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2004

with data for 2002

INTERNATIONAL CLEARINGHOUSE FOR BIRTH DEFECTS MONITORING SYSTEMS

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THE INTERNATIONAL CLEARINGHOUSE FOR BIRTH DEFECTS MONITORING SYSTEMS

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INTERNATIONAL CLEARINGHOUSE FOR BIRTH DEFECTS MONITORING SYSTEMS ANNUAL REPORT 2004 (WITH DATA FOR 2002)

Introduction

Pierpaolo Mastroiacovo
Director, International Centre on Birth Defects (ICBD)

A word on the structure of the report

Because of collaborative monitoring and research are the most important functions of the International Clearinghouse for Birth Defects Monitoring Systems (ICBDMS), summaries of these activities open this report.

Descriptions of the individual Programmes and tabulations of their data follow.

Make sure that you read these pages before looking at individual programmes tables and graphs

Each monitoring system monitors all birth defects. However, the tables and the graphs present data for selected defects. The selection is made at the Annual Meeting and is quite arbitrary, moreover it may change year by year.

The main aim of the tables and graphs is to show the time variation in the rates of some specific defects in each monitoring system. Figures are presented in:

(a) a table showing data for 2002,
(b) a table showing data for the longest available period of each register and for each malformation up to 2002
(c) some graphs showing the rate trends represented in the following style:
  a. bars represent real patterns of prevalence,
  b. blue bars stand for live+still births rates
  c. black bars stand for termination of pregnancy rates.
  d. blue continuous line stands for the three-year moving average of live and still births rates (the value shown for each year correspond to the average of that year, the previous and the following year).

The tables for 2002 have a standard format for all the registries. If a malformation is not reported the row says "not reported".

The tables for temporal trend have a flexible format. Only malformations with data are reported
The prevalence rates graphs are presented only for those malformations which have:
(a) figures at least for 8 years,
(b) number of cases per year different from zero in at least half the available years.

This way of presenting data underlines the recommendation to avoid the comparison of rates of a birth defect among Programmes, as there are important differences in the methodology of registration, in defining live births, still births and abortions, including birth defects observed in pregnancy terminations, and last but not least, in defining every single birth defect. Some of the differences in birth defects definitions are highlighted in the description of each monitoring system and in the table "Synopsis of Monitoring Systems" and in the table "Deviations from the ICBDMS definitions by Registry".

Birth defect rates are calculated by including all cases of each defect, whether isolated or associated to other defects. In some instances, therefore, the same baby may be counted more than once in the tables (i.e.: a baby with cleft lip and limb deficiency is counted twice). In the data from Hungary, however, only isolated defects are reported.

Not all Registries report pregnancy terminations either because the data are not available to the Registry or pregnancy termination is not legal in that country. The inclusion of pregnancy terminations is noted in the tables.

For a better understanding of the statistical analysis, it may be helpful to read the notes on the box.

Some pages of the report show the overall picture of the results of 2002 year monitoring for selected defects. This is the most important piece of information and attemps to answer the questions of what happened in 2002 and whether any relevant cluster noted in more than one or two Registries. If so, then these clusters may need to be investigated further.

1 Introduction

Notes on statistical analysis

Rates

When calculating rates among live born infants and stillbirths, the denominator used is total births. When terminations are included, the total number of terminations for birth defects is added to the denominator. The denominator used for age-specific rates for Down syndrome consists of the total number of live born infants, stillbirths and, if appropriate, terminations for Down syndrome, whose mothers are in that age group.

Observed / expected ratio
An iterative procedure is applied to calculate the expected rates: baseline series is tested, using the Chi squared trend test, in order to find a stable sub sample of observations-years. At the start of the procedure the whole series is tested; then, step by step, years are dropped until the test identifies a stable period. The observations-years kept in the sample are used as baseline to calculate the expected number of cases. Hence the observed / expected ratio is tested using an approximated procedure of the Poisson test at 95% significance level. In the column "YB" the number of observations-years in the baseline is found; the "Remark" column shows the significant values.

Time trend analysis
As terminations were not recorded in the past, the time trend analyses are based on live and stillbirths with the exception of New Zealand and South Africa (live births only). The generalised apparent fall in rates is likely to be, at least in part, the consequence of prenatal diagnosis and pregnancy termination for those registries whose countries allow terminations. Time trends are computed using annual rates even though data in the trend tables is presented by five year intervals so as to make the tables more readable.
We have studied the Chi-Squared for trend in order to test the time tendency. The arrows in the column "trend" show the significant increase or decrease: upward arrows locate the significant increasing trends, downward arrows the significant decreasing trends. It is important to underline that this kind of test is counts-sensitive: statistical significance is easier to reach when the number of cases per year is high.

References

Feller W. 1968. An introduction to probability theory and its application. Vol. 1 3rd ed. New York: John Wiley & Sons
Breslow N.E., Day N.E. 1980. Statistical methods in cancer research. IARC Scientific Publications No.32
Armitage P., Berry G. 1994. Statistical methods in medical research. 3rd ed. Blackwell Science

2.1 Routinely Performed Projects

2.1.1 Malformations and Drug Exposure (MADRE) Database Analysis

Elisabeth Robert Gnansia (France, Central East)
Pierpaolo Mastroiacovo (ICBD, Rome)
Alessandra Lisi (ICBD, Rome)

During the year 2004 the MADRE Database was revised and the more clinically oriented coding system, commonly used for the "ICBDMS Multimalformed Surveillance Projects", was added. This means that all the material, at present and in the future, will be coded with ICD 9 or 10 plus the ICBDMS codes. As usual each clearinghouse drug was coded by Elisabeth Robert Gnansia with the ATC classification system.
On January 2005 all the material - 15,342 cases (see table 1) - was analyzed.

Table 1: Number of cases registered and % of number of drugs per case by programme

Registries	Years	Total cases	Number of drugs registered per case (%)						
			1	2	3	4	5	6	7
Australia	1990-1992	68	63,2	27,9	0,0	7,4	1,5		
Czech Republic	1996-2003	1004	71,0	23,1	5,9				
France: CE	1990-2003	2374	58,6	25,0	9,5	4,3	2,7		
France: Paris	1992-2000	1351	69,9	20,7	7,0	1,5	1,0		
Israel	1990-2004	233	74,7	19,3	6,0				
Italy: IMER	1990-2002	888	74,7	19,5	4,1	1,5	0,3		
Italy: IPIMC	1990-1994	1638	67,8	22,3	9,3	0,4	0,1		
Italy: ISMAC	1991-1996	94	86,2	13,8					
Italy: Tuscany	1992-2001	1081	78,3	19,1	2,7				
Japan	1990-2004	914	67,4	22,3	6,1	2,8	1,3		
Northern Netherlands	1981-2001	2315	60,2	25,5	9,7	2,8	1,3	0,3	0,2
South America	1990-1996	3382	65,3	24,7	6,9	2,1	1,0		
TOTAL		**15342**	66,4	23,2	7,3	2,0	1,0		

Analysis
In MADRE, drugs are cross-tabulated against malformations, and a two-by-two table is constructed for each combination of drug and malformation, for each participating register. An infant is defined as case-infant if it has the malformation in question and a control-infant otherwise. An infant is defined as exposed if the mother used the drug in question during the first trimester, and unexposed otherwise. If exposures and malformations are unrelated, drug types and malformation types should be randomly distributed, and deviations from this distribution show up as increased odds ratios. Such deviations can be used to screen for associations that deserve further study.
For each exposure – defect combination a Mantel – Haenszel Odds Ratio (M-H OR) is computed, stratified by register. $P<0.01$ is considered statistically significant. The Breslow-Day test is used to test the homogeneity of ORs among registries.$P<0.10$ is considered statistically significant for heterogeneity.

In this report we present the analysis conducted on "48 specified major malformations" (see list) at various level of specificity of ATC code: 3, 4, 5 digit level.

We planned to analyze the material in three steps:

a. analysis of the cases with isolated malformations, more homogeneous from the etiological point of view, to detect statistically significant association ($p<0.01$)
b. evaluation of the statistically significant associations seen in (a) in the cases with associated malformation,
c. analysis of the total cases to detect association not appeared in (a)

In this report we present the results obtained in the (a) first step. Only the associations observed in more than 10 cases, with a M-H OR homogeneous among registries, are shown and commented. All the other results will be presented and discussed in future reports.

Results
Results are shown in table 2.

Table 2 : Results of the analysis described in the text

	Malformation	ATC Code	Drugs	N. of cases	OR	CI 95%	
Text Ref						Inf	Sup
1	Spina Bifida aperta	N03AG	Fatty acid derivatives	27	8,19	5,49	12,22
2	Cleft lip with or without palate Cleft palate (included P. Robin) Left obstructive defect	N03AA N03A N03A	Barbiturates and derivatives Antiepileptics Antiepileptics	21 21 11	3,58 1,88 2,75	2,23 1,18 1,48	5,75 2,98 5,12
3	Cystic Kidney Kidney a/dysgenesis	H03AA H03	Thyroid hormones Thyroid hormones	17 13	3,08 2,16	1,88 1,21	5,06 3,86
4	Anencephaly	N02BB	Pyrazolones	14	2,59	1,47	4,55
5	Ventricular septal defect	A03AX	Other synthetic anticholinergic agents	13	2,48	1,30	4,75
6	Cleft lip with or without palate	H02	Corticosteroids	19	1,89	1,17	3,06
7	Cleft lip with or without palate	N05BA	Benzodiazepine derivatives	29	1,84	1,24	2,73
8	Cleft lip with or without palate	J01C	Beta lactam antibacterials, penicillins	60	1,49	1,13	1,98
9	Hypospadias Hypospadias	C04AA G03DA	2 amino 1 phenylethanol derivatives Pregnen 4 derivatives	124 89	1,49 1,45	1,18 1,12	1,88 1,86
10	Spina Bifida aperta	B03BB	Folic acid and derivatives	17	2,03	1,23	3,36
11	Hypospadias	B03BB	Folic acid and derivatives	64	1,56	1,12	2,17

In this table only the associations with the most specific ATC code are shown. This means that if a malformation shows an association with the ATC code at three digits and this is due to the association at ATC four and five digits level, only the more specific level is shown.

1 - <u>Spina bifida and fatty acid derivatives.</u>

This is a well known association. Twenty-seven cases of isolated spina bifida exposed to fatty acid derivatives (valproic acid - VPA) have been registered so far. Table 3 shows the distribution by register of these cases and the register specific ORs. The answer to the question why 26 cases out of 27 were registered in the two French registries is given in the last three columns of table 3. High proportion of VPA exposed cases, as shown in column 1 (among all the drug-exposed malformed subjects, which suggests a high prevalence of VPA use) and a high number of spina bifida cases, as shown in column 2. In column 3 the expected number of exposed to VPA spina bifida cases is computed on the hypothesis that the risk observed in France Central East is the same as in all the other registries. It can be seen that the major discrepancy observed in Czech Republic (no cases observed against 2.9 expected) can be random.

Table 3: Number of spina bifida cases exposed to VPA, OR and CI 95% observed and explanation why almost all cases have been registered in French registries (see text for details).

Programme	Spina bifida exposed to VPA	OR	95% Conf.Int		1 VPA exposure proportion (%)	2 Spina bifida isolated total	3 Expected
Australia	0	0,00	0,00	.	1,47	1	0,1
Czech Republic	0	0,00	0,00	8,87	2,49	13	2,9
France: CE	20	10,42	5,46	19,25	3,41	65	20,0
France: Paris	6	17,09	4,92	51,91	2,29	20	4,1
Israel	0	.	.	.	0,00	0	0,0
Italy: IMER	0	0,00	0,00	81,24	0,34	12	0,4
Italy: IPIMC	0	0,00	0,00	39,74	0,24	32	0,7
Italy: ISMAC	0	.	.	.	0,00	5	0,0
Italy: Tuscany	0	.	.	.	0,00	5	0,0
Japan	0	0,00	0,00	18,52	0,88	17	1,3
Northern Netherlands	1	55,04	0,93	756,46	0,17	9	0,1
South America	0	0,00	0,00	25,28	0,12	96	1,0
Total and MH OR	**27**	**8,19**	**5,15**	**13,04**	**1,05**	**275**	**25,8**

2 - <u>Barbiturates and cleft lip +/- palate, antiepileptics and cleft palate, antiepileptics and left obstructive defects</u>

These associations are well known. In this analysis, left obstructive defects which include hypoplastic left heart syndrome, coarctation of aorta and other less frequent defects (aortic atresia/hypoplasia, congenital stenosis of aortic valve, congenital mitral stenosis/insufficiency, supra-aortic stenosis, congenital insufficiency of aortic valve), appear to be more specifically associated to antiepileptics than other CHD malformations.

3 - <u>Thyroid hormones and unilateral kidney agenesis or cystic kidneys</u>

This association is not known in the common "drugs in pregnancy" literature. It is based on 17 cases of cystic kidneys (unilateral or bilateral) and on 13 cases of unilateral kidney agenesis. The M-H ORs are respectively 3.08 (CI 95% 1.83-5.21) and 2.16 (CI95% 1.20-3.91). The exposed cases have been registered in 8 registries (table 4)

Table 4: Association between cystic kidney(s) or unilateral kidney a/dysgenesis and thyroid hormones. Only registries with at least one exposed case are shown.

	Cystic kidney(s)				Unilateral kidney a/dysgenesis			
Programme	N. exposed Cases	OR	95% Conf.Int		N. exposed Cases	OR	95% Conf.Int	
France: CE	2	1,76	0,19	7,65	8	4,96	1,87	11,77
France: Paris	4	3,19	0,77	9,94	3	1,50	0,29	5,03
Italy: IMER	2	3,03	0,31	14,55	1	2,04	0,04	15,82
Italy: IPIMC	4	7,77	1,82	24,93	0	0,00	0,00	10,15
Italy: Tuscany	0	0,00	0,00	4,33	1	2,28	0,05	19,36
Japan	3	8,93	1,26	53,96	0	0,00	0,00	10,99
Northern Netherlands	1	6,57	0,14	50,99	0	0,00	0,00	37,70
South America	1	3,94	0,09	26,25	0	0,00	0,00	35,90
Total and MH OR	**17**	**3,08**	**1,83**	**5,21**	**13**	**2,16**	**1,20**	**3,91**

This association is interesting and should be tested in other databases, considering the underlying diseases. A few arguments in favour of a real association exist in the literature. Rodriguez-Garcia et al (1999) reported a case of bilateral renal agenesis in a girl born to a hyperthyroid mother who received methimazole in early pregnancy. Tan et al (1997) administrated propylthiouracil (PTU) to pregnant rats in order to obtund thyroid hormone levels. They showed that thyroid hormone is likely to set the stage for trophic control of renal development by neural input, and hypothyroidism during a critical window can be expected to result in abnormal renal functional development. Ali & Clos (1986) also showed in rats that thyroid deficiency induced by daily PTU treatment, strongly affects the development of the renal cortex.

4 - Anencephaly and pyrazolones

This association is based on 14 cases exposed. All of them have been registered in South America, with a specific OR of 2.72 (CI95% 1.40-4.96). The proportion of pyrazolones use among all cases as well as the number of isolated anencephalies registered in South America and in other countries is shown in table 5. The fact that the number of cases of anencephaly or the proportional use of pyrazolones is low in other registries explains why this association has been found only in South America.

Programme	Anencephaly exposed to pyrazolones	OR	95% Conf.Int		Pyrazolones exposure proportion (%) (1)	Anenc isolated	Expected (2)
Australia	0				0,00	0	0,0
Czech Republic	0				0,10	4	0,0
France: CE	0				0,00	23	0,0
France: Paris	0				0,00	26	0,0
Israel	0				0,00	0	0,0
Italy: IMER	0				1,69	0	0,0
Italy: IPIMC	0				3,11	6	0,6
Italy: ISMAC	0				4,26	0	0,0
Italy: Tuscany	0				0,00	4	0,0
Japan	0				0,00	9	0,0
Northern Netherlands	0				0,17	20	0,1
South America	14	2,72	1,40	4,96	4,08	112	14,0
Total and MH OR	**14**	**2,59**	**1,44**	**4,64**	**1,39**	**204**	**14,7**

5 - VSD and other synthetic anthicolinergic agent

This association is based on 13 cases, all registered in the IPIMC material. The specific OR is 2.57 (CI 95% 1.20-5.20)I. The drug used is always "Spasmex", always used as mild (!?) pregnancy protective (!?)???. The reason why the association is found only in IPIMC material is the same: low prevalence of the drug in other registries or low number of VSD (as discussed for associations number 1 and 4)

6 - Corticosteroids and cleft lip +/- palate

This association has been discussed in detail in a recent paper where, more or less, the same material was analyzed.
Pradat P, Robert-Gnansia E, Di Tanna GL, Rosano A, Lisi A, Mastroiacovo P;Contributors to the MADRE database. First trimester exposure to corticosteroids and oral clefts. Birth Defects Res A Clin Mol Teratol. 2003 Dec;67(12):968-70.

7 - Cleft lip and palate and benzodiazepines

This association has been widely discussed in the literature: Dolovich LR, Addis A, Vaillancourt JM, Power JD, Koren G, Einarson TR. Benzodiazepine use in pregnancy and major malformations or oral cleft: meta-analysis of cohort and case-control studies.BMJ. 1998 Sep 26;317(7162):839-43.
In the MADRE database the association is based on 29 isolated cases (table 6) with M-H OR of 1.84 (1.23-1.75). Five cases were exposed also to antiepileptics.
Using the 24 cases not exposed also to antiepileptics the OR decreases to 1.67 (1.08-2.58). These 24 cases were exposed to: diazepam (3),

oxazepam (5), clorazepam (3), lorazepam (2), bromazepam (4), clobazam (2), prazepam (1) alprazolam (3), unspecified (1). Some of these drugs, more specifically diazepam, lorazepam and clobazam are used sometimes for epilepsy and we know that the use of benzodiazepines is often associated with smoking. This means that the association may be due to confounding factors as maternal epilepsy or smoking. This means also that we (ICBDMS Members) should seriously consider to collect some more information in the MADRE database in the near future..

Table 6: Association between Cleft lip and palate and benzodiazepines. Only registries with at least one exposed case are shown.

Programme	N. exposed Cases	OR	95% Conf.Int	
Japan	3	2,78	0,44	13,25
France: CE	11	1,42	0,67	2,77
Italy: IMER	2	8,19	0,79	44,38
Italy: IPIMC	1	0,58	0,01	3,58
South America	2	1,38	0,16	5,54
France: Paris	4	5,34	1,27	16,92
Northern Netherlands	5	2,04	0,60	5,58
Czech Republic	1	2,70	0,06	20,61
Total and MH OR	**29**	**1,84**	**1,23**	**2,75**

8 - Cleft lip +/- palate (CL(P))and penicillins

This association is based on 60 cases (table 7). Four registries estimate an OR higher than 1.5. The overall M-H OR is 1.49 (CI 95% 1.13-1.98). 51 cases out of 60 have been exposed to ampicillin or amoxicillin alone or in combination with beta-lactamase inhibitors.

Table 7: Association between cleft lip +/- palate (CL(P)) and penicillins

Programme	N. exposed Cases	OR	95% Conf.Int	
Australia	0	0,00	0,00	4,15
Czech Republic	9	2,22	0,88	5,17
France: CE	16	1,76	0,94	3,13
France: Paris	3	1,00	0,19	3,37
Israel	0	.	.	.
Italy: IMER	1	1,17	0,03	7,84
Italy: IPIMC	4	1,11	0,28	3,11
Italy: ISMAC	0	0,00	0,00	.
Italy: Tuscany	0	.	.	.
Japan	3	1,50	0,26	5,83
Northern Netherlands	11	2,00	0,92	4,01
South America	13	1,20	0,61	2,18
Total and M-H OR	60	1,49	1,13	1,98

Because this class of drugs have been extensively studied and is not considered as teratogenic, a more likely explanation is that clefts are linked with either viral disease or hyperthermia. No virus is known to increase the risk for CL(P), but several recent studies suggested that hypethermia/fever may be at risk: Shaw et al (1982) studied interactions between maternal fever and use of vitamines They found, in case of combination of no vitamin use and fever, after adjustment for maternal body

mass index, education and race/ethnicity, an odds ratio of 2.9 (1.4-5.8) for cleft lip with or without cleft palate. Effects tended to be highest among those women who did not use vitamins, had fever, and did not use fever-reducing medications. Botto et al (2002) evaluated whether multivitamin use modified birth defect risks associated with febrile illness. They selected seven defects including cleft lip and palate because of their inverse relation with multivitamin supplement use and defined four exposure categories from combinations of periconceptional multivitamin use (use compared with no use) and febrile illness (early pregnancy compared with no illness). The reference category was no multivitamin use and no illness. Febrile illness with no multivitamin use was associated with generally increased risk for all defects, including orofacial clefts (odds ratio = 1.7). Peterka et al (1994) analysed the retrospective interview data on probable febrile illness during critical period of orofacial clefts development in 992 mothers of infants with orofacial clefts, and found that 24% to 33% of mothers gave a positive answer. They consider the results as a support for the hypothesis of a harmful effect of febrile illness on craniofacial development.

The most interesting findings related to this association is that the M-H OR for penicillins and cleft palate is 0.54 (CI 95% 0.28-1.02). Although a negative association in the MADRE Database must be evaluated on the light of "positive" associations (taken off), it should be carefully evaluated on other samples whether fever is associated to CL(P) only or to any oral cleft.

9 - <u>Hypospadias and 2 amino 1 phenylethanol derivatives, hypospadias and Pregnen 4 derivatives</u>

All cases of hypospadias associated to 2 amino 1 phenylethanol derivatives are associated to isoxsuprine a peripheral vasolidator used (without evidence of efficacy) as "mild" prevention of spontaneous abortion mainly in Italy (table 8). Out of 124 cases involved in this association 112 (90%) have been registered in the three Italian registries. Almost all cases of hypospadias associated to pregnen-4-derivatives are progesterone, a well know drug used as prevention of spontaneous abortion (without evidence of efficacy in most cases) . The possible association between sex hormones and hypospadias has been widely debated in the literature. The current view is that the observed association is biased by subfertility as underlying condition which brings to the use of progesterone as hypothetic pregnancy protector. The findings here reported confirm this hypothesis since the association is also found with isoxsuprine, used as alternative to progesterone. Table 8 shows the distribution of exposed cases among participating programmes and their specific OR.

Table 8: Association between hypospadias and isoxsuprine or with pregnene derivates. Only programmes with at least one exposed case shown.

	Exposed to isoxsuprine				Exposed to pregnene derivatives			
Programme	**Hypospadias N. exposed Cases**	**OR**	**95% Conf.Int**		**Hypospadias N. exposed Cases**	**OR**	**95% Conf.Int**	
France: CE	2	1,76	0,19	7,65	8	4,96	1,87	11,77
Japan	9	3,21	1,20	8,06	0	0,00	0,00	7,77
France: CE	0	.	.	.	8	1,01	0,41	2,14
Italy: IMER	44	1,97	1,24	3,13	5	0,58	0,18	1,50
Italy: IPIMC	65	1,20	0,86	1,66	62	2,13	1,49	3,01
South America	3	0,95	0,19	2,95	1	1,09	0,03	6,89
France: Paris	0	.	.	.	5	0,95	0,28	2,48
Israel	0	.	.	.	2	4,58	0,38	32,77
Italy: ISMAC	3	2,58	0,37	13,51	3	2,05	0,30	10,32
Czech Republic	0	.	.	.	3	0,62	0,12	2,02
Total and M-H OR	**124**	**1,49**	**1,18**	**1,88**	**89**	**1,45**	**1,12**	**1,86**

10 - <u>Spina bifida and folic acid and derivatives</u>

This is an interesting finding showing that the MADRE methodology works well. Out of the 17 cases 8 are registered in France Central East and 7 of them in association with valproic acid. The association in France Central East and in all the material disappears when folic acid is analyzed

without the association with valproic acid. The paradox is so explained: folic acid is more often prescribed to treated epileptic women than to healthy women, and it probably doesn't have a preventive effect on valproate-induced spina bifida.

11 - Hypospadias and folic acid

This association is based on 63 cases (table 9). While in France Central East again, out of 7 cases, 5 were exposed to valproic acid and 1 to progesterone, explaining entirely the association (and paradox !), this does not appear in the other three programmes. Out of 56 cases in the other three programmes, 40 cases are associated to folic acid only. Since we assume that the MADRE methodology works well and gives interesting results, we should try to have good interpretation of the results. This finding raises two reasonable questions: (a) is folic acid more often registered when no other drugs have been taken and the defect is mild; (b) if subfertility is linked to hypospadias, is folic acid used more often by subfertile women ? Is there any other good hypothesis ?

Table 9: Association between hypospadias and folic acid

Programme	N. exposed Cases	OR	95% Conf.Int	
Czech Republic	5	2,98	0,83	8,84
France: CE	7	2,53	0,93	5,88
Northern Netherlands	47	1,35	0,86	2,13
South America	4	1,35	0,35	3,71
Total and M-H OR	**63**	**1,56**	**1,11**	**2,19**

2.1.2 Multiple Congenital Anomalies (MCA), 2002

Jorge Lopez-Camelo (South America, ECLAMC)
Monica Rittler (South America, ECLAMC)

Purpose and rationale

The annual review of cases of multiple congenital anomalies (MCA) is designed as an additional tool to detect increases in birth defect occurrence due to teratogens. Because at least some teratogens (eg. rubella, thalidomide, and retinoic acid) cause MCAs rather than isolated defects, the systematic evaluation of combinations of MCA can be a useful adjunct to standard monitoring, which usually examines one defect at a time. Here we report the occurrence of defects, alone and in combination, in MCA cases.

Methods and data

This year, eleven programmes participated in the annual monitoring of MCA (Table 1), which evaluated birth outcomes that occurred in 2002. Collectively, the eleven programmes provided information on 2,286 cases ascertained among nearly 690,000 births. For each case, programme directors provided a case listing that included a description of the defects. This case information was reviewed and the defects were coded. We then focused on the subset of 1,165 cases of two or more major unrelated defects of unknown etiology (Table 1). These 1,165 cases form the basis of the remainder of the report. Rates were computed using liveborn infants as denominators, although we included stillborn infants among the cases (numerators).

Classification and comparisons

We used a coding system specifically devised for MCA analysis to code and classify defects. These defects were then collapsed into 48 groups (Table 2). To identify unusual MCA occurrences in the current year, we compared rates and MCA patterns for these cases with those in the accumulated baseline of MCA cases born during 1992-2001. We computed rates for each of the 48 MCA components as well as for defect combinations. The latter included all combinations of the 48 defect groups (two- or three-defect combinations), as well as certain combinations that have been

associated with recognized teratogens, such as rubella, retinoic acid and thalidomide. We also searched for new defect combinations, i.e., combinations that had not been seen in the baseline. Statistical significance was determined, based on a p=0.001 cutoff of the appropriate Poisson distribution. In the analysis we focused mainly on combinations of major defects.

Findings and comments

The overall rate of MCA cases (2 or more unrelated defects of unknown etiology) was 16.9 per 10,000 births (Table 1), although rates varied noticeably across programmes. However, because programmes vary in the ascertainment, diagnostic follow-up, and reporting of cases, the comparison of rates between registries is probably not very informative in the absence of further information.

Monitoring of individual component defects is summarized in Table 2. For each defect group we show the observed number among MCA cases and the number of cases expected from the baseline. To assess the extent and impact of rate variations, we present rate ratios and rate differences. From the latter we estimated the number of excess cases observed in 2002; this number will be positive when more cases than expected were observed, and negative when less cases were observed. The table is ordered by these excess number of cases. Finally, we noted which rate variations fell outside Poisson expectations (*p<0.01; **p<0.001). For example, six increases fell beyond the p=0.01, and other six beyond the p=0.001 threshold, while no decrease fell beyond expectations.

Overall, there were nearly 600 more defect occurrences in this period (sum of excess cases) than expected from the baseline. Six defect groups appeared over-represented, namely, congenital heart defects, other urinary tract defects, hypospadias, omphalocele, laryngo-tracheal defects, and vessel anomalies. Two of them, congenital heart defects and other urinary tract anomalies, also surfaced in the evaluation of both two- and three-defect combinations. Laryngo-tracheal anomalies and vessel anomalies only appeared in excess in the two-defect combinations, and omphalocele in the three-defect combinations.

Finally, no increase of patterns attributable to the selected known teratogens were identified.

Summary

The latest review flagged several defect groups, among whom CHD appeared by far as the most outstanding group, perhaps indicating a better ascertainment and diagnosis of the anomalies. No increase in MCA patterns associated with known teratogens was noted.

Table 1: Cases and rates of multiple congenital anomalies (MCA) by source and type, ICBDMS

Registry	Births	Total cases evaluated	Cases of known etiology	< 2 major defects	2 or more	
					Number	Rate
Canada: British Columbia	40201	363	53	209	101	25.1
Finland	55768	141	57	15	69	12.4
France: Central East	107008	218	49	26	143	13.4
France: Paris	38700	68	1	4	63	16.3
France: Strasbourg	13481	41	6	1	34	25.2
Israel	23117	38	2	9	27	11.7
Italy: Emilia Romagna	26010	46	1	15	30	11.5
Japan	89255	579	189	249	141	15.8
Mexico: RYVEMCE	21830	34	9	7	18	8.2
South America: ECLAMC	223305	620	97	77	446	19.9
USA: Atlanta	51174	138	38	7	93	18.2
TOTAL	**689849**	**2286**	**502**	**619**	**1165**	**16.9**

Table 2: Occurrence of component defects in MCA patterns and comparison with baseline, ICBDMS

Defect group	Observed	Expected	Rate Ratio	Rate Difference	Excess	Poisson
Congenital heart defect	517	353.1	1.5	23.8	163.9	**
Other urinary tract defect	215	126.5	1.7	12.8	88.5	**
Hypospadias	86	52.5	1.6	4.9	33.5	**
Anorectal atresia	136	104.1	1.3	4.6	32.0	*
Esophageal atresia	112	80.5	1.4	4.6	31.6	*
Cleft lip+/-palate	125	97.2	1.3	4.0	27.8	*
Renal a/dysgenesis	85	58.0	1.5	3.9	27.0	*
Omphalocele	72	46.0	1.6	3.8	26.0	**
Other brain defect	94	70.4	1.3	3.4	23.6	*
Diaphragmatic hernia	59	42.9	1.4	2.3	16.1	
Other axial skeleton defect	106	91.7	1.2	2.1	14.3	
Severe genitalia defect	74	60.2	1.2	2.0	13.8	
Limb reduction defect, preaxial	42	29.3	1.4	1.8	12.7	
Limb reduction defect	32	19.9	1.6	1.8	12.1	
Duodenal atresia	26	14.6	1.8	1.7	11.4	*
Laryngeo-tracheal defect	17	6.1	2.8	1.6	10.9	**
Situs inversus	20	10.6	1.9	1.4	9.4	
Other ear anomaly	17	8.3	2.1	1.3	8.7	
Vessel anomaly	9	1.0	9.2	1.2	8.0	**
A/polysplenia	20	12.0	1.7	1.2	8.0	
Polydactyly	90	82.4	1.1	1.1	7.6	
Other small intestinal atresia	45	38.6	1.2	0.9	6.5	
Cystic kidney	43	37.2	1.2	0.8	5.8	
Choanal atresia	18	12.4	1.5	0.8	5.6	
Anencephaly	19	14.2	1.3	0.7	4.8	
Spina Bifida	41	36.8	1.1	0.6	4.2	
Holoprosencephaly	17	13.4	1.3	0.5	3.6	
An-microphtalmia	34	30.5	1.1	0.5	3.5	
Neck anomaly	16	12.6	1.3	0.5	3.4	
Other eye anomaly	33	29.9	1.1	0.4	3.1	
Cleft palate	75	72.0	1.0	0.4	3.0	
Syndactyly	33	30.1	1.1	0.4	2.9	
Lumbo-sacral axial skeleton def.	8	7.3	1.1	0.1	0.7	
Broncho-pulmonary defect	40	40.3	1.0	0.0	-0.3	
Teratoma, sirenomelia	5	5.3	0.9	0.0	-0.3	
Deformation	130	131.0	1.0	-0.1	-1.0	
Encephalocele	18	19.5	0.9	-0.2	-1.5	
Craniostenosis	8	9.6	0.8	-0.2	-1.6	
Gut malrotation	10	11.8	0.8	-0.3	-1.8	
Microcephaly	38	40.3	0.9	-0.3	-2.3	
Other severe craniofacial defect	18	20.3	0.9	-0.3	-2.3	
Limb reduction defect, other type	28	30.7	0.9	-0.4	-2.7	
Hydrocephaly	81	85.6	0.9	-0.7	-4.6	
Gastroschisis	11	16.3	0.7	-0.8	-5.3	
An-microtia	43	48.6	0.9	-0.8	-5.6	
Bladder extrophy/epispadias	3	10.6	0.3	-1.1	-7.6	

Table 3: Two-defect combinations among MCA cases, ICBDMS, 2002

Defect combinations	Observed	Expected	Rate	Rate	Excess	Poisson
	No.	No.	Ratio	Difference	no. cases	flag
Congenital heart defect + other urinary tract defect	83	52.7	1.6	10.5	30.3	**
Laryngo-tracheal defect + congenital heart defect	14	2.7	5.2	1.9	11.3	**
Cleft lip +/- cleft palate + other urinary tract defect	15	4.9	3.1	2.1	10.1	**
An-microphthalmia + congenital heart defect	5	0.6	8.3	0.7	4.4	**
Vessel anomaly + other urinary tract defect	3	0			3	**
Omphalocele and syndactyly	3	0,6	4,9	0,4	2,4	**

Table 4: Three-defect combinations among MCA cases, ICBDMS, 2002

Defect combinations	Observed	Expected	Rate	Rate	Excess	Poisson
	No.	No.	Ratio	Difference	no. cases	flag
Congenital heart defect + limb reduction defect + other axial skeleton defect	11	2.9	3.8	1.5	8.1	**
Cleft palate + other urinary tract defect + other axial skeleton defect	5	0.2	25	0.7	4.8	**
Esophageal atresia + other small intestinal atresia + other urinary tract defect	4	0.2	20	0.6	3.8	**
Other small intestinal atresia + oth urinary tract defect + oth axial skeleton defect	4	0.2	20	0.6	3.8	**
Congenital heart defect + cystic kidney + polydactyly	3	0			3	**
Cleft palate + anorectal atresia + syndactyly	3	0			3	**
Neck anomaly + omphalocele + congenital heart defect	3	0			3	**

2.1.3 Prenatal diagnosis and Down Syndrome, 2002

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Introduction

The "Prenatal Diagnosis Committee" (PDC) of the International Clearinghouse, has had the responsibility, since 1993, for a specific analysis of prenatal diagnosis of Down Syndrome (DS). The aim of the survey is to assess the progressive increase in use and spread of prenatal diagnostic techniques and the impact of elective termination on prevalence rates at birth of DS, in countries where elective abortions are performed.

Participation in the Clearinghouse programmes worldwide provides a unique opportunity to analyse international variations on the use of prenatal diagnosis (Chorion Villus Sampling = CVS, Amniocentesis = AC, Cordocentesis= CC), and access to screening, as well as differences in advice and abortion legislation. In addition, repeating this study over time has made it possible to follow the evolution of these techniques and to evaluate the impact of each practice on the prevalence of DS.

2002 Data

During 2002, 17 programmes (one more than last year) provided data on 2331 DS newborns, 1287 of them (54.1%) were prenatally diagnosed and terminated (Table 1).

The total number of births under surveillance in 2001 was 1,390,037.

The percentage of terminations of pregnancy (ToP) ranged from the lowest values in Northern Netherlands (10.0 %), USA:Atlanta (22.9%) and Canada: Alberta (25.8%), to the highest in France: Paris and Strasbourg, that reached 84.0% and 85.2% respectively (Table 2). Other Registries show percentages of terminations over 60%: Australia:Victoria (62.4%), Czech Republic (67.1%) and two Italian Registries: IMER and Tuscany (61.9% and 76.2% respectively).
In the European registries that provided a data set of 10 years (1993-2002), a regular increase in the percentage of ToP has been observed: 41.5% in 1993, 45.9% in 1994, 48.5% in 1995, 50.9% in 1996, 52.2% in 1997, 53.8% in 1998, 55.2% in 1999, 57.8% in 2000, 57.1% in 2001 and 58.7% in 2002. The comparison of the rate of ToP in 2002, between European Countries and non-European Countries (i.e. Australia:Victoria, Canada:Alberta and USA:Atlanta) is significantly different (58.8% vs 44.9% , c2 = 175.91 p< 0.001)
The terminations are related to the maternal age as shown in Table 2: the percentage of ToPs is lower in the lowest maternal age class (<=29 years) as in USA:Atlanta: 4.5%, and in Scandinavian Countries: Sweden: 17.9% and Finland: 18.2% and in some Italian registries as Italy:North-East (20%) and Italy:BDRCam (29.4%). On the contrary in the higher maternal age classes: i.e. over 35 years (38-39 and >= 40) the percentage of terminations is higher: some registries show percentages of ToPs of about 80-90% (Czech Republic: 90.9% and 77.8%; France:Paris 90.3% and 84.0%; France:Central-East: 100% and 76.6%, Italy:Tuscany: 75.0% and 94.4%).

Overall, the proportion of DS pregnancies which were terminated among women at higher risk (≥35 years old), was over 80% in the France Registries: Strasbourg, Paris and Central-East (87.5, 85.7 and 85.6% respectively), in two Italian Registries: Tuscany (86.7%) and IMER (84.6%) and in Czech Republic (82.7%) while percentages of ToPs less than 40% were observed in Germany-Saxony-Anhalt (35.7%), Canada:Alberta (35.1%) and USA:Atlanta (31.0%). The lowest percentage of ToPs in mothers aged 35 and over, was observed in the Northern-Netherlands Registry: 7.7% (Table 3).

In the Registries that provided a data set for 10 years (1993-2002), a regular increase in the percentage of ToP was observed. The increase is seen in both groups of maternal age: younger (<35 years) and older (≥35 years) women, although the majority of ToPs occur in the older group: 854/1287 (66.4%) The impact of prenatal diagnosis over time is less evident in the older mothers: 63% in 1993, 65.3% in 1994, 65.4% in 1995, 66.0% in 1996, 67.7% in 1997, 65.3% in 1998, 68.3% in 1999, 64.7% in 2000, 69.2% in 2001 and 66.4% in 2002. In the group of younger mothers (<35 years) the increase of ToP through the years is more evident: 24.7% in 1993, 31.2% in 1994, 33.3% in 1995, 36.3% in 1996, 39.4% in 1997, 43.6% in 1998, 45.5% in 1999, 41.9% in 2000, 44.4% in 2001 and 41.1% in 2002.
This significant trend (p<0.001) in the younger group may be explained by a better identification of women who may be at risk from factors other than maternal age, as in England and Wales (OSCAR Project) and in France. It may also be due to a better knowledge of ultrasonographic signs in the first trimester (i.e. NT screening) and consequently a better yield of routine ultrasound, or it may be related to multiple-marker screening in other countries. This may explain the increased detection in the younger group of women.

The most common technique of prenatal diagnosis remained amniocentesis in 2002 (Table 4), with a mean value of 68.4%. CVS, with a mean value of 28.6% has a progressive increase year by year: 18.3% in 1995, 19.0% in 1996, 19.3% in 1997, 18.2% in 1998, 20.2% in 1999 and 21.8% in 2000, 22.9% in 2001 and 28.6 in 2002.
In Australia:Victoria CVS is the first technique of prenatal detection used with a rate of 65.5%, while AC is less used. CVS has been used mainly in England and Wales (44%) and in Finland (35.4%). In the Registries of France the mean percentage is 19.2% while the mean value in Italy is 9.4%. The programmes, where CVS is more frequently adopted, show the lowest mean gestational ages at pregnancy termination in the older maternal age group (≥35) as in Australia:Victoria (14.2±2.4wks) and in England and Wales (15.6±3.0wks) (Table 5).
The mean age (wks) of terminations is heterogeneous and significantly different among the programs in both maternal age groups. In the younger group (<35 years) there is a lower limit of 15.4±2.3 wks in Australia:Victoria, to an upper limit of 21 and over in USA.Atlanta , Italy:BDRCam, Israel:IBDMS and France:Central East. (Table 5).

The prevalence at birth of DS has decreased over the past 10 years in the majority of the programmes: Czech Republic, all three registries of France (Central-East, Paris and Strasbourg), and all four Italian registries (Campania, IMER, North East and Tuscany) (Table 6) . These are the programmes that showed the highest rate of terminations and an increase in the terminations year by year. In the same way the highest rates of prevalence at birth were observed in the Programmes where terminations were lowest (Canada:Alberta and USA:Atlanta). Controversial data are showed by Scandinavian Registries where despite quite a high rate of ToP (about 45% see Table 2) it is possible to observe high rates of prevalence at birth, respectively 13.31 per 10.000 in Sweden and 14.16 in Finland.

Table 1. List of the programs participating in the Prenatal Diagnosis Study in the years.

	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002
AUSTRALIA: Victoria	X	X	X	X	X	X				X
CANADA: Alberta					X	X	X	X	X	X
CZECH REPUBLIC	X	X	X	X	X	X	X	X	X	X
ENGLAND & WALES	X	X	X	X	X	X	X	X	X	X
FINLAND	X	X	X	X	X	X	X	X		X
FRANCE: Central-East	X	X	X	X	X	X	X	X	X	X
FRANCE: Paris	X	X	X	X	X	X	X	X	X	X
FRANCE: Strasbourg	X	X	X	X	X	X	X	X	X	X
GERMANY: Saxony–Anhalt								X	X	X
ISRAEL: IBDMS	X	X	X	X	X	X	X	X	X	X
ITALY: BDRCam	X	X	X	X	X	X	X	X	X	X
ITALY: IMER	X	X	X	X	X	X	X	X	X	X
ITALY: North-East	X	X	X	X	X	X	X	X	X	X
ITALY: Tuscany	X	X	X	X	X	X	X	X	X	X
Northern Netherlands	X	X	X	X	X	X	X	X	X	X
SWEDEN								X	X	X
USA: Atlanata	X	X	X	X	X	X	X	X	X	X

Table 2. Percentage (%) of terminations (ToP) among the total number of cases recorded in 2002

Monitoring Program	Maternal Age (years)					
	<= 29	30 – 34	35 – 37	38 – 39	>= 40	Total
Australia: Victoria	33.0	56.8	68.1	82.1	67.6	62.4
Canada: Alberta	26.7	0	38.5	14.3	60.0	25.8
Czech Republic	58.1	65.7	82.6	90.9	77.8	67.1
England & Wales	32.4	47.8	59.8	66.4	58.2	51.2
Finland	18.2	40.7	29.4	69.6	64.1	45.5
France: Central East	64.4	84.3	86.1	100	76.6	75.0
France: Paris	68.8	86.2	83.3	90.3	84.0	84.0
France: Strasbourg	66.7	100	100	75.0	83.3	85.2
Germany: Saxony–Anhalt	28.6	60.0	40.0	0	42.9	40.7
Israel: IBDMS	50.0	20.0	87.5	50.0	56.0	
Italy: BDRCam	29.4	50.0	46.7	55.6	81.8	50.7
Italy: IMER	40.0	18.2	100	80.0	75.0	61.9
Italy: North East	20.0	43.8	77.8	63.6	46.4	
Italy: Tuscany	0	85.7	75.0	75.0	94.4	76.2
Northern Netherlands	0	11.1	0	0	16.7	10.0
Sweden	17.9	17.9	70.8	55.2	78.0	45.8
USA: Atlanta	4.5	22.2	37.5	27.3	26.7	22.9

Table 3. Percentage of mothers aged 35 and over in the monitoring programs participating in the study and percentage of terminations (ToP) in the same group of mothers.Prevalence rate in live and stillbirths (per 10,000) and comparison with the rate after inclusion of ToP

Monitoring Program	% of mothers	% of ToP in mothers	Prevalence rate (* 10,000)	
	aged >=35	aged >=35	L+S	L+S+ToP
Australia: Victoria	20.6	71.6	23.8	83.6
Canada: Alberta	14.5	35.1	42.8	66.0
Czech Republic	7.3	82.7	13.3	77.1
England & Wales	18.1	61.1	14.2	36.5
Finland	19.4	53.1	41.6	88.8
France: Central East	17.7	85.6	9.0	62.4
France: Paris	28.0	85.7	13.8	96.8
France: Strasbourg	14.7	87.5	10.1	80.5
Germany: Saxony-Anhalt	10.9	35.7	20.9	73.0
Israel: IBDMS	15.8	71.4	10.9	38.2
Italy: BDRCam	19.1	60.0	11.7	29.2
Italy: IMER	24.1	84.6	6.4	41.5
Italy: Tuscany	25.5	86.7	4.4	44.3
Northern Netherlands	19.4	7.7	30.5	33.0
Sweden	18.6	70.1	21.2	71.0
USA: Atlanta	16.4	31.0	34.6	50.2

* estimated

Table 4 . Down Syndrome techniques of prenatal diagnosis (number of cases) registered in 2002 grouped in maternal age classes.

Monitoring Program	<35				35-39				>39				Tot*			
	CVS	AC	CC	UK	CVS	AC	CC	UK	CVS	AC	CC	UK	CVS	AC	CC	UK
Australia:Victoria	15	16	0	0	39	15	0	1	17	6	0	0	72	38	0	1
Canada: Alberta	0	1	0	3	1	5	0	1	0	4	0	2	1	10	0	6
Czech Republic	0	57	2	0	0	28	1	0	0	14	0	0	0	99	3	0
England & Wales	52	63	11	4	67	69	15	2	39	38	5	7	158	170	31	13
Finland	2	13	0	0	7	18	0	1	14	11	0	0	23	42	0	1
France: Central East	10	51	1	10	3	53	1	8	3	32	0	1	16	136	2	19
France: Paris	9	27	0	0	13	35	0	0	10	31	0	1	32	93	0	1
France: Strasbourg	4	5	0	0	3	6	0	0	3	2	0	0	10	13	0	0
Germany:Saxony-Anhalt	0	5	0	0	2	2	0	0	0	1	0	0	2	9	0	0
Israel: IBDMS	1	3	0	0	0	7	0	0	0	3	0	0	1	13	0	0
Italy: BDRCam	0	11	0	0	0	12	0	0	0	9	0	0	0	35	0	0
Italy: IMER	1	3	0	0	2	11	0	0	4	5	0	0	7	19	0	0
Italy: Tuscany	1	5	0	6	0	9	0	3	0	17	0	1	1	31	0	10
Northern Netherlands	0	1	0	0	0	0	0	0	1	0	0	0	1	1	0	0
Sweden	8	11	0	0	4	46	0	0	5	34	0	0	17	91	0	0
USA: Atlanta	0	5	0	0	1	9	0	0	0	4	0	0	1	18	0	0
Total	103	277	14	23	142	325	17	16	96	211	5	12	342	818	36	51

CVS = Chorion Villus sampling
AC = Amniocentesis
CC = Chordocentesis
UK = Unknown
*+casi con età materna non nota

Table 5. Mean gestational age (weeks) and Standard Deviation of induced abortions by maternal age group and by type of prenatal diagnosis.

Monitoring Program	<35			>=35		
	CVS	AC	Total	CVS	AC	Total
Australia:Victoria	13.60±1.45	17.19±1.42	15.45±2.31	13.08±1.49	17.35±1.46	14.26±2.43
Canada: Alberta	-	22.00±0	22.00±0	16.00±0	18.00±0.50	17.80±0.79
Czech Republic	-	20.15±1.92	20.15±1.92	-	20.00±1.74	20.00±1.74
England & Wales	13.71±1.79	19.59±2.69	16.93±3.74	13.40±1.31	18.09±2.30	15.65±2.97
Finland	17.00±1.41	18.92±2.81	18.67±2.72	14.00±1.52	17.55±1.15	16.06±2.20
France: Central East	14.50±2.17	22.58±5.19	21.06±5.73	14.80±0.45	19.52±2.97	19.20±3.11
France: Paris	13.11±0.93	21.59±5.29	19.47±5.91	13.65±1.15	20.88±4.28	18.94±4.91
France: Strasbourg	17.00±1.41	22.00±6.20	19.78±5.19	15.17±1.60	20.13±2.85	18.00±3.44
Germany: Saxony-Anhalt	-	18.80±1.48	18.80±1.48	13.00±1.41	18.33±3.79	16.20±4.02
Israel: IBDMS	20.00±0	21.67±2.89	21.25±2.50	-	23.70±3.13	23.70±3.13
Italy: BDRCam	-	21.75±1.49	21.75±1.49	-	20.80±0.95	20.80±0.95
Italy: IMER	15.0±0	20.33±2.08	19.00±3.16	13.67±1.51	18.69±1.35	17.32±2.66
Italy: Tuscany	14.00±0	19.60±1.34	18.67±2.58	-	18.42±1.36	18.42±1.36
N. Netherlands	13.00±0	-	13.00±0	-	18.00±.	18.00±0
USA: Atlanta	-	21.80±1.30	21.80±1.30	12.0±0	18.57±1.40	17.75±2.66

Table 6. Prevalence at birth (x 10,000) in the years of DS in the programs participating in the survey.

	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002
Australia:Victoria										9.98
Canada: Alberta	11.45	11.07	13.15	8.49	11.14	14.02	11.56	14.65	15.2	12.71
Czech Republic	7.52	7.67	7.26	5.51	5.06	6.72	6.57	5.37	5.51	5.37
England & Wales	4.59	4.73	4.91	5.50	6.39	7.18	6.71	6.60	6.27	5.9
Finland	13.21	12.83	12.94	10.33	10.07	11.33	10.04	11.76	14.18	14.16
France: Central East	10.98	10.43	8.91	9.47	9.01	6.83	4.86	5.83	5.85	5.51
France: Paris	10.61	9.19	7.05	9.67	7.78	10.48	5.24	7.87	7.79	6.20
France: Strasbourg	16.75	17.87	24.04	17.44	27.95	2.20	4.34	5.62	2.23	2.96
Germany: Saxony-Anhalt	5.79	6.33	7.43	7.86	8.33	13.65	6.09	6.38	8.26	9.08
Israel: IBDMS	5.06	5.03	6.32	4.87	9.13	3.28	6.01	4.74	6.15	4.75
Italy: BDRCam	10.94	7.63	10.01	9.22	6.74	8.73	6.33	2.99	6.83	5.42
Italy: IMER	8.97	9.27	10.24	7.97	7.27	9.36	9.58	6.47	6.33	6.15
Italy: North East	12.87	10.31	11.46	9.14	7.15	7.23	7.17	6.90	7.83	9.04
Italy: Tuscany	11.83	9.80	11.42	6.91	7.34	6.28	6.14	4.90	5.70	3.76
Northern Netherlands	9.86	5.74	9.38	13.74	11.91	10.03	8.43	6.35	9.32	13.31
Sweden							14.01	11.01	14.59	13.31
USA: Atlanta	12.02	13.81	10.93	11.98	10.49	11.46	12.00	11.08	13.25	12:56

2.2 Ad Hoc Projects

2.2.1 Gender and congenital malformations: an international perspective

Alessandra Lisi (ICBD, Rome)

The study evaluated the sex distribution of major isolated malformations and common trisomies among a large and geographically varied sample. Eighteen registries from 24 countries contributed cases, which were centrally reviewed and classified in three clinical types as isolated, associated, or syndromic. We selected cases of 26 major defects (n.108,534); trisomy 21, 18, and 13 (n.30,114); other syndromes (n.2,898); and multiple congenital anomalies (n.24,197), for a total of 165,743 cases. We observed a significant deviation of sex distribution (compared to a sex ratio of 1.06 or male proportion of 51.4%) for 24 of the 29 groups (a maleexcess in 16, a female excess in 8), and in 8 of such groups these estimates varied significantly across registries. A male excess was noted for two left obstructive cardiac defects (hypoplastic left heart and coarctation of the aorta) and a female excess for all the main types of neural tube defects. A male excess was seen for omphalocele but not gastroschisis. For neural tube defects the female excess tended to be stronger in areas with historically high prevalence for these defects. For 15 of the 26 birth defects the sex distribution differed among isolated, associated, and syndromic cases. Some of these epidemiologic commonalities are consistent with know or putative developmental processes. Further, the geographical variation for some defects may reflect local prevalences rates and risk factors. Finally, the findings underscore the need for clinical classification (e.g. into isolated, multiple, syndromes) in studies of birth defects.

3.1 World Health Organization

The International Clearinghouse for Birth Defects Monitoring Systems (ICBDMS) is a non-governmental organisation with an official relation with the World Health Organization. WHO is represented at Annual Meetings of the ICBDMS by Dr Victor Boulyzhenkov, Director of Human Genetics Program.
WHO supports the Annual Meeting of the ICBDMS.

The World Atlas of Birth Defects – 2nd Edition was published in April 2003 in collaboration with European Surveillance of Congenital Anomalies (EUROCAT) and in cooperation with Human Genetics Program – WHO. The aim of this second edition is to provide to the users tables and maps to illustrate the actual prevalence of congenital malformations in the world, using the data collected by the ICBDMS and EUROCAT throughout the period 1993-1998.

In October 2002 an agreement between WHO – Human Genetic Program and ICBD was signed to develop an International Database on Cranio-Facial Anomalies (IDCFA)

3.2 European Surveillance of Congenital Anomalies (EUROCAT)

Funded by the Public Health Programme of the European Commission Public Health Directorate
WHO Collaborating Centre for the Epidemiologic Surveillance of Congenital Anomalies

What is EUROCAT?

- European Network of population-based registries for the epidemiologic surveillance of congenital anomalies.
- Started in 1979.
- Over 1.2 million births per year in Europe surveyed by 40 registries in 19 ountries of Europe, more than one quarter of European Union births.
- Standardised central database on more than 300,000 cases of congenital anomaly among livebirths, stillbirths and terminations of pregnancy, updated every year.

The objectives of EUROCAT

- To provide essential epidemiologic information on congenital anomalies in Europe.
- To facilitate the early warning of teratogenic exposures.
- To evaluate the effectiveness of primary prevention.
- To assess the impact of developments in prenatal screening.
- To act as an information and resource centre regarding clusters, exposures or risk factors of concern.
- To provide a ready collaborative network and infrastructure for research related to the causes and prevention of congenital anomalies and the treatment and care of affected children.
- To act as a catalyst for the setting up of registries throughout Europe collecting comparable, standardised data.

Available on the website

Member registry descriptions
(www.eurocat.ulster.ac.uk/memberreg/memberreg.html)
1980-2002 Prevalence Data Tables: Prevalence rates of 88 congenital anomaly subgroups (livebirths, stillbirths and terminations of pregnancy following prenatal diagnosis), in customized tables for the years and registers of user's choice ***(www.eurocat.ulster.ac.uk/pubdata/tables.html)***
Cluster Advisory Service: collected experience on how to investigate a cluster of congenital anomalies and an extensive literature review of environmental risk factors ***(www.eurocat.ulster.ac.uk/clusteradservice.html)*** EUROCAT Special Report ***(www.eurocat.ulster.ac.uk/pubdata/)*** and publications on a variety of subjects including assessment of the prevention of neural tube defects in Europe.
Revised Guide 3: For the Description and Classification of Congenital Limb Defects ***(www.eurocat.ulster.ac.uk/pubdata)***

3 Relations with other Organisations

News

Available soon on the website: EUROCAT Guide 1.3 : revised instructions for registration and revised common dataset (for all births from 2005) ; EUROCAT Guide 6: Guide to Coding of Syndromes; A report on prenatal diagnosis policies in each European country.
8th European Symposium on the Prevention of Congenital Anomalies. Poznan, Poland, 10 June 2005. All welcome. Abstract submission via ***www.rejestrwad.pl***
EUROCAT Steering Committee 2004-5: D Lillis (Ireland, President of the EUROCAT Association), H Dolk (UK, EUROCAT Project Leader), L Abramsky (UK), I Barisic (Croatia), F Bianchi (Italy), E Calzolari (Italy), C de Vigan (France), E Garne (Denmark), A Latos-Bielenska (Poland) and A Queisser-Luft (Germany)

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The International Clearinghouse Strategic Direction

John A. Harris M.D.,M.P.H., California Birth Defects Monitoring Program
Barry Borman Ph. D., Public Health Intelligence, New Zealand

Background

The International Clearinghouse for Birth Defects Monitoring Systems (ICBDMS) was founded in 1974, post thalidomide tragedy, to enable monitoring of major structural congenital anomalies among interested programs throughout the world. On the occasion of the organization's 30th anniversary, under the chairmanship of one of the authors (B.B.), the ICBDMS initiated a strategic planning process in order to critically examine current activities and to redirect its efforts going forward. The Strategic Planning Team (SPT) consisted of a selective group of committed Program Directors* with diverse opinions. As is the case with any strategic planning process, the lessons learned about past activities—both strengths and weaknesses—were uncovered as a way to inform future direction.

30 Year Lessons Learned, 1974-2004

First, monitoring congenital anomalies and publishing the demographics of who is at risk among large populations throughout the world has been an important first step. However, going forward, "surveillance" of birth defects needs to become the critical activity for Clearinghouse members. The SPT defined "monitoring" as an activity for which the primary task is accurately counting. "Surveillance," on the other hand, begins with counting, but involves systematic public health **action** as follow up. This **action** could be etiologic research, advocacy, educating policy makers, or assessing the effectiveness of interventions like folic acid fortification.

Second, conducting etiologic research, while an activity of some individual Clearinghouse members, has been under-emphasized by the Clearinghouse as an organization. Since congenital anomalies are common—approximately 1 in 33 live births—and causes are mostly unknown, the only way to develop effective prevention strategies in the future is to increase understanding about **why** congenital anomalies occur.

Third, between 1974 and 2004 the Clearinghouse had as membership criteria that programs must monitor structural congenital anomalies. Many organizations that were effectively monitoring other common children's disabilities with high morbidity, such as prematurity or cerebral palsy, have not been part of the Clearinghouse.

Fourth, quarterly statistical surveillance and investigation of clusters of congenital anomalies, while useful services to communities, have not in 30 years of Clearinghouse operation resulted in the discovery of even one cause of any structural congenital anomaly anywhere in the world.

Strategic Direction of the Clearinghouse, 2004 Going Forward

The Clearinghouse has provided an invaluable international forum where population-based data on structural congenital anomalies has been compiled, exchanged and published. These activities will continue. However, going forward the SPT recommended the following changes, subject to member ratification:

1. Surveillance rather than monitoring will be emphasized.
2. Non Clearinghouse researchers will be invited to collaborate with Clearinghouse members to utilize the diverse population-based data, the core strength of Clearinghouse programs, to test important research hypotheses.
3. Surveillance programs, which include children's disabilities other than structural congenital anomalies, will be invited to join the Clearinghouse.
4. There will be less emphasis on quarterly statistical monitoring and more emphasis on constant communication among Clearinghouse members.
5. The name of the organization will be changed to the International Clearinghouse for Birth Defects Surveillance and Research to reflect the strategic direction.

* Acknowledgments. We would like to acknowledge the following Clearinghouse members involved in the Strategic Planning Team: Chairman, Barry Borman – New Zealand; Participants, Eduardo Castilla- Brazil and Argentina, Hermien de Walle- Netherlands, David Erickson- United States, Miriam Gatt- Malta, Lorentz Irgens- Norway, Brian Lowry- Canada, Pierpaolo Mastriocova- Italy, Elisabeth Robert- France; Facilitator, John Harris- United States.

Monitoring Program	Coverage	Year Joined ICBDMS	Maximum age at diagnosis	Criteria defining stillbirths
Australia: National	Population-based National	1981	1 year	20 weeks or 400 grams
Australia:VBDR	Population-based Statewide	2002	Up to 15 years	20 weeks or 400 grams
Australia: WABDR	Population-based Regional	2002	Up to 6 years	20 weeks or 400 grams
Canada: Alberta	Population-based Provincial	1996	1 year	20 weeks or 500 grams
Canada British Columbia	Population-based Provincial	2001	No limit	At least 20 weeks or 500 grams
Canada National	Population-based National	1996	1 year	20 weeks or 500 grams
Chile-Maule	Hospital-based Regional	2003		
China: Beijing	Population-based Four Provinces	1997	6 weeks	20 weeks
China: CBDMN	Hospital-based	1985	7 days	28 weeks
Costa Rica: CREC	Population-based National	2003	3 days	22 weeks or 500 grams
Cuba	Hospital based National	2003	Hospital discharge	500 grams
Czech Republic	Population-based National	1974	Up to 15 years	non-viable fetuses, 28 weeks or >1000 grams
England and Wales	Population-based National	1974	1995 onwards no limit	24 weeks
Finland	Population-based National	1974	1 year	22 weeks or 500 grams
France: Central-East	Population-based Regional	1974	1 year	22 weeks
France: Paris	Population-based Regional	1982	Hospital discharge	22 weeks
France: Strasbourg	Population-based Regional	1982	1 year	26 weeks
Germany: Saxony-Anhalt	Population-based (Federal State)	2001	Hospital discharge (first week of life)	< 500 grams
Hungary	Population-based National	1974	1 year	24 weeks or 500 grams
Ireland: Dublin	Population-based Regional	1997	5 years	24 weeks or 500 grams
Israel: IBDMS	Hospital-based Regional	1974	Hospital discharge 2-5 days	20weeks
Italy: BDRCam	Population-based Regional	1996	7 days	180 days (25 weeks + 5 days)
Italy: IMER	Population-based Regional	1985	7 days	180 days (25 weeks + 5 days)
Italy: ISMAC	Hospital-based Regional	1991	1 year	180 days (25 weeks + 5 days)
Italy: North East	Population-based Regional	1997	7 days	180 days (25 weeks + 5 days)
Italy: Tuscany	Population-based Regional	1998	1 year	180 days (25 weeks + 5 days)
Japan: JAOG	Hospital-based National	1988	7 days	22 weeks
Malta	Population-based National	2000	1 year	20 weeks
Mexico: RYVEMCE	Population-based National	1980	72 hours	20 weeks or 500 grams
New Zealand	Population-based National	1979	1 year	20 weeks or 400 grams
Northern Netherlands	Population-based Regional	1993	No limit	24 weeks
Norway	Population-based National	1974	Hospital discharge Lifelong for mortality (from 2002 1 year)	16 weeks (12 weeks from 1999)
Russia Moscow Region	Population-based Regional	2001	1 year	28 weeks
South Africa: SABDSS	Hospital-based	1992	Hospital discharge (usually 4 days)	Stillbirths not recorded
South America: ECLAMC	Hospital-based Multinational	1977	3 days	500 grams
Spain: ECEMC	Hospital-based National	1979	3 days	24 weeks or 500 grams
Sweden	Population-based National	1974	28 days	22 weeks
Ukraine	Population-based Regional	2001	7 days	500 grams
United Arab Emirates	Hospital-based Regional	1995	7 days	23 weeks
USA: Atlanta	Population-based Regional	1974	6 years	20 weeks

The following definitions have been adopted by all monitoring systems except when indicated in the Table 7.1

1. Anencephaly: a congenital malformation characterized by the total or partial absence of the cranial vault, the covering skin, and the brain missing or reduced to small mass. Incl. craniorachischisis. Incl. infants with iniencephaly and other neural tube defects as encephalocele or open spina bifida, when associated with anencephaly. Excl. acephaly, that is, absence of head observed in amorphous acardiac twins.

2. Spina bifida: a family of congenital malformation defects in the closure of the spinal column characterized by herniation or exposure of the spinal cord and/or meninges through an incompletely closed spine. Incl. meningocele, meningomyelocele, myelocele, myelomeningocele, rachischisis. Spina bifida is not counted when present with anencephaly. Excl. spina bifida occulta, sacrococcygeal teratoma without dysraphism .

3. Encephalocele: a congenital malformation characterized by herniation of the brain and/or meninges through a defect in the skull. Encephalocele is not counted when present with spina bifida.

4. Microcephaly: a congenitally small cranium, defined by an occipito-frontal circumference (OFC) 3 standard deviation below the age- and sex-appropriate distribution curves. [If using a different definition or cut-off point (e.g., 2 standard deviations), report but specify criteria]. Excl. microcephaly associated with anencephaly or encephalocele.

5. **Arhinencephaly/holoprosencephaly**: a congenital malformation of the brain, characterized by various degrees of incomplete lobation of the brain hemispheres. Olfactory nerve tract may be absent. Holoprosencephaly includes cyclopia, ethmocephaly, cebocephaly, and premaxillary agenesis.

6. Hydrocephaly: a congenital malformation characterized by dilatation of the cerebral ventricles, not associated with a primary brain atrophy, with or without enlargement of the head, and diagnosed at birth. Not counted when present with encephalocele or spina bifida. Excl. macrocephaly without dilatation of ventricular system, skull of macerated fetus, hydranencephaly, holoprosencephaly, and postnatally acquired hydrocephalus.

7. Anophthalmos/microphthalmos: apparently absent or small eyes. Some normal adnexal elements and eyelids are usually present. In microphthalmia, the corneal diameter is usually less than 10 mm. and the antero-posterior diameter of the globe is less than 20 mm.

8. Anotia/microtia: a congenital malformation characterized by absent parts of the pinna (with or without atresia of the ear canal) commonly expressed in grades (I-IV) of which the extreme form (grade IV) is anotia, absence of pinna.
Excl. small, normally shaped ears, imperforate auditory meatus with a normal pinna, dysplastic and low set ears.

9. Transposition of great vessels: a cardiac defect where the aorta exits from the right ventricle and the pulmonary artery from the left ventricle, with or without other cardiac defects. Incl. double outlet ventricle so-called corrected transposition.

10. Tetralogy of Fallot: a condition characterized by ventricular septal defect, overriding aorta, infundibular pulmonary stenosis, and often right ventricular hypertrophy.

11. Hypoplastic left heart syndrome: a cardiac defect with a hypoplastic left ventricle, associated with aortic and/or mitral valve atresia, with or without other cardiac defect.

12. Coarctation of the aorta: an obstruction in the descending aorta, almost invariably at the insertion of the ductus arteriosus

13. Choanal atresia, bilateral: congenital obstruction (membraneous or osseous) of the posterior choana or choanae. Excl. choanal stenosis and congestion of nasal mucosa.

14. Cleft palate without cleft lip: a congenital malformation characterized by a closure defect of the hard and/or soft palate behind the foramen incisivum without cleft lip. Incl. submucous cleft palate. Excl. cleft palate with cleft lip, cleft uvula, functional short palate, and high narrow palate.

15. Cleft lip with or without cleft palate: a congenital malformation characterized by partial or complete clefting of the upper lip, with or without clefting of the alveolar ridge or the hard palate. Excl. midline cleft of upper or lower lip and oblique facial fissure (going towards the eye).

16. Oesophageal atresia/stenosis: a congenital malformation characterized by absence of continuity or narrowing of the esophagus, with or without tracheal fistula. Incl. tracheoesophageal fistula with or without mention of atresia or stenosis of oesophagus.

6 ICBDMS Definitions of the Reported Malformations

17. Small intestine atresia/stenosis: complete or partial occlusion of the lumen of a segment of the small intestine. It can involve a single area or multiples areas of the jejunum or ileum. Excl. duodenal atresia.

18. Anorectal atresia/stenosis: a congenital malformation characterized by absence of continuity of the anorectal canal or of communication between rectum and anus, or narrowing of anal canal, with or without fistula to neighboring organs. Excl. mild stenosis which does not need correction, and ectopic anus.

19. Undescended testis: bilateral undescended testes in at term newborn or at least unilateral undescended testis in males more than 1 year of age. Excl. retractrile testis.

20. Hypospadias: a congenital malformation characterized by the opening of the urethra on the ventral side of the penis, distally to the sulcus. Incl. penile, scrotal, and perineal hypospadias. Excl. glandular or first-degree hypospadias and ambiguous genitalia (intersex or pseudohermaphroditism).

21. Epispadias: a congenital malformation characterized by the opening of the urethra on the dorsal surface of the penis. Not counted when part of exstrophy of the bladder.

22. Indeterminate sex: genital ambiguity at birth that does not readily allow for phenotypic sex determination.
Incl. male or female true or pseudohermaphroditism.

23. Renal agenesis: a congenital malformation characterized by complete absence of kidneys bilaterally or severely dysplastic kidneys.

24. Cystic kidney: a congenital malformation characterized by multiple cysts in the kidney. Incl. infantile polycystic kidney, multicystic kidney, other forms of cystic kidney and unspecified cystic kidney. Excl. single kidney cyst.

25. Bladder exstrophy: complex malformation characterized by a defect in the closure of the lower abdominal wall and bladder. Bladder opens in the ventral wall of the abdomen between the umbilicus and the symphysis pubis. It is often associated with epispadias and structural anomalies of the pubic bones.

26. Polydactyly, preaxial: extra digit(s) on the radial side of the upper limb or the tibial side of the lower limb.
It can affect the hand, the foot, or both.

27. Limb reduction defects: a congenital malformation characterized by total or partial absence or severe hypoplasia of skeletal structures of the limbs. Incl. femoral hypoplasia. Excl. mild hypoplasia with normal shape of skeletal parts, brachydactyly, finger or toe reduction directly associated with syndactyly, general skeletal dysplasia and sirenomelia.

28. Diaphragmatic hernia: a congenital malformation characterized by herniation into the thorax of abdominal contents through a defect of the diaphragm. Incl. total absence of the diaphragm. Excl. hiatus hernia, eventration and phrenic palsy.

29. Abdominal wall defects: cases specified as omphalocele and/or gastroschisis plus unspecified cases.

30. Omphalocele: a congenital malformation characterized by herniation of abdominal contents through the umbilical insertion and covered by a membrane which may or may not be intact. Excl. gastroschisis (para-umbilical hernia), a - or hypoplasia of abdominal muscles, skin-covered umbilical hernia.

31. Gastroschisis: a congenital malformation characterized by visceral herniation through a right side abdominal wall defect to an intact umbilical cord and not covered by a membrane. Excl. a-or hypoplasia of abdominal muscles, skin-covered umbilical hernia, omphalocele.

32. Prune belly sequence: a complex congenital malformation characterized by deficient abdominal muscle and urinary obstruction/distension. It can be caused by urethral obstruction secondary to posterior urethral valves or urethral atresia. In the affected fetus the deficiency of the abdominal muscle may not be evident. It can be associated with undescended testes, clubfoot, and limb deficiencies.

33. Trisomy 13: a congenital chromosomal malformation syndrome associated with extra chromosome 13 material. Incl. translocation and mosaic trisomy 13.

34. Trisomy 18: a congenital chromosomal malformation syndrome associated with extra chromosome 18 material.
Incl. translocation and mosaic trisomy 18

35. Down syndrome: a congenital chromosomal malformation syndrome characterized by a well known pattern of minor and major anomalies and associated with excess chromosomal 21 material. Incl. trisomy mosaicism and translocations of chromosome 21.

6.1 Deviations from the ICBDMS Definitions by Registry

	Encephalocele	Microcephaly	Arhinencephaly / Holoprosencephaly	Hydrocephaly	Anophthalmos / Microphthalmos	Anotia	Transposition of great vessels	Tetralogy of Fallot	Choanal atresia, bilateral	Cleft palate without cleft lip	Cleft lip with or without cleft palate	Oesophageal atresia / stenosis	Small intestine atresia / stenosis	Anorectal atresia / stenosis	Undescended testis	Hypospadias	Epispadias	Indeterminate sex	Renal agenesis	Cystic kidney	Polydactyly, preaxial	Limb reduction defects	Prune belly sequenze	Trisomy 13	Trisomy 18	Down syndrome
Australia: VBDR									11							25					36					
Australia: WABDR				42					11										29/43		36	44				45
Canada: Alberta		2			2	7	8		11\12							25					36					2
Canada: British Columbia	1	2	4	6	2	7	8	10	11\12	13	15		18\19			25	25\26	28	29	31	36	38		2	2	2
Canada: National	1	1\2		6	2				11\12	14			18	21	23	25	26		29	32	36		41	2	2	2
China: Beijing																					36					
China: CBDMN	1	2		6	2	7	9		12				18			25		28	29	32	36	38		2	2	2
Costa Rica: CREC				6			9		11\12								26	28	29	32	36			2	2	2
Czech Republic																25					36					
England and Wales																										
Finland	1	2			2		8		11							25		28		33		38		2	2	2
France: Central East																25										2
France: Paris																25										
France: Strasbourg		2			2		9						18\19			25			29\30	31\34						
Germany: Saxony-Anhalt					2	7	9	10					18\19			25		28		33		38				2
Hungary	1	2			2		9									25	26				36	39\40		2	2	2
Ireland: Dublin		2			2				11				18\19			25	26				36			2	2	2
Israel: IBDMS							8									25				34						
Italy: BDRCAM																								2	2	2
Italy: IMER																25					36					
Italy: ISMAC																25										
Italy: North East			5		2					13	15	17	18\20	22					30		36					2
Italy: Tuscany							8																			
Japan: JAOG		2			2															32						
Malta		2			2		9		11									28		32	36	38		2	2	2
Mexico: RYVEMCE	1	2			2				11\12				18					28	29	31	36	38		2	2	2
New Zealand					2											25	26							2	2	2
Northern Netherlands															24	25					36					
Norway																25				35						
Russia: Moscow region		2					9			13	15		18			25				32	37					2
South Africa: SABDSS	1	2			2				11\12							25		28		32	36	38		2	2	2
South America: ECLAMC																25										
Spain: ECEMC		2			2			10					18				27	28		34	37	38				2
Sweden		2			2				11							25			29	33						2
Ukraine		2\3		6	2	7	9				16							28						2	2	2
United Arab Emirates		2			2	7	8	10	11				18						29/30	32						
USA: Atlanta									12		16															

6 ICBDMS Definitions of the Reported Malformations

1 = when present with spina bifida counted
2 = clinical diagnosis included
3 = OCF below 3rd percentile
4 = there may be other defects with the same code
5 = only cyclopia included
6 = hydranencephaly included
7 = absence of auricle
8 = double outlet right ventricle excluded
9 = all kind of transposition included
10 = Trilogy of Fallot included
11 = unilateral cases included
12 = stenosis included
13 = submucous cleft palate excluded
14 = Cleft uvula included
15 = midline and oblique facial clefts included
16 = clefts of the alveolar ridge without cleft lip included
17 = stenosis excluded
18 = doudenal atresia included
19 = doudenal stenosis excluded
20 = intestinal stenosis excluded
21 = Large intestine atresia/stenosis included
22 = tenosis excluded
23 = No gestational age information
24 = Registered when it is combined with other defects
25 = all types included
26 = epispadias counted with hypospadias
27 = epispadias included also when part of bladder exstrophy
28 = genital ambiguity and absent genitalia included
29 = unilateral defects included
30 = severely dysplastic kidneys excluded
31 = single cyst included
32 = all kind of cystic kidney included
33 = all cystic kidneys are included except for single renal cysts
34 = AR polycystic kidney excluded
35 = some autosomalrecessive polycystyc kidneys are not excluded
36 = any type of polydactyly included
37 = polysyndactyly preaxial excluded
38 = any hypoplasia of skeletal limb structures included except branchydactyly and hypoplasia as part of skeletal dysplasia
39 = any hypoplasia of skeletal structures included
40 = sirenomalia included
41 = Prune belly sequence counted with Total abdominal wall defects

Australia: VBDR
Victoria Birth Defects Registry

History:
In 1979 the Commonwealth Government agreed in principle to collect more information about births and birth defects. It was decided that the States would be responsible for setting up their own systems and the Commonwealth would establish a National Perinatal Statistics Unit, to collate information from all the states and provide an overall picture. The Victorian Perinatal Data Collection Unit (PDCU), established under the Health Act of 1958, operates under the aegis of the Consultative Council on Obstetric and Paediatric Mortality and Morbidity (the Council). One of the fundamental purposes of the PDCU was the establishment and maintenance of a Birth Defects/Congenital Malformations Register (BDR). The PDCU and BDR were established in 1982.

Size and coverage:
The BDR collects information on all birth defects for livebirths, stillbirths and terminations of pregnancy pre 20 wks gestation and children up to 15 yrs of age (irrespective of the age at diagnosis). Approximately 3.6% of babies are born with a birth defect at or after 20 weeks gestation. We also follow up terminations for malformations before 20 weeks, once these are included the overall prevalence is approximately 4%. Birth defects are notified to the register for those babies/fetus' who were born in Victoria

Legislation and funding:
The ongoing maintenance of the BDR is enshrined in the legislation pertaining to the PDCU (Health Act 1958) and is an ongoing function of the PDCU, however notification of birth defects outside the reporting period on
the Perinatal Morbidity Statistics form (28 days) is a voluntary process. There is a section for reporting of birth defects on the Perinatal form which is completed at the time of birth. Several measures are taken to ensure the ascertainment of birth defects outside this reporting period which will be specified in 'sources of ascertainment'. The PDCU & BDR are funded by the Department of Human Services (State Government)

Sources of ascertainment:
Perinatal forms (approx 52.5%)
Hospital listings* (aprox 27.1%)
Perinatal Death Certificates (approx 5.2%)
Autopsy Reports (approx 2.9%)
Cytogenetic Reports (approx 6.7%)
Maternal & Child Health Nurse (approx 4.7%)
Other professionals/parents (approx 0.1%)

* these include obtaining inpatient listings from the Royal Children's Hospital (RCH) detailing all children born since 1982 who have been subsequently admitted to the RCH with a birth defect. We also obtain listings of all children born since 1982 who have visited the RCH Cardiology Unit and Metabolic Clinic, either as an inpatient or an outpatient. This procedure has also been adopted for Monash Medical Centre. Other listing received include cystic fibrosis, hypothyroidism, cerebral palsy.

Exposure information:
No exposure information is available

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Australia: Victoria, 2002

Live births (L)	62678
Stillbirths (S)	391
Total births	63069
Number of terminations of pregnancy (ToP) for birth defects	289

Birth Defects	Number of cases			Rates*10.000		O/E	YB	Remark
	L	S	ToP	L+S	L+S+ToP	L+S		
Anencephaly	3	5	25	1.27	5.21	0.79	13	
Spina bifida	7	9	17	2.54	5.21	0.64	10	
Encephalocele	2	1	4	0.48	1.10	0.36	18	
Microcephaly	14	1	0	2.38	2.37	0.85	15	
Arhinencephaly / Holoprosencephaly	2	1	11	0.48	2.21	0.52	19	
Hydrocephaly	43	8	13	8.09	10.10	0.99	5	
Total Anophthalmos / Microphthalmos (include unspecified)	2	1	0	0.48	0.47	0.50	14	
Anophthalmos	1	1	0	0.32	0.32	1.59	19	
Microphthalmos	1	0	0	0.16	0.16	0.21	14	
Total Anotia / Microtia (include unspecified)	6	2	0	1.27	1.26	1.06	19	
Anotia	3	2	0	0.79	0.79	0.94	19	
Microtia	3	0	0	0.48	0.47	1.30	19	
Transposition of great vessels	14	1	0	2.38	2.37	0.81	17	
Tetralogy of Fallot	22	1	0	3.65	3.63	0.90	10	
Hypoplastic left heart syndrome	19	3	3	3.49	3.95	1.35	19	
Coarctation of aorta	20	2	1	3.49	3.63	0.84	11	
Choanal atresia, any**	8	0	0	1.27	1.26	0.66	19	
Cleft palate without cleft lip	36	2	1	6.03	6.16	0.78	19	
Cleft lip with or without cleft palate	47	4	8	8.09	9.31	0.82	19	
Oesophageal atresia / stenosis with or without fistula	13	1	0	2.22	2.21	0.63	19	
Small intestine atresia / stenosis	19	4	1	3.65	3.79	1.34	18	
Anorectal atresia / stenosis	15	2	8	2.70	3.95	0.70	19	
Undescended testis (37 weeks of gestation or later)***	277	0	0	43.92	43.72	0.95	10	
Hypospadias	211	2	0	33.77	33.62	1.00	10	
Epispadias	1	0	0	0.16	0.16	0.36	17	
Indeterminate sex	12	1	0	2.06	2.05	1.02	19	
Renal agenesis	29	5	5	5.39	6.16	1.01	11	
Cystic kidney	40	5	3	7.14	7.58	1.24	8	
Bladder exstrophy	3	0	2	0.48	0.79	1.27	19	
Polydactyly, any****	52	1	4	8.40	9.00	0.87	13	
Total Limb reduction defects (include unspecified)	18	9	11	4.28	6.00	0.77	19	
Transverse	nr	nr	nr	nc	nc			
Preaxial	nr	nr	nr	nc	nc			
Postaxial	nr	nr	nr	nc	nc			
Intercalary	nr	nr	nr	nc	nc			
Mixed	nr	nr	nr	nc	nc			
Diaphragmatic hernia	17	2	1	3.01	3.16	0.93	19	
Total Abdominal wall defects (include unspecified)	22	7	15	4.60	6.94	0.73	13	
Omphalocele	9	5	15	2.22	4.58	1.04	19	
Gastroschisis	11	2	0	2.06	2.05	0.90	10	
Prune belly sequence	1	0	0	0.16	0.16	0.61	19	
Trisomy 13	3	4	10	1.11	2.68	1.21	19	
Trisomy 18	7	7	26	2.22	6.31	0.98	19	
Down syndrome, all ages (include age unknown)	57	10	102	10.62	26.67	0.89	19	
<20	1	0	0	5.19	5.19	0.81	19	
20-24	6	0	3	7.93	11.90	1.10	19	
25-29	12	2	7	8.17	12.26	1.22	12	
30-34	14	2	20	6.83	15.35	0.54	15	▼
35-39	14	5	47	17.33	59.96	0.77	15	
40-44	10	1	22	55.64	165.08	1.01	19	
45+	0	0	1	0.00	129.87	0.00	19	

** Choanal atresia includes any, not just bilateral
*** UDT includes from 37 weeks gestation, rather than 36 wks
**** Polydactyly includes any, not just preaxial

Australia: VBDR, time trend analysis 1983-2002

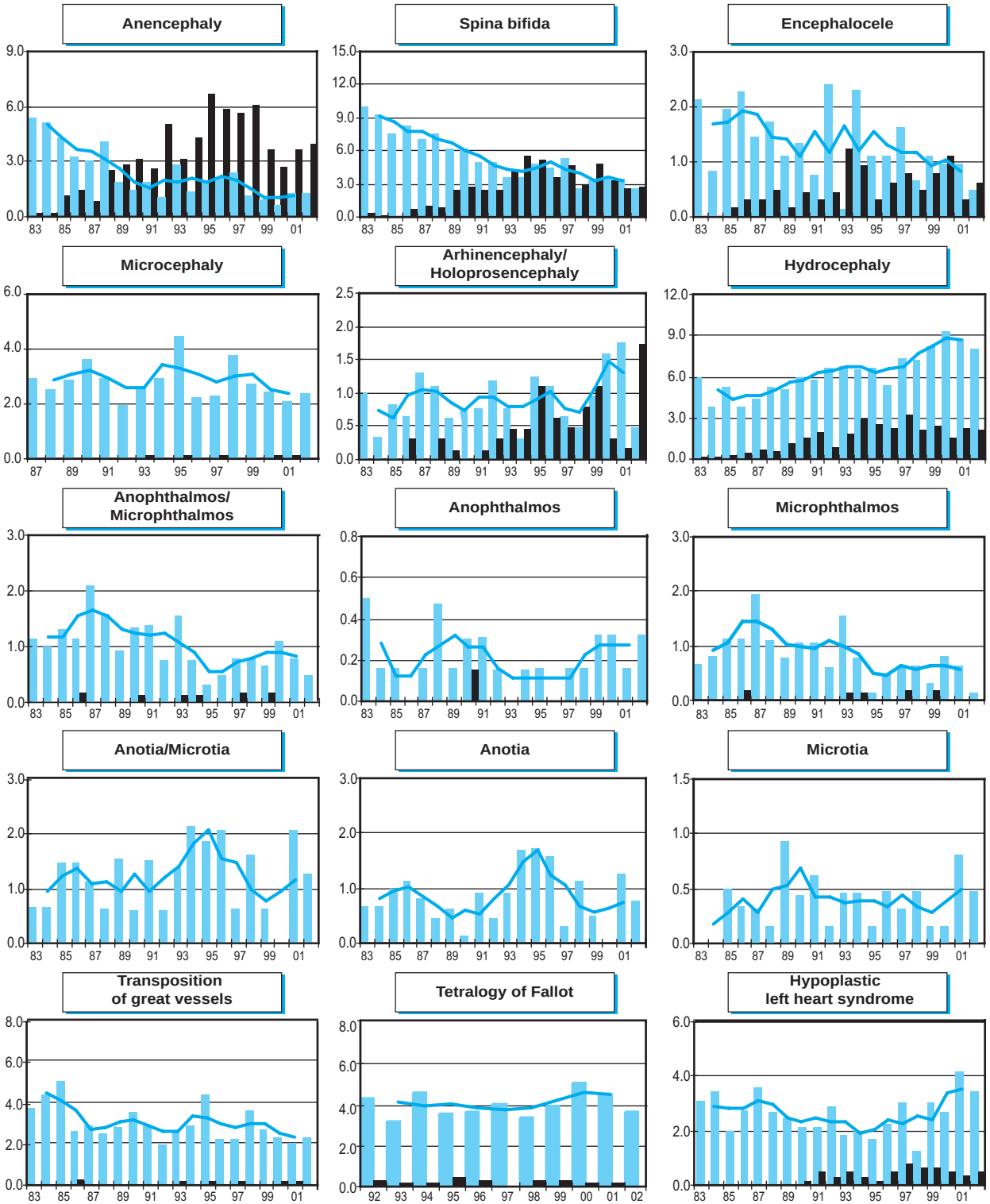
Birth prevalence rates: (L+S) * 10,000

	1974-81	1982-86*	1987-91	1992-96	1997-01	2002	Trend	RR
Births		243,807	321,614	322,642	311,801	63,069		
Anencephaly		4.51	2.46	1.83	1.28	1.27	▼	0.921
Spina bifida		8.82	6.41	4.31	3.62	2.54	▼	0.939
Encephalocele		1.80	1.27	1.43	1.06	0.48	▼	0.962
Microcephaly			2.95	2.82	2.63	2.38		
Arhinencephaly / Holoprosencephaly		0.70	0.90	0.93	1.09	0.48		
Hydrocephaly		4.68	5.32	6.38	8.15	8.09	▲	1.036
Total Anophthalmos / Microphthalmos (include unspecified)		1.15	1.46	0.77	0.83	0.48	▼	0.959
Anophthalmos		0.21	0.28	0.09	0.22	0.32		
Microphthalmos		0.94	1.18	0.71	0.61	0.16	▼	0.952
Total Anotia / Microtia (include unspecified)		1.07	1.09	1.61	0.99	1.27		
Anotia		0.86	0.59	1.27	0.64	0.79		
Microtia		0.21	0.50	0.34	0.38	0.48		
Transposition of great vessels		3.98	2.95	2.82	2.63	2.38	▼	0.976
Tetralogy of Fallot				3.91	4.20	3.65		
Hypoplastic left heart syndrome		2.83	2.58	2.14	2.85	3.49		
Coarctation of aorta		7.01	5.69	4.71	3.69	3.49	▼	0.960
Choanal atresia, bilateral		1.56	2.08	2.26	1.73	1.27		
Cleft palate without cleft lip		8.12	6.59	7.90	8.27	6.03		
Cleft lip with or without cleft palate		10.25	10.23	9.05	9.94	8.09		
Oesophageal atresia / stenosis with or without fistula		4.02	2.89	4.00	3.37	2.22		
Small intestine atresia / stenosis		2.05	2.83	2.26	3.34	3.65	▲	1.026
Anorectal atresia / stenosis		3.65	3.23	4.62	3.88	2.70		
Undescended testis (36 weeks of gestation or later)				47.17	45.12	43.92		
Hypospadias				33.91	33.84	33.77		
Epispadias		0.21	0.40	0.31	0.64	0.16		
Indeterminate sex		1.15	2.95	2.29	1.44	2.06		
Renal agenesis		4.68	4.63	5.05	5.45	5.39	▲	1.017
Cystic kidney		2.95	3.73	4.84	6.19	7.14	▲	1.051
Bladder exstrophy		0.45	0.31	0.40	0.35	0.48		
Polydactyly, preaxial		7.67	8.02	9.61	10.36	8.40	▲	1.018
Total Limb reduction defects (include unspecified)		5.66	5.47	6.23	4.94	4.28		
Transverse								
Preaxial								
Postaxial								
Intercalary								
Mixed								
Diaphragmatic hernia		3.24	3.05	3.63	3.01	3.01		
Total Abdominal wall defects (include unspecified)		3.86	5.07	5.95	7.22	4.60	▲	1.031
Omphalocele		2.09	2.74	1.74	1.96	2.22		
Gastroschisis		0.74	1.15	1.89	2.73	2.06	▲	1.071
Prune belly sequence		0.41	0.12	0.40	0.13	0.16		
Trisomy 13		1.07	0.93	0.93	0.77	1.11		
Trisomy 18		2.13	2.36	2.36	2.15	2.22		
Down syndrome, all ages (include age unknown)		12.67	12.69	11.65	11.13	10.62		
<20		10.53	7.27	5.30	1.96	5.19		
20-24		7.31	9.21	5.55	6.18	7.93		
25-29		9.33	8.27	6.70	6.27	8.17	▼	0.977
30-34		14.72	13.15	14.08	11.05	6.83	▼	0.976
35-39		34.10	27.90	20.87	20.76	17.33	▼	0.968
40-44		83.37	48.77	60.33	46.72	55.64		
45+		168.07	71.94	182.65	66.23	0.00		

* = data include less than five years

Australia: VBDR

'Time trends 1983-2002 (Birth prevalence rates per 10,000)



Note: L+S rates, ToP rates — 3-year moving average trend

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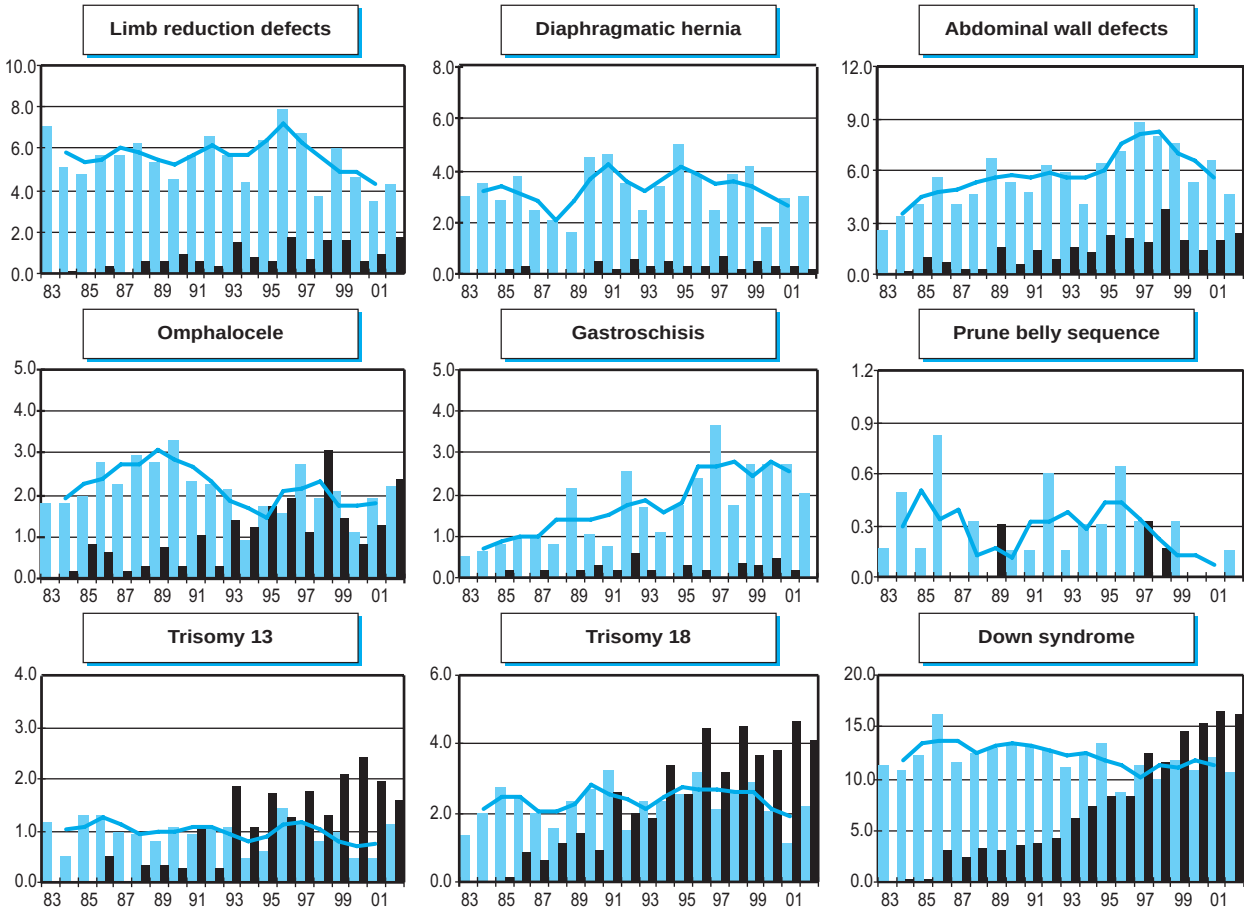

Note: L+S rates, ToP rates — 3-year moving average trend

Australia: WABDR
Western Australian Birth Defects Registry

History:
The Registry was established in 1980, and is currently located in a teaching obstetric hospital. The objectives of the Registry have always been to establish how often birth defects occur, to conduct research into causes and prevention of birth defects, provide health professionals and the public with information about birth defects, and to monitor and evaluate screening, treatment and prevention programmes.

Size and coverage:
Population-based in the state of Western Australia. 25,000 birth a year, ~6% reported with a birth defect.
Birth defects in livebirths, stillbirths and terminations of pregnancy, diagnosed prenatally or up to the age of 6 years, are included.

Legislation and funding:
Following a period of short term funding from both Federal and State sources, the Registry is now wholly funded by the Western Australian Department of Health. There are several statutory sources of information (birth, death and hospital data collections), and a large number of voluntary sources. Statutory notification is being considered by the Department of Health.

Sources of ascertainment:
Statutory sources:
Midwives' Notification of Birth Forms (all births over 20 weeks gestation), Death Certificates (perinatal, infant and childhood), Hospital Morbidity (all hospital discharges in Western Australia).
Voluntary sources:
Maternity and paediatric hospitals
Obstetricians, paediatricians, orthopaedic surgeons
Community and Child Health Nurses
Cytogenetic laboratories
Pathology services (including prenatal screening services)
Ultrasound practices
Genetic services
Disability services.

Exposure information:
No exposure information is routinely collected.

Background information:
The data on the Registry are routinely linked to the Maternal and Child Health Research Data Base, a linked dataset of all births, deaths and hospital admissions for Western Australia. This linkage provides information on variables such as maternal and paternal age, labour and delivery data, and maternal illnesses, for both cases of birth defects (numerators) and all births in Western Australia (denominators).
Data from the Registry are provided to the National Perinatal Statistics Unit for monitoring birth defects in Australia as a whole.

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Website:
http://wchs.health.wa.gov.au/services/b/birth_defects.htm

Australia: Western, 2002

Live births (L)	24590
Stillbirths (S)	176
Total births	24766
Number of terminations of pregnancy (ToP) for birth defects	160

Birth Defects	Number of cases			Rates*10.000		O/E	YB	Remark
	L	S	ToP	L+S	L+S+ToP	L+S		
Anencephaly	0	0	17	0.00	6.82			
Spina bifida	7	0	9	2.83	6.42			
Encephalocele	0	0	1	0.00	0.40			
Microcephaly	9	1	0	4.04	4.01			
Arhinencephaly / Holoprosencephaly	0	0	4	0.00	1.60			
Hydrocephaly	7	0	14	2.83	8.42			
Total Anophthalmos / Microphthalmos (include unspecified)	3	0	3	1.21	2.41			
Anophthalmos	0	0	1	0.00	0.40			
Microphthalmos	3	0	2	1.21	2.01			
Total Anotia / Microtia (include unspecified)	3	1	0	1.62	1.60			
Anotia	2	1	0	1.21	1.20			
Microtia	1	0	0	0.40	0.40			
Transposition of great vessels	10	0	5	4.04	6.02			
Tetralogy of Fallot	9	0	3	3.63	4.81			
Hypoplastic left heart syndrome	2	0	1	0.81	1.20			
Coarctation of aorta	15	1	4	6.46	8.02			
Choanal atresia, bilateral	4	0	0	1.62	1.60			
Cleft palate without cleft lip	28	0	1	11.31	11.63			
Cleft lip with or without cleft palate	24	0	6	9.69	12.04			
Oesophageal atresia / stenosis with or without fistula	5	2	4	2.83	4.41			
Small intestine atresia / stenosis	4	1	0	2.02	2.01			
Anorectal atresia / stenosis	10	1	3	4.44	5.62			
Undescended testis (36 weeks of gestation or later)	77	0	0	31.09	30.89			
Hypospadias	71	0	1	28.67	28.89			
Epispadias	0	0	0	0.00	0.00			
Indeterminate sex	1	0	0	0.40	0.40			
Renal agenesis	8	0	6	3.23	5.62			
Cystic kidney	13	0	8	5.25	8.42			
Bladder exstrophy	0	0	0	0.00	0.00			
Polydactyly, preaxial	11	0	6	4.44	6.82			
Total Limb reduction defects (include unspecified)	7	1	11	3.23	7.62			
Transverse	nr	nr	nr	nc	nc			
Preaxial	nr	nr	nr	nc	nc			
Postaxial	nr	nr	nr	nc	nc			
Intercalary	nr	nr	nr	nc	nc			
Mixed	nr	nr	nr	nc	nc			
Diaphragmatic hernia	4	1	2	2.02	2.81			
Total Abdominal wall defects (include unspecified)	11	2	12	5.25	10.03			
Omphalocele	4	2	8	2.42	5.62			
Gastroschisis	6	0	3	2.42	3.61			
Prune belly sequence	0	0	0	0.00	0.00			
Trisomy 13	0	0	5	0.00	2.01			
Trisomy 18	0	1	13	0.40	5.62			
Down syndrome, all ages (include age unknown)	28	2	39	12.11	27.68			
<20	3	0	0	20.75	20.75			
20-24	0	0	1	0.00	2.46			
25-29	6	0	3	8.37	12.55			
30-34	7	0	12	8.84	23.95			
35-39	4	1	14	14.26	53.96			
40-44	5	1	8	94.34	217.39			
45+	3	0	1	967.74	1250.00			

Canada: National

Canadian Congenital Anomalies Surveillance Network (CCASN)

History:
The Programme was started in 1966. The Programme was a full member until 1987, when it became an associate member. The Programme was discontinued as an associate member of the ICBDMS in the early 1990s, and reinstated its associate member status in 1996.

Size and coverage:
This system presently monitors about 330,000 births annually, which captures virtually all births in the 10 provinces and 3 territories of Canada. Data from Nova Scotia have not been included in the national statistics provided to the ICBDMS, however, efforts are being made to include this province in future submissions.
Live births to 1 year of age and registered stillbirths (a birth weight of greater or equal to 500 grams, or greater than or equal to 20 weeks in pregnancy) are captured.

Legislation and funding:
Reporting is based on an agreement between the Canadian Institute for Health Information (CIHI), a non-profit organization, which collects and disseminates data on hospital admission/separation in Canada, and the central registry, which is run and funded by Health Canada. The Alberta Congenital Anomalies Surveillance System, the Manitoba provincial government and Med-Echo (Système de maintenance et d'exploitation des données pour l'étude de la clientèle hospitalière) for the province of Québec provide their data separately.

Sources of ascertainment:
Cases from most provinces and territories are ascertained from hospital admission/separation summary records collected by the Canadian Institute for Health Information and Med-Echo. Two exceptions are Alberta and Manitoba. The Alberta Congenital Anomalies Surveillance System and the Manitoba government provide their own separate provincial data. Follow-up continues to one year of age.

Exposure information:
No exposure information is routinely collected in the central registry.

Background information:
Background information is based on hospital admission/separation summary records from the Canadian Institute for Health Information and Med-Echo. Alberta Congenital Anomalies Surveillance System and Manitoba provincial government provide their own background information.

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Canada: National*, 2002

Live births (L)	315206
Stillbirths (S)	1940
Total births	317146
Number of terminations of pregnancy (ToP) for birth defects	nr

Birth Defects	Number of cases			Rates*10.000		O/E	YB	Remark
	L	S	ToP	L+S	L+S+ToP	L+S		
Anencephaly	18	18	nr	1.14	nc	1.02	4	
Spina bifida	99	11	nr	3.47	nc	0.84	2	
Encephalocele	20	6	nr	0.82	nc	0.98	4	
Microcephaly	175	1	nr	5.55	nc	1.03	11	
Arhinencephaly / Holoprosencephaly	nr	nr	nr	nc	nc	nc		
Hydrocephaly	190	30	nr	6.94	nc	1.00	11	
Total Anophthalmos / Microphthalmos (include unspecified)	42	1	nr	1.36	nc	1.04	11	
Anophthalmos	10	0	nr	0.32	nc	1.08	11	
Microphthalmos	33	1	nr	1.07	nc	1.03	11	
Total Anotia / Microtia (include unspecified)	nr	nr	nr	nc	nc	nc		
Anotia	nr	nr	nr	nc	nc	nc		
Microtia	nr	nr	nr	nc	nc	nc		
Transposition of great vessels	159	0	nr	5.01	nc	0.95	6	
Tetralogy of Fallot	179	2	nr	5.71	nc	1.19	11	
Hypoplastic left heart syndrome	93	10	nr	3.25	nc	1.15	11	
Coarctation of aorta	184	2	nr	5.86	nc	1.01	8	
Choanal atresia, bilateral	79	0	nr	2.49	nc	0.86	3	
Cleft palate without cleft lip	211	3	nr	6.75	nc	0.93	11	
Cleft lip with or without cleft palate	326	15	nr	10.75	nc	0.97	11	
Oesophageal atresia / stenosis with or without fistula	99	1	nr	3.15	nc	0.92	11	
Small intestine atresia / stenosis	120	0	nr	3.78	nc	1.08	11	
Anorectal atresia / stenosis	137	5	nr	4.48	nc	0.88	11	
Undescended testis	955	2	nr	30.18	nc	0.91	9	▼
Hypospadias	787	0	nr	24.82	nc	0.92	11	▼
Epispadias nr	nr	nr	nc	nc	nc			
Indeterminate sex	19	2	nr	0.66	nc	0.95	11	
Renal agenesis	137	7	nr	4.54	nc	0.90	11	
Cystic kidney	181	13	nr	6.12	nc	0.97	3	
Bladder exstrophy	7	2	nr	0.28	nc	0.71	11	
Polydactyly, preaxial	421	3	nr	13.37	nc	1.12	11	
Total Limb reduction defects (include unspecified)	113	8	nr	3.82	nc	0.91	7	
Transverse	nr	nr	nr	nc	nc	nc		
Preaxial	nr	nr	nr	nc	nc	nc		
Postaxial	nr	nr	nr	nc	nc	nc		
Intercalary	nr	nr	nr	nc	nc	nc		
Mixed	nr	nr	nr	nc	nc	nc		
Diaphragmatic hernia	119	4	nr	3.88	nc	1.05	11	
Total Abdominal wall defects (include unspecified)	196	13	nr	6.59	nc	1.13	10	
Omphalocele	nr	nr	nr	nc	nc	nc		
Gastroschisis	nr	nr	nr	nc	nc	nc		
Prune belly sequence	nr	nr	nr	nc	nc	nc		
Trisomy 13	24	10	nr	1.07	nc	0.94	11	
Trisomy 18	34	42	nr	2.40	nc	1.07	11	
Down syndrome, all ages (include age unknown)	448	51	nr	15.73	nc	1.19	11	▲
<20	nr	nr	nr	nc	nc	nc		
20-24	nr	nr	nr	nc	nc	nc		
25-29	nr	nr	nr	nc	nc	nc		
30-34	nr	nr	nr	nc	nc	nc		
35-39	nr	nr	nr	nc	nc	nc		
40-44	nr	nr	nr	nc	nc	nc		
45+	nr	nr	nr	nc	nc	nc		

* excluding Nova Scotia
nr = not reported
nc = not calculable

Canada: National, time trend analysis 1989-2000

Birth prevalence rates: (L+S) * 10,000

	1974-79	1980-84	1985-89*	1990-94	1995-99	2000	Trend	RR
Births			375,840	1,918,123	1,728,310	317,146		
Anencephaly			2.16	1.90	1.26	1.14	▼	0.930
Spina bifida			7.96	6.88	5.07	3.47	▼	0.935
Encephalocele			1.46	1.36	0.93	0.82	▼	0.941
Microcephaly			5.40	5.49	5.29	5.55		
Arhinencephaly / Holoprosencephaly								
Hydrocephaly			7.21	7.05	6.79	6.94		
Total Anophthalmos / Microphthalmos (include unspecified)			1.01	1.42	1.31	1.39		
Anophthalmos			0.19	0.35	0.25	0.32		
Microphthalmos			0.82	1.07	1.06	1.07		
Total Anotia / Microtia (include unspecified)								
Anotia								
Microtia								
Transposition of great vessels			3.86	4.57	5.54	5.01	▲	1.024
Tetralogy of Fallot			4.98	4.48	5.11	5.71	▲	1.013
Hypoplastic left heart syndrome			2.87	2.86	2.80	3.25		
Coarctation of aorta			5.51	5.34	5.95	5.86	▲	1.014
Choanal atresia, bilateral			2.66	2.03	2.46	2.49	▲	1.030
Cleft palate without cleft lip			6.70	7.17	7.38	6.75		
Cleft lip with or without cleft palate			10.70	11.37	10.90	10.75		
Oesophageal atresia / stenosis with or without fistula			3.35	3.47	3.36	3.15		
Small intestine atresia / stenosis			3.49	3.47	3.55	3.78		
Anorectal atresia / stenosis			5.75	5.13	4.91	4.48	▼	0.987
Undescended testis (36 weeks of gestation or later)			36.03	34.29	32.74	30.18	▼	0.988
Hypospadias			27.11	26.78	26.93	24.82		
Epispadias								
Indeterminate sex			0.88	0.67	0.69	0.66		
Renal agenesis			5.27	4.97	5.05	4.54		
Cystic kidney			4.47	4.96	5.99	6.12	▲	1.038
Bladder exstrophy			0.35	0.45	0.36	0.28		
Polydactyly, preaxial			12.21	11.88	11.95	13.37		
Total Limb reduction defects (include unspecified)			4.76	4.65	4.14	3.82	▼	0.978
Transverse								
Preaxial								
Postaxial								
Intercalary								
Mixed								
Diaphragmatic hernia			3.59	3.77	3.60	3.88		
Total Abdominal wall defects (include unspecified)			3.72	5.67	5.99	6.59	▲	1.029
Omphalocele								
Gastroschisis								
Prune belly sequence								
Trisomy 13			1.41	1.13	1.11	1.07		
Trisomy 18			2.02	2.18	2.37	2.40		
Down syndrome, all ages (include age unknown)			12.13	13.21	13.48	15.73	▲	1.011
<20								
20-24								
25-29								
30-34								
35-39								
40-44								
45+								

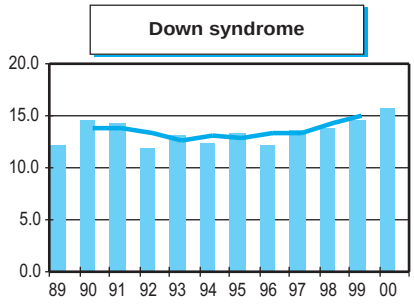
* = data include less than five years

Canada: National

'Time trends 1989-2000 (Birth prevalence rates per 10,000)

Note: L+S rates, ToP rates — 3-year moving average trend

Note: L+S rates, ToP rates — 3-year moving average trend



Note: L+S rates, ToP rates 3-year moving average trend

Canada: Alberta

Alberta Congenital Anomalies Surveillance System (ACASS)

History:
This Programme began in 1966 as a general Registry for Handicapped Children. This was disbanded in 1980 and continued as a surveillance Programme for live and stillborn infants with congenital anomalies who were born in the Province of Alberta. The Programme became an associate member of the ICBDMS in 1996.

Size and coverage:
All live and stillbirths in the province are included which at present comprises about 38,000 births per year. The definition of stillbirth is 20 weeks or more or 500 grams or more. The vast majority of births occur in hospital (approximately 97%). In 1997 a special fetal congenital anomalies surveillance system was started to include those fetuses with congenital anomalies who were either spontaneously lost prior to 20 weeks or where there was termination as a result of prenatal diagnosis.

Legislation and funding:
Reporting is voluntary but there is legislation permitting us to request information from physicians, hospitals, clinics and laboratories. The system is run by members of the Department of Medical Genetics, Alberta Children's Hospital/University of Calgary in conjunction with Alberta Health Surveillance and reporting to Alberta Health. Funding is from Alberta Ministry of Health.

Sources of ascertainment:
Reports are obtained from physician's notice of birth, live birth and stillbirth registration, death registrations and a special congenital anomalies reporting form (CARF) from hospitals. This is based on discharge diagnosis, including readmissions for any reason up to one year of age. Additional sources are specialty clinics, such as medical genetics and cytogenetics laboratories.

Exposure information:
None is routinely collected.

Background information:
Linkage studies are possible with other statistical data from Alberta Health.

Research Projects

- Impact of folic acid fortification on the epidemiology of neural tube defects in Canada. 1993 - 2002. P.I. Philippe de Wals. Alberta Co-Investigator R. Brian Lowry.
- Review of Anophthalmia and Microphthalmia in the Alberta Congenital Anomalies Surveillance System – 1991 – 2001.
- Anorectal Malformations in Alberta reported by the Alberta Congenital Anomalies Surveillance System 1990 – 2001 with a comment on the Canadian Congenital Anomalies Surveillance System.

Education:
Personnel from the Alberta Congenital Anomaly Surveillance System played a large role in the 2nd Annual Scientific meeting of the Canadian Congenital Anomalies Surveillance Network which was held in Edmonton, Alberta October 19 • 21, 2003. These included platform and poster presentations on the following:

- Surveillance from the global perspective
- Fluctuations in Alberta Congenital Anomaly Rates 1980 – 2001. Is changing ascertainment a factor
- Time Trend of Fetal Anomalies in Northern and Central Alberta, 1996 – 2001
- Birth Prevalence of Congenital Anomalies in Chinese, First Nations, Vietnamese and Hutterite Populations, Alberta, 1995 - 2001

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Canada: Alberta, 2002

Live births (L)	38282
Stillbirths (S)	249
Total births	38531
Number of terminations of pregnancy (ToP) for birth defects	59

Birth Defects	Number of cases			Rates*10.000		O/E	YB	Remark
	L	S	ToP	L+S	L+S+ToP	L+S		
Anencephaly	2	1	4	0.78	1.81	0.42	12	
Spina bifida	5	1	2	1.56	2.07	0.47	6	
Encephalocele	5	1	1	1.56	1.81	1.67	22	
Microcephaly	7	0	0	1.82	1.81	0.57	22	
Arhinencephaly / Holoprosencephaly	2	1	2	0.78	1.30	0.66	17	
Hydrocephaly	13	4	1	4.41	4.66	0.95	20	
Total Anophthalmos / Microphthalmos (include unspecified)	0	0	0	0.00	0.00	0.00	22	
Anophthalmos	0	0	0	0.00	0.00	0.00	22	
Microphthalmos	0	0	0	0.00	0.00	0.00	22	
Total Anotia / Microtia (include unspecified)	6	0	0	1.56	1.55	1.20	17	
Anotia	2	0	0	0.52	0.52	1.75	19	
Microtia	4	0	0	1.04	1.04	1.13	18	
Transposition of great vessels	17	0	1	4.41	4.66	1.44	22	
Tetralogy of Fallot	9	1	0	2.60	2.59	0.96	21	
Hypoplastic left heart syndrome	6	0	0	1.56	1.55	0.68	22	
Coarctation of aorta	18	1	0	4.93	4.92	1.12	22	
Choanal atresia, bilateral	3	0	0	0.78	0.78	0.62	22	
Cleft palate without cleft lip	30	3	0	8.56	8.55	1.09	18	
Cleft lip with or without cleft palate	51	0	1	13.24	13.47	1.17	22	
Oesophageal atresia / stenosis with or without fistula	8	1	0	2.34	2.33	0.91	22	
Small intestine atresia / stenosis	7	0	0	1.82	1.81	1.19	15	
Anorectal atresia / stenosis	24	0	4	6.23	7.26	1.41	22	
Undescended testis (36 weeks of gestation or later)	99	0	0	25.69	25.65	1.09	10	
Hypospadias	61	0	0	15.83	15.81	0.77	22	▼
Epispadias	1	0	0	0.26	0.26	0.58	22	
Indeterminate sex	2	0	0	0.52	0.52	0.66	20	
Renal agenesis	22	2	3	6.23	7.00	1.42	21	
Cystic kidney	26	1	3	7.01	7.77	1.57	16	
Bladder exstrophy	2	0	0	0.52	0.52	1.67	22	
Polydactyly, preaxial	50	2	1	13.50	13.73	0.99	19	
Total Limb reduction defects (include unspecified)	29	1	1	7.79	8.03	0.87	19	
Transverse	nr	nr	nr	nc	nc	nc		
Preaxial	nr	nr	nr	nc	nc	nc		
Postaxial	nr	nr	nr	nc	nc	nc		
Intercalary	nr	nr	nr	nc	nc	nc		
Mixed	nr	nr	nr	nc	nc	nc		
Diaphragmatic hernia	14	2	1	4.15	4.41	1.32	22	
Total Abdominal wall defects (include unspecified)	20	2	2	5.71	6.22	1.31	22	
Omphalocele	4	2	2	1.56	2.07	0.81	22	
Gastroschisis	16	0	0	4.15	4.15	2.17	20	▲
Prune belly sequence	0	0	0	0.00	0.00	0.00	22	
Trisomy 13	3	1	1	1.04	1.30	1.11	22	
Trisomy 18	8	4	6	3.11	4.66	1.04	10	
Down syndrome, all ages (include age unknown)	45	4	17	12.72	17.10	1.06	12	
<20	1	0	1	4.47	8.93	2.13	2	
20-24	2	0	0	2.55	2.55	0.66	4	
25-29	8	0	3	6.73	9.25	0.59	4	
30-34	13	1	0	12.77	12.77	0.96	4	
35-39	17	3	7	42.01	56.63	1.51	4	
40-44	4	0	6	49.32	122.40	0.54	4	
45+	0	0	0	0.00	0.00	0.00	4	

***= Terminations of Pregnancy**
nr = not reported
nc = not calculable

Canada: Alberta, time trend analysis 1980-2002

Birth prevalence rates: (L+S) * 10,000

	1974-81*	1982-86	1987-91	1992-96	1997-01	2002	Trend	RR
Births	82,118	221,349	212,720	198,350	187,033	38,531		
Anencephaly	3.53	3.61	2.73	1.92	1.55	0.78	▼	0.948
Spina bifida 4.26	5.38	4.89	5.04	3.10	1.56		▼	0.977
Encephalocele	0.97	1.08	0.80	0.91	0.91	1.56		
Microcephaly	3.41	3.43	3.48	2.57	3.21	1.82		
Arhinencephaly / Holoprosencephaly	0.37	0.54	1.08	1.16	1.50	0.78	▲	1.050
Hydrocephaly	6.21	5.65	4.04	4.59	4.28	4.41	▼	0.984
Total Anophthalmos / Microphthalmos (include unspecified)	1.22	1.22	1.60	1.06	2.03	0.00		
Anophthalmos	0.12	0.36	0.47	0.30	0.32	0.00		
Microphthalmos	1.10	0.86	1.13	0.76	1.71	0.00		
Total Anotia / Microtia (include unspecified)	0.12	0.63	0.85	1.61	1.55	1.56	▲	1.069
Anotia	0.00	0.18	0.19	0.30	0.48	0.52	▲	1.089
Microtia	0.12	0.45	0.66	1.31	1.07	1.04	▲	1.063
Transposition of great vessels	2.44	2.85	3.29	3.18	3.26	4.41		
Tetralogy of Fallot	1.22	2.17	3.15	3.08	2.73	2.60	▲	1.021
Hypoplastic left heart syndrome	2.31	2.26	2.12	2.02	2.73	1.56		
Coarctation of aorta	2.92	4.34	4.14	5.80	3.90	4.93		
Choanal atresia, bilateral	0.85	1.40	1.55	1.56	0.64	0.78		
Cleft palate without cleft lip	6.45	6.01	8.56	7.41	9.04	8.56	▲	1.017
Cleft lip with or without cleft palate	10.11	10.35	12.69	12.05	10.69	13.24		
Oesophageal atresia / stenosis with or without fistula	1.46	2.94	3.34	2.02	2.30	2.34		
Small intestine atresia / stenosis	0.61	0.81	1.36	1.31	1.92	1.82	▲	1.052
Anorectal atresia / stenosis	2.92	3.70	5.64	4.64	4.22	6.23		
Undescended testis (36 weeks of gestation or later)	25.33	26.97	30.32	23.75	23.47	25.69	▼	0.992
Hypospadias	16.68	19.11	25.20	21.33	18.50	15.83		
Epispadias	0.61	0.41	0.38	0.40	0.53	0.26		
Indeterminate sex	0.24	0.41	0.89	0.86	1.02	0.52	▲	1.043
Renal agenesis	2.56	3.57	5.22	4.64	4.44	6.23	▲	1.020
Cystic kidney	0.85	3.07	4.18	4.74	4.81	7.01	▲	1.045
Bladder exstrophy	0.12	0.36	0.28	0.25	0.43	0.52		
Polydactyly, preaxial	11.08	9.62	16.17	14.82	12.78	13.50	▲	1.013
Total Limb reduction defects (include unspecified)	5.97	7.14	9.78	8.92	9.46	7.79	▲	1.017
Transverse								
Preaxial								
Postaxial								
Intercalary								
Mixed								
Diaphragmatic hernia	3.29	3.57	2.87	2.62	3.42	4.15		
Total Abdominal wall defects (include unspecified)	2.92	4.11	4.75	3.88	5.40	5.71	▲	1.016
Omphalocele	0.97	1.90	2.59	1.51	2.03	1.56		
Gastroschisis	1.34	1.63	1.69	1.92	2.51	4.15	▲	1.037
Prune belly sequence	0.61	0.41	0.33	0.05	0.48	0.00		
Trisomy 13	0.73	0.72	1.03	1.06	1.02	1.04		
Trisomy 18	1.34	1.58	1.97	2.57	3.42	3.11	▲	1.049
Down syndrome, all ages (include age unknown)	10.11	8.76	10.86	10.54	13.37	12.72	▲	1.021
<20					8.95*	4.47		
20-24					3.90*	2.55		
25-29					11.42*	6.73		
30-34					13.24*	12.77		
35-39					27.83*	42.01		
40-44					91.42*	49.32		
45+					166.02*	0.00		

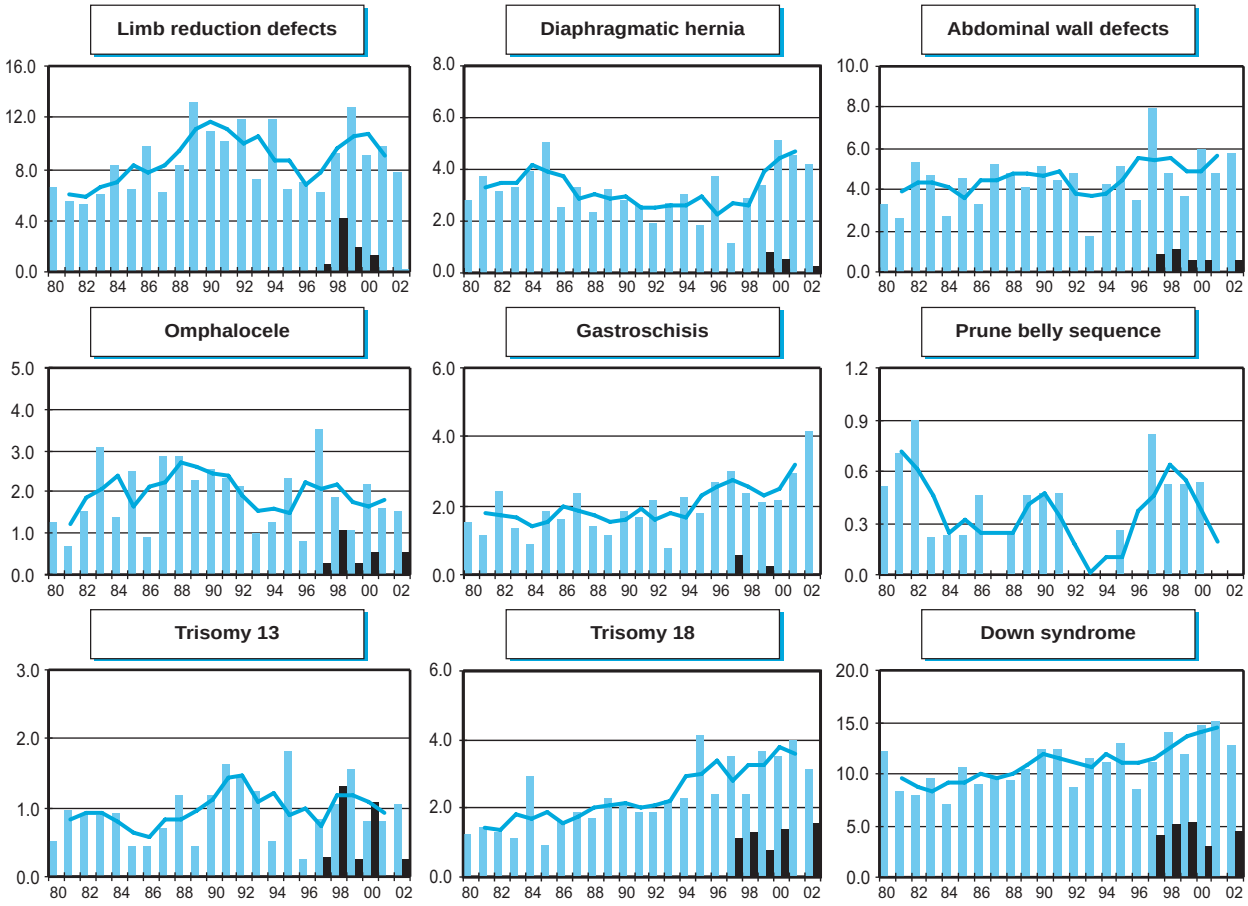
* = data include less than eight and five years

Canada: Alberta

'Time trends 1980-2002 (Birth prevalence rates per 10,000)

Note: L+S rates, ToP rates — 3-year moving average trend

Note: L+S rates, ToP rates — 3-year moving average trend



Note: L+S rates, ToP rates 3-year moving average trend

Canada: British Columbia

British Columbia Health Status Registry, Congenital Anomaly Surveillance System

The BC Health Status Registry (BCHSR), established in 1952 is a comprehensive database of information on individuals with congenital anomalies, genetic conditions and selected disabilities managed by the British Columbia Vital Statistics Agency under the Health Act.

Mission, Mandate, & General Objectives:
- To record and classify information concerning congenital anomalies, genetic conditions for any age and selected handicapping conditions of children;
- To assist health care planners and others in the planning and development of appropriate services by providing accurate and reliable data on congenital anomalies, genetic conditions and chronic handicapping conditions; and
- To undertake statistical analysis of the data collected and to assist medical and genetic research .

Additional Objectives are:
- To keep the public informed by producing timely and accurate statistical-related products, while maintaining the confidentiality of the data;
- To respond to research requests from a worldwide and varied audience, such as governments, universities, private and public organizations, health-related researchers, and administrators;
- To develop the BCHSR as a useful tool that will be utilized by the health care system.

Registration Criteria:
Since January 01, 1993, the criteria for registration of case/individual within the BCHSR is as follows:
- A person of any age who is diagnosed as having a congenital anomaly or a genetic condition, which is not necessarily disabling; or
- A person who is 19 years or less and is diagnosed as having a physical, mental and/or emotional problem which effects, to interfere substantially with education, or to prevent full and open functional employment.

Medical Coding of Diagnoses:
Based upon the medical diagnoses reported to the BCHSR, Registered Nurses trained in medical coding assign codes to the data using ICD-10 published by the WHO. In addition, an etiology code identifying the probable cause of the disease or condition is also assigned. A 6-digit McKusick code may be given in order to provide geneticists with the specific diagnostic detail they require.

Major Reporting Sources:
- Notice of Live Births, Stillbirths and Deaths
- Medical Genetics Clinics
- Hospital Admission and Discharge Abstracts
- Children's Hospital and Cystic Fibrosis Clinic
- Provincial Health Regions

Current Major Activities:
- Improving data qualities and ascertainments by cross-checking through the various multiple sources;
- Undertaking development and implementation of the Patient Record management System;
- Collecting and maintaining cases having the medically terminated pregnancies due to congenital anomalies;
- Publishing BCHSR annual congenital anomaly surveillance report;
- Producing BC Birth Defect Monitoring report by Health Region for Medical Health Officers;
- Participating various research activities based on BCHSR data.

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Phone: 1-250-9522567

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Web site:http://www.vs.gov.bc.ca

Canada: British Columbia, 2002

Live births (L)	39902
Stillbirths (S)	299
Total births	40201
Number of terminations of pregnancy (ToP) for birth defects	nr

Birth Defects	Number of cases			Rates*10.000		O/E	YB	Remark
	L	S	ToP	L+S	L+S+ToP	L+S		
Anencephaly	2	5	nr	1.74	nc	0.86	15	
Spina bifida	11	2	nr	3.23	nc	0.63	9	
Encephalocele	0	2	nr	0.50	nc	0.44	12	
Microcephaly	17	0	nr	4.23	nc	0.57	20	▼
Arhinencephaly / Holoprosencephaly	37	8	nr	11.19	nc	0.76	1	
Hydrocephaly	10	2	nr	2.99	nc	0.55	6	▼
Total Anophthalmos / Microphthalmos (include unspecified)	5	0	nr	1.24	nc	0.67	28	
Anophthalmos	0	0	nr	0.00	nc	0.00	28	
Microphthalmos	5	0	nr	1.24	nc	0.78	28	
Total Anotia / Microtia (include unspecified)	7	0	nr	1.74	nc	nc	1	
Anotia	1	0	nr	0.25	nc	nc	28	
Microtia	1	0	nr	0.25	nc	nc	1	
Transposition of great vessels	10	1	nr	2.74	nc	0.56	28	
Tetralogy of Fallot	17	0	nr	4.23	nc	0.82	28	
Hypoplastic left heart syndrome	12	4	nr	3.98	nc	1.48	28	
Coarctation of aorta	17	0	nr	4.23	nc	0.64	8	
Choanal atresia, bilateral	9	0	nr	2.24	nc	1.20	28	
Cleft palate without cleft lip	34	0	nr	8.46	nc	0.74	10	
Cleft lip with or without cleft palate	42	3	nr	11.19	nc	0.79	28	
Oesophageal atresia / stenosis with or without fistula	14	1	nr	3.73	nc	1.09	28	
Small intestine atresia / stenosis	11	0	nr	2.74	nc	0.79	28	
Anorectal atresia / stenosis	28	0	nr	6.97	nc	1.42	28	
Undescended testis (36 weeks of gestation or later)	93	0	nr	23.13	nc	0.44	5	▼
Hypospadias	71	0	nr	17.66	nc	0.49	14	▼
Epispadias 2	0	nr	0.50	nc	6.41	6		
Indeterminate sex	0	0	nr	0.00	nc	0.00	28	▼
Renal agenesis	4	4	nr	1.99	nc	2.02	1	
Cystic kidney	1	0	nr	0.25	nc	0.14	1	▼
Bladder exstrophy	1	0	nr	0.25	nc	0.54	28	
Polydactyly, preaxial	39	1	nr	9.95	nc	0.46	28	▼
Total Limb reduction defects (include unspecified)	8	0	nr	1.99	nc	0.35	6	▼
Transverse	nr	nr	nr	nc	nc	nc		
Preaxial	nr	nr	nr	nc	nc	nc		
Postaxial	nr	nr	nr	nc	nc	nc		
Intercalary	nr	nr	nr	nc	nc	nc		
Mixed	nr	nr	nr	nc	nc	nc		
Diaphragmatic hernia	10	1	nr	2.74	nc	0.68	22	
Total Abdominal wall defects (include unspecified)	28	7	nr	8.71	nc	1.00	18	
Omphalocele	11	4	nr	3.73	nc	nc	2	
Gastroschisis	16	2	nr	4.48	nc	nc	2	
Prune belly sequence	1	0	nr	0.25	nc	nc	28	
Trisomy 13	1	4	nr	1.24	nc	1.22	28	
Trisomy 18	7	17	nr	5.97	nc	2.02	12	▲
Down syndrome, all ages (include age unknown)	49	23	nr	17.91	nc	1.16	24	
<20	2	0	nr	12.49	nc	0.99	25	
20-24	6	1	nr	11.34	nc	1.89	25	
25-29	6	4	nr	8.84	nc	1.09	25	
30-34	9	7	nr	12.35	nc	0.83	25	
35-39	12	7	nr	28.22	nc	1.07	25	
40-44	8	3	nr	80.88	nc	1.13	25	
45+	1	1	nr	363.64	nc	0.51	8	

Canada: British Columbia, time trend analysis 1974-2002

Birth prevalence rates: (L+S) * 10,000

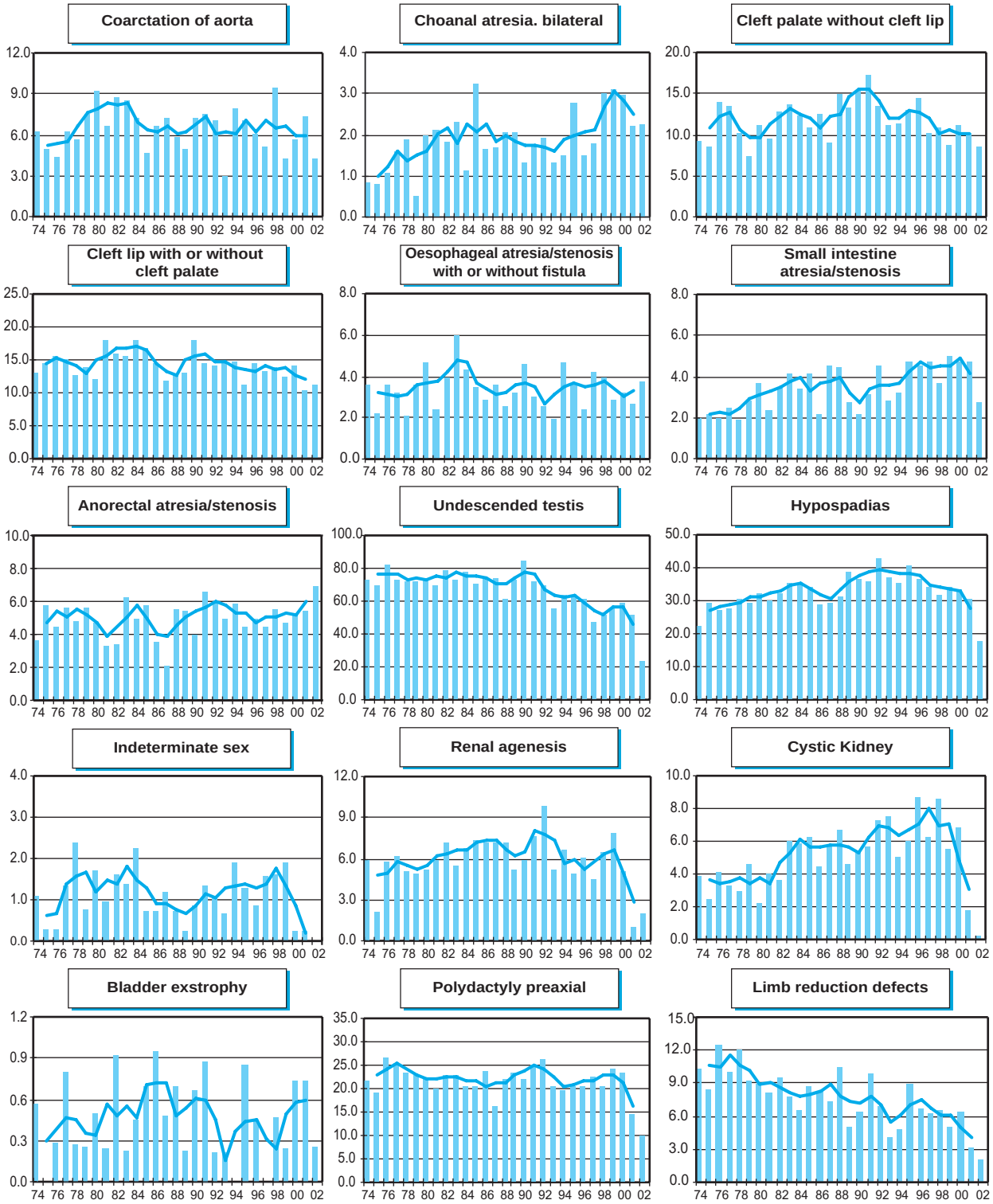
	1974-81	1982-86	1987-91	1992-96	1997-01	2002	Trend	RR
Births	304,516	216,300	220,249	233,019	211,365	40,201		
Anencephaly	5.85	3.65	2.45	1.93	1.70	1.74	▼	0.942
Spina bifida 10.25	7.67	7.08	6.57	4.64	3.23		▼	0.965
Encephalocele	1.77	1.16	1.95	1.46	0.52	0.50	▼	0.972
Microcephaly	5.25	6.47	6.63	9.14	7.24	4.23	▲	1.016
Arhinencephaly / Holoprosencephaly	1.97	4.44	4.49	3.95	7.48	11.19	▲	1.054
Hydrocephaly	11.07	6.33	7.76	6.27	5.20	2.99	▼	0.970
Total Anophthalmos / Microphthalmos (include unspecified)	2.04	1.94	1.91	1.63	1.70	1.24		
Anophthalmos	0.46	0.37	0.54	0.26	0.33	0.00		
Microphthalmos	1.64	1.66	1.50	1.50	1.66	1.24		
Total Anotia / Microtia (include unspecified)	47.26	69.63	51.08	26.22	9.27	1.74	nc	
Anotia	2.76	3.05	2.68	2.36	1.75	0.25	nc	
Microtia	42.10	64.08	46.67	22.36	5.91	0.25	nc	
Transposition of great vessels	4.60	4.85	4.77	5.06	5.06	2.74		
Tetralogy of Fallot	5.29	5.46	5.81	4.21	5.20	4.23		
Hypoplastic left heart syndrome	2.33	2.73	2.59	2.79	3.12	3.98	▲	1.016
Coarctation of aorta	6.37	7.17	6.54	6.22	6.39	4.23		
Choanal atresia, bilateral	1.38	2.03	1.77	1.80	2.60	2.24	▲	1.023
Cleft palate without cleft lip	10.34	12.34	13.94	12.57	10.17	8.46		
Cleft lip with or without cleft palate	14.28	16.04	14.03	13.69	12.77	11.19	▼	0.994
Oesophageal atresia / stenosis with or without fistula	3.19	4.11	3.41	3.05	3.41	3.73		
Small intestine atresia / stenosis	2.43	3.47	3.36	3.95	4.54	2.74	▲	1.022
Anorectal atresia / stenosis	4.73	4.81	4.77	5.28	5.06	6.97		
Undescended testis (36 weeks of gestation or later)	72.94	74.71	73.10	62.66	52.66	23.13	▼	0.984
Hypospadias	28.64	33.06	34.51	38.37	32.74	17.66	▲	1.005
Epispadias	0.00	0.05	0.00	0.00	0.09	0.50	▲	1.157
Indeterminate sex	1.12	1.34	0.86	1.16	1.14	0.00		
Renal agenesis	5.16	6.80	6.63	6.52	5.02	1.99		
Cystic kidney	3.45	5.27	5.58	6.91	5.82	0.25	▲	1.015
Bladder exstrophy	0.36	0.65	0.59	0.34	0.43	0.25		
Polydactyly, preaxial	22.53	22.01	21.88	21.41	21.01	9.95	▼	0.993
Total Limb reduction defects (include unspecified)	9.88	8.18	7.81	6.31	5.49	1.99	▼	0.971
Transverse								
Preaxial								
Postaxial								
Intercalary								
Mixed								
Diaphragmatic hernia	4.40	3.93	3.86	4.25	3.97	2.74		
Total Abdominal wall defects (include unspecified)	25.98	12.94	7.31	8.33	10.08	8.71	▼	0.945
Omphalocele	0.00	0.05	0.00	0.09	0.62	3.73	nc	
Gastroschisis	0.00	0.00	0.05	0.13	1.94	4.48	nc	
Prune belly sequence	0.00	0.05	0.00	0.04	0.05	0.25	nc	
Trisomy 13	0.62	0.92	1.09	1.16	1.47	1.24	▲	1.035
Trisomy 18	1.71	1.90	2.04	2.62	3.55	5.97	▲	1.044
Down syndrome, all ages (include age unknown)	12.84	14.24	15.53	15.75	17.46	17.91	▲	1.014
<20	8.72*	11.88	14.52	15.33	15.27	12.49		
20-24	5.28*	5.43	5.63	7.48	6.91	11.34		
25-29	7.48*	7.31	6.86	8.41	10.95	8.84		
30-34	16.09*	14.08	15.05	14.34	15.15	12.35	▼	0.983
35-39	42.01*	23.13	22.41	24.14	28.67	26.73		
40-44	110.44*	75.60	94.75	65.80	57.64	88.24	▼	0.942
45+	434.78*	689.66*	416.67*	533.33*	1454.55*	363.64		

* = data include less than five years

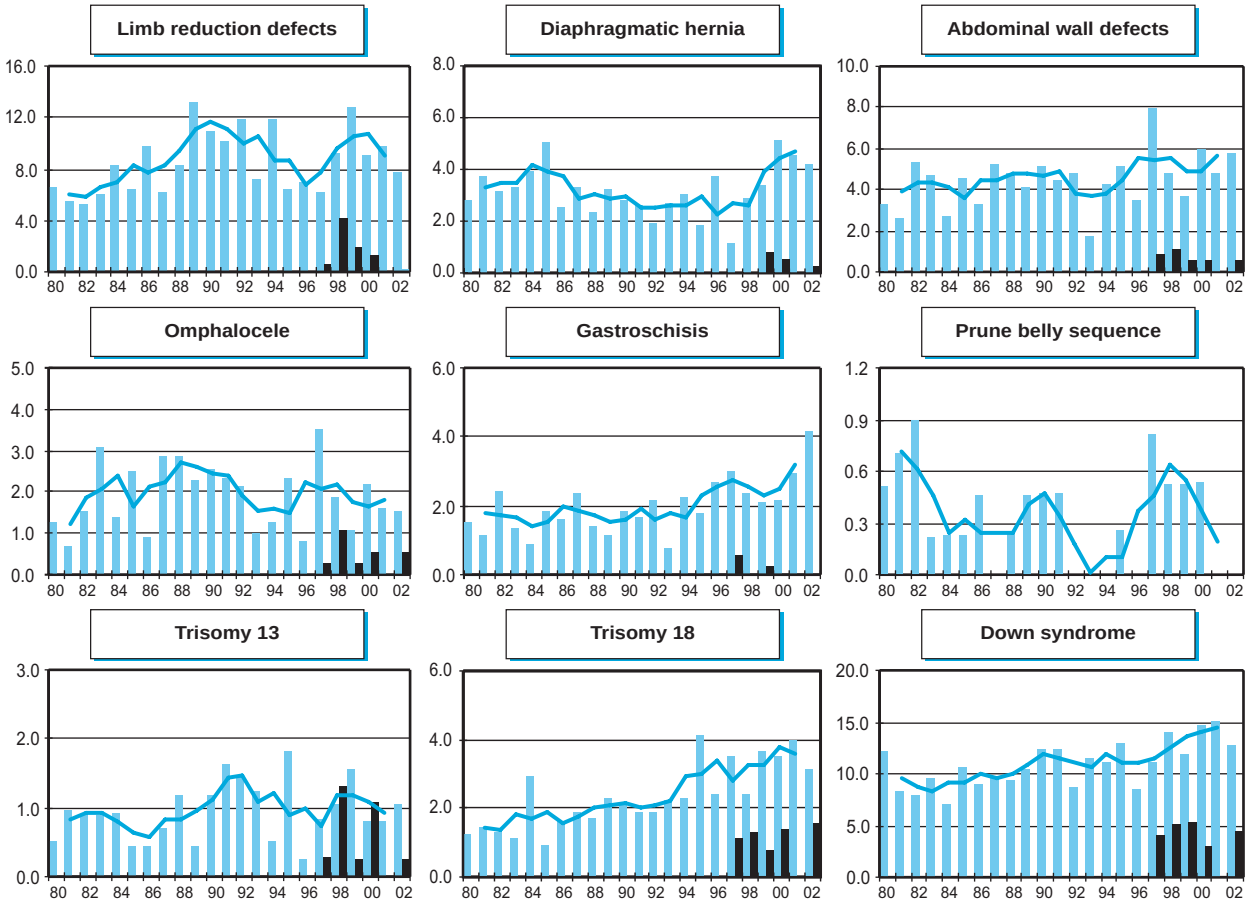
Canada: British Columbia

Time trends 1974-2002 (Birth prevalence rates per 10,000)

Note: L+S rates, 3-year moving average trend



Note: L+S rates, 3-year moving average trend



Note: L+S rates, ToP rates 3-year moving average trend

Chile, Maule: RRMC-SSM

Regional Register Congenital Malformational Maule Health Service

History:
The register started in 2001 defined by order of Director Maule Health Service and assesored for South America.ECLAMC, Eduardo Castilla.
RRMC-SSM became an associated member of ICBDMS in 2003.

Size and coverage:
RRMC-SSM is located in a Region in the center of Chile, in Talca Maule Region.
Maule Region is situated between 34° 41' & 36° 33' S and 70° 20' & 72° 44' W. The surface is 30.535 kms2 (4 % of Chile). 930,306 habitants. 37,4% rurality. Cellulosa producer and agricultural products.

The number of participating are 13 public hospitals from 2001 and since 2004 will include the unique private maternity of the region.
There are around 13.500 births annually (2002).
The information about livebirths and stillbirths are collected from 13 maternity hospitals in the region for pediatricians and midwives.
Stillbirths of at least 500g birthweight have been included since 2001.

Legislation and funding:
The registry is based on the information of births and notification of congenital malformation ECLAMC from 2001 and funded by the Maule health Service.

Sources of ascertainment:
Reporting is made by collaborating pediatricians and midwives at the delivery units of participating hospitals.

Exposure information:
Detailed information on various risk factor exposures, maternal and paternal occupation, diseases and other information available.

Background information:
Epidemiological information on all births is available from participating hospitals and statistical units.

Addres for further information:
M.Aurora Canessa, Linares Hospital, Maule Region - Chile.
AV. BRAZIL 753, LINARES, Chile.

Phone: 56-73-563276, 56-73-219879.

Fax: 56-73-219111, 56-73-219879.

E-mail: rrmc@ssmaule.cl

Chile : RRMC-SSM , 2002

Live births (L)	13607
Stillbirths (S)	83
Total births	13690
Number of terminations of pregnancy (ToP) for birth defects	not permitted

Birth Defects	Number of cases			Rates*10.000		O/E	YB	Remark
	L	S	ToP	L+S	L+S+ToP	L+S		
Anencephaly	2	0		1.46				
Spina bifida	3	0		2.19				
Encephalocele	3	0		2.19				
Microcephaly	3	0		2.19				
Arhinencephaly / Holoprosencephaly	0	0		0.00				
Hydrocephaly	1	2		2.19				
Total Anophthalmos / Microphthalmos (include unspecified)	1	0		0.73				
Anophthalmos	0	0		0.00				
Microphthalmos	1	0		0.73				
Total Anotia / Microtia (include unspecified)	3	0		2.19				
Anotia	0	0		0.00				
Microtia	3	0		2.19				
Transposition of great vessels	2	0		1.46				
Tetralogy of Fallot	4	0		2.92				
Hypoplastic left heart syndrome	0	0		0.00				
Coarctation of aorta	0	0		0.00				
Choanal atresia, bilateral	0	0		0.00				
Cleft palate without cleft lip	6	0		4.38				
Cleft lip with or without cleft palate	12	0		8.77				
Oesophageal atresia / stenosis with or without fistula	2	0		1.46				
Small intestine atresia / stenosis	3	0		2.19				
Anorectal atresia / stenosis	2	0		1.46				
Undescended testis (36 weeks of gestation or later)	6	0		4.38				
Hypospadias	15	0		10.96				
Epispadias	0	0		0.00				
Indeterminate sex	0	0		0.00				
Renal agenesis	0	0		0.00				
Cystic kidney	0	0		0.00				
Bladder exstrophy	0	0		0.00				
Polydactyly, preaxial, postaxial and unspecified	15	0		10.96				
Total Limb reduction defects (include unspecified)	3	0		2.19				
Transverse	3	0		2.19				
Preaxial	0	0		0.00				
Postaxial	0	0		0.00				
Intercalary	0	0		0.00				
Mixed	0	0		0.00				
Diaphragmatic hernia	2	0		1.46				
Total Abdominal wall defects (include unspecified)	1	2		2.19				
Omphalocele	0	2		1.46				
Gastroschisis	1	0		0.73				
Prune belly sequence	1	0		0.73				
Trisomy 13	1	0		0.73				
Trisomy 18	1	1		1.46				
Down syndrome, all ages (include age unknown)	24	1		18.26				
<20	0	0		0.00				
20-24	0	0		0.00				
25-29	3	1		10.93				
30-34	3	0		12.73				
35-39	9	0		58.37				
40-44	9	0		223.33				
45+	0	0		0.00				

China: Beijing - BDSS

Birth Defect Surveillance System in Thirty Counties of Four Provinces, People's Republic of China

History:
The Programme began in 1992. It became a full member of the ICBDMS in 1997.

Size and coverage:
This is a population based monitoring system. Reports were obtained from all hospitals and village health stations, which together cover all geographically defined population. Total number of population in these areas is around 17 millions and total number of births per year is around 150,000.

Legislation and funding:
Funding is from China Ministry of Health and local health authorities.

Sources of ascertainment:
Reports are obtained from delivery units, paediatric clinics, ultrasound departments, pathology departments and perinatal health care departments of different level hospitals, MCH institutes and village health stations in the participating counties and cites.

Exposure information:
Exposure information is obtained from the perinatal health care surveillance system (PHCSS) in the same areas for all women and their babies from pre-marital examination till six weeks after birth. BDSS data is linked with PHCSS data by using an ID number assigned to each woman.

Background information:
Background information is also obtained from PHCSS data.

Address for further information:
Zhu Li, M.D., M.P.H., China National Centre for Maternal and Infant Health, Be Medical University, 38 College Road, Beijing 100083, PR China.

Phone: 86-10-62091138

Fax: 86-10-62091141

China: Beijing, 2002

Live births (L)	141225
Stillbirths (S)	562
Total births	141787
Number of terminations of pregnancy (ToP) for birth defects	nr

Birth Defects	Number of cases			Rates*10.000		O/E	YB	Remark
	L	S	ToP	L+S	L+S+ToP	L+S		
Anencephaly	0	43	nr	3.03	nc	0.85	5	
Spina bifida	14	28	nr	2.96	nc	1.16	4	
Encephalocele	4	16	nr	1.41	nc	1.08	5	
Microcephaly	4	0	nr	0.28	nc	0.74	5	
Arhinencephaly / Holoprosencephaly	2	6	nr	0.56	nc	1.33	5	
Hydrocephaly	6	60	nr	4.65	nc	0.85	5	
Total Anophthalmos / Microphthalmos (include unspecified)	2	2	nr	0.28	nc	1.16	5	
Anophthalmos	0	1	nr	0.07	nc	0.58	5	
Microphthalmos	2	1	nr	0.21	nc	1.74	5	
Total Anotia / Microtia (include unspecified)	36	5	nr	2.89	nc	1.05	5	
Anotia	3	1	nr	0.28	nc	2.07	5	
Microtia	33	4	nr	2.61	nc	1.00	5	
Transposition of great vessels	nr	nr	nr	nc	nc	nc		
Tetralogy of Fallot	nr	nr	nr	nc	nc	nc		
Hypoplastic left heart syndrome	nr	nr	nr	nc	nc	nc		
Coarctation of aorta	nr	nr	nr	nc	nc	nc		
Choanal atresia, bilateral	nr	nr	nr	nc	nc	nc		
Cleft palate without cleft lip	41	3	nr	3.10	nc	1.15	5	
Cleft lip with or without cleft palate	135	31	nr	11.71	nc	1.22	4	
Oesophageal atresia / stenosis with or without fistula	nr	nr	nr	nc	nc	nc		
Small intestine atresia / stenosis	nr	nr	nr	nc	nc	nc		
Anorectal atresia / stenosis	20	3	nr	1.62	nc	0.98	5	
Undescended testis (36 weeks of gestation or later)	3	0	nr	0.21	nc	0.93	5	
Hypospadias	19	0	nr	1.34	nc	1.09	5	
Epispadias	1	0	nr	0.07	nc	nc	1	
Indeterminate sex	12	6	nr	1.27	nc	1.13	5	
Renal agenesis	nr	nr	nr	nc	nc	nc		
Cystic kidney	nr	nr	nr	nc	nc	nc		
Bladder exstrophy	0	0	nr	0.00	nc	0.00	5	
Polydactyly, preaxial	82	1	nr	5.85	nc	0.87	5	
Total Limb reduction defects (include unspecified)	26	5	nr	2.19	nc	0.88	5	
Transverse	21	1	nr	1.55	nc	0.90	4	
Preaxial	0	3	nr	0.21	nc	0.65	4	
Postaxial	0	0	nr	0.00	nc	nc	1	
Intercalary	0	0	nr	0.00	nc	0.00	4	
Mixed	0	0	nr	0.00	nc	0.00	4	
Diaphragmatic hernia	nr	nr	nr	nc	nc	nc		
Total Abdominal wall defects (include unspecified)	14	26	nr	2.82	nc	0.97	5	
Omphalocele	6	7	nr	0.92	nc	0.88	5	
Gastroschisis	8	19	nr	1.90	nc	0.97	4	
Prune belly sequence	0	10	nr	0.71	nc	0.60	4	
Trisomy 13	nr	nr	nr	nc	nc	nc		
Trisomy 18	nr	nr	nr	nc	nc	nc		
Down syndrome, all ages (include age unknown)	nr	nr	nr	nc	nc	nc		
<20	nr	nr	nr	nc	nc	nc		
20-24	nr	nr	nr	nc	nc	nc		
25-29	nr	nr	nr	nc	nc	nc		
30-34	nr	nr	nr	nc	nc	nc		
35-39	nr	nr	nr	nc	nc	nc		
40-44	nr	nr	nr	nc	nc	nc		
45+	nr	nr	nr	nc	nc	nc		

nr = not reported
nc = not calculable

China: Beijing, time trend analysis 1997-2002

Birth prevalence rates: (L+S) * 10,000

	1974-81	1982-86	1987-91	1992-96	1997-01	2002	Trend	RR
Births					660,041	141,787		
Anencephaly					3.56	3.03		
Spina bifida					2.83	2.96		
Encephalocele					1.30	1.41		
Microcephaly					0.38	0.28		
Arhinencephaly / Holoprosencephaly					0.42	0.56		
Hydrocephaly					5.48	4.65	▼	0.945
Total Anophthalmos / Microphthalmos (include unspecified)					0.24	0.28		
Anophthalmos					0.12	0.07		
Microphthalmos					0.12	0.21		
Total Anotia / Microtia (include unspecified)					2.74	2.89		
Anotia					0.14	0.28		
Microtia					2.61	2.61		
Transposition of great vessels								
Tetralogy of Fallot								
Hypoplastic left heart syndrome								
Coarctation of aorta								
Choanal atresia, bilateral								
Cleft palate without cleft lip					2.70	3.10		
Cleft lip with or without cleft palate					10.89	11.71		
Oesophageal atresia / stenosis with or without fistula								
Small intestine atresia / stenosis								
Anorectal atresia / stenosis					1.65	1.62		
Undescended testis (36 weeks of gestation or later)					0.23	0.21		
Hypospadias					1.23	1.34		
Epispadias					0.00	0.07		
Indeterminate sex					1.12	1.27		
Renal agenesis								
Cystic kidney								
Bladder exstrophy					0.05	0.00		
Polydactyly, preaxial					6.70	5.85		
Total Limb reduction defects (include unspecified)					2.48	2.19		
Transverse					1.73*	1.55		
Preaxial					0.33*	0.21		
Postaxial					0.00*	0.00		
Intercalary					0.02*	0.00		
Mixed					0.04*	0.00		
Diaphragmatic hernia								
Total Abdominal wall defects (include unspecified)					2.89	2.82		
Omphalocele					1.05	0.92		
Gastroschisis					1.85	1.90		
Prune belly sequence					1.38	0.71	▼	0.807
Trisomy 13								
Trisomy 18								
Down syndrome, all ages (include age unknown)								
<20								
20-24								
25-29								
30-34								
35-39								
40-44								
45+								

* = data include less than five years

China: CBDMN

Chinese Birth Defects Program of Sichuan Province, China (until 1994)
Chinese Birth Defects Monitoring Network

History:
The Programme began in 1984. It became an associate member of the ICBDMS in 1985 and a full member in 1987.

Size and coverage:
In 1984, reports were obtained from 100 hospitals but participation has increased. In 1985,205 hospitals participated. At present, the Programme covers approximately 260,000 births annually in 31 provinces.

Since we resumed reporting data, only one part of data (20 provinces, I remember apprising you by email several years ago) is sent to ICBD. The nationwide programme covers approximately 450,000~500,000 births annually in provinces.

Legislation and funding:
Participation is voluntary. Funding is mainly from local health authorities, also supported by Ministry of health.

Sources of ascertainment:
Reports are obtained from delivery units, paediatric clinics, and pathology departments of the participating hospitals.

Exposure information:
Exposure information is obtained by interviews of mothers of the reported malformed infants. No information is available on exposures in controls.

Background information:
Total number of births from each participating hospital is known.

Address for further information:
Zhu Jun, National Center for Birth Defects Monitoring, West China University of Medical Sciences, No.17 section 3 Ren Min Nan Lu, Chengdu-PRC-China.

Phone: 86-28-5501363

Fax: 86-28-5501363

E-mail: cnbdms@mail.sc.cninfo.net

E-mail: lzh@public.bta.net.cn

China: CBDMN, 2002

Live births (L)	362771
Stillbirths (S)	4820
Total births	367591
Number of terminations of pregnancy (ToP) for birth defects	nr

Birth Defects	Number of cases			Rates*10.000		O/E	YB	Remark
	L	S	ToP	L+S	L+S+ToP	L+S		
Anencephaly	21	88	nr	2.97	nc	0.73	2	▼
Spina bifida	115	130	nr	6.67	nc	0.89	6	
Encephalocele	31	29	nr	1.63	nc	0.91	6	
Microcephaly	6	2	nr	0.22	nc	0.80	5	
Arhinencephaly / Holoprosencephaly	nr	nr	nr	nc	nc	nc		
Hydrocephaly	55	218	nr	7.43	nc	1.14	6	
Total Anophthalmos / Microphthalmos (include unspecified)	8	1	nr	0.24	nc	0.63	6	
Anophthalmos	nr	nr	nr	nc	nc	nc		
Microphthalmos	nr	nr	nr	nc	nc	nc		
Total Anotia / Microtia (include unspecified)	107	7	nr	3.10	nc	1.06	6	
Anotia	nr	nr	nr	nc	nc	nc		
Microtia	nr	nr	nr	nc	nc	nc		
Transposition of great vessels	nr	nr	nr	nc	nc	nc		
Tetralogy of Fallot	nr	nr	nr	nc	nc	nc		
Hypoplastic left heart syndrome	nr	nr	nr	nc	nc	nc		
Coarctation of aorta	nr	nr	nr	nc	nc	nc		
Choanal atresia, bilateral	nr	nr	nr	nc	nc	nc		
Cleft palate without cleft lip	90	4	nr	2.56	nc	1.09	6	
Cleft lip with or without cleft palate	437	63	nr	13.60	nc	0.98	6	
Oesophageal atresia / stenosis with or without fistula	27	5	nr	0.87	nc	1.15	6	
Small intestine atresia / stenosis	nr	nr	nr	nc	nc	nc		
Anorectal atresia / stenosis	103	17	nr	3.26	nc	1.14	6	
Undescended testis (36 weeks of gestation or later)	29	3	nr	0.87	nc	1.45	6	
Hypospadias	175	2	nr	4.82	nc	1.11	3	
Epispadias	nr	nr	nr	nc	nc	nc		
Indeterminate sex	38	18	nr	1.52	nc	1.40	6	
Renal agenesis	5	7	nr	0.33	nc	1.47	5	
Cystic kidney	15	29	nr	1.20	nc	1.35	5	
Bladder exstrophy	3	2	nr	0.14	nc	1.50	6	
Polydactyly, total	426	15	nr	12.00	nc	nc		
Total Limb reduction defects (include unspecified)	154	75	nr	6.23	nc	1.18	6	
Transverse	nr	nr	nr	nc	nc	nc		
Preaxial	nr	nr	nr	nc	nc	nc		
Postaxial	nr	nr	nr	nc	nc	nc		
Intercalary	nr	nr	nr	nc	nc	nc		
Mixed	nr	nr	nr	nc	nc	nc		
Diaphragmatic hernia	8	3	nr	0.30	nc	0.54	6	
Total Abdominal wall defects (include unspecified)	86	62	nr	4.03	nc	0.99	6	
Omphalocele	38	22	nr	1.63	nc	1.20	6	
Gastroschisis	48	40	nr	2.39	nc	0.88	6	
Prune belly sequence	nr	nr	nr	nc	nc	nc		
Trisomy 13	0	1	nr	0.03	nc	nc		
Trisomy 18	3	1	nr	0.11	nc	nc		
Down syndrome, all ages (include age unknown)	81	4	nr	2.31	nc	1.07	4	
<20	0	0	nr	0.00	nc	0.00	5	
20-24	12	1	nr	1.54	nc	1.40	6	
25-29	32	1	nr	1.70	nc	0.89	3	
30-34	20	1	nr	2.97	nc	1.16	6	
35+	17	1	nr	10.57	nc	0.97	6	
	nr	nr	nr	nc	nc	nc		
	nr	nr	nr	nc	nc	nc		

China: CBDMN, time trend analysis 1996-2002

Birth prevalence rates: (L+S) * 10,000

	1974-81	1982-86	1987-91	1992-96*	1997-01	2002	Trend	RR
Births				295,243	1,574,814	367,591		
Anencephaly				6.71	4.73	2.97	▼	0.881
Spina bifida				7.35	7.48	6.67	▼	
Encephalocele				1.86	1.78	1.63		0.946
Microcephaly				0.07	0.27	0.22		
Arhinencephaly / Holoprosencephaly								
Hydrocephaly				6.40	6.54	7.43		
Total Anophthalmos / Microphthalmos (include unspecified)				0.47	0.37	0.24		
Anophthalmos								
Microphthalmos								
Total Anotia / Microtia (include unspecified)				3.08	2.91	3.10		
Anotia								
Microtia								
Transposition of great vessels								
Tetralogy of Fallot								
Hypoplastic left heart syndrome								
Coarctation of aorta								
Choanal atresia, bilateral								
Cleft palate without cleft lip				2.00	2.42	2.56		
Cleft lip with or without cleft palate				14.12	13.86	13.60		
Oesophageal atresia / stenosis with or without fistula				0.71	0.76	0.87		
Small intestine atresia / stenosis								
Anorectal atresia / stenosis				2.68	2.91	3.26	▲	1.046
Undescended testis (36 weeks of gestation or later)				0.37	0.64	0.87	▲	1.096
Hypospadias				3.05	3.80	4.82	▲	1.112
Epispadias								
Indeterminate sex				0.75	1.15	1.52		
Renal agenesis				0.10	0.25*	0.33		
Cystic kidney				0.58	0.89	1.20	▲	1.130
Bladder exstrophy				0.07	0.10	0.14		
Polydactyly, preaxial						12.00	nc	
Total Limb reduction defects (include unspecified)				4.84	5.34	6.23	▲	1.038
Transverse								
Preaxial								
Postaxial								
Intercalary								
Mixed								
Diaphragmatic hernia				0.75	0.52	0.30		
Total Abdominal wall defects (include unspecified)				4.03	4.08	4.03		
Omphalocele				1.25	1.38	1.63		
Gastroschisis				2.78	2.70	2.39		
Prune belly sequence								
Trisomy 13						0.03	nc	
Trisomy 18						0.11	nc	
Down syndrome, all ages (include age unknown)				1.73	2.01	2.31	▲	1.090
<20				0.00	4.98	0.00		
20-24				1.01	1.12	1.54		
25-29				1.38	1.61	1.70	▲	1.076
30-34				3.37	2.45	2.97		
35+				9.05	11.17	10.57		

* = data include less than five years

Costa Rica: CREC
Costa Rican Birth Defects Register Center

History:
The registry was created in 1986, based in a government decret by which birth defects became subject of obligatory notification.
The program became an ICBDMS member in September 2003.

Size and coverage:
The program is population based it. Includes all births from the National Security System (CCSS) which covers about 98% of all births occurred in the country, and births of private hospitals.
There are approximately 75000 annual births in Costa Rica.

Legislation and funding:
The Registry is financed by the government as a program of the Costa Rican Institute of Research and Training in Nutrition and Health (INCIENSA), Institute that depends from the Ministry of Health.

Sources of ascertainment:
Reporting is made by neonatologists, pediatricians and physicians before newborns discharge from maternity services, with biostatistics personal collaboration.

Exposure information:
None is routinely collected at present.

Background information:
Linkage studies are possible with other statistical data from the National Statistics Center and the National Security System Statistical Center

Address for further information:
Lila Umaña, Department of Genetics, Costa Rican Institute of Research and training in Nutrition and Health. PO Box 4-2250 Tres Ríos, Cartago. Costa Rica, Central America.

Phone: (506) 2799911

Fax: (506) 2795546

E-mail: lumana@inciensa.sa.cr

Costa Rica: CREC, 2002

Live births (L)	70679
Stillbirths (S)	465
Total births	71144
Number of terminations of pregnancy (ToP) for birth defects	not permitted

Birth Defects	Number of cases			Rates*10.000		O/E	YB	Remark
	L	S	ToP	L+S	L+S+ToP	L+S		
Anencephaly	10	4		1.97				
Spina bifida	20	3		3.23				
Encephalocele	4	1		0.70				
Microcephaly	6	1		0.98				
Arhinencephaly / Holoprosencephaly	2	0		0.28				
Hydrocephaly	10	0		1.41				
Total Anophthalmos / Microphthalmos (include unspecified)	1	0		0.14				
Anophthalmos	1	0		0.14				
Microphthalmos	0	0		0.00				
Total Anotia / Microtia (include unspecified)	13	0		1.83				
Anotia	1	0		0.14				
Microtia	12	0		1.69				
Transposition of great vessels	1	0		0.14				
Tetralogy of Fallot	2	0		0.28				
Hypoplastic left heart syndrome	3	0		0.42				
Coarctation of aorta	1	0		0.14				
Choanal atresia, bilateral	2	0		0.28				
Cleft palate without cleft lip	16	1		2.39				
Cleft lip with or without cleft palate	50	3		7.45				
Oesophageal atresia / stenosis with or without fistula	7	0		0.98				
Small intestine atresia / stenosis	3	0		0.42				
Anorectal atresia / stenosis	13	0		1.83				
Undescended testis (36 weeks of gestation or later)	62	0		8.71				
Hypospadias	40	0		5.62				
Epispadias	0	0		0.00				
Indeterminate sex	12	0		1.69				
Renal agenesis	4	0		0.56				
Cystic kidney	3	1		0.56				
Bladder exstrophy	0	0		0.00				
Polydactyly, preaxial	47	1		6.75				
Total Limb reduction defects (include unspecified)	33	2		4.92				
Transverse	nr	nr		nc				
Preaxial	nr	nr		nc				
Postaxial	nr	nr		nc				
Intercalary	nr	nr		nc				
Mixed	nr	nr		nc				
Diaphragmatic hernia	11	0		1.55				
Total Abdominal wall defects (include unspecified)	12	0		1.69				
Omphalocele	0	0		0.00				
Gastroschisis	6	0		0.84				
Prune belly sequence	1	0		0.14				
Trisomy 13	10	0		1.41				
Trisomy 18	5	1		0.84				
Down syndrome, all ages (include age unknown)	56	0		7.87				
<20	10	0		6.92				
20-24	14	0		6.54				
25-29	8	0		4.99				
30-34	11	0		9.70				
35-39	10	0		16.53				
40-44	3	0		19.78				
45+	0	0		0.00				

Cuba: RECUMAC

Cuban Register of Congenital Malformation

History:
The program started in 1985 and has grown in size and coverage. The registry became a member of the ICBDMS in 2003.

Size and coverage:
Reports are obtained from hospitals distributed all over Cuba. The number of participating hospitals has grown in 1986 to 54 at the present time. The annual number of birth is approximately 140 000 representing almost 95 % of all births.

Legislation and funding:
It is a research programme with voluntary participation of hospitals. The registry is associated with the National Center of Medical Genetics, and is financed by Health Public Ministery of Cuba.

Sources and ascertainment:
Reports are obtained from delivery units paediatric departments of the participating hospitals. Mothers are also interviewed directly to gather information and fill in the RECUMAC standard protocols.

Exposure information:
The mother of each reported infant and the mother of a control infant, the next non malformed infant born at the hospital with the same sex as the proband are interviewed on various exposures, including drug usage and parental occupation.

Background information:
Total number of births by sex and number of twin pairs in each participating hospital are know. Other background information is obtained partly from summarizing tables of births in each participating hospitals, partly from the control material.

Address for further information:
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Cuba: RECUMAC, 2002

Live births (L)	141276
Stillbirths (S)	1869
Total births	143145
Number of terminations of pregnancy (ToP) for birth defects	686

Birth Defects	Number of cases			Rates*10.000		O/E	YB	Remark
	L	S	ToP	L+S	L+S+ToP	L+S		
Anencephaly	0	1	68	0.07	4.80			
Spina bifida	16	0	51	1.12	4.66			
Encephalocele	1	1	3	0.14	0.35			
Microcephaly	6	0	2	0.42	0.56			
Arhinencephaly / Holoprosencephaly	1	0	1	0.07	0.14			
Hydrocephaly	27	2	95	2.03	8.62			
Total Anophthalmos / Microphthalmos (include unspecified)	3	0	1	0.21	0.28			
Anophthalmos	1	0	0	0.07	0.07			
Microphthalmos	2	0	1	0.14	0.21			
Total Anotia / Microtia (include unspecified)	6	0	0	0.42	0.42			
Anotia	2	0	0	0.14	0.14			
Microtia	4	0	0	0.28	0.28			
Transposition of great vessels	24	0	4	1.68	1.95			
Tetralogy of Fallot	33	0	3	2.31	2.50			
Hypoplastic left heart syndrome	2	1	10	0.21	0.90			
Coarctation of aorta	3	0	3	0.21	0.42			
Choanal atresia, bilateral	3	1	1	0.28	0.35			
Cleft palate without cleft lip	23	1	3	1.68	1.88			
Cleft lip with or without cleft palate	66	1	14	4.68	5.63			
Oesophageal atresia / stenosis with or without fistula	24	2	11	1.82	2.57			
Small intestine atresia / stenosis	12	0	8	0.84	1.39			
Anorectal atresia / stenosis	27	0	0	1.89	1.88			
Undescended testis (36 weeks of gestation or later)	38	0	0	2.65	2.64			
Hypospadias	100	0	0	6.99	6.95			
Epispadias	1	0	0	0.07	0.07			
Indeterminate sex	7	0	0	0.49	0.49			
Renal agenesis	6	2	7	0.56	1.04			
Cystic kidney	5	0	33	0.35	2.64			
Bladder exstrophy	2	0	0	0.14	0.14			
Polydactyly, preaxial	12	0	0	0.84	0.83			
Total Limb reduction defects (include unspecified)	27	0	10	1.89	2.57			
Transverse	9	0	0	0.63	0.63			
Preaxial	0	0	0	0.00	0.00			
Postaxial	0	0	0	0.00	0.00			
Intercalary	0	0	0	0.00	0.00			
Mixed	0	0	0	0.00	0.00			
Diaphragmatic hernia	18	0	13	1.26	2.16			
Total Abdominal wall defects (include unspecified)	20	0	59	1.40	5.49			
Omphalocele	11	0	17	0.77	1.95			
Gastroschisis	9	0	42	0.63	3.55			
Prune belly sequence	0	0	0	0.00	0.00			
Trisomy 13	3	0	9	0.21	0.83			
Trisomy 18	1	0	5	0.07	0.42			
Down syndrome, all ages (include age unknown)	114	0	25	7.96	9.66			
<20	6	0	0	nc	nc			
20-24	6	0	0	nc	nc			
25-29	22	0	0	nc	nc			
30-34	22	0	0	nc	nc			
35-39	24	0	0	nc	nc			
40-44	16	0	0	nc	nc			
45+	3	0	0	nc	nc			

Cuba: RECUMAC, time trend analysis 1985-2002

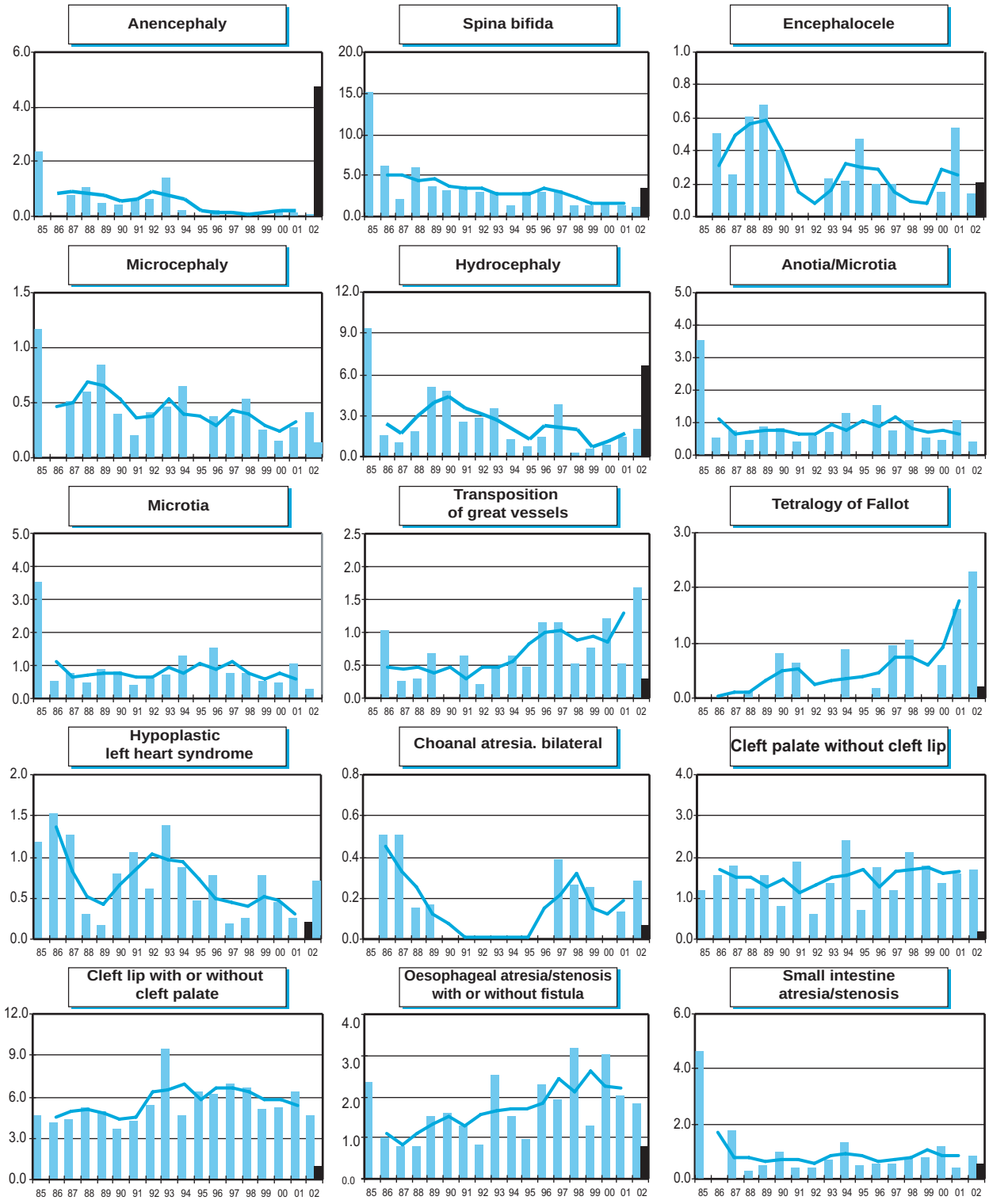
Birth prevalence rates: (L+S) * 10,000

	1974-81	1982-86*	1987-91	1992-96	1997-01	2002	Trend	RR
Births		28,122	260,474	231,977	269,593	143,145		
Anencephaly		0.71	0.69	0.47	0.07	0.07		
Spina bifida	8.89	3.84	2.72	1.78	1.12			
Encephalocele		0.36	0.42	0.22	0.22	0.14		
Microcephaly		0.36	0.54	0.39	0.30	0.42		
Arhinencephaly / Holoprosencephaly		0.71	0.12	0.09	0.04	0.07		
Hydrocephaly		3.91	3.15	1.94	1.48	2.03		
Total Anophthalmos / Microphthalmos (include unspecified)		0.00	0.15	0.00	0.26	0.21		
Anophthalmos		0.00	0.08	0.00	0.07	0.07		
Microphthalmos		0.00	0.08	0.00	0.19	0.14		
Total Anotia / Microtia (include unspecified)		1.42	0.65	0.86	0.78	0.42		
Anotia		0.00	0.00	0.00	0.04	0.14		
Microtia		1.42	0.65	0.86	0.74	0.28		
Transposition of great vessels		0.71	0.38	0.60	0.85	1.68		
Tetralogy of Fallot		0.00	0.31	0.22	0.93	2.31		
Hypoplastic left heart syndrome		1.42	0.65	0.82	0.37	0.21		
Coarctation of aorta		0.00	0.08	0.09	0.15	0.21		
Choanal atresia, bilateral		0.36	0.15	0.00	0.19	0.28		
Cleft palate without cleft lip		1.42	1.42	1.38	1.56	1.68		
Cleft lip with or without cleft palate		4.27	4.53	6.34	6.05	4.68		
Oesophageal atresia / stenosis with or without fistula		1.42	1.19	1.64	2.30	1.82		
Small intestine atresia / stenosis		1.42	0.73	0.69	0.74	0.84		
Anorectal atresia / stenosis		2.49	1.07	1.51	1.34	1.89		
Undescended testis (36 weeks of gestation or later)		4.62	3.80	4.66	2.08	2.65		
Hypospadias		14.58	14.86	11.68	10.09	6.99		
Epispadias		0.00	0.31	0.13	0.22	0.07		
Indeterminate sex		0.36	0.19	0.22	0.22	0.49		
Renal agenesis		1.78	0.38	0.30	0.22	0.56		
Cystic kidney		1.42	1.11	0.86	0.59	0.35		
Bladder exstrophy		0.71	0.12	0.22	0.15	0.14		
Polydactyly, preaxial		0.71	0.08	0.17	0.67	0.84		
Total Limb reduction defects (include unspecified)		4.62	2.34	2.85	2.56	1.89		
Transverse		2.13	0.92	0.95	0.56	0.63		
Preaxial					0.27*	0.00		
Postaxial					0.00*	0.00		
Intercalary					0.40*	0.00		
Mixed					1.21*	0.00		
Diaphragmatic hernia		1.42	1.54	1.38	1.48	1.26		
Total Abdominal wall defects (include unspecified)		2.49	1.00	1.08	0.56	1.40		
Omphalocele		2.13	0.58	0.65	0.26	0.77		
Gastroschisis		0.00	0.38	0.56	0.33	0.63		
Prune belly sequence		0.00	0.15	0.04	0.00	0.00		
Trisomy 13		0.36	0.54	0.39	0.52	0.21		
Trisomy 18		0.36	0.08	0.39	0.33	0.07		
Down syndrome, all ages (include age unknown)		11.73	7.56	7.41	7.68	7.96		
<20								
20-24								
25-29								
30-34								
35-39								
40-44								
45+								

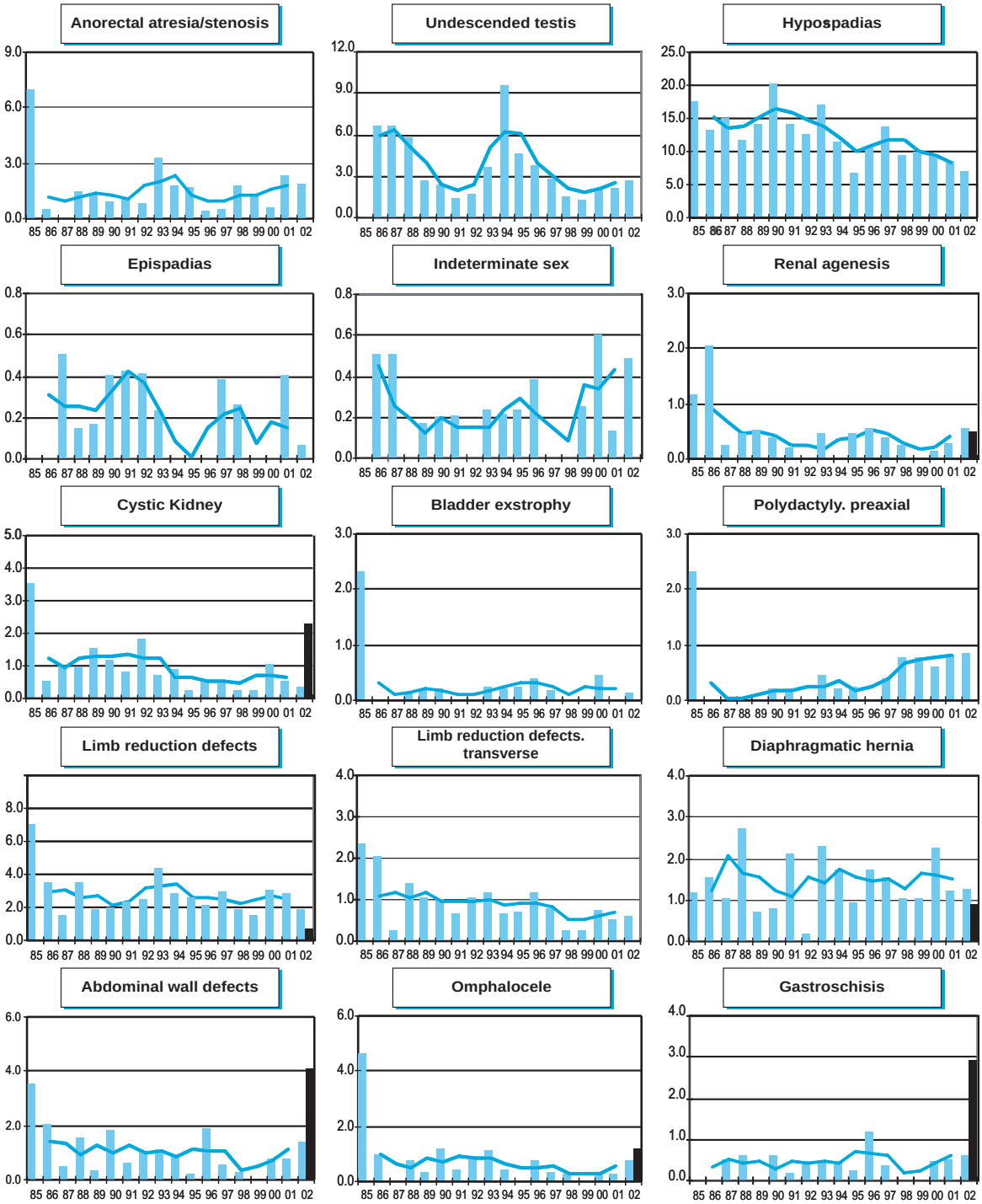
* = data include less than five years

Cuba RECUMAC

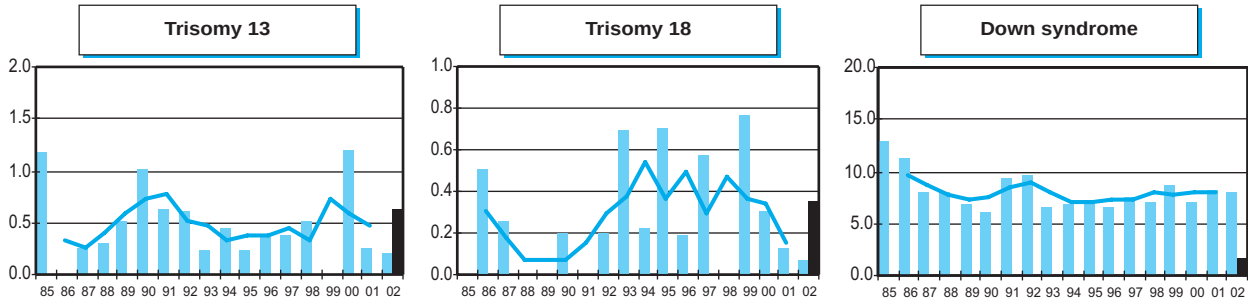
'Time trends 1985-2002 (Birth prevalence rates per 10,000)



Note: L+S rates, ToP rates — 3-year moving average trend



Note: L+S rates, ToP rates — 3-year moving average trend



Note: L+S rates, ToP rates 3-year moving average trend

Czech Republic

Congenital Malformations Monitoring Program of the Czech Republic

History:
A registration of congenital malformation began in 1961 and regular monitoring started in 1975. The programme was a founding member of the Clearinghouse and is a full member.

Size and coverage:
All births in the Czech Republic (Bohemia, Moravia and Silesia regions) are covered, at present comprising approximately 90,000 annual births. Stillbirths weighting at least 1,000g are included.

Legislation and funding:
Reporting is compulsory. The registration is financed and run by the government in the Institute of Health Information and Statistics of the Czech Republic. Analysis of data is supported by Grant project NJ 7516-3 of Grant Agency Ministry of Health of the Czech Republic in the Institute for Care of Mother and Child.

Sources of ascertainment:
Reports are obtained from delivery units, neonatal, pediatric, child surgery, pathology departments and cytogenetic laboratories. Reporting to the central registry occurs via Regional Department of Institute of Health Information and Statistics.

Exposure information:
Some exposure information is available on malformed infants, at present none on controls.

Background information:
Information's on all births are available in the Institute of Health Information and Statistics of the Czech Republic.

Research projects
a) started or ongoing in 2003 – 2004: data analyses from the CM register – incidences of CMs in pre- and postnatally diagnosed cases. Submitting data for MADRE, AWD project, cleft lip/palate project, prenatal diagnostics of Down syndrome and congenital heart defects.
b) finished during 2003 – 2004 period: CM in children after assisted reproduction in the Czech Republic.

Education or promotion project
None

Other relevant information to the scientific community about the activity of the registry:
In early 2004, a new Act on Health Registers was adopted by the Czech Parliament. This will allow, among others, further activities of the Congenital Malformations Register. A grant support of the CM Register will be provided in the 2003 – 2005 period .

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Czech Republic, 2002

Live births (L)	92786
Stillbirths (S)	261
Total births	93047
Number of terminations of pregnancy (ToP) for birth defects	489

Birth Defects	Number of cases			Rates*10.000		O/E	YB	Remark
	L	S	ToP	L+S	L+S+ToP	L+S		
Anencephaly	0	0	18	0.00	1.92	0.00	12	
Spina bifida	17	0	20	1.83	3.96	1.09	11	
Encephalocele	4	0	4	0.43	0.86	1.08	17	
Microcephaly	16	0	1	1.72	1.82	2.02	25	
Arhinencephaly / Holoprosencephaly	6	0	nr	0.64	nc	5.17	7	▲
Hydrocephaly	23	4	24	2.90	5.45	1.10	28	
Total Anophthalmos / Microphthalmos (include unspecified)	6	0	nr	0.64	nc	1.30	9	
Anophthalmos	1	0	nr	0.11	nc	1.96	4	
Microphthalmos	5	0	nr	0.54	nc	2.44	4	
Total Anotia / Microtia (include unspecified)	10	0	nr	1.07	nc	0.10	3	▼
Anotia	6	0	nr	0.64	nc	0.67	3	
Microtia	4	0	nr	0.43	nc	1.30	3	
Transposition of great vessels	34	0	5	3.65	4.17	1.55	25	
Tetralogy of Fallot	23	0	4	2.47	2.89	0.83	7	
Hypoplastic left heart syndrome	11	0	17	1.18	2.99	0.70	8	
Coarctation of aorta	35	0	10	3.76	4.81	1.06	8	
Choanal atresia, bilateral	5	0	nr	0.54	nc	2.12	8	
Cleft palate without cleft lip	78	0	9	8.38	9.30	1.39	28	▲
Cleft lip with or without cleft palate	119	1	nr	12.90	nc	1.29	28	▲
Oesophageal atresia / stenosis with or without fistula	31	0	nr	3.33	nc	1.31	7	
Small intestine atresia / stenosis	28	0	nr	3.01	nc	1.38	8	
Anorectal atresia / stenosis	32	0	nr	3.44	nc	1.09	6	
Undescended testis (36 weeks of gestation or later)	193	0	nr	20.74	nc	0.82	1	▼
Hypospadias	306	0	nr	32.89	nc	1.12	3	
Epispadias	2	0	nr	0.21	nc	0.49	8	
Indeterminate sex	3	1	nr	0.43	nc	0.95	8	
Renal agenesis	50	1	12	5.48	6.74	3.60	28	▲
Cystic kidney	50	0	8	5.37	6.20	2.19	28	▲
Bladder exstrophy	1	0	nr	0.11	nc	0.84	25	
Polydactyly, preaxial	134	1	nr	14.51	nc	1.15	14	
Total Limb reduction defects (include unspecified)	43	1	4	4.73	5.13	0.96	26	
Transverse	nr	nr	nr	nc	nc	nc		
Preaxial	nr	nr	nr	nc	nc	nc		
Postaxial	nr	nr	nr	nc	nc	nc		
Intercalary	nr	nr	nr	nc	nc	nc		
Mixed	nr	nr	nr	nc	nc	nc		
Diaphragmatic hernia	29	0	7	3.12	3.85	1.71	16	▲
Total Abdominal wall defects (include unspecified)	15	0	31	1.61	4.92	0.83	11	
Omphalocele	9	0	9	0.97	1.92	0.78	8	
Gastroschisis	6	0	22	0.64	2.99	0.94	11	
Prune belly sequence	nr	nr	nr	nc	nc	nc		
Trisomy 13	3	0	10	0.32	1.39	0.89	8	
Trisomy 18	8	3	33	1.18	4.70	1.73	8	
Down syndrome, all ages (include age unknown)	50	0	102	5.37	16.25	0.84	15	
<20	0	0	0	0.00	0.00	0.00	28	
20-24	9	0	13	3.97	9.70	0.93	25	
25-29	17	0	23	4.11	9.67	0.77	15	
30-34	12	0	23	6.50	18.93	0.74	26	
35-39	5	0	29	8.59	58.11	0.76	8	
40-44	3	0	13	33.56	176.41	0.60	20	
45+	1	0	1	333.33	645.16	1.39	28	

Czech Republic, time trend analysis 1974-2002

Birth prevalence rates: (L+S) * 10,000

	1974-81	1982-86	1987-91	1992-96	1997-01	2002	Trend	RR
Births	1,412,636	688,659	654,036	536,751	453,680	93,047		
Anencephaly	3.28	2.43	0.70	0.11	0.09	0.00	▼	0.915
Spina bifida 3.96	3.94	2.83	1.81	1.63	1.83		▼	0.965
Encephalocele	0.52	0.62	0.64	0.26	0.26	0.43	▼	0.982
Microcephaly	1.08	0.89	0.81	0.61	0.86	1.72		
Arhinencephaly / Holoprosencephaly				0.11*	0.13	0.64		
Hydrocephaly	2.39	2.88	2.89	2.81	2.53	2.90		
Total Anophthalmos / Microphthalmos (include unspecified)			1.11*	0.75	0.37	0.64	▼	0.908
Anophthalmos					0.06*	0.11		
Microphthalmos					0.22*	0.54		
Total Anotia / Microtia (include unspecified)	0.09	0.13	0.08*	0.24*	6.81	1.07	▲	1.197
Anotia					0.96*	0.64	nc	
Microtia					0.33*	0.43	nc	
Transposition of great vessels	2.63	1.86	1.47*	1.84*	3.66	3.65		
Tetralogy of Fallot				1.97*	3.24	2.47		
Hypoplastic left heart syndrome	0.57	0.74	0.65*	1.73*	1.68	1.18	▲	1.052
Coarctation of aorta				3.54*	3.57	3.76		
Choanal atresia, bilateral				0.31*	0.22	0.54		
Cleft palate without cleft lip	5.83	6.53	5.61	5.83	6.79	8.38	▲	1.006
Cleft lip with or without cleft palate	10.00	10.47	10.24	9.95	9.30	12.90		
Oesophageal atresia / stenosis with or without fistula	1.20	1.19	1.01	1.92	2.67	3.33	▲	1.040
Small intestine atresia / stenosis				1.87*	2.38	3.01	▲	1.061
Anorectal atresia / stenosis	1.32	1.12	0.73	2.40	3.11	3.44	▲	1.043
Undescended testis (36 weeks of gestation or later)				4.76*	16.36	20.74	▲	1.223
Hypospadias	18.73	20.52	23.48	23.88	27.27	32.89	▲	1.018
Epispadias				0.31*	0.53	0.21		
Indeterminate sex				0.34*	0.53	0.43		
Renal agenesis	1.62	1.29	1.18	1.45	2.14	5.48	▲	1.019
Cystic kidney	2.51	2.48	1.97	1.94	3.59	5.37	▲	1.012
Bladder exstrophy	0.16	0.06	0.02*	0.17*	0.22	0.11		
Polydactyly, preaxial			12.29*	13.34	12.19	14.51		
Total Limb reduction defects (include unspecified)	4.36	5.33	5.18*	4.92	4.72	4.73	▲	1.006
Transverse								
Preaxial								
Postaxial								
Intercalary								
Mixed								
Diaphragmatic hernia	2.55	2.58	1.85	1.77	1.76	3.12	▼	0.984
Total Abdominal wall defects (include unspecified)	3.38	3.67	3.16	2.25	1.68	1.61	▼	0.977
Omphalocele	2.28	2.29	2.43	1.88	1.06	0.97	▼	0.980
Gastroschisis	1.10	1.38	0.91*	0.68*	0.60	0.64	▼	0.979
Prune belly sequence				0.00*	0.00*		nc	
Trisomy 13				0.34*	0.37	0.32		
Trisomy 18				0.85*	0.57	1.18		
Down syndrome, all ages (include age unknown)	8.46	7.86	6.21	7.21	5.84	5.37	▼	0.985
<20	4.51	5.92	3.52	3.47	4.87	0.00		
20-24	5.40	4.88	2.95	4.03	4.63	3.97	▼	0.984
25-29	8.27	8.11	5.16	6.44	4.67	4.11	▼	0.976
30-34	11.35	8.43	8.24	10.13	7.47	6.50	▼	0.981
35-39	31.02	31.22	25.62	19.00	8.55	8.59	▼	0.959
40-44	123.18	77.10	57.84	45.15	46.88	33.56		0.954
45+	242.21	200.00	404.04	359.71	0.00	333.33	▼	

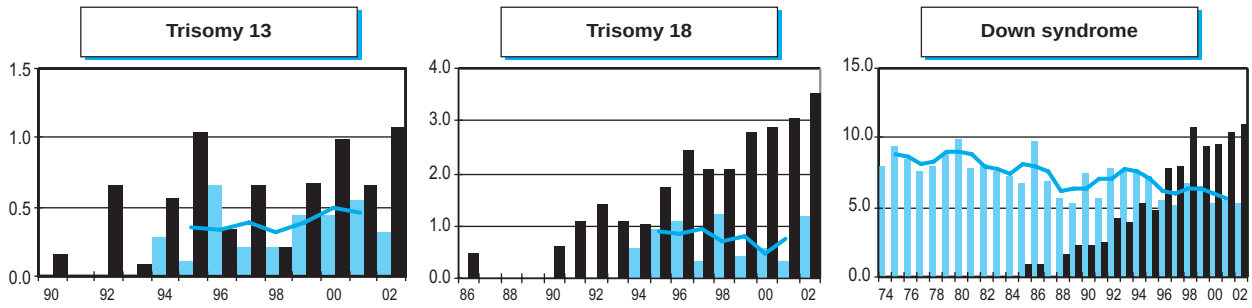
* = data include less than five years

Czech Republic

'Time trends 1974-2002 (Birth prevalence rates per 10,000)

Note: L+S rates, ToP rates — 3-year moving average trend

Note: L+S rates, ToP rates — 3-year moving average trend



Note: L+S rates, ToP rates — 3-year moving average trend

England and Wales
The National Congenital Anomaly System

History:
The monitoring Programme was started in 1964. It was a founding member of the Clearinghouse and is a full member.

Size and coverage:
All births in England and Wales are covered, at present approximately 600,000 annually. Stillbirths of 24 weeks or more gestation are registered.

Legislation and funding:
Reporting is voluntary. The governmental Office for National Statistics finances the National Congenital Anomaly System.

Sources of ascertainment:
Reports are mainly based on notifications of births prepared by attendants at birth, either physicians or midwives, supplemented by other reports from neonatal intensive care units, special care baby units etc. Improvements to NCAS have been made through collaboration with local congenital anomaly registers. In 1998 the Wales regional congenital anomaly register began exchanging information, followed in 1999 by the East Midlands & South Yorkshire congenital anomaly register (formerly known as Trent). In 2000 reporting started from the Merseyside and Cheshire register and the North Thames West register. Now in 2002 two further registers began reporting to NCAS – Wessex and Oxfordshire. These six registers together use several sources for ascertainment and cover 33% of the births in England and Wales.

Exposure information:
Parents' occupation is known.

Background information:
Information on all births is available from birth certificates.

Address for further information:
Nirupa Dattani, Office for National Statistics, B6/10, 1 Drummond Gate, London SW1V 2QQ, England

Phone: 44-20-7533 5205

Fax : 44-20-7533 5635

E-mail: nirupa.dattani@ons.gov.uk

England and Wales, 2002

Live births (L)	595914
Stillbirths (S)	3365
Total births	599279
Number of terminations of pregnancy (ToP) for birth defects	1863

Birth Defects	Number of cases			Rates*10.000		O/E	YB	Remark
	L	S	ToP	L+S	L+S+ToP	L+S		
Anencephaly	13	17	137	0.50	2.78	1.19	15	
Spina bifida	60	13	98	1.22	2.84	1.14	11	
Encephalocele	10	4	20	0.23	0.57	1.13	12	
Microcephaly	25	6	4	0.52	0.58	1.03	15	
Arhinencephaly / Holoprosencephaly	19	10	25	0.48	0.90	3.77	19	▲
Hydrocephaly	52	26	33	1.30	1.85	1.05	13	
Total Anophthalmos / Microphthalmos (include unspecified)	11	4	0	0.25	0.25	0.77	19	
Anophthalmos	1	2	0	0.05	0.05	0.46	12	
Microphthalmos	10	2	0	0.20	0.20	1.14	23	
Total Anotia / Microtia (include unspecified)	11	1	0	0.20	0.20	0.76	3	
Anotia	8	0	0	0.13	0.13	0.84	4	
Microtia	3	1	0	0.07	0.07	1.34	7	
Transposition of great vessels	56	1	1	0.95	0.96	0.93	3	
Tetralogy of Fallot	59	2	4	1.02	1.08	0.99	3	
Hypoplastic left heart syndrome	32	8	15	0.67	0.91	1.00	3	
Coarctation of aorta	79	1	1	1.33	1.35	1.29	3	
Choanal atresia, bilateral	12	0	0	0.20	0.20	1.30	15	
Cleft palate without cleft lip	196	6	0	3.37	3.36	1.04	13	
Cleft lip with or without cleft palate	346	10	1	5.94	5.94	0.94	9	
Oesophageal atresia / stenosis with or without fistula	65	1	0	1.10	1.10	1.15	15	
Small intestine atresia / stenosis	52	1	0	0.88	0.88	0.92	4	
Anorectal atresia / stenosis	83	3	1	1.44	1.45	1.00	10	
Undescended testis (36 weeks of gestation or later)	16	0	0	0.27	0.27	0.43	3	▼
Hypospadias	488	0	0	8.14	8.12	0.85	3	▼
Epispadias	8	0	0	0.13	0.13	0.46	8	
Indeterminate sex	37	5	0	0.70	0.70	0.99	23	
Renal agenesis	66	8	19	1.23	1.55	1.32	27	
Cystic kidney	138	13	20	2.52	2.84	1.13	3	
Bladder exstrophy	9	1	1	0.17	0.18	0.99	19	
Polydactyly, preaxial	45	0	nr	0.75	nc	0.84	2	
Total Limb reduction defects (include unspecified)	168	17	3	3.09	3.13	1.01	13	
Transverse	76	6	nr	1.37	nc	0.81	12	
Preaxial	14	1	nr	0.25	nc	1.21	12	
Postaxial	8	0	nr	0.13	nc	1.05	12	
Intercalary	51	9	nr	1.00	nc	1.30	4	
Mixed	10	1	nr	0.18	nc	1.02	12	
Diaphragmatic hernia	75	4	16	1.32	1.58	1.20	14	
Total Abdominal wall defects (include unspecified)	188	22	20	3.50	3.83	1.25	13	▲
Omphalocele	52	13	12	1.08	1.28	1.06	3	
Gastroschisis	109	7	4	1.94	2.00	1.05	4	
Prune belly sequence	1	1	2	0.03	0.07	0.99	7	
Trisomy 13	17	4	50	0.35	1.18	1.74	23	
Trisomy 18	24	24	136	0.80	3.06	1.45	23	
Down syndrome, all ages (include age unknown)	329	25	372	5.91	12.08	0.96	17	
<20	13	0	4	2.97	3.89	0.82	15	
20-24	21	3	15	2.15	3.49	0.60	15	▼
25-29	54	3	26	3.70	5.38	1.03	11	
30-34	85	8	85	5.13	9.81	0.88	12	
35-39	80	10	153	9.89	26.67	0.77	12	▼
40-44	60	1	83	36.83	86.50	1.03	15	
45+	3	0	6	33.33	99.34	0.47	15	

England and Wales, time trend analysis 1974-2002

Birth prevalence rates: (L+S) * 10,000

	1974-81	1982-86	1987-91	1992-96	1997-01	2002	Trend	RR
Births	4,961,573	3,225,714	3,482,903	3,341,363	3,114,770	599,279		
Anencephaly	8.89	1.49	0.44	0.40	0.42	0.50	▼	0.872
Spina bifida	14.43	6.02	2.08	1.02	1.01	1.22	▼	0.894
Encephalocele	1.90	0.77	0.35	0.16	0.21	0.23	▼	0.901
Microcephaly	1.24*	0.96	0.57	0.40	0.54	0.52	▼	0.951
Arhinencephaly / Holoprosencephaly	0.07*	0.08	0.13	0.13	0.15	0.48	▲	1.059
Hydrocephaly	8.72	4.47	1.55	1.13	1.28	1.30	▼	0.911
Total Anophthalmos / Microphthalmos (include unspecified)	0.43*	0.41	0.28	0.32	0.30	0.25	▼	0.980
Anophthalmos	0.28*	0.22	0.16	0.15	0.08	0.05	▼	0.942
Microphthalmos	0.15*	0.20	0.13	0.17	0.23	0.20		
Total Anotia / Microtia (include unspecified)				0.15*	0.17	0.20	▲	1.130
Anotia				0.08*	0.13	0.13	▲	1.153
Microtia				0.06*	0.04	0.07		
Transposition of great vessels	0.40	0.61	0.48	0.50	0.82	0.95	▲	1.029
Tetralogy of Fallot			0.29*	0.36	0.81	1.02	▲	1.135
Hypoplastic left heart syndrome	0.12*	0.29	0.22	0.29	0.56	0.67	▲	1.064
Coarctation of aorta			0.31*	0.31	0.80	1.33	▲	1.148
Choanal atresia, bilateral	0.21*	0.23	0.20	0.11	0.15	0.20	▼	0.976
Cleft palate without cleft lip	10.38	9.77	3.65	3.01	3.27	3.37	▼	0.943
Cleft lip with or without cleft palate	9.71	8.93	7.83	6.79	6.22	5.94	▼	0.979
Oesophageal atresia / stenosis with or without fistula	1.66	1.62	1.05	0.84	0.98	1.10	▼	0.972
Small intestine atresia / stenosis	0.49*	0.63	0.64	0.58	0.86	0.88	▲	1.023
Anorectal atresia / stenosis	2.83	2.57	1.95	1.49	1.37	1.44	▼	0.967
Undescended testis (36 weeks of gestation or later)	5.70*	8.64	5.11	0.21	0.47	0.27	▼	0.892
Hypospadias				7.51*	8.82	8.14	▲	1.036
Epispadias			0.00*	0.35*	0.25	0.13		
Indeterminate sex	0.80*	0.82	0.57	0.58	0.82	0.70		
Renal agenesis	0.78	1.15	0.87	0.76	1.09	1.23	▲	1.011
Cystic kidney	0.40*	0.60	0.87	1.14	1.89	2.52	▲	1.079
Bladder exstrophy	0.22*	0.21	0.19	0.13	0.17	0.17	▼	0.978
Polydactyly, preaxial				0.61*	0.75	0.75	▲	1.067
Total Limb reduction defects (include unspecified)	5.11	5.09	3.71	2.94	3.06	3.09	▼	0.973
Transverse			1.88*	1.67	1.60	1.37		
Preaxial			0.23*	0.21	0.20	0.25		
Postaxial			0.13*	0.16	0.10	0.13		
Intercalary			0.56*	0.45	0.67	1.00	▲	1.053
Mixed			0.15*	0.18	0.19	0.18		
Diaphragmatic hernia	1.36*	1.52	1.32	0.89	1.13	1.32	▼	0.984
Total Abdominal wall defects (include unspecified)	7.10	6.71	4.32	2.44	3.04	3.50	▼	0.958
Omphalocele			2.25*	1.54	0.86	1.08	▼	0.914
Gastroschisis				1.36*	1.75	1.94	▲	1.058
Prune belly sequence				0.04*	0.03	0.03		
Trisomy 13	0.13*	0.19	0.24	0.19	0.23	0.35	▲	1.020
Trisomy 18	0.45*	0.64	0.57	0.48	0.57	0.80		
Down syndrome, all ages (include age unknown)	7.10	7.49	6.40	5.09	6.74	5.91	▼	0.992
<20			3.70	3.27	3.84	2.97		
20-24			3.85	3.26	3.59	2.15		
25-29			4.53	3.46	3.63	3.70	▼	0.978
30-34			7.63	5.19	6.21	5.13	▼	0.978
35-39			17.71	10.69	13.46	9.89	▼	0.970
40-44			36.06	31.11	38.94	36.83		
45+			61.82	67.16	82.85	33.33		

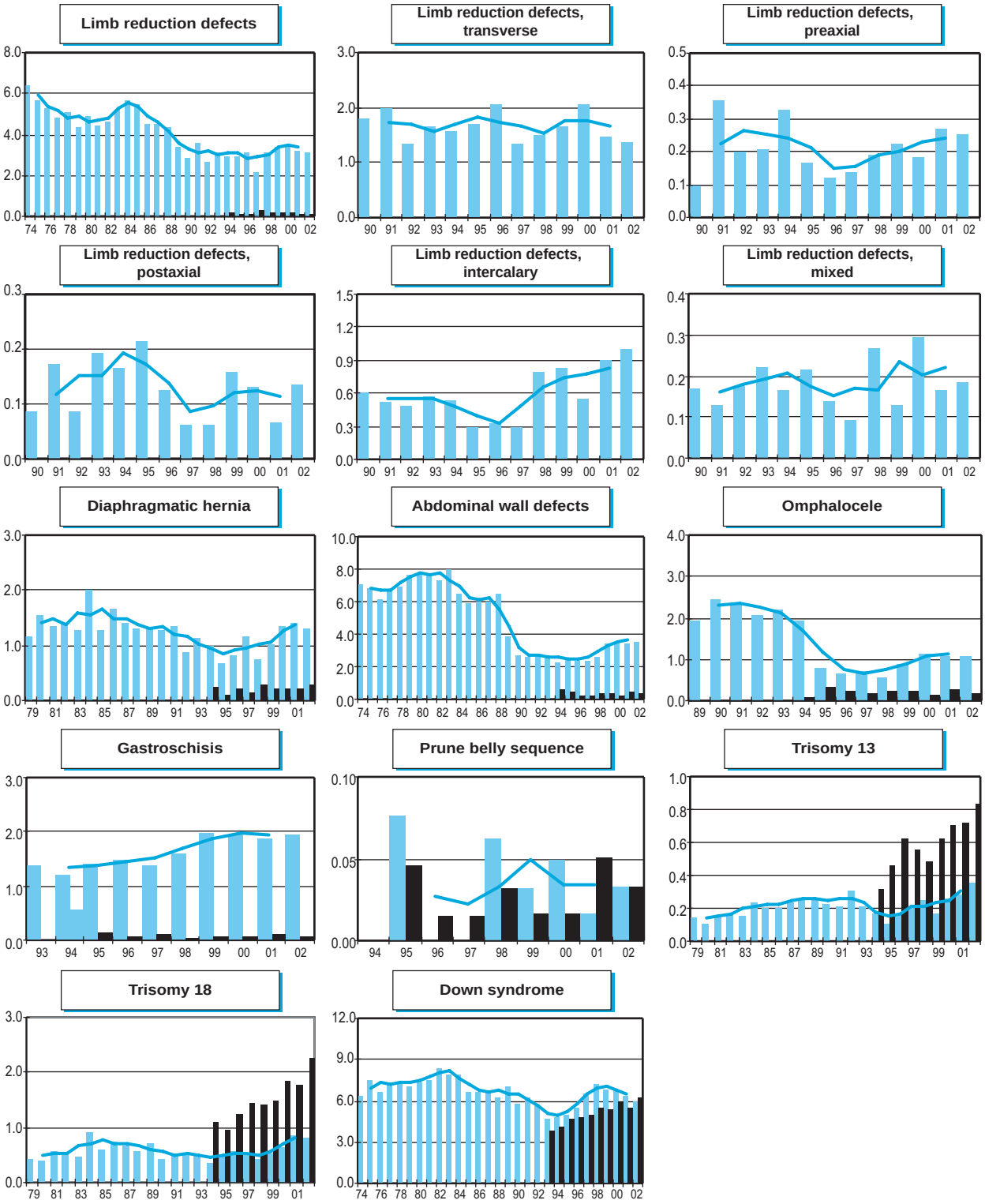
* = data include less than eight and five years

England and Wales

Time trends 1974-2002 (Birth prevalence rates per 10,000)

Note: L+S rates, ToP rates — 3-year moving average trend

Note: L+S rates, ToP rates — 3-year moving average trend



Note: L+S rates, ToP rates — 3-year moving average trend

Finland

The Finnish Register of Congenital Malformations

History:
The registry was established in 1963 and regular monitoring started in 1977. It was a founding member of the ICBDMS and is a full member. In 1998 the registry became an associate member of EUROCAT. The registry system (data collection etc.) has been changed twice, in 1985 and in 1993.

Size and coverage:
The registry is national and population based. All births in Finland are covered, at present approximately 56,000 annually. Stillbirths of 22 weeks / 500 g or more are registered. Information on malformations is principally collected up to 1 year of age, but later information is also included. Selective terminations of pregnancy for fetal reasons and spontaneous abortions with malformations have been included since 1993.

Legislation and funding:
Reporting is compulsory. The registry is regulated by the act and statute on the national health care registers with personal data. The registry is run and financed by STAKES, the governmental National Research and Development Centre for Welfare and Health (under the Ministry of Social Affairs and Health).

Sources and ascertainment:
Reports are obtained from delivery units, neonatal, paediatric and pathology departments, death certificates and cytogenetic laboratories. Case information is also received from the national Medical Birth Register, Abortion Register and Hospital Discharge Register. The diagnoses of the malformation cases received from other sources are confirmed from the hospitals.

Exposure information:
Until 1986, extensive exposure information was obtained from maternity health centres and by personal interview for cases with selected malformations and their controls. In 1987-1992 only parental occupation was reported. Exposure information, like maternal occupation, medication, X-rays and diseases, etc., has been obtained since 1993. Some exposure information on all births is also available in the Medical Birth Register since 1987.

Background information:
Epidemiological background data are available on all births in the Medical Birth Register and in the Statistics Finland.

Address for further information:
Annukka Ritvanen, The Finnish Register of Congenital Malformations, The National Research and Development Centre for Welfare and Health, STAKES, Lintulahdenkuja 4, P.O. Box 220, SF 00531-Helsinki - Finland

Phone: +358-9-39672376

Fax: +358-9-39672459

E-mail: annukka.ritvanen@stakes.fi

Website: http://www.stakes.fi/

Finland, 2002

Live births (L)	55555
Stillbirths (S)	213
Total births	55768
Number of terminations of pregnancy (ToP) for birth defects	255

Birth Defects	Number of cases			Rates*10.000		O/E	YB	Remark
	L	S	ToP	L+S	L+S+ToP	L+S		
Anencephaly	1	0	12	0.18	2.32	0.51	9	
Spina bifida	11	1	13	2.15	4.46	0.70	9	
Encephalocele	6	0	10	1.08	2.86	3.24	9	▲
Microcephaly	4	0	1	0.72	0.89	0.36	9	▼
Arhinencephaly / Holoprosencephaly	0	0	5	0.00	0.89	0.00	9	▼
Hydrocephaly	22	2	12	4.30	6.43	0.93	9	
Total Anophthalmos / Microphthalmos (include unspecified)	7	1	4	1.43	2.14	0.83	9	
Anophthalmos	3	0	2	0.54	0.89	1.46	9	
Microphthalmos	4	1	2	0.90	1.25	0.66	9	
Total Anotia / Microtia (include unspecified)	16	0	1	2.87	3.03	0.64	9	
Anotia	nr	nr	nr	nc	nc	nc		
Microtia	nr	nr	nr	nc	nc	nc		
Transposition of great vessels	22	0	0	3.94	3.93	0.99	9	
Tetralogy of Fallot	17	0	0	3.05	3.03	0.86	7	
Hypoplastic left heart syndrome	12	1	7	2.33	3.57	0.69	9	
Coarctation of aorta	40	1	4	7.35	8.03	0.71	4	▼
Choanal atresia, bilateral	4	0	0	0.72	0.71	0.76	9	
Cleft palate without cleft lip	76	1	1	13.81	13.92	1.05	8	
Cleft lip with or without cleft palate	53	0	9	9.50	11.07	0.95	9	
Oesophageal atresia / stenosis with or without fistula	24	1	0	4.48	4.46	1.32	9	
Small intestine atresia / stenosis	7	1	0	1.43	1.43	1.32	9	
Anorectal atresia / stenosis	17	1	1	3.23	3.39	0.68	9	
Undescended testis (36 weeks of gestation or later)	nr	nr	nr	nc	nc	nc		
Hypospadias	69	1	1	12.55	12.67	0.86	9	
Epispadias	1	0	0	0.18	0.18	0.61	9	
Indeterminate sex	7	0	1	1.26	1.43	0.77	3	
Renal agenesis	3	2	1	0.90	1.07	0.97	9	
Cystic kidney	27	2	15	5.20	7.85	1.11	9	
Bladder exstrophy	4	0	1	0.72	0.89	1.56	9	
Polydactyly, preaxial	18	0	0	3.23	3.21	0.77	9	
Total Limb reduction defects (include unspecified)	37	0	9	6.63	8.21	1.15	9	
Transverse	14	0	2	2.51	2.86	0.73	9	
Preaxial	16	0	7	2.87	4.11	2.11	9	▲
Postaxial	3	0	0	0.54	0.54	1.95	9	
Intercalary	2	0	0	0.36	0.36	1.39	9	
Mixed	1	0	0	0.18	0.18	0.69	9	
Diaphragmatic hernia	11	1	1	2.15	2.32	1.00	9	
Total Abdominal wall defects (include unspecified)	16	4	28	3.59	8.57	1.01	9	
Omphalocele	9	3	19	2.15	5.53	1.08	9	
Gastroschisis	7	1	8	1.43	2.86	1.00	9	
Prune belly sequence	1	0	1	0.18	0.36	1.08	9	
Trisomy 13	4	1	8	0.90	2.32	0.72	9	
Trisomy 18	9	5	20	2.51	6.07	0.91	9	
Down syndrome, all ages (include age unknown)	75	4	66	14.17	25.88	1.18	9	
<20	1	1	0	11.14	11.14	1.45	9	
20-24	6	0	0	6.55	6.55	1.10	9	
25-29	9	1	4	5.75	8.05	0.71	9	
30-34	15	1	11	9.63	16.24	0.85	9	
35-39	30	1	26	35.03	64.22	1.80	9	▲
40-44	11	0	24	59.78	187.77	1.02	9	
45+	3	0	1	254.24	336.13	1.34	9	

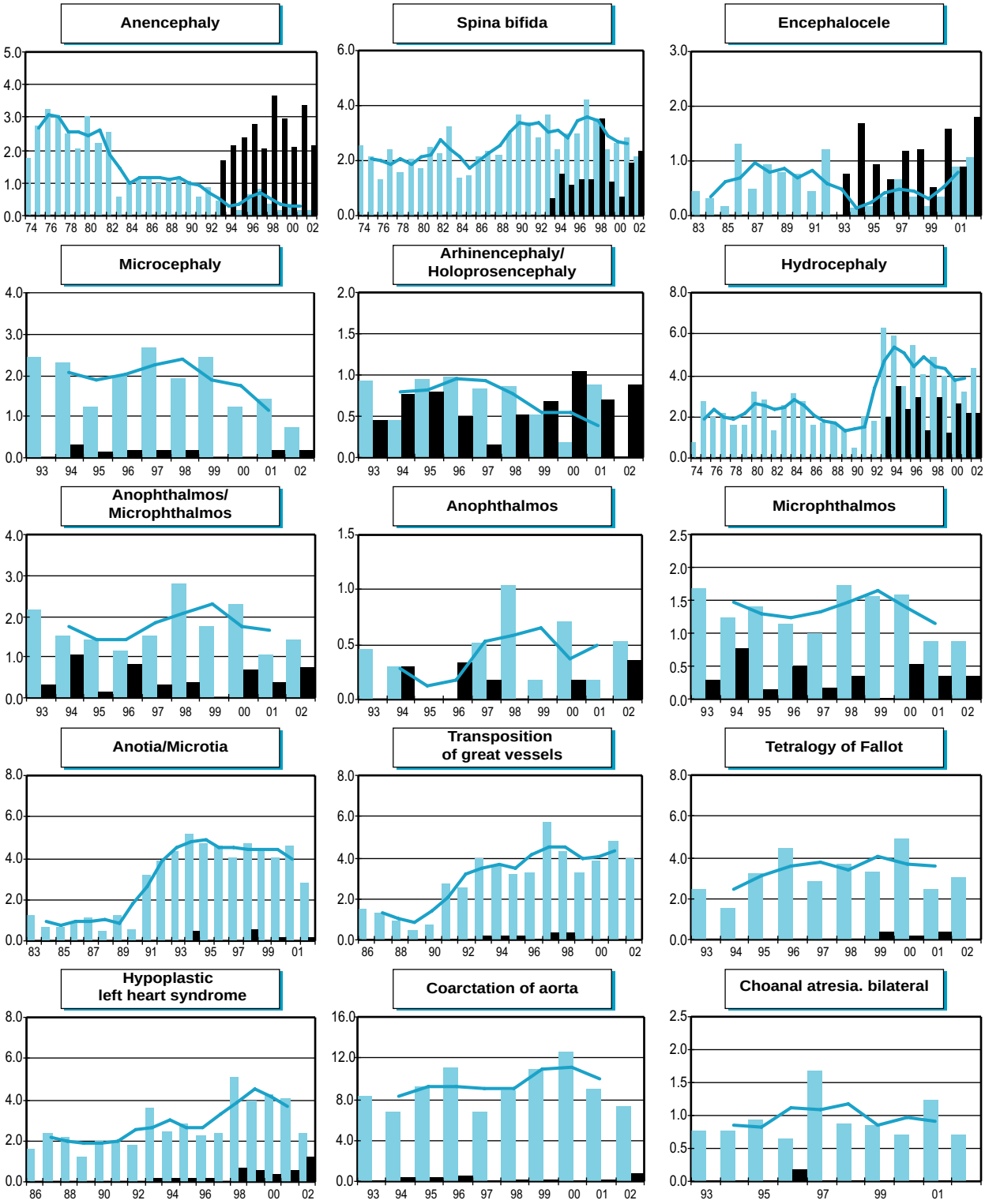
Finland, time trend analysis 1993-2002

Birth prevalence rates: (L+S) * 10,000

	1974-81	1982-86	1987-91	1992-96*	1997-01	2002	Trend	RR
Births				254,911	288,062	55,768		
Anencephaly				0.31	0.38	0.18		
Spina bifida				3.02	3.12	2.15		
Encephalocele				0.16	0.49	1.08	▲	1.263
Microcephaly				2.00	1.94	0.72	▼	0.932
Arhinencephaly / Holoprosencephaly				0.82	0.66	0.00		
Hydrocephaly				5.30	3.99	4.30	▼	0.947
Total Anophthalmos / Microphthalmos (include unspecified)				1.57	1.87	1.43		
Anophthalmos				0.20	0.52	0.54		
Microphthalmos				1.37	1.35	0.90		
Total Anotia / Microtia (include unspecified)				4.71	4.34	2.87		
Anotia				0.00	0.00*			
Microtia				0.00	0.00*			
Transposition of great vessels				3.53	4.41	3.94		
Tetralogy of Fallot				2.86	3.44	3.05		
Hypoplastic left heart syndrome				2.79	3.92	2.33		
Coarctation of aorta				8.83	9.62	7.35		
Choanal atresia, bilateral				0.78	1.08	0.72		
Cleft palate without cleft lip				14.48	12.91	13.81	▼	0.969
Cleft lip with or without cleft palate				10.08	9.86	9.50		
Oesophageal atresia / stenosis with or without fistula				3.02	3.75	4.48	▲	1.054
Small intestine atresia / stenosis				1.02	1.15	1.43		
Anorectal atresia / stenosis				4.55	4.86	3.23		
Undescended testis (36 weeks of gestation or later)				0.00	0.00*			
Hypospadias				15.14	14.06	12.55		
Epispadias				0.24	0.35	0.18		
Indeterminate sex				0.59	1.11	1.26	▲	1.175
Renal agenesis				1.10	0.76	0.90		
Cystic kidney				4.43	4.89	5.20		
Bladder exstrophy				0.47	0.45	0.72		
Polydactyly, preaxial				4.24	4.20	3.23		
Total Limb reduction defects (include unspecified)				6.36	5.24	6.63		
Transverse				4.12	2.85	2.51	▼	0.942
Preaxial				1.29	1.42	2.87		
Postaxial				0.16	0.38	0.54		
Intercalary				0.31	0.21	0.36		
Mixed				0.35	0.17	0.18		
Diaphragmatic hernia				2.04	2.26	2.15		
Total Abdominal wall defects (include unspecified)				3.33	3.71	3.59		
Omphalocele				2.12	1.87	2.15		
Gastroschisis				1.10	1.74	1.43		
Prune belly sequence				0.20	0.14	0.18		
Trisomy 13				1.49	1.04	0.90		
Trisomy 18				3.02	2.53	2.51		
Down syndrome, all ages (include age unknown)				12.40	11.59	14.17		
<20				14.01	2.54	11.14		
20-24				5.10	6.65	6.55		
25-29				9.21	6.89	5.75		
30-34				12.34	10.54	9.63		
35-39				18.52	20.15	35.03	▲	1.054
40-44				64.07	54.61	59.78		
45+				201.15	181.82	254.24		

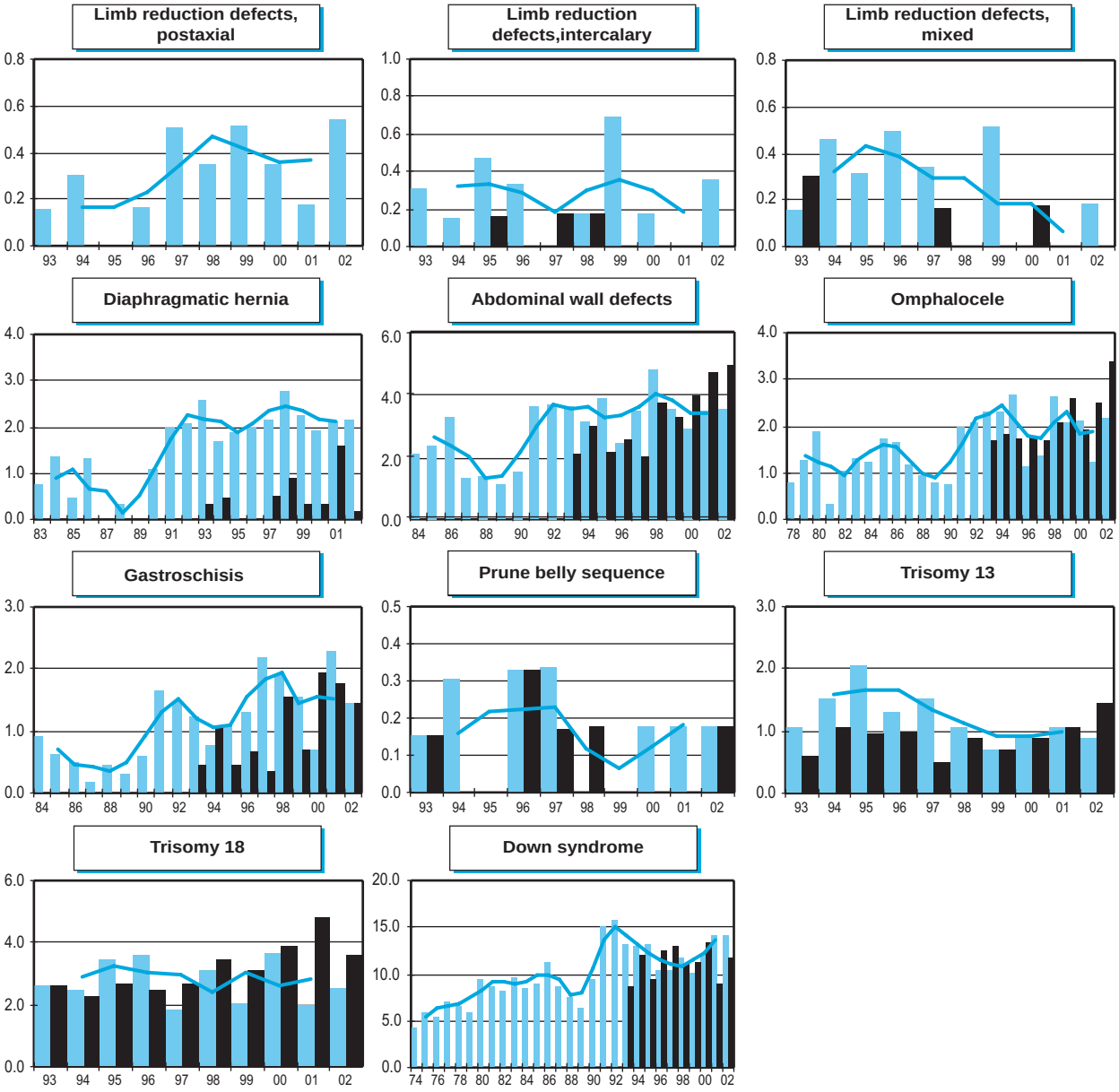
Finland

'Time trends 1974-2002 (Birth prevalence rates per 10,000)



Note: L+S rates, ToP rates — 3-year moving average trend

Note: L+S rates, ToP rates — 3-year moving average trend



Note: L+S rates, ToP rates — 3-year moving average trend

France: Central-East

Central-East France Register of Congenital Malformations.

History:
The registry began in 1973 within the Rhone-Alps area -the Auvergne region was added in 1983, the Jura area in 1985, the Côte d'Or & Nièvre in 1989 and Saône-et-Loire in 1990. The Programme was a founding member of the ICBDMS and is a full member. In 1998 the registry was split up and the Auvergne region became financially independent, under the responsibility of Christine Francannet under the acronym CEMC. The collaboration between Auvergne and the rest of the FCE-registry is maintained and common results are published.

Size and coverage:
The registry covers all births in the area, approximately 100,000 births annually, which represent about 13% of all births in France. Stillbirths of 22 weeks or more gestation are included.

Legislation and funding:
Reporting is voluntary. The system is run by a privately funded research organisation. It is now officially recognised by the French Ministry of Health and partially supported by an annual grant voted by the National Committee of Registries.

Sources of ascertainment:
Reports are received from delivery units, pediatric and child surgery clinics, pathology departments, and cytogenetic laboratories. Infants up to the age of one are registered, as well as fetuses delivered after medical abortion.

Exposure information:
Information on maternal and paternal occupation, drug use, diseases, etc. is collected by interviews of the mothers of the malformed infants. No controls are interviewed.

Background information:
Distribution of births according to maternal age, sex, and place of parental residence is available from the general population national statistics.

Research projects
Started during the year (2003 – 2004):
- Case-control study for exploring a possible association between residence close to a municipal solid waste incinerator and urinary malformations (data collection is ongoing).
- ENTIS collaborative studies on drug exposures durng pregnancy (H2 inhibitors, PPI inhibitors, anticoagulants, mesalazine)

Finished during the year (2003 – 2004) but not yet published:
Gene polymorphism, and gene environment interaction in oral clefts
A population-based study of 706 cases of major congenital malformations : influence of medical and non medical factors on prenatal management and neonatal mortality. Submitted to BMJ
Maternal drug use, fertility problems, and infant craniostenosis. A study from Sweden (1995-2002) and France (1988-2002). Submitted to J Craniofac Genet Develop Med

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France: Central East, 2002

Live births (L)	106211
Stillbirths (S)	797
Total births	107008
Number of terminations of pregnancy (ToP) for birth defects	599

Birth Defects	Number of cases			Rates*10.000		O/E	YB	Remark
	L	S	ToP	L+S	L+S+ToP	L+S		
Anencephaly	1	0	15	0.09	1.49	1.06	12	
Spina bifida	9	0	40	0.84	4.55	1.58	3	
Encephalocele	4	0	15	0.37	1.77	1.32	18	
Microcephaly	10	1	5	1.03	1.49	0.80	10	
Arhinencephaly / Holoprosencephaly	1	0	8	0.09	0.84	0.16	24	
Hydrocephaly	23	1	47	2.24	6.60	0.89	24	
Total Anophthalmos / Microphthalmos (include unspecified)	3	0	4	0.28	0.65	0.25	24	▼
Anophthalmos	0	0	0	0.00	0.00	0.00	24	
Microphthalmos	3	0	4	0.28	0.65	0.29	24	
Total Anotia / Microtia (include unspecified)	5	0	1	0.47	0.56	0.72	24	
Anotia	2	0	0	0.19	0.19	0.51	24	
Microtia	3	0	1	0.28	0.37	0.99	24	
Transposition of great vessels	27	0	11	2.52	3.53	0.82	24	
Tetralogy of Fallot	19	0	6	1.78	2.32	0.85	24	
Hypoplastic left heart syndrome	10	1	23	1.03	3.16	0.58	24	
Coarctation of aorta	9	1	2	0.93	1.12	0.38	24	▼
Choanal atresia, bilateral	0	0	7	0.00	0.65	0.00	24	
Cleft palate without cleft lip	53	0	2	4.95	5.11	0.93	21	
Cleft lip with or without cleft palate	55	0	7	5.14	5.76	0.77	24	
Oesophageal atresia / stenosis with or without fistula	26	1	3	2.52	2.79	0.96	23	
Small intestine atresia / stenosis	23	0	3	2.15	2.42	1.03	17	
Anorectal atresia / stenosis	30	1	9	2.90	3.72	0.97	24	
Undescended testis (36 weeks of gestation or later)	nr	nr	nr	nc	nc	nc		
Hypospadias	124	1	2	11.68	11.80	1.00	7	
Epispadias	0	0	0	0.00	0.00	0.00	24	
Indeterminate sex	5	0	2	0.47	0.65	1.16	11	
Renal agenesis	2	0	12	0.19	1.30	1.14	7	
Cystic kidney	29	0	24	2.71	4.93	1.00	17	
Bladder exstrophy	1	0	1	0.09	0.19	0.34	24	
Polydactyly, preaxial	15	0	0	1.40	1.39	0.78	16	
Total Limb reduction defects (include unspecified)	32	3	21	3.27	5.20	0.82	21	
Transverse	19	1	6	1.87	2.42	0.83	24	
Preaxial	5	1	10	0.56	1.49	0.89	24	
Postaxial	2	1	2	0.28	0.46	0.81	24	
Intercalary	3	0	2	0.28	0.46	0.66	24	
Mixed	3	0	1	0.28	0.37	1.01	18	
Diaphragmatic hernia	19	2	9	1.96	2.79	0.81	24	
Total Abdominal wall defects (include unspecified)	31	1	17	2.99	4.55	1.41	23	
Omphalocele	12	0	13	1.12	2.32	0.97	24	
Gastroschisis	19	1	4	1.87	2.23	1.93	23	▲
Prune belly sequence	0	0	2	0.00	0.19	0.00	24	
Trisomy 13	1	1	23	0.19	2.32	0.30	24	
Trisomy 18	4	0	28	0.37	2.97	0.29	24	▼
Down syndrome, all ages (include age unknown)	56	3	177	5.51	21.93	0.94	4	
<20	1	0	0	5.74	5.74	0.91	24	
20-24	5	0	6	3.61	7.94	0.71	18	
25-29	9	1	23	2.79	9.19	0.98	5	
30-34	8	0	43	2.18	13.91	0.62	4	
35-39	5	1	65	3.85	45.32	0.45	4	
40-44	9	1	34	31.82	138.50	0.98	11	
45+	1	0	2	66.67	197.37	0.64	24	

France: Central East, time trend analysis 1978-2002

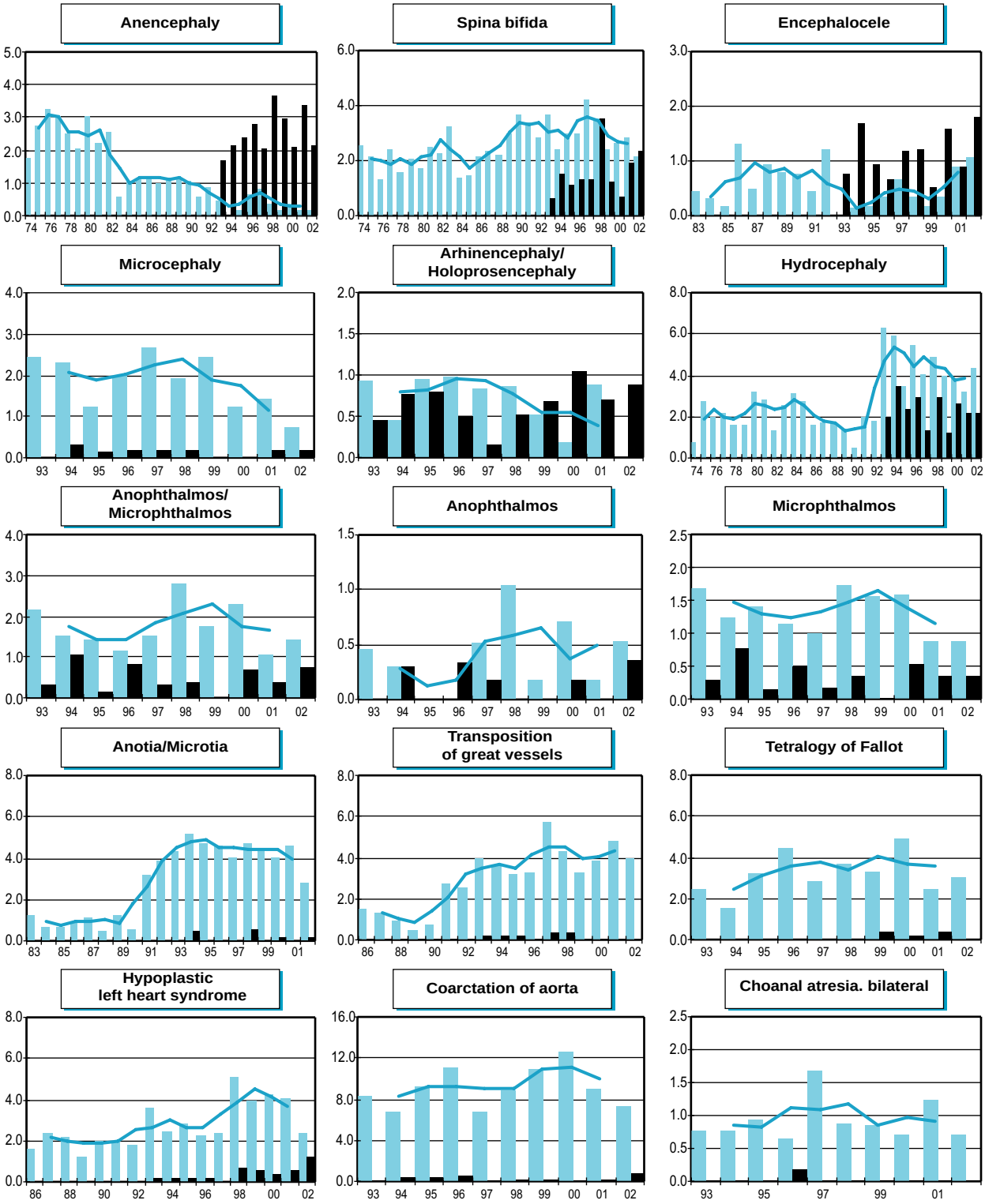
Birth prevalence rates: (L+S) * 10,000

	1974-81*	1982-86	1987-91	1992-96	1997-01	2002	Trend	RR
Births	291,826	431,925	495,329	508,996	523,282	107,008		
Anencephaly	0.82	0.81	0.36	0.14	0.02	0.09	▼	0.868
Spina bifida	4.04	3.40	2.06	2.04	0.80	0.84	▼	0.911
Encephalocele	0.69	0.69	0.36	0.29	0.15	0.37	▼	0.921
Microcephaly	1.40	2.43	2.20	1.49	1.07	1.03	▼	0.953
Arhinencephaly / Holoprosencephaly	0.31	0.51	0.91	0.79	0.29	0.09		
Hydrocephaly	1.78	2.99	2.99	2.40	2.27	2.24	▼	0.982
Total Anophthalmos / Microphthalmos (include unspecified)	1.30	1.04	1.47	0.96	0.84	0.28	▼	0.976
Anophthalmos	0.31	0.05	0.24	0.10	0.10	0.00	▼	0.948
Microphthalmos	0.99	1.00	1.23	0.86	0.75	0.28	▼	0.980
Total Anotia / Microtia (include unspecified)	0.38	0.56	0.79	0.81	0.61	0.47		
Anotia	0.24	0.30	0.50	0.41	0.32	0.19		
Microtia	0.14	0.25	0.28	0.39	0.29	0.28		
Transposition of great vessels	2.95	3.13	3.69	3.03	2.60	2.52	▼	0.975
Tetralogy of Fallot	1.85	2.41	2.42	1.98	1.74	1.78		
Hypoplastic left heart syndrome	1.51	1.97	2.38	1.49	1.40	1.03	▼	0.975
Coarctation of aorta	1.95	2.76	2.95	2.34	2.03	0.93	▼	0.985
Choanal atresia, bilateral	0.65	0.67	0.85	0.53	0.90	0.00		
Cleft palate without cleft lip	4.15	5.07	4.64	6.25	5.48	4.95		
Cleft lip with or without cleft palate	6.82	6.11	6.48	7.70	6.31	5.14	▼	0.980
Oesophageal atresia / stenosis with or without fistula	2.02	2.36	3.03	2.57	2.64	2.52	▼	0.993
Small intestine atresia / stenosis	1.64	1.53	1.78	1.87	2.52	2.15		
Anorectal atresia / stenosis	2.09	3.19	3.15	3.18	2.96	2.90		
Undescended testis (36 weeks of gestation or later)								
Hypospadias	6.23	6.90	10.20	9.67	11.94	11.68	▲	1.030
Epispadias	0.17	0.19	0.32	0.14	0.15	0.00		
Indeterminate sex	0.55	0.81	0.77	0.45	0.32	0.47	▼	0.951
Renal agenesis	0.48	0.90	0.46	0.49	0.15	0.19	▼	0.939
Cystic kidney	0.65	1.46	2.73	2.77	3.04	2.71	▲	1.040
Bladder exstrophy	0.17	0.23	0.38	0.26	0.27	0.09		
Polydactyly, preaxial	0.82	0.86	1.59	2.00	1.87	1.40	▲	1.027
Total Limb reduction defects (include unspecified)	4.69	4.07	4.06	4.15	3.65	3.27	▼	0.989
Transverse	2.36	2.06	2.42	2.30	2.16	1.87		
Preaxial	0.62	0.76	0.52	0.69	0.57	0.56		
Postaxial	0.31	0.25	0.52	0.26	0.36	0.28		
Intercalary	0.55	0.49	0.32	0.55	0.29	0.28		
Mixed	0.62	0.49	0.26	0.29	0.21	0.28	▼	0.948
Diaphragmatic hernia	1.92	2.80	2.28	2.87	2.06	1.96	▼	0.980
Total Abdominal wall defects (include unspecified)	1.61	1.83	2.30	2.02	2.47	2.99	▲	1.017
Omphalocele	1.06	1.09	1.27	0.94	1.36	1.12		
Gastroschisis	0.55	0.74	1.03	1.08	1.11	1.87	▲	1.030
Prune belly sequence	0.27	0.16	0.38	0.28	0.15	0.00		
Trisomy 13	0.41	0.58	1.09	0.69	0.31	0.19	▼	0.961
Trisomy 18	0.89	1.02	2.30	1.65	0.52	0.37	▼	0.968
Down syndrome, all ages (include age unknown)	11.38	11.11	10.96	9.94	6.46	5.51	▼	0.973
<20	7.79	3.32	7.46	4.94	8.99	5.74		
20-24	6.47	6.40	5.74	6.01	3.16	3.61	▼	0.973
25-29	5.59	5.95	6.60	4.82	2.83	2.79	▼	0.969
30-34	11.80	10.23	9.05	7.84	4.16	2.18	▼	0.949
35-39	26.78	29.09	22.03	17.25	9.62	3.85	▼	0.937
40-44	102.73	60.73	51.43	35.94	26.92	31.82	▼	0.936
45+	91.46	109.89	127.93	130.29	62.70	66.67		

* = data include less than eight years

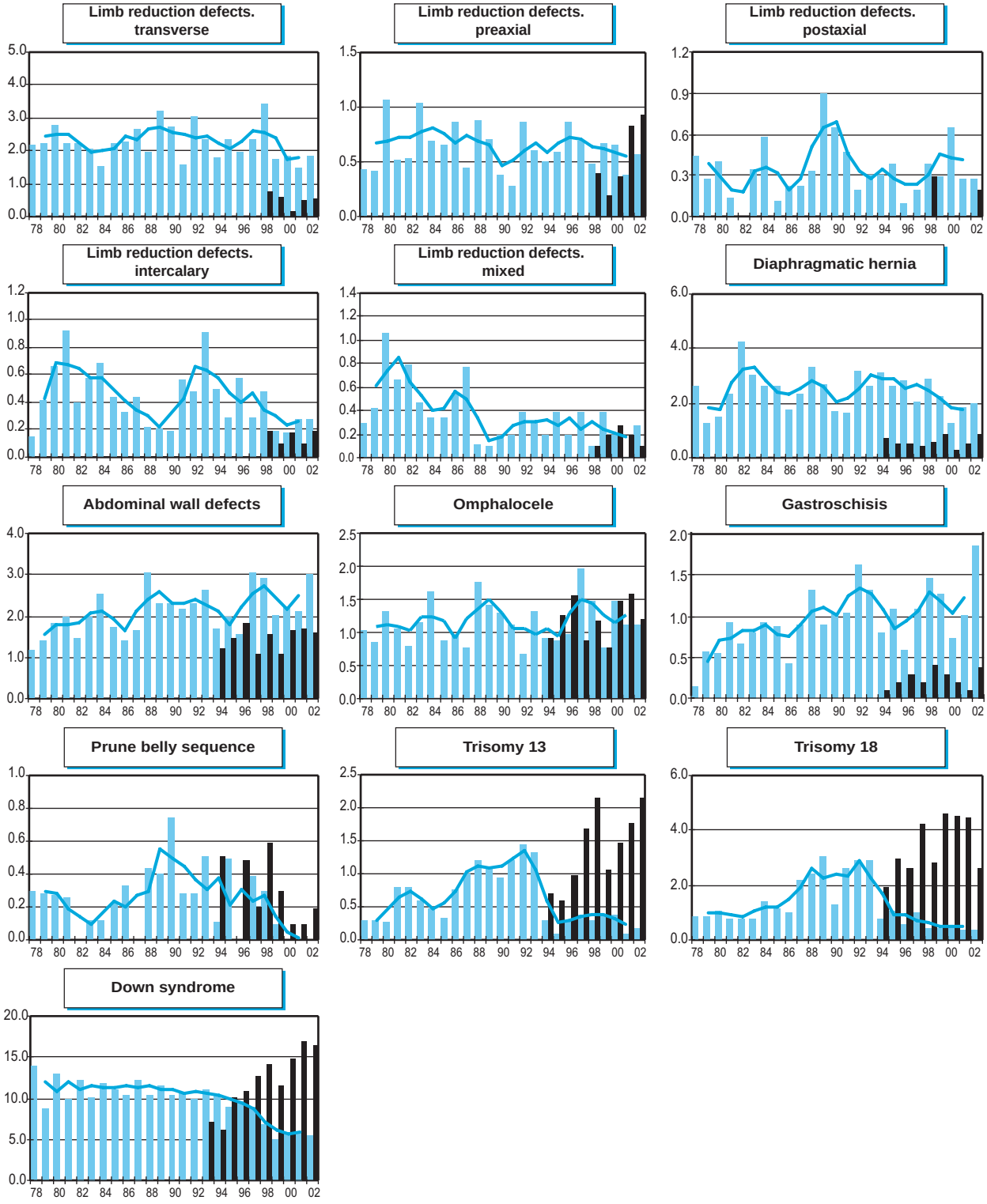
France: Central East

'Time trends 1978-2002 (Birth prevalence rates per 10,000)



Note: L+S rates, ToP rates — 3-year moving average trend

Note: L+S rates, ToP rates — 3-year moving average trend



Note: L+S rates, ToP rates — 3-year moving average trend

France: Paris

History:
The Programme was initiated in 1975, but the registry really started in 1981. It became an associate member of the ICBDMS in 1982. It is also a member of EUROCAT.

Size and coverage:
The registry covers 38.500 annual births (about 5% of all births in France), those are all births (live and still births of 22 weeks or more) and terminations of pregnancy in the population of Greater Paris delivering in Paris maternity units. The estimation of the coverage of the registry is around 95%.

Legislation and funding:
Reporting is voluntary. The registry is part of a research unit of INSERM (National Institute of Health and Medical Research). The registry has been officially recognized by the French National Comity of Registries, and is renewed for four years (2001-2004) and supported by an annual grant from INSERM and Institut de la Veille Sanitaire (Institute for Health Surveillance).

Sources of ascertainment:
Reports are actively collected from delivery units, pediatric departments, cytogenetic laboratories, and pathology departments. Terminations of pregnancy are included. Case information is also received from the health certificates of the first week.

Exposure information:
Information on maternal drug use, maternal and paternal diseases and occupations, outcome of previous pregnancies, is available for the malformed cases.

Prenatal diagnosis information: Data about techniques of prenatal screening (ultrasound, serum markers) and prenatal diagnosis are systematically collected.

Background information:
Background data on births are available from the National Institute of Statistics (INSEE)

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France: Paris, 2002

Live births (L)	38500
Stillbirths (S)	200
Total births	38700
Number of terminations of pregnancy (ToP) for birth defects	520

Birth Defects	Number of cases			Rates*10.000		O/E	YB	Remark
	L	S	ToP	L+S	L+S+ToP	L+S		
Anencephaly	0	2	27	0.52	7.39	1.92	14	
Spina bifida	3	1	16	1.03	5.10	1.01	15	
Encephalocele	0	0	8	0.00	2.04	0.00	21	
Microcephaly	0	1	7	0.26	2.04	0.16	15	
Arhinencephaly / Holoprosencephaly	0	0	16	0.00	4.08	0.00	21	
Hydrocephaly	27	2	30	7.49	15.04	1.58	9	
Total Anophthalmos / Microphthalmos (include unspecified)	2	1	3	0.78	1.53	0.68	21	
Anophthalmos	0	0	0	0.00	0.00	0.00	21	
Microphthalmos	2	1	3	0.78	1.53	0.84	21	
Total Anotia / Microtia (include unspecified)	5	0	1	1.29	1.53	1.29	20	
Anotia	3	0	0	0.78	0.76	1.47	19	
Microtia	2	0	1	0.52	0.76	1.11	21	
Transposition of great vessels	18	0	4	4.65	5.61	1.07	9	
Tetralogy of Fallot	15	0	4	3.88	4.84	1.42	13	
Hypoplastic left heart syndrome	5	0	8	1.29	3.31	1.20	18	
Coarctation of aorta	13	0	2	3.36	3.82	1.00	10	
Choanal atresia, bilateral	0	0	0	0.00	0.00	0.00	21	
Cleft palate without cleft lip	21	0	6	5.43	6.88	1.18	15	
Cleft lip with or without cleft palate	16	0	1	4.13	4.33	0.64	21	
Oesophageal atresia / stenosis with or without fistula	14	0	2	3.62	4.08	1.25	21	
Small intestine atresia / stenosis	8	1	1	2.33	2.55	1.36	15	
Anorectal atresia / stenosis	11	0	3	2.84	3.57	1.14	21	
Undescended testis (36 weeks of gestation or later)	25	0	1	6.46	6.63	1.12	6	
Hypospadias	61	0	3	15.76	16.32	1.35	21	
Epispadias	0	0	0	0.00	0.00	0.00	21	
Indeterminate sex	2	0	3	0.52	1.27	0.44	21	
Renal agenesis	1	0	9	0.26	2.55	0.68	14	
Cystic kidney	27	1	23	7.24	13.00	1.42	11	
Bladder exstrophy	0	0	1	0.00	0.25	0.00	21	
Polydactyly, preaxial	0	0	0	0.00	0.00	0.00	14	
Total Limb reduction defects (include unspecified)	14	3	15	4.39	8.16	1.25	7	
Transverse	11	3	10	3.62	6.12	1.62	7	
Preaxial	0	0	2	0.00	0.51	0.00	7	
Postaxial	2	0	2	0.52	1.02	2.27	7	
Intercalary	1	0	0	0.26	0.25	0.76	7	
Mixed	0	0	0	0.00	0.00	0.00	7	
Diaphragmatic hernia	17	0	8	4.39	6.37	1.37	19	
Total Abdominal wall defects (include unspecified)	20	1	18	5.43	9.94	0.99	7	
Omphalocele	12	1	12	3.36	6.37	1.75	21	
Gastroschisis	8	0	3	2.07	2.80	0.43	2	▼
Prune belly sequence	0	0	1	0.00	0.25	0.00	21	
Trisomy 13	1	0	21	0.26	5.61	0.54	21	
Trisomy 18	4	3	46	1.81	13.51	1.71	21	
Down syndrome, all ages (include age unknown)	21	3	126	6.20	38.25	0.73	10	
<20	0	0	0	0.00	0.00	0.00	21	
20-24	1	1	0	6.45	6.45	0.95	21	
25-29	3	0	4	2.90	6.76	0.49	21	
30-34	3	1	25	2.86	20.68	0.44	9	
35-39	6	1	48	8.38	65.49	0.80	10	
40-44	5	0	38	20.83	176.37	0.67	21	
45+	3	0	4	300.00	673.08	2.04	21	

France: Paris, time trend analysis 1981-2002

Birth prevalence rates: (L+S) * 10,000

	1974-81*	1982-86	1987-91	1992-96	1997-01	2002	Trend	RR
Births	36,917	181,346	184,461	182,327	190,578	38,700		
Anencephaly	2.17	0.88	0.65	0.27	0.10	0.52	▼	0.895
Spina bifida	5.42	2.70	1.30	0.71	1.05	1.03	▼	0.924
Encephalocele	0.00	0.72	0.81	0.49	0.47	0.00		
Microcephaly	2.17	2.48	1.95	1.70	1.15	0.26	▼	0.954
Arhinencephaly / Holoprosencephaly	0.00	0.44	0.27	0.22	0.42	0.00		
Hydrocephaly	5.15	3.36	3.20	3.73	5.35	7.49	▲	1.030
Total Anophthalmos / Microphthalmos (include unspecified)	0.27	1.21	1.30	1.10	1.10	0.78		
Anophthalmos	0.27	0.22	0.22	0.27	0.21	0.00		
Microphthalmos	0.00	0.99	1.14	0.88	0.89	0.78		
Total Anotia / Microtia (include unspecified)	0.00	0.66	1.03	1.04	1.26	1.29	▲	1.042
Anotia	0.00	0.28	0.38	0.71	0.68	0.78	▲	1.065
Microtia	0.00	0.39	0.65	0.33	0.58	0.52		
Transposition of great vessels	0.81	2.65	2.33	3.57	4.83	4.65	▲	1.049
Tetralogy of Fallot	1.08	1.05	1.73	2.19	3.46	3.88	▲	1.069
Hypoplastic left heart syndrome	1.08	1.76	1.41	0.93	0.79	1.29	▼	0.962
Coarctation of aorta	0.54	1.43	2.28	3.02	3.67	3.36	▲	1.058
Choanal atresia, bilateral	0.81	0.50	0.76	0.33	0.47	0.00		
Cleft palate without cleft lip	2.17	3.58	4.23	4.44	5.14	5.43	▲	1.026
Cleft lip with or without cleft palate	6.23	6.01	6.61	6.69	6.61	4.13		
Oesophageal atresia / stenosis with or without fistula	2.17	2.37	3.58	2.69	3.10	3.62		
Small intestine atresia / stenosis	0.00	0.50	1.41	1.70	1.99	2.33	▲	1.076
Anorectal atresia / stenosis	2.71	3.09	2.11	3.07	1.73	2.84		
Undescended testis (36 weeks of gestation or later)	6.77	10.15	12.69	10.86	5.19	6.46	▼	0.975
Hypospadias	10.29	10.09	12.96	13.05	11.02	15.76		
Epispadias	0.00	0.33	0.60	0.33	0.42	0.00		
Indeterminate sex	1.90	1.32	1.36	1.10	0.79	0.52	▼	0.966
Renal agenesis	1.08	1.10	0.76	0.27	0.37	0.26	▼	0.925
Cystic kidney	0.81	2.15	3.47	4.28	6.03	7.24	▲	1.064
Bladder exstrophy	0.00	0.39	0.22	0.38	0.26	0.00		
Polydactyly, preaxial	0.27	0.72	1.08	1.92	2.26	0.00	▲	1.052
Total Limb reduction defects (include unspecified)				2.97*	3.73	4.39		
Transverse				1.62*	2.47	3.62		
Preaxial				0.40*	0.58	0.00		
Postaxial				0.40*	0.16	0.52		
Intercalary				0.40*	0.31	0.26		
Mixed				0.13*	0.16	0.00		
Diaphragmatic hernia	1.90	2.48	2.82	3.29	3.78	4.39	▲	1.028
Total Abdominal wall defects (include unspecified)	0.81	2.92	3.47	4.39	5.51	5.43	▲	1.050
Omphalocele	0.81	1.76	2.01	1.86	2.26	3.36	▲	1.028
Gastroschisis	0.00	0.61	1.25	2.36	3.10	2.07	▲	1.093
Prune belly sequence	0.00	0.17	0.05	0.05	0.00	0.00		
Trisomy 13	0.81	0.39	0.60	0.38	0.47	0.26		
Trisomy 18	0.81	1.43	1.19	0.55	1.10	1.81		
Down syndrome, all ages (include age unknown)	10.84	12.02	12.14	9.10	7.87	6.20	▼	0.974
<20	9.03	11.59	10.77	5.81	16.94	0.00		
20-24	10.74	6.22	6.53	8.06	4.73	6.45		
25-29	3.71	7.46	6.82	4.74	4.64	2.90	▼	0.973
30-34	8.12	12.15	12.53	8.50	5.66	2.86	▼	0.953
35-39	17.11	28.49	24.81	12.23	8.94	8.38	▼	0.933
40-44	90.25	31.81	25.14	30.38	31.54	20.83		
45+	810.81	91.74	129.45	97.32	174.67	300.00		

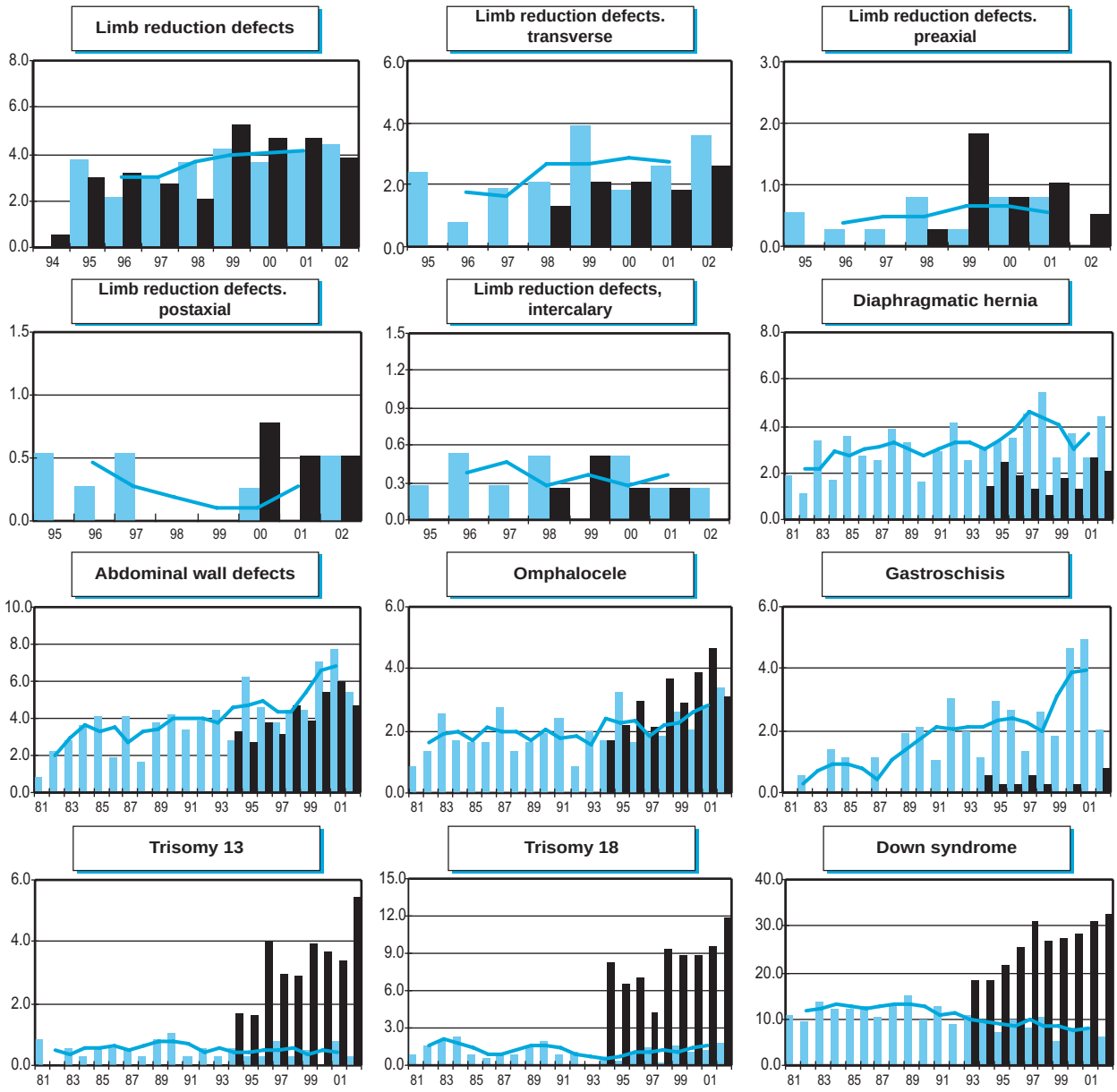
* = data include less than eight and five years

France: Paris

'Time trends 1981-2002 (Birth prevalence rates per 10,000)

Note: L+S rates, ToP rates — 3-year moving average trend

Note: L+S rates, ToP rates — 3-year moving average trend



Note: L+S rates, ToP rates — 3-year moving average trend

France: Strasbourg

Strasbourg Prospective Study of Congenital Malformations.

History:
The registry was started in 1979. The Programme became an associate member of the ICBDMS in 1982.

Size and coverage:
All births in an area including those around Strasbourg and the Bas-Rhin are covered -13,000 to 13,500 annually, or 1.8% of all births in France.

Legislation and funding:
The Programme is a research program, recognized by the local health authorities and funded by Social Security, Ministry of Health and INSERM.

Sources of ascertainment:
Reports are obtained from pediatricians examining the newborn infants. A control infant is selected for each malformed one: the next infant of the same sex as the proband born at that hospital.

Exposure information:
Detailed information on various exposures is obtained by interview of the mothers of the malformed infants and their controls. The children are followed to the age of one year.

Background information:
General demographic information is obtained from the National Institute of Statistics. Further information is obtained from Social Security Records and Health Sheets.

Research projects
Evaluation and impact of prenatal diagnosis,epidemiology and genetics of Down syndrome, neural tube defects(mothers folic acid intake),congenital heart defects,oral clefts,and limb reduction defects from 1979 to 2002,risk factors in congenital eye defects and urinary anomalies.
No rumors.

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France: Strasbourg, 2002

Live births (L)	13374
Stillbirths (S)	107
Total births	13481
Number of terminations of pregnancy (ToP) for birth defects	74

Birth Defects	Number of cases			Rates*10.000		O/E	YB	Remark
	L	S	ToP	L+S	L+S+ToP	L+S		
Anencephaly	0	0	8	0.00	5.90	0.00	8	
Spina bifida	1	0	3	0.74	2.95	0.56	9	
Encephalocele	0	0	0	0.00	0.00	0.00	17	
Microcephaly	0	0	0	0.00	0.00	0.00	7	
Arhinencephaly / Holoprosencephaly	0	0	2	0.00	1.48	0.00	7	
Hydrocephaly	1	0	4	0.74	3.69	0.39	9	
Total Anophthalmos / Microphthalmos (include unspecified)	1	0	0	0.74	0.74	0.31	19	
Anophthalmos	1	0	0	0.74	0.74	2.38	19	
Microphthalmos	0	0	0	0.00	0.00	0.00	19	
Total Anotia / Microtia (include unspecified)	2	0	0	1.48	1.48	0.90	19	
Anotia	0	0	0	0.00	0.00	0.00	19	
Microtia	2	0	0	1.48	1.48	1.05	19	
Transposition of great vessels	7	0	3	5.19	7.38	1.16	19	
Tetralogy of Fallot	2	0	1	1.48	2.21	0.44	19	
Hypoplastic left heart syndrome	0	0	4	0.00	2.95	0.00	12	
Coarctation of aorta	4	0	3	2.97	5.16	0.66	19	
Choanal atresia, bilateral	1	0	0	0.74	0.74	7.14	7	
Cleft palate without cleft lip	7	0	1	5.19	5.90	0.73	12	
Cleft lip with or without cleft palate	12	0	4	8.90	11.80	0.85	19	
Oesophageal atresia / stenosis with or without fistula	5	0	1	3.71	4.43	1.41	19	
Small intestine atresia / stenosis	4	0	1	2.97	3.69	1.76	7	
Anorectal atresia / stenosis	1	0	2	0.74	2.21	0.16	19	
Undescended testis (36 weeks of gestation or later)	nr	nr	nr	nc	nc	nc		
Hypospadias	30	0	1	22.25	22.87	0.97	19	
Epispadias	0	0	0	0.00	0.00	0.00	6	
Indeterminate sex	0	0	0	0.00	0.00	0.00	7	
Renal agenesis	8	0	4	5.93	8.85	0.95	3	
Cystic kidney	10	0	2	7.42	8.85	1.14	7	
Bladder exstrophy	0	0	0	0.00	0.00	0.00	7	
Polydactyly, preaxial	7	0	2	5.19	6.64	1.49	7	
Total Limb reduction defects (include unspecified)	9	0	1	6.68	7.38	0.96	19	
Transverse	7	0	0	5.19	5.16	1.21	19	
Preaxial	0	0	1	0.00	0.74	0.00	19	
Postaxial	0	0	0	0.00	0.00	0.00	19	
Intercalary	0	0	0	0.00	0.00	0.00	19	
Mixed	2	0	0	1.48	1.48	3.13	19	
Diaphragmatic hernia	1	0	1	0.74	1.48	0.18	19	
Total Abdominal wall defects (include unspecified)	7	0	4	5.19	8.12	1.06	19	
Omphalocele	1	0	1	0.74	1.48	0.25	19	
Gastroschisis	6	0	0	4.45	4.43	2.58	19	
Prune belly sequence	0	0	0	0.00	0.00	nc		
Trisomy 13	0	0	1	0.00	0.74	0.00	7	
Trisomy 18	0	1	6	0.74	5.16	1.41	7	
Down syndrome, all ages (include age unknown)	4	0	23	2.97	19.92	0.20	19	▼
<20	0	0	1	0.00	24.04	0.00	19	
20-24	1	0	3	4.17	16.65	0.54	19	
25-29	1	0	0	2.17	2.17	0.28	19	
30-34	0	0	5	0.00	12.24	0.00	19	
35-39	1	0	9	5.94	59.07	0.96	4	
40-44	1	0	5	34.36	202.70	1.37	4	
45+	0	0	0	0.00	0.00	0.00	19	

nr= not reported
nc= not calculable

France: Strasbourg, time trend analysis 1983-2002

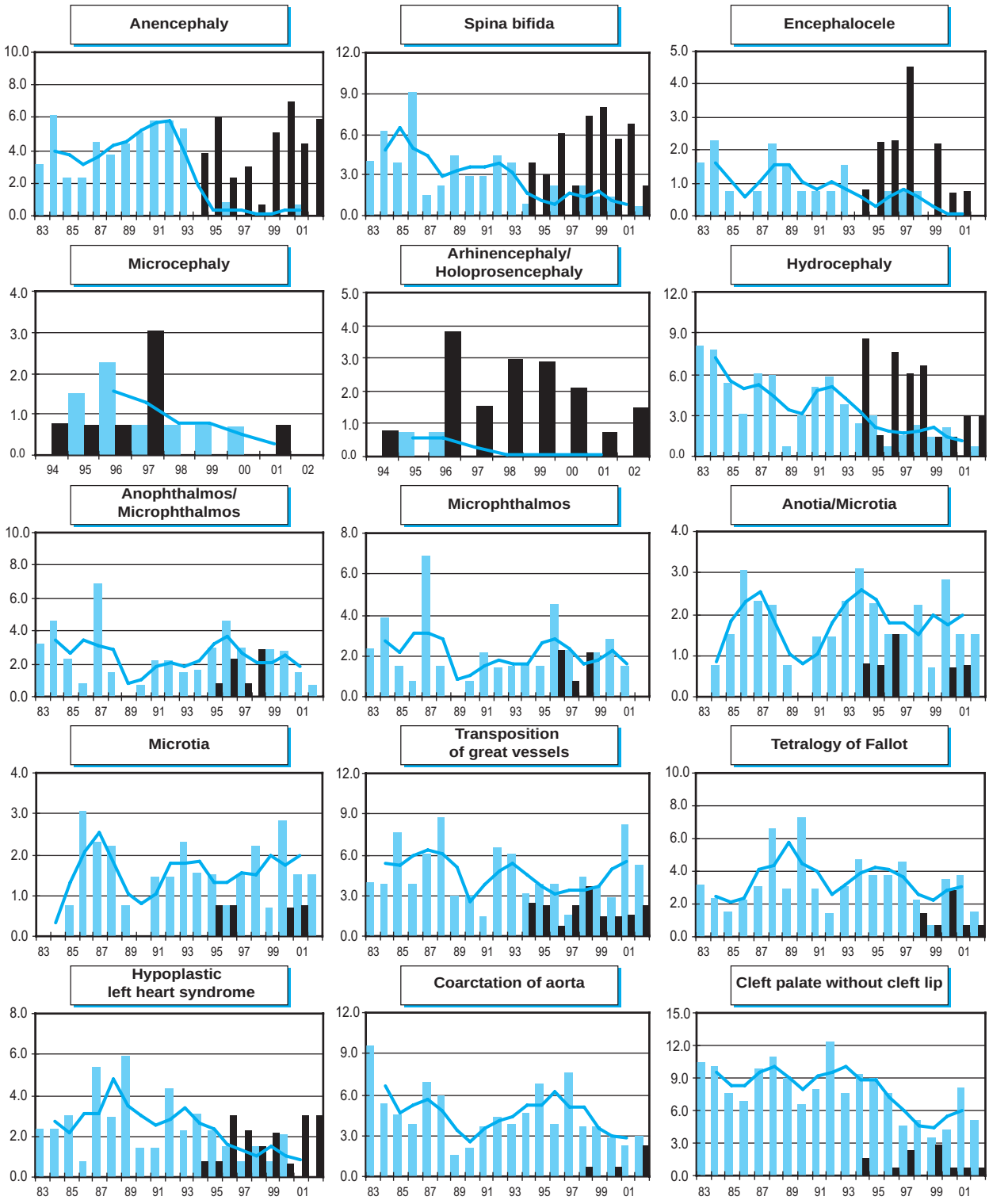
Birth prevalence rates: (L+S) * 10,000

	1974-81	1982-86*	1987-91	1992-96	1997-01	2002	Trend	RR
Births		51,759	67,715	66,248	68,364	13,481		
Anencephaly		3.48	4.73	2.42	0.15	0.00	▼	0.891
Spina bifida		5.80	2.81	2.26	1.02	0.74	▼	0.887
Encephalocele		1.16	1.18	0.60	0.29	0.00	▼	0.869
Microcephaly				1.89*	0.59	0.00	▼	0.738
Arhinencephaly / Holoprosencephaly				0.75*	0.00	0.00		
Hydrocephaly		5.99	4.13	3.17	1.46	0.74	▼	0.888
Total Anophthalmos / Microphthalmos (include unspecified)		2.70	2.22	2.57	2.05	0.74		
Anophthalmos		0.58	0.00	0.45	0.29	0.74		
Microphthalmos		2.13	2.22	2.11	1.76	0.00		
Total Anotia / Microtia (include unspecified)		1.35	1.33	2.11	1.76	1.48		
Anotia		0.39	0.00	0.60	0.00	0.00		
Microtia		0.97	1.33	1.51	1.76	1.48		
Transposition of great vessels		4.83	4.43	4.68	4.10	5.19		
Tetralogy of Fallot		2.32	4.58	3.32	2.93	1.48		
Hypoplastic left heart syndrome		2.13	3.40	2.72	1.02	0.00	▼	0.923
Coarctation of aorta		5.80	3.99	4.68	3.95	2.97		
Choanal atresia, bilateral				0.00*	0.15	0.74		
Cleft palate without cleft lip		8.69	8.86	9.21	5.12	5.19	▼	0.960
Cleft lip with or without cleft palate		8.50	9.45	12.83	10.68	8.90		
Oesophageal atresia / stenosis with or without fistula		2.13	3.10	1.96	3.22	3.71		
Small intestine atresia / stenosis				1.89*	1.61	2.97		
Anorectal atresia / stenosis		4.83	4.58	5.43	3.95	0.74	▼	0.964
Undescended testis (36 weeks of gestation or later)				1.52*			nc	
Hypospadias		17.97	26.14	24.76	21.80	22.25		
Epispadias				0.00*	0.29	0.00		
Indeterminate sex				0.00*	0.15	0.00		
Renal agenesis				0.76*	3.95	5.93	▲	1.330
Cystic kidney				6.04*	6.73	7.42		
Bladder exstrophy				0.38*	0.29	0.00		
Polydactyly, preaxial				3.77*	3.36	5.19		
Total Limb reduction defects (include unspecified)		5.60	7.38	7.70	6.73	6.68		
Transverse		3.67	4.73	3.77	4.83	5.19		
Preaxial		1.55	1.77	1.81	0.59	0.00		
Postaxial		0.19	0.44	0.30	0.44	0.00		
Intercalary		0.00	0.00	1.21	0.29	0.00		
Mixed		0.19	0.44	0.60	0.59	1.48		
Diaphragmatic hernia		4.06	4.58	3.62	3.95	0.74	▼	0.958
Total Abdominal wall defects (include unspecified)		4.06	6.35	6.49	2.63	5.19		
Omphalocele		2.51	3.69	3.62	1.76	0.74		
Gastroschisis		1.55	2.22	2.42	0.73	4.45		
Prune belly sequence				0.00*	0.00	0.00		
Trisomy 13				0.00*	0.15	0.00		
Trisomy 18				0.75*	0.44	0.74		
Down syndrome, all ages (include age unknown)		10.63	17.57	19.93	9.36	2.97	▼	0.977
<20		7.88	14.59	14.01	4.73	0.00		
20-24		7.56	8.46	11.10	2.71	4.17		
25-29		5.03	8.95	8.89	7.02	2.17		
30-34		10.89	17.44	15.64	9.97	0.00		
35-39		40.94	59.36	63.47	20.23	5.94	▼	0.938
40-44		180.41	222.48	206.28	41.67	34.36	▼	0.910
45+		400.00	0.00	222.22	0.00	0.00		

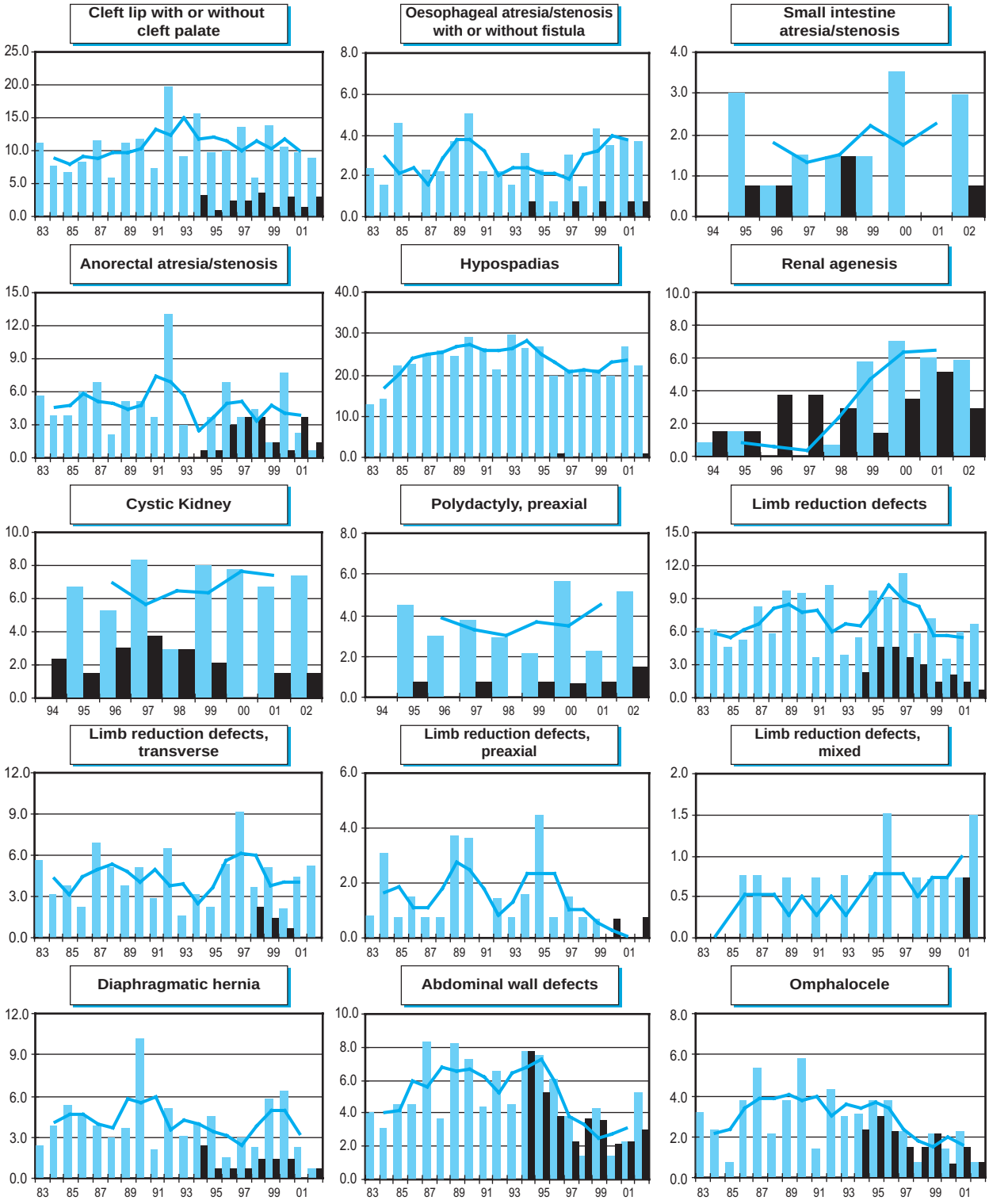
* = data include less than five years

France: Strasbourg

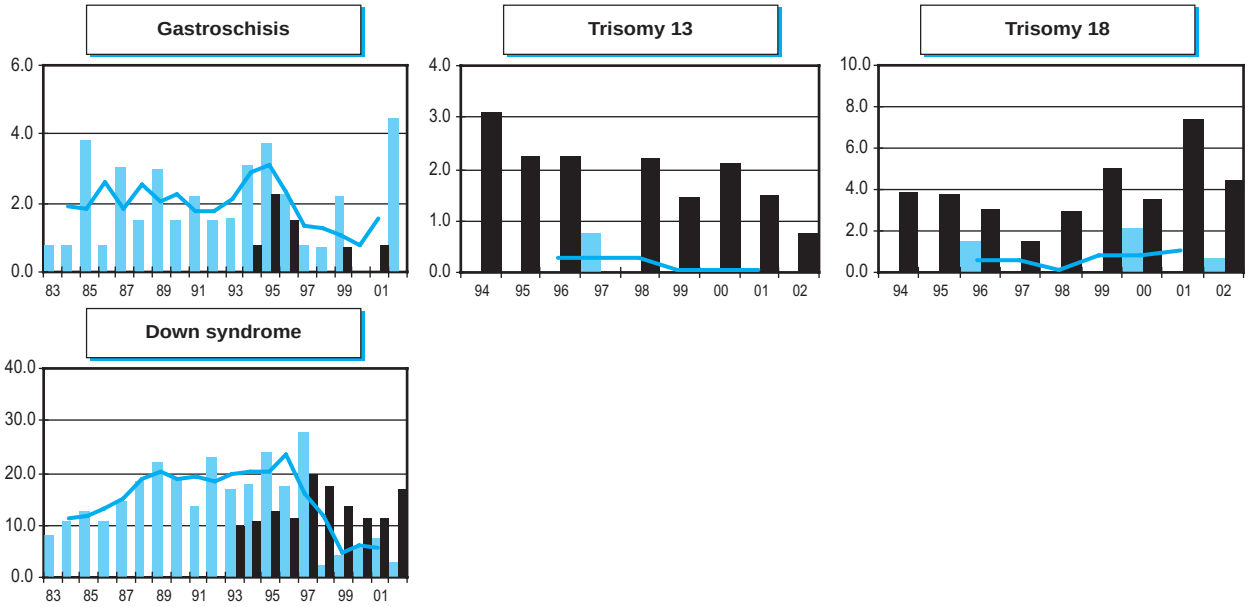
'Time trends 1983-2002 (Birth prevalence rates per 10,000)



Note: L+S rates, ToP rates — 3-year moving average trend



Note: L+S rates, ToP rates — 3-year moving average trend



Note: L+S rates, ToP rates 3-year moving average trend

Germany: Saxony-Anhalt
Malformation Monitoring Saxony-Anhalt

History:
Since 1980 in the city of Magdeburg all live- and stillbirths, abortions after the 16th week of gestation (spontaneous and induced abortions according to medical evidence based on prenatal diagnoses of congenital defects), and postnatal anomalies or congenital defects have been recorded up to the first week of life. After the reunification of Germany and the creation of the Federal State of Saxony-Anhalt, the survey of congenital defects included approximately two-thirds of all births with postnatal anomalies and congenital defects in the same federal state. Since 1 January 2000 the survey region includes the entire state of Saxony-Anhalt. Saxony-Anhalt has 2.65 million inhabitants and annual births at a rate of about 18,000 children.
The survey system works as a multicentre and population based study .
The programme became an associate member of the ICBDMS in 2001 and is also a member of EUROCAT since 1992.

Legislation and funding:
1980 to 1989: Ministry of Health of the former German Democratic Republic
1990 to 1992: Academy of Medicine, Magdeburg
1993 to 1995: Ministry of Health, Federal Republic of Germany
since 1995: Ministry of Health and Social Affairs of the Federal State of Saxony-Anhalt.
The Malformation Monitoring is working in order of Ministry of Health and Social Affairs of the Federal State of Saxony-Anhalt.

Sources of ascertainment:
The co-operation partner are:
- 31 obstetrics departments
- 29 children hospitals
- 11 institutions of prenatal diagnostic
- 6 departments of pathology

Exposure information:
maternal and paternal occupation (in groups); occupation risk; drugs in pregnancy (ATC-code); alcohol, nicotine, drug abuse.
Background:
population based registry (Federal State Saxony-Anhalt); written informed consent of the mother (parents); name and address don't registered; two healthy "controls" per one malformed child; inclusion of terminations of pregnancy, spontaneous abortions after 16th week of gestation, live and stillborn babies; definition of stillbirth: < 500 grams; maximum age to include diagnoses: 1 year, almost 1th week of life; annual reports (in German).

Working projects:
1. Since 1998 in Saxony-Anhalt we have a working group "Folic acid - for you my child". In October 2003 we started a public action with support of the famous swimmer Dagmar Hase with flyer and poster in pharmacies and with the gynaecologists to assist the periconceptional intake of folic acid against the development of neural tube defects.
2. In March this year we asked school children (16 to 19 years old in different school forms) to the knowledge about folic acid, vitamins and some minerals. About 3,000 questionnaires came back.
3. Prof. Steinbicker and myself also member of the German project: Folic acid and nutrition.
4. Our group is working together with the German National Registry of congenital heart defects and in the German registry of limb reduction defects.

Address for further information:
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Dr. Christine Rösch

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Germany: Saxony-Anhalt, 2002

Live births (L)	17617
Stillbirths (S)	71
Total births	17688
Number of terminations of pregnancy (ToP) for birth defects	67

Birth Defects	Number of cases			Rates*10.000		O/E	YB	Remark
	L	S	ToP	L+S	L+S+ToP	L+S		
Anencephaly	1	0	3	0.57	2.25	2.08	2	
Spina bifida	2	0	7	1.13	5.07	0.60	2	
Encephalocele	0	0	2	0.00	1.13	0.00	2	
Microcephaly	24	0	0	13.57	13.52	2.28	2	▲
Arhinencephaly / Holoprosencephaly	0	0	1	0.00	0.56	0.00	2	
Hydrocephaly	12	1	7	7.35	11.26	1.60	2	
Total Anophthalmos / Microphthalmos (include unspecified)	2	0	0	1.13	1.13	nc		
Anophthalmos	0	0	0	0.00	0.00	nc		
Microphthalmos	2	0	0	1.13	1.13	nc		
Total Anotia / Microtia (include unspecified)	4	0	0	2.26	2.25	2.08	2	
Anotia	0	0	0	0.00	0.00	nc		
Microtia	4	0	0	2.26	2.25	2.08	2	
Transposition of great vessels	6	1	3	3.96	5.63	0.97	2	
Tetralogy of Fallot	6	0	0	3.39	3.38	1.57	2	
Hypoplastic left heart syndrome	6	0	3	3.39	5.07	1.25	2	
Coarctation of aorta	6	1	1	3.96	4.51	1.46	2	
Choanal atresia, bilateral	1	0	0	0.57	0.56	0.69	2	
Cleft palate without cleft lip	16	0	0	9.05	9.01	0.93	2	
Cleft lip with or without cleft palate	20	0	3	11.31	12.95	0.79	2	
Oesophageal atresia / stenosis with or without fistula	6	0	0	3.39	3.38	1.57	2	
Small intestine atresia / stenosis	5	0	0	2.83	2.82	1.16	2	
Anorectal atresia / stenosis	6	0	2	3.39	4.51	1.39	2	
Undescended testis (36 weeks of gestation or later)	17	0	0	9.61	9.57	1.27	2	
Hypospadias	15	0	0	8.48	8.45	0.95	2	
Epispadias	0	0	0	0.00	0.00	0.00	2	
Indeterminate sex	1	0	1	0.57	1.13	0.69	2	
Renal agenesis	1	0	3	0.57	2.25	1.04	2	
Cystic kidney	6	0	0	3.39	3.38	1.25	2	
Bladder exstrophy	0	0	0	0.00	0.00	nc		
Polydactyly, preaxial	6	0	0	3.39	3.38	nc		
Total Limb reduction defects (include unspecified)	6	0	2	3.39	4.51	0.52	2	
Transverse	5	0	1	2.83	3.38	0.80	2	
Preaxial	0	0	0	0.00	0.00	0.00	2	
Postaxial	0	0	0	0.00	0.00	nc		
Intercalary	0	0	0	0.00	0.00	0.00	2	
Mixed	1	0	1	0.57	1.13	0.35	2	
Diaphragmatic hernia	6	0	1	3.39	3.94	2.09	2	
Total Abdominal wall defects (include unspecified)	5	0	6	2.83	6.20	0.75	2	
Omphalocele	2	0	4	1.13	3.38	0.84	2	
Gastroschisis	3	0	2	1.70	2.82	0.78	2	
Prune belly sequence	0	0	3	0.00	1.69	0.00	2	
Trisomy 13	1	0	0	0.57	0.56	nc		
Trisomy 18	1	0	4	0.57	2.82	1.04	2	
Down syndrome, all ages (include age unknown)	17	0	11	9.61	15.77	1.11	2	
<20	0	0	1	0.00	7.71	nc		
20-24	2	0	0	4.56	4.56	nc		
25-29	4	0	1	7.54	9.42	nc		
30-34	3	0	3	6.36	12.72	nc		
35-39	5	0	2	30.01	41.97	nc		
40-44	2	0	3	82.99	204.92	nc		
45+	1	0	0	909.09	909.09	nc		

* only the last 3 years(2000-2001-2002) have been considered to calculate the O/E ratio

Germany: Saxony Anhalt, time trend analysis 1980-2002

Birth prevalence rates: (L+S) * 10,000

	1974-81*	1982-86	1987-91	1992-96	1997-01	2002	Trend	RR
Births	35,995	86,498	72,876	39,433	68,296	17,688		
Anencephaly	1.11	1.73	0.69	0.76	0.44	0.57		
Spina bifida	3.06	6.24	6.45	3.30	1.90	1.13		
Encephalocele	0.28	0.58	0.55	0.76	0.29	0.00		
Microcephaly			2.06	4.31	7.61	13.57		
Arhinencephaly / Holoprosencephaly			1.37	0.00	0.44	0.00		
Hydrocephaly			3.70	5.33	5.12	7.35		
Total Anophthalmos / Microphthalmos (include unspecified)			1.10	2.03	0.15	1.13		
Anophthalmos			0.00	1.01	0.00	0.00		
Microphthalmos			1.10	1.01	0.15	1.13		
Total Anotia / Microtia (include unspecified)			0.14	0.25	0.73	2.26		
Anotia			0.00	0.25	0.00	0.00		
Microtia			0.18*	0.00	0.73	2.26		
Transposition of great vessels			2.47	3.80	5.42	3.96		
Tetralogy of Fallot			0.69	2.03	2.78	3.39		
Hypoplastic left heart syndrome			3.98	3.55	2.78	3.39		
Coarctation of aorta			1.51	1.52	2.78	3.96		
Choanal atresia, bilateral			0.96	1.27	0.88	0.57		
Cleft palate without cleft lip			5.08	5.58	9.37	9.05		
Cleft lip with or without cleft palate			13.45	12.68	15.67	11.31		
Oesophageal atresia / stenosis with or without fistula			2.06	2.03	2.20	3.39		
Small intestine atresia / stenosis			1.37	2.79	1.76	2.83		
Anorectal atresia / stenosis			3.16	2.54	2.34	3.39		
Undescended testis (36 weeks of gestation or later)			12.35	17.24	10.84	9.61		
Hypospadias			13.31	20.79	13.03	8.48		
Epispadias			0.27	0.76	0.29	0.00		
Indeterminate sex			0.41	0.00	0.88	0.57		
Renal agenesis			0.69	0.51	1.02	0.57		
Cystic kidney			1.10	3.55	2.93	3.39		
Bladder exstrophy			0.41	0.51	0.00	0.00		
Polydactyly, preaxial			0.41	3.04	4.54	3.39		
Total Limb reduction defects (include unspecified)			5.35	5.07	7.32	3.39		
Transverse					3.52*	2.83		
Preaxial					0.27*	0.00		
Postaxial					0.00*	0.00		
Intercalary					1.08*	0.00		
Mixed					1.62*	0.57		
Diaphragmatic hernia			1.92	0.00	1.61	3.39		
Total Abdominal wall defects (include unspecified)			4.94	3.30	3.51	2.83		
Omphalocele			3.57	1.78	1.02	1.13		
Gastroschisis			1.37	1.52	2.34	1.70		
Prune belly sequence			0.27	0.51	0.59	0.00		
Trisomy 13	0.00	0.35	0.55	0.25	0.73	0.57		
Trisomy 18	0.00	0.92	0.82	0.51	0.44	0.57		
Down syndrome, all ages (include age unknown)	6.95	9.13	7.41	7.61	8.93	9.61		
<20					0.00*	0.00		
20-24					4.37*	4.56		
25-29					4.73*	7.54		
30-34					10.67*	6.36		
35-39					0.00*	30.01		
40-44					80.32*	82.99		
45+					0.00*	909.09		

* = data include less than eight and five years

Germany: Saxony Anhalt

'Time trends 1980-2002 (Birth prevalence rates per 10,000)

Note: L+S rates, ToP rates — 3-year moving average trend

Note: L+S rates, ToP rates — 3-year moving average trend

Note: L+S rates, ToP rates — 3-year moving average trend

Hungary
Hungarian Congenital Abnormality Registry

History:
Centralized registration of congenital abnormalities began in Hungary in 1962, and came under our co-ordination in 1970. Monitoring began in 1973. The Programme was a founding member of the International Clearinghouse and is a full member.

Size and coverage:
The registry covers all births in Hungary, approximately 100,000 annually. Criteria to define stillbirth was changed in 1998. At present, stillbirths of at least 24 weeks gestation or 500 grams are registered. Prenatally diagnosed and terminated fetuses are also registered.

Legislation and funding:
Reporting is compulsory. The registry is run and financed by the governmental National Center for Epidemiology (formerly the National Institute of Public Health).

Sources of ascertainment:
Reports are obtained from delivery units, neonatal and pediatric surgery, pathology, and prenatal diagnostic centers. Abnormalities detected before the age of one are reported. Variations in figures (especially in the1990s) may reflect incomplete notification.

Exposure information:
Exposure information has been available since 1980, when a case-control system was initiated. Mothers of selected malformed infants and controls are interviewed by community nurses to collect information. The case-control system was interrupted due to temporary problems of the legislative background. Therefore, exposure information was not collected in 2003. Our expectation is that the formal system will be restart in 2004.

Background information:
General background information on all births is available from central statistics.

Research projects
a. Started during the year (2003 – 2004) Epidemiology of orofacial clefts
b. Finished during the year (2003 – 2004) but not yet published (do not describe projects that have been published) None

Education or promotion project
c. Describe the main activity your registry promoted or was involved in related to education and prevention promotion The Registry started a training program for field workers in order to improve the quality of data and case ascertainment.

Address for further information:
Csaba Siffel/Julia Metneki, Department of Human Genetics and Teratology, National Center for Epidemiology, Gyali ut 2-6., H-1966 Budapest, Pf. 64., Hungary.

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Hungary, 2002

Live births (L)	96804
Stillbirths (S)	523
Total births	97327
Number of terminations of pregnancy (ToP) for birth defects	179

Birth Defects	Number of cases			Rates*10.000		O/E	YB	Remark
	L	S	ToP	L+S	L+S+ToP	L+S		
Anencephaly	3	1	16	0.41	2.05	1.45	10	
Spina bifida	12	0	13	1.23	2.56	0.73	11	
Encephalocele	3	1	5	0.41	0.92	1.29	10	
Microcephaly	8	0	0	0.82	0.82	1.29	15	
Arhinencephaly / Holoprosencephaly	8	0	3	0.82	1.13	3.29	21	▲
Hydrocephaly	19	2	14	2.16	3.59	1.48	11	
Total Anophthalmos / Microphthalmos (include unspecified)	0	0	0	0.00	0.00	0.00	22	
Anophthalmos	0	0	0	0.00	0.00	0.00	26	
Microphthalmos	0	0	0	0.00	0.00	0.00	22	
Total Anotia / Microtia (include unspecified)	5	0	0	0.51	0.51	0.62	3	
Anotia	4	0	0	0.41	0.41	0.61	4	
Microtia	1	0	0	0.10	0.10	3.23	28	
Transposition of great vessels	13	0	0	1.34	1.33	0.97	24	
Tetralogy of Fallot	22	0	0	2.26	2.26	1.85	28	
Hypoplastic left heart syndrome	7	0	2	0.72	0.92	1.25	24	
Coarctation of aorta	13	0	0	1.34	1.33	0.75	27	
Choanal atresia, bilateral	1	0	0	0.10	0.10	0.88	22	
Cleft palate without cleft lip	28	0	0	2.88	2.87	0.90	15	
Cleft lip with or without cleft palate	58	0	1	5.96	6.05	0.84	9	
Oesophageal atresia / stenosis with or without fistula	11	1	0	1.23	1.23	1.28	10	
Small intestine atresia / stenosis	7	1	0	0.82	0.82	1.36	9	
Anorectal atresia / stenosis	6	0	0	0.62	0.62	0.72	8	
Undescended testis (36 weeks of gestation or later)	135	0	0	13.87	13.85	1.38	6	▲
Hypospadias & Epispadias	225	0	0	23.12	23.08	1.11	22	
Indeterminate sex	5	0	0	0.51	0.51	3.23	12	
Renal agenesis	0	0	1	0.00	0.10	0.00	9	
Cystic kidney	25	0	0	2.57	2.56	1.76	6	
Bladder exstrophy	0	0	0	0.00	0.00	0.00	13	
Polydactyly, preaxial	86	0	0	8.84	8.82	1.12	5	
Total Limb reduction defects (include unspecified)	23	1	1	2.47	2.56	0.80	15	
Transverse	nr	nr	nr	nc	nc	nc		
Preaxial	nr	nr	nr	nc	nc	nc		
Postaxial	nr	nr	nr	nc	nc	nc		
Intercalary	nr	nr	nr	nc	nc	nc		
Mixed	nr	nr	nr	nc	nc	nc		
Diaphragmatic hernia	3	0	0	0.31	0.31	0.47	9	
Total Abdominal wall defects (include unspecified)	6	1	11	0.72	1.85	0.74	10	
Omphalocele	5	0	7	0.51	1.23	0.76	13	
Gastroschisis	1	1	4	0.21	0.62	0.44	20	
Prune belly sequence	0	0	0	0.00	0.00	nc		
Trisomy 13	0	0	7	0.00	0.72	0.00	20	
Trisomy 18	7	0	7	0.72	1.44	2.47	20	
Down syndrome, all ages (include age unknown)	94	0	47	9.66	14.46	1.31	19	
<20	2	0	1	2.87	4.31	1.47	20	
20-24	16	0	4	7.04	8.80	2.59	19	▲
25-29	28	0	6	7.39	8.98	2.04	20	▲
30-34	18	0	7	8.42	11.69	1.62	20	
35-39	19	0	18	27.34	53.10	1.91	20	
40+	11	0	11	76.34	151.52	1.45	20	

Note: only isolated birth defects are reported
nr = not reported
nc = not calculable

Hungary, time trend analysis 1974-2002

Birth prevalence rates: (L+S) * 10,000

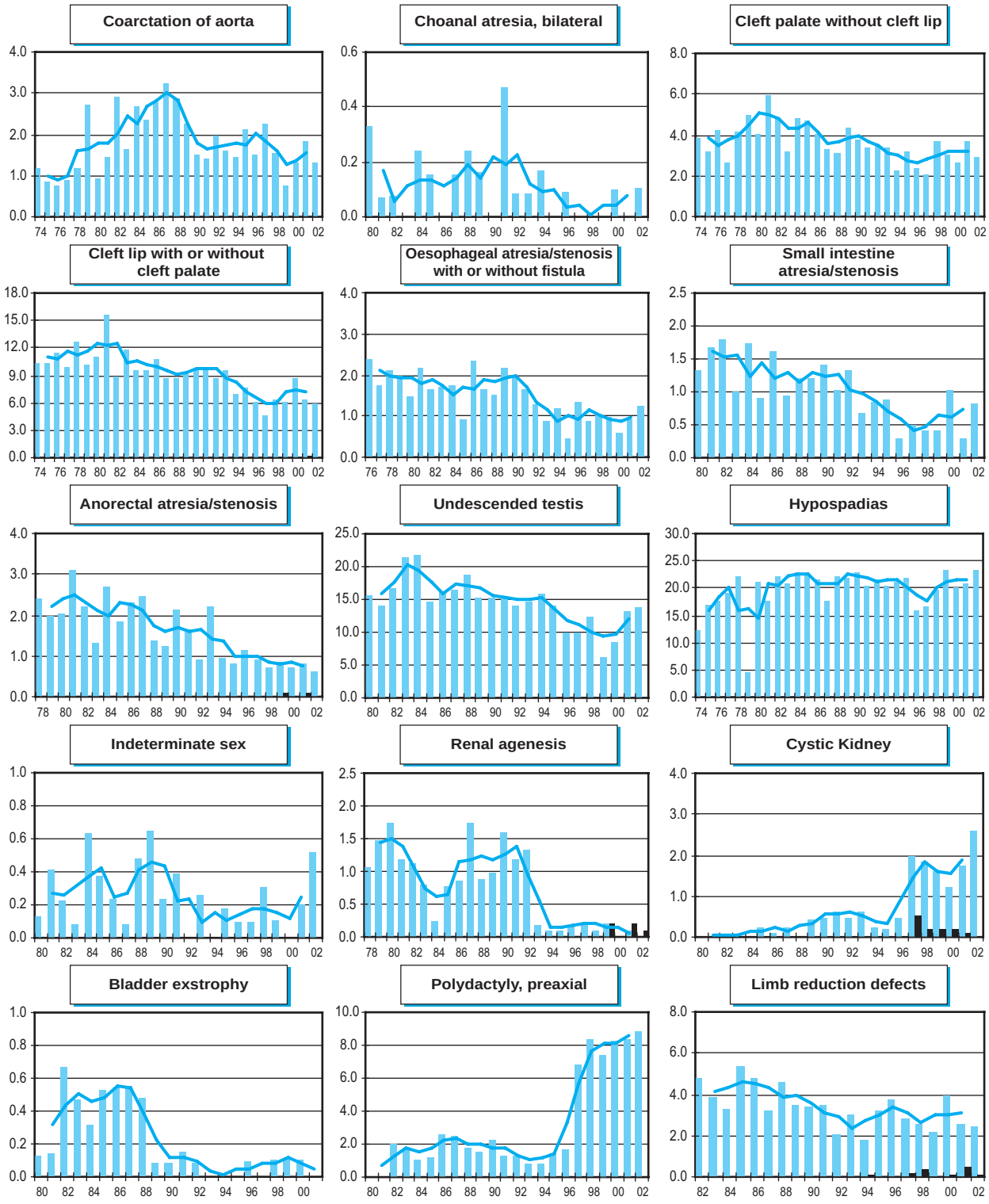
	1974-81	1982-86	1987-91	1992-96	1997-01	2002	Trend	RR
Births	1,374,956	648,927	629,899	573,811	489,639	97,327		
Anencephaly	7.05	4.41	1.37	0.31	0.25	0.41	▼	0.908
Spina bifida	10.26	7.87	4.52	1.52	1.59	1.23	▼	0.931
Encephalocele	1.54*	1.62	1.05	0.37	0.27	0.41	▼	0.929
Microcephaly	1.67*	1.17	0.71	0.64	0.53	0.82	▼	0.947
Arhinencephaly / Holoprosencephaly	0.14*	0.29	0.16	0.05	0.55	0.82	▼	1.060
Hydrocephaly	6.57	3.76	2.87	1.10	1.49	2.16	▼	0.936
Total Anophthalmos / Microphthalmos (include unspecified)	0.29	0.26	0.10	0.14	0.14	0.00	▼	0.957
Anophthalmos	0.11	0.08	0.05	0.05	0.04	0.00	▼	0.951
Microphthalmos	0.18	0.18	0.05	0.09	0.10	0.00	▼	0.960
Total Anotia / Microtia (include unspecified)	0.14	0.20	0.22	0.23	0.65	0.51	▲	1.070
Anotia	0.09	0.18	0.21	0.19	0.61	0.41	▲	1.081
Microtia	0.04	0.02	0.02	0.03	0.04	0.10		
Transposition of great vessels	0.98*	1.66	1.79	1.12	1.27	1.34		
Tetralogy of Fallot	1.32	1.11	0.98	0.94	1.72	2.26		
Hypoplastic left heart syndrome	0.38*	0.46	0.92	0.44	0.67	0.72		
Coarctation of aorta	1.22	2.48	2.25	1.74	1.55	1.34	▲	1.010
Choanal atresia, bilateral	0.20*	0.09	0.21	0.09	0.02	0.10		
Cleft palate without cleft lip	4.07	4.30	3.59	2.95	3.02	2.88	▼	0.987
Cleft lip with or without cleft palate	11.38	10.14	9.21	7.89	6.47	5.96	▼	0.980
Oesophageal atresia / stenosis with or without fistula	1.99*	1.66	1.79	1.03	0.88	1.23	▼	0.969
Small intestine atresia / stenosis	1.50*	1.42	1.16	0.82	0.53	0.82	▼	0.953
Anorectal atresia / stenosis	2.37*	2.08	1.76	1.20	0.80	0.62	▼	0.954
Undescended testis (36 weeks of gestation or later)	14.97*	18.12	16.27	13.80	10.07	13.87	▼	0.977
Hypospadias & Epispadias	16.42	22.04	21.00	20.32	20.01	23.12	▲	1.010
Indeterminate sex	0.27*	0.31	0.37	0.10	0.14	0.51		
Renal agenesis	1.36*	0.76	1.27	0.38	0.12	0.00	▼	0.930
Cystic kidney	0.00*	0.06	0.35	0.40	1.67	2.57	▲	1.171
Bladder exstrophy	0.14*	0.51	0.27	0.03	0.06	0.00	▼	0.907
Polydactyly, preaxial	0.00*	1.74	1.86	1.19	7.86	8.84	▲	1.124
Total Limb reduction defects (include unspecified)		4.44	3.62	2.74	2.82	2.47	▼	0.971
Transverse								
Preaxial								
Postaxial								
Intercalary								
Mixed								
Diaphragmatic hernia	2.05	2.30	2.16	0.94	0.65	0.31	▼	0.962
Total Abdominal wall defects (include unspecified)		2.53	1.51	1.01	0.92	0.72	▼	0.934
Omphalocele		1.99	0.95	0.63	0.55	0.51	▼	0.918
Gastroschisis		0.54	0.56	0.38	0.37	0.21		
Prune belly sequence				0.00*	0.00	0.00		
Trisomy 13		0.26	0.16	0.16	0.08	0.00	▼	0.943
Trisomy 18		0.25	0.33	0.17	0.43	0.72	▲	1.044
Down syndrome, all ages (include age unknown)	8.94	7.77	8.54	6.43	6.82	9.66	▼	0.990
<20		1.56	2.52	1.30	2.81	2.87		
20-24		2.04	3.03	1.85	3.86	7.04	▲	1.045
25-29		3.46	4.25	2.14	4.71	7.39	▲	1.022
30-34		4.80	5.64	3.90	6.26	8.42		
35-39		11.05	18.96	11.62	14.82	27.34		
40+		56.53	64.97	30.28	62.90	76.34		

* = data include less than eight and five years

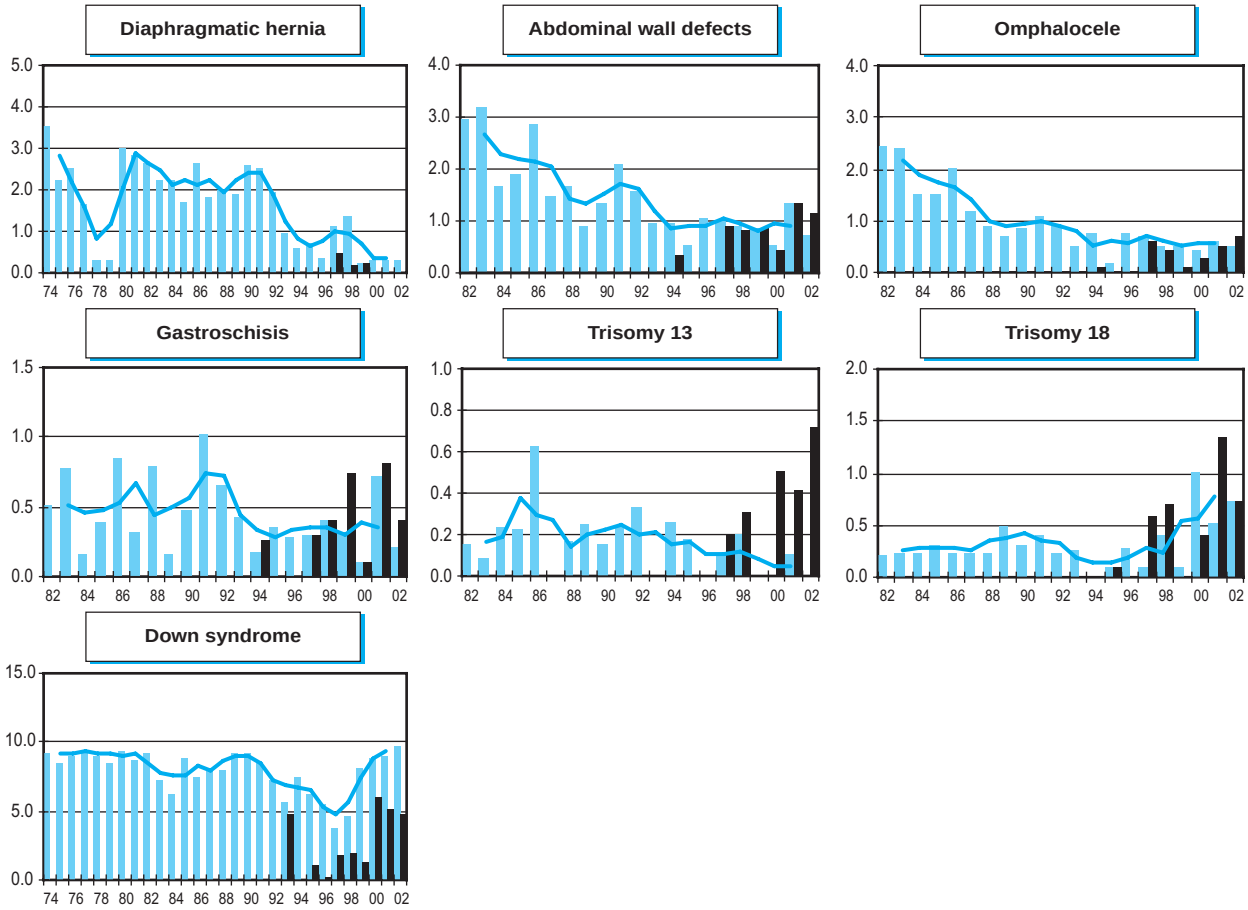
Hungary

'Time trends 1974-2002 (Birth prevalence rates per 10,000)

Note: L+S rates, ToP rates — 3-year moving average trend



Note: L+S rates, ToP rates — 3-year moving average trend



Note: L+S rates, ToP rates — 3-year moving average trend

Ireland: Dublin
Dublin EUROCAT Registry

History:
Register began in September 1979 and joined EUROCAT at the same time. Joined ICBDMS in 1997.

Size and coverage:
The Registry is population-based and situated in the East of Ireland covering the counties of Dublin, Wicklow and Kildare. About one third (20,000 births) of all births in Ireland occur in this area.

Legislation and funding:
The Registry is located within the Public Health Department of the Eastern Regional Health Authority. Staffing includes a full time nurse/researcher and a part time secretary plus a part-time public health specialist. Funding is provided by the Department of Health through the Eastern Regional Health Authority. There is a Steering Committee comprising specialists from each of Maternity and Paediatric Hospitals in the catchment plus a representative from the Department of Health.

Exposure information:
For each malformed infant reported, limited information is given on certain exposures. No information is available on controls.

Sources of ascertainment:
All live and still births are covered. Abortion is illegal in Ireland.

Address for further information:
Robert Mc Donnell, Department of Public Health, Eastern Regional Health Authority, Dr. Steeven's Hospital, Dublin 8, Ireland.

Phone: 353-1-6352750

Fax: 353-1-6352745

E-mail: bob.mcdonnell@erha.ie

Ireland: Dublin, 2002

Live births (L)	ESTIMATE	22671
Stillbirths (S)	ESTIMATE	130
Total births	ESTIMATE	22801
Number of terminations of pregnancy (ToP) for birth defects		not permitted

Birth Defects	Number of cases			Rates*10.000		O/E	YB	Remark
	L	S	ToP	L+S	L+S+ToP	L+S		
Anencephaly	4	5		3.95		1.02	11	
Spina bifida	7	0		3.07		0.54	13	
Encephalocele	0	1		0.44		0.22	22	
Microcephaly	7	0		3.07		0.81	22	
Arhinencephaly / Holoprosencephaly	2	0		0.88		0.81	10	
Hydrocephaly	2	0		0.88		0.34	6	
Total Anophthalmos / Microphthalmos (include unspecified)	1	0		0.44		0.19	14	
Anophthalmos	1	0		0.44		1.37	21	
Microphthalmos	0	0		0.00		0.00	14	
Total Anotia / Microtia (include unspecified)	1	0		0.44		2.50	22	
Anotia	1	nr		nc		nc		
Microtia	nr	nr		nc		nc		
Transposition of great vessels	11	0		4.82		0.90	6	
Tetralogy of Fallot	5	0		2.19		0.74	22	
Hypoplastic left heart syndrome	7	0		3.07		1.46	22	
Coarctation of aorta	11	0		4.82		0.85	22	
Choanal atresia, bilateral	5	0		2.19		1.86	16	
Cleft palate without cleft lip	15	0		6.58		0.85	22	
Cleft lip with or without cleft palate	24	0		10.53		1.19	22	
Oesophageal atresia / stenosis with or without fistula	3	0		1.32		0.38	22	
Small intestine atresia / stenosis	5	1		2.63		1.09	22	
Anorectal atresia / stenosis	4	0		1.75		0.56	22	
Undescended testis (36 weeks of gestation or later)	nr	nr		nc		nc		
Hypospadias & Epispadias	23	0		10.09		0.76	22	
Indeterminate sex	0	0		0.00		0.00	22	
Renal agenesis	3	1		1.75		0.41	22	
Cystic kidney	7	0		3.07		0.93	22	
Bladder exstrophy	nr	nr		nc		nc		
Polydactyly, preaxial	15	0		6.58		1.03	21	
Total Limb reduction defects (include unspecified)	9	0		3.95		0.98	22	
Transverse	nr	nr		nc		nc		
Preaxial	nr	nr		nc		nc		
Postaxial	nr	nr		nc		nc		
Intercalary	nr	nr		nc		nc		
Mixed	nr	nr		nc		nc		
Diaphragmatic hernia	9	3		5.26		1.31	22	
Total Abdominal wall defects (include unspecified)	10	2		5.26		0.88	4	
Omphalocele	5	2		3.07		1.20	22	
Gastroschisis	5	0		2.19		1.01	9	
Prune belly sequence	nr	nr		nc		nc		
Trisomy 13	6	2		3.51		1.16	7	
Trisomy 18	4	3		3.07		0.88	13	
Down syndrome, all ages (include age unknown)	43	3		20.17		0.96	17	
<20	0	0		0.00		0.00	8	
20-24	4	0		11.75		1.49	10	
25-29	2	0		3.65		0.38	10	
30-34	11	2		17.38		1.00	10	
35-39	16	1		38.46		0.80	10	
40-44	10	0		139.66		0.84	10	
45+	0	0		0.00		0.00	9	

Ireland: Dublin, time trend analysis 1980-2002

Birth prevalence rates: (L+S) * 10,000

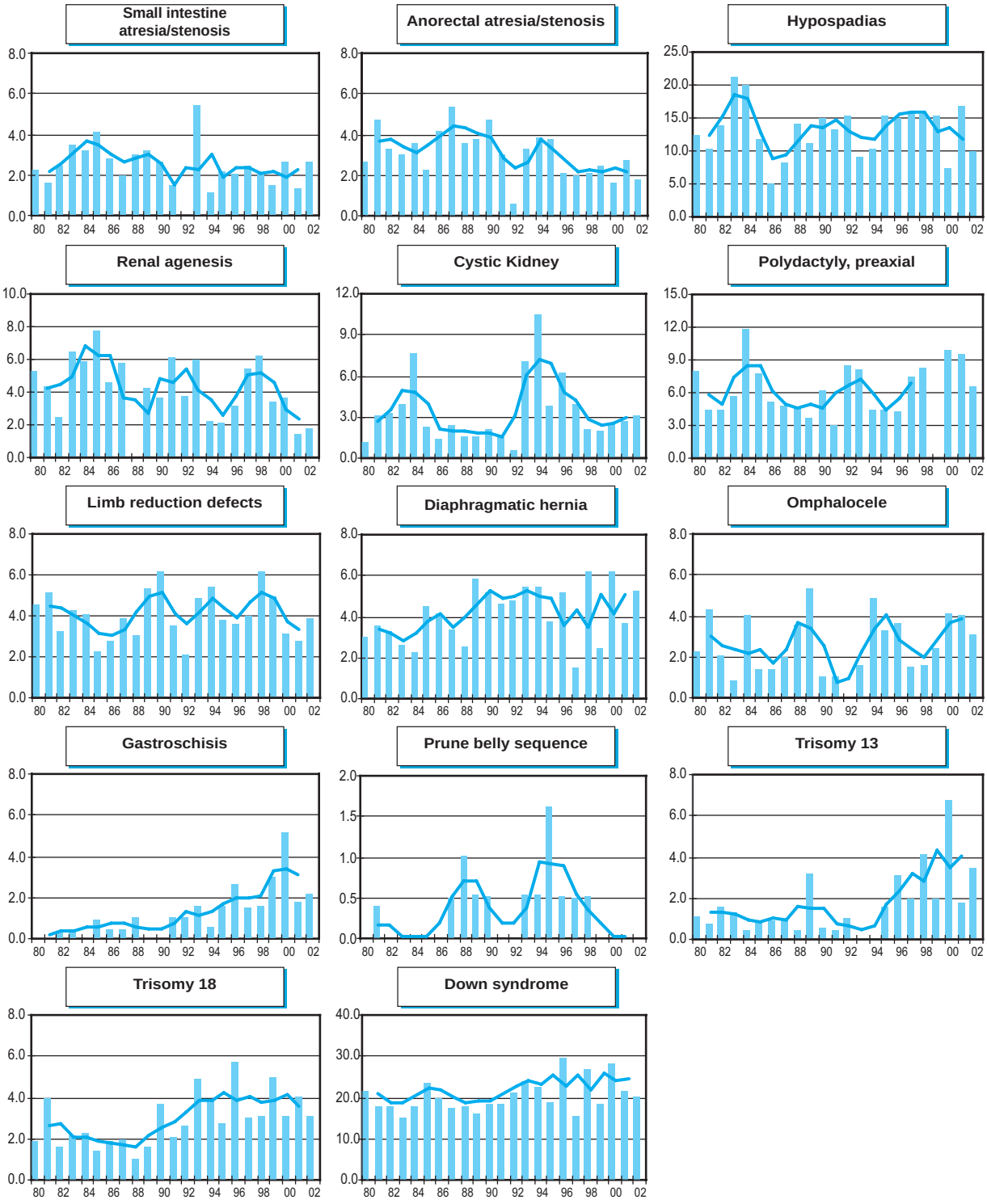
	1974-81*	1982-86	1987-91	1992-96	1997-01	2002	Trend	RR
Births	51,519	113,387	98,055	93,154	100,815	22,801		
Anencephaly	17.08	11.82	7.34	4.08	3.47	3.95	▼	0.922
Spina bifida	9.71	15.96	8.46	6.01	4.86	3.07	▼	0.942
Encephalocele	3.49	1.76	1.63	2.25	1.79	0.44		
Microcephaly	3.69	4.15	2.55	5.37	3.17	3.07		
Arhinencephaly / Holoprosencephaly	0.00	0.35	0.51	0.64	1.49	0.88	▲	1.094
Hydrocephaly				2.08*	2.68	0.88		
Total Anophthalmos / Microphthalmos (include unspecified)	0.58	1.15	1.33	2.68	2.68	0.44	▲	1.054
Anophthalmos	0.39	0.18	0.00	0.64	0.50*	0.44		
Microphthalmos	0.19	0.97	1.33	2.04	2.23*	0.00	▲	1.055
Total Anotia / Microtia (include unspecified)	0.19	0.09	0.10	0.43	0.10	0.44		
Anotia								
Microtia								
Transposition of great vessels				4.69*	5.46	4.82		
Tetralogy of Fallot	3.11	2.91	2.24	3.65	3.07	2.19		
Hypoplastic left heart syndrome	1.16	2.73	1.84	2.36	1.88	3.07		
Coarctation of aorta	4.27	5.91	5.71	6.23	5.46	4.82		
Choanal atresia, bilateral	0.19	0.53	0.61	1.50	1.49	2.19	▲	1.080
Cleft palate without cleft lip	7.57	6.79	7.75	8.16	8.53	6.58		
Cleft lip with or without cleft palate	11.06	8.73	8.26	8.48	8.73	10.53		
Oesophageal atresia / stenosis with or without fistula	4.27	3.26	3.47	3.44	3.27	1.32		
Small intestine atresia / stenosis	1.94	3.17	2.45	2.15	1.98	2.63		
Anorectal atresia / stenosis	3.69	3.26	4.08	2.68	2.18	1.75	▼	0.975
Undescended testis (36 weeks of gestation or later)								
Hypospadias & Epispadias	11.26	14.46	12.34	13.10	14.28	10.09		
Indeterminate sex	0.19	0.18	0.20	0.32	0.20	0.00		
Renal agenesis	4.85	5.38	3.98	3.44	3.97	1.75	▼	0.975
Cystic kidney	2.14	3.70	1.84	5.58	2.68	3.07		
Bladder exstrophy				2.61*	0.49*		nc	
Polydactyly, preaxial	6.21	6.88	4.49	5.90	8.81*	6.58		
Total Limb reduction defects (include unspecified)	4.85	3.35	4.39	3.97	4.17	3.95		
Transverse								
Preaxial								
Postaxial								
Intercalary								
Mixed								
Diaphragmatic hernia	3.30	3.35	4.28	4.94	3.97	5.26		
Total Abdominal wall defects (include unspecified)					5.95*	5.26		
Omphalocele	3.30	1.94	2.55	2.68	2.78	3.07		
Gastroschisis	0.00	0.44	0.51	1.50	2.58	2.19	▲	1.122
Prune belly sequence	0.19	0.00	0.51	0.64	0.51*		▲	1.116
Trisomy 13	0.97	1.06	1.12	1.18	3.27	3.51	▲	1.074
Trisomy 18	2.91	1.85	2.04	3.97	3.67	3.07	▲	1.034
Down syndrome, all ages (include age unknown)	19.80	18.87	17.54	23.29	22.02	20.17	▲	1.011
<20				17.75	3.20	0.00	▼	0.790
20-24				8.99	6.80	11.75		
25-29				10.10	9.00	3.65		
30-34				19.62	15.38	17.38		
35-39				46.14	49.91	38.46		
40-44				172.03	159.51	139.66		
45+				1029.41*	576.92	0.00		

* = data include less than eight and five years

Ireland: Dublin

Time trends 1980-2001 (Birth prevalence rates per 10,000)

Note: L+S rates, 3-year moving average trend



Note: L+S rates, 3-year moving average trend

Israel: IBDMS

Israel Birth Defects Monitoring System

History:
The Programme started in one hospital in 1966 and was a founding member of the Clearinghouse. It was a full member until 1986, when it became an associate member.

Size and coverage:
Reports are now obtained from three hospitals located in the central region of the country, with more than 20,000 annual births (more than 15% of all births in Israel). Stillbirths of 20 weeks gestation or more and 500 gm or more are included. The registry of termination of pregnancy began in 1995.

Legislation and funding:
The Registry is a research programme supported by research grants without any governmental support.

Sources of ascertainment:
Reporting is voluntary. Reports are obtained from delivery units and neonatal departments in the participating hospitals. The three included hospitals are: Rabin Medical Center, Beilinson Campus' Petah Tikva; Kaplan Hospital, Rehovot (Dr, Kohan Dr, Shinwell) and Lis Medical Center, Tel Aviv (Prof. Mimouni, Prof. Dolberg). These hospitals are affiliated to Sackler School of Medicine, Tel-Aviv University.

Exposure information:
Complete anamneses are obtained by interviews of mothers of all malformed infants. All the other women with normal newborns complete a similar form at discharge.

Background information:
Epidemiological information on all births occurring in the participating hospitals is available.

Address for further information:
Paul Merlob, Department of Neonatology, Rabin Medical Center, Beilinson Campus, 49100 Petah Tikva, Israel:
IBDMS.

Phone: 972-3-9377474/2/3

Fax: 972-3-9220068

E-mail: merlobp@post.tau.ac.il

Israel: IBDMS, 2002

Live births (L)	22886
Stillbirths (S)	231
Total births	23117
Number of terminations of pregnancy (ToP) for birth defects	32

Birth Defects	Number of cases			Rates*10.000		O/E	YB	Remark
	L	S	ToP	L+S	L+S+ToP	L+S		
Anencephaly	2	1	2	1.30	2.16	1.58	14	
Spina bifida	6	0	1	2.60	3.02	0.97	15	
Encephalocele	1	0	0	0.43	0.43	0.88	28	
Microcephaly	10	0	0	4.33	4.32	4.88	3	▲
Arhinencephaly / Holoprosencephaly	0	0	0	0.00	0.00	0.00	18	
Hydrocephaly	10	0	4	4.33	6.05	1.17	28	
Total Anophthalmos / Microphthalmos (include unspecified)	2	0	0	0.87	0.86	1.40	28	
Anophthalmos	2	0	0	0.87	0.86	nc		
Microphthalmos	0	0	0	0.00	0.00	0.00	28	
Total Anotia / Microtia (include unspecified)	3	0	0	1.30	1.30	0.99	28	
Anotia	0	0	0	0.00	0.00	0.00	28	
Microtia	3	0	0	1.30	1.30	1.01	28	
Transposition of great vessels	4	0	5	1.73	3.89	0.49	16	
Tetralogy of Fallot	11	0	1	4.76	5.18	1.80	19	
Hypoplastic left heart syndrome	1	0	2	0.43	1.30	0.21	16	
Coarctation of aorta	5	0	0	2.16	2.16	0.91	16	
Choanal atresia, bilateral	0	0	0	0.00	0.00	0.00	18	
Cleft palate without cleft lip	7	0	0	3.03	3.02	0.63	28	
Cleft lip with or without cleft palate	10	1	1	4.76	5.18	0.93	28	
Oesophageal atresia / stenosis with or without fistula	3	1	0	1.73	1.73	0.74	28	
Small intestine atresia / stenosis	0	0	0	0.00	0.00	0.00	18	
Anorectal atresia / stenosis	1	1	0	0.87	0.86	0.30	28	
Undescended testis (36 weeks of gestation or later)	nr	nr	nr	nc	nc	nc		
Hypospadias	89	0	0	38.50	38.45	1.04	17	
Epispadias	1	0	0	0.43	0.43	3.33	28	
Indeterminate sex	nr	nr	nr	nc	nc	nc		
Renal agenesis	0	0	0	0.00	0.00	0.00	16	
Cystic kidney	8	0	0	3.46	3.46	3.08	26	
Bladder exstrophy	0	0	0	0.00	0.00	0.00	28	
Polydactyly, preaxial	1	0	0	0.43	0.43	0.63	23	
Total Limb reduction defects (include unspecified)	5	0	0	2.16	2.16	2.23	6	
Transverse	2	0	0	0.87	0.86	0.95	20	
Preaxial	2	0	0	0.87	0.86	1.85	20	
Postaxial	1	0	0	0.43	0.43	1.56	20	
Intercalary	0	0	0	0.00	0.00	0.00	20	
Mixed	0	0	0	0.00	0.00	0.00	17	
Diaphragmatic hernia	3	0	1	1.30	1.73	0.64	24	
Total Abdominal wall defects (include unspecified)	2	0	1	0.87	1.30	0.89	17	
Omphalocele	2	0	0	0.87	0.86	1.16	17	
Gastroschisis	0	0	1	0.00	0.43	0.00	24	
Prune belly sequence	1	0	0	0.43	0.43	4.76	25	
Trisomy 13	0	0	0	0.00	0.00	0.00	18	
Trisomy 18	2	0	1	0.87	1.30	1.28	18	
Down syndrome, all ages (include age unknown)	11	0	14	4.76	10.80	0.80	11	
<20	1	0	0	23.42	23.42	nc		
20-24	0	0	0	0.00	0.00	0.00	10	
25-29	2	0	3	2.45	6.12	0.74	11	
30-34	4	0	1	5.80	7.25	1.27	11	
35-39	1	0	7	3.37	26.89	0.29	11	
40-44	1	0	3	15.46	61.54	0.39	11	
45+	2	0	0	434.78	434.78	4.88	11	

nr = not reported
nc = not calculable

Israel: IBDMS, time trend analysis 1974-2002

Birth prevalence rates: (L+S) * 10,000

	1974-81	1982-86	1987-91	1992-96	1997-01	2002	Trend	RR
Births	105,116	89,839	85,221	79,784	107,578	23,117		
Anencephaly	5.14	4.01	1.64	0.63	0.56	1.30	▼	0.915
Spina bifida	3.62	6.12	3.29	2.01	2.70	2.60	▼	0.976
Encephalocele	0.29	0.45	0.94	0.63	0.28	0.43		
Microcephaly					0.89*	4.33	nc	
Arhinencephaly / Holoprosencephaly		0.19*	0.23	0.38	0.00	0.00		
Hydrocephaly	3.62	3.78	2.58	4.01	4.37	4.33		
Total Anophthalmos / Microphthalmos (include unspecified)	0.67	0.00	0.82	0.38	1.12	0.87		
Anophthalmos	0.00	0.00	0.00	0.00	0.00	0.87	▲	1.210
Microphthalmos	0.67	0.00	0.82	0.38	1.12	0.00		
Total Anotia / Microtia (include unspecified)	0.67	1.22	1.53	2.76	0.74	1.30		
Anotia	0.00	0.00	0.00	0.13	0.00	0.00		
Microtia	0.67	1.22	1.53	2.63	0.74	1.30		
Transposition of great vessels		1.14*	3.64	3.38	4.00	1.73		
Tetralogy of Fallot	0.81*	0.78	3.52	3.38	2.70	4.76	▲	1.051
Hypoplastic left heart syndrome		1.71*	2.11	2.76	1.49	0.43		
Coarctation of aorta	0.00*	0.45	2.23	2.51	2.79	2.16	▲	1.076
Choanal atresia, bilateral		0.37*	0.12	0.25	0.28	0.00		
Cleft palate without cleft lip	4.09	4.79	5.52	4.89	4.83	3.03		
Cleft lip with or without cleft palate	4.76	5.34	6.34	3.38	5.48	4.76		
Oesophageal atresia / stenosis with or without fistula	1.81	1.56	3.05	3.89	1.86	1.73		
Small intestine atresia / stenosis		1.12*	1.17	1.25	0.65	0.00		
Anorectal atresia / stenosis	2.09	3.23	3.87	3.89	1.67	0.87		
Undescended testis (36 weeks of gestation or later)								
Hypospadias	28.54	27.16	37.55	39.73	36.90	38.50	▲	1.015
Epispadias	0.10	0.11	0.00	0.25	0.19	0.43		
Indeterminate sex					0.00*		nc	
Renal agenesis		0.57*	0.82	0.63	0.46	0.00		
Cystic kidney	0.57	0.89	1.41	0.88	1.67	3.46	▲	1.050
Bladder exstrophy	0.19	0.22	0.82	0.25	0.28	0.00		
Polydactyly, preaxial	0.29	0.56	0.47	0.75	1.12	0.43		
Total Limb reduction defects (include unspecified)	3.33	2.89	2.70	3.01	0.93	2.16	▼	0.966
Transverse		0.78	1.64	1.00	0.37	0.87		
Preaxial		0.67	0.47	0.38	0.37	0.87		
Postaxial		0.33	0.12	0.75	0.00	0.43		
Intercalary		0.45	0.12	0.25	0.19	0.00		
Mixed		0.67	0.35	0.63	0.00	0.00	▼	0.903
Diaphragmatic hernia	2.03*	2.67	2.11	2.13	1.39	1.30		
Total Abdominal wall defects (include unspecified)	2.09	2.78	1.06	0.75	0.74	0.87	▼	0.948
Omphalocele	2.00	2.00	0.94	0.75	0.56	0.87	▼	0.946
Gastroschisis	0.14*	0.78	0.12	0.00	0.19	0.00		
Prune belly sequence	0.38	0.11	0.12	0.00	0.00	0.43		
Trisomy 13		0.56*	0.47	0.25	0.37	0.00		
Trisomy 18		0.56*	0.59	1.00	0.56	0.87		
Down syndrome, all ages (include age unknown)	10.27	12.02	10.44	5.77	5.76	4.76	▼	0.968
<20			0.00*	0.00	0.00	23.42		
20-24			0.00*	0.63	3.16	0.00		
25-29			0.00*	3.19	3.88	2.45		
30-34			9.62*	4.38	3.97	5.80		
35-39			24.73*	13.85	7.90	3.37	▼	0.885
40-44			60.98*	29.85	44.62	15.46		
45+			0.00*	95.54	87.46	434.78		

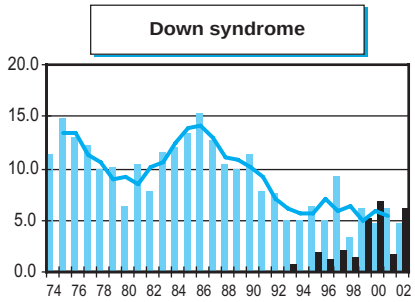
* = data include less than eight nad five years

Israel: IBDMS

'Time trends 1974-2002 (Birth prevalence rates per 10,000)

Note: L+S rates, ToP rates — 3-year moving average trend

Note: L+S rates, ToP rates — 3-year moving average trend



Note: L+S rates, ToP rates 3-year moving average trend

Italy: BDRCam
Birth Defects Registry of Campania

History:
The Registry started in 1991and became a full member of the ICBDMS in 1996.

Size and coverage:
The Registry is based on reporting from hospitals distributed in Campania, a region in southern Italy. Naples is the main city. Initially 38 hospitals reported and the annual number of births was 38.000. Until 2001 the registry is hospital-based covering approximately 50.000 annual births. Actually beginning from 2002, the registry is population based covering approximately 100% of all births. Stillbirths and induced abortions are included. In 2002 is started officially a link with birth regional registry.

Legislation and funding:
The Registry is a surveillance programme supported by grants from Regional Health Authorities. Participation was voluntary up to 1995. From 1996 participation is mandatory.

Sources of ascertainment:
Reports are obtained from delivery units and pediatric clinics at the participating hospitals. For selected malformations multiple sources are used with follow-up to one year using specific records from pediatric specialties departments dealing with malformed infants.

Exposure information:
For each malformed infant reported, information is given on certain exposures, including maternal drug usage and parental occupation. Beginning from 2002 informations on controls are available but only partially on induced abortions.

Background information:
Always from 2002 background information is given on certain exposures, including maternal drug usage and parental occupation. Informations on controls are available.

Address for further information:
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Phone: +39- 0824-57374

Fax: + 39-0824-57495

E-mail: giorecam@tin.it

Gioacchino Scarano, Osservatorio Epidemiologico Regionale,Assessorato alla Sanità - Regione Campania, Centro Direzionale isola C3, Naples, Italy

Fax : +39-081-7969347

Italy: BDRCam, 2002

Live births (L)	62577
Stillbirths (S)	131
Total births	62708
Number of terminations of pregnancy (ToP) for birth defects	179

Birth Defects	Number of cases			Rates*10.000		O/E	YB	Remark
	L	S	ToP	L+S	L+S+ToP	L+S		
Anencephaly	1	0	16	0.16	2.70	0.24	11	
Spina bifida	6	0	7	0.96	2.07	0.45	11	
Encephalocele	1	0	6	0.16	1.11	0.35	11	
Microcephaly	2	0	1	0.32	0.48	0.35	11	
Arhinencephaly / Holoprosencephaly	1	0	3	0.16	0.64	0.38	11	
Hydrocephaly	4	0	21	0.64	3.98	0.23	11	▼
Total Anophthalmos / Microphthalmos (include unspecified)	4	0	3	0.64	1.11	1.06	11	
Anophthalmos	1	0	1	0.16	0.32	0.94	6	
Microphthalmos	3	0	2	0.48	0.80	1.99	11	
Total Anotia / Microtia (include unspecified)	4	0	2	0.64	0.95	0.57	11	
Anotia	2	0	2	0.32	0.64	0.59	11	
Microtia	2	0	0	0.32	0.32	0.55	11	
Transposition of great vessels	5	0	0	0.80	0.80	0.46	11	
Tetralogy of Fallot	8	0	2	1.28	1.59	0.52	11	
Hypoplastic left heart syndrome	4	0	8	0.64	1.91	0.64	11	
Coarctation of aorta	3	0	2	0.48	0.80	0.29	11	
Choanal atresia, bilateral	1	0	0	0.16	0.16	0.79	11	
Cleft palate without cleft lip	20	0	2	3.19	3.50	0.69	11	
Cleft lip with or without cleft palate	29	0	3	4.62	5.09	0.72	11	
Oesophageal atresia / stenosis with or without fistula	8	0	1	1.28	1.43	0.62	11	
Small intestine atresia / stenosis	7	0	0	1.12	1.11	0.58	11	
Anorectal atresia / stenosis	12	0	4	1.91	2.54	0.67	11	
Undescended testis (36 weeks of gestation or later)	nr	nr	nr	nc	nc	nc		
Hypospadias**	47	0	0	7.50	7.47	2.05	11	▲
Epispadias	2	0	0	0.32	0.32	1.59	11	
Indeterminate sex	2	0	2	0.32	0.64	0.66	11	
Renal agenesis	11	0	6	1.75	2.70	0.81	8	
Cystic kidney	1	0	11	0.16	1.91	0.10	11	▼
Bladder exstrophy	0	0	0	0.00	0.00	0.00	11	
Polydactyly, preaxial	2	0	0	0.32	0.32	0.18	11	▼
Total Limb reduction defects (include unspecified)	24	1	4	3.99	4.61	0.90	11	
Transverse	15	0	2	2.39	2.70	0.81	11	
Preaxial	1	1	2	0.32	0.64	0.47	11	
Postaxial	5	0	0	0.80	0.80	2.49	11	
Intercalary	2	0	0	0.32	0.32	0.84	11	
Mixed	1	0	0	0.16	0.16	1.59	11	
Diaphragmatic hernia	10	0	2	1.59	1.91	0.72	8	
Total Abdominal wall defects (include unspecified)	4	1	10	0.80	2.39	0.63	11	
Omphalocele	3	0	9	0.48	1.91	0.51	11	
Gastroschisis	1	1	1	0.32	0.48	1.00	11	
Prune belly sequence	0	0	0	0.00	0.00	0.00	5	
Trisomy 13	2	0	2	0.32	0.64	1.35	9	
Trisomy 18	1	0	4	0.16	0.80	0.33	11	
Down syndrome, all ages (include age unknown)	34	0	35	5.42	10.97	0.86	5	
<20	2	0	0	12.26	12.26	3.70	11	
20-24	2	0	0	1.99	1.99	0.49	9	
25-29	8	0	5	4.24	6.89	1.12	8	
30-34	6	0	6	2.97	5.94	0.60	5	
35-39	12	0	12	12.11	24.19	0.92	7	
40-44	2	0	9	10.29	56.32	0.22	11	
45+	0	0	0	0.00	0.00	0.00	11	

** EXCLUDED GLANDULAR

Italy: BDRCam, time trend analysis 1991-2002

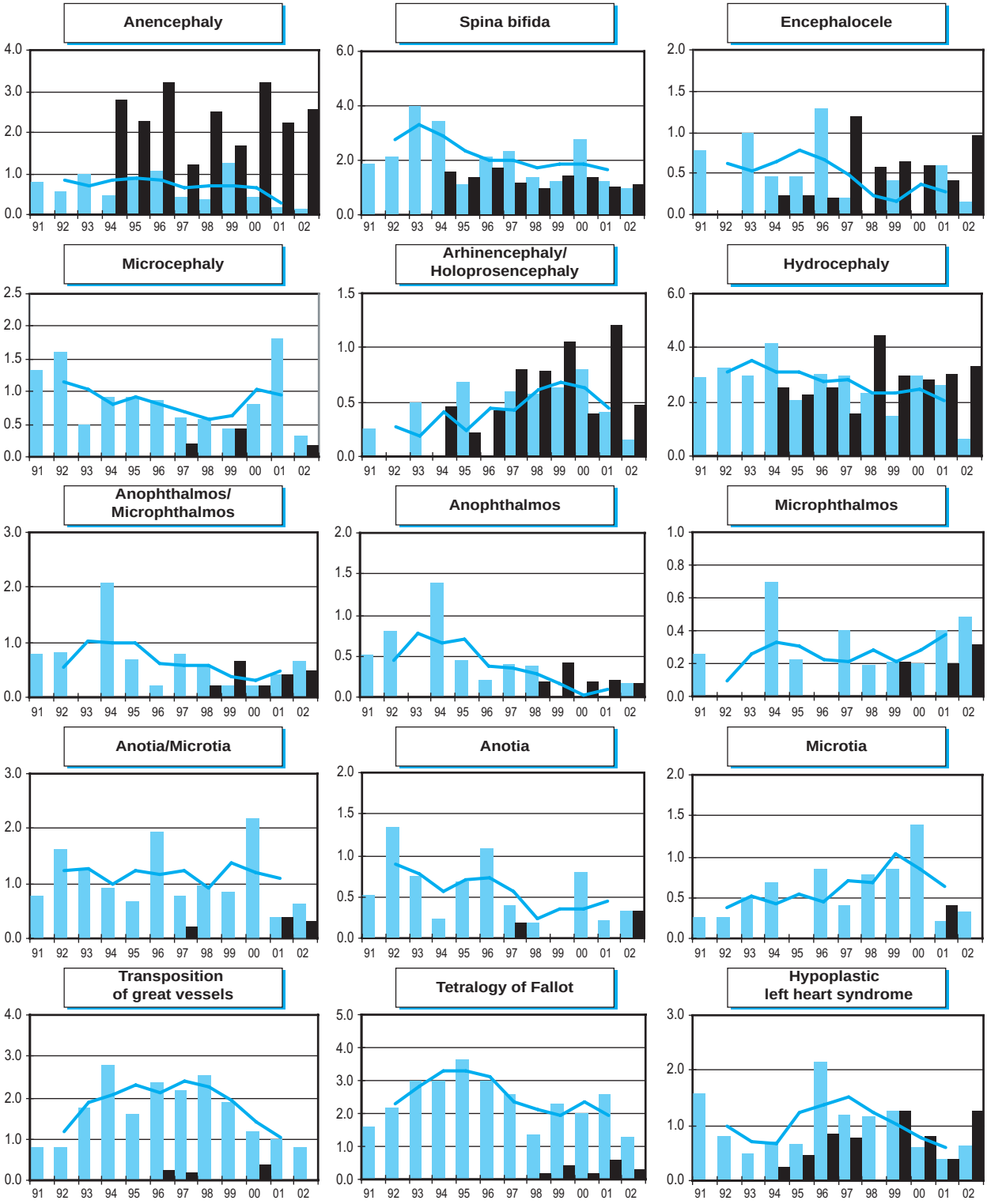
Birth prevalence rates: (L+S) * 10,000

	1974-81	1982-86	1987-91*	1992-96	1997-01	2002	Trend	RR
Births			37,978	211,162	249,308	62,708		
Anencephaly			0.79	0.81	0.52	0.16		
Spina bifida			1.84	2.56	1.80	0.96	▼	0.935
Encephalocele			0.79	0.66	0.24	0.16		
Microcephaly			1.32	0.95	0.84	0.32		
Arhinencephaly / Holoprosencephaly			0.26	0.24	0.60	0.16		
Hydrocephaly			2.90	3.08	2.49	0.64	▼	0.938
Total Anophthalmos / Microphthalmos (include unspecified)			0.79	0.76	0.44	0.64		
Anophthalmos			0.53	0.57	0.16	0.16	▼	0.832
Microphthalmos			0.26	0.19	0.28	0.48		
Total Anotia / Microtia (include unspecified)			0.79	1.28	1.04	0.64		
Anotia			0.53	0.81	0.32	0.32		
Microtia			0.26	0.47	0.72	0.32		
Transposition of great vessels			0.79	1.89	1.76	0.80		
Tetralogy of Fallot			1.58	2.98	2.17	1.28		
Hypoplastic left heart syndrome			1.58	0.99	0.92	0.64		
Coarctation of aorta			1.05	1.75	1.60	0.48		
Choanal atresia, bilateral			0.00	0.24	0.20	0.16		
Cleft palate without cleft lip			5.00	4.36	4.73	3.19		
Cleft lip with or without cleft palate			5.79	6.82	6.26	4.62		
Oesophageal atresia / stenosis with or without fistula			1.58	2.37	1.85	1.28		
Small intestine atresia / stenosis			2.37	2.08	1.72	1.12		
Anorectal atresia / stenosis			2.63	2.65	3.05	1.91		
Undescended testis (36 weeks of gestation or later)								
Hypospadias			3.95	3.36	3.85	7.50	▲	1.070
Epispadias			0.00	0.33	0.12	0.32		
Indeterminate sex			0.26	0.38	0.60	0.32		
Renal agenesis			1.32	1.47	2.37	1.75	▲	1.073
Cystic kidney			0.53	1.56	1.93	0.16		
Bladder exstrophy			0.26	0.33	0.12	0.00		
Polydactyly, preaxial			2.11	1.80	1.64	0.32		
Total Limb reduction defects (include unspecified)			5.79	4.74	4.01	3.99		
Transverse			4.21	3.27	2.53	2.39	▼	0.955
Preaxial			1.05	0.62	0.68	0.32		
Postaxial			0.26	0.28	0.36	0.80		
Intercalary			0.00	0.43	0.40	0.32		
Mixed			0.26	0.14	0.04	0.16		
Diaphragmatic hernia			1.58	1.75	2.29	1.59		
Total Abdominal wall defects (include unspecified)			1.05	1.42	1.16	0.80		
Omphalocele			0.79	1.14	0.80	0.48	▼	0.921
Gastroschisis			0.26	0.28	0.36	0.32		
Prune belly sequence			0.00	0.21*	0.07*	0.00		
Trisomy 13			1.05	0.47	0.12	0.32	▼	0.836
Trisomy 18			0.26	0.62	0.40	0.16		
Down syndrome, all ages (include age unknown)			9.48	9.90	6.34	5.42	▼	0.933
<20			6.63	3.53	2.51	12.26		
20-24			7.07	5.66	2.79	1.99	▼	0.894
25-29			8.80	6.07	3.13	4.24	▼	0.909
30-34			11.96	10.06	4.98	2.97	▼	0.872
35-39			34.75	25.09	10.83	12.11	▼	0.877
40-44			55.87	56.98	39.33	10.29		
45+			0.00	58.82	0.00	0.00		

* = data include less than five years

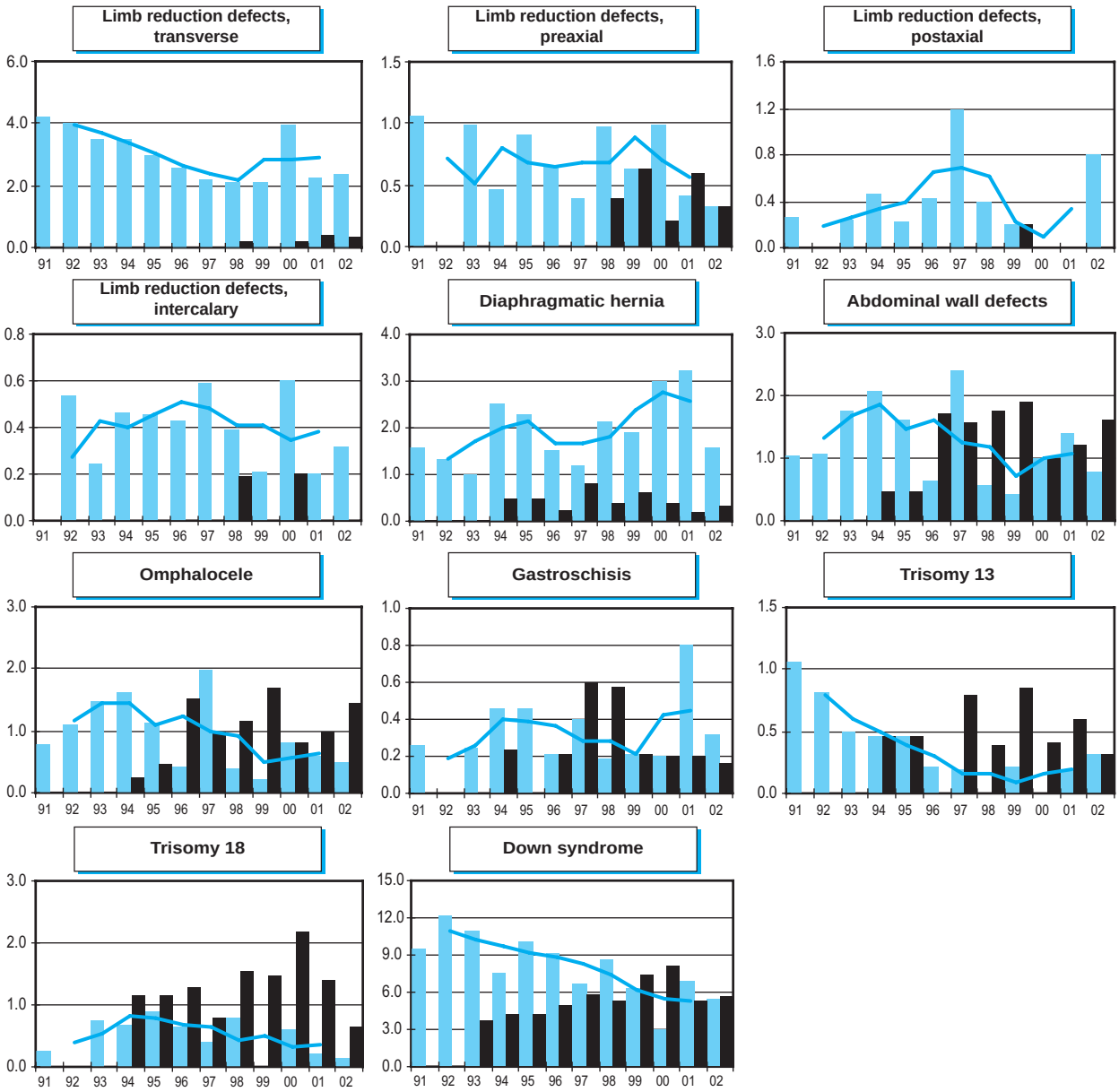
Italy: BDRCam

'Time trends 1991-2002 (Birth prevalence rates per 10,000)



Note: L+S rates, ToP rates — 3-year moving average trend

Note: L+S rates, ToP rates — 3-year moving average trend



Note: L+S rates, ToP rates 3-year moving average trend

Italy: IMER
Emilia-Romagna Registry of Congenital Malformations

History:
The registry started in 1978 in 4 hospitals and has increased in size to include now 39 delivery units. The Programme joined the ICBDMS in 1985 as an associate member.

Size and coverage:
The Programme is population-based (about 95% of all births in the Emilia-Romagna region) and covers approximately 28,000 annual births. Stillbirths of 28 weeks of gestation are included.

Legislation and funding:
The Programme is recognised and financed by the Health Authorities, the National Research Council, and the Regional Health Council. Hospital participation is voluntary.

Sources of ascertainment:
Reporting is made by neonatologists and pediatricians during the first week of the infant's life. Selected malformations are followed up.

Exposure information:
Detailed exposure information is obtained by interviews of the mothers of malformed infants.

Background information:
Some general demographic information is known for all births in the area. For each participating hospital, the number of livebirths and stillbirths are known.

Address for further information:
Guido Cocchi, Istituto Clinico di Pediatria Preventiva e Neonatologia, Università di Bologna, Via Massarenti 11, 40138 Bologna, Italy.

Phone: 39-051-342754 / 6363654

Fax: 39-051-342754

E-mail: cocchi@med.unibo.it

Italy: IMER, 2002

Live births (L)	25919
Stillbirths (S)	91
Total births	26010
Number of terminations of pregnancy (ToP) for birth defects	85

Birth Defects	Number of cases			Rates*10.000		O/E	YB	Remark
	L	S	ToP	L+S	L+S+ToP	L+S		
Anencephaly	0	1	2	0.38	1.15	0.68	19	
Spina bifida	2	0	5	0.77	2.68	0.42	9	
Encephalocele	0	0	1	0.00	0.38	0.00	24	
Microcephaly	5	0	0	1.92	1.92	1.79	12	
Arhinencephaly / Holoprosencephaly	2	1	2	1.15	1.92	2.29	20	
Hydrocephaly	8	0	5	3.08	4.98	1.24	11	
Total Anophthalmos / Microphthalmos (include unspecified)	2	0	0	0.77	0.77	0.93	24	
Anophthalmos	1	0	0	0.38	0.38	2.00	24	
Microphthalmos	1	0	0	0.38	0.38	0.60	24	
Total Anotia / Microtia (include unspecified)	2	0	0	0.77	0.77	0.57	24	
Anotia	1	0	0	0.38	0.38	0.70	8	
Microtia	1	0	0	0.38	0.38	0.64	8	
Transposition of great vessels	11	0	1	4.23	4.60	1.03	7	
Tetralogy of Fallot	10	0	2	3.84	4.60	2.07	21	
Hypoplastic left heart syndrome	4	0	3	1.54	2.68	0.96	24	
Coarctation of aorta	4	0	1	1.54	1.92	0.66	22	
Choanal atresia, bilateral	2	0	0	0.77	0.77	3.33	24	
Cleft palate without cleft lip	10	0	0	3.84	3.83	0.75	24	
Cleft lip with or without cleft palate	11	1	3	4.61	5.75	0.75	17	
Oesophageal atresia / stenosis with or without fistula	8	0	0	3.08	3.07	0.86	24	
Small intestine atresia / stenosis	8	0	0	3.08	3.07	1.04	24	
Anorectal atresia / stenosis	6	0	3	2.31	3.45	0.84	24	
Undescended testis (36 weeks of gestation or later)	nr	nr	nr	nc	nc	nc		
Hypospadias	39	0	0	14.99	14.95	0.81	22	
Epispadias	0	0	0	0.00	0.00	nc		
Indeterminate sex	1	0	0	0.38	0.38	1.67	7	
Renal agenesis	8	0	2	3.08	3.83	1.79	24	
Cystic kidney	6	0	3	2.31	3.45	1.00	8	
Bladder exstrophy	1	0	0	0.38	0.38	1.10	24	
Polydactyly, preaxial	4	0	1	1.54	1.92	0.43	9	
Total Limb reduction defects (include unspecified)	4	0	1	1.54	1.92	0.37	11	
Transverse	2	0	0	0.77	0.77	0.43	10	
Preaxial	0	0	0	0.00	0.00	0.00	17	
Postaxial	1	0	0	0.38	0.38	0.76	17	
Intercalary	1	0	0	0.38	0.38	0.66	17	
Mixed	0	0	1	0.00	0.38	0.00	17	
Diaphragmatic hernia	4	0	2	1.54	2.30	0.60	20	
Total Abdominal wall defects (include unspecified)	0	0	4	0.00	1.53	0.00	9	
Omphalocele	0	0	3	0.00	1.15	0.00	24	
Gastroschisis	0	0	1	0.00	0.38	0.00	24	
Prune belly sequence	0	0	1	0.00	0.38	0.00	24	
Trisomy 13	2	0	4	0.77	2.30	2.02	15	
Trisomy 18	1	0	4	0.38	1.92	0.46	24	
Down syndrome, all ages (include age unknown)	17	0	22	6.54	14.95	0.77	10	
<20	1	0	0	25.64	25.64	5.56	17	
20-24	2	0	0	7.77	7.77	1.37	17	
25-29	0	0	1	0.00	1.42	0.00	12	
30-34	9	0	1	9.25	10.28	1.06	11	
35-39	1	0	7	1.88	15.06	0.15	12	
40-44	3	0	6	32.05	95.54	0.69	17	
45+	0	0	1	0.00	370.37	0.00	17	

Italy: IMER, time trend analysis 1978-2002

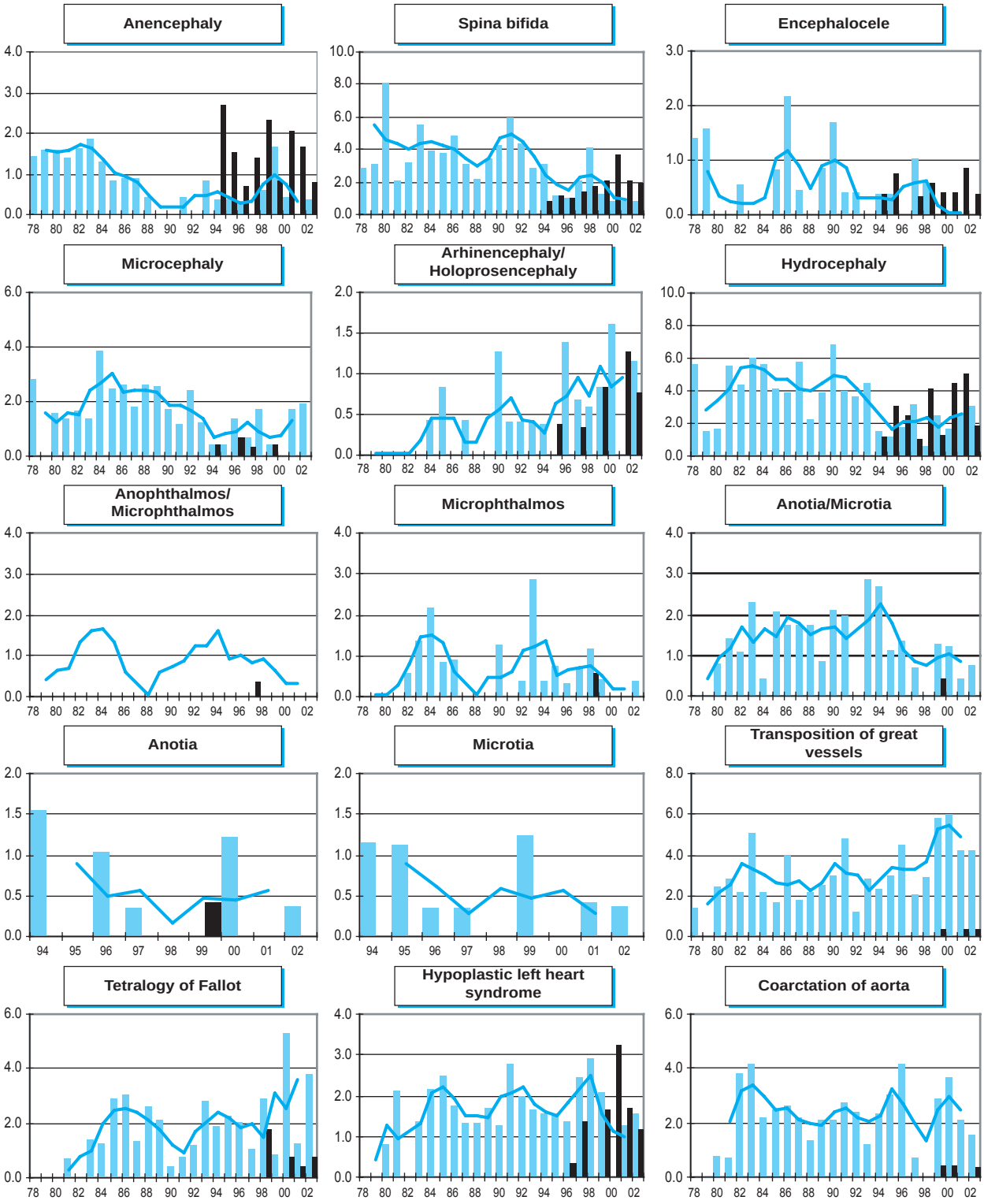
Birth prevalence rates: (L+S) * 10,000

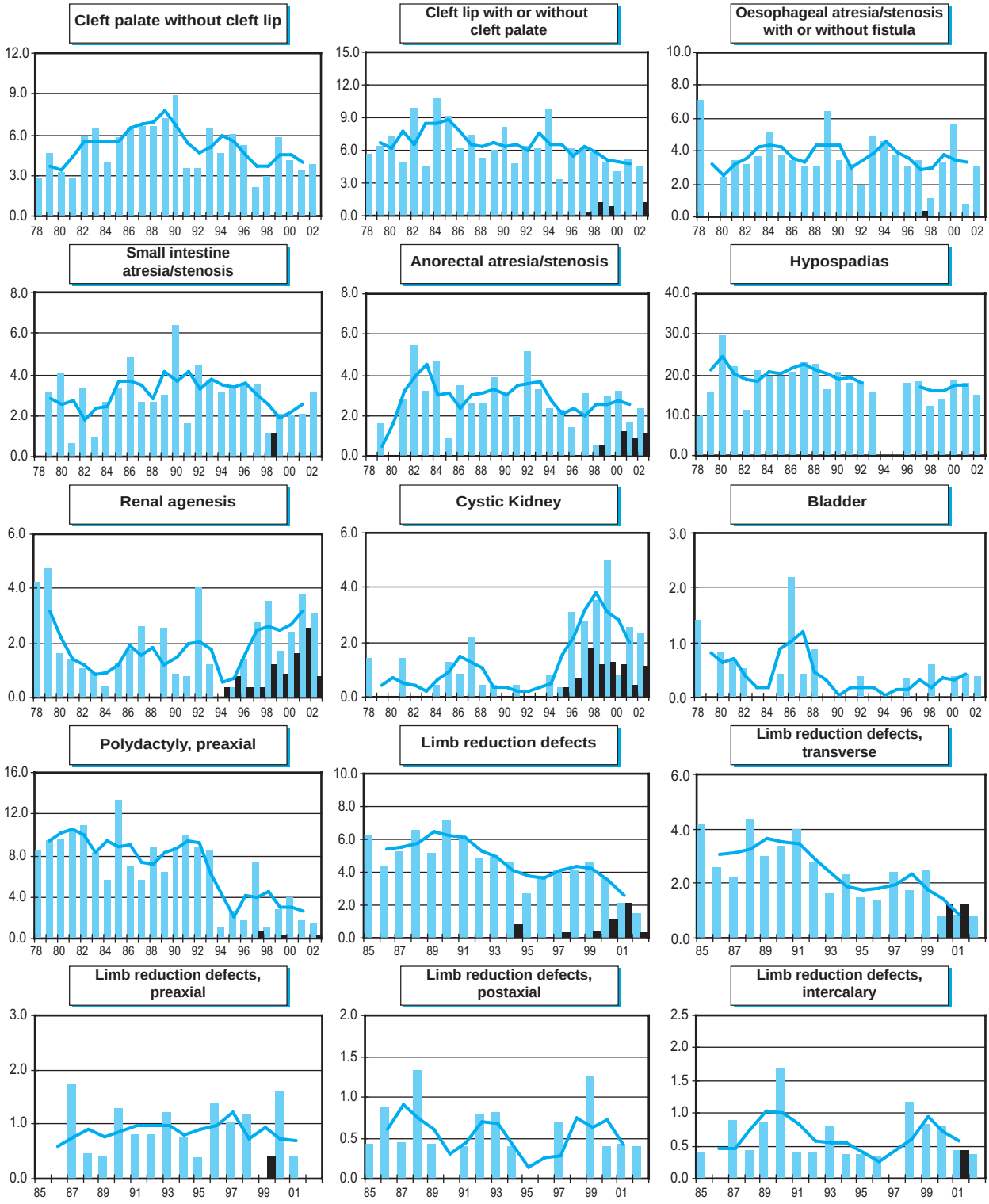
	1974-81*	1982-86	1987-91	1992-96	1997-01	2002	Trend	RR
Births	40,200	110,168	117,589	130,693	118,338	26,010		
Anencephaly	1.49	1.27	0.34	0.38	0.51	0.38	▼	0.927
Spina bifida	4.23	4.27	3.83	2.45	1.69	0.77	▼	0.945
Encephalocele	0.50	0.73	0.68	0.23	0.34	0.00		
Microcephaly	1.49	2.45	1.96	1.15	0.85	1.92	▼	0.959
Arhinencephaly / Holoprosencephaly	0.00	0.27	0.43	0.54	0.76	1.15	▲	1.085
Hydrocephaly	3.73	4.81	4.51	2.45	2.20	3.08	▼	0.959
Total Anophthalmos / Microphthalmos (include unspecified)	0.75	1.27	0.43	1.15	0.51	0.77		
Anophthalmos	0.75	0.09	0.17	0.23	0.08	0.38		
Microphthalmos	0.00	1.18	0.26	0.92	0.42	0.38		
Total Anotia / Microtia (include unspecified)	0.75	1.54	1.70	1.61	0.76	0.77		
Anotia				0.86*	0.34	0.38		
Microtia				0.86*	0.42	0.38		
Transposition of great vessels	1.99	3.00	2.89	2.83	4.23	4.23	▲	1.034
Tetralogy of Fallot	0.37	1.82	1.45	2.07	2.20	3.84	▲	1.043
Hypoplastic left heart syndrome	1.00	1.63	1.70	1.61	1.69	1.54		
Coarctation of aorta	0.75	3.00	2.13	2.68	1.94	1.54		
Choanal atresia, bilateral	0.00	0.18	0.43	0.15	0.25	0.77		
Cleft palate without cleft lip	3.23	5.72	6.55	5.20	3.63	3.84		
Cleft lip with or without cleft palate	5.97	8.08	6.29	6.35	5.24	4.61	▼	0.980
Oesophageal atresia / stenosis with or without fistula	3.23	3.90	3.83	3.67	3.04	3.08		
Small intestine atresia / stenosis	1.99	3.00	3.23	3.60	2.28	3.08		
Anorectal atresia / stenosis	1.24	3.45	2.81	2.83	2.45	2.31		
Undescended testis (36 weeks of gestation or later)								
Hypospadias	21.39	18.79	20.07	17.21*	16.56	14.99	▼	0.989
Epispadias				0.00*	0.00	0.00		
Indeterminate sex				0.00*	0.34	0.38		
Renal agenesis	2.49	1.09	1.36	1.38	2.79	3.08		
Cystic kidney	0.75	0.54	0.68	0.92	2.87	2.31	▲	1.094
Bladder exstrophy	0.75	0.64	0.26	0.15	0.25	0.38		
Polydactyly, preaxial	9.70	8.99	7.99	4.44	3.72	1.54	▼	0.940
Total Limb reduction defects (include unspecified)		5.33*	6.04	4.13	3.72	1.54	▼	0.954
Transverse		3.41*	3.40	1.91	1.69	0.77	▼	0.933
Preaxial		0.00*	0.94	0.92	0.85	0.00		
Postaxial		0.64*	0.51	0.38	0.59	0.38		
Intercalary		0.21*	0.85	0.46	0.59	0.38		
Mixed		0.43*	0.34	0.31	0.00	0.00		
Diaphragmatic hernia	0.75	1.72	2.38	3.44	2.62	1.54	▲	1.032
Total Abdominal wall defects (include unspecified)	2.99	3.09	3.57	2.60	1.69	0.00	▼	0.960
Omphalocele	1.74	1.82	1.70	1.76	0.93	0.00	▼	0.961
Gastroschisis	0.75	0.91	0.77	0.77	0.76	0.00		
Prune belly sequence	0.50	0.36	0.34	0.15	0.08	0.00		
Trisomy 13	1.49	1.36	0.51	0.38	0.25	0.77	▼	0.916
Trisomy 18	0.50	1.27	1.02	0.54	0.68	0.38		
Down syndrome, all ages (include age unknown)	16.92	12.80	12.33	9.26	7.69	6.54	▼	0.962
<20		2.90*	3.65	4.10	14.09	25.64	▲	1.173
20-24		5.25*	5.17	4.37	8.90	7.77		
25-29		12.46*	9.07	6.48	3.94	0.00	▼	0.920
30-34		11.64*	17.70	8.92	7.49	9.25	▼	0.949
35-39		38.51*	23.43	17.15	8.16	1.88	▼	0.878
40-44		49.14*	68.03	41.45	35.57	32.05		
45+		133.33*	0.00	160.00	67.57	0.00		

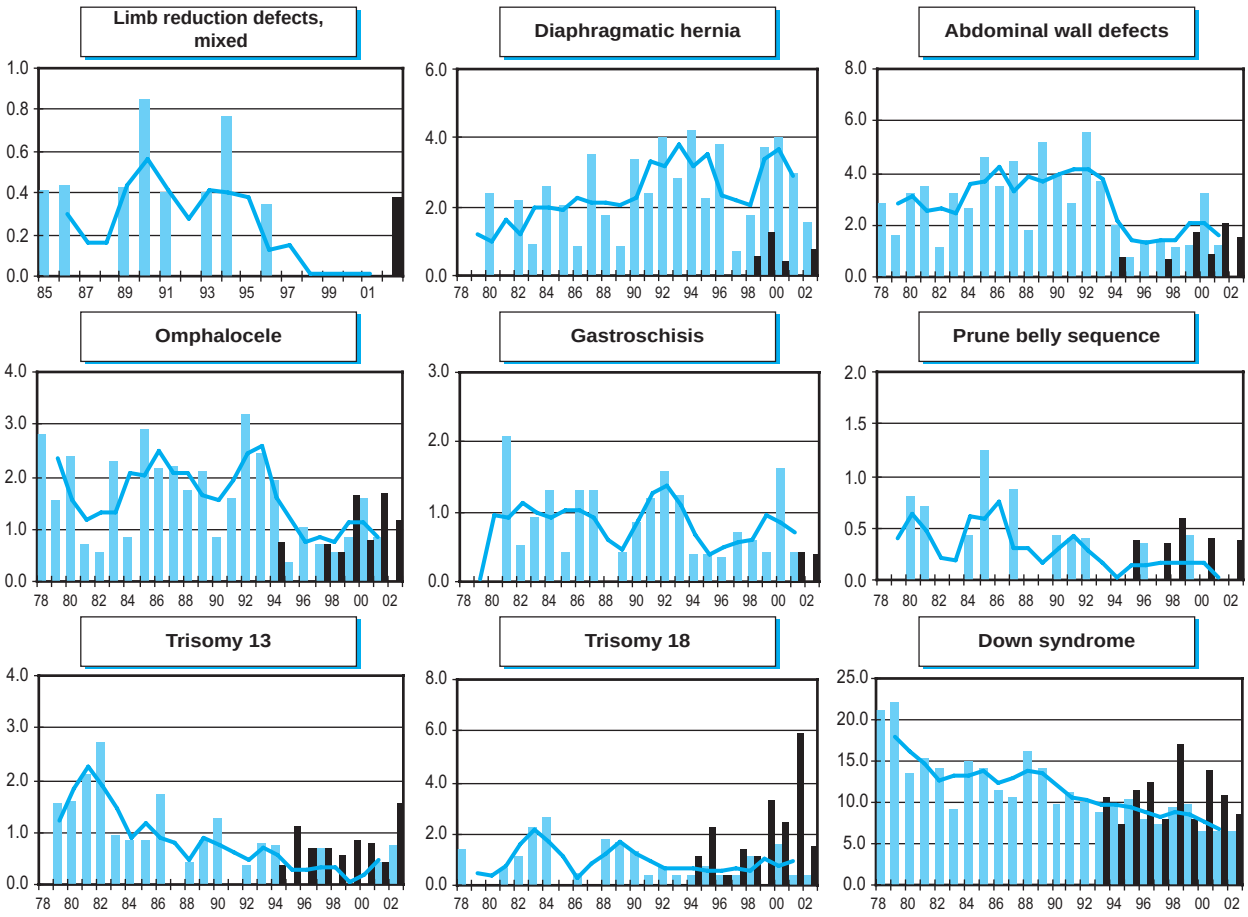
* = data include less than eight and five years

Italy: IMER

Time trends 1978-2001 (Birth prevalence rates per 10,000)




Cleft palate without cleft lip
Cleft lip with or without cleft palate
Oesophageal atresia/stenosis with or without fistula
Small intestine atresia/stenosis
Anorectal atresia/stenosis
Hypospadias
Renal agenesis
Cystic Kidney
Bladder
Polydactyly, preaxial
Limb reduction defects
Limb reduction defects, transverse
Limb reduction defects, preaxial
Limb reduction defects, postaxial
Limb reduction defects, intercalary
Note: L+S rates, ToP rates 3-year moving average trend



Note: L+S rates, ToP rates — 3-year moving average trend

Italy: ISMAC
Sicilian Registry of Congenital Malformations

History:
The Registry started in 1991 and became an ICB-DMS associate member in 1996. Sicilian Registry is also member of EUROCAT and collaborates with other Italian Registries under supervision of Italian National Institute of Health Rome.

Size and coverage:
It is hospital based and actually collaborates with four southeast provinces of the nine Sicilian provinces, (with a covering rate higher than 75%) and with more than 19,000 controlled newborns by year.

Legislation and funding:
The Programme is on a voluntary basis, supported at local level by A.S.MA.C, Sicilian association for congenital malformations prevention.

Sources of ascertainment:
Reports are obtained from delivery units, pediatric units and other specialistic departments.

Exposure information:
For each malformed reported (livebirth, stillbirth and voluntary abortion), information is given on certain exposures, including maternal drug usage and parental occupation. Up to now no information on controls is available.

Address for further information:
Sebastiano Bianca, Dipartimento di Pediatria, via S. Sofia, 78 – 95123 Catania, Italy

Fax: 39-095-222532

E-mail:sebastiano.bianca@tiscali.it

Italy: ISMAC, 2002

Live births (L)	16073
Stillbirths (S)	nr
Total births	16073
Number of terminations of pregnancy (ToP) for birth defects	nr

Birth Defects	Number of cases			Rates*10.000		O/E	YB	Remark
	L	S	ToP	L+S	L+S+ToP	L+S		
Anencephaly	1	nr	nr	0.62	nc	1.12	10	
Spina bifida	7	nr	nr	4.36	nc	1.52	10	
Encephalocele	2	nr	nr	1.24	nc	5.00	11	
Microcephaly	2	nr	nr	1.24	nc	0.86	11	
Arhinencephaly / Holoprosencephaly	1	nr	nr	0.62	nc	1.79	11	
Hydrocephaly	4	nr	nr	2.49	nc	0.80	11	
Total Anophthalmos / Microphthalmos (include unspecified)	5	nr	nr	3.11	nc	7.81	11	▲
Anophthalmos	2	nr	nr	1.24	nc	12.50	11	
Microphthalmos	3	nr	nr	1.87	nc	4.69	11	
Total Anotia / Microtia (include unspecified)	0	nr	nr	0.00	nc	0.00	5	
Anotia	0	nr	nr	0.00	nc	0.00	4	
Microtia	0	nr	nr	0.00	nc	0.00	4	
Transposition of great vessels	2	nr	nr	1.24	nc	0.40	11	
Tetralogy of Fallot	6	nr	nr	3.73	nc	2.48	4	
Hypoplastic left heart syndrome	3	nr	nr	1.87	nc	1.76	9	
Coarctation of aorta	4	nr	nr	2.49	nc	2.76	4	
Choanal atresia, bilateral	6	nr	nr	3.73	nc	13.64	10	▲
Cleft palate without cleft lip	6	nr	nr	3.73	nc	0.75	11	
Cleft lip with or without cleft palate	9	nr	nr	5.60	nc	0.86	11	
Oesophageal atresia / stenosis with or without fistula	1	nr	nr	0.62	nc	0.21	11	
Small intestine atresia / stenosis	8	nr	nr	4.98	nc	2.92	7	
Anorectal atresia / stenosis	5	nr	nr	3.11	nc	1.13	11	
Undescended testis (36 weeks of gestation or later)	35	nr	nr	21.78	nc	0.88	2	
Hypospadias	47	nr	nr	29.24	nc	1.17	3	
Epispadias	1	nr	nr	0.62	nc	1.92	7	
Indeterminate sex	1	nr	nr	0.62	nc	1.25	11	
Renal agenesis	2	nr	nr	1.24	nc	1.00	11	
Cystic kidney	6	nr	nr	3.73	nc	1.38	4	
Bladder exstrophy	1	nr	nr	0.62	nc	1.89	10	
Polydactyly, preaxial	5	nr	nr	3.11	nc	1.20	5	
Total Limb reduction defects (include unspecified)	4	nr	nr	2.49	nc	0.82	11	
Transverse	4	nr	nr	2.49	nc	1.03	4	
Preaxial	0	nr	nr	0.00	nc	nc		
Postaxial	0	nr	nr	0.00	nc	0.00	4	
Intercalary	0	nr	nr	0.00	nc	nc		
Mixed	0	nr	nr	0.00	nc	nc		
Diaphragmatic hernia	7	nr	nr	4.36	nc	2.64	11	
Total Abdominal wall defects (include unspecified)	3	nr	nr	1.87	nc	0.85	11	
Omphalocele	1	nr	nr	0.62	nc	0.44	11	
Gastroschisis	2	nr	nr	1.24	nc	1.56	11	
Prune belly sequence	0	nr	nr	0.00	nc	0.00	10	
Trisomy 13	1	nr	nr	0.62	nc	0.88	8	
Trisomy 18	1	nr	nr	0.62	nc	1.14	11	
Down syndrome, all ages (include age unknown)	14	nr	nr	8.71	nc	0.74	11	
<20	0	nr	nr	nc	nc	nc		
20-24	0	nr	nr	nc	nc	nc		
25-29	1	nr	nr	nc	nc	nc		
30-34	2	nr	nr	nc	nc	nc		
35-39	3	nr	nr	nc	nc	nc		
40-44	0	nr	nr	nc	nc	nc		
45+	1	nr	nr	nc	nc	nc		

Italy: ISMAC, time trend analysis 1991-2002

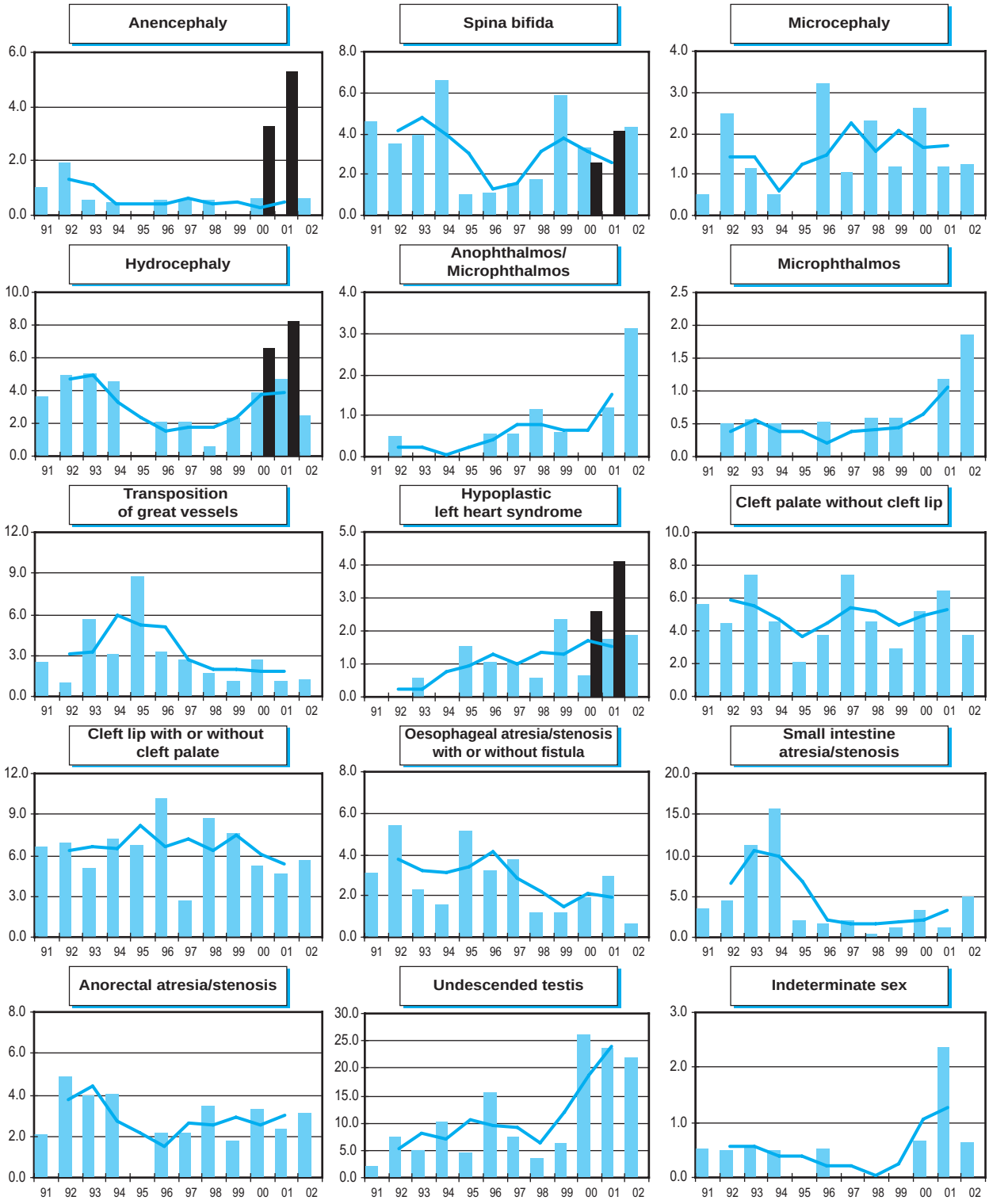
Birth prevalence rates: (L+S) * 10,000

	1974-81	1982-86	1987-91*	1992-96	1997-01	2002	Trend	RR
Births			19,430	95,516	85,238	16,073		
Anencephaly			1.03	0.73	0.35	0.62		
Spina bifida			4.63	3.25	2.46	4.36		
Encephalocele			0.00	0.31	0.23	1.24		
Microcephaly			0.51	1.47	1.64	1.24		
Arhinencephaly / Holoprosencephaly			0.00	0.42	0.35	0.62		
Hydrocephaly			3.60	3.35	2.70	2.49		
Total Anophthalmos / Microphthalmos (include unspecified)			0.00	0.21	0.70	3.11	▲	1.307
Anophthalmos			0.00	0.00	0.23	1.24		
Microphthalmos			0.00	0.42	0.47	1.87		
Total Anotia / Microtia (include unspecified)			0.00	0.26*	1.06	0.00		
Anotia					0.60*	0.00		
Microtia					0.45*	0.00		
Transposition of great vessels			2.57	4.29	1.88	1.24		
Tetralogy of Fallot					1.51*	3.73		
Hypoplastic left heart syndrome			0.00	0.63	1.29	1.87	▲	1.196
Coarctation of aorta					0.90*	2.49		
Choanal atresia, bilateral			0.00	0.13*	0.47	3.73		
Cleft palate without cleft lip			5.66	4.40	5.40	3.73		
Cleft lip with or without cleft palate			6.69	7.22	5.75	5.60		
Oesophageal atresia / stenosis with or without fistula			3.09	3.56	2.23	0.62	▼	0.921
Small intestine atresia / stenosis			3.60	7.01	1.64	4.98	▼	0.888
Anorectal atresia / stenosis			2.06	3.04	2.58	3.11		
Undescended testis (36 weeks of gestation or later)			2.06	8.58	13.02	21.78	▲	1.165
Hypospadias				17.62*	19.94	29.24		
Epispadias			0.00	0.00*	0.47	0.62		
Indeterminate sex			0.51	0.42	0.59	0.62		
Renal agenesis			0.00	1.78	0.94	1.24		
Cystic kidney			0.51	0.94	2.23	3.73	▲	1.222
Bladder exstrophy			0.51	0.00*	0.59	0.62		
Polydactyly, preaxial			0.00	0.26*	2.58	3.11		
Total Limb reduction defects (include unspecified)			6.69	2.41	2.93	2.49		
Transverse					2.41*	2.49		
Preaxial					0.00*	0.00		
Postaxial					0.30*	0.00		
Intercalary					0.00*	0.00		
Mixed					0.00*	0.00		
Diaphragmatic hernia			1.54	1.99	1.29	4.36		
Total Abdominal wall defects (include unspecified)			1.03	2.93	1.64	1.87		
Omphalocele			1.03	1.99	0.82	0.62		
Gastroschisis			0.00	0.94	0.82	1.24		
Prune belly sequence			0.00	0.00*	0.12	0.00		
Trisomy 13			0.00	0.26*	0.94	0.62		
Trisomy 18			0.51	0.63	0.47	0.62		
Down syndrome, all ages (include age unknown)			9.78	12.98	10.79	8.71	▼	0.963
<20								
20-24								
25-29								
30-34								
35-39								
40-44								
45+								

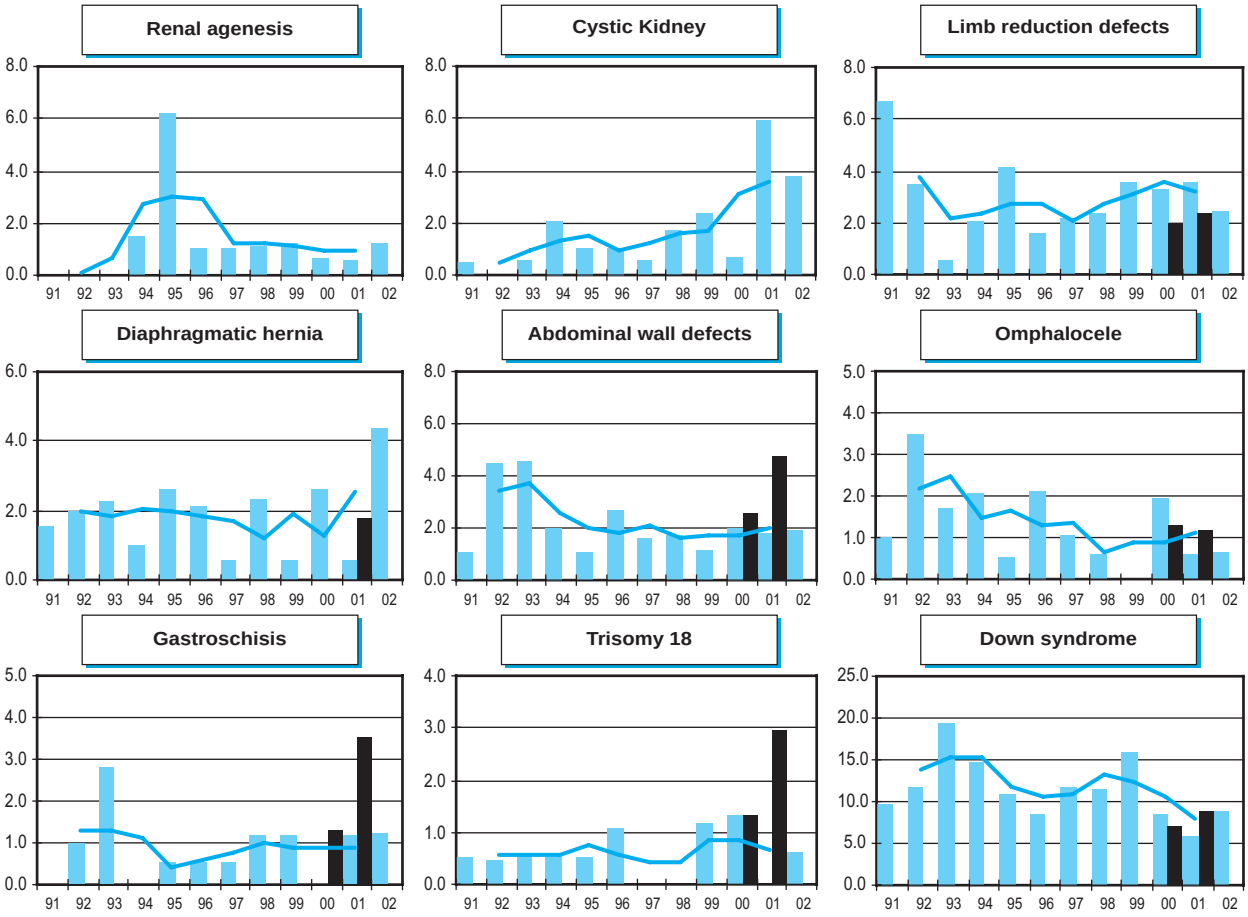
* = data include less than five years

Italy: ISMAC

'Time trends 1991-2002 (Birth prevalence rates per 10,000)



Note: L+S rates, ToP rates — 3-year moving average trend



Note: L+S rates, ToP rates — 3-year moving average trend

Italy: North East

North East Italy Registry of Congenital Malformations

History

The Registry was established in 1981 to include the Veneto and Friuli Venezia Giulia regions. The Trentino Alto Adige region was added in 1990. The Registry became a member of EUROCAT in 1985, and an associate member of the ICBDMS in 1997.

Size and coverage

The registry is population-based II: it includes all mothers delivering within the Veneto, Friuli-Venezia, Giulia and Trentino-Alto Adige Regions, irrespective of place of residence. Reports are obtained from 66 participating hospitals, with a total of approximately 57,000 annual births; the actual coverage is estimated at 99%.

Legislation and funding

Reporting is voluntary. The programme is partly run by privately funded research organisations and partly by Regional Health Authorities. Since 1998 NEI Registry is the Regional Center for the congenital malformations of the Veneto.

Sources of ascertainment

Reports are obtained on specific forms from delivery units, induced abortion units, pediatric, cardiology, ophthalmology and pathology departments, regional induced abortion database and cytogenetic laboratories. Thirty-two selected malformations are recorded within 7 days from birth (within 3 years of age for cardiovascular and ophthalmologic anomalies only). In terminated fetuses all anomalies are recorded. Since 1st January 2000 we are registering all congenital anomalies adopting the EUROCAT list of exclusions (revision 1985).
Up to 1999 we did not register cases of: microcephaly, cystic kidney disease, indeterminate sex, diaphraghmatic hernia, Patau syndrome (Trisomy 13), Edward syndrome (Trisomy 18) and we do not separately code for (not included) cases of: common arterial truncus, transposition of the great vesssels (complete), congenital absence, atresia and/or stenosis of duodenum, congenital absence, atresia and/or stenosis of other specified parts of the small intestine.
Since 2000 we don't register control cases.
In 2003 we have been allowed to use the Regional Hospital Discharge Records of the years 2001 and 2002 to update and to complete the data of the NEI Registry. We adopted a complex procedure before introducing new cases in our Registry, checking directly the Hospital charts when necessary.

Exposure information

Detailed information on various exposures, including maternal or paternal occupation, diseases and drug use is obtained by interview of the mothers at the birth of the malformed infants and their controls.

Background information

Some epidemiological background data of all births are available. For each participating hospital the number of livebirths and stillbirths by sex and number of twin pairs are known.

Address for further information

Prof. Romano Tenconi, Clinical and Epidemiological Genetic Service, Pediatric Department, Via Giustiniani 3, 35128 Padova, Italy

Tel: +39 049 8213513

Fax: +39 049 8211425

E-mail: romano.tenconi@unipd.it

Website: http://www.genetica.pediatria.unipd.it

Italy: North East, 2002

Live births (L)	57339
Stillbirths (S)	156
Total births	57495
Number of terminations of pregnancy (ToP) for birth defects	140

Birth Defects	Number of cases			Rates*10.000		O/E	YB	Remark
	L	S	ToP	L+S	L+S+ToP	L+S		
Anencephaly	0	1	2	0.17	0.52	0.51	13	
Spina bifida	7	0	4	1.22	1.91	0.90	11	
Encephalocele	0	0	2	0.00	0.35	0.00	14	
Microcephaly	6	0	0	1.04	1.04	2.74	2	
Arhinencephaly / Holoprosencephaly	0	1	5	0.17	1.04	0.97	18	
Hydrocephaly	7	1	3	1.39	1.91	1.18	21	
Total Anophthalmos / Microphthalmos (include unspecified)	2	0	0	0.35	0.35	0.52	21	
Anophthalmos	0	0	0	0.00	0.00	0.00	14	
Microphthalmos	2	0	0	0.35	0.35	0.60	13	
Total Anotia / Microtia (include unspecified)	3	1	0	0.70	0.69	0.37	21	
Anotia	0	0	0	0.00	0.00	0.00	21	
Microtia	3	1	0	0.70	0.69	0.41	20	
Transposition of great vessels	1	0	0	0.17	0.17	0.19	10	
Tetralogy of Fallot	14	0	0	2.43	2.43	1.32	10	
Hypoplastic left heart syndrome	0	0	1	0.00	0.17	0.00	8	
Coarctation of aorta	4	0	0	0.70	0.69	0.99	8	
Choanal atresia, bilateral	3	0	0	0.52	0.52	2.73	2	
Cleft palate without cleft lip	20	0	2	3.48	3.82	0.78	21	
Cleft lip with or without cleft palate	24	0	7	4.17	5.38	0.74	10	
Oesophageal atresia / stenosis with or without fistula	15	0	1	2.61	2.78	1.20	21	
Small intestine atresia / stenosis	3	0	0	0.52	0.52	0.71	21	
Anorectal atresia / stenosis	8	0	3	1.39	1.91	0.65	15	
Undescended testis (36 weeks of gestation or later)	nr	nr	nr	nc	nc	nc		
Hypospadias	21	0	0	3.65	3.64	1.14	6	
Epispadias	1	0	0	0.17	0.17	1.23	21	
Indeterminate sex	nr	nr	nr	nc	nc	nc		
Renal agenesis	1	0	1	0.17	0.35	0.56	13	
Cystic kidney	5	0	0	0.87	0.87	2.28	2	
Bladder exstrophy	1	0	2	0.17	0.52	0.79	21	
Polydactyly, preaxial	7	0	1	1.22	1.39	0.60	21	
Total Limb reduction defects (include unspecified)	20	0	3	3.48	3.99	0.85	11	
Transverse	10	0	1	1.74	1.91	0.64	19	
Preaxial	2	0	0	0.35	0.35	1.41	17	
Postaxial	1	0	0	0.17	0.17	1.25	19	
Intercalary	2	0	0	0.35	0.35	0.67	21	
Mixed	5	0	2	0.87	1.21	1.17	11	
Diaphragmatic hernia	3	0	1	0.52	0.69	1.37	2	
Total Abdominal wall defects (include unspecified)	3	0	4	0.52	1.21	0.84	11	
Omphalocele	2	0	2	0.35	0.69	0.72	11	
Gastroschisis	1	0	2	0.17	0.52	0.97	14	
Prune belly sequence	0	0	0	0.00	0.00	0.00	2	
Trisomy 13	3	1	7	0.70	1.91	1.83	2	
Trisomy 18	3	1	9	0.70	2.26	1.83	2	
Down syndrome, all ages (include age unknown)	52	0	45	9.04	16.83	1.19	6	
<20	0	0	0	nc	nc	nc		
20-24	0	0	0	nc	nc	nc		
25-29	4	0	1	nc	nc	nc		
30-34	9	0	7	nc	nc	nc		
35-39	8	0	28	nc	nc	nc		
40-44	4	0	7	nc	nc	nc		
45+	0	0	0	nc	nc	nc		

nr = not reported
nc = not calculable

Italy: North East, time trend analysis 1981-2002

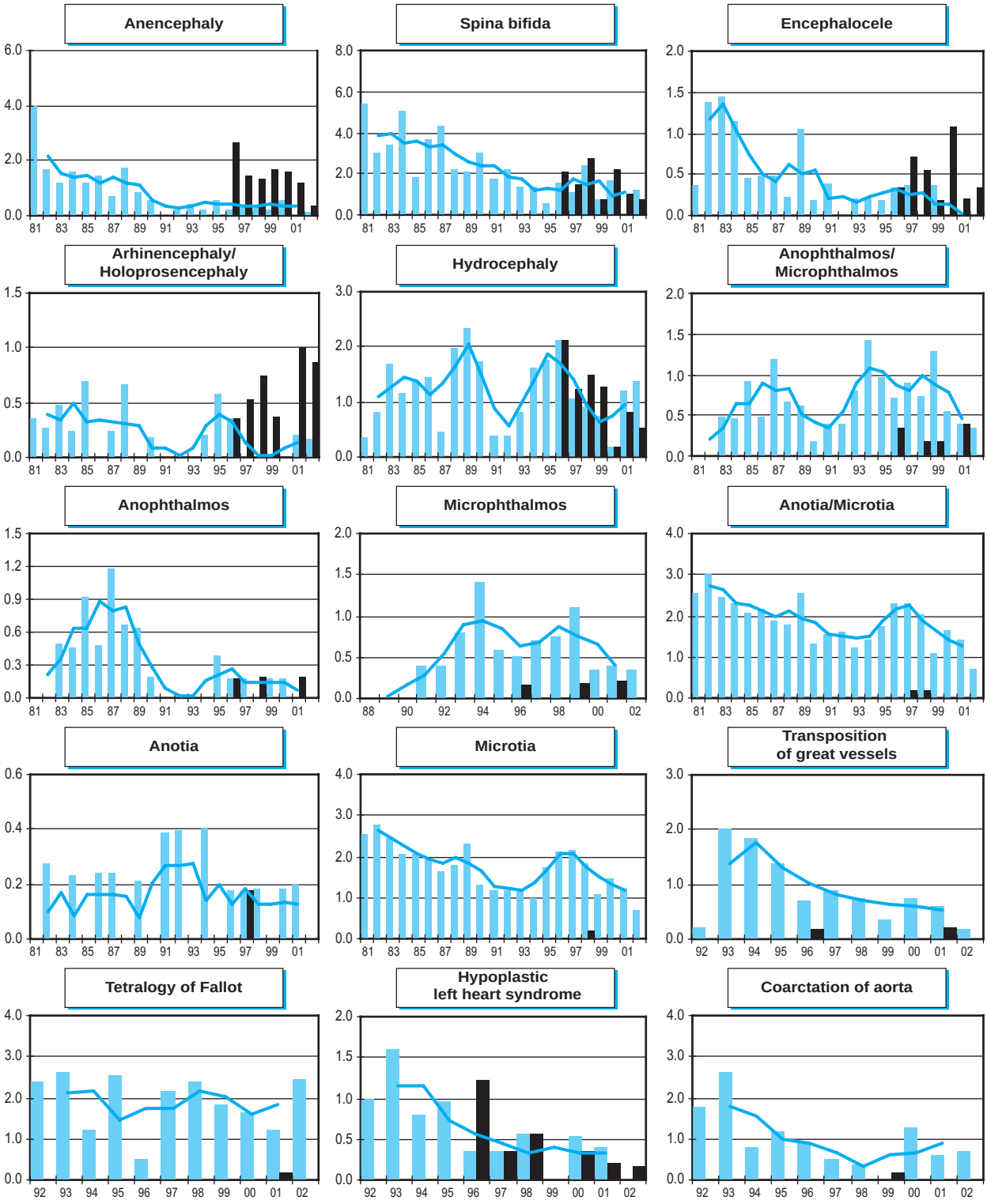
Birth prevalence rates: (L+S) * 10,000

	1974-81*	1982-86	1987-91	1992-96	1997-01	2002	Trend	RR
Births	27,708	205,384	238,168	257,873	269,026	57,495		
Anencephaly	3.97	1.41	0.76	0.31	0.30	0.17	▼	0.879
Spina bifida	5.41	3.41	2.65	1.43	1.19	1.22	▼	0.925
Encephalocele	0.36	0.97	0.46	0.19	0.15	0.00	▼	0.884
Microcephaly					0.38*	1.04	nc	
Arhinencephaly / Holoprosencephaly	0.36	0.34	0.21	0.23	0.04	0.17		
Hydrocephaly	0.36	1.31	1.39	1.36	0.82	1.39		
Total Anophthalmos / Microphthalmos (include unspecified)	0.00	0.49	0.59	0.85	0.78	0.35		
Anophthalmos	0.00	0.49	0.50	0.12	0.11	0.00	▼	0.908
Microphthalmos			0.10*	0.74	0.67	0.35		
Total Anotia / Microtia (include unspecified)	2.53	2.39	1.81	1.67	1.71	0.70	▼	0.970
Anotia	0.00	0.15	0.17	0.19	0.15	0.00		
Microtia	2.53	2.24	1.64	1.47	1.56	0.70	▼	0.968
Transposition of great vessels				1.20	0.67	0.17		0.886
Tetralogy of Fallot				1.82	1.86	2.43		
Hypoplastic left heart syndrome				0.93	0.37	0.00	▼	0.820
Coarctation of aorta				1.43	0.56	0.70	▼	0.867
Choanal atresia, bilateral					0.19*	0.52	nc	
Cleft palate without cleft lip	0.72	5.11	5.16	4.34	3.75	3.48		
Cleft lip with or without cleft palate	11.55	8.72	7.98	6.17	5.20	4.17	▼	0.963
Oesophageal atresia / stenosis with or without fistula	3.25	2.53	1.89	2.83	1.41	2.61		
Small intestine atresia / stenosis	0.36	0.49	0.84	1.01	0.59	0.52		
Anorectal atresia / stenosis	2.89	2.92	2.44	2.02	2.04	1.39	▼	0.974
Undescended testis (36 weeks of gestation or later)								
Hypospadias	10.83	5.79	7.01	5.35	3.01	3.65	▼	0.956
Epispadias	0.00	0.15	0.08	0.12	0.22	0.17		
Indeterminate sex								
Renal agenesis	0.36	0.73	0.67	0.16	0.26	0.17	▼	0.929
Cystic kidney					0.38*	0.87	nc	
Bladder exstrophy	0.36	0.19	0.42	0.19	0.07	0.17		
Polydactyly, preaxial	1.80	1.90	2.60	2.13	1.49	1.22		
Total Limb reduction defects (include unspecified)	6.14	5.70	5.88	4.11	3.90	3.48	▼	0.973
Transverse	2.89	3.31	3.36	2.40	2.27	1.74	▼	0.974
Preaxial	0.36	0.00	0.17	0.27	0.37	0.35	▲	1.082
Postaxial	0.00	0.05	0.08	0.19	0.19	0.17	▲	1.096
Intercalary	1.08	0.54	0.67	0.47	0.37	0.35		
Mixed	2.17	1.80	1.60	0.78	0.71	0.87	▼	0.940
Diaphragmatic hernia					0.38*	0.52	nc	
Total Abdominal wall defects (include unspecified)	1.80	2.53	1.55	0.78	0.45	0.52		0.905
Omphalocele	0.72	1.66	1.09	0.62	0.33	0.35		0.916
Gastroschisis	1.08	0.88	0.46	0.16	0.11	0.17		0.880
Prune belly sequence					0.10*	0.00	nc	
Trisomy 13					0.38*	0.70	nc	
Trisomy 18					0.38*	0.70	nc	
Down syndrome, all ages (include age unknown)	15.52	14.46	14.07	10.66	7.25	9.04	▼	0.961
<20	0.00	4.88	6.17	10.75	4.76*			
20-24	5.95	8.12	7.71	3.43	2.77*		▼	0.959
25-29	9.40	5.89	7.42	7.19	4.05*			
30-34	8.70	12.95	11.14	8.78	5.35*			
35-39	37.83	45.09	31.68	20.04	7.01*		▼	0.915
40-44	137.84	83.70	82.31	40.86	22.74*		▼	0.937
45+		140.85*	26.25*	121.95*	85.47*			

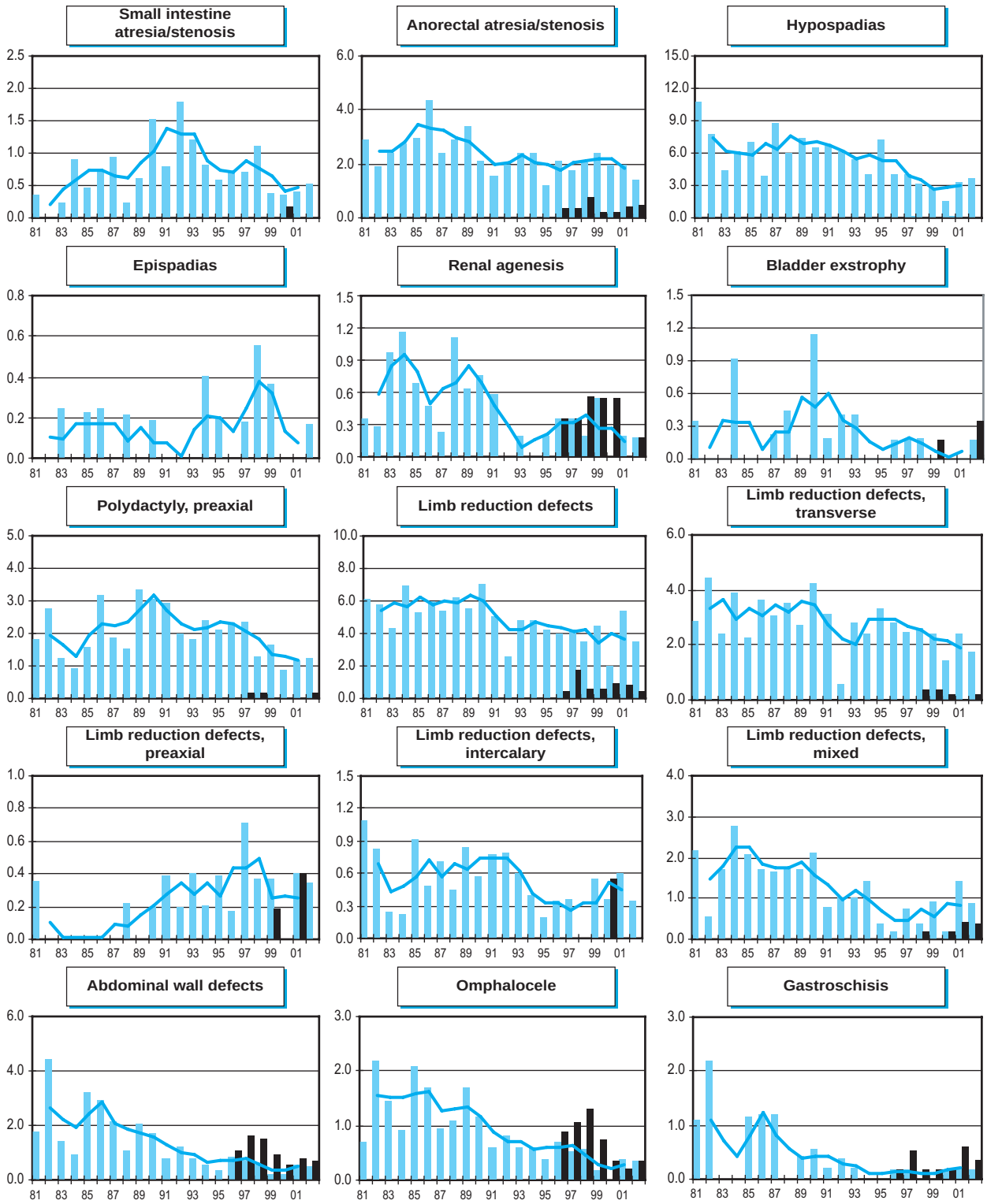
* = data include less than eight and five years

Italy: North East

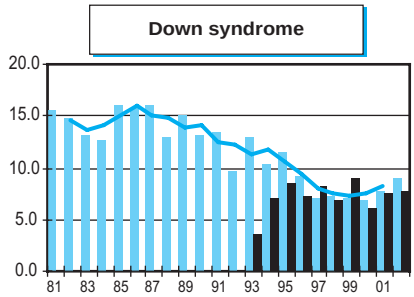
'Time trends 1981-2002 (Birth prevalence rates per 10,000)



Note: L+S rates, ToP rates — 3-year moving average trend



Note: L+S rates, ToP rates — 3-year moving average trend



Note: L+S rates, ToP rates 3-year moving average trend

Italy: Tuscany
Tuscany Registry of Congenital Defects

History:
The registry started in 1979 in the province of Florence and from 1992 in the whole Tuscany region. The Programme became a full member of the ICBMDS in 1998.

Size and coverage:
The Programme is population based, involves all the regional hospitals and the coverage is around 95% of all births in the Tuscany region (approximately 3.5 millions inhabitants and 25,000 births/year). Stillbirths of 20 weeks or more gestation and induced abortions after prenatal diagnosis of birth defects are systematically included. Malformed babies diagnosed within the first year of life are also registered.

Legislation and funding:
The Registry is a surveillance Programmeincluded in the Regional Statistics System; it is formally recognised and supported by the Tuscany Region Health Authority.

Sources and ascertainment:
Multiple sources are used to ascertain malformed infants; records are obtained from all obstetrical and maternity units, pediatric departments, neonatal and pediatric surgery units, prenatal diagnostic centers and pathology services. Mothers are interviewed by using a standardized questionnaire.

Exposure information:
Exposure information on maternal and paternal occupation, life-style, and socio-economical characteristics are obtained by interviews of mothers of malformed infants.

Background information:
Vital statistics and other epidemiological information are obtained by the birth medical records collected by the Regional Bureau of Statistics. Selected information is obtained from the control material collected.

Address for further information:
Fabrizio Bianchi, Sezione di Epidemiologia e Biostatistica, Istituto di Fisiologia Clinica del Consiglio Nazionale delle Ricerche, Area della Ricerca di S. Cataldo, Via Moruzzi, 1, 56127 Pisa, italy.

Phone: 39-050-3152100

Fax: 39-050 3152095

E-mail: fabrizio.bianchi@ifc.cnr.it

Italy: Tuscany, 2002

Live births (L)	26511
Stillbirths (S)	82
Total births	26593
Number of terminations of pregnancy (ToP) for birth defects	98

Birth Defects	Number of cases			Rates*10.000		O/E	YB	Remark
	L	S	ToP	L+S	L+S+ToP	L+S		
Anencephaly	0	0	2	0.00	0.75	0.00	10	
Spina bifida	0	0	6	0.00	2.25	0.00	10	
Encephalocele	0	0	1	0.00	0.37	0.00	9	
Microcephaly	1	0	0	0.38	0.37	0.38	10	
Arhinencephaly / Holoprosencephaly	0	0	3	0.00	1.12	0.00	10	
Hydrocephaly	2	0	2	0.75	1.50	0.63	10	
Total Anophthalmos / Microphthalmos (include unspecified)	3	0	0	1.13	1.12	1.79	10	
Anophthalmos	2	0	0	0.75	0.75	6.25	10	
Microphthalmos	1	0	0	0.38	0.37	0.73	10	
Total Anotia / Microtia (include unspecified)	0	0	0	0.00	0.00	0.00	10	
Anotia	0	0	0	0.00	0.00	0.00	10	
Microtia	0	0	0	0.00	0.00	0.00	10	
Transposition of great vessels	5	1	0	2.26	2.25	1.06	10	
Tetralogy of Fallot	5	0	1	1.88	2.25	0.77	10	
Hypoplastic left heart syndrome	3	0	4	1.13	2.62	0.77	10	
Coarctation of aorta	3	0	0	1.13	1.12	0.41	10	
Choanal atresia, bilateral	2	0	0	0.75	0.75	3.77	10	
Cleft palate without cleft lip	11	0	0	4.14	4.12	1.19	10	
Cleft lip with or without cleft palate	11	0	4	4.14	5.62	0.66	10	
Oesophageal atresia / stenosis with or without fistula	7	0	0	2.63	2.62	1.13	10	
Small intestine atresia / stenosis	1	1	0	0.75	0.75	1.06	10	
Anorectal atresia / stenosis	5	0	2	1.88	2.62	0.99	10	
Undescended testis (36 weeks of gestation or later)	29	0	0	10.91	10.87	1.04	4	
Hypospadias	25	0	1	9.40	9.74	2.16	10	▲
Epispadias	1	0	0	0.38	0.37	1.59	10	
Indeterminate sex	0	0	0	0.00	0.00	0.00	10	
Renal agenesis	1	0	1	0.38	0.75	0.41	10	
Cystic kidney	9	0	4	3.38	4.87	1.20	10	
Bladder exstrophy	1	0	0	0.38	0.37	1.59	10	
Polydactyly, preaxial	3	0	0	1.13	1.12	1.19	10	
Total Limb reduction defects (include unspecified)	13	0	3	4.89	5.99	1.14	10	
Transverse	9	0	3	3.38	4.50	1.06	10	
Preaxial	1	0	0	0.38	0.37	1.35	10	
Postaxial	0	0	0	0.00	0.00	0.00	10	
Intercalary	0	0	0	0.00	0.00	0.00	10	
Mixed	0	0	0	0.00	0.00	0.00	10	
Diaphragmatic hernia	5	0	0	1.88	1.87	1.40	10	
Total Abdominal wall defects (include unspecified)	2	0	2	0.75	1.50	0.66	10	
Omphalocele	2	0	2	0.75	1.50	0.90	10	
Gastroschisis	0	0	0	0.00	0.00	0.00	10	
Prune belly sequence	0	0	0	0.00	0.00	0.00	10	
Trisomy 13	0	0	3	0.00	1.12	0.00	10	
Trisomy 18	2	0	7	0.75	3.37	1.36	10	
Down syndrome, all ages (include age unknown)	9	1	32	3.76	15.74	0.63	6	
<20	0	0	0	0.00	0.00	nc		
20-24	3	0	0	12.88	12.88	3.26	10	
25-29	2	0	0	2.90	2.90	0.56	10	
30-34	1	0	6	0.99	6.90	0.12	10	▼
35-39	3	0	9	5.22	20.85	0.97	7	
40-44	0	1	16	10.19	170.51	0.37	10	
45+	0	0	1	0.00	212.77	0.00	10	

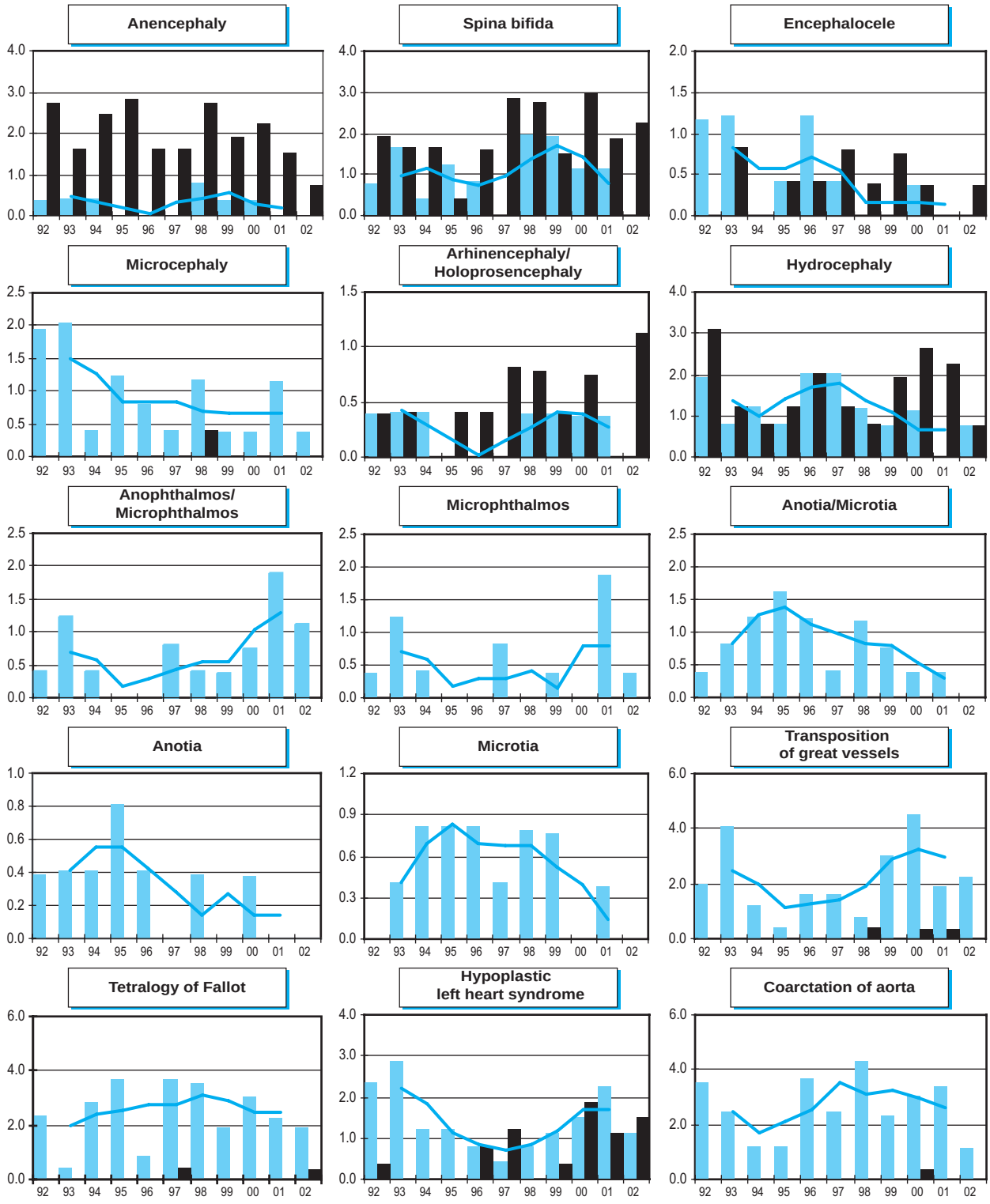
Italy: Tuscany, time trend analysis 1992-2002

Birth prevalence rates: (L+S) * 10,000

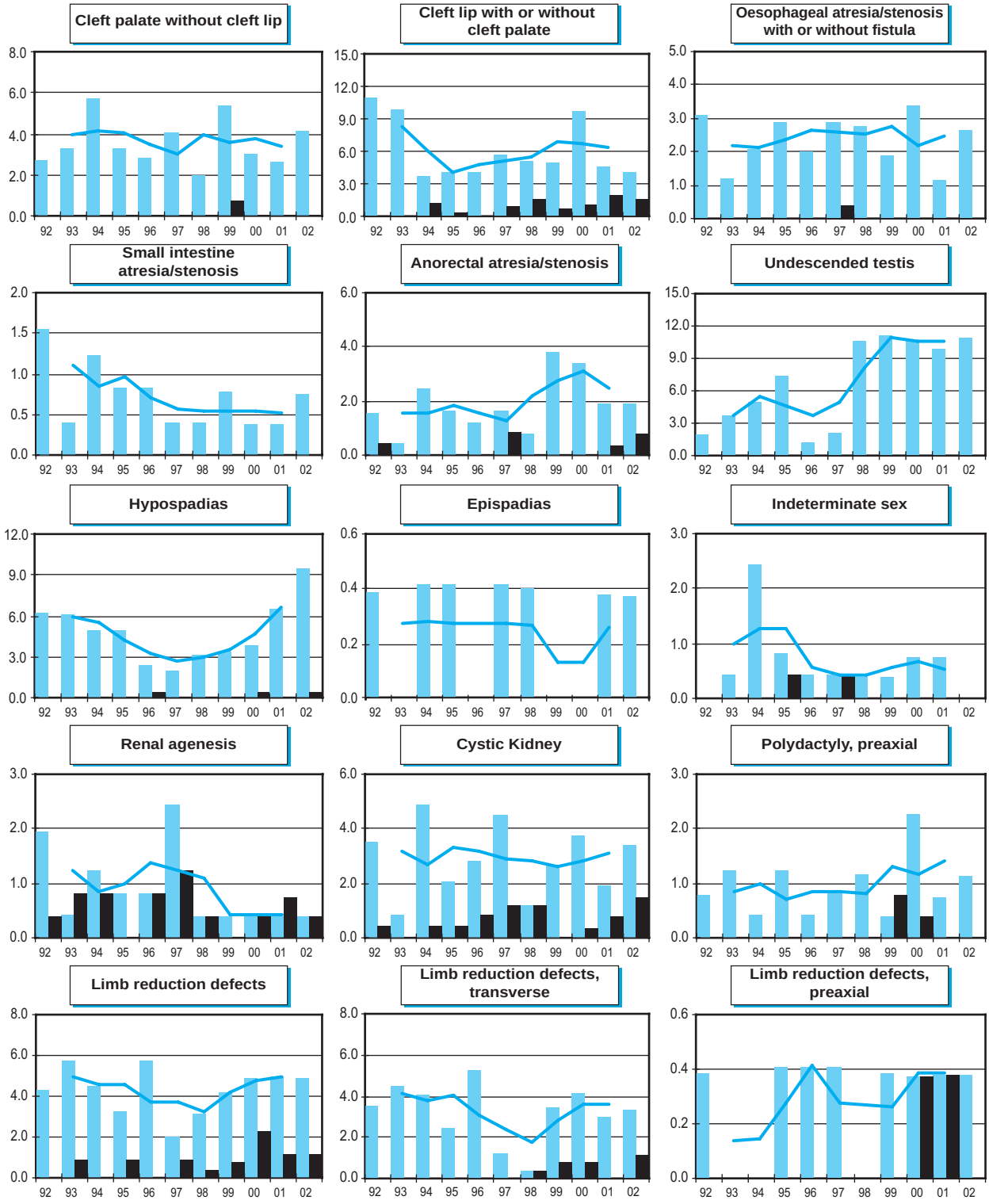
	1974-81	1982-86	1987-91	1992-96	1997-01	2002	Trend	RR
Births				123,787	129,059	26,593		
Anencephaly				0.24	0.31	0.00		
Spina bifida				0.97	1.24	0.00		
Encephalocele				0.81	0.15	0.00	▼	0.779
Microcephaly				1.29	0.70	0.38	▼	0.880
Arhinencephaly / Holoprosencephaly				0.24	0.31	0.00		
Hydrocephaly				1.37	1.01	0.75		
Total Anophthalmos / Microphthalmos (include unspecified)				0.40	0.85	1.13		
Anophthalmos				0.00	0.23	0.75		
Microphthalmos				0.40	0.62	0.38		
Total Anotia / Microtia (include unspecified)				1.05	0.62	0.00		
Anotia				0.48	0.15	0.00		
Microtia				0.57	0.46	0.00		
Transposition of great vessels				1.86	2.40	2.26		
Tetralogy of Fallot				2.02	2.87	1.88		
Hypoplastic left heart syndrome				1.70	1.24	1.13		
Coarctation of aorta				2.42	3.10	1.13		
Choanal atresia, bilateral				0.08	0.31	0.75		
Cleft palate without cleft lip				3.55	3.41	4.14		
Cleft lip with or without cleft palate				6.54	6.04	4.14	▼	0.950
Oesophageal atresia / stenosis with or without fistula				2.26	2.40	2.63		
Small intestine atresia / stenosis				0.97	0.46	0.75		
Anorectal atresia / stenosis				1.45	2.32	1.88		
Undescended testis (36 weeks of gestation or later)				3.80	8.91	10.91	▲	1.150
Hypospadias				4.93	3.80	9.40		
Epispadias				0.24	0.23	0.38		
Indeterminate sex				0.81	0.54	0.00		
Renal agenesis				1.05	0.77	0.38		
Cystic kidney				2.83	2.79	3.38		
Bladder exstrophy				0.32	0.15	0.38		
Polydactyly, preaxial				0.81	1.08	1.13		
Total Limb reduction defects (include unspecified)				4.69	3.87	4.89		
Transverse				3.96	2.48	3.38		
Preaxial				0.24	0.31	0.38		
Postaxial				0.16	0.31	0.00		
Intercalary				0.24	0.62	0.00		
Mixed				0.48	0.39	0.00		
Diaphragmatic hernia				1.37	1.32	1.88		
Total Abdominal wall defects (include unspecified)				1.29	1.01	0.75		
Omphalocele				0.97	0.70	0.75		
Gastroschisis				0.16	0.15	0.00		
Prune belly sequence				0.08	0.08	0.00		
Trisomy 13				0.08	0.31	0.00		
Trisomy 18				0.65	0.46	0.75		
Down syndrome, all ages (include age unknown)				9.53	5.81	3.76	▼	0.911
<20				0.00	0.00	0.00		
20-24				4.96	2.53	12.88		
25-29				5.93	4.26	2.90		
30-34				10.57	6.87	0.99		
35-39				17.21	5.16	5.22		
40-44				37.69	20.76	10.19		
45+				78.74	0.00	0.00		

Italy: Tuscany

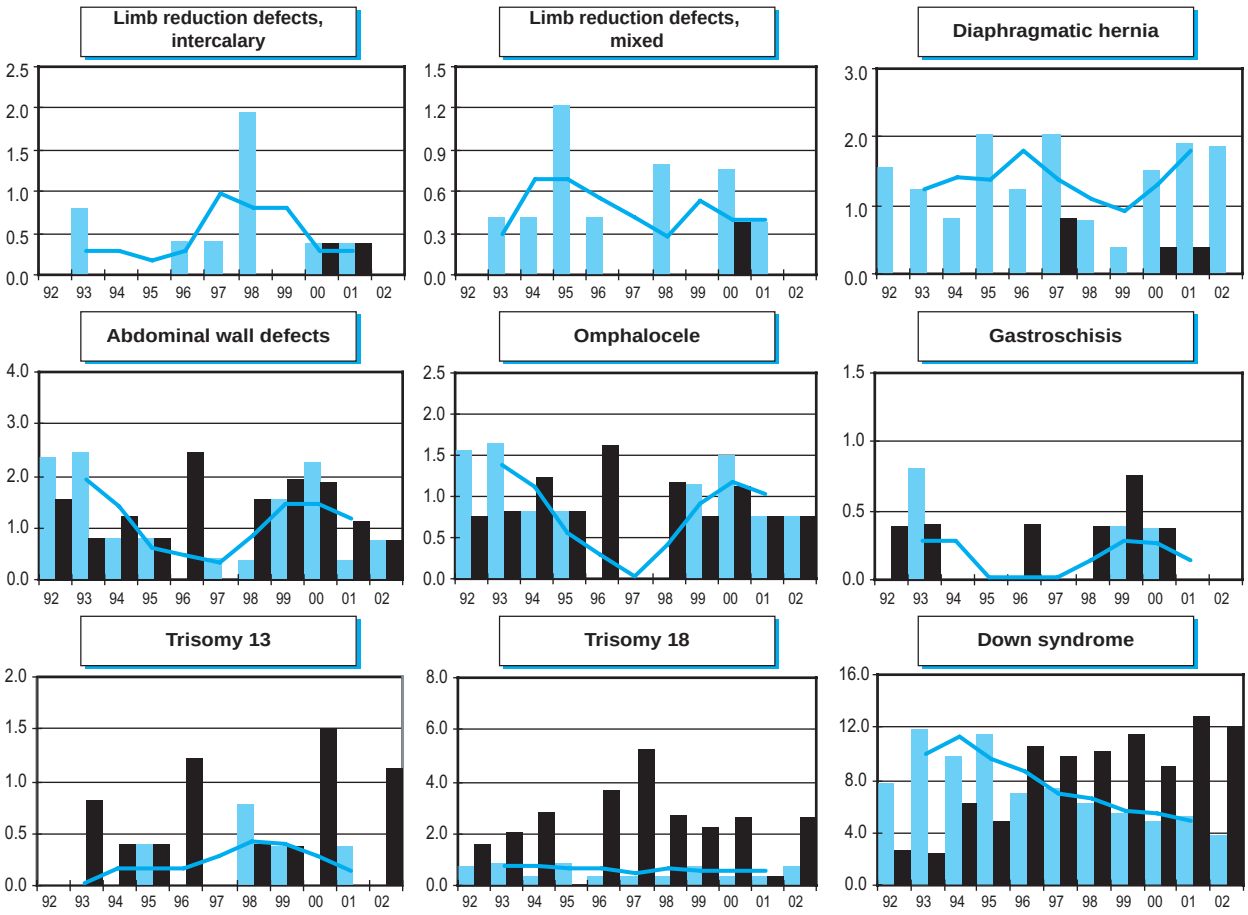
Time trends 1992-2002 (Birth prevalence rates per 10,000)



Note: L+S rates, ToP rates — 3-year moving average trend



Note: L+S rates, ToP rates — 3-year moving average trend



Note: L+S rates, ToP rates — 3-year moving average trend

Japan: JAOG

Japan Association of Maternal Welfare (Until 1994)
Japan Association of Obstetricians and Gynecologists

History:
The Programme started in 1972 and became a full member of ICBDMS in 1988.

Size and coverage:
The Programme is based on reports from 330 hospitals throughout Japan.
At present, approximately 89,255(2002) births are covered representing about 8% of all Japanese births. Still births of 22 weeks or more gestation are included.

Legislation and funding:
The Programme is a research programme acknowledged by the Ministry of Welfare, Labor and Health and supported by JAOG and Ogyaa-Donation.

Sources of ascertainment:
Reports are obtained from delivery units and pediatric clinics of participating hospitals.

Exposure information:
Detailed information on various exposures including maternal or paternal occupation, Chronic diseases and drug use including Folic acid supplementation, X-ray and viral infections are available.

Background informations:
Basic epidemiological information on all births is available from each participating hospitals.

Address for further information:
Yoshio Sumiyoshi, JAOG, Yokohama City University, Urafune Hospital, 4-57, Urafune-cho, Minami-ku, Yokohama, 232-0024

Phone: 81-45-2533668

Fax: 81-45-2533668

E-mail: fuhira@hamakko.or.jp

Japan: JAOG, 2002

Live births (L)	88556
Stillbirths (S)	699
Total births	89255
Number of terminations of pregnancy (ToP) for birth defects	nr

Birth Defects	Number of cases			Rates*10.000		O/E	YB	Remark
	L	S	ToP	L+S	L+S+ToP	L+S		
Anencephaly	4	8	nr	1.34	nc	0.83	6	
Spina bifida	44	5	nr	5.49	nc	1.39	10	
Encephalocele	7	1	nr	0.90	nc	0.84	28	
Microcephaly	10	3	nr	1.46	nc	1.14	24	
Arhinencephaly / Holoprosencephaly	9	2	nr	1.23	nc	1.22	7	
Hydrocephaly	62	7	nr	7.73	nc	1.11	14	
Total Anophthalmos / Microphthalmos (include unspecified)	6	3	nr	1.01	nc	1.37	11	
Anophthalmos	2	2	nr	0.45	nc	2.37	9	
Microphthalmos	4	1	nr	0.56	nc	1.01	28	
Total Anotia / Microtia (include unspecified)	nr	nr	nr	nc	nc	nc		
Anotia	nr	nr	nr	nc	nc	nc		
Microtia	11	1	nr	1.34	nc	1.17	28	
Transposition of great vessels	20	3	nr	2.58	nc	1.02	4	
Tetralogy of Fallot	33	1	nr	3.81	nc	1.28	4	
Hypoplastic left heart syndrome	19	0	nr	2.13	nc	1.32	5	
Coarctation of aorta	21	2	nr	2.58	nc	1.14	4	
Choanal atresia, bilateral	nr	nr	nr	nc	nc	nc		
Cleft palate without cleft lip	27	3	nr	3.36	nc	0.67	19	▼
Cleft lip with or without cleft palate	181	17	nr	22.18	nc	1.37	12	▲
Oesophageal atresia / stenosis with or without fistula	30	5	nr	3.92	nc	1.03	4	
Small intestine atresia / stenosis	48	4	nr	5.83	nc	1.26	5	
Anorectal atresia / stenosis	36	9	nr	5.04	nc	1.19	19	
Undescended testis (36 weeks of gestation or later)	nr	nr	nr	nc	nc	nc		
Hypospadias	38	2	nr	4.48	nc	1.45	13	
Epispadias	nr	nr	nr	nc	nc	nc		
Indeterminate sex	nr	nr	nr	nc	nc	nc		
Renal agenesis	12	7	nr	2.13	nc	1.41	13	
Cystic kidney	38	4	nr	4.71	nc	1.34	4	
Bladder exstrophy	2	0	nr	0.22	nc	1.39	26	
Polydactyly, preaxial	50	0	nr	5.60	nc	0.90	13	
Total Limb reduction defects (include unspecified)	29	8	nr	4.15	nc	1.26	9	
Transverse	2	0	nr	0.22	nc	0.63	9	
Preaxial	4	2	nr	0.67	nc	1.18	9	
Postaxial	3	1	nr	0.45	nc	1.61	9	
Intercalary	11	2	nr	1.46	nc	1.63	6	
Mixed	7	1	nr	0.90	nc	1.43	9	
Diaphragmatic hernia	48	5	nr	5.94	nc	1.07	4	
Total Abdominal wall defects (include unspecified)	2	1	nr	0.34	nc	0.08	19	▼
Omphalocele	24	12	nr	4.03	nc	1.32	17	
Gastroschisis	17	2	nr	2.13	nc	0.98	6	
Prune belly sequence	0	0	nr	0.00	nc	0.00	7	
Trisomy 13	11	1	nr	1.34	nc	1.46	7	
Trisomy 18	48	37	nr	9.52	nc	1.52	2	▲
Down syndrome, all ages (include age unknown)	89	6	nr	10.64	nc	1.33	8	▲
<20	1	0	nr	6.89	nc	1.54	9	
20-24	2	0	nr	2.09	nc	0.76	9	
25-29	17	3	nr	6.72	nc	1.42	9	
30-34	29	2	nr	9.47	nc	1.34	9	
35-39	31	0	nr	22.82	nc	1.30	9	
40+	9	1	nr	46.40	nc	0.84	9	

nr = not repoted
nc = not calculable

Japan: JAOG, time trend analysis 1974-2002

Birth prevalence rates: (L+S) * 10,000

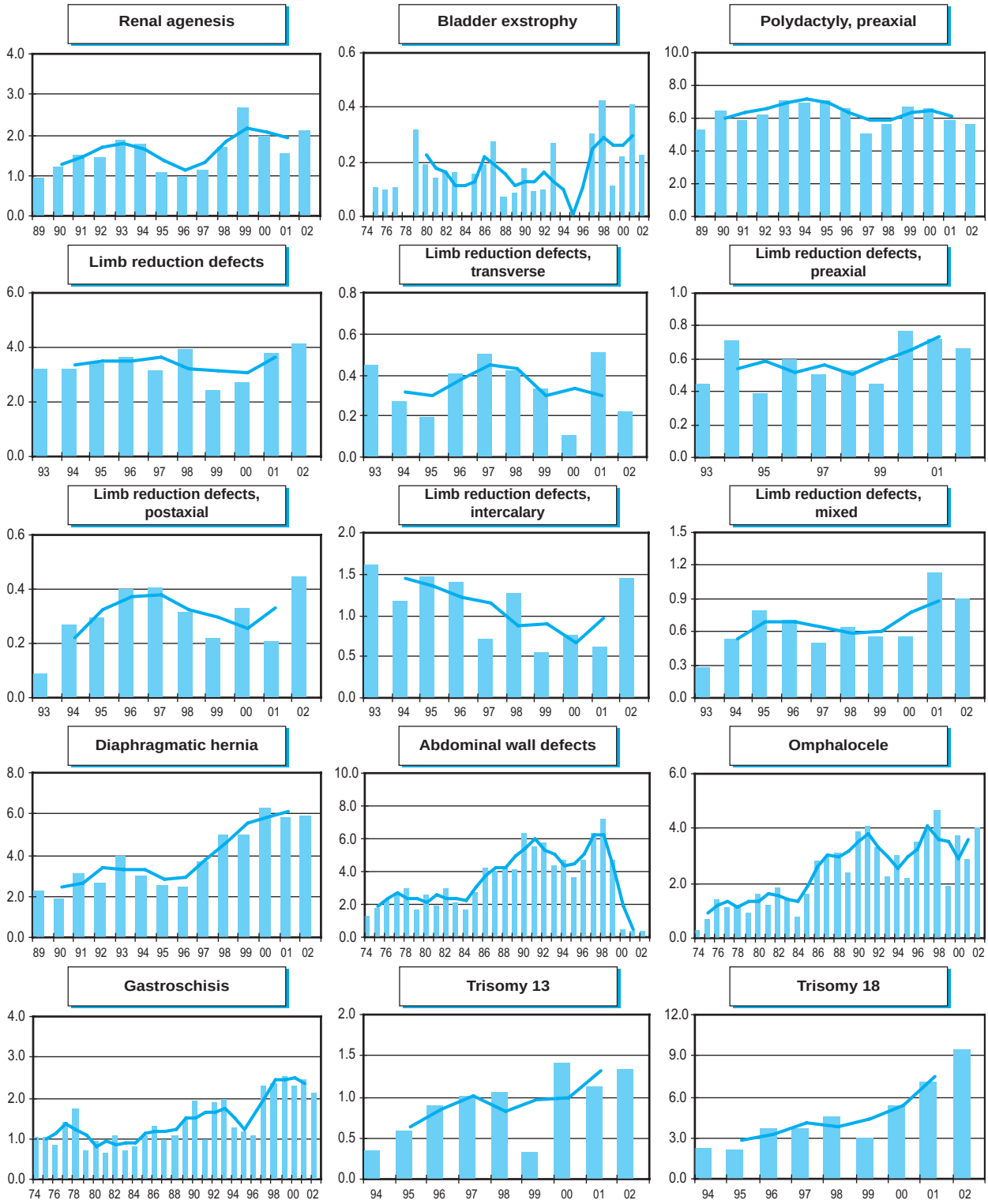
	1974-81	1982-86	1987-91	1992-96	1997-01	2002	Trend	RR
Births	925,762	659,696	625,335	525,703	472,208	89,255		
Anencephaly	9.27	8.47	5.96	2.93	1.63	1.34	▼	0.942
Spina bifida	1.96	3.02	3.10	3.73	4.17	5.49	▲	1.036
Encephalocele	1.05	1.20	1.18	0.99	0.83	0.90		
Microcephaly	0.96	1.24	1.38	1.35	1.42	1.46	▲	1.018
Arhinencephaly / Holoprosencephaly				0.70*	1.14	1.23		
Hydrocephaly	2.93	4.64	6.28	6.81	7.28	7.73	▲	1.042
Total Anophthalmos / Microphthalmos (include unspecified)	1.30	1.53	1.14	0.82	0.59	1.01	▼	0.971
Anophthalmos	0.76	0.88	0.54	0.27	0.19	0.45	▼	0.951
Microphthalmos	0.54	0.65	0.59	0.55	0.40	0.56		
Total Anotia / Microtia (include unspecified)								
Anotia								
Microtia	1.12	1.02	1.17	1.18	1.33	1.34		
Transposition of great vessels					2.33	2.58		
Tetralogy of Fallot					2.77	3.81		
Hypoplastic left heart syndrome					1.61	2.13		
Coarctation of aorta					1.91	2.58		
Choanal atresia, bilateral								
Cleft palate without cleft lip	12.72	5.24	5.49	4.87	4.64	3.36	▼	0.951
Cleft lip with or without cleft palate	13.85	13.93	14.68	15.67	16.88	22.18	▲	1.011
Oesophageal atresia / stenosis with or without fistula	1.20*	1.20	1.70	2.40	3.60	3.92	▲	1.066
Small intestine atresia / stenosis					4.62	5.83		
Anorectal atresia / stenosis	3.90	3.97	4.17	4.24	4.60	5.04	▲	1.009
Undescended testis (36 weeks of gestation or later)								
Hypospadias	1.92	2.40	2.53	2.87	3.43	4.48	▲	1.031
Epispadias								
Indeterminate sex								
Renal agenesis			1.23*	1.46	1.78	2.13	▲	1.040
Cystic kidney					3.18	4.71		
Bladder exstrophy	0.17*	0.14	0.14	0.08	0.30	0.22		
Polydactyly, preaxial			5.89*	6.79	5.93	5.60		
Total Limb reduction defects (include unspecified)				3.37*	3.22	4.15		
Transverse				0.33*	0.38	0.22		
Preaxial				0.54*	0.59	0.67		
Postaxial				0.26*	0.30	0.45		
Intercalary				1.42*	0.78	1.46		
Mixed				0.57*	0.68	0.90		
Diaphragmatic hernia			2.39*	2.95	5.15	5.94	▲	1.088
Total Abdominal wall defects (include unspecified)	2.11	2.77	4.73	4.64	3.83	0.34	▲	1.023
Omphalocele	1.11	1.76	3.26	2.85	3.43	4.03	▲	1.050
Gastroschisis	0.99	1.02	1.26	1.48	2.39	2.13	▲	1.039
Prune belly sequence				0.10*	0.02	0.00		
Trisomy 13				0.61*	1.00	1.34	▲	1.119
Trisomy 18				2.65*	4.72	9.52	▲	1.188
Down syndrome, all ages (include age unknown)	4.25*	5.24	5.95	6.60	8.68	10.64	▲	1.036
<20				4.39*	4.56	6.89		
20-24				2.58*	2.90	2.09		
25-29				4.26*	5.19	6.72		
30-34				5.85*	8.11	9.47		
35-39				15.76*	18.95	22.82		
40+				60.67*	51.27	46.40		

* = data include less than eight and five years

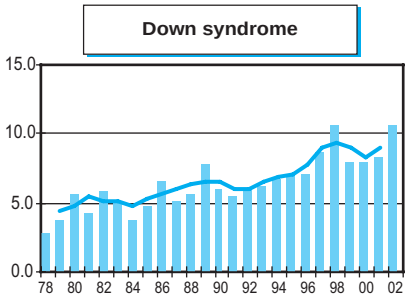
Japan: JAOG

Time trends 1974-2001 (Birth prevalence rates per 10,000)

Note: L+S rates, 3-year moving average trend



Note: L+S rates, 3-year moving average trend



Note: L+S rates, ToP rates 3-year moving average trend

Malta
Congenital Anomalies Register

History:
The register started in 1985 as a research project of the University of Malta. It started as a hospital based register collecting data regarding congenital anomalies diagnosed in babies born at the main general hospital. It became a member of EUROCAT in 1986. Funding for the research project was stopped in 1995 and in 1997 the Department of Health Information resumed the functions of the registry increasing coverage to all hospitals on the islands making it a population based register. Several new sources of data were included at this stage. The Register was accepted as an associate member of the International Clearinghouse in 2000.

Size and Coverage:
The registry is population based and presently covers about 4500 births per year. Stillbirths of 20 weeks gestation or more are registered. Termination of pregnancy is illegal in Malta.

Legislation and Funding:
Reporting is voluntary. The registry is run and funded by the government Department of Health Information.

Sources of ascertainment:
The registry employs active data collection from multiple sources including: labour, postnatal and nursery wards, cardiac lab records, genetics clinic records, National Mortality Register, National Obstetric Systems database, Hospital Activity Analysis database, National Cancer Register and the hypothyroid screening Program. Voluntary reporting by doctors is also available. These sources cover the whole population of the Maltese Islands.

Exposure information:
Information regarding maternal disease and exposure to medicinal drugs, smoking, alcohol and drug abuse as well as parental occupation are collected for all malformed infants.

Background information:
Epidemiological background data on all births are available from the National Obstetric Information Systems database and the National Statistics Office (NSO).

Health Promotion Project:
The Malta Congenital Anomalies Registry is collaborating with the Health Promotion Department which is organising a national campaign promoting healthy pregnancies and periconceptional folic acid supplementation. The Registry will be responsible for co-ordinating two surveys investigating maternal knowledge and periconceptional folic acid uptake before and then 2 years after the health promotion campaign. Data collection for the first survey is scheduled to start in October 2004.

Address for further information:
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Tel: 356-21234915

Fax: 356-21235910

E-mail: miriam.gatt@gov.mt

Malta, 2002

Live births (L)	3805
Stillbirths (S)	21
Total births	3826
Number of terminations of pregnancy (ToP) for birth defects	not permitted

Birth Defects	Number of cases			Rates*10.000		O/E	YB	Remark
	L	S	ToP	L+S	L+S+ToP	L+S		
Anencephaly	0	2		5.23		1.45	9	
Spina bifida	2	0		5.23		0.78	9	
Encephalocele	1	0		2.61		1.20	9	
Microcephaly	1	0		2.61		0.78	9	
Arhinencephaly / Holoprosencephaly	0	0		0.00		0.00	9	
Hydrocephaly	0	0		0.00		0.00	9	
Total Anophthalmos / Microphthalmos (include unspecified)	0	0		0.00		0.00	9	
Anophthalmos	0	0		0.00		0.00	9	
Microphthalmos	0	0		0.00		0.00	9	
Total Anotia / Microtia (include unspecified)	0	0		0.00		nc		
Anotia	0	0		0.00		nc		
Microtia	0	0		0.00		nc		
Transposition of great vessels	1	0		2.61		0.49	9	
Tetralogy of Fallot	0	0		0.00		0.00	9	
Hypoplastic left heart syndrome	2	0		5.23		3.64	9	
Coarctation of aorta	2	0		5.23		0.94	9	
Choanal atresia, bilateral	1	0		2.61		5.56	9	
Cleft palate without cleft lip	3	0		7.84		0.55	9	
Cleft lip with or without cleft palate	1	0		2.61		0.26	9	
Oesophageal atresia / stenosis with or without fistula	1	0		2.61		1.20	9	
Small intestine atresia / stenosis	0	0		0.00		0.00	9	
Anorectal atresia / stenosis	4	0		10.45		2.55	9	
Undescended testis (36 weeks of gestation or later)	nr	nr		nc		nc		
Hypospadias	8	0		20.91		0.86	5	
Epispadias	0	0		0.00		0.00	9	
Indeterminate sex	0	0		0.00		0.00	9	
Renal agenesis	1	0		2.61		0.99	9	
Cystic kidney	0	0		0.00		0.00	9	
Bladder exstrophy	0	0		0.00		nc		
Polydactyly, all	8	0		20.91		1.34	9	
Total Limb reduction defects (include unspecified)	2	0		5.23		0.94	9	
Transverse	nr	nr		nc		nc		
Preaxial	nr	nr		nc		nc		
Postaxial	nr	nr		nc		nc		
Intercalary	nr	nr		nc		nc		
Mixed	nr	nr		nc		nc		
Diaphragmatic hernia	4	0		10.45		1.89	9	
Total Abdominal wall defects (include unspecified)	1	0		2.61		0.72	9	
Omphalocele	1	0		2.61		1.09	9	
Gastroschisis	0	0		0.00		0.00	9	
Prune belly sequence	0	0		0.00		0.00	9	
Trisomy 13	0	0		0.00		0.00	9	
Trisomy 18	2	0		5.23		1.98	9	
Down syndrome, all ages (include age unknown)	15	0		39.21		2.33	9	▲
<20	0	0		0.00		0.00	3	
20-24	0	0		0.00		nc		
25-29	5	0		32.59		5.05	3	▲
30-34	3	0		33.94		2.01	3	
35-39	4	0		108.40		1.92	3	
40-44	3	0		375.00		2.52	3	
45+	0	0		0.00		nc		

nr = not reported
nc = not calculable

Malta, time trend analysis 1993-2002

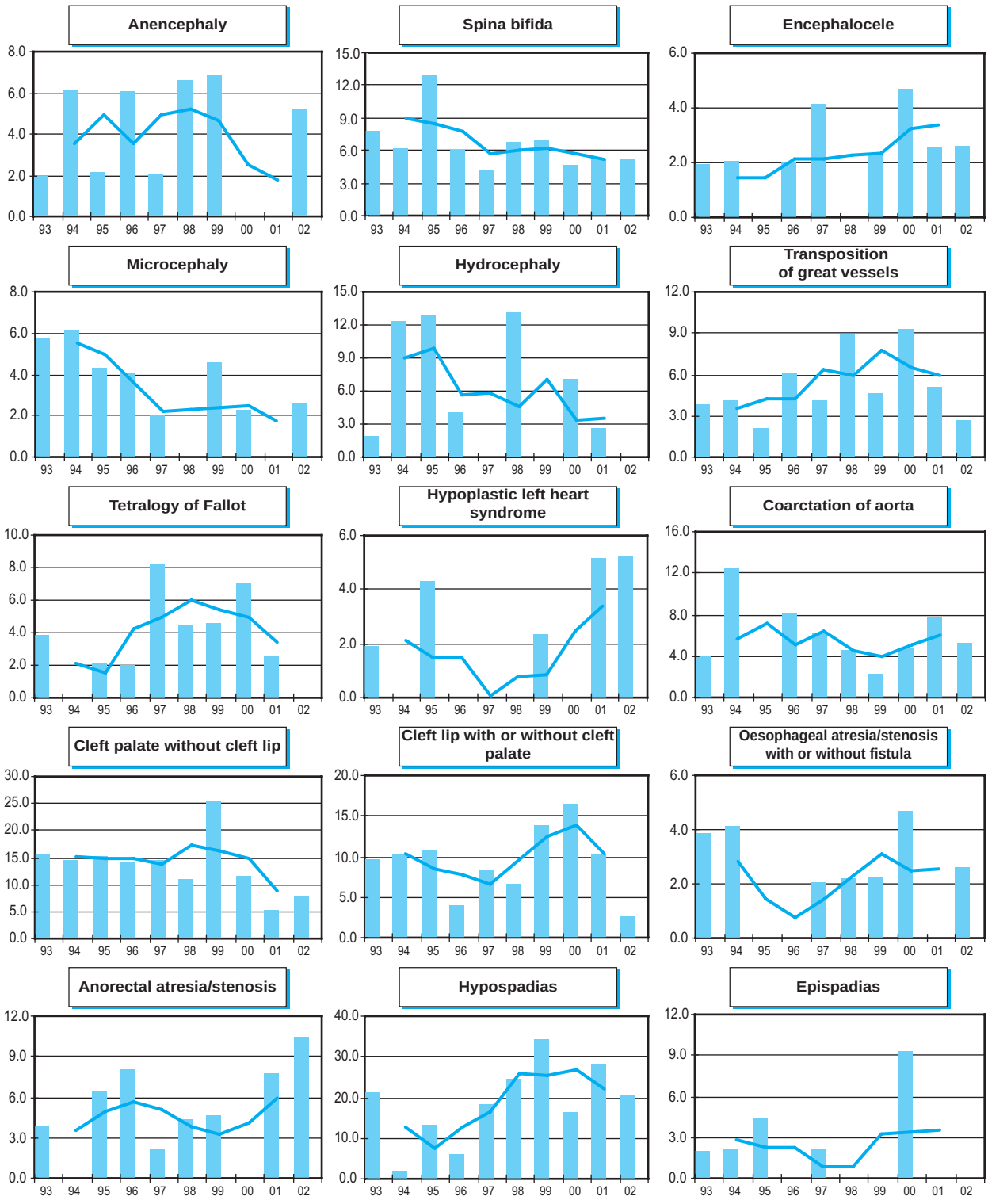
Birth prevalence rates: (L+S) * 10,000

	1974-81	1982-86	1987-91	1992-96*	1997-01	2002	Trend	RR
Births				19,646	21,869	3,826		
Anencephaly				4.07	3.20	5.23		
Spina bifida				8.14	5.49	5.23		
Encephalocele				1.53	2.74	2.61		
Microcephaly				5.09	1.83	2.61		
Arhinencephaly / Holoprosencephaly				0.51	1.37	0.00		
Hydrocephaly				7.64	4.57	0.00		
Total Anophthalmos / Microphthalmos (include unspecified)				1.02	1.37	0.00		
Anophthalmos				0.51	0.46	0.00		
Microphthalmos				0.51	0.91	0.00		
Total Anotia / Microtia (include unspecified)				0.00	0.00	0.00		
Anotia				0.00	0.00	0.00		
Microtia				0.00	0.00	0.00		
Transposition of great vessels				4.07	6.40	2.61		
Tetralogy of Fallot				2.04	5.49	0.00		
Hypoplastic left heart syndrome				1.53	1.37	5.23		
Coarctation of aorta				6.11	5.03	5.23		
Choanal atresia, bilateral				0.51	0.46	2.61		
Cleft palate without cleft lip				14.76	13.72	7.84		
Cleft lip with or without cleft palate				8.65	10.97	2.61		
Oesophageal atresia / stenosis with or without fistula				2.04	2.29	2.61		
Small intestine atresia / stenosis				0.51	1.37	0.00		
Anorectal atresia / stenosis				4.58	3.66	10.45		
Undescended testis (36 weeks of gestation or later)								
Hypospadias				10.69	24.24	20.91	▲	1.097
Epispadias				2.04	2.29	0.00		
Indeterminate sex				1.53	1.37	0.00		
Renal agenesis				3.05	2.29	2.61		
Cystic kidney				4.58	4.12	0.00		
Bladder exstrophy				0.00	0.00	0.00		
Polydactyly, all				13.74	17.38	20.91		
Total Limb reduction defects (include unspecified)				4.58	6.40	5.23		
Transverse								
Preaxial								
Postaxial								
Intercalary								
Mixed								
Diaphragmatic hernia				6.11	5.03	10.45		
Total Abdominal wall defects (include unspecified)				4.58	2.74	2.61		
Omphalocele				3.56	1.37	2.61		
Gastroschisis				1.02	1.37	0.00		
Prune belly sequence				1.02	0.00	0.00		
Trisomy 13				0.00	0.46	0.00		
Trisomy 18				2.04	3.20	5.23		
Down syndrome, all ages (include age unknown)				19.34	14.63	39.21		
<20					27.97*	0.00	nc	
20-24					0.00*	0.00	nc	
25-29					6.44*	32.59	nc	
30-34					16.80*	33.94	nc	
35-39					56.36*	108.40	nc	
40-44					149.25*	375.00	nc	
45+					0.00*	0.00	nc	

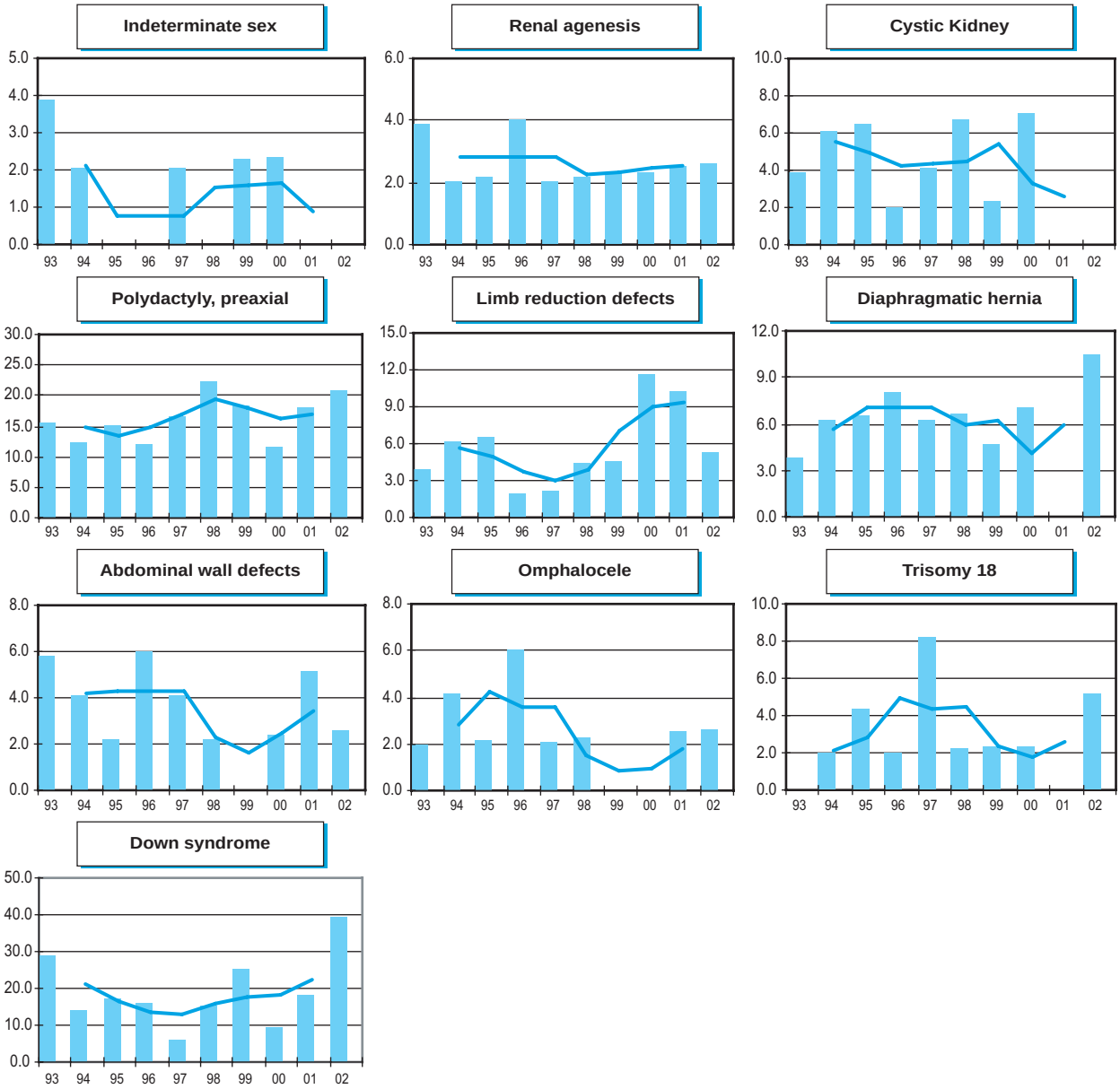
* = data include less than five years

Malta

'Time trends 1993-2002 (Birth prevalence rates per 10,000)



Note: L+S rates, 3-year moving average trend



Note: L+S rates, 3-year moving average trend

Mexico: RYVEMCE

Mexican Registry and Epidemiological Surveillance of External Congenital Malformations

History:
The Programme was started in 1978. The Programme became a full member of the ICBDMS in 1980.

Size and coverage:
Reports are obtained from 15 hospitals in 11 cities in Mexico. Participation is voluntary. The annual number of births is approximately 40.000, about 3.5% of all births in Mexico. Stillbirths of 20 weeks or more gestation and/or at least 500g birthweight are included.

Legislation and funding:
The Programme is a research Programmeand is funded by research grants.

Sources of ascertainment:
Reports are obtained from the delivery units and pediatric departments of the participating hospitals.

Exposure information:
The mother of each reported infant and the mother of a control infant-the next non-malformed infant born at that hospital with the same sex as the proband - are interviewed on various exposures, including drug usage and parental occupation.

Background information:
The total number of births in the hospitals is known.

Address for further information:
Osvaldo Mutchinick, Departamento de Genetica, Instituto Nacional de Nutricion, Salvador Zubiran, Vasco de Quiroga 15, Tlalpan, 14000 Mexico, D.F., Mexico.

Phone: 52-5-5731200/ 52-5-5730611, 52-5-5737333 (ext 2426, 2425)

Fax: 52-5-6556138

E-mail: osvaldo@servidor.unam.mx

Mexico: RYVEMCE, 2002

Live births (L)	21585
Stillbirths (S)	245
Total births	21830
Number of terminations of pregnancy (ToP) for birth defects	not permitted

Birth Defects	Number of cases			Rates*10.000		O/E	YB	Remark
	L	S	ToP	L+S	L+S+ToP	L+S		
Anencephaly	6	6		5.50		0.70	2	
Spina bifida	13	0		5.96		0.38	22	
Encephalocele	0	1		0.46		0.18	21	
Microcephaly	1	1		0.92		0.46	15	
Arhinencephaly / Holoprosencephaly	2	1		1.37		2.36	5	
Hydrocephaly	12	2		6.41		1.12	22	
Total Anophthalmos / Microphthalmos (include unspecified)	3	2		2.29		1.45	17	
Anophthalmos	nr	nr		nc		nc		
Microphthalmos	nr	nr		nc		nc		
Total Anotia / Microtia (include unspecified)	15	0		6.87		1.04	22	
Anotia	nr	nr		nc		nc		
Microtia	nr	nr		nc		nc		
Transposition of great vessels	0	0		0.00		0.00	7	
Tetralogy of Fallot	nr	nr		nc		nc		
Hypoplastic left heart syndrome	1	0		0.46		nc		
Coarctation of aorta	nr	nr		nc		nc		
Choanal atresia, bilateral	0	0		0.00		0.00	22	
Cleft palate without cleft lip	5	0		2.29		0.69	22	
Cleft lip with or without cleft palate	29	3		14.66		1.16	22	
Oesophageal atresia / stenosis with or without fistula	5	0		2.29		1.14	20	
Small intestine atresia / stenosis	4	0		1.83		1.50	17	
Anorectal atresia / stenosis	11	0		5.04		1.11	22	
Undescended testis (36 weeks of gestation or later)	nr	nr		nc		nc		
Hypospadias	9	1		4.58		1.07	22	
Epispadias	nr	nr		nc		nc		
Indeterminate sex	9	2		5.04		2.40	22	
Renal agenesis	2	0		0.92		1.72	8	
Cystic kidney	3	2		2.29		2.09	10	
Bladder exstrophy	1	0		0.46		1.03	22	
Polydactyly, preaxial	36	3		17.87		1.42	21	
Total Limb reduction defects (include unspecified)	13	0		5.96		1.00	22	
Transverse	8	0		3.66		1.09	19	
Preaxial	3	0		1.37		1.82	10	
Postaxial	1	0		0.46		1.52	19	
Intercalary	1	0		0.46		1.45	19	
Mixed	0	0		0.00		0.00	19	
Diaphragmatic hernia	2	0		0.92		1.04	22	
Total Abdominal wall defects (include unspecified)	16	4		9.16		2.02	22	
Omphalocele	4	2		2.75		1.69	22	
Gastroschisis	12	2		6.41		2.10	8	
Prune belly sequence	2	0		0.92		0.91	22	
Trisomy 13	2	0		0.92		4.17	22	
Trisomy 18	1	0		0.46		2.27	11	
Down syndrome, all ages (include age unknown)	21	0		9.62		0.74	22	
<20	6	0		12.49		1.50	22	
20-24	2	0		2.74		0.42	22	
25-29	4	0		8.14		0.93	22	
30-34	6	0		21.57		1.52	22	
35-39	1	0		7.01		0.17	22	
40-44	2	0		62.11		0.44	22	
45+	0	0		0.00		0.00	20	

Mexico: RYVEMCE, time trend analysis 1980-2002

Birth prevalence rates: (L+S) * 10,000

	1974-81*	1982-86	1987-91	1992-96	1997-01	2002	Trend	RR
Births	76,228	155,109	234,777	282,882	155,036	21,830		
Anencephaly	18.37	18.70	18.70	16.19	11.61	5.50	▼	0.974
Spina bifida	15.61	14.44	18.36	15.38	13.80	5.96	▼	0.989
Encephalocele	3.41	3.61	2.60	2.26	2.32	0.46	▼	0.969
Microcephaly	2.49	2.58	2.56	1.77*	1.61	0.92	▼	0.972
Arhinencephaly / Holoprosencephaly				0.12	0.58	1.37	▲	1.435
Hydrocephaly	6.03	5.35	4.86	6.01	6.84	6.41		
Total Anophthalmos / Microphthalmos (include unspecified)	2.23	2.45	1.87	1.52	1.23	2.29	▼	0.967
Anophthalmos					0.00*		nc	
Microphthalmos					0.00*		nc	
Total Anotia / Microtia (include unspecified)	6.30	6.83	6.90	5.90	7.35	6.87		
Anotia					0.00*		nc	
Microtia					0.00*		nc	
Transposition of great vessels				0.10*	0.32	0.00		
Tetralogy of Fallot					0.16*		nc	
Hypoplastic left heart syndrome				0.00*	0.00	0.46		
Coarctation of aorta					0.00*		nc	
Choanal atresia, bilateral	0.13	0.26	0.38	0.57	0.06	0.00		
Cleft palate without cleft lip	3.54	3.16	3.62	3.46	2.71	2.29		
Cleft lip with or without cleft palate	12.20	13.41	12.35	12.66	12.71	14.66		
Oesophageal atresia / stenosis with or without fistula	1.18	1.22	2.17	2.09	2.45	2.29	▲	1.028
Small intestine atresia / stenosis	0.92	0.64	1.06	1.24	1.48	1.83	▲	1.042
Anorectal atresia / stenosis	3.80	4.64	4.43	4.88	4.45	5.04		
Undescended testis (36 weeks of gestation or later)					0.00*		nc	
Hypospadias	3.54	4.13	4.51	5.09	2.90	4.58		
Epispadias				0.00*	0.00*		nc	
Indeterminate sex	1.71	2.00	2.21	2.58	1.35	5.04		
Renal agenesis				0.60*	0.45	0.92		
Cystic kidney	0.26	0.32	0.47	0.92	1.42	2.29	▲	1.089
Bladder exstrophy	0.26	0.64	0.38	0.39	0.52	0.46		
Polydactyly, preaxial	11.81	11.99	13.59	12.86*	11.87	17.87		
Total Limb reduction defects (include unspecified)	6.56	6.06	6.26	5.97	5.16	5.96		
Transverse		2.57*	3.36	3.82	3.10	3.66		
Preaxial		1.08*	1.41	0.88	0.52	1.37		
Postaxial		0.17*	0.30	0.42	0.19	0.46		
Intercalary		0.17*	0.34	0.25	0.52	0.46		
Mixed		1.41*	0.55	0.49	0.77	0.00		
Diaphragmatic hernia	0.52	0.45	1.06	0.99	1.03	0.92		
Total Abdominal wall defects (include unspecified)	4.46	4.26	4.39	4.35	5.48	9.16	▲	1.019
Omphalocele	1.97	1.61	1.36	1.84	1.48	2.75		
Gastroschisis	1.44	1.29	1.70	2.16	3.81	6.41	▲	1.068
Prune belly sequence	1.05	1.35	1.32	0.67	0.77	0.92		
Trisomy 13	0.52	0.19	0.34	0.11	0.13	0.92		
Trisomy 18	1.05	0.52	0.47	0.28	0.06	0.46	▼	0.915
Down syndrome, all ages (include age unknown)	14.17	12.12	14.10	13.33	11.42	9.62		
<20	10.73	8.79	10.46	6.43	7.05	12.49		
20-24	6.66	6.55	5.98	7.18	5.79	2.74		
25-29	7.58	6.59	10.60	8.17	9.76	8.14		
30-34	11.32	10.12	15.71	16.09	14.20	21.57		
35-39	46.18	41.43	38.45	48.68	35.60	7.01		
40-44	177.94	126.86	167.58	143.88	96.49	62.11		
45+	361.45	295.86	195.31	145.63	88.76	0.00	▼	0.937

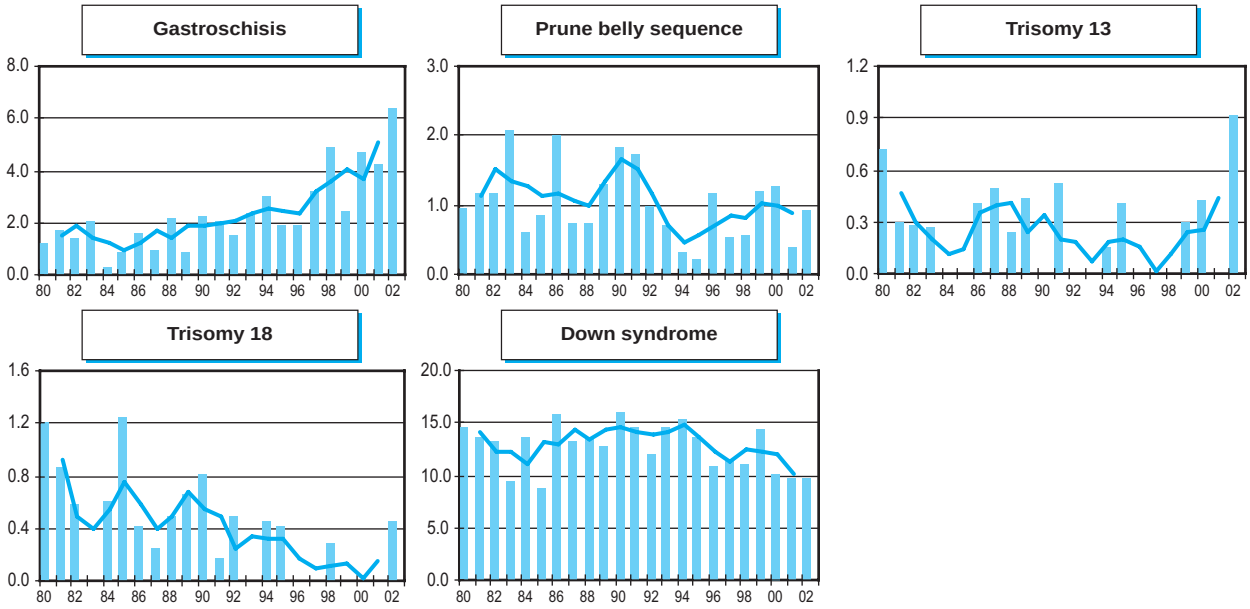
* = data include less than eight nad five years

Mexico: RYVEMCE

'Time trends 1980-2002 (Birth prevalence rates per 10,000)

Note: L+S rates, 3-year moving average trend

Note: L+S rates, 3-year moving average trend



Note: L+S rates, 3-year moving average trend

New Zealand

New Zealand Birth Defects Monitoring Program

History:
The Programme began in 1975 and became a full member of the ICBDMS in 1979.

Size and coverage:
The Programme covers all livebirths (approximately 56,000 per year) delivered or treated in a New Zealand publicly funded hospital. Only these data are included in the quarterly and annual reports to the ICBDMS. Data on stillbirths are retrospectively added to the database together with additional cases derived from the national perinatal and mortality databases. In late 1995 the definition of stillbirth was changed from 28 weeks completed gestation to 20 weeks or more gestation and/or 400g birthweight.

Legislation and funding:
The Programme is run and funded by Public Health Intelligence, Ministry of Health. Exposure information: No exposure data are currently available, but attempts are being made to obtain such data.

Background information:
General epidemiological characteristics for all births are available.

Address for further information:
Dr Barry Borman, Public Health Intelligence, Public Health, Directorate, Ministry of Health, PO Box 5013 Wellington, New Zealand.

Phone: 64-4-495-4379

Fax: 64-4-495-4401

E-mail: barry_borman@moh,govt.nz

New Zealand, 2002

Live births (L)	55,214
Stillbirths (S)	325
Total births	55539
Number of terminations of pregnancy (ToP) for birth defects	nr

Birth Defects	Number of cases			Rates*10.000		O/E	YB	Remark
	L	S	ToP	L+S	L+S+ToP	L+S		
Anencephaly	3	nr	nr	0.54	nc	1.11	10	
Spina bifida	12	nr	nr	2.16	nc	0.76	7	
Encephalocele	2	nr	nr	0.36	nc	0.71	13	
Microcephaly	14	nr	nr	2.52	nc	0.88	6	
Arhinencephaly / Holoprosencephaly	nr	nr	nr	nc	nc	nc		
Hydrocephaly	20	nr	nr	3.60	nc	1.02	22	
Total Anophthalmos / Microphthalmos (include unspecified)	8	nr	nr	1.44	nc	2.13	6	
Anophthalmos	1	nr	nr	0.18	nc	nc		
Microphthalmos	7	nr	nr	1.26	nc	1.87	6	
Total Anotia / Microtia (include unspecified)	nr	nr	nr	nc	nc	nc		
Anotia	nr	nr	nr	nc	nc	nc		
Microtia	nr	nr	nr	nc	nc	nc		
Transposition of great vessels	30	nr	nr	5.40	nc	1.08	6	
Tetralogy of Fallot	15	nr	nr	2.70	nc	0.59	4	
Hypoplastic left heart syndrome	4	nr	nr	0.72	nc	0.55	9	
Coarctation of aorta	21	nr	nr	3.78	nc	1.58	4	
Choanal atresia, bilateral	9	nr	nr	1.62	nc	1.58	6	
Cleft palate without cleft lip	55	nr	nr	9.90	nc	1.02	5	
Cleft lip with or without cleft palate	29	nr	nr	5.22	nc	1.09	13	
Oesophageal atresia / stenosis with or without fistula	5	nr	nr	0.90	nc	0.45	22	
Small intestine atresia / stenosis	nr	nr	nr	nc	nc	nc		
Anorectal atresia / stenosis	18	nr	nr	3.24	nc	1.30	22	
Undescended testis	438	nr	nr	78.86	nc	1.03	3	
Hypospadias + epispadias	163	nr	nr	29.35	nc	1.06	4	
Epispadias	nr	nr	nr	nc	nc	nc		
Indeterminate sex	2	nr	nr	0.36	nc	0.68	5	
Renal agenesis	14	nr	nr	2.52	nc	0.75	5	
Cystic kidney	26	nr	nr	4.68	nc	0.78	6	
Bladder exstrophy	1	nr	nr	0.18	nc	0.43	5	
Polydactyly60	nr	nr	10.80	nc	1.27	2		
Total Limb reduction defects (include unspecified)	21	nr	nr	3.78	nc	1.45	18	
Transverse	nr	nr	nr	nc	nc	nc		
Preaxial	nr	nr	nr	nc	nc	nc		
Postaxial	nr	nr	nr	nc	nc	nc		
Intercalary	nr	nr	nr	nc	nc	nc		
Mixed	nr	nr	nr	nc	nc	nc		
Diaphragmatic hernia	11	nr	nr	1.98	nc	0.84	5	
Total Abdominal wall defects (include unspecified)	35	nr	nr	6.30	nc	1.80	8	▲
Omphalocele	nr	nr	nr	nc	nc	nc		
Gastroschisis	nr	nr	nr	nc	nc	nc		
Prune belly sequence	nr	nr	nr	nc	nc	nc		
Trisomy 13	3	nr	nr	0.54	nc	1.32	6	
Trisomy 18	11	nr	nr	1.98	nc	1.93	6	
Down syndrome, all ages (include age unknown)	78	nr	nr	14.04	nc	1.18	5	
<20	nr	nr	nr	nc	nc	nc		
20-24	nr	nr	nr	nc	nc	nc		
25-29	nr	nr	nr	nc	nc	nc		
30-34	nr	nr	nr	nc	nc	nc		
35-39	nr	nr	nr	nc	nc	nc		
40-44	nr	nr	nr	nc	nc	nc		
45+	nr	nr	nr	nc	nc	nc		

New Zealand, time trend analysis 1980-2002

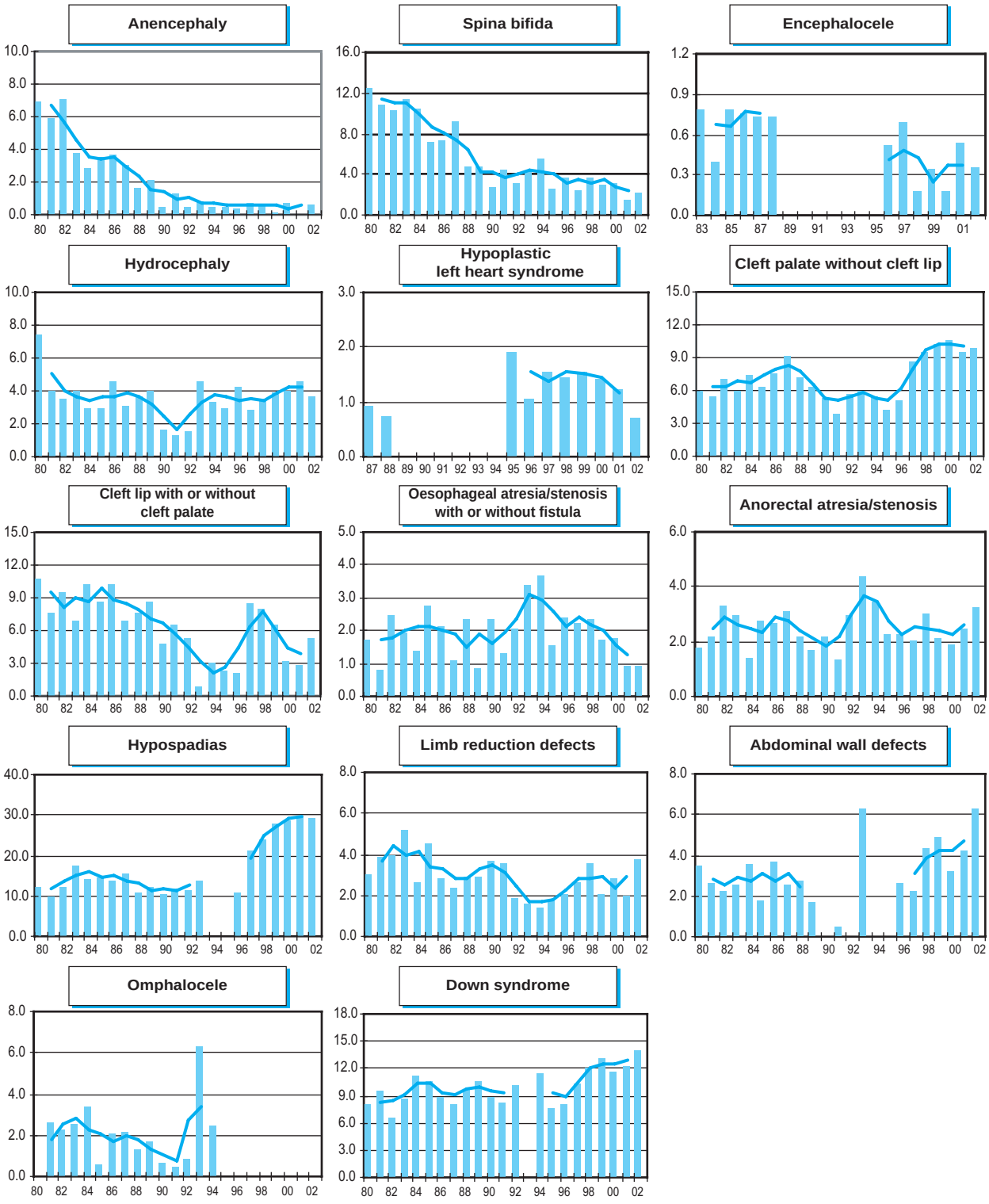
Birth prevalence rates: (L+S) * 10,000

	1974-81*	1982-86	1987-91	1992-96	1997-01	2002	Trend	RR
Births	95,943	252,560	286,647	291,957	283,638	55,539		
Anencephaly	6.36	4.12	1.71	0.55	0.42	0.54	▼	0.870
Spina bifida	11.67	9.38	5.13	3.84	2.71	2.16	▼	0.922
Encephalocele		0.69*	0.73*	0.26*	0.39	0.36		
Microcephaly				0.70*	3.31	2.52		
Arhinencephaly / Holoprosencephaly								
Hydrocephaly	5.63	3.60	2.72	3.32	3.74	3.60		
Total Anophthalmos / Microphthalmos (include unspecified)				0.52*	0.71	1.44		
Anophthalmos					0.00	0.18		
Microphthalmos				0.52*	0.71	1.26		
Total Anotia / Microtia (include unspecified)		0.69*	0.37*	0.52*	0.00*		▼	0.910
Anotia								
Microtia								
Transposition of great vessels			0.55*	5.92*	4.79	5.40	▲	1.087
Tetralogy of Fallot					4.56*	2.70		
Hypoplastic left heart syndrome			0.82*	1.48*	1.45	0.72		
Coarctation of aorta					2.39*	3.78	▲	1.229
Choanal atresia, bilateral				0.52*	1.13	1.62	▲	1.169
Cleft palate without cleft lip	5.73	6.89	6.35	5.27	9.70	9.90	▲	1.020
Cleft lip with or without cleft palate	9.17	9.11	6.87	2.67	5.78	5.22	▲	0.958
Oesophageal atresia / stenosis with or without fistula	1.25	2.14	1.60	2.64	1.80	0.90		
Small intestine atresia / stenosis				1.74*	1.80			
Anorectal atresia / stenosis	1.98	2.61	2.09	3.08	2.33	3.24		
Undescended testis (36 weeks of gestation or later)					69.03	78.86	▲	1.081
Hypospadias	10.94	14.41	12.11	11.83*	26.34	29.35	▲	1.047
Epispadias								
Indeterminate sex					0.53	0.36		
Renal agenesis		0.13*	0.64*		3.35	2.52	▲	1.106
Cystic kidney				5.05*	6.24	4.68		
Bladder exstrophy				0.17*	0.48*	0.18		
Polydactyly, preaxial				4.88*	8.52*	10.80	nc	
Total Limb reduction defects (include unspecified)	3.44	3.80	3.10	1.75	2.61	3.78	▼	0.978
Transverse								
Preaxial								
Postaxial								
Intercalary								
Mixed								
Diaphragmatic hernia		1.52*	1.46*		2.57*	1.98	▲	1.034
Total Abdominal wall defects (include unspecified)	3.02	2.77	1.85*	3.06*	3.77	6.30	▲	1.030
Omphalocele	2.61	2.18	1.26	3.28*				
Gastroschisis	0.00	0.36	0.73*				▲	1.411
Prune belly sequence								
Trisomy 13				0.35*	0.42	0.54		
Trisomy 18				0.70*	1.09	1.98		
Down syndrome, all ages (include age unknown)	8.76	9.23	9.14	9.33*	11.88	14.04	▲	1.018
<20	2.55	7.43	4.32*				▲	1.264
20-24	6.32	3.86	1.40*					
25-29	8.75	8.61	7.92*				▲	1.120
30-34	8.75	9.78	9.29*				▲	1.138
35-39	34.79	31.66	34.31*					
40-44	65.62	102.54	452.49*				▲	1.392
45+	0.00	215.83	0.00*					

* = data include less than eight and five years

New Zealand

Time trends 1980-2001 (Birth prevalence rates per 10,000)



Note: L+S rates, ToP rates — 3-year moving average trend

Northern Netherlands

EUROCAT Registration Northern Netherlands

History:
The Programme started in 1981, and became an associate member of ICBDMS in 1993.

Size and coverage:
In the beginning the Programme covered 7,500 births annually. Coverage was gradually increased to 19,000 births annually in the provinces Groningen, Friesland and Drenthe from 1989 onwards. Home deliveries (30% of births) are included.

Legislation and funding:
The Programme is funded by the Dutch Ministry of Public Health, Welfare and Sports. The registry is carried out in the Department of Medical Genetics of the University of Groningen.

Sources of ascertainment:
Obstetricians, paediatricians, clinical geneticists, surgeons, general practitioners, midwives, well-baby clinics, pathologists and the national obstetric registry send information to the registry on a voluntary basis. Informed consent of the parents is needed. Registry personnel are actively involved in data collection. No age limits are applied.

Exposure information:
Since 1997 parents are asked to fill out a questionnaire including questions on occupational activities and drug use. Besides, data from community pharmacies are used to collect maternal drug exposure data.

Background information:
General statistics are available from the Dutch Central Bureau of Statistics (CBS).

Address for further information:
Hermien de Walle, Department of Medical Genetics, Ant. Deusinglaan 4, 9713 AW Groningen, The Netherlands.

Phone: 31-50- 3633193/3632952

Fax: 31-50-3187268

E-mail: H.E.K.de.Walle@medgen.azg.nl

Northern Netherlands, 2002

Live births (L)	20273
Stillbirths (S)	159
Total births	20432
Number of terminations of pregnancy (ToP) for birth defects	22

Birth Defects	Number of cases			Rates*10.000		O/E	YB	Remark
	L	S	ToP	L+S	L+S+ToP	L+S		
Anencephaly	4	1	1	2.45	2.93	2.02	17	
Spina bifida	5	1	0	2.94	2.93	0.56	21	
Encephalocele	1	0	0	0.49	0.49	0.70	19	
Microcephaly	2	0	0	0.98	0.98	0.26	21	
Arhinencephaly / Holoprosencephaly	2	0	1	0.98	1.47	1.15	21	
Hydrocephaly	3	3	1	2.94	3.42	0.95	21	
Total Anophthalmos / Microphthalmos (include unspecified)	1	0	0	0.49	0.49	0.29	21	
Anophthalmos	1	0	0	0.49	0.49	1.79	21	
Microphthalmos	0	0	0	0.00	0.00	0.00	21	
Total Anotia / Microtia (include unspecified)	3	0	0	1.47	1.47	0.99	21	
Anotia	0	0	0	0.00	0.00	0.00	20	
Microtia	3	0	0	1.47	1.47	1.72	21	
Transposition of great vessels	6	0	0	2.94	2.93	0.74	21	
Tetralogy of Fallot	2	1	0	1.47	1.47	0.46	21	
Hypoplastic left heart syndrome	3	0	0	1.47	1.47	0.62	21	
Coarctation of aorta	8	0	0	3.92	3.91	0.91	11	
Choanal atresia, bilateral	0	0	0	0.00	0.00	0.00	21	
Cleft palate without cleft lip	9	0	2	4.40	5.38	0.65	21	
Cleft lip with or without cleft palate	23	0	1	11.26	11.73	0.77	21	
Oesophageal atresia / stenosis with or without fistula	7	0	0	3.43	3.42	1.14	21	
Small intestine atresia / stenosis	4	0	0	1.96	1.96	0.83	21	
Anorectal atresia / stenosis	0	0	0	0.00	0.00	0.00	21	
Undescended testis (36 weeks of gestation or later)	1	0	0	0.49	0.49	0.29	21	
Hypospadias	17	0	0	8.32	8.31	0.68	21	
Epispadias	0	0	0	0.00	0.00	0.00	21	
Indeterminate sex	1	0	0	0.49	0.49	2.33	21	
Renal agenesis	6	2	1	3.92	4.40	1.07	21	
Cystic kidney	5	2	1	3.43	3.91	0.95	21	
Bladder exstrophy	0	0	0	0.00	0.00	0.00	21	
Polydactyly, preaxial	0	0	0	0.00	0.00	0.00	21	
Total Limb reduction defects (include unspecified)	12	0	0	5.87	5.87	0.96	21	
Transverse	7	0	0	3.43	3.42	0.98	21	
Preaxial	1	0	0	0.49	0.49	0.65	21	
Postaxial	4	0	0	1.96	1.96	1.84	21	
Intercalary	0	0	0	0.00	0.00	0.00	21	
Mixed	0	0	0	0.00	0.00	0.00	21	
Diaphragmatic hernia	3	0	0	1.47	1.47	0.59	21	
Total Abdominal wall defects (include unspecified)	2	1	0	1.47	1.47	0.56	21	
Omphalocele	1	0	0	0.49	0.49	0.24	21	
Gastroschisis	1	1	0	0.98	0.98	1.54	21	
Prune belly sequence	0	0	0	0.00	0.00	0.00	21	
Trisomy 13	2	0	1	0.98	1.47	1.15	21	
Trisomy 18	2	1	5	1.47	3.91	0.91	21	
Down syndrome, all ages (include age unknown)	25	2	3	13.21	14.67	1.22	21	
<20	0	0	0	0.00	0.00	nc		
20-24	0	0	0	0.00	0.00	0.00	21	
25-29	6	0	0	10.45	10.45	1.36	21	
30-34	8	0	1	9.32	10.49	0.82	21	
35-39	6	1	0	20.43	20.43	0.87	21	
40-44	4	1	1	100.40	120.24	1.61	16	
45+	0	0	0	0.00	0.00	nc		

Northern Netherlands, time trend analysis 1981-2002

Birth prevalence rates: (L+S) * 10,000

	1974-81*	1982-86	1987-91	1992-96	1997-01	2002	Trend	RR
Births	7,877	42,560	82,023	96,139	100,453	20,432		
Anencephaly	1.27	4.46	1.34	0.83	1.29	2.45	▼	0.935
Spina bifida	5.08	5.40	7.56	4.68	3.98	2.94	▼	0.972
Encephalocele	1.27	1.64	0.37	1.04	0.40	0.49	▼	0.926
Microcephaly	3.81	4.46	3.29	3.64	3.88	0.98		
Arhinencephaly / Holoprosencephaly	1.27	0.94	1.10	0.52	0.90	0.98		
Hydrocephaly	1.27	3.29	2.68	3.43	3.19	2.94		
Total Anophthalmos / Microphthalmos (include unspecified)	1.27	2.11	1.83	2.08	1.10	0.49		
Anophthalmos	0.00	0.23	0.49	0.21	0.20	0.49		
Microphthalmos	1.27	1.88	1.34	1.87	0.90	0.00		
Total Anotia / Microtia (include unspecified)	2.54	2.58	1.22	1.46	1.19	1.47		
Anotia	2.54	2.35	0.61	1.04	0.80	0.00	▼	0.930
Microtia	1.27	0.70	0.98	0.94	0.70	1.47		
Transposition of great vessels	0.00	4.23	3.41	4.47	4.18	2.94		
Tetralogy of Fallot	3.81	3.76	3.41	3.22	2.69	1.47	▼	0.964
Hypoplastic left heart syndrome	2.54	2.58	2.44	2.29	2.29	1.47		
Coarctation of aorta	6.35	5.87	5.85	5.62	2.99	3.92	▼	0.967
Choanal atresia, bilateral	0.00	0.70	0.24	0.73	0.30	0.00		
Cleft palate without cleft lip	13.96	6.34	6.46	7.49	6.07	4.40		
Cleft lip with or without cleft palate	15.23	16.92	13.90	15.08	13.74	11.26		
Oesophageal atresia / stenosis with or without fistula	0.00	2.58	2.68	3.02	3.68	3.43		
Small intestine atresia / stenosis	2.54	2.35	2.32	2.81	1.99	1.96		
Anorectal atresia / stenosis	1.27	2.82	3.66	2.91	3.58	0.00		
Undescended testis (36 weeks of gestation or later)	1.27	2.11	2.07	1.35	1.49	0.49		
Hypospadias	19.04	13.63	9.88	10.40	14.73	8.32		
Epispadias	0.00	0.23	0.73	0.52	0.70	0.00		
Indeterminate sex	0.00	0.23	0.24	0.10	0.30	0.49		
Renal agenesis	3.81	3.76	3.29	4.06	3.48	3.92		
Cystic kidney	0.00	1.64	5.36	3.95	2.99	3.43		
Bladder exstrophy	0.00	0.23	0.24	0.10	0.20	0.00		
Polydactyly, preaxial	0.00	2.35	1.46	2.08	2.39	0.00		
Total Limb reduction defects (include unspecified)	6.35	6.81	5.36	7.28	5.38	5.87		
Transverse	5.08	3.99	2.56	4.16	3.29	3.43		
Preaxial	0.00	1.17	0.61	0.94	0.60	0.49		
Postaxial	1.27	0.47	1.22	1.46	0.80	1.96		
Intercalary	0.00	0.00	0.00	0.21	0.20	0.00		
Mixed	0.00	0.00	0.37	0.31	0.30	0.00		
Diaphragmatic hernia	2.54	2.35	2.44	2.39	2.69	1.47		
Total Abdominal wall defects (include unspecified)	3.81	2.58	2.56	2.70	2.59	1.47		
Omphalocele	2.54	1.41	2.19	2.50	1.69	0.49		
Gastroschisis	1.27	1.17	0.37	0.21	1.00	0.98		
Prune belly sequence	0.00	0.23	0.49	0.21	0.10	0.00		
Trisomy 13	0.00	0.94	1.10	0.94	0.60	0.98		
Trisomy 18	2.54	1.64	1.46	1.25	1.99	1.47		
Down syndrome, all ages (include age unknown)	10.16	11.75	10.97	10.24	11.06	13.21		
<20	0.00	0.00	0.00	0.00	0.00	0.00		
20-24	9.63	8.17	7.46	7.10	2.18	0.00		
25-29	5.93	8.10	10.10	4.33	8.67	10.45		
30-34	11.47	14.95	10.45	13.44	9.35	9.32		
35-39	54.79	38.20	20.08	21.49	23.27	20.43		
40-44	0.00	35.34	86.58*	71.74*	56.86*	100.40		
45+	0.00	0.00	0.00	0.00	0.00	0.00		

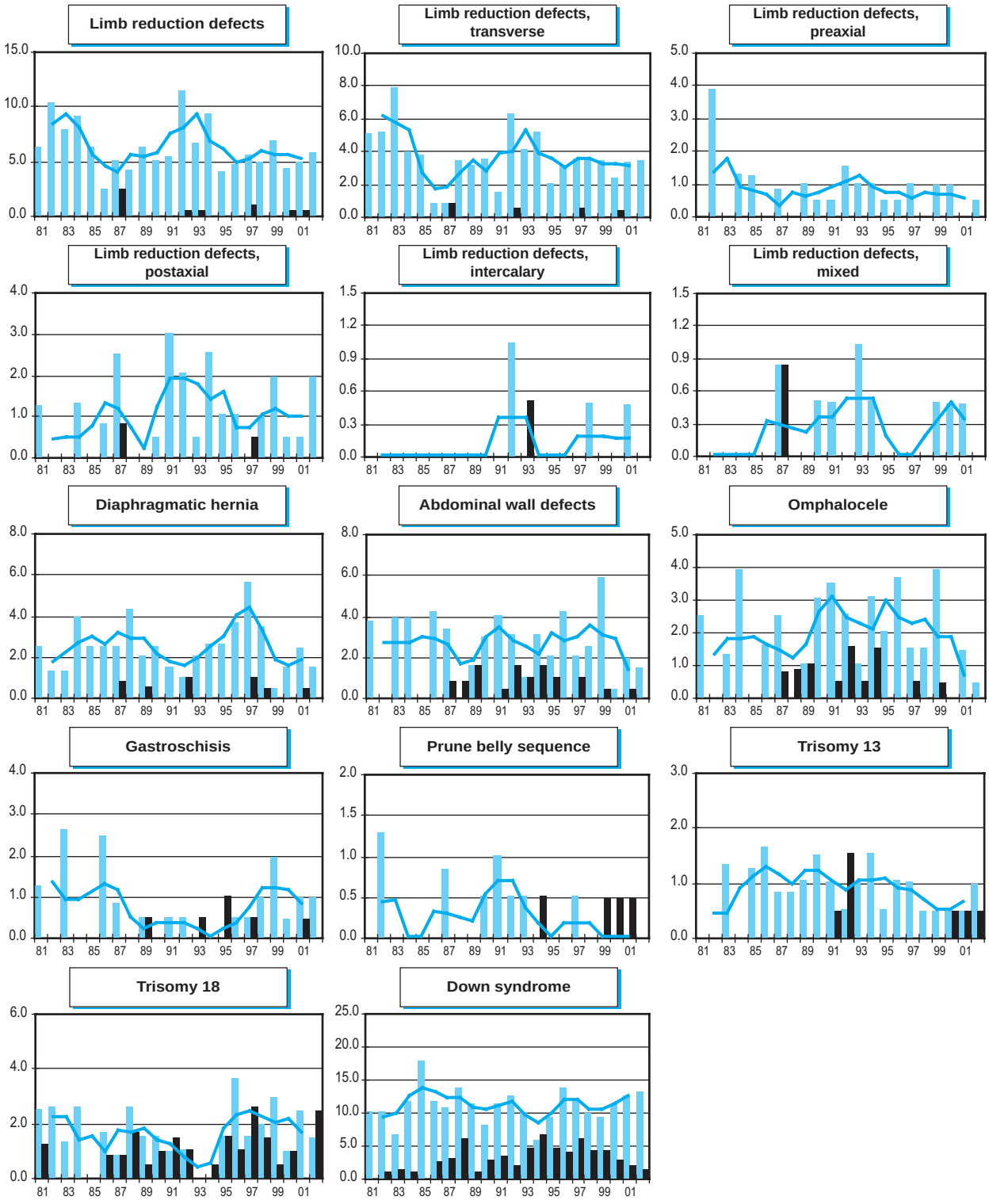
* = data include less than eight and five years

Northern Netherlands

'Time trends 1981-2002 (Birth prevalence rates per 10,000)

Note: L+S rates, ToP rates — 3-year moving average trend

Note: L+S rates, ToP rates — 3-year moving average trend



Note: L+S rates, ToP rates — 3-year moving average trend

Norway
Medical Birth Registry of Norway

History:
The Programme was started in 1967. The Programme was a founding member of the ICBDMS and is a full member.

Size and coverage:
The Programme covers all births in Norway, approximately 60,000 annual births. Stillbirths of 16 weeks or more gestation are included (12 weeks or more from 2002 onwards).

Legislation and funding:
The Programme is funded and run by the Norwegian Institute of Public Health, in close cooperation with the University of Bergen. Reporting is compulsory.

Sources of ascertainment:
The registry is based on the notification of births from the delivery units and since 1999 also from the neonatal units.

Exposure information: Some basic information, such as maternal disease and since 1999:smoking and occupation, is collected on all infants, malformed or not.

Background information:
All information available for reported malformed infants is also available for the total population of births.

Address for further information:
Lorentz M. Irgens, Department of Medical Birth Registry of Norway, Kalfarveien 31, NO-5018 Bergen, Norway.

Phone: 47-53204002

Fax: 47-53204001

E-mail: lorentz.irgens@mfr.uib.no

Norway, 2002

Live births (L)	55943
Stillbirths (S)	429
Total births	56372
Number of terminations of pregnancy (ToP) for birth defects	170

Birth Defects	Number of cases			Rates*10.000		O/E	YB	Remark
	L	S	ToP	L+S	L+S+ToP	L+S		
Anencephaly	3	2	25	0.89	5.31	0.63	15	
Spina bifida	5	0	13	0.89	3.18	0.23	14	▼
Encephalocele	2	0	7	0.35	1.59	0.75	28	
Microcephaly	1	0	1	0.18	0.35	0.29	28	
Arhinencephaly / Holoprosencephaly	2	0	0	0.35	0.35	0.88	24	
Hydrocephaly	14	0	9	2.48	4.07	0.81	21	
Total Anophthalmos / Microphthalmos (include unspecified)	0	0	0	0.00	0.00	0.00	28	
Anophthalmos	0	0	0	0.00	0.00	0.00	28	
Microphthalmos	0	0	0	0.00	0.00	0.00	28	
Total Anotia / Microtia (include unspecified)	7	0	0	1.24	1.24	1.99	12	
Anotia	5	0	0	0.89	0.88	5.38	28	▲
Microtia	2	0	0	0.35	0.35	0.75	12	
Transposition of great vessels	8	0	1	1.42	1.59	0.60	14	
Tetralogy of Fallot	18	0	1	3.19	3.36	1.34	4	
Hypoplastic left heart syndrome	10	0	6	1.77	2.83	0.96	12	
Coarctation of aorta	6	0	1	1.06	1.24	0.53	4	
Choanal atresia, bilateral	4	0	0	0.71	0.71	1.60	28	
Cleft palate without cleft lip	33	0	0	5.85	5.84	1.09	26	
Cleft lip with or without cleft palate	62	0	3	11.00	11.50	0.81	28	
Oesophageal atresia / stenosis with or without fistula	19	1	0	3.55	3.54	1.69	28	
Small intestine atresia / stenosis	6	0	0	1.06	1.06	0.90	28	
Anorectal atresia / stenosis	16	0	0	2.84	2.83	1.41	28	
Undescended testis (36 weeks of gestation or later)	155	0	0	27.50	27.41	1.06	2	
Hypospadias	107	0	0	18.98	18.92	1.27	26	
Epispadias	3	0	0	0.53	0.53	1.71	28	
Indeterminate sex	1	1	2	0.35	0.71	0.09	26	▼
Renal agenesis	0	0	3	0.00	0.53	0.00	24	
Cystic kidney	15	0	14	2.66	5.13	1.03	12	
Bladder exstrophy	1	0	1	0.18	0.35	0.56	28	
Polydactyly, preaxial	47	0	0	8.34	8.31	1.06	3	
Total Limb reduction defects (include unspecified)	15	0	1	2.66	2.83	0.74	3	
Transverse	10	0	1	1.77	1.95	0.82	6	
Preaxial	2	0	0	0.35	0.35	1.01	10	
Postaxial	1	0	0	0.18	0.18	0.56	10	
Intercalary	1	0	0	0.18	0.18	0.53	13	
Mixed	3	0	0	0.53	0.53	0.46	8	
Diaphragmatic hernia	12	0	1	2.13	2.30	0.92	28	
Total Abdominal wall defects (include unspecified)	20	2	9	3.90	5.48	1.00	28	
Omphalocele	8	0	5	1.42	2.30	0.71	28	
Gastroschisis	12	2	4	2.48	3.18	1.11	18	
Prune belly sequence	1	0	2	0.18	0.53	0.17	3	
Trisomy 13	2	0	0	0.35	0.35	0.45	3	
Trisomy 18	1	0	0	0.18	0.18	0.17	3	
Down syndrome, all ages (include age unknown)	65	1	11	11.71	13.62	1.12	28	
<20	1	0	0	7.25	7.25	2.33	28	
20-24	6	0	0	7.27	7.27	2.26	10	
25-29	10	0	3	5.30	6.89	0.77	28	
30-34	17	0	3	8.88	10.45	0.76	28	
35-39	25	0	1	33.48	34.81	1.09	28	
40-44	6	1	4	57.10	89.43	0.69	27	
45+	0	0	0	0.00	0.00	0.00	28	

Norway, time trend analysis 1974-2002

Birth prevalence rates: (L+S) * 10,000

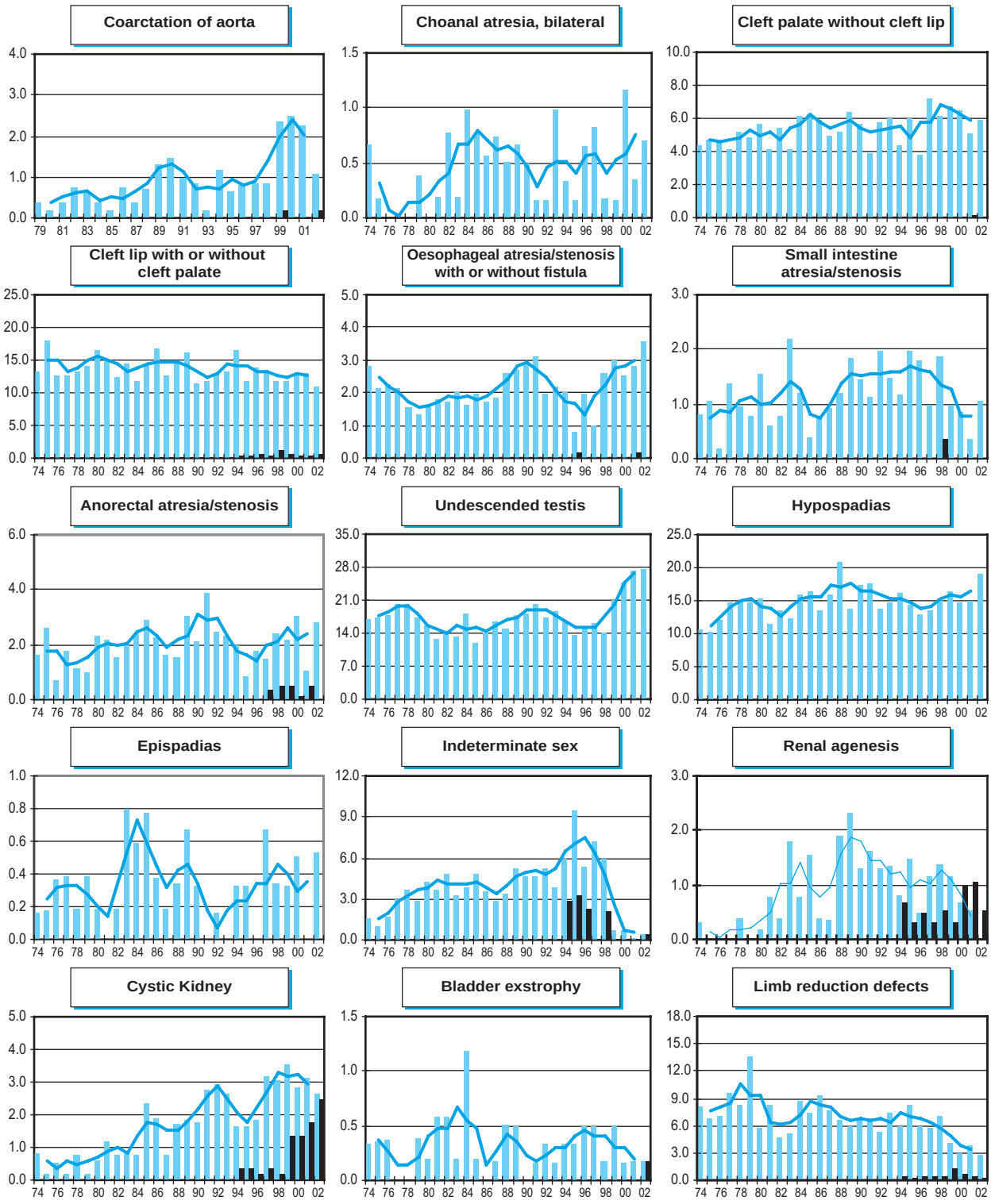
	1974-81	1982-86	1987-91	1992-96	1997-01	2002	Trend	RR
Births	430,040	256,935	295,188	303,100	295,668	56,372		
Anencephaly	4.07	2.92	1.46	1.65	1.08	0.89	▼	0.944
Spina bifida	5.14	5.18	4.51	3.93	3.28	0.89	▼	0.977
Encephalocele	0.49	0.74	0.47	0.40	0.30	0.35		
Microcephaly	0.60	0.74	0.54	0.53	0.68	0.18		
Arhinencephaly / Holoprosencephaly	0.05	0.47	0.47	0.63	0.30	0.35	▲	1.046
Hydrocephaly	4.07	3.78	3.08	2.54	2.98	2.48	▼	0.981
Total Anophthalmos / Microphthalmos (include unspecified)	0.19	0.43	0.54	0.26	0.34	0.00		
Anophthalmos	0.05	0.12	0.20	0.07	0.07	0.00		
Microphthalmos	0.14	0.31	0.34	0.20	0.27	0.00		
Total Anotia / Microtia (include unspecified)		0.76*	1.46	0.46	0.61	1.24	▼	0.942
Anotia	0.09	0.39	0.10	0.20	0.10	0.89		
Microtia		0.76*	1.36	0.26	0.51	0.35	▼	0.904
Transposition of great vessels	0.51	0.62	2.13	1.68	2.91	1.42	▲	1.066
Tetralogy of Fallot	0.16	0.35	0.85	1.02	2.10	3.19	▲	1.102
Hypoplastic left heart syndrome			1.12	1.72	2.03	1.77	▲	1.061
Coarctation of aorta	0.32*	0.54	0.98	0.73	1.76	1.06	▲	1.069
Choanal atresia, bilateral	0.19	0.66	0.51	0.46	0.54	0.71		
Cleft palate without cleft lip	4.67	5.57	5.22	5.15	6.32	5.85	▲	1.009
Cleft lip with or without cleft palate	14.49	13.89	13.18	13.63	12.58	11.00	▼	0.994
Oesophageal atresia / stenosis with or without fistula	1.95	1.79	2.64	1.78	2.37	3.55		
Small intestine atresia / stenosis	0.91	1.05	1.32	1.68	1.01	1.06		
Anorectal atresia / stenosis	1.67	2.22	2.47	1.88	2.03	2.84		
Undescended testis (36 weeks of gestation or later)	17.21	14.32	17.48	16.13	20.56	27.50	▲	1.010
Hypospadias	12.91	14.40	17.11	14.42	15.02	18.98	▲	1.009
Epispadias	0.23	0.54	0.30	0.16	0.37	0.53		
Indeterminate sex	2.65	4.05	4.20	5.97	2.94	0.35		
Renal agenesis	0.21	0.97	1.52	1.09	0.98	0.00	▲	1.033
Cystic kidney	0.56	1.32	1.80	2.14	3.15	2.66	▲	1.063
Bladder exstrophy	0.28	0.43	0.27	0.33	0.30	0.18		
Polydactyly, preaxial					7.85*	8.34	nc	
Total Limb reduction defects (include unspecified)	8.37	7.04	6.74	6.57	4.70	2.66	▼	0.978
Transverse			3.23*	3.83	2.06	1.77	▼	0.951
Preaxial			0.93*	0.40	0.30	0.35	▼	0.901
Postaxial			0.88*	0.40	0.24	0.18	▼	0.873
Intercalary			0.16*	0.49	0.27	0.18		
Mixed			0.65*	0.73	1.35	0.53	▲	1.067
Diaphragmatic hernia	2.09	2.26	2.57	2.28	2.44	2.13		
Total Abdominal wall defects (include unspecified)	3.58	3.50	3.93	4.55	4.09	3.90		
Omphalocele	2.30	1.95	1.96	2.08	1.59	1.42	▼	0.986
Gastroschisis	1.28	1.56	1.96	2.47	2.50	2.48	▲	1.030
Prune belly sequence					1.07*	0.18	nc	
Trisomy 13					0.79*	0.35	nc	
Trisomy 18					1.02*	0.18	nc	
Down syndrome, all ages (include age unknown)	9.95	10.90	10.60	9.67	11.63	11.71		
<20	2.55	4.43	3.59	3.01	2.55	7.25		
20-24	6.46	7.79	6.17	3.91	2.29	7.27	▼	0.978
25-29	7.86	6.92	5.50	7.06	6.67	5.30		
30-34	10.87	14.44	13.72	11.12	9.67	8.88		
35-39	36.75	34.27	33.39	19.47	33.35	33.48		
40-44	129.56	63.69	74.78	69.46	86.67	57.10	▼	0.979
45+	178.57	99.01	327.87	326.80	225.99	0.00		

* = data include less than eight and five years

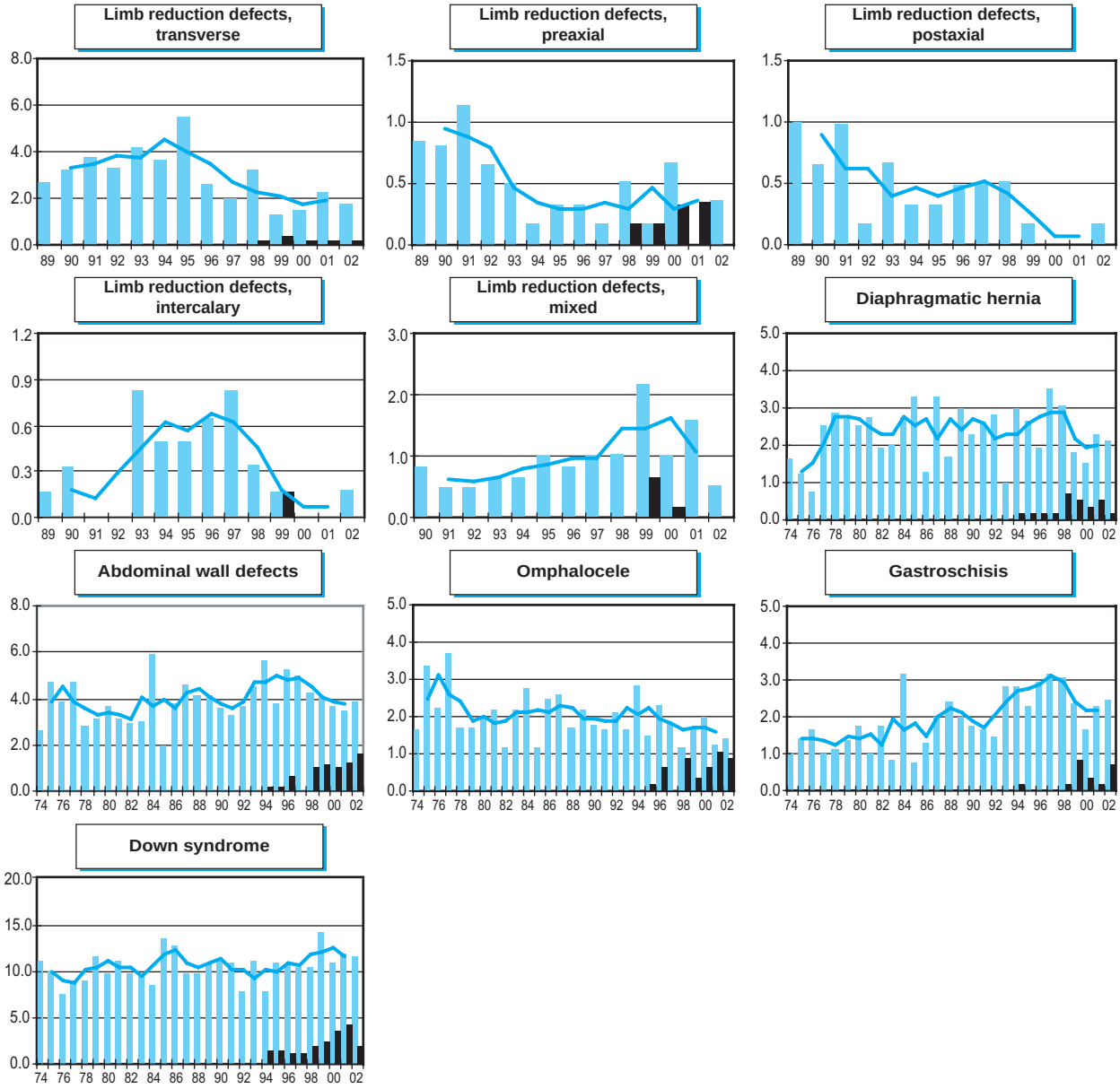
Norway

'Time trends 1974-2002 (Birth prevalence rates per 10,000)

Note: L+S rates, ToP rates — 3-year moving average trend



Note: L+S rates, ToP rates — 3-year moving average trend



Note: L+S rates, ToP rates 3-year moving average trend

Russia: MRRCM

Moscow Regional Registry of Congenital Malformation

History:
Moscow Regional Registry of Congenital Malformation (MRRCM) started the activity in 1999 and legally defined by the order of the Ministry of Health Care of Russian Federation. MRRCM became a Member of ICBDMS in 2001.

Size and coverage:
MRRCM is located in a section of Moscow Regional Medical genetic consultation by The Moscow Regional Research institute of obstetrics and gynecology (MONIIAG).
Director of the MONIIAG is Professor Vladislav Krasnopolsky.
The Head of the Moscow Regional Medical genetic consultation and Director of the Programme of MRRCM is Ludmila Jouthenko.

Size and coverage:
The Programme of Monitoring of Birth defects covers all births in Moscow Region. In 1999 MRRCM observed 45,000 births. There are about 55,000 births annually (2002). The information about babies and fetuses with birth defects are collected from 54 maternity hospitals also from all women's consultations and clinics, children's clinics. Prenatally diagnosed and terminated fetuses are also registered.

Legislation and funding:
Monitoring of the birth of fetuses and babies with congenital malformations is legally defined by the Order of the Ministry of Health Care of Russian Federation in 1999.

Sources of ascertainment:
Reporting is made by neonatologist during the first week of the infant's life in maternity hospitals and by pediatricians during the first year – in pediatric clinics and departments. Reports are collected form cytogenetic laboratories, pathology departments.

Exposure information:
No exposure information is routinely collected in the registry.

Background information:
Background information on all births is available from statistics department.

Address for further information:
Ludmila Joutchenko, Moscow Regional Research Institute of Obstetrics and Gynecology (MONIIAG), Pokrovka st 22 A, Moscow, Russia, 101000

Phone/Fax: 7-095-9215398

E-mail: mrrcm@mail.ru

Russia: Moscow region, 2002

Live births (L)	49920
Stillbirths (S)	382
Total births	50302
Number of terminations of pregnancy (ToP) for birth defects	123

Birth Defects	Number of cases			Rates*10.000		O/E	YB	Remark
	L	S	ToP	L+S	L+S+ToP	L+S		
Anencephaly	0	0	19	0.00	3.77			
Spina bifida	14	0	7	2.78	4.16			
Encephalocele	4	0	0	0.80	0.79			
Microcephaly	6	0	1	1.19	1.39			
Arhinencephaly / Holoprosencephaly	0	0	1	0.00	0.20			
Hydrocephaly	18	0	15	3.58	6.54			
Total Anophthalmos / Microphthalmos (include unspecified)	1	0	0	0.20	0.20			
Anophthalmos	1	0	0	0.20	0.20			
Microphthalmos	0	0	0	0.00	0.00			
Total Anotia / Microtia (include unspecified)	6	0	0	1.19	1.19			
Anotia	0	0	0	0.00	0.00			
Microtia	1	0	0	0.20	0.20			
Transposition of great vessels	11	0	1	2.19	2.38			
Tetralogy of Fallot	10	0	0	1.99	1.98			
Hypoplastic left heart syndrome	3	0	0	0.60	0.59			
Coarctation of aorta	0	0	0	0.00	0.00			
Choanal atresia, bilateral	0	0	0	0.00	0.00			
Cleft palate without cleft lip	29	0	0	5.77	5.75			
Cleft lip with or without cleft palate	39	0	0	7.75	7.73			
Oesophageal atresia / stenosis with or without fistula	9	0	0	1.79	1.78			
Small intestine atresia / stenosis	3	0	0	0.60	0.59			
Anorectal atresia / stenosis	14	0	0	2.78	2.78			
Undescended testis (36 weeks of gestation or later)	124	0	0	24.65	24.59			
Hypospadias	87	0	0	17.30	17.25			
Epispadias	0	0	0	0.00	0.00			
Indeterminate sex	5	0	0	0.99	0.99			
Renal agenesis	7	0	5	1.39	2.38			
Cystic kidney	16	0	1	3.18	3.37			
Bladder exstrophy	0	0	0	0.00	0.00			
Polydactyly, preaxial	57	0	0	11.33	11.30			
Total Limb reduction defects (include unspecified)	20	0	0	3.98	3.97			
Transverse	8	0	0	1.59	1.59			
Preaxial	3	0	0	0.60	0.59			
Postaxial	2	0	0	0.40	0.40			
Intercalary	0	0	0	0.00	0.00			
Mixed	1	0	0	0.20	0.20			
Diaphragmatic hernia	6	0	1	1.19	1.39			
Total Abdominal wall defects (include unspecified)	36	0	7	7.16	8.53			
Omphalocele	28	3	5	6.16	7.14			
Gastroschisis	8	2	2	1.99	2.38			
Prune belly sequence	0	1	0	0.20	0.20			
Trisomy 13	1	0	0	0.20	0.20			
Trisomy 18	0	0	0	0.00	0.00			
Down syndrome, all ages (include age unknown)	55	0	0	10.93	10.91			
<20	4	0	0	nc	nc			
20-24	12	0	0	nc	nc			
25-29	14	0	0	nc	nc			
30-34	7	0	0	nc	nc			
35-39	14	0	0	nc	nc			
40-44	4	0	0	nc	nc			
45+	0	0	0	nc	nc			

South Africa: SABDSS

South African Birth Defects Surveillance Systems

History:
The programme started in 1988 and became a full member of the ICBDMS in 1992.

Size and coverage:
The programme is hospital based covering 9 sentinel sites in the country with approximately 22,000 annual or 2% of all births in South Africa.

Legislation and Funding:
Participation in the programme is voluntary and is funded by the Department of National Health.

Sources of ascertainment:
Notifications are obtained from delivery units and paediatric units of the participating hospitals.

Exposure information:
No exposure information is routinely available.

Background information:
Total births for some participating hospitals are not accurately known.

Address for further information:
Rauf Sayed and David Bourne: Programme Directors, School of Public Health and Family Medicine, Medical School, University of Cape Town, Observatory 7925, South Africa.

Phone: 27-21-4066275

Fax: 27-21-4066163

Email: rauf@phfm.uct.ac.za
db@phfm.uct.ac.z

South Africa: SABDSS, 2002

aLive births (L)	21259
Stillbirths (S)	nr
Total births	nr
Number of terminations of pregnancy (ToP) for birth defects	nr

Birth Defects	Number of cases			Rates*10.000		O/E	YB	Remark
	L	S	ToP	L+S	L+S+ToP	L+S		
Anencephaly	8	nr	nr	3.76	nc	0.89	3	
Spina bifida	10	nr	nr	4.70	nc	0.39	2	▼
Encephalocele	1	nr	nr	0.47	nc	0.35	3	
Microcephaly	1	nr	nr	0.47	nc	0.63	3	
Arhinencephaly / Holoprosencephaly	3	nr	nr	1.41	nc	2.34	3	
Hydrocephaly	19	nr	nr	8.94	nc	1.91	3	
Total Anophthalmos / Microphthalmos (include unspecified)	nr	nr	nr	nc	nc	nc		
Anophthalmos	nr	nr	nr	nc	nc	nc		
Microphthalmos	nr	nr	nr	nc	nc	nc		
Total Anotia / Microtia (include unspecified)	nr	nr	nr	nc	nc	nc		
Anotia	nr	nr	nr	nc	nc	nc		
Microtia	nr	nr	nr	nc	nc	nc		
Transposition of great vessels	3	nr	nr	1.41	nc	1.17	3	
Tetralogy of Fallot	nr	nr	nr	nc	nc	nc		
Hypoplastic left heart syndrome	1	nr	nr	0.47	nc	1.56	3	
Coarctation of aorta	nr	nr	nr	nc	nc	nc		
Choanal atresia, bilateral	10	nr	nr	4.70	nc	1.84	3	
Cleft palate without cleft lip	2	nr	nr	0.94	nc	0.35	3	
Cleft lip with or without cleft palate	6	nr	nr	2.82	nc	0.81	3	
Oesophageal atresia / stenosis with or without fistula	12	nr	nr	5.64	nc	1.39	3	
Small intestine atresia / stenosis	10	nr	nr	4.70	nc	1.74	3	
Anorectal atresia / stenosis	10	nr	nr	4.70	nc	1.42	3	
Undescended testis (36 weeks of gestation or later)	2	nr	nr	0.94	nc	0.30	2	
Hypospadias	10	nr	nr	4.70	nc	1.20	3	
Epispadias	nr	nr	nr	nc	nc	nc		
Indeterminate sex	1	nr	nr	0.47	nc	0.52	2	
Renal agenesis	2	nr	nr	0.94	nc	0.63	3	
Cystic kidney	nr	nr	nr	nc	nc	nc		
Bladder exstrophy	2	nr	nr	0.94	nc	0.82	2	
Polydactyly, preaxial	nr	nr	nr	nc	nc	nc		
Total Limb reduction defects (include unspecified)	4	nr	nr	1.88	nc	0.60	3	
Transverse	nr	nr	nr	nc	nc	nc		
Preaxial	nr	nr	nr	nc	nc	nc		
Postaxial	nr	nr	nr	nc	nc	nc		
Intercalary	nr	nr	nr	nc	nc	nc		
Mixed	nr	nr	nr	nc	nc	nc		
Diaphragmatic hernia	3	nr	nr	1.41	nc	0.94	3	
Total Abdominal wall defects (include unspecified)	nr	nr	nr	nc	nc	nc	3	
Omphalocele	11	nr	nr	5.17	nc	1.18	3	
Gastroschisis	4	nr	nr	1.88	nc	1.04	3	
Prune belly sequence	3	nr	nr	1.41	nc	1.57	2	
Trisomy 13	4	nr	nr	1.88	nc	0.83	3	
Trisomy 18	nr	nr	nr	nc	nc	nc		
Down syndrome, all ages (include age unknown)	16	nr	nr	7.53	nc	0.76	2	
<20	nr	nr	nr	nc	nc	nc		
20-24	2	nr	nr	3.24	nc	1.04	3	
25-29	1	nr	nr	1.81	nc	0.35	3	
30-34	3	nr	nr	8.82	nc	0.87	2	
35-39	5	nr	nr	29.39	nc	1.30	3	
40-44	1	nr	nr	23.53	nc	0.45	3	
45+	nr	nr	nr	nc	nc	nc		

South America: ECLAMC

Latin American Collaborative Study of Congenital Malformations

History:
The Programme started in 1967 and has grown in size and coverage. The Programme became a full member of the ICBDMS in 1977.

Size and coverage:
The number of participating hospitals has grown from 20 in 1977 to 70 at the present time, distributed over most South American countries. The annual number of births covered is at present approximately 150,000, less than 1% of all births. Stillbirths of at least 500g birthweight have been included since 1978.

Legislation and funding:
The Registry is a research programme with voluntary participation of hospitals and funded by research grants provided from several sources, mainly the national research councils of Argentina and Brazil.

Sources of ascertainment:
Reporting is made by collaborating pediatricians at the delivery units of participating hospitals.

Exposure information:
The mother of each reported infant and the mother of a control infant - the next non-malformed infant born at that hospital with the same sex as the proband - are interviewed on various exposures, including drug usage and parental occupation.

Background information:
Background information is obtained partly from summarising tables of births in each participating hospitals, partly from the matched control newborns.

Research Projects
Starting in 2003:
Birth Defects Treatment and Prevention Program, Global Network for Women's and Children's Health Research. Tertiary prevention of complications in cleft lip and/or palate through sistematin pediatric intervention during the first two years of life. Funded by NICHD-NIH through the University of Iowa, a Subcontract HD-40561.

Monitoring the impact of folic acid food fortification on the birth prevalence rate of neural tube defects and other major anomalies in South American Countries. Funded by Centers for Disease Control, Purchase # 0000384785.

Bank of DNA from Latin American Collaborative Study of Congenital Malformations: ECLAMC. Funded by March of Dimes Foundation, Grant # FY-02-212.

Ending in 2003:
None.

Education and prevention promotion performed in 2003
Consultation with the Government of Argentina to discuss the monitoring of the impact on the frequency of neural tube defects by folic acid fortification of wheat flour, which started in November 2003.

Consultation with the Government of Brazil to discuss estrategies for food fortification with folic acid, to start on June 2004, and projects to monitor the impact on the frequency of neural tube defects. In Brazil, 2500 cases of spina bifida are born every year, and half of them could be easily prevented by adequate food fortification.

Address for further information:
Eduardo Castilla, ECLAMC/Dept. Genetica/ FIOCRUZ, C.P. 926, 20010-970 Rio de Janeiro, Brazil.

Phone: 55-21-25984358

Fax: 55-21-22604282

E-mail: castilla@centroin.com.br

South America: ECLAMC, 2002

Live births (L)	220562
Stillbirths (S)	2743
Total births	223305
Number of terminations of pregnancy (ToP) for birth defects	not permitted

Birth Defects	Number of cases			Rates*10.000		O/E	YB	Remark
	L	S	ToP	L+S	L+S+ToP	L+S		
Anencephaly	86	70		6.99		0.98	15	
Spina bifida	206	11		9.72		0.95	7	
Encephalocele	56	5		2.73		0.98	6	
Microcephaly	75	4		3.54		1.01	8	
Arhinencephaly / Holoprosencephaly	28	5		1.48		0.97	4	
Hydrocephaly	237	24		11.69		1.01	8	
Total Anophthalmos / Microphthalmos (include unspecified)	47	7		2.42		1.29	15	
Anophthalmos	11	2		0.58		1.57	28	
Microphthalmos	36	5		1.84		1.27	16	
Total Anotia / Microtia (include unspecified)	106	5		4.97		1.16	28	
Anotia	7	1		0.36		1.06	5	
Microtia	99	4		4.61		1.17	5	
Transposition of great vessels	33	1		1.52		0.89	4	
Tetralogy of Fallot	39	1		1.79		1.10	9	
Hypoplastic left heart syndrome	26	0		1.16		1.08	6	
Coarctation of aorta	23	1		1.07		1.16	9	
Choanal atresia, bilateral	6	0		0.27		1.63	28	
Cleft palate without cleft lip	91	3		4.21		0.97	8	
Cleft lip with or without cleft palate	285	22		13.75		1.10	8	
Oesophageal atresia / stenosis with or without fistula	88	4		4.12		1.28	11	
Small intestine atresia / stenosis	54	2		2.51		0.86	3	
Anorectal atresia / stenosis	106	12		5.28		1.03	8	
Undescended testis (36 weeks of gestation or later)	144	0		6.45		0.98	3	
Hypospadias	100	0		4.48		0.88	9	
Epispadias	6	0		0.27		1.00	28	
Indeterminate sex	36	10		2.06		1.10	27	
Renal agenesis	40	13		2.37		1.05	9	
Cystic kidney	91	4		4.25		1.00	6	
Bladder exstrophy	4	0		0.18		0.61	24	
Polydactyly, preaxial	87	3		4.03		1.31	9	
Total Limb reduction defects (include unspecified)	131	18		6.67		1.09	10	
Transverse	79	8		3.90		1.38	24	▲
Preaxial	24	7		1.39		0.96	10	
Postaxial	7	0		0.31		0.81	28	
Intercalary	6	0		0.27		0.56	28	
Mixed	9	1		0.45		0.86	28	
Diaphragmatic hernia	89	7		4.30		1.20	8	
Total Abdominal wall defects (include unspecified)	139	25		7.34		1.01	6	
Omphalocele	55	17		3.22		1.06	9	
Gastroschisis	55	1		2.51		0.90	7	
Prune belly sequence	28	2		1.34		1.21	9	
Trisomy 13	18	5		1.03		1.23	9	
Trisomy 18	40	9		2.19		1.12	7	
Down syndrome, all ages (include age unknown)	420	11		19.30		1.03	7	
<20	24	1		5.85		0.81	28	
20-24	63	1		10.27		1.19	12	
25-29	46	2		9.78		1.07	13	
30-34	60	2		17.98		1.13	28	
35-39	108	3		55.98		1.15	28	
40-44	102	2		181.75		1.15	28	
45+	10	0		276.24		0.94	28	

South America: ECLAMC, time trend analysis 1974-2002

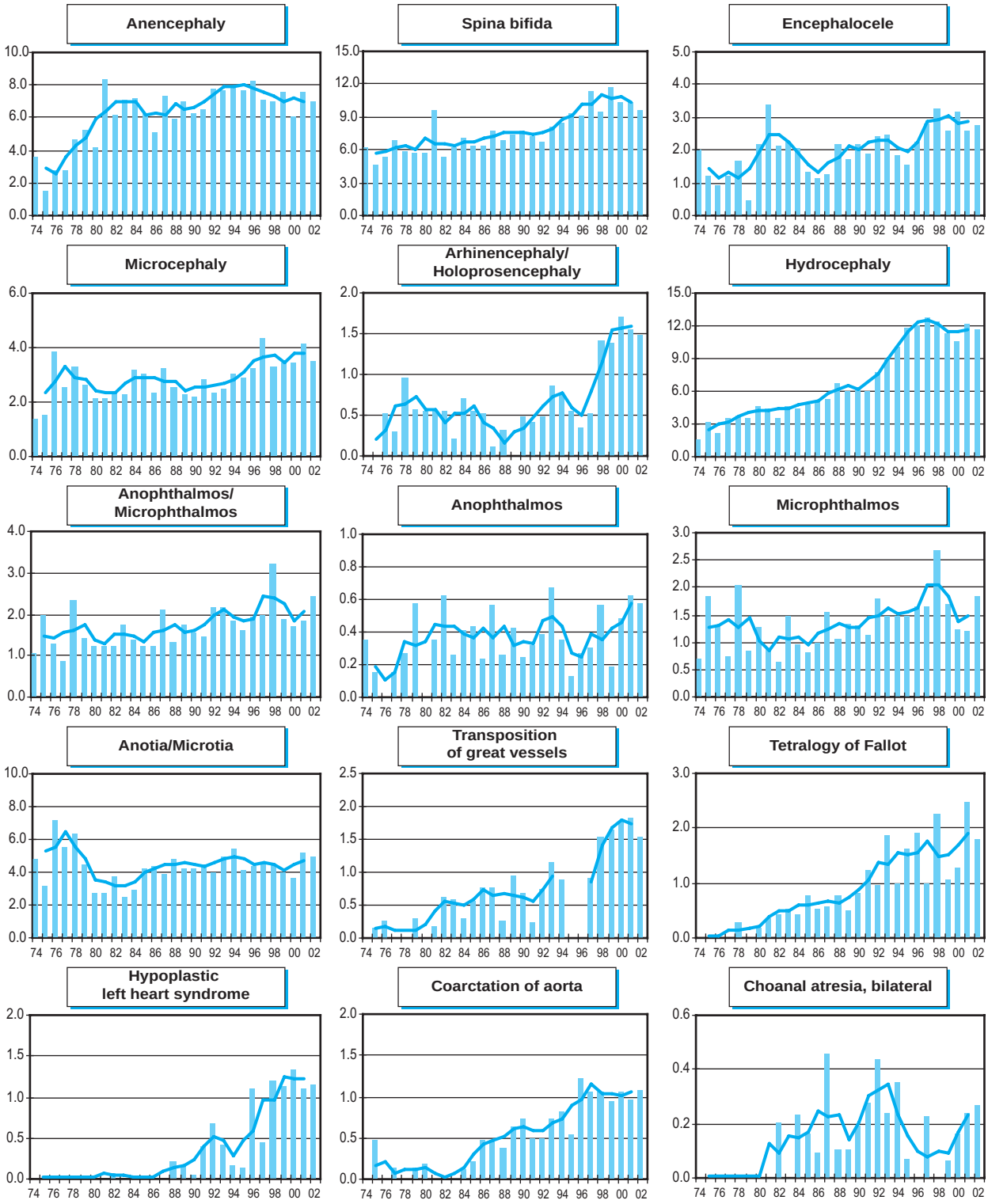
Birth prevalence rates: (L+S) * 10,000

	1974-81	1982-86	1987-91	1992-96	1997-01	2002	Trend	RR
Births	549,219	861,574	1,001,967	878,906	827,434	223,305		
Anencephaly	4.04	6.28	6.58	7.84	7.07	6.99	▲	1.018
Spina bifida	6.21	6.29	7.44	8.25	10.62	9.72	▲	1.026
Encephalocele	1.57	1.73	1.87	2.14	2.88	2.73	▲	1.026
Microcephaly	2.46	2.63	2.61	2.75	3.75	3.54	▲	1.018
Arhinencephaly / Holoprosencephaly	0.42	0.51	0.27	0.61	1.37	1.48	▲	1.068
Hydrocephaly	3.20	4.53	6.01	9.88	11.74	11.69	▲	1.056
Total Anophthalmos / Microphthalmos (include unspecified)	1.44	1.36	1.63	1.97	2.08	2.42	▲	1.020
Anophthalmos	0.24	0.38	0.36	0.39	0.45	0.58		
Microphthalmos	1.20	0.97	1.27	1.58	1.63	1.84	▲	1.020
Total Anotia / Microtia (include unspecified)	4.77	3.61	4.31	4.59	4.37	4.97		
Anotia					0.34	0.36		
Microtia					3.93	4.61		
Transposition of great vessels	0.11	0.57	0.57	0.74*	1.58	1.52	▲	1.076
Tetralogy of Fallot	0.09	0.53	0.79	1.46	1.66	1.79	▲	1.079
Hypoplastic left heart syndrome	0.00	0.01	0.17	0.50	1.08	1.16	▲	1.138
Coarctation of aorta	0.11	0.19	0.54	0.74	1.02	1.07	▲	1.081
Choanal atresia, bilateral	0.00	0.14	0.23	0.24	0.15	0.27	▲	1.034
Cleft palate without cleft lip	3.10	3.49	3.41	3.81	4.53	4.21	▲	1.016
Cleft lip with or without cleft palate	11.00	10.40	10.46	11.54	12.69	13.75	▲	1.009
Oesophageal atresia / stenosis with or without fistula	2.02	2.39	2.90	2.90	3.55	4.12	▲	1.024
Small intestine atresia / stenosis	0.71	1.56	1.52	1.90	2.62	2.51	▲	1.044
Anorectal atresia / stenosis	2.93	3.69	3.97	4.78	5.21	5.28	▲	1.025
Undescended testis (36 weeks of gestation or later)	1.78	4.02	4.61	4.95	6.03	6.45	▲	1.039
Hypospadias	3.71	4.87	3.66	4.86	5.23	4.48	▲	1.012
Epispadias	0.11	0.37	0.35	0.22	0.23	0.27		
Indeterminate sex	1.20	2.25	1.66	1.92	2.07	2.06	▲	1.011
Renal agenesis	0.44	0.71	1.11	1.92	2.41	2.37	▲	1.069
Cystic kidney	0.58	1.17	1.80	2.47	4.40	4.25	▲	1.077
Bladder exstrophy	0.13	0.26	0.29	0.32	0.35	0.18	▲	1.030
Polydactyly, preaxial	2.66	2.44	2.64	2.74	3.23	4.03	▲	1.014
Total Limb reduction defects (include unspecified)	4.32	5.26	4.90	5.72	6.51	6.67	▲	1.016
Transverse	2.28	2.62	2.56	2.88	3.24	3.90	▲	1.017
Preaxial	0.71	1.09	0.92	1.29	1.62	1.39	▲	1.031
Postaxial	0.31	0.41	0.28	0.49	0.44	0.31		
Intercalary	0.47	0.45	0.47	0.40	0.60	0.27		
Mixed	0.42	0.59	0.54	0.51	0.51	0.45		
Diaphragmatic hernia	0.86	1.35	1.99	2.58	3.76	4.30	▲	1.063
Total Abdominal wall defects (include unspecified)	1.78	3.16	3.29	5.23	7.44	7.34	▲	1.059
Omphalocele	1.29	2.19	2.26	2.73	3.21	3.22	▲	1.033
Gastroschisis	0.15	0.53	0.70	1.75	2.96	2.51	▲	1.100
Prune belly sequence	0.02	0.70	0.72	0.96	1.15	1.34	▲	1.059
Trisomy 13	0.18	0.55	0.42	0.66	0.94	1.03	▲	1.054
Trisomy 18	0.24	0.93	0.93	1.23	2.07	2.19	▲	1.066
Down syndrome, all ages (include age unknown)	14.71	14.53	15.80	16.35	18.95	19.30	▲	1.013
<20	7.79	6.23	7.08	7.29	8.01	5.85		
20-24	7.28	6.40	7.37	8.35	9.26	10.27	▲	1.016
25-29	8.20	7.67	7.39	8.86	10.09	9.78	▲	1.013
30-34	15.13	14.04	17.04	15.04	17.62	17.98		
35-39	53.69	42.10	48.65	45.92	55.03	55.98		
40-44	169.35	147.69	142.88	167.15	168.63	181.75	▲	1.007
45+	309.83	240.47	312.15	266.38	372.26	276.24		

* = data include less than five years

South America: ECLAMC

'Time trends 1974-2002 (Birth prevalence rates per 10,000)



Note: L+S rates, 3-year moving average trend

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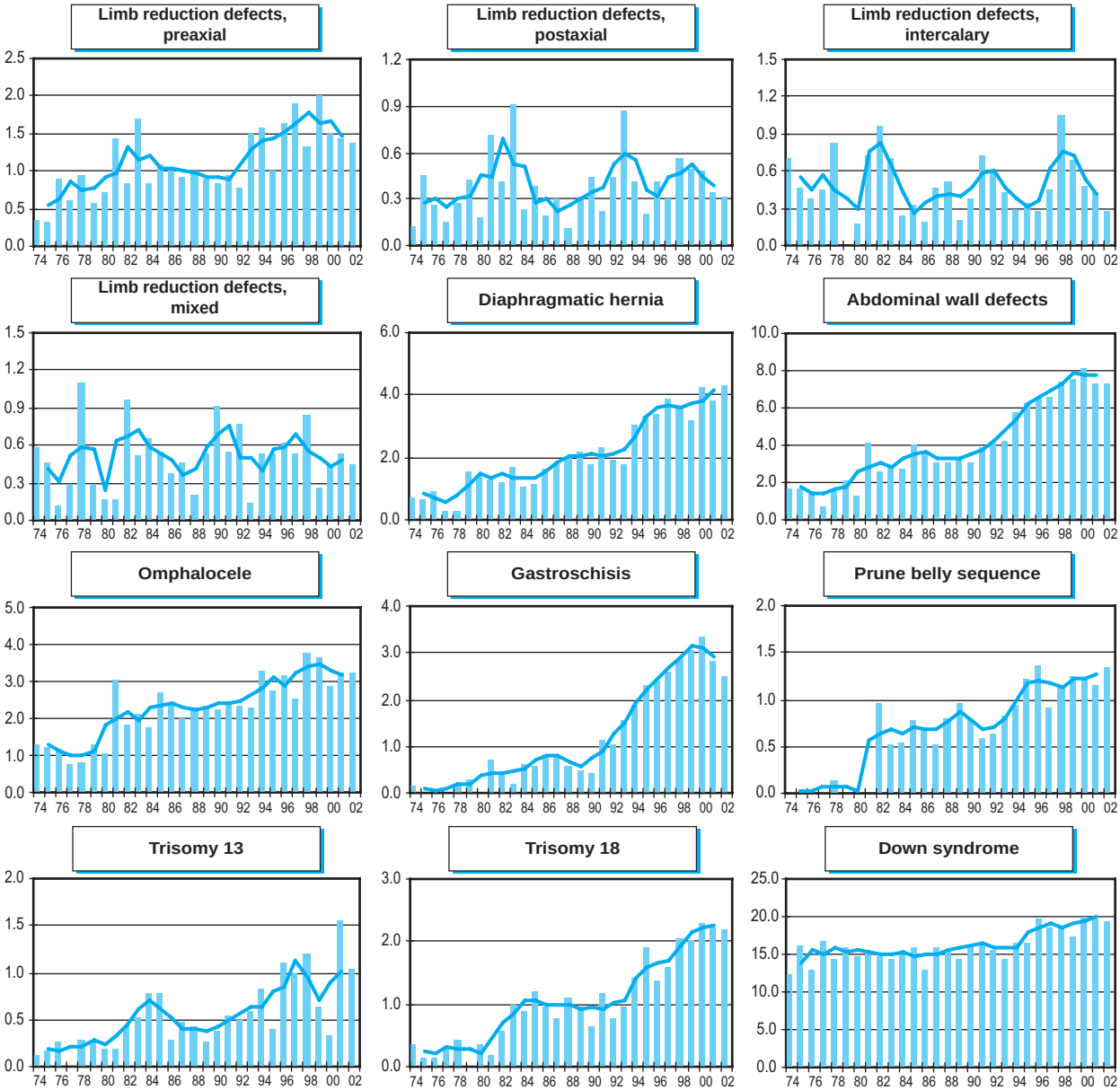

Note: L+S rates, 3-year moving average trend

7 Monitoring Systems

Spain: ECEMC
Spanish Collaborative Study of Congenital Malformations

History:
The programme was created in 1976 by Prof. Dr. María Luisa Martínez-Frías, as a hospital-based case-control study and surveillance system. It became a full member of the ICBDMS in 1979. In January 2002 the ECEMC Programme became integrated into the CIAC (Research Center on Congenital Anomalies), of the Instituto de Salud Carlos III (ISCIII) from the Ministerio de Sanidad y Consumo of Spain, and is also directed by Prof. Martínez-Frías. Activity of the CIAC is coordinated in agreement with the IIER (Institute of Research on Rare Diseases), of the ISCIII too. The ECEMC has 2 Teratogen Information Services since 1991, one for the general population and another one for physicians.

Size and coverage:
Reports are obtained from hospitals (82 at present) distributed all over Spain. The annual number of births surpasses 100,000, representing 25.6% of all Spanish births. Stillbirths of at least 24 weeks or 500 g. have been included since 1980.

Legislation and funding:
It is a research programme with voluntary participation of hospitals, and is financed mainly by the Spanish Administration and, partially, by non-governmental organisations.

Sources of ascertainment:
The detection period is the first 3 days of life, including major and/or minor/mild defects. Reports come from delivery units and paediatric departments of the participating hospitals. Mothers are interviewed directly to fill in the ECEMC standard protocols, which include more than 300 data for each child (family history, demographic and obstetrical data, prenatal exposures, etc), whether case or control. Controls are defined as the next non-malformed infant born at the same hospital that the case with the same sex as the malformed infant. In many instances, photographs, imaging studies, high-resolution bands karyotypes and molecular analysis when needed (which are performed at the central group of the ECEMC), and other complementary studies are available.

Exposure information:
The mother of each reported infant (case or control) is interviewed on various exposures (parental occupation, maternal acute or chronic diseases, drug usage, exposure to other chemical or physical factors) within the first three days after delivery.

Background information:
Total number of births by sex and number of twin pairs in each participating hospital are gathered. Other background information is obtained from the control material.

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Spain: ECEMC, 2002

Live births (L)	110500
Stillbirths (S)	454
Total births	110954
Number of terminations of pregnancy (ToP) for birth defects	nr

Birth Defects	Number of cases			Rates*10.000		O/E	YB	Remark
	L	S	ToP	L+S	L+S+ToP	L+S		
Anencephaly	1	0	nr	0.09	nc	0.34	4	
Spina bifida	8	0	nr	0.72	nc	0.35	7	▼
Encephalocele	4	0	nr	0.36	nc	1.98	6	
Microcephaly	11	0	nr	0.99	nc	0.52	19	
Arhinencephaly / Holoprosencephaly	1	0	nr	0.09	nc	0.19	22	
Hydrocephaly	18	1	nr	1.71	nc	0.66	22	
Total Anophthalmos / Microphthalmos (include unspecified)	12	0	nr	1.08	nc	0.80	8	
Anophthalmos	2	0	nr	0.18	nc	0.81	16	
Microphthalmos	12	0	nr	1.08	nc	0.84	9	
Total Anotia / Microtia (include unspecified)	28	0	nr	2.52	nc	1.53	21	
Anotia	0	0	nr	0.00	nc	0.00	21	
Microtia	28	0	nr	2.52	nc	1.71	17	
Transposition of great vessels	5	0	nr	0.45	nc	0.37	19	
Tetralogy of Fallot	14	0	nr	1.26	nc	1.08	15	
Hypoplastic left heart syndrome	2	1	nr	0.27	nc	0.39	22	
Coarctation of aorta	5	0	nr	0.45	nc	0.58	16	
Choanal atresia, bilateral	1	0	nr	0.09	nc	0.40	22	
Cleft palate without cleft lip	46	0	nr	4.15	nc	0.97	18	
Cleft lip with or without cleft palate	44	0	nr	3.97	nc	1.32	2	
Oesophageal atresia / stenosis with or without fistula	19	0	nr	1.71	nc	0.88	22	
Small intestine atresia / stenosis	11	0	nr	0.99	nc	0.89	22	
Anorectal atresia / stenosis	20	0	nr	1.80	nc	0.81	22	
Undescended testis (36 weeks of gestation or later)	19	0	nr	1.71	nc	0.65	20	
Hypospadias	36	1	nr	3.33	nc	1.71	17	▲
Epispadias	1	0	nr	0.09	nc	0.32	22	
Indeterminate sex	2	0	nr	0.18	nc	0.22	22	
Renal agenesis	0	0	nr	0.00	nc	0.00	4	
Cystic kidney	12	0	nr	1.08	nc	0.69	22	
Bladder exstrophy	0	0	nr	0.00	nc	0.00	22	
Polydactyly, preaxial	12	0	nr	1.08	nc	0.57	22	
Total Limb reduction defects (include unspecified)	41	0	nr	3.70	nc	0.67	7	▼
Transverse	15	0	nr	1.35	nc	0.55	17	
Preaxial	4	0	nr	0.36	nc	0.43	18	
Postaxial	2	0	nr	0.18	nc	1.01	22	
Intercalary	5	0	nr	0.45	nc	1.27	19	
Mixed	5	0	nr	0.45	nc	0.41	22	
Diaphragmatic hernia	5	0	nr	0.45	nc	0.40	5	
Total Abdominal wall defects (include unspecified)	7	0	nr	0.63	nc	0.50	10	
Omphalocele	5	0	nr	0.45	nc	0.56	10	
Gastroschisis	2	0	nr	0.18	nc	0.41	22	
Prune belly sequence	1	0	nr	0.09	nc	0.35	9	
Trisomy 13	4	0	nr	0.36	nc	0.83	22	
Trisomy 18	3	2	nr	0.45	nc	0.52	22	
Down syndrome, all ages (include age unknown)	91	0	nr	8.20	nc	0.92	3	
<20	1	0	nr	2.74	nc	1.64	9	
20-24	6	0	nr	5.13	nc	0.89	22	
25-29	13	0	nr	4.10	nc	0.60	22	
30-34	32	0	nr	7.63	nc	0.93	4	
35-39	27	0	nr	14.09	nc	1.00	3	
40-44	11	0	nr	40.77	nc	0.71	12	
45+	0	0	nr	0.00	nc	0.00	21	

nr = not reported
nc = not calculable

Spain: ECEMC, time trend analysis 1980-2002

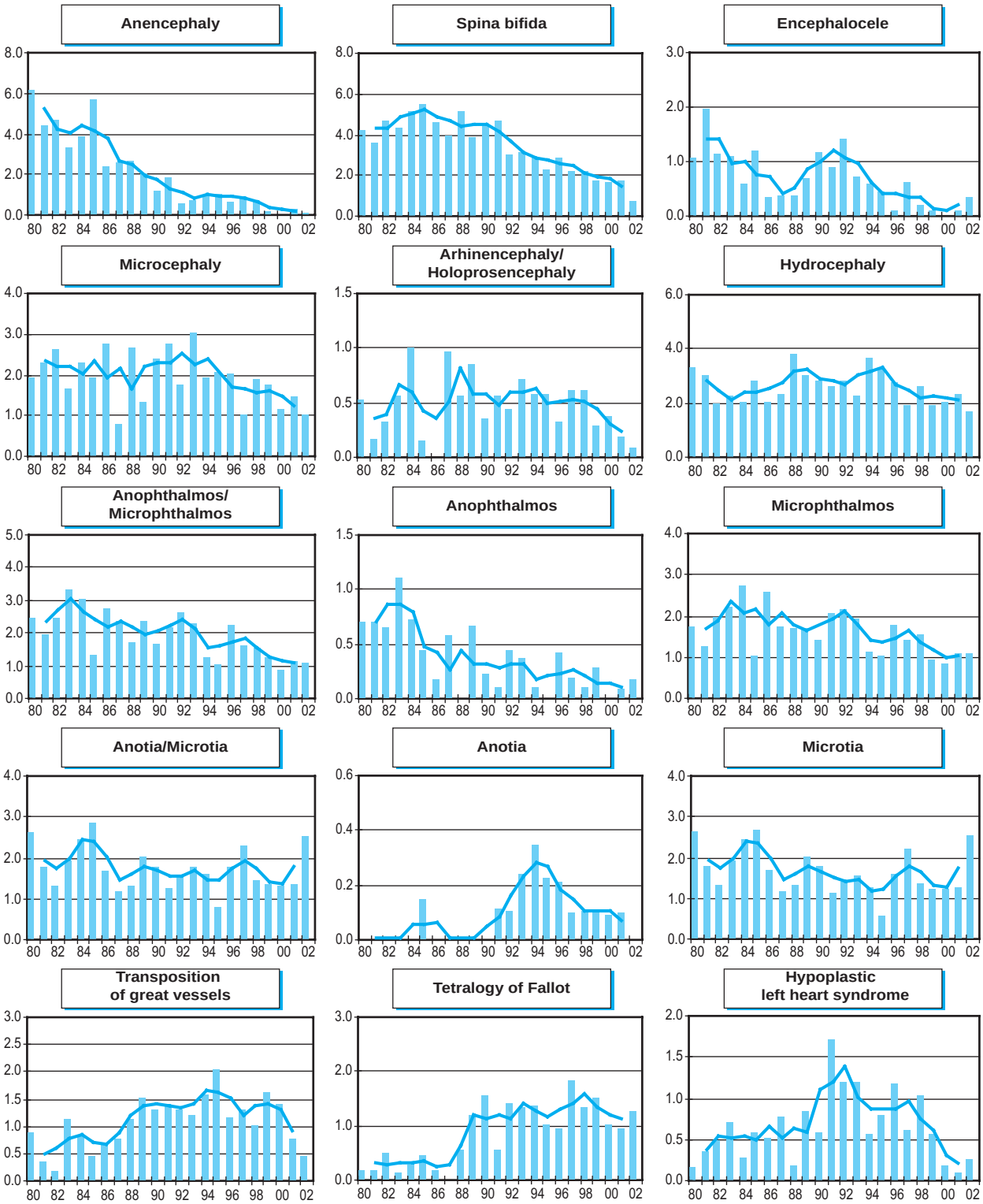
Birth prevalence rates: (L+S) * 10,000

	1974-81*	1982-86	1987-91	1992-96	1997-01	2002	Trend	RR
Births	113,012	327,623	334,870	443,187	509,009	110,954		
Anencephaly	5.31	4.03	1.94	0.77	0.37	0.09	▼	0.869
Spina bifida	3.89	4.88	4.42	2.84	1.91	0.72	▼	0.945
Encephalocele	1.50	0.89	0.78	0.65	0.20	0.36	▼	0.921
Microcephaly	2.12	2.23	2.09	2.14	1.43	0.99	▼	0.977
Arhinencephaly / Holoprosencephaly	0.35	0.43	0.63	0.52	0.41	0.09		
Hydrocephaly	3.19	2.23	2.90	2.98	2.16	1.71		
Total Anophthalmos / Microphthalmos (include unspecified)	2.21	2.59	2.03	1.90	1.28	1.08	▼	0.962
Anophthalmos	0.71	0.64	0.30	0.27	0.14	0.18	▼	0.912
Microphthalmos	1.50	2.11	1.73	1.62	1.16	1.08	▼	0.971
Total Anotia / Microtia (include unspecified)	2.21	2.08	1.52	1.51	1.55	2.52		
Anotia	0.00	0.03	0.03	0.23	0.10	0.00		
Microtia	2.21	2.05	1.49	1.29	1.45	2.52		
Transposition of great vessels	0.62	0.67	1.25	1.47	1.24	0.45		
Tetralogy of Fallot	0.18	0.31	0.84	1.22	1.34	1.26	▲	1.062
Hypoplastic left heart syndrome	0.27	0.52	0.90	0.99	0.49	0.27	▲	
Coarctation of aorta	0.71	0.24	0.66	0.79	0.86	0.45		1.034
Choanal atresia, bilateral	0.00	0.15	0.51	0.18	0.18	0.09		
Cleft palate without cleft lip	4.96	4.88	5.05	4.31	3.77	4.15	▼	0.985
Cleft lip with or without cleft palate	5.93	5.71	5.76	5.26	3.73	3.97	▼	0.977
Oesophageal atresia / stenosis with or without fistula	1.68	2.41	1.85	2.14	1.57	1.71		
Small intestine atresia / stenosis	1.06	1.13	1.16	1.47	0.77	0.99		
Anorectal atresia / stenosis	2.48	2.66	1.97	2.10	2.20	1.80		
Undescended testis (36 weeks of gestation or later)	1.24	2.14	2.66	2.57	3.05	1.71	▲	1.016
Hypospadias	2.65	2.66	2.21	1.69	1.93	3.33		
Epispadias	0.53	0.24	0.42	0.16	0.26	0.09		
Indeterminate sex	0.53	1.16	1.08	0.65	0.67	0.18	▼	0.968
Renal agenesis	0.62	0.73	0.87	0.59	0.26	0.00	▼	0.942
Cystic kidney	1.50	1.13	1.67	1.67	1.69	1.08		
Bladder exstrophy	0.27	0.27	0.27	0.25	0.31	0.00		
Polydactyly, preaxial	1.77	1.86	1.97	1.87	1.93	1.08		
Total Limb reduction defects (include unspecified)	7.52	6.84	7.20	6.57	5.21	3.70	▼	0.980
Transverse	2.83	3.11	3.05	2.21	2.24	1.35	▼	0.976
Preaxial	1.15	1.13	0.93	0.90	0.67	0.36	▼	0.962
Postaxial	0.27	0.09	0.15	0.25	0.18	0.18		
Intercalary	0.53	0.46	0.33	0.59	0.16	0.45		
Mixed	1.50	0.95	1.28	1.08	1.04	0.45		
Diaphragmatic hernia	2.48	2.56	2.21	2.08	1.12	0.45	▼	0.951
Total Abdominal wall defects (include unspecified)	3.19	2.26	2.30	1.47	1.08	0.63	▼	0.945
Omphalocele	2.12	1.50	1.49	1.02	0.61	0.45	▼	0.942
Gastroschisis	0.80	0.40	0.48	0.36	0.41	0.18		
Prune belly sequence	0.44	0.55	0.66	0.38	0.20	0.09	▼	0.943
Trisomy 13	0.27	0.37	0.48	0.45	0.47	0.36		
Trisomy 18	0.44	1.34	0.90	0.81	0.67	0.45	▼	0.972
Down syndrome, all ages (include age unknown)	14.60	15.02	13.92	11.76	9.80	8.20	▼	0.973
<20	8.72	7.08	10.76	3.34	1.18	2.74	▼	0.942
20-24	8.44	5.86	5.27	5.69	4.72	5.13		
25-29	5.33	7.23	8.17	6.55	6.11	4.10		
30-34	12.31	11.74	14.28	12.88	9.04	7.63	▼	0.975
35-39	40.80	48.10	39.94	32.58	17.70	14.09	▼	0.939
40-44	117.61	189.43	129.80	51.00	51.98	40.77	▼	0.932
45+	163.27	246.91	137.93	265.49	2666.67*	0.00		

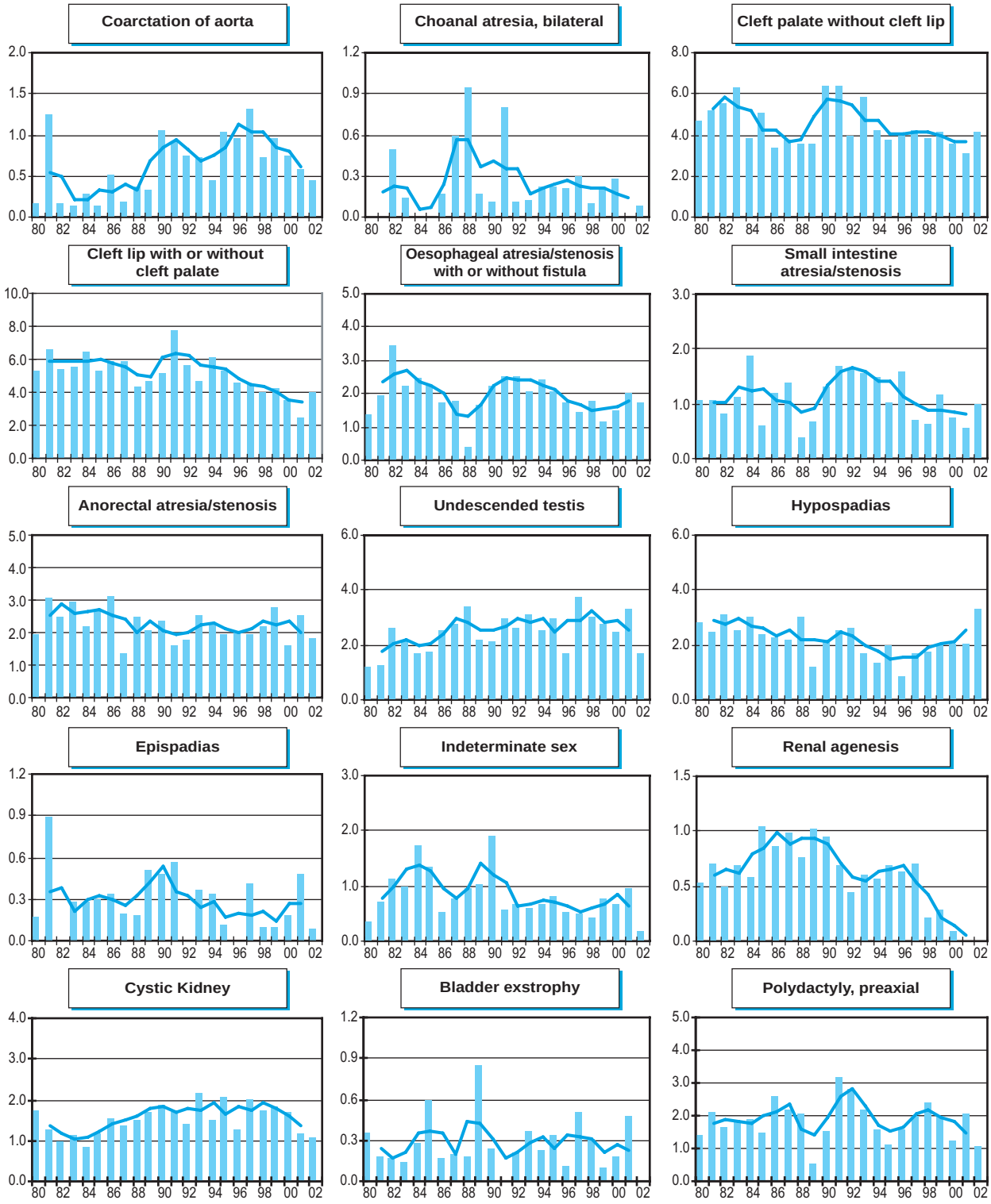
* = data include less than eight and five years* = data include less than eight and five years

Spain: ECEMC

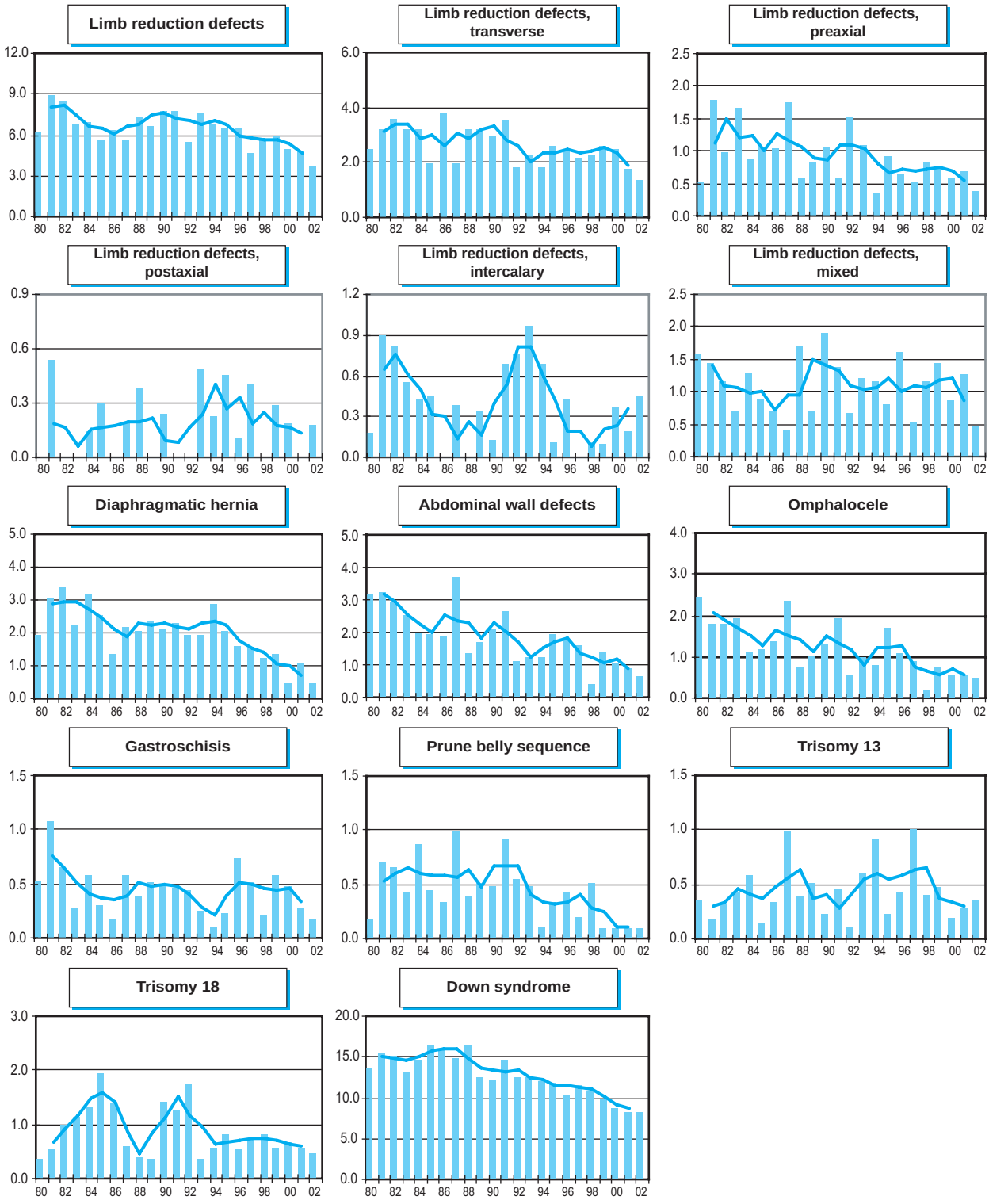
'Time trends 1980-2002 (Birth prevalence rates per 10,000)



Note: L+S rates, 3-year moving average trend



Note: L+S rates, 3-year moving average trend



Note: L+S rates, 3-year moving average trend

Sweden

The Swedish Registry of Congenital Malformations and the Medical Birth Registry.

History:
The Registry of Congenital Malformations started in 1964 and the Medical Birth Registry in 1973. The Programme was a founding member of the ICBDMS and contributed with data until 1994. The registry has a new regime from 1999 and is since then again a full member of the ICBDMS.

Size and coverage:
All births in Sweden are included, approximately 100,000-120,000 annual births. The definition of stillbirth in Sweden is more than 28 weeks. Since 1999 all fetal deaths with congenital malformations more than 22 weeks are reported to the Swedish Registry of Congenital Malformations. In 1999 a special fetal congenital anomalies surveillance system was started to include those fetuses with congenital malformations who were terminated as a result of prenatal diagnosis.

Legislation and funding:
Reporting is compulsory for children with malformations, but not for terminated pregnancies with fetuses with congenital malformations.

Sources of ascertainment:
Reports are received from delivery units, paediatric clinics, pathology departments, child cardiology clinics, and cytogenetic laboratories.

Exposure information:
Some exposure information for all births is available in the Medical Birth Registry; maternal occupation, socio-economic factors, maternal smoking, drug use during pregnancy, contraceptive usage, maternal diseases.

Background information:
Epidemiological background data are available on all birth in the Medical Birth Registry.

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Sweden, 2002

Live births (L)	95815
Stillbirths (S)	352
Total births	96167
Number of terminations of pregnancy (ToP) for birth defects	380

Birth Defects	Number of cases			Rates*10.000		O/E	YB	Remark
	L	S	ToP	L+S	L+S+ToP	L+S		
Anencephaly	2	0	43	0.21	4.66	0.81	3	
Spina bifida	24	0	27	2.50	5.28	1.47	3	
Encephalocele	2	0	8	0.21	1.04	0.95	2	
Microcephaly	1	0	0	0.10	0.10	0.26	3	
Arhinencephaly / Holoprosencephaly	2	1	10	0.31	1.35	1.41	3	
Hydrocephaly	10	0	20	1.04	3.11	0.72	3	
Total Anophthalmos / Microphthalmos (include unspecified)	2	0	1	0.21	0.31	0.38	3	
Anophthalmos	1	0	0	0.10	0.10	0.56	3	
Microphthalmos	1	0	1	0.10	0.21	0.28	3	
Total Anotia / Microtia (include unspecified)	4	0	0	0.42	0.41	0.31	3	▼
Anotia	3	0	0	0.31	0.31	0.25	3	▼
Microtia	1	0	0	0.10	0.10	1.41	3	
Transposition of great vessels	36	1	6	3.85	4.45	1.37	3	
Tetralogy of Fallot	24	0	1	2.50	2.59	1.03	3	
Hypoplastic left heart syndrome	17	0	4	1.77	2.18	0.94	3	
Coarctation of aorta	27	0	3	2.81	3.11	0.74	3	
Choanal atresia, bilateral	5	0	1	0.52	0.62	0.83	3	
Cleft palate without cleft lip	52	0	1	5.41	5.49	0.95	3	
Cleft lip with or without cleft palate	98	0	12	10.19	11.39	1.32	2	▲
Oesophageal atresia / stenosis with or without fistula	19	0	0	1.98	1.97	0.97	3	
Small intestine atresia / stenosis	21	1	1	2.29	2.38	1.17	3	
Anorectal atresia / stenosis	28	2	9	3.12	4.04	1.30	3	
Undescended testis (36 weeks of gestation or later)	nr	nr	nr	nc	nc	nc		
Hypospadias	214	0	0	22.25	22.17	1.09	3	
Epispadias	3	0	0	0.31	0.31	2.83	3	
Indeterminate sex	5	1	0	0.62	0.62	3.39	3	
Renal agenesis	8	1	4	0.94	1.35	0.82	3	
Cystic kidney	18	1	11	1.98	3.11	1.28	3	
Bladder exstrophy	4	0	0	0.42	0.41	2.26	3	
Polydactyly, preaxial	35	0	5	3.64	4.14	0.86	2	
Total Limb reduction defects (include unspecified)	50	0	9	5.20	6.11	1.36	3	
Transverse	41	0	8	4.26	5.08	1.78	3	▲
Preaxial	2	0	1	0.21	0.31	1.13	3	
Postaxial	0	0	0	0.00	0.00	0.00	3	
Intercalary	3	0	0	0.31	0.31	2.83	3	
Mixed	4	0	0	0.42	0.41	0.43	3	
Diaphragmatic hernia	12	0	8	1.25	2.07	0.64	3	
Total Abdominal wall defects (include unspecified)	18	1	19	1.98	3.94	0.78	3	
Omphalocele	12	1	12	1.35	2.59	1.11	3	
Gastroschisis	6	0	7	0.62	1.35	0.47	3	
Prune belly sequence	0	0	2	0.00	0.21	nc		
Trisomy 13	1	0	15	0.10	1.66	0.19	3	
Trisomy 18	16	0	31	1.66	4.87	1.07	3	
Down syndrome, all ages (include age unknown)	128	0	108	13.31	24.44	1.01	3	
<20	2	0	0	11.74	11.74	1.49	3	
20-24	7	0	2	5.77	7.42	0.95	3	
25-29	23	0	5	7.44	9.06	0.70	1	
30-34	55	0	12	16.40	19.97	1.54	3	▲
35-39	27	0	50	17.74	50.42	0.68	3	
40-44	11	0	35	42.82	176.65	0.88	3	
45+	0	0	4	0.00	380.95	0.00	3	

Ukraine: UABDP
Ukrainian-American Birth Defects Program

History:
The Programme was established in 1998. Birth defects surveillance began in 2000. It became an associate member of the ICBDMS in 2001.

Size and coverage:
The Programme monitors nearly 27,000 births in two provinces (Rivne and Volyn).

Legislation and funding:
Participation is an integral part of the State Health System. Funding is in part provided by the United States Agency for International Development, by the Ukrainian Ministry of Health, by the Oblasts (Province) Health Administration and private sources.

Sources of ascertainment:
Reports are obtained from delivery, neonatology and pediatric units. Hospital admission/discharge summaries are reviewed. Cytogenetic, pathology and other sources of data are also explored.

Exposure information:
Routine information collection is minimal except when ad hoc circumstances are noted. Plans for systematic collection of exposure data are being drawn.

Prenatal diagnosis information:
Birth defects data collection teams include specialists in prenatal diagnosis. However, rural areas are under served.

Rumors
During 2000-2002 in one of the oblasts covered by UABDP Registry we observed 3 cases of conjoined twins. Occurrence rate is 0,74 per 10000 (live births + stillbirths), prevalence – 1 case per 13509 births (live births + stillbirths).

Research projects
a. In 2003 we participated in the following ICBD MS projects - "Case-Control Study on Gastroschisis" and "International Database on Craniofacial Anomalies".

Education or promotion projects
a. Within the framework of Ukrainian-American Birth Defects Program 6 Resource Centers (RC) were established as a component of Birth Defects (BD) Surveillance, case and prevention programs, as well as to activate the creation of parental support organizations, other community-based resources and to expedite international partnership.
   The key elements of an RC are: trained informed officers who are English-competent and knowledgeable of electronic information sources and web-technology; trained medical/clinical experts cognizant of BD, genetics and teratology; access to printed, electronic or web-based information resources; access to national and international consultants; RC staff located in major pediatric health care centers who, therefore, implicitly partake in RC activities; easy access to RC by professionals and the public through the extension of operating hours beyond standard working hours, electronic publication and dissemination of information resources developed by local authors; partnership with medical and other teaching/training programs.
   The impact of RCs is evident from the large number of visitors (>10,000 per year) and utilization of RCs by a variety of clinicians, allied health pro fessionals, and parental organizations, among others. RC teams published and disseminated novel information resources (e.g. growth standards for infants with or without BD and other disorders) and serve as sites for teleconsultations linking rural medical care providers with Ukrainian and international expert.

b. Educational project "NTD recurrence prevention in women of risk-group" has been started since 2002 aimed at free distribution of folic acid pills, distribution of informational materials about NTD and the role of folic acid in NTD occurrence and recurrence prevention.

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Ukraine, 2002

Live births (L)	24805
Stillbirths (S)	115
Total births	24920
Number of terminations of pregnancy (ToP) for birth defects	nr

Birth Defects	Number of cases			Rates*10.000		O/E	YB	Remark
	L	S	ToP	L+S	L+S+ToP	L+S		
Anencephaly	0	2	20	0.80	8.83	0.58	2	
Spina bifida	12	1	12	5.22	10.03	1.15	2	
Encephalocele	0	0	5	0.00	2.01	0.00	2	
Microcephaly	10	0	nr	4.01	nc	1.70	2	
Arhinencephaly / Holoprosencephaly	0	0	nr	0.00	nc	nc		
Hydrocephaly	11	3	nr	5.62	nc	0.89	2	
Total Anophthalmos / Microphthalmos (include unspecified)	1	0	nr	0.40	nc	0.20	2	
Anophthalmos	0	0	nr	0.00	nc	0.00	2	
Microphthalmos	1	0	nr	0.40	nc	0.23	2	
Total Anotia / Microtia (include unspecified)	4	0	nr	1.61	nc	1.02	2	
Anotia	1	0	nr	0.40	nc	2.04	2	
Microtia	3	0	nr	1.20	nc	0.87	2	
Transposition of great vessels	11	0	nr	4.41	nc	1.12	2	
Tetralogy of Fallot	7	1	nr	3.21	nc	2.33	2	
Hypoplastic left heart syndrome	1	0	nr	0.40	nc	0.68	2	
Coarctation of aorta	1	0	nr	0.40	nc	0.51	2	
Choanal atresia, bilateral	0	0	nr	0.00	nc	nc		
Cleft palate without cleft lip	17	1	nr	7.22	nc	2.45	2	▲
Cleft lip with or without cleft palate	27	0	nr	10.83	nc	1.25	2	
Oesophageal atresia / stenosis with or without fistula	3	0	nr	1.20	nc	0.68	2	
Small intestine atresia / stenosis	6	0	nr	2.41	nc	1.74	2	
Anorectal atresia / stenosis	6	1	nr	2.81	nc	1.19	2	
Undescended testis (36 weeks of gestation or later)	109	0	nr	43.74	nc	1.19	2	
Hypospadias	9	0	nr	3.61	nc	1.02	2	
Epispadias	1	0	nr	0.40	nc	0.68	2	
Indeterminate sex	2	0	nr	0.80	nc	1.36	2	
Renal agenesis	0	3	nr	1.20	nc	1.53	2	
Cystic kidney	2	0	nr	0.80	nc	0.82	2	
Bladder exstrophy	2	0	nr	0.80	nc	1.02	2	
Polydactyly, preaxial	14	0	nr	5.62	nc	2.04	2	
Total Limb reduction defects (include unspecified)	11	0	nr	4.41	nc	1.02	2	
Transverse	4	0	nr	1.61	nc	0.63	2	
Preaxial	2	0	nr	0.80	nc	2.04	2	
Postaxial	0	0	nr	0.00	nc	0.00	2	
Intercalary	1	0	nr	0.40	nc	1.02	2	
Mixed	1	0	nr	0.40	nc	2.04	2	
Diaphragmatic hernia	4	1	nr	2.01	nc	0.93	2	
Total Abdominal wall defects (include unspecified)	10	0	nr	4.01	nc	2.54	2	
Omphalocele	5	0	nr	2.01	nc	2.04	2	
Gastroschisis	5	0	nr	2.01	nc	3.40	2	
Prune belly sequence	0	0	nr	0.00	nc	nc		
Trisomy 13	1	0	nr	0.40	nc	2.04	2	
Trisomy 18	0	0	nr	0.00	nc	0.00	2	
Down syndrome, all ages (include age unknown)	42	0	nr	16.85	nc	1.56	2	▲
<20	3	0	nr	10.63	nc	1.20	2	
20-24	10	0	nr	9.75	nc	1.72	2	
25-29	9	0	nr	13.04	nc	1.66	2	
30-34	8	0	nr	24.16	nc	1.56	2	
35-39	8	0	nr	62.89	nc	4.17	2	▲
40-44	2	0	nr	57.14	nc	0.42	2	
45+	2	0	nr	2500.00	nc	1.50	1	

nr = not repored
nc = not calculable

United Arab Emirates

Program: Congenital abnormality study group

History:
The Program was initiated in 1992, but continuous monitoring did not begin until 1994. It is now an Associate Member of the ICBDMS.

Size and coverage:
The Programme covers about 8000 births a year and includes all births occurring in three major hospitals of the Al Ain Medical District, situated in the eastern part of the Abu Dhabi Emirate. It has a population of about 270,000. Still births with a weight of more than 500 gm are included.

Legislation and funding:
The Programme is funded by the Faculty of Medicine and Health Sciences of the UAE University.

Sources of ascertainment:
In each hospital, there is a neonatologist who examines, identifies abnormalities and records at birth in a template provided. The diagnosis is further assisted by a clinical geneticist/dysmorphologist and pediatricians.

Exposure information:
Some basic information on exposure and maternal disease is collected in all cases.

Background information:
General epidemiological data for all births are available.

Activities
Members of the Congenital Abnormality Study Group had regular meetings in Al Ain and discussed issues and concerns of congenital anomalies in the area. We also had meetings with speakers drawn from local scientists as well as overseas visitors. In conjunction with the Development and Genetics Priority Research Group of the Faculty of Medicine and Health Sciences, UAE University we had an international meeting this year (December 9-11, 2004). It was titled "International Genetics Congress:Global Challenge, Regional Focus on Advances in Community and Preventive Genetics. Participants came from 32 countries. There were 52 platform presentations and 114 poster presentations in all. Participants enjoyed good science and an excellent social program during the three days of the meeting. Procedings of the Congress are being published in Community Medicine as a supplementary issue with Lihadh Al Gazali (UAE) and Alan H Bittles (Edith Cowan University, Perth Australia) as Editors.

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Padmanabhan Krishna Rengasamy
E-mail: padamanabhanr@uaeu.ac.ae

United Arab Emirates, 2002

Live births (L)	8331
Stillbirths (S)	72
Total births	8403
Number of terminations of pregnancy (ToP) for birth defects	not permitted

Birth Defects	Number of cases			Rates*10.000		O/E	YB	Remark
	L	S	ToP	L+S	L+S+ToP	L+S		
Anencephaly	0	6		7.14		1.27	6	
Spina bifida	10	1		13.09		1.74	6	
Encephalocele	2	2		4.76		1.58	6	
Microcephaly	9	0		10.71		4.52	6	▲
Arhinencephaly / Holoprosencephaly	0	0		0.00		0.00	6	
Hydrocephaly	7	2		10.71		1.99	6	
Total Anophthalmos / Microphthalmos (include unspecified)	1	0		1.19		5.56	6	
Anophthalmos	1	0		1.19		5.56	6	
Microphthalmos	0	0		0.00		nc		
Total Anotia / Microtia (include unspecified)	2	0		2.38		1.83	6	
Anotia	0	0		0.00		nc		
Microtia	2	0		2.38		1.83	6	
Transposition of great vessels	1	0		1.19		0.50	6	
Tetralogy of Fallot	4	0		4.76		3.03	4	
Hypoplastic left heart syndrome	2	0		2.38		0.61	6	
Coarctation of aorta	2	0		2.38		3.77	4	
Choanal atresia, bilateral	0	0		0.00		0.00	6	
Cleft palate without cleft lip	6	0		7.14		2.07	6	
Cleft lip with or without cleft palate	10	0		11.90		1.84	6	
Oesophageal atresia / stenosis with or without fistula	1	0		1.19		0.50	6	
Small intestine atresia / stenosis	4	0		4.76		1.23	6	
Anorectal atresia / stenosis	1	0		1.19		0.22	6	
Undescended testis (36 weeks of gestation or later)	nr	nr		nc		nc		
Hypospadias	nr	nr		nc		nc		
Epispadias	nr	nr		nc		nc		
Indeterminate sex	0	0		0.00		0.00	6	
Renal agenesis	2	0		2.38		1.10	6	
Cystic kidney	6	1		8.33		1.76	6	
Bladder exstrophy	0	0		0.00		0.00	6	
Polydactyly, preaxial	0	0		0.00		0.00	6	
Total Limb reduction defects (include unspecified)	1	0		1.19		0.47	5	
Transverse	1	0		1.19		1.89	4	
Preaxial	0	0		0.00		0.00	4	
Postaxial	0	0		0.00		0.00	4	
Intercalary	0	0		0.00		nc		
Mixed	0	0		0.00		nc		
Diaphragmatic hernia	8	0		9.52		1.77	6	
Total Abdominal wall defects (include unspecified)	0	1		1.19		0.37	6	
Omphalocele	0	0		0.00		0.00	6	
Gastroschisis	0	1		1.19		1.39	6	
Prune belly sequence	0	0		0.00		0.00	6	
Trisomy 13	0	0		0.00		0.00	6	
Trisomy 18	3	0		3.57		3.49	5	
Down syndrome, all ages (include age unknown)	16	0		19.04		0.95	6	
<20	0	0		nc		nc		
20-24	0	0		nc		nc		
25-29	2	0		nc		nc		
30-34	5	0		nc		nc		
35-39	2	0		nc		nc		
40-44	2	0		nc		nc		
45+	4	0		nc		nc		

United Arab Emirates, time trend analysis 1996-2002

Birth prevalence rates: (L+S) * 10,000

	1974-81	1982-86	1987-91	1992-96*	1997-01	2002	Trend	RR
Births				7,412	39,006	8,403		
Anencephaly				1.35	6.41	7.14		
Spina bifida				9.44	7.18	13.09	▲	1.167
Encephalocele				2.70	3.08	4.76		
Microcephaly				4.05	2.05	10.71	▲	1.265
Arhinencephaly / Holoprosencephaly				2.70	1.28	0.00		
Hydrocephaly				4.05	5.64	10.71		
Total Anophthalmos / Microphthalmos (include unspecified)				0.00	0.26	1.19		
Anophthalmos				0.00	0.26	1.19		
Microphthalmos				0.00	0.00	0.00		
Total Anotia / Microtia (include unspecified)				0.00	1.54	2.38		
Anotia				0.00	0.00	0.00		
Microtia				0.00	1.54	2.38		
Transposition of great vessels				5.40	1.79	1.19		
Tetralogy of Fallot					1.57*	4.76		
Hypoplastic left heart syndrome				4.05	3.85	2.38		
Coarctation of aorta					0.63*	2.38		
Choanal atresia, bilateral				1.35	1.03	0.00		
Cleft palate without cleft lip				2.70	3.59	7.14		
Cleft lip with or without cleft palate				8.09	6.15	11.90		
Oesophageal atresia / stenosis with or without fistula				2.70	2.31	1.19		
Small intestine atresia / stenosis				2.70	4.10	4.76		
Anorectal atresia / stenosis				8.09	4.87	1.19	▼	0.797
Undescended testis (36 weeks of gestation or later)								
Hypospadias								
Epispadias								
Indeterminate sex				0.00	2.31	0.00		
Renal agenesis				1.35	2.31	2.38		
Cystic kidney				2.70	5.13	8.33		
Bladder exstrophy				0.00	0.77	0.00		
Polydactyly, preaxial				0.00	0.51	0.00		
Total Limb reduction defects (include unspecified)				5.40	2.56	1.19	▼	0.757
Transverse					0.63*	1.19		
Preaxial					0.94*	0.00	▼	0.331
Postaxial					0.31*	0.00		
Intercalary					0.00*	0.00		
Mixed					0.00*	0.00		
Diaphragmatic hernia				5.40	5.38	9.52		
Total Abdominal wall defects (include unspecified)				1.35	3.59	1.19		
Omphalocele				1.35	2.56	0.00		
Gastroschisis				0.00	1.03	1.19		
Prune belly sequence				2.70	1.54	0.00		
Trisomy 13				1.35	1.79	0.00		
Trisomy 18				4.05	1.03	3.57		
Down syndrome, all ages (include age unknown)				14.84	21.02	19.04		
<20								
20-24								
25-29								
30-34								
35-39								
40-44								
45+								

* = data include less than five years

USA: Atlanta

Metropolitan Atlanta Congenital Defects Program

History:
The Programme started in 1967 and was a founding member of the ICBDMS. The Programme is a full member of the ICBDMS.

Size and coverage:
The Programme covers all births within a five county area in metropolitan Atlanta, Georgia. The annual number of births in this area is approximately 50,000. Stillbirths and terminations of at least 20 weeks gestations are included. Terminations less than 20 weeks are included for selected defects.

Legislation and funding:
In 1994 the Georgia Department of Human Resources (GDHR) added birth defects to the list of legally reportable conditions in Georgia. In 1997 the GDHR authorized the Birth Defects Branch at the Centers for Disease Control and Prevention (CDC) to act with and on its behalf to collect health information on children with birth defects. The Programme is funded by the Centers for Disease Control and Prevention.

Sources of ascertainment:
Multiple sources, such as delivery units, pediatric departments, laboratories, prenatal diagnostic centers and other specialties, are used to ascertained malformed infants born in the defined area with a follow-up to age six years.

Exposure information:
Exposure information is obtained by interview for mothers of reported malformed infants who participate in various research projects.

Background information:
Number of live births and demographic information on the five counties are obtained from vital statistics.

Address for further information:
Dave Erickson, Centers for Disease Control and Prevention, National Center on Birth Defects and Developmental Disabilities, Mailstop E-86, 1600 Clifton Road, Atlanta, GA 30333, USA

Phone: 1-404-498-3550

Fax: 1-404-495 3890

E-mail: DErickson@cdc.gov

USA: Atlanta, 2002

Live births (L)	50543
Stillbirths (S)	631
Total births	51174
Number of terminations of pregnancy (ToP) for birth defects	nr

Birth Defects	Number of cases			Rates*10.000		O/E	YB	Remark
	L	S	ToP	L+S	L+S+ToP	L+S		
Anencephaly	2	1	9	0.59	nc	0.35	15	
Spina bifida	16	1	4	3.32	nc	1.28	11	
Encephalocele	4	0	3	0.78	nc	0.76	15	
Microcephaly	36	0	0	7.03	nc	0.99	9	
Arhinencephaly / Holoprosencephaly	3	0	0	0.59	nc	0.70	28	
Hydrocephaly	24	2	3	5.08	nc	0.78	21	
Total Anophthalmos / Microphthalmos (include unspecified)	21	0	0	4.10	nc	1.25	16	
Anophthalmos	1	0	0	0.20	nc	0.38	28	
Microphthalmos	20	0	0	3.91	nc	1.34	20	
Total Anotia / Microtia (include unspecified)	5	0	0	0.98	nc	0.63	28	
Anotia	2	0	0	0.39	nc	2.22	28	
Microtia	3	0	0	0.59	nc	0.42	28	
Transposition of great vessels	28	0	0	5.47	nc	1.06	28	
Tetralogy of Fallot	31	1	0	6.25	nc	1.65	28	
Hypoplastic left heart syndrome	10	1	1	2.15	nc	0.82	28	
Coarctation of aorta	32	0	0	6.25	nc	1.35	27	
Choanal atresia, bilateral	3	0	0	0.59	nc	1.72	28	
Cleft palate without cleft lip	22	0	0	4.30	nc	0.77	28	
Cleft lip with or without cleft palate	43	0	2	8.40	nc	0.96	18	
Oesophageal atresia / stenosis with or without fistula	8	0	0	1.56	nc	0.68	28	
Small intestine atresia / stenosis	8	0	0	1.56	nc	0.90	28	
Anorectal atresia / stenosis	16	0	1	3.13	nc	0.83	28	
Undescended testis (36 weeks of gestation or later)	47	0	0	9.18	nc	0.61	2	▼
Hypospadias	45	0	0	8.79	nc	1.01	6	
Epispadias	2	0	0	0.39	nc	0.77	19	
Indeterminate sex	11	2	0	2.54	nc	1.90	23	
Renal agenesis	4	1	2	0.98	nc	0.99	17	
Cystic kidney	28	1	2	5.67	nc	1.10	11	
Bladder exstrophy	2	0	0	0.39	nc	1.59	28	
Polydactyly, preaxial	11	0	0	2.15	nc	0.86	28	
Total Limb reduction defects (include unspecified)	27	0	2	5.28	nc	0.99	28	
Transverse	18	0	0	3.52	nc	1.07	28	
Preaxial	4	0	1	0.78	nc	0.82	28	
Postaxial	1	0	0	0.20	nc	0.76	28	
Intercalary	0	0	0	0.00	nc	0.00	28	
Mixed	4	0	0	0.78	nc	1.16	9	
Diaphragmatic hernia	16	0	0	3.13	nc	1.34	28	
Total Abdominal wall defects (include unspecified)	21	3	2	4.69	nc	0.98	28	
Omphalocele	8	1	1	1.76	nc	0.73	20	
Gastroschisis	13	2	1	2.93	nc	1.39	28	
Prune belly sequence	1	0	0	0.20	nc	0.45	28	
Trisomy 13	5	1	8	1.17	nc	1.05	28	
Trisomy 18	9	5	10	2.74	nc	1.45	24	
Down syndrome, all ages (include age unknown)	61	3	20	12.51	nc	1.12	23	
<20	3	0	0	6.44	nc	0.90	22	
20-24	6	0	0	5.35	nc	0.74	22	
25-29	10	2	1	9.08	nc	1.24	22	
30-34	13	1	4	10.22	nc	0.91	20	
35-39	18	0	9	25.70	nc	1.00	15	
40-44	10	0	4	76.75	nc	1.25	22	
45+	1	0	0	149.25	nc	0.87	22	

USA: Atlanta, time trend analysis 1974-2002

Birth prevalence rates: (L+S) * 10,000

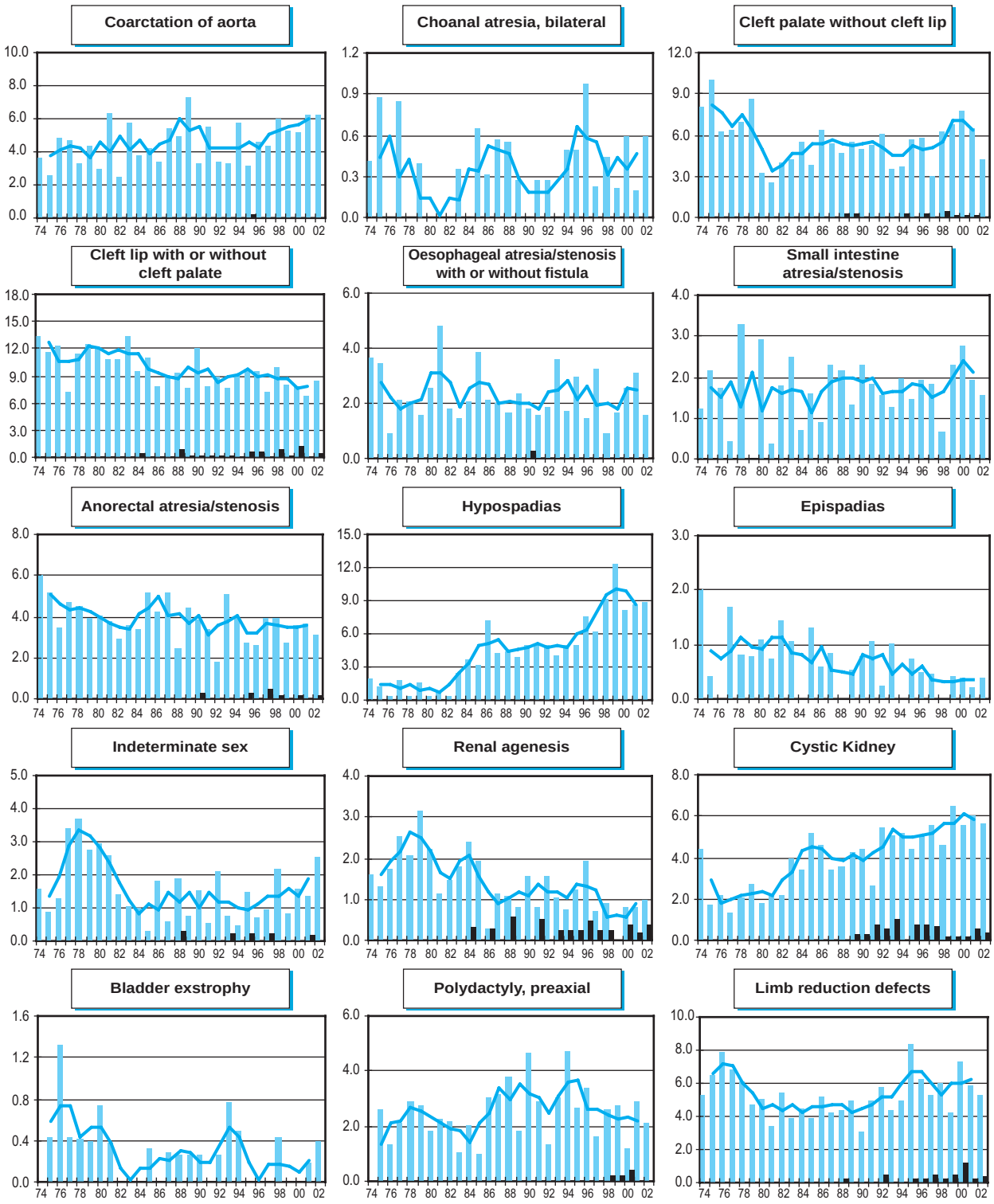
	1974-81	1982-86	1987-91	1992-96	1997-01	2002	Trend	RR
Births	198,119	148,828	186,757	199,529	237,898	51,174		
Anencephaly	5.20	3.29	2.30	1.20	1.60	0.59	▼	0.936
Spina bifida	6.92	6.85	4.50	2.56	2.56	3.32	▼	0.951
Encephalocele	2.22	2.22	1.23	1.15	0.76	0.78	▼	0.954
Microcephaly	5.70	5.58	5.46	5.91	7.69	7.03	▲	1.014
Arhinencephaly / Holoprosencephaly	0.56	0.74	1.34	1.05	0.55	0.59		
Hydrocephaly	10.55	8.00	5.62	5.56	6.89	5.08	▼	0.979
Total Anophthalmos / Microphthalmos (include unspecified)	4.64	4.37	3.16	3.76	2.69	4.10	▼	0.983
Anophthalmos	0.61	0.54	0.54	0.65	0.29	0.20		
Microphthalmos	4.04	3.83	2.62	3.11	2.40	3.91	▼	0.984
Total Anotia / Microtia (include unspecified)	1.41	1.61	1.77	1.55	1.43	0.98		
Anotia	0.15	0.20	0.11	0.20	0.21	0.39		
Microtia	1.26	1.41	1.66	1.40	1.22	0.59		
Transposition of great vessels	4.80	5.64	4.93	5.46	5.17	5.47		
Tetralogy of Fallot	3.18	3.83	4.12	4.11	3.70	6.25	▲	1.014
Hypoplastic left heart syndrome	2.47	2.49	3.00	2.41	2.77	2.15		
Coarctation of aorta	4.09	3.90	5.30	4.06	5.42	6.25	▲	1.014
Choanal atresia, bilateral	0.30	0.27	0.32	0.45	0.34	0.59		
Cleft palate without cleft lip	6.41	4.84	5.14	4.96	6.10	4.30		
Cleft lip with or without cleft palate	11.46	10.41	9.16	9.02	7.90	8.40	▼	0.984
Oesophageal atresia / stenosis with or without fistula	2.68	2.28	1.87	2.31	2.31	1.56		
Small intestine atresia / stenosis	1.51	1.48	1.98	1.65	1.93	1.56		
Anorectal atresia / stenosis	4.44	3.90	3.86	3.26	3.57	3.13	▼	0.987
Undescended testis (36 weeks of gestation or later)					15.13*	9.18	nc	
Hypospadias	1.06	3.56	4.50	5.31	8.95	8.79	▲	1.068
Epispadias	0.96	0.87	0.64	0.50	0.29	0.39	▼	0.953
Indeterminate sex	2.42	1.14	1.07	1.10	1.39	2.54		
Renal agenesis	1.97	1.55	1.07	1.30	0.63	0.98	▼	0.961
Cystic kidney	2.32	3.90	3.64	5.06	5.67	5.67	▲	1.034
Bladder exstrophy	0.50	0.07	0.21	0.30	0.13	0.39		
Polydactyly, preaxial	1.97	1.88	3.27	3.06	2.23	2.15		
Total Limb reduction defects (include unspecified)	5.65	4.57	4.34	5.96	5.76	5.28		
Transverse	3.48	3.36	2.62	4.01	2.94	3.52		
Preaxial	1.06	0.47	0.75	0.95	1.30	0.78		
Postaxial	0.25	0.13	0.32	0.30	0.25	0.20		
Intercalary	0.45	0.20	0.32	0.25	0.13	0.00	▼	0.949
Mixed	0.10	0.34	0.21	0.30	0.92	0.78	▲	1.072
Diaphragmatic hernia	2.42	2.35	2.95	1.90	2.14	3.13		
Total Abdominal wall defects (include unspecified)	5.45	5.38	4.87	4.36	4.20	4.69		
Omphalocele	3.84	3.43	2.14	2.16	2.14	1.76	▼	0.970
Gastroschisis	1.62	1.95	2.73	2.21	2.06	2.93		
Prune belly sequence	0.76	0.47	0.27	0.15	0.50	0.20		
Trisomy 13	1.06	1.28	1.07	1.00	1.18	1.17		
Trisomy 18	0.91	1.88	1.50	2.05	2.31	2.74	▲	1.034
Down syndrome, all ages (include age unknown)	9.84	9.81	10.71	11.13	12.06	12.51	▲	1.012
<20	10.62*	5.62	7.36	7.70	6.46	6.44		
20-24	6.78*	7.47	7.85	6.88	6.84	5.35		
25-29	11.33*	6.42	6.97	8.15	6.50	9.08		
30-34	17.63*	14.38	12.86	10.03	9.68	10.22	▼	0.977
35-39	31.52*	16.85	22.08	21.82	30.20	25.70		
40-44	106.38*	67.34	49.02	57.79	65.24	76.75		
45+	0.00*	0.00	0.00	241.94	196.85	149.25		

* = data include less than eight and five years

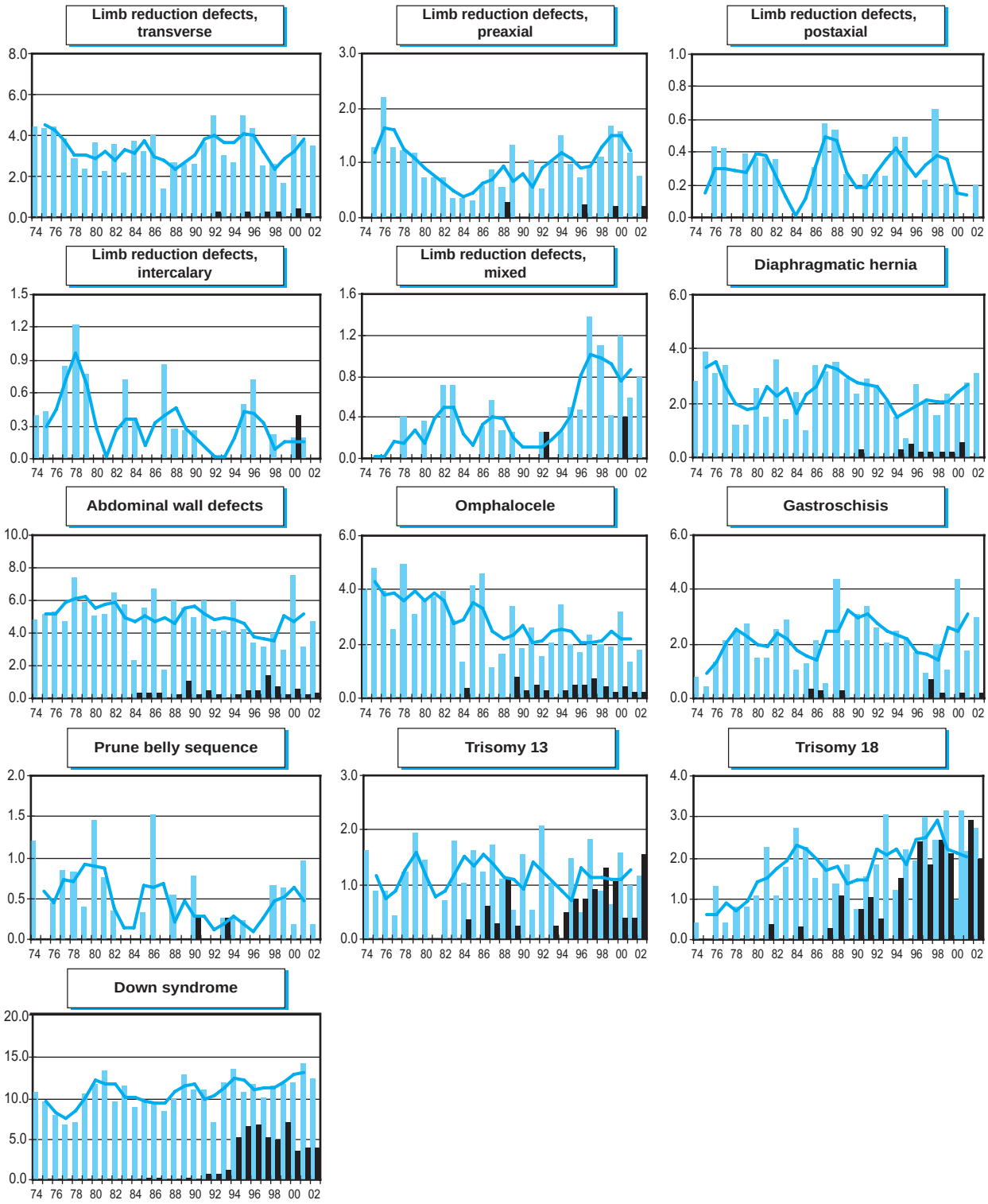
USA: Atlanta

'Time trends 1974-2002 (Birth prevalence rates per 10,000)

Note: L+S rates, ToP rates — 3-year moving average trend



Note: L+S rates, ToP rates — 3-year moving average trend



Note: L+S rates, ToP rates 3-year moving average trend

7.1 Monitoring Systems, not contributing with Annual Data:

Australia

Australian Birth Defects Monitoring System

History:
The mechanism for national monitoring of birth defects was initiated in 1979 with the establishment of the National Perinatal Statistics Unit (NPSU). The national collation of birth defects data began in 1981 with data from four states, and all states and territories provided data from 1986. The national program became an associate member of the Clearinghouse in 1982 and full member in 1984.However, Australia has not contributed national data to the Clearinghouse for the last 3 years. Australia has recently undertaken a review of the National Congenital Malformations and Birth Defects Data Collection, which identified a lack of national consistency in birth anomalies data. A significant program of data development will be undertaken to achieve national standardisation of the scope, the data and clinical definitions used, and the classification of birth anomalies. It is anticipated the resumption of data contribution to the ICBDMS will be possible in the foreseeable future. In 2005, national data for 1998–2001 will be reported.

Size and coverage:
All births in Australia are covered. Births have remained stable at approximately 250,000 annual births for the last 10 years. All births of 20 weeks or 400 grams gestation are registered. A recommendation of the review was to extend the scope of the new national collection to initially include data for birth anomalies notified up to 1 year of age and to include terminations of pregnancies with birth anomalies where termination data are available.

Legislation and funding:
There is no national legislation requiring the reporting of birth defects at the national level. Most jurisdictions have legislation which covers the notification of birth anomalies and this is enacted through their respective Public Health Acts. The coverage of this legislation varies among the jurisdictions, however, and legislation does not cover all sources of data in some jurisdictions. For example, notification of terminations of pregnancies with birth anomalies is not enacted through legislation in some jurisdictions. Therefore, although legislation which covers notification of birth anomalies exists, notification is voluntary from some sources. In most states and territories, birth defect data are collected as part of the perinatal data collection, and funding, if any is determined by the jurisdiction. The state and territory health authorities report to the central data custodian (the NPSU) which receives funding from the Australian Institute of Health and Welfare.

Sources of ascertainment:
Birth defects are notified to state and territory birth defect registers mainly through their perinatal data collections. Other sources of notification may include death certificates/mortality data, hospital morbidity data, primary health care staff, disability services staff, medical officers, and screening and diagnostic The states and territories then provide the data to the National Perinatal Statistics Unit for national collation and reporting.

Exposure information:
Currently not available.

Address for further information:
Dr Elizabeth Sullivan, AIHW National Perinatal Statistics Unit, 2nd Floor, McNevin Dickson Building, Randwick Hospitals Campus, Randwick NSW 2031 Australia

Phone: 61-2-93821014

Fax: 61-2-93821025

E-mail: e.sullivan@unsw.edu.au

Website: http://www.npsu.unsw.edu.au

USA: California

California Birth Defects Monitoring Program

History:
The California Birth Defects Monitoring Program was established in 1983 to monitor rates and trends and conduct epidemiological investigations to find causes of birth defects. The Programme is funded through the California Department of Health Services and jointly operated with the March of Dimes Birth Defects Foundation. In 1997 the Centers for Disease Control designated the Programme one of eight Centers of Excellence in Birth Defects Research. The Programme is an associate member of the Clearinghouse.

Size and coverage:
The Programme operates a population-based registry among 56,000 births. The registry includes 8 counties whose birth defects rates and trends are representative of California and who reflect the state's racial/ethnic diversity.

Legislation and funding:
The Programme operates under statutory authority: Health and Safety Code, Division 102, Part 2, Chapter 1, Sections 103825-103855. State funding is appropriated each year through the state budget. The Programme also receives research grants from the National Institutes of Health and the Centers for Disease Control.

Sources of ascertainment:
Staff actively ascertains data at hospitals and genetic centers by reviewing logs and identifying children with structural birth defects (BPA 740-759) diagnosed prenatally through age 1. All diagnostic information is abstracted directly from medical records; registry files are cross-linked with vital statistics data to verify demographic information.

Exposure information:
Bilingual interviewers collect environmental exposure information through large, case-control interview studies. Exposures under investigation include nutrition, health status and family history, medications, lifestyle, and chemical exposures through hobbies and occupation. Study participants also submit biological samples for analysis of genetic factors that might be contributing. The Programme has published more than 200 articles reporting research and registry findings in medical and scientific journals.

Background information:
Registry data, research findings, publications, and a description of Programme activities are available on their website www.cbdmp.org.

Address for further information:
John Harris, Jackie Wynne, MOD/CBDMP, 3031 F Street, Suite 200, Sacramento, CA 95816-3844.

Phone: 1-888-898-2229

Fax: 1-916-443-6657

E-mail: jwy@cbdmp.org

Website: http://www.npsu.unsw.edu.au

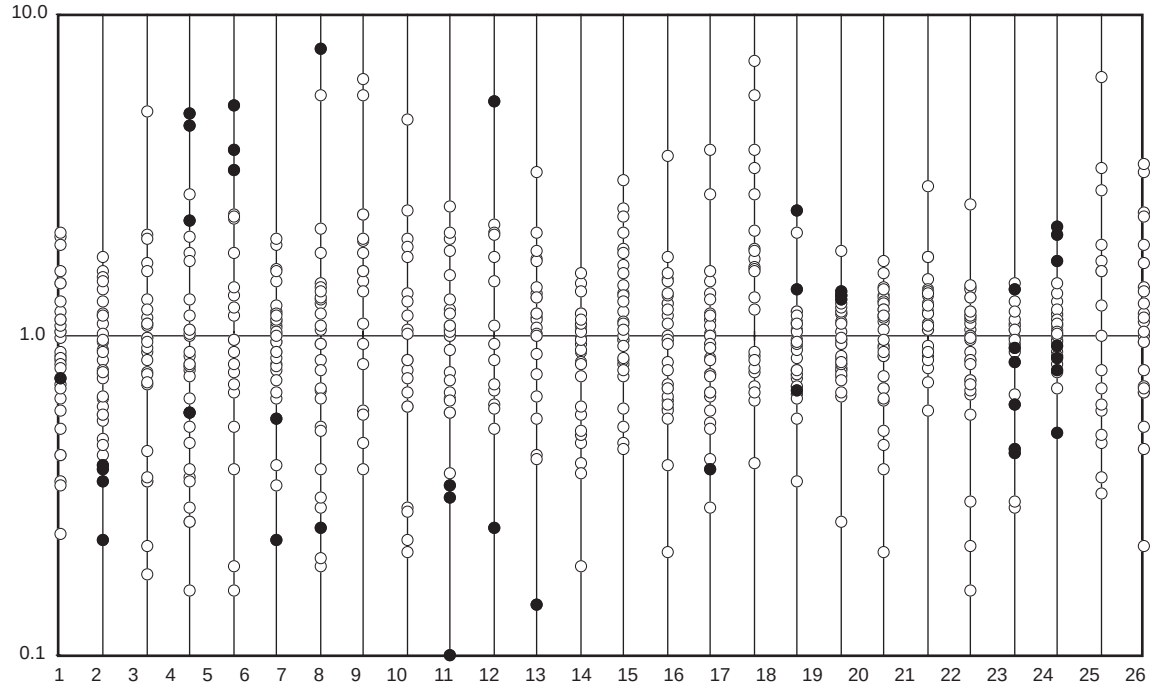
8.1 Summary of the Results of the Observed to Expected Ratios, 2002

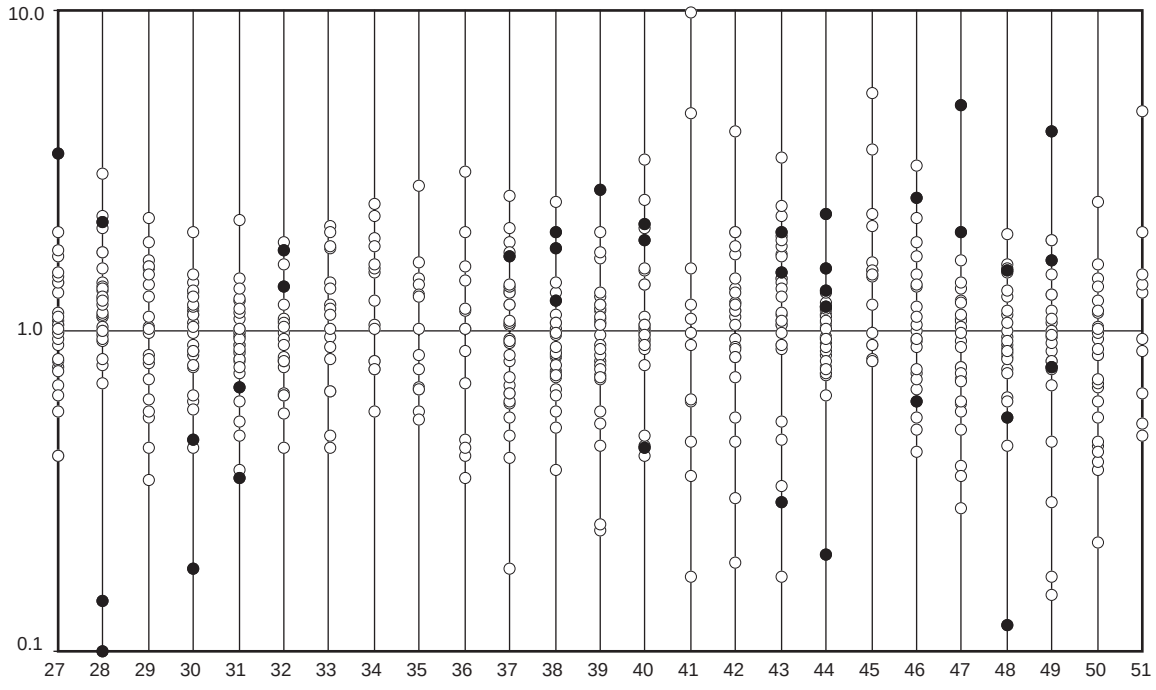
Malformation	O/E ratio >1		O/E ratio <=1	
	Number	Statistically significant	Number	Statistically significant
Anencephaly	13	0	21	1
Spina bifida	11	0	23	4
Encephalocele	11	0	23	0
Microcephaly	12	3	22	1
Arhinencephaly / Holoprosencephaly	11	3	19	0
Hydrocephaly	16	0	18	2
Total Anophthalmos / Microphthalmos (include unspecified)	13	1	19	1
Anophthalmos	13	0	15	0
Microphthalmos	10	0	19	0
Total Anotia / Microtia (include unspecified)	13	0	16	3
Anotia	7	1	16	2
Microtia	15	0	11	1
Transposition of great vessels	13	0	19	0
Tetralogy of Fallot	16	0	14	0
Hypoplastic left heart syndrome	12	0	19	0
Coarctation of aorta	11	0	19	1
Choanal atresia, bilateral	15	1	15	0
Cleft palate without cleft lip	12	2	22	1
Cleft lip with or without cleft palate	13	3	21	0
Oesophageal atresia / stenosis with or without fistula	18	0	15	0
Small intestine atresia / stenosis	20	0	11	0
Anorectal atresia / stenosis	16	0	18	0
Undescended testis (36 weeks of gestation or later)	9	1	12	5
Hypospadias	19	3	14	4
Epispadias	8	0	15	0
Indeterminate sex	13	0	18	2
Renal agenesis	15	1	18	0
Cystic kidney	20	1	12	2
Bladder exstrophy	12	0	19	0
Polydactyly, preaxial	13	0	18	2
Total Limb reduction defects (include unspecified)	11	0	23	2
Transverse	9	2	14	0
Preaxial	10	0	12	0
Postaxial	10	0	11	0
Intercalary	7	0	14	0
Mixed	8	0	13	0
Diaphragmatic hernia	17	1	16	0
Total Abdominal wall defects (include unspecified)	10	3	23	1
Omphalocele	15	1	17	0
Gastroschisis	14	2	18	1
Prune belly sequence	5	0	20	0
Trisomy 13	15	0	16	0
Trisomy 18	21	2	10	1
Down syndrome, all ages (include age unknown)	17	4	16	1
<20	11	0	12	0
20-24	11	1	15	1
25-29	11	2	16	0
30-34	10	1	17	2
35-39	10	2	17	1
40-44	9	0	17	0
45+	5	0	16	0
Total	636	41	854	42

Note: The total number of ratios was 1,490. The reasons why the number of ratios is different malformation by malformation are due to the fact that some registries did not contribute in some malformations and that some expected ratios were not computable. The number of ratios is very high so we expect to have a certain number (about 5%) of significant ratios just by chance. The exact calculation of the number of "chance" significance is obstructed by the presence of correlated ratios (e.g. the ones related to the Down syndrome).

8.2 Graph of the Observed to Expected Ratios, 2002

Observed to Expected Ratio, 2002





Ratio of observed and expected number of selected malformations, 2002, plotted on a log scale. Expected numbers are calculated as mentioned in the "notes on statistical analysis".
Significant ratios are indicated by closed circles, the others by open circles.

Legend

1 Anencephaly
2 Spina bifida
3 Encephalocele
4 Microcephaly
5 Arhinencephaly / Holoprosencephaly
6 Hydrocephaly
7 Total Anophthalmos / Microphthalmos (incl. unspecified)
8 Anophthalmos
9 Microphthalmos
10 Total Anotia / Microtia (incl. unspecified)
11 Anotia
12 Microtia
13 Transposition of great vessels
14 Tetralogy of Fallot
15 Hypoplastic left heart syndrome
16 Coarctation of aorta
17 Choanal atresia, bilateral
18 Cleft palate without cleft lip
19 Cleft lip with or without cleft palate
20 Oesophageal atresia / stenosis with or without fistula
21 Small intestine atresia / stenosis
22 Anorectal atresia / stenosis
23 Undescended testis (36 weeks of gestation or later)
24 Hypospadias
25 Epispadias
26 Indeterminate sex
27 Renal agenesis
28 Cystic kidney
29 Bladder exstrophy
30 Polydactyly, preaxial
31 Total Limb reduction defects (incl. unspecified)
32 LRD, Transverse
33 LRD, Preaxial
34 LRD, Postaxial
35 LRD, Intercalary
36 LRD, Mixed
37 Diaphragmatic hernia
38 Total Abdominal wall defects (incl. unspecified)
39 Omphalocele
40 Gastroschisis
41 Prune belly sequence
42 Trisomy 13
43 Trisomy 18
44 Down syndrome, all ages (incl. age unknown)
45 Down syndrome, <20
46 Down syndrome, 20-24
47 Down syndrome, 25-29
48 Down syndrome, 30-34
49 Down syndrome, 35-39
50 Down syndrome, 40-44
51 Down syndrome, 45+

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Selection of papers by Programme Directors and their collaborators are reported as following. The details are sent from the Programme Directors only for the listed Monitoring Systems. The collaborative publications, made by two or more ICBDMS members in any context, are first shown and not repeated in the specific registry section.
Papers can be obtained contacting authors.

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