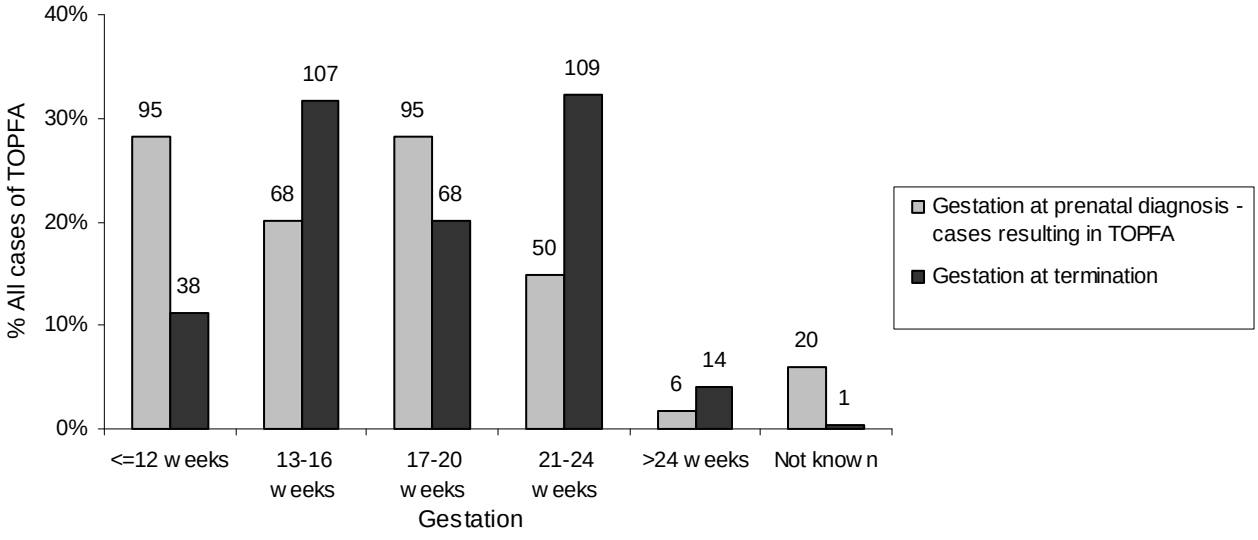


Figure 5 Percentage and number of cases resulting in termination of pregnancy for fetal anomaly (TOPFA), by gestation period at prenatal diagnosis and at termination, n = 337



NB 14 pregnancies terminated at >24 weeks gestation (brain, cardiac, fetal hydrops and chromosome anomalies). These included some selective reduction of twin pregnancies.

Part 3 - Rates of congenital anomalies

Table 7 Table of cases and anomalies and rate per 1,000 births using data from CAROBB held by EUROCAT 2005 and 2006 (Total births: 55,993)

Please note: *The reason for the lower the rate of births with congenital anomalies than that shown in Table 5 is that not all births notified to CAROBB are transmitted to EUROCAT e.g. miscarriages of less than 20 weeks of gestation.

Diagnostic Category	ICD 10 code	Live births, stillbirths and fetal deaths >=20weeks (n)	Termination of pregnancy (n)	Including chromosomal anomalies Rate per 1,000 births		Excluding chromosomal anomalies Rate per 1,000 births	
				Live births, stillbirths, fetal deaths and termination of pregnancy (n)	Live births, stillbirths, fetal deaths and termination of pregnancy (rate)	Live births, stillbirths, fetal deaths and termination of pregnancy (n)	Live births, stillbirths, fetal deaths and termination of pregnancy (rate)
All births with congenital anomalies		**627**	**321**	**948**	**16.9***	**664**	**11.9**
The list below is a list of all anomalies, not individual births. Some births will have more than one anomaly present. An anomaly listed as resulting in termination of pregnancy may be part of a multiple anomaly case.							
Nervous system anomalies	Q00 – Q07	**44**	**83**	**127**	**2.3**	**120**	**2.1**
Neural Tube Defects		10	51	61	1.1	57	1.1
Anencephalus, encephalocele and similar	Q00 – Q01	5	27	32	0.6	32	5.9
Spina Bifida	Q05	5	24	29	0.6	25	0.4
Hydrocephaly	Q03	23	12	35	0.6	34	0.6
Other		11	20	31	0.6	29	0.6
Congenital heart anomalies	Q20 - Q26	**139**	**38**	**177**	**3.2**	**136**	**2.4**
Ventricular septal defect	Q210	53	0	53	0.9	42	0.8
Atrioventricular septal defect	Q212	16	5	21	0.4	8	0.1
Hypoplastic left heart	Q234	6	9	15	0.3	13	0.3
Coarctation of aorta	Q251	15	0	15	0.3	14	0.3
Other		49	24	73	1.3	59	1.1
Respiratory anomalies	Q30 – Q34	**20**	**5**	**25**	**0.4**	**23**	**0.4**
Oro-facial clefts	Q35 - Q37	**67**	**7**	**74**	**1.3**	**69**	**1.2**

Digestive system anomalies	Q38 – Q39, Q402, Q408, Q409, Q41 – Q45	**50**	**4**	**54**	**1.0**	**49**	**0.9**
Oesophageal atresia with or without tracheo-oesophagal fistula	Q390 - Q3914	9	0	9	0.2	9	0.2
Duodenal atresia or stenosis	Q410	9	0	9	0.2	5	0.09
Hirchspung's disease	Q431	6	0	6	0.1	6	0.1
Other		26	4	30	0.5	29	0.5
Genital anomalies	Q50 – Q52, Q54 – Q56	**50**	**4**	**54**	**1.0**	**52**	**0.9**
Urinary anomalies	Q60 - Q64, Q794	**86**	**19**	**105**	**1.9**	**100**	**1.8**
Cystic kidney disease	Q61	23	5	28	0.5	28	0.5
Other		63	14	77	1.4	72	1.3
Limb anomalies		**74**	**29**	**87**	**1.6**	**78**	**1.4**
Reduction defects	Q71 – Q73	24	15	39	0.7	35	0.6
Club foot – talipes equinovarus	Q660	34	14	48	0.9	43	0.8
Musculo-skeletal, skeletal dysplasias	Q750 – Q751, Q754 – Q759, Q761 – Q764, Q766 – Q769, Q77 – Q78, Q796 –Q799	**19**	**23**	**42**	**0.8**	**40**	**0.7**
Abdominal wall defects Gastroschisis and Omphalocele	Q792, Q793	**24**	**11**	**35**	**0.6**	**31**	**0.6**
Other anomalies	Q27 – Q28, Q80 – Q85, Q89	**29**	**7**	**36**	**0.6**	**33**	**0.6**
Genetic syndromes & microdeletions	Q87, Q936, D821	**25**	**14**	**39**	**0.7**	**39**	**0.7**
Chromosomal anomalies	Q90 – Q93, Q96 – Q99	**122**	**162**	**284**	**5.1**	**0**	**0**
Down's Syndrome (Trisomy 21)	Q90	77	77	154	2.8	0	0
Patau syndrome (Trisomy 13)	Q914 – Q917	5	14	19	0.3	0	0
Edward syndrome (Trisomy 18)	Q910 – Q913	8	35	43	0.8	0	0
Turner's syndrome	Q96	10	11	21	0.4	0	0
Other chromosomal		22	25	47	0.8	0	0

Part 4 - Information about specific anomalies

1. Open Neural Tube Defects (NTD)

Anencephaly: **Definition:** Total or partial absence of the cranial vault, covering skin and brain tissue.

Encephalocoele: **Definition:** Herniation of the brain and/or meninges through a defect in the skull.

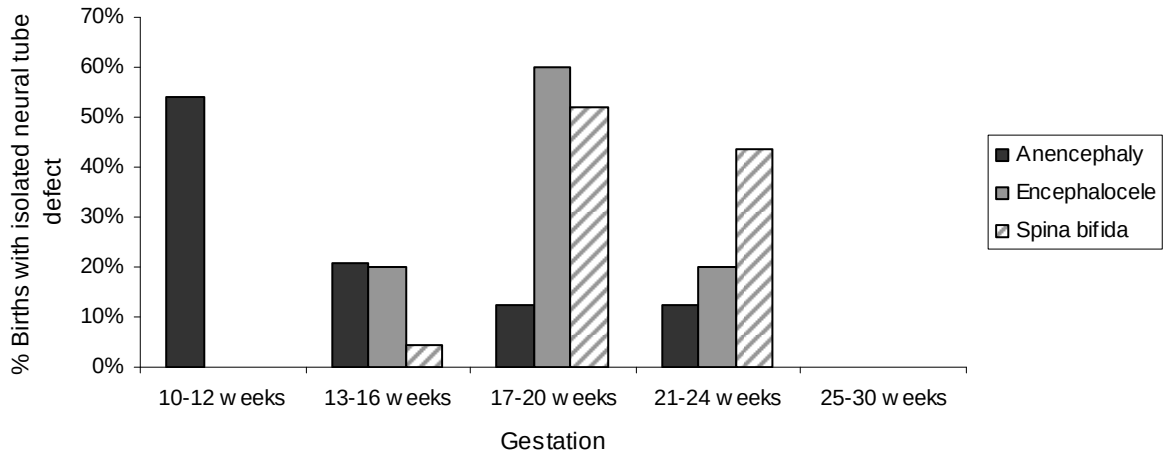
Spina bifida: **Definition:** Non-closure of the spine resulting in herniation or exposure of the spinal cord and /or meninges. Hydrocephaly may or may not be present.

Summary Information

Prenatal Investigation:	Ultrasound scan +/- maternal serum alpha feto protein screening
Rate:	n = 53
Isolated neural tube defects	0.9 per 1000 births
Isolated and non-isolated neural tube defects n=60	1.1 per 1000 births
Prenatal detection rate for isolated cases:	52/53 (98%)
ICD 10 codes:	Q00.0 (anencephaly); Q01.2 (encephalocele) Q05 – Q05.9 (spina bifida)

Of the 53 isolated cases (24 anencephaly, 5 encephalocele, 24 spina bifida), 52 were prenatally suspected.

Figure 7 Percentage of isolated Neural Tube Defects diagnosed at different gestational periods



2. Cardiac Anomalies

Definition: Group of anomalies with abnormal structure of the heart.*

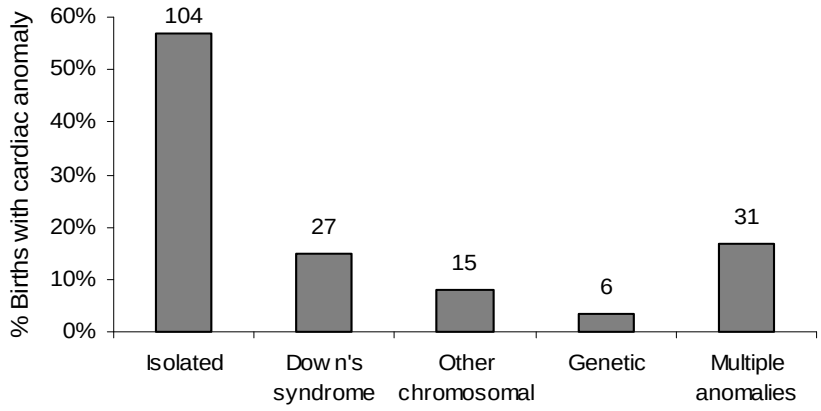
Summary information

Prenatal Investigation:	Ultrasound scan
Rate: all notified structural cardiac anomalies isolated and non-isolated cases	n = 183 3.3[#] per 1000
Prenatal detection rate of isolated cardiac cases <30 weeks	44/104 (42%)
ICD 10 Codes	Q20 – Q26.9

*For a description of individual anomalies see Knowles R, Griebsch I, Dezateux C, Brown J, Bull C, Wren C. Newborn screening for congenital heart defects: a systematic review and cost-effectiveness analysis. *Health Technol Assess* 2005;9(44). www.ncchta.org/fullmono/mon944.pdf

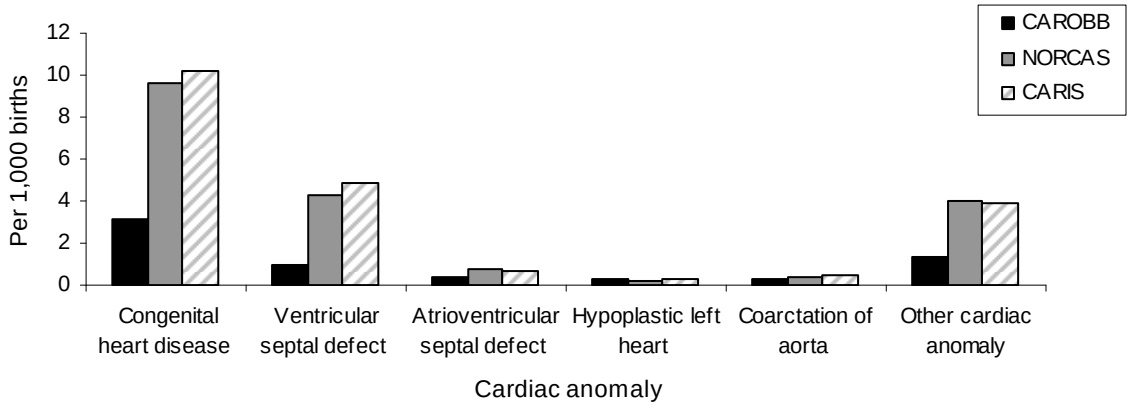
[#]Expected rate 8 per 1,000, also described by Knowles et al.

Figure 8 Percentage and number of births with a cardiac anomaly categorised by type, n=183



The low rate of cardiac anomalies is clearly due to under-ascertainment. Figure 9 illustrates the rate of cardiac anomalies notified to CAROBB compared to rates in Wales (CARIS, Congenital Anomaly Register and Information Service), and the Northern Region (NorCAS, Northern Congenital Anomaly Survey). Very few cases with cardiac anomalies diagnosed after the neonatal period are notified to CAROBB. We now have access to an additional in-patient information source at the John Radcliffe Hospital. During the next year we hope to work with the paediatricians and paediatric cardiologists covering all hospitals to improve ascertainment. Please contact us on carobb@npeu.ox.ac.uk if you have any ideas.

Figure 9 Comparison of rates of cardiac anomalies ascertained to three different UK Congenital Anomaly Registers using EUROCAT data



3. Cleft Lip with or without Cleft Palate (Cleft lip +/- Palate)

Cleft lip: **Definition** - Clefting of the upper lip without clefting of the alveolar ridge and palate.

Cleft lip and palate: **Definition** - Clefting of the upper lip with clefting of the alveolar ridge and palate.

Summary Information

Prenatal Investigation:	Ultrasound scan
Rate: **Isolated cleft lip +/- palate**	n = 34 0.6 / 1,000
Prenatal detection rate:	25 / 34 (74%)
ICD 10 Codes	Q36 – 37.9

We report the prenatal detection of cleft lip with or without cleft palate. It is not possible to visualise isolated cleft palate by ultrasound prenatally. Very minor clefts (forme fruste) have been excluded from this analysis.
There were 34 cases of isolated cleft lip +/- palate of which 25 (74%) were prenatally diagnosed. In addition there were 14 cases of non-isolated cleft lip +/- palate. The associated anomalies are shown in Table 8.

Figure 10 Percentage and number of births with isolated Cleft lip +/- palate diagnosed at different gestational periods, n = 25

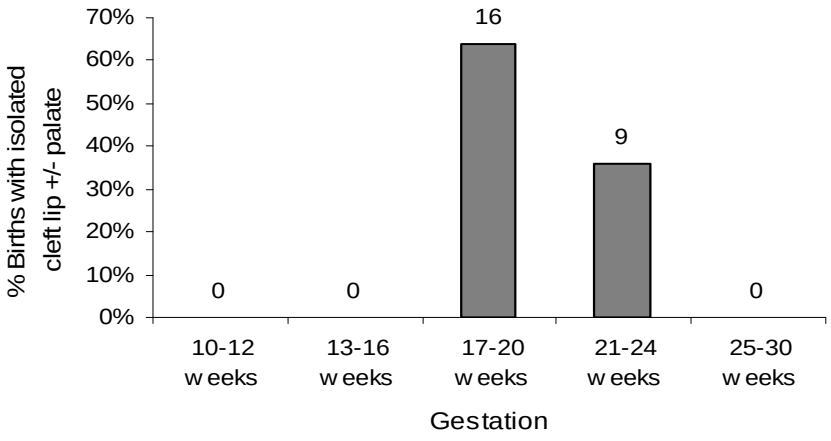


Table 8 Anomalies associated with non-isolated cleft lip +/- palate (30% of cases)

Non Chromosomal	Chromosomal
Limb body wall complex	Trisomy 21
TRAP sequence	Trisomy 13
Lissencephaly Type 2	Turner's syndrome mosaic
Conjoined twins	Structural chromosome anomalies
Multiple congenital anomalies	

4. Diaphragmatic Hernia, Exomphalos and Gastroschisis

a. Diaphragmatic hernia: **Definition -** Herniation of the abdominal organs into the thorax through a defect in the diaphragm.

b. Exomphalos: **Definition -** Herniation of abdominal contents through umbilical insertion and covered by membrane which may or may not remain intact.
Excluded exomphalos minor / cord root exomphalos

c. Gastroschisis: **Definition -** Visceral herniation through an abdominal wall defect lateral to an intact umbilical cord.

Summary information

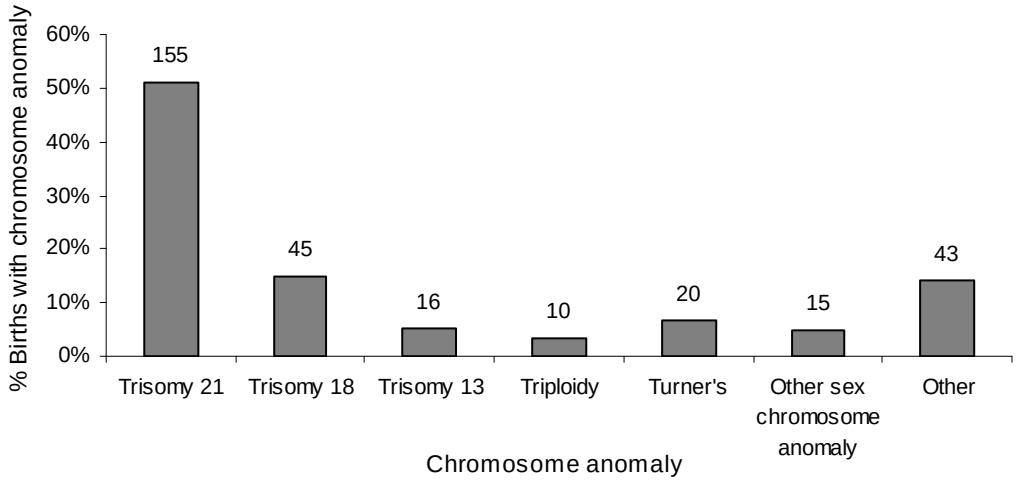
	Diaphragmatic Hernia	Exomphalos	Gastroschisis
Prenatal Investigation	Ultrasound scan	Ultrasound scan +/- maternal serum AFP screening	Ultrasound scan +/- maternal serum AFP screening
Number of isolated cases	11	8	15
Non isolated cases	6 non isolated cases: (chromosomal, cardiac and renal anomalies)	11 non isolated cases: (Trisomy 18, Beckwith-Wiedemann syndrome)	All cases of gastroschisis notified were isolated
Rate:			
Isolated cases	0.2 / 1,000	0.1 / 1,000	0.3 / 1,000
Isolated and non-isolated cases	0.3 /1,000	0.4 / 1,000	0.3 / 1,000
Prenatal detection rate for isolated cases	8/11 (73%)	8/8 (100%)	15/15 (100%)
ICD 10 Codes	Q79.0	Q79.2	Q79.3

There was a high prenatal diagnosis rate for these three anomalies (100% for exomphalos and gastroschisis and 73% for diaphragmatic hernia). Because of the small numbers of cases we cannot disclose gestation at diagnosis for the individual anomalies but overall 35% were suspected before 16 weeks of gestation, 42% between 17 and 20 weeks and 23% after 20 weeks gestation.

It is well recognised that gastroschisis is more common in babies born to younger mothers and that it is more likely to be an isolated lesion compared to both diaphragmatic hernia and exomphalos. All the gastroschisis cases, 65% of diaphragmatic herniae and 42% of exomphalos had isolated lesions in the cases reported to CAROBB and born in 2005 and 2006. The mean age (range) of mothers of babies with gastroschisis was 23 years (18-36 years) compared to 32 years (19-43 years) for isolated exomphalos and 31 years (24-37 years) for isolated diaphragmatic hernia.

5. Chromosome Anomalies

Figure 11 All Chromosome anomalies, percentage of cases by chromosome type, n = 304



6. Down's Syndrome (Trisomy 21)

Definition: Additional chromosome 21.

Summary information

Prenatal Investigation:	First and second trimester screening tests. Karyotyping performed because higher risk for Down's syndrome for one of the following reasons; older mother, positive family history, translocation carrier, higher risk screening test or suspicion on ultrasound scan.
Rate:	n = 155
From 12 weeks gestation	2.8 / 1,000
Prenatal detection rate:	84 / 155 (54%)
ICD 10 Codes	Q90 – Q90.9

Over the last few years there has been a move from offering pregnant women at higher risk for having a baby with Down's syndrome a prenatal diagnostic test, to a national programme for prenatal screening tests to be offered to all pregnant women. The National Screening Committee set performance standards for the screening programme so that that by 2004/05 a detection rate of at least 60% with a false positive rate of 5% or less should have been achieved, and by April 2007 a detection rate of at least 75% with a false positive rate of 3% or less. There are a range of different screening tests offered at different gestation periods (see http://nscfa.web.its.manchester.ac.uk/ for details of the NHS Fetal Anomaly Screening Programme).

In the CAROBB area there were a variety of screening tests for Down's syndrome in place in 2005 and 2006. In Oxfordshire the second trimester serum screening Triple test was introduced in March 2005. In Buckinghamshire there has been a move from offering the Double to the Triple test and in Berkshire the first trimester nuchal scan has been offered in some areas and the Triple test in others. In all areas there are private clinics offering first trimester nuchal combined screening.

There were 155 births with Down's syndrome in 2005 / 2006. Eighty four (54%) of the 155 cases were prenatally diagnosed before 24 weeks gestation. The majority (75%) of the prenatal diagnoses were due to a positive first or second trimester screening test (Figure 12 and Table 9).

Twenty three of the 71 cases diagnosed postnatally or after 24 weeks gestation could potentially have been prenatally diagnosed but either screening was declined (12 cases) or karyotyping was declined after a screen positive test (9 cases) or suspicious scan (2 cases). If all high risk cases had accepted karyotyping the prenatal detection rate would have been 69%. This figure may be an under-estimate because in 36 postnatally diagnosed cases no information was given about prenatal screening. We are hoping to improve collection of data on Down's syndrome screening and will be working with the team from the National Screening Committee as well as with local screening co-ordinators.

Figure 12 Prenatal detection of Down's Syndrome – percentage and number of cases grouped by reason for karyotyping, n = 84

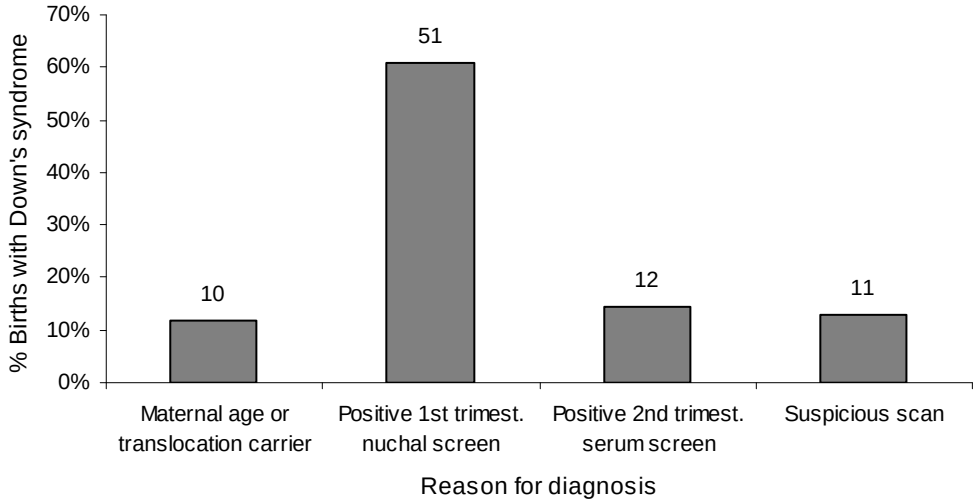


Figure 13 Percentage of Down's syndrome cases prenatally diagnosed at <24 weeks gestation / not prenatally diagnosed, by maternal age groups
(4 age not known, excluded)

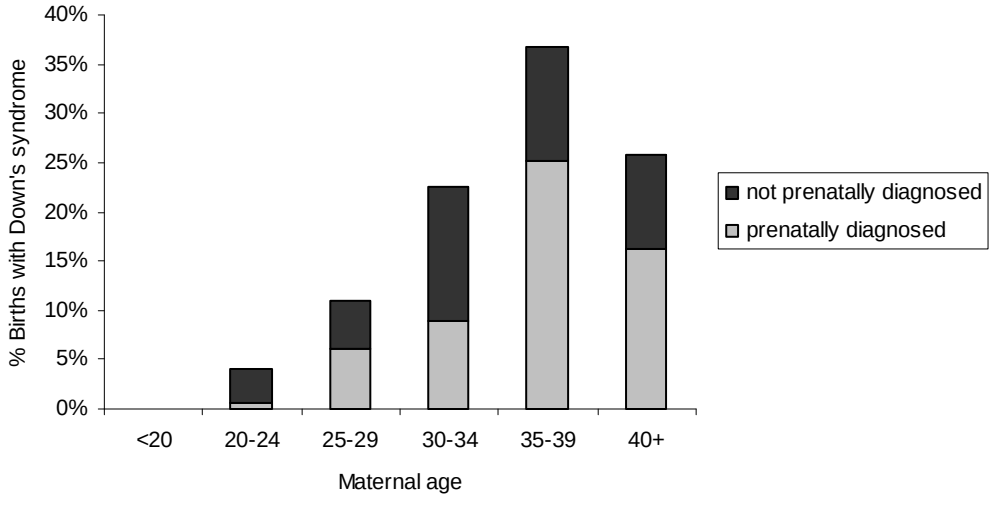


Table 9 **Number of cases of Down's syndrome (n = 155) diagnosed prenatally with reason for prenatal detection, (n = 84), postnatally diagnosed cases (n = 71), with number of potentially detectable cases**

	Prenatal Diagnosis Primary reason for karyotyping in cases prenatally diagnosed before 24 weeks of gestation n = 84					Postnatal Diagnosis or after 24 weeks gestation n = 71						Total with Down's syndrome
						Potentially detectable prenatally n = 23						
Year	**Maternal age or translocation carrier**	**+ve1st trimester nuchal screen**	**+ve2nd trimester serum screen**	**Suspicion on scan**		**+ve 1st trimester screen karyotyping declined**	**+ve 2st trimester screen karyotyping declined**	**Suspicious scan <24 weeks karyotyping declined**	**Screening or karyotyping declined**	**Screen negative 1st / 2nd trimester tests.**	**No prenatal suspicion or no information provided**	
2005, 2006	10	51	12	11		4	5	2	12	12	36	155

Appendices

Congenital Anomalies in Oxford from 1991-2006 using data from OXCAR and CAROBB

Summary table

Table 1A: Prenatal detection of selected congenital anomalies in the local Oxford population, 1991 – 2006

Defect	Prenatal investigation	Number of pregnancies notified with prenatal suspicion of anomaly (not including false positive diagnoses)	Number of cases notified with anomaly confirmed at birth	Rate / 1,000 births	Prenatal detection rate
Isolated Neural Tube Defects (anencephaly & spina bifida)	Ultrasound Scanning +/- MS AFP[1]	102	105[3]	1.2	97%
Isolated Cardiac anomaly	Ultrasound scanning	60	190	2.1[4]	32%
Isolated Cleft lip +/- palate	Ultrasound scanning	35	61	0.7	57%
Down's Syndrome	Karyotyping Prenatal detection because MA[2]>35 (n=32) or 1st (n=33) or 2nd (30) trimester or Ultrasound scanning (n=49)	144	232	2.5	62%
Isolated Diaphragmatic hernia	Ultrasound scanning	16	26	0.3	62%
Isolated Exomphalos (excludes exomphalos minor)	Ultrasound scanning +/- MS AFP	12	17	0.2	71%
Isolated Gastroschisis	Ultrasound scanning +/- MS AFP	25	25	0.3	100%

1 MS AFP Maternal Serum Alpha feto protein screening
2 MA Maternal age > 35 years at expected date of delivery (EDD)
3 One woman declined screening
4 There is under reporting of cardiac anomalies diagnosed after discharge from the maternity unit

Background

The Oxford Congenital Anomaly Register (OXCAR) was established in 1991 after consultation with local experts (obstetricians, midwives, paediatricians, neonatologists, paediatric cardiologists, paediatric pathologists, geneticists, biochemists and public health physicians) who gave full support to the register. One of the main aims of the register at that time was to monitor the newly developing techniques used in prenatal diagnosis and particularly the accuracy of antenatal ultrasound scanning. The first six years of data are summarised in a paper in the Lancet (see Appendix 4 reference 34).

Appendix 1

Other aims were to improve ascertainment to the National Congenital Anomaly System, to provide data for health care policies and planning and for research on aetiology and natural history of congenital anomalies to enable better advice to be given to parents. In 2003 funding from the Department of Health enabled the expansion of OXCAR to Berkshire and Buckinghamshire (i.e. to cover Thames Valley) and the name was changed to CAROBB. Because there is now 16 years of data for the Oxford area, we are, in this Appendix to the main CAROBB report, summarising these data. More detailed information is available on individual anomalies, prenatal detection rates and outcome of pregnancy. Please contact us by email at carobb@npeu.ox.ac.uk if you would like further information.

The population studied

Anomalies suspected and or confirmed in fetuses / babies booked for delivery at the Oxford Women's Centre, community hospital or home delivery within the catchment area of the Women's Centre and with an OX postcode during 1991 - 2006 inclusive. Denominator data for this population was provided by the Oxford Radcliffe Hospitals NHS Trust Performance & Information Department. There were 90,992 births in this category in the 16 year study period. Please note this population does not equate with the data from the whole of Oxfordshire used in the CAROBB report. The population used here gives the best approximation available to the unselected local Oxford population.

Table 2A: Total births and notifications in the local Oxford population, (John Radcliffe Women's Centre booking, with OX postcodes), 1991-2006 inclusive; number prenatally suspected with and without congenital anomaly at birth, number resulting in termination of pregnancy for fetal anomaly (TOPFA), in four four-year periods

Year	1991-1994	1995-1998	1999-2002	2003-2006	1991-2006
Total births	23,438	22,703	21,765	23,086	90,992
Total notifications	566	752	875	687	2,880
Total notifications made prenatally (including 'markers') (% of total notified)	290 (51%)	639 (85%)	746 (85%)	543 (79%)	2,218 (77%)
Notifications made prenatally with anomaly at birth (% of total)	232 (41%)	344 (46%)	408 (47%)	344 (50%)	1,328 (46%)
Notifications made prenatally & considered normal at birth (% of total notified prenatally)	58 (20%)	295 (45%)	381 (51%)	196 (36%)	930 (42%)
Notifications made prenatally and resulting in TOPFA (% of prenatally diagnosed cases with anomaly confirmed)	100 (43%)	138 (40%)	142 (35%)	154 (45%)	534 (40%)
Total with anomaly at delivery. (% of total births)	508 (2.2%)	457 (2.0%)	495 (2.3%)	489 (2.1%)	1,949 (2.1%)

Table 2A gives the number of notifications to the OXCAR population in four four-year periods from 1991 – 2006. During these time periods the number of cases notified prenatally changed from 51% in 1991-1994, to 85% in the middle time periods and to 79% during 2003-2006. However in the same time periods the number of cases where there was a prenatal suspicion but the baby was apparently normal at birth rose from 20% of prenatal notifications in 1991 – 1994 to 45% in 1995-1998 and reached a high level of 51% during 1999-2002 but dropping to 36% for the years 2003-2006.

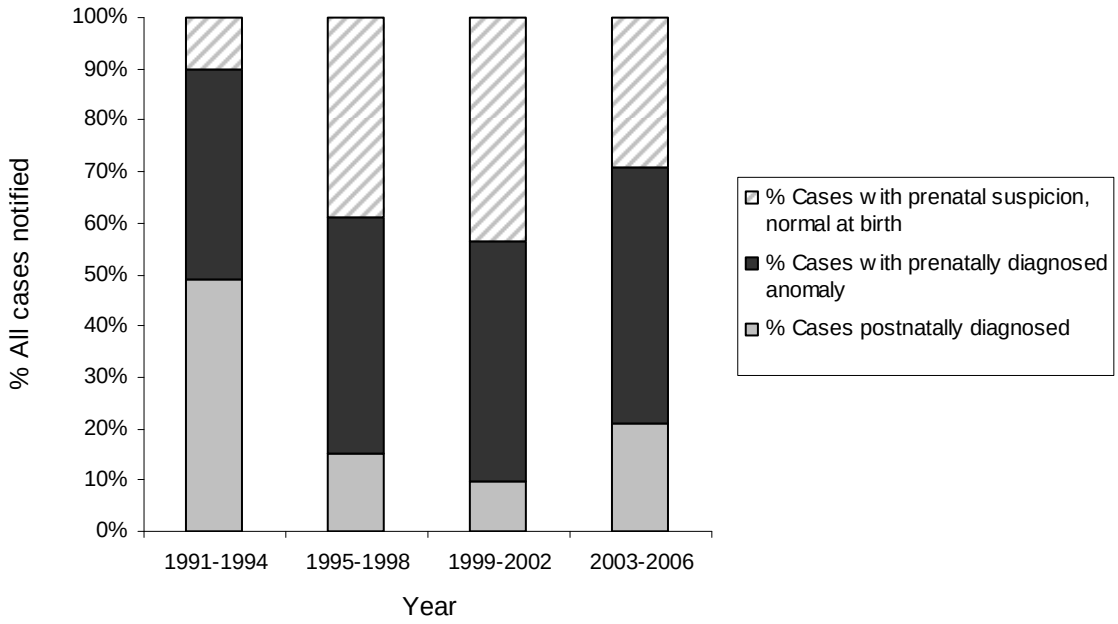
This trend is illustrated in Figure 2A and Table 3 which demonstrate the evolution of reporting ultrasound soft markers (such as echogenic bowel and nuchal thickening). Ultrasound soft markers started to be reported regularly in the early 1990s. By the mid-1990s it was realised that most babies with these usually normal variants were normal and local protocols were drawn up to guide professionals on the management of such markers, when to report specific markers and what further tests might be indicated.

The change in management clearly had an effect. The prenatal diagnosis rate increased sharply from 51% to a high of 85% during the years 1995 to 2002. The number of women informed of a possible fetal abnormality when in fact the baby was normal has fallen from a high of 1 in 57 to 1 in 118 following the change in policy concerning ultrasound soft markers, with a small fall in prenatal diagnosis rate to 79%.

Trends in prenatal diagnosis - the impact of reporting ultrasound soft markers;

Figure 2A Cases reported to OXCAR/CAROBB in four 4-year periods from 1991-2006;

Percentage postnatally diagnosed, percentage prenatally suspected with anomaly confirmed at birth, and percentage with prenatal suspicion, baby normal at birth



Appendix 1

Table 3A: Changes in prenatal detection rates in four four-year periods and proportion of total births with prenatal suspicion (ultrasound soft markers) and baby normal at birth

	1991 – 1994	**1995 – 1998**	**1999 - 2002**	**2003 – 2006**
Total births	23,438	22,703	21,765	23,086
% babies with anomaly at birth	2.2 %	2.0%	2.3%	2.1%
% babies with anomaly detected prenatally	51%	85%	85%	79%
Proportion of total births with prenatal suspicion*, baby normal at birth	1 in 404	1 in 77	1 in 57	1 in 118

* ultrasound soft markers

CAROBB Notification form

The standard notification form is shown overleaf but we are happy to accept information in other ways eg copies of discharge letters or clinic lists.

Please contact us if you would like to discuss how best to notify to the register.

We will provide copies of forms on request or forms can be printed from our website: www.npeu.ox.ac.uk/carobb

Appendix 2

CAROBB NOTIFICATION FORM

Congenital Anomaly Register for Oxfordshire, Berkshire and Buckinghamshire

Office use only - Case no

Dup | Con | From

Please register any actual OR prenatally suspected anomaly - structural, chromosomal or biochemical in fetus/baby. (See reverse of form for more information about the register and exclusion list)

MOTHER DETAILS

(Sticky label, if available)

Surname……

Forename……..**Hosp No**……

NHS Number……

Postcode *(essential field)*

Mother's DoB *(essential field)*

Booking hosp……

To deliver at……
(If different from booking hospital)

EDD *(essential field)*

Multiple pregnancy?……**Zygosity:** MCMA / MCDA / DCDA

Assisted conception? ……
If yes, (please state method, if known)

No of previous pregnancies/births

……Livebirth ……Miscarriage/TOP *(<24 weeks)* ……Stillbirth/TOP *(>24 weeks)*

Ethnic origin of mother *(please circle)*

White / Asian / Black / Mixed / Chinese / Other……

BABY DETAILS

(Sticky label, if available)

Surname……

Forename……..**Hosp No**……

NHS Number……

Sex Male / Female / Ambiguous / Not known
(please circle)

Date of delivery
(or date of TOP)

Place of delivery……

Gest at delivery……weeks

Weight g ☐ Not weighed

Outcome *(when possible, please report date of delivery, gest, sex, weight and details of any anomalies, whatever the outcome)*

- ☐ Liveborn, no anomaly identified, no follow up requested
- ☐ Liveborn, anomaly present or req' further tests *(please give details)*
- ☐ Miscarriage/IUD *(<24 weeks)*
- ☐ Stillbirth/IUD *(>24 weeks)*
- ☐ Termination
- ☐ Neonatal death

Date of neonatal death

Post mortem? Yes / No / Not known

PRENATAL INVESTIGATIONS

Screening and Diagnostic tests

Gest	Test *(please circle)*	Result
……	Nuchal / Combined	NT measurement ……mm
…….	Double / Triple	Down's risk 1 in ……
…….	Other ……	Tri 13 / 18 risk 1 in ……
		Not offered / Declined
……	CVS	Normal / Abnormal *(state karyotype if known)*
…….	Amnio	……
…….	FBS	Not offered / Declined
…….	Other *(please state)* ……	

Gest	Ultrasound scan findings *(& any other relevant details)*
……	……
…….	……
……	……
……	……
……	……
……	……
…….	……

POSTNATAL DETAILS OF ANOMALY

Prenatally suspected? ☐ Yes ☐ No

……

……

……

……

……

……

……

Additional details *(eg previous congenital anomalies, consanguinity, illness in mother, exposure to potentially harmful substances)*

……

……

……

……

……

……

Referred to:……

Notified by:……Date:……Hospital:……Dept:……Tel:……

Confidential: Please send in a sealed envelope to: CAROBB, NPEU, Old Road Campus, Oxford OX3 7LF or use confidential fax: 01865 289720. Any queries contact Cath Rounding: Tel: 01865 289721, E-mail: CAROBB@npeu.ox.ac.uk.

Congenital Anomaly Register for Oxfordshire, Berkshire and Buckinghamshire (CAROBB)

Please complete the form overleaf as fully as possible, registering any anomalies found at whatever stage you become aware of them in the pregnancy/postnatal period.

Uses of the register:

- Audit for prenatal diagnosis
- Evaluation and monitoring of new invasive and non invasive prenatal tests
- Evaluation of new screening programmes
- Provision of data for health care policies and planning
- Provision of data for the investigation of cluster of abnormalities
- Investigation of putative teratogens
- Research on aetiology and natural history of particular malformations
- Improving ascertainment to the National Congenital Anomaly System

Congenital anomalies exclusion list

It is not necessary to report any of the following conditions to us POSTNATALLY, unless there was a prenatal suspicion of an anomaly.

- Spina bifida occulta uncomplicated
- Phymosis
- Stenosis or stricture of lacrimal duct
- Minor skin anomalies less than 4cm^2: skin tag, naevus, angioma, haemangioma, glomus tumor, lymphangioma, birth mark
- Minor anomaly of auricle
- Clicking hip
- Minor anomaly of face or nose
- Minor anomaly of nipple, accessory or ectopic nipple
- Postural clubfoot
- Minor anomalies of the foot: hallux valgus/varus, "orteil en marteau", metatarus valgus/adductus
- Postural talipes calcaneovalgus or pes calcaneovalgus
- Congenital umbilical hernia, inguinal or para umbilical
- Functional or unspecified cardiac murmur
- Absence or hypoplasia of umbilical artery
- Congenital hydrocele or hydrocele of testis

If in doubt, report to us, we will feed back any inappropriate reporting

Confidentiality and data protection

All information held on the register is strictly confidential. Data are stored in a secure environment at the National Perinatal Epidemiology Unit, University of Oxford (data protection registration number: Z575783X). Any research undertaken is subject to ethical approval. The register holds Patient Information Advisory Group approval.

Confidential: Please fax or send in a sealed envelope to:

Cath Rounding
CAROBB Co-ordinator
National Perinatal Epidemiology Unit
University of Oxford
Old Road Campus
Headington
Oxford OX3 7LF

Confidential fax: 01865 289720

Please do not hesitate to contact us with any queries, or requests for more forms.

Tel: 01865 289721
E-mail: carobb@npeu.ox.ac.uk
Website: http://www.npeu.ox.ac.uk/carobb/

PLEASE DO NOT SEND ANY NOTIFICATIONS BY E-MAIL

Appendix 3

Research Projects using data from CAROBB

1.	**Project title:**	Arthrogryposis multiplex congenita (AMC) – causes and risk factors
	Investigators:	Dr Jana Midelfart Hoff
	Collaboration:	EUROCAT
	Status of study:	Ongoing
	Additional Information:	1) To study occurrence of AMC in Europe based on data from the EUROCAT database 2) To look at risk factors and possible targets for prevention of AMC 3) To look at different subgroups of AMC: Isolated condition, part of a syndrome with generalized affection, different grades of affection. 4) To study the connection between maternal myasthenia gravis (MG) and AMC, and to study a possible preventive effect of thymectomy.
2.	**Project title:**	Audit of prenatal lung lesions versus pathological diagnosis
	Investigators:	P. Teong, K Lakhoo, L Impey
	Collaboration:	Local
	Status of study:	Ongoing
3.	**Project title:**	Fraser Syndrome
	Investigators:	Prof Helen Dolk, Dr Ingeborg Barisic
	Collaboration:	EUROCAT
	Status of study:	Ongoing
4.	**Project title:**	Cognitive and behavioural outcomes of children with an extra sex chromosome
	Investigators:	Prof Pat Jacob, Prof Dorothy Bishop, Dr Gaia Scerif
	Collaboration:	Dept of Experimental Psychology, Oxford University; Wessex Regional Genetics Laboratory
	Status of study:	Ongoing
	Additional Information:	Funded by BDF Newlife
5.	**Project title:**	Antenatal diagnosis of duodenal atresia and postnatal outcome
	Investigators:	Ms PG Roy, Miss K Lakhoo, Dr P Boyd
	Collaboration:	Local
	Status of study:	Ongoing
	Additional Information:	To assess accuracy of prenatal scan diagnosis of duodenal atresia with the actual postnatal outcome.
6.	**Project title:**	Oro-facial Clefts. World-wide Recent Total Prevalence Data.
	Investigators:	Prof Pierpaolo Mastroiacovo
	Collaboration:	EUROCAT
	Status of study:	Ongoing
	Additional Information:	To describe the total prevalence rate of OC in various countries by contributing registries, grouped by country and/or by larger areas

7.	**Project title:**	How have babies born with spina bifida in the 1990's fared?
	Investigators:	Dr Jenny Kurinczuk, Dr Jenny Calvert, Dr Patricia Boyd, Dr Paul Chamberlain, Dr Mary Anthony
	Collaboration:	Action Medical Research
	Status of study:	Complete, submitted for publication
8.	**Project title:**	Sentinel phenotypes
	Investigators:	Ms Suzhuang Hong, Prof Helen Dolk, Marlene Sinclair, Diana Wellesley, Ingeborg Barisic, Maria Loane, Ian Bradbury
	Collaboration:	EUROCAT
	Status of study:	Ongoing
9.	**Project title:**	FOCAL – Follow-up Of Children with Congenital Anomalies Long-term. Pilot study of diaphragmatic hernia
	Investigators:	FOCAL
	Collaboration:	BINOCAR & BDF Newlife
	Status of study:	Ongoing
	Additional Information:	The feasibility of investigating the outcomes at age two years for children born with congenital diaphragmatic hernia. Funded by BDF Newlife
10.	**Project title:**	Isolated cleft lip and palate audit
	Investigators:	Dr Dorothy Halliday, Dr Patricia Boyd
	Collaboration:	Local
	Status of study:	Complete
11.	**Project title:**	Gastroschisis
	Investigators:	Dr Elizabeth Draper
	Collaboration:	BINOCAR
	Status of study:	Ongoing
	Additional Information:	Pooling of data from BINOCAR registries to assess possible increasing incidence
12.	**Project title:**	Congenital hydrocephalus
	Investigators:	Dr Ester Garne
	Collaboration:	EUROCAT
	Status of study:	Ongoing
13.	**Project title:**	Myotonic dystrophy audit
	Investigators:	Dr Paul Chamberlain
	Collaboration:	Local
	Status of study:	Complete (see Appendix 4 reference 4)
14.	**Project title:**	Chlorination of water supplies and birth defects
	Investigators:	Prof Paul Elliott
	Collaboration:	SASHU
	Status of study:	Complete (see Appendix 4 reference 1)
15.	**Project title:**	Absent stomach bubble/TOF/OA
	Investigators:	Dr Paul Chamberlain, Miss Kokila Lakhoo, Dr Patricia Boyd
	Collaboration:	Local

Appendix 3

	Status of study:	Complete (see Appendix 4 reference 5)
16.	**Project title:**	Clinical genetics audit of late TOP
	Investigators:	Dr Dorothy Halliday, Dr Patricia Boyd
	Collaboration:	Local
	Status of study:	Complete
17.	**Project title:**	Geographical variation in overall rates of congenital abnomalities and the rates for specific abnormalities
	Investigators:	Prof Helen Dolk
	Collaboration:	EUROCAT
	Status of study:	Complete (see Appendix 4 reference 7)
18.	**Project title:**	Audit of screening offered to parents of those babies born with down syndrome
	Investigators:	Dr Gail Whitehead
	Collaboration:	Local
	Status of study:	Complete
19.	**Project title:**	Audit of gastroschisis 1995-2005
	Investigators:	Dr Gail Whitehead
	Collaboration:	Local
	Status of study:	Complete
20.	**Project title:**	Prenatal screening in Europe
	Investigators:	Dr Patricia Boyd
	Collaboration:	EUROCAT
	Status of study:	Complete (see Appendix 4 reference 2)
21.	**Project title:**	Cornelia de Lange Syndrome
	Investigators:	Prof Helen Dolk, Dr Ingeborg Barisic
	Collaboration:	EUROCAT
	Status of study:	Complete (see Appendix 4 reference 3)
22.	**Project title:**	Audit of screening of fetuses with echogenic bowel
	Investigators:	Dr Gail Whitehead
	Collaboration:	Local
	Status of study:	Complete

Publications to which CAROBB / OXCAR have contributed information

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4. Zaki M, Boyd PA, Impey L, Roberts A, and Chamberlain P. Congenital myotonic dystrophy - prenatal findings and pregnancy outcome. Ultrasound in Obsterics and Gynecology. 2007; 29(3):284-8.

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of trisomy 21: experience from 19 European registers. Annales de Genetique. 2004; 47:373-480.

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Data Protection and handling requests for data

5a PIAG approval documentation

5b MREC approval documentation

5c Application form and guidelines for use of CAROBB data

Appendix 5a

Patient Information Advisory Group (PIAG) approval for CAROBB (as part of BINOCAR) to collect identifiable information without explicit consent from individuals registered.

Application Number	0011	
PIAG Reference	PIAG 2-08(e)/2002	
Other PIAG Refs		
Application Title	Congenital Anomalies Register (BINOCAR)	
Application Summary	To provide continuous epidemiological monitoring of the frequency, nature, cause and outcomes of congenital anomalies by means of national, regional and disease specific registers of congenital anomalies.	
Applicant Organisation Name	British Isles Network of Congenital Anomalies Register (BINOCAR)	
Contact Name	Elizabeth S Draper,Chair of BINOCAR	
Address	Department of Health Sciences, University of Leicester	
	22-28 Princess Road West	
	Leicester	
Postcode	LE1 6TP	
Telephone	0116 252 3210	
Fax		
Email	jlsb1@leicester.ac.uk	
Medical Purposes	Y	the surveillance and analysis of health and disease;
	□	the monitoring and audit of health and health related care provision and outcomes where such provision has been made;
	□	the planning and administration of the provision made for health and health related care;
	□	medical research approved by research ethics committees;
	□	the provision of information about individuals who have suffered from a particular disease or condition
Cohort/Population	UK-wide: patients with congenital anomalies	
Description of confidential patient information used	Mother's name, address, postcode, hospital number, NHS number, date of birth. Baby's name, address, postcode, hospital number, NHS number, date of birth, date of death.	
S60 Class(es)	□	Specific Support
	Y	Class I - making the person less readily identifiable
	Y	Class II - present or past geographical locations of patients
	Y	Class III - to identify and contact patients to obtain consent
	Y	Class IV - linking multiple sources;validating quality and completeness; avoiding error
	Y	Class V - audit, monitoring, & analysis of healthcare provision
	Y	Class VI - granting of access to data for purposes I-V
NHS Sponsor		
Status	Approved	
Date Applied		
Date Approved	20/06/02	
Date S60 Granted	20/06/02	
Expiry Date		
Next Review Date	20/06/08	
Details of Approval	PIAG gave Section 60 support for the BINOCAR application.	
Notes		

NHS

Trent Multi-centre Research Ethics Committee

Derwent Shared Services
Laurie House
Colyear Street
Derby
DE1 1LJ

Chairman: **Dr Robert Bing**
Administrator: **Jill Marshall**

Your Ref:

Telephone: 01332 868905
Fax: 01332 868930
Email: Jill.Marshall@derwentsharedservices.nhs.uk

19 July 2004

Mrs Elizabeth Draper
Director, East Midlands and South Yorkshire Congenital
Anomalies Register (BINOCAR)
Department of Health Sciences
University of Leicester
22-28 Princess Road West
LEICESTER
LE1 6TP

Dear Mrs Draper

Full title of study: The regional and national registration of congenital anomalies in England, Scotland and Wales - the British Isles Network of Congenital Anomaly Registers (BINOCAR).
REC reference number: 04/MRE04/25
Protocol number: Designated 1

Thank you for your letter of 08 July 2004, responding to the Committee's request for further information on the above research.

The further information has been considered on behalf of the Committee by the Chairman.

Confirmation of ethical opinion

On behalf of the Committee, I am pleased to confirm a favourable ethical opinion for the above research on the basis described in the application form, protocol and supporting documentation.

Conditions of approval

The favourable opinion is given provided that you comply with the conditions set out in the attached document. You are advised to study the conditions carefully. **I confirm that this is a 'No Local Investigator' study, therefore no site specific assessment need be sought from LRECs.**

Approved documents

The final list of documents reviewed and approved by the Committee is as follows:

Document Type: Application
Version:
Dated: 02/04/2004
Date Received: 15/04/2004

Appendix 5c

CAROBB

Congenital Anomaly Register for Oxfordshire, Berkshire and Buckinghamshire

Application to use data from CAROBB

Title of project: _____

Name(s) of researcher(s): _____

Current position(s)

Address: _____ **Tel:** _____

e-mail address(es) _____

Name of supervisor *(see guidelines):* _____

Current status of project:

In preparation: Yes No

Funding applied for: Yes No N/A

Funding secured: Yes No N/A

Funding agency _____

Other - (*please describe)*: _____

Principal grant holder: _____

Address if different from above: _____

_____

Ethics approval: Has been granted: Yes No N/A

Name(s) of Committee(s): _____

_____

Proposed start date: _____ Completion date: _____

Please turn over

Peer review: Study protocol has been reviewed: Yes No

To whom submitted: _____

_____

Aims and objectives:

Background:

Methods:

Main outcome measures:

1. I have read and agree to conform to the Guidelines for Users of CAROBB.

Name (*please print*): _____ **Signed:** _____

Date: _____

2. I agree to act as supervisor for this research project.

Name of supervisor: _____ **Signed:** _____
(*please print*)

Date: _____

e-mail address: _____ **Tel:** _____

Please return the completed form to:

Catherine Rounding, CAROBB Co-ordinator, National Perinatal Epidemiology Unit, University of Oxford, Old Road Campus, Headington, Oxford OX3 7LF. Tel: 01865 289721 E-mail: **carobb@npeu.ox.ac.uk**

Appendix 5c

GUIDELINES for users CAROBB

Congenital Anomaly Register for Oxfordshire, Berkshire and Buckinghamshire

CAROBB (Congenital Anomaly Register for Oxfordshire, Berkshire and Buckinghamshire) was awarded funding by the Department of Health in 2003 to establish a database of information on babies born with suspected or confirmed congenital anomalies for the three counties. Prior to 2003, the register was known as OXCAR and included cases seen at the John Radcliffe Hospital since 1991.

The principal objectives of CAROBB are:

- Provide data for research on the aetiology and natural history of particular malformations to enable better advice based on accurate information to be given to parents
- Enable the evaluation and monitoring of new invasive and non invasive prenatal tests.
- Evaluate new prenatal screening programmes and to provide data for health care policies and planning
- Provide data to investigate clusters of abnormalities and putative teratogens by the monitoring of incidence over time and in population trends such as maternal age, ethnicity, and health inequalities.

CAROBB can be used as a basis for other studies and there are increasing numbers of requests for access to the data for research purposes. The Management Group wishes to encourage the use of the register in this way and the following guidelines have been drawn up to help potential register users. CAROBB conforms to the Data Protection Act 1998 and the Health and Social Care Act 2001.

Please feel free to contact the Register Co-ordinator for a discussion of your proposal at an early stage. It is important to be clear about what information you wish to collect and what information you will be able to obtain through the register.

1. All requests for access to CAROBB data should be made through the research co-ordinator using the accompanying form.

2. The request should be accompanied by a study protocol. The protocol must be approved by CAROBB. Approval by an ethics committee will not guarantee approval by CAROBB. Any amendments required by an ethics committee must be approved by CAROBB before data will be released.

3. If appropriate, the researcher will be responsible for obtaining approval from Ethics Committees in the areas in which the cases live. A copy of the approval must be supplied to the register co-ordinator before data will be released for the study.

4. Researchers are expected to seek peer review of the proposed study.

5. Researchers will need to seek the permission of the parent/child's general practitioner prior to contacting parents and children. If necessary, permission must

also be sought from the appropriate consultant for access to hospital notes.

6. If the researcher has little or no previous experience of research the Management Group will require a written assurance from a supervisor that the work will be carried out and completed satisfactorily.

7. It is the responsibility of the researcher to apply for funds to carry out the proposed study. A small administrative charge may be made to cover the cost of accessing cases from CAROBB.

8. Data supplied by CAROBB must not be passed to a third party, nor should it be re-used for later study without applying to CAROBB for permission. Personal data must not be uploaded to a researchers home computer. Researchers are expected to deposit datasets which have been derived from the original data, with suitable documentation, in the CAROBB database.

9. In compliance with the Data Protection Act, 1998, to keep the database as accurate as possible, researchers will be expected to inform CAROBB of changes to subjects details during the course of the study.

10. The Management Group will request a short progress report at intervals during the course of the study and evidence of the final results in the form of a report or paper. Any change in contact addresses or personnel working on the project should be notified to the Management Group.

11. The Management Group would like to see an advanced draft of any publication, or abstract submitted for a meeting, in which CAROBB data have been used. Congenital Anomaly Register for Oxfordshire, Berkshire and Buckinghamshire should be acknowledged in any publication or presentation, arising from CAROBB data, using the sentence "The Management Group of Congenital Anomaly Register for Oxfordshire, Berkshire and Buckinghamshire approved the release of register data for this study. CAROBB is funded by the Department of Health."

12. On completion of the analysis and after copy datasets have been supplied to CAROBB, ALL PERSONAL IDENTIFIABLE INFORMATION MUST BE DESTROYED, in accordance with any requirements of the ethics approval for the study. If you are unsure on this point, contact CAROBB for clarification.

Please complete the application form enclosed and return to the CAROBB office.

Appendix 6

Publicity

6a Poster for clinic waiting rooms

6b Leaflet for clinic waiting rooms

carobb

Congenital Anomaly Register for Oxfordshire, Berkshire & Buckinghamshire

Congenital Anomaly Register for Oxfordshire, Berkshire and Buckinghamshire

Most babies are born healthy,

but

if a baby is born with a birth defect (congenital anomaly)

or

a problem is suspected on scan before birth

information about the defect and the pregnancy is recorded on a local register and on a National one at the Office of National Statistics which was set up in the 1960s following the birth of babies affected by Thalidomide.

Why is this information collected?

- To improve our understanding of congenital anomalies and help research into causes, treatment and prevention
- To help identify possible clusters of birth defects
- To check how good antenatal scans and screening tests are at picking up problems
- To help plan and develop NHS services

The information collected is held securely and is strictly confidential. If you have any questions or concerns about the information that might be held about you or your baby, please contact:

CAROBB, National Perinatal Epidemiology Unit, University of Oxford, Old Road Campus, Headington, Oxford OX3 7LF
E-mail: CAROBB@npeu.ox.ac.uk.
Website: www.npeu.ox.ac.uk/carobb

npeu
National Perinatal Epidemiology Unit

How is information collected?

A member of staff from the hospital who treats you or your baby, completes a notification to the register when the anomaly is identified. The register often receives several notifications from different departments about the same baby. Any information reported in the early stages can be improved or confirmed later by these multiple notifications.

Names and postcodes are included so that information can be updated on the correct case and the same baby is not counted several times.

Information is collected on paper and stored electronically on a computer. This information is held securely by CAROBB, which is based at The National Perinatal Epidemiology Unit, in Oxford.

Does my name or my baby's name have to go on the Register?

We hope everyone will want to be included on the Register, to help us plan and improve services for future mothers and babies. However, your details can be removed at any time.

Will the database be secure and confidential?

The information recorded on the Register about you or your baby is confidential. It is held in a responsible way which respects the rights and privacy of individuals.

The Register follows a strict policy on security and confidentiality. This policy is available to the public. The register conforms to the requirements of legislation on data protection.

How can I find out more about CAROBB?

If you have any questions or concerns regarding the information that could be held on you or your baby, please contact the registry:

CAROBB
National Perinatal Epidemiology Unit
University of Oxford
Old Road Campus
Headington
Oxford OX3 7LF

Tel: 01865 289721
Fax: 01865 289720
E-mail: carobb@npeu.ox.ac.uk
Website: www.npeu.ox.ac.uk/carobb/

CAROBB and The National Perinatal Epidemiology Unit are funded by the Department of Health

Congenital Anomaly Register for Oxfordshire, Berkshire and Buckinghamshire

Information for parents

Every parent hopes that their baby will be healthy and most babies are.

However, a few babies do have problems (abnormalities) such as cleft palate, spina bifida, or Down's syndrome. These are sometimes called congenital anomalies or congenital malformations.

Some congenital anomalies are detected during pregnancy, some are found at birth, while others become apparent only as a baby grows older.

Why is information collected about babies with congenital anomalies?

CAROBB collects information:

- To increase our understanding of congenital anomalies and help research into their causes, treatment and prevention.
- To monitor how good antenatal screening tests (serum screening and ultrasound scans) are at picking-up problems.
- To look at trends - for example changes in the number of babies born with congenital anomalies, or changes in the pattern of where they are born.
- To give health professionals information to help them advise families about their chances of having a baby with a congenital anomaly.
- To help plan and develop NHS services.

What is CAROBB?

***CAROBB* (Congenital Anomaly Register for Oxfordshire, Berkshire and Buckinghamshire) is a database of information on babies born with suspected or confirmed congenital anomalies.**

What information is collected?

Information held by the register includes:

- Descriptions of each anomaly.
- Details and results of any investigations carried out during pregnancy (for example, the results of any ultrasound scans).
- Details about mother and baby.

Who sees the information?

There are very strict regulations controlling access to personal information - that is names and addresses. This information will only be available to members of hospital staff treating you or your baby, and to those who work on CAROBB.

Information is also sent to the National Congenital Anomaly Surveillance System, which collects information for the whole country. When this happens only the first three letters of the baby's name are sent.

Information that is used by researchers or published in reports does not contain anything to identify either mother or baby, such as names and addresses.

Can I see the records on the Register?

Yes - you have the right to request a copy of the information held on you or your baby.

To do this, please make your wishes known to a member of your healthcare team or contact CAROBB by telephone or e-mail.

Appendix 7

Management Group and Steering Committee Members and Terms of Reference

Management Group members

Dr Patricia Boyd	Senior Clinical Research Fellow/ Director CAROBB, National Perinatal Epidemiology Unit
Prof Peter Brocklehurst	Director National Perinatal Epidemiology Unit, National Perinatal Epidemiology Unit
Dr Paul Chamberlain	Consultant obstetrician, John Radcliffe Hospital
Dr Jenny Kurinczuk	Consultant Clinical Epidemiologist, Deputy Director, National Perinatal Epidemiology Unit
Mrs Jackie Lovstrom	Prenatal diagnosis specialist midwife, John Radcliffe Hospital
Ms Catherine Rounding	Co-ordinator CAROBB, National Perinatal Epidemiology Unit
Ms Geraldine Surman	4Child, National Perinatal Epidemiology Unit

Steering Committee members 2008

Mrs Beverley Beaumont	Radiographer, Horton Hospital
Dr Patricia Boyd	Senior Clinical Research Fellow/ Director CAROBB, National Perinatal Epidemiology Unit
Prof Peter Brocklehurst	Director National Perinatal Epidemiology Unit, National Perinatal Epidemiology Unit
Dr Paul Chamberlain	Consultant obstetrician, John Radcliffe Hospital
Ms Catryn Dixon	Antenatal screening co-ordinator, Wycombe General Hospital
Dr Sanjay Salgia	Consultant Paediatrician, Wycombe General Hospital
Miss Jacqueline Hall	Consultant Gynaecologist , Stoke Mandeville Hospital
Mrs Julia Horsnell	Lay member
Dr Jenny Kurinczuk	Consultant Clinical Epidemiologist, Deputy Director, National Perinatal Epidemiology Unit
Mrs Jackie Lovstrom	Prenatal diagnosis specialist midwife, John Radcliffe Hospital
Ms Catherine Rounding	Co-ordinator CAROBB, National Perinatal Epidemiology Unit
Dr Rekha Sanghavi	Consultant Paediatrician, Wexham Park Hospital

Miss Pampa Sarkar	Consultant Obstetrician, Wexham Park Hospital
Dr Nick Hicks	Director of Public Health, Milton Keynes
Ms Alison Wainright	Antenatal Screening Co-ordinator, Stoke Mandeville Hospital
Ms Geraldine Surman	4Child, National Perinatal Epidemiology Unit
Prof Andrew Wilkinson	Consultant neonatal paediatrician, John Radcliffe Hospital
Dr Ann Gordon	Consultant Paediatrician, Royal Berkshire Hospital
Ms Louise Abbott	Antenatal Screening co-ordinator, Milton Keynes General Hospital

CAROBB Steering Committee Terms of Reference

1) Terms of Reference
    a. To monitor and supervise the progress of the register towards its interim and overall objectives.
    b. To be accountable to the Department of Health for the register and associated projects.
    c. To determine the strategies for the use and development of the register.
    d. To propose and develop research projects using the register and to encourage the development of satellite projects.
    e. To encourage collaboration with other registers with similar functions in the development of joint projects and pooling of data.
    f. To develop strategies, within existing and future legislation and government guidelines, which authorise the release of personal data from the register to support research as appropriate.
2) Membership
    a. Chair
        i. independent of the management group of the project;
        ii. should be reviewed every three years;
        iii. should serve no more than two consecutive terms;
    b. Vice chair[1]
        i. independent of the management group of the project;
        ii. should be reviewed every three years;
    c. Minimum of two other independent members;
    d. One or two principal contributors;
    e. At least one lay/consumer representative;
    f. Project co-ordinator;
    g. Other members of the project management group should attend as appropriate;
    h. Observers from the funding body and host institution should be invited to all meetings.
    i. Members failing to attend two consecutive meetings may be asked to stand down;
    j. Members with particular difficulty in attending meetings e.g. through disability, child-care, may be asked to contribute to the group by email/telephone with the agreement of other members;

k. Members should aim to serve on the committee for at least three years. Membership should be reviewed after three years for long-running projects.

3) Meetings
   a. Should be organised before the start of a project to finalise the protocol where appropriate;
   b. Should be held at least annually;
   c. Papers for meetings should be circulated in advance;
   d. Meetings should be held face-to-face but in exceptional circumstances telephone conferencing can be considered an acceptable alternative;
   e. Where less than 50 per cent of independent members are able to attend, the meeting should be declared inquorate and a new meeting date arranged;
   f. Accurate minutes of the meeting should be prepared and agreed by all members of the steering committee.

1. This should answer the difficulty when the chair is unable to attend.