ANNUAL REPORT

2005

with data for 2003

INTERNATIONAL CLEARINGHOUSE FOR BIRTH DEFECTS SURVEILLANCE AND RESEARCH

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THE CENTRE OF THE INTERNATIONAL CLEARINGHOUSE FOR BIRTH DEFECTS SURVEILLANCE AND RESEARCH

Via Carlo Mirabello, 19 - 00195 Roma - Italy

This Annual Report was finalized for publication in October 2006, only a few days after the tragic accident that took the young life of ***Alessandra Lisi****, its principal author. Over the years, Alessandra's skill, work ethic, grace, and kindness made her an increasingly central part of all ICBD activities. We mourn her loss, miss her beyond words.*
We dedicate this volume to her.

INTERNATIONAL CLEARINGHOUSE FOR BIRTH DEFECTS SURVEILLANCE AND RESEARCH (ICBDSR)

A non-governmental organisation in official relations
with the World Health Organization

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INTERNATIONAL CLEARINGHOUSE FOR BIRTH DEFECTS SURVEILLANCE AND RESEARCH

ANNUAL REPORT 2005 (WITH DATA FOR 2003)

Contents

Introduction

A word on the structure of the report

Because of collaborative research is the most important function of the International Clearinghouse for Birth Defects Surveillance and Research (ICBDSR), summaries of these activities open this report.

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

Each monitoring system monitors all birth defects. However, the tables and 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 some basic data and the rates of some specific defects in each surveillance system. Figures are presented in:

(a) a graph showing the total number of births per year
(b) two graphs showing the percentage of births per year and maternal age classes (<20, 20-24, 25-29; 30-34, 35-39, 40+)
(c) a table showing data for 2003
(d) a table showing data for the previous longest available period of each register and for each malformation up to 2003
(e) some graphs showing the yearly rates represented in the following style:
  a. bars represent real patterns of prevalence
  b. blue bars stand for live+still births rates
  c. grey bars stand for termination of pregnancy rates.

The tables have a standard format for all the registries. If a malformation is not reported the row says "not reported".
The prevalence rates graphs are presented only for those malformations which have: figures at least for 8 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 surveillance system and in the table "Synopsis of Surveillance Systems" and in the table "Deviations from the ICBDSR 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.

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.

2. Collaborative Research Projects

2.1. Post-marketing surveillance and pregnancy: The MADRE Project.

A short letter to British Medical Journal, March 25, 2005

Editor,

In her recent letter (BMJ 2005;330:308, doi:10.1136/bmj.330.7486.308) Patricia Yeargin rightly stresses the importance of including the effects during pregnancy in post-marketing surveillance of medications. Physicians and women can benefit when they know more about the reproductive toxicity of medications, and, crucially, when the evidence does not support claims or fears of teratogenicity. This knowledge can help prevent unnecessary abortions when fears arise about medications taken before pregnancy is recognized, as well as help use effective medications safely in pregnant women. We would like to share with the readers of the journal some findings of one such ongoing post marketing surveillance that is being carried out since the late 1980's by the International Clearinghouse for Birth Defects Surveillance and Research [ICBDSR previously known as ICBDMS] (1). The Clearinghouse is a network of registries that exchange information and track over time the occurrence of major birth defects, including multiple congenital anomalies, chromosomal conditions, and teratogen-associated phenotypes.

As part of such collaborative exchange, the Clearinghouse has implemented the MADRE (MAlformations DRug Exposure) project, which tracks first trimester use of medications among pregnancies whose outcome was a birth with major congenital anomalies (2). MADRE uses such data which is routinely collected by selected registries around the world as a screening tool for potentially teratogenic medications.

To screen for potential teratogenicity the MADRE data is assessed with an "exposed case-only " design. The study population consists of cases (infants or terminations of pregnancy with birth defects) all of which were exposed to some medication during the first trimester of pregnancy. Medications are cross-tabulated against birth defects. In the simplest approach, for each combination of medication and malformation, a two-by-two table is constructed and evaluated using an odds ratio, stratified by registry. In this table, a case is a subject (infant or fetus) if it has the malformation in question and a control otherwise (really an affected control because it has other defects). A subject is defined as exposed if the mother used during the first trimester the medication under study, and unexposed otherwise (although exposed to other medications). If medications and malformations are not specifically associated, then they should be randomly distributed in the sample, otherwise deviations from this distribution are signalled by increased odds ratios for the corresponding tables. We use such deviations and corresponding odds ratios to screen for associations that deserve further study.

The MADRE database now includes over 15,000 cases exposed to first trimester medications, reported from France, Israel, Italy, Japan, Northern Netherlands and Latin America. Such international setting and large sample improves statistical power and provides, to some extent, internal indicators of consistency. For example, an association is more likely to be due to factors other than chance if it occurs simultaneously in different registries. Moreover, because all subjects are affected, differential maternal recall of medication use is less of a concern compared to when unaffected controls are utilized. Conducting these analyses as ongoing surveillance allows also for further confirmation over time.

As an example of findings, we report selected associations. Of note, classic associations were confirmed: phenobarbital with oral clefts and heart defects; valproic acid with spina bifida, hypospadias, and heart defects; and carbamazepine with heart defects (3). Novel associations were also detected and are considered as hypotheses to be tested on further samples. For example, the association between corticosteroids and orofacial clefts was initially noted in 1994 (2), was later confirmed as a weak association by three epidemiological studies (4-6), and further confirmed in 2003 using MADRE data (7).

Another use of MADRE data database is to test associations as they appear in the literature. For example, we confirmed the suggested association between valproic acid and craniosynostosis (mainly trigonocephaly) (8), and were unable to replicate the reported association between trimethoprim and malformations such as neural tube and cardiac defects (9). Another example is the putative association of thyroid therapy and renal anomalies. A case report noted bilateral renal agenesis in a girl born to a hyperthyroid mother who received methimazole in early pregnancy (10), and experimental data in rats suggests that

pharmacologic hypothyroidism during a critical window might affect renal development (11 -12). In the MADRE database, we identified a significant association of thyroid therapy with cystic kidney [23 exposed cases, odds ratio 1.9, 95% confidence interval 1.2 to 2.9], and with unilateral kidney agenesis [18 exposed cases, odds ratio 2.3, 95% confidence interval 1.4-3.7]. Potential associations such as these warrant further testing in other samples. These are only selected examples and other can be found in the Annual Report of the Clearinghouse (13).

We think that the MADRE approach, which leverages the strength of existing birth defect registries and is relatively inexpensive, can be a useful adjunct tool and resource for postmarketing surveillance of the pregnancy effects of medications, and should be expanded. Moreover, physicians and researchers who wish to test selected associations between first trimester use of medications and structural malformations are welcome to contact us.

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The MADRE project was created after an idea from B Källén (Lund) and would not be possible without the ongoing effort and collaboration of the directors and staff of participating birth defects registries, which we gratefully acknowledge: France Central East (E Robert-Gnansia), France Paris (C De Vigan), Israel (P Merlob), Italy IMER (G Cocchi), Italy BDRCAM (G Scarano) Japan JAOG (Y Sumiyoshi), Latin America ECLAMC (E Castilla), Northern Netherlands (H de Walle).

We thank A Lisi (ICBDSR, Rome) and M Atkinson and D Gambrell (CDC, USA) for help in the statistical analysis of data from the MADRE project.

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2.2. International Database on CranioFacial Anomalies (IDCFA)

A world-wide initiative promoted and supported by WHO - Human Genetics Programme / NIDCR (National Institute of Dental and Craniofacial Research)

The WHO Human Genetics Programme in collaboration with the International Clearinghouse for Birth Defects Surveillance and Research (ICBDSR) established a databases' project on craniofacial anomalies in order to achieve one of the three main objectives of the International Collaborative Research on craniofacial anomalies started in 2000. It was recognised that gaps in present database collections could limit the understanding of the causes of craniofacial anomalies as well as the possibilities to implement useful actions to improve the quality of life of persons with craniofacial anomaly.

The promoters of this initiative are confident that collection and dissemination of data on persons affected by a craniofacial defects could improve their health and help researchers find to innovative solutions to prevent undue suffering.

The main aims of the International Database on Craniofacial Anomalies (IDCFA) are:

- to stimulate existing birth defects registries to share their data creating a specific worldwide database : International Perinatal Database on Craniofacial Anomalies (IPDTOC).
- to present the collected data in a suitable way or to make available more specific data to stimulate research addressing primary and tertiary prevention as well as better treatment of craniofacial anomalies.
- to encourage the establishment of new database to contribute to the worldwide IDCFA.
- to stimulate scientific and lay organizations to collect and share relevant data and information on persons affected by a craniofacial anomaly.

The development of the IDFCA is taking place in two phases:

Phase 1: The IPDTOC will collect simple information on new born children with cleft lip and/or palate named collectively as Typical Orofacial Clefts (TOC) from existing ongoing and well designed registries of birth defects.

Phase 2: Following this basic collection, IDCFA will expand to include:

- simple data on TOC from less developed or new birth defects registries.
- more complex information from birth defects registries on risk factors associated to TOC.
- data on less frequent craniofacial anomalies and syndromes.
- information on clinical pattern, quality of life and quality of services from registries as well as from medical departments and support organizations.

More information at:
http:**//www.who.int/genomics/anomalies/cfadatabase/en/** .

2 Collaborative Research Projects

Table 1. Typical Orofacial Clefts-cumulative data by Register
Updated: February 2006

Register	Period Sent	Births	Cleft Lip	Cleft Lip/Palate	Cleft Palate	Pierre Robin	Total Cases	% CL+CLP	Total Rate	95% CI Total rate*10,000	
South Africa SABDSS	2001-2002-2003	69.321	4	16	10	3	33	60,6	4,76	3,28	6,69
Italy-North East	2002	57.495	12	14	10	2	38	68,4	6,61	4,68	9,07
Spain-Basque Countries	2001-2002-2003	55.188	9	20	9	5	43	67,4	7,79	5,64	10,50
USA-West Virginia	2000-2001-2002-2003	80.743	16	26	22	2	66	63,6	8,17	6,32	10,40
Italy-BDRCAM	2001-2002-2003	172.300	32	47	55	8	142	55,6	8,24	6,94	9,71
USA-Tennessee*	2000-2001	157.857	41	39	52	0	132	60,6	8,36	7,00	9,92
France-Central East	2001-2002-2003-2004	430.028	63	152	111	43	369	58,3	8,58	7,73	9,50
Southern Portugal	2001-2002	37.163	6	18	9	3	36	66,7	9,69	6,79	13,41
Italy-IMER	2001-2002-2003	81.642	12	36	25	7	80	60,0	9,80	7,77	12,20
Croatia	2001-2002-2003	16.739	4	7	6	0	17	64,7	10,16	5,92	16,26
Israel IBDMS	2002-2003-2004	26.317	13	6	7	1	27	70,4	10,26	6,76	14,93
USA-Illinois	2000-2001	369.025	65	166	143	8	382	60,5	10,35	9,34	11,44
Italy-Tuscany	2001-2002-2003	80.505	16	32	33	3	84	57,1	10,43	8,32	12,92
Uruguay	2001-2002	20.923	6	10	5	1	22	72,7	10,51	6,59	15,92
USA-Rhode Island	2000-2001-2002-2003	49.451	13	27	11	1	52	76,9	10,52	7,85	13,79
United Arab Emirates	2002-2003	17.188	6	6	5	2	19	63,2	11,05	6,66	17,26
Malta	2001-2002-2003	11.629	6	2	3	2	13	61,5	11,18	5,95	19,12
Spain-Asturias	2001-2002-2003	20.911	5	9	8	2	24	58,3	11,48	7,36	17,08
Hungary	2002	97.327	27	48	36	5	116	64,7	11,92	9,85	14,30
Russia Moscow Region	2002-2003	104.403	25	47	51	6	129	55,8	12,36	10,32	14,68
UK-North Thames	2001-2002-2003	140.672	43	83	50	6	182	69,2	12,74	10,67	15,10
Canada-British Columbia	2001-2002-2003-2004	162.030	59	85	59	4	207	69,6	12,78	11,09	14,64
Venezuela	2001-2002	42.850	12	34	7	2	55	83,6	12,84	9,67	16,71
Ukraine	2001-2002-2003-2004	101.510	43	44	40	6	133	65,4	13,10	10,97	15,53
USA-Atlanta	2001-2002-2003	154.714	41	86	56	32	215	59,1	13,90	12,10	15,88
Austria-Styria	2001	10.050	2	9	2	1	14	78,6	13,93	7,62	23,37
Belgium-Hainaut	2001-2002-2003	36.461	14	15	21	1	51	56,9	13,99	10,42	18,39
Italy-ISMAC	2001-2002	33.022	7	18	19	3	47	53,2	14,23	10,46	18,93
USA-Hawaii	2000-2001-2002	52.272	16	31	20	8	75	62,7	14,35	11,29	17,99
UK-Wessex	2001-2002-2003	77.785	34	36	42	5	117	59,8	15,04	12,44	18,03
Czech Republic	2001-2002	375.947	137	200	228	12	577	58,4	15,35	14,12	16,65
Poland**	2001-2002-2003	724.742	229	412	457	20	1.118	57,3	15,43	14,54	16,36
Ecuador	2001-2002	22.836	2	30	3	1	36	88,9	15,76	11,04	21,83
USA-Arkansas	2001-2002	74.423	21	64	25	8	118	72,0	15,86	13,12	18,99
USA-Colorado	2000-2001	132.434	47	98	64	2	211	68,7	15,93	13,86	18,23
Slovak Republic	2001-2002-2003-2004	203.487	59	147	110	11	327	63,0	16,07	14,38	17,91
Chile	2001-2002	116.624	32	86	64	8	190	62,1	16,29	14,06	18,78
UK-Oxford	2001-2002-2003	18.334	4	11	14	1	30	50,0	16,36	11,04	23,36
Colombia	2001-2002	8.428	4	8	2	0	14	85,7	16,61	9,08	27,87
France-Paris	2002-2003	77.000	25	58	29	17	129	64,3	16,75	13,99	19,91
USA-Kentucky	2000-2001-2002	164.946	49	113	94	23	279	58,1	16,91	14,99	19,02
USA-Michigan	2001-2002	262.765	36	255	135	21	447	65,1	17,01	15,47	18,66
Ireland-Dublin	2001-2002-2003	68.469	24	32	46	15	117	47,9	17,09	14,13	20,48
Switzerland - Vaud	2001-2002-2003	20.942	9	13	10	4	36	61,1	17,19	12,04	23,80
Mexico RYVEMCE	2002-2003	34.128	8	44	6	1	59	88,1	17,29	13,16	22,30
Australia VBDR	2001-2002	125.218	46	68	74	31	219	52,1	17,49	15,25	19,96
Belgium-Antwerp	2001-2002-2003	52.868	24	38	25	7	94	66,0	17,78	14,37	21,76
Argentina	2001-2002	117.553	30	131	37	13	211	76,3	17,95	15,61	20,54
UK-Wales	2001-2002-2003	92.470	32	57	57	21	167	53,3	18,06	15,43	21,02
USA-Alabama	2000-2001-2002-2003	64.733	26	49	31	15	121	62,0	18,69	15,51	22,34
France-Strasbourg	2001	13.860	8	6	7	5	26	53,8	18,76	12,26	27,50
Canada-Alberta	2002-2003	78.400	39	58	38	21	156	62,2	19,90	16,90	23,28
USA-Oklahoma	2000-2001-2002-2003	200.925	79	192	100	30	401	67,6	19,96	18,05	22,01
Brasile	2001-2002	79.058	34	79	45	7	165	68,5	20,87	17,81	24,31
Northern Netherlands	2001-2002-2003	60.924	35	54	30	11	130	68,5	21,34	17,83	25,34
USA-Utah	2000-2001-2002-2003	194.220	121	167	103	46	437	65,9	22,50	20,44	24,71
Paraguay	2001-2002	8.829	3	13	2	2	20	80,0	22,65	13,84	34,98
Germany-Saxony Anhalt	2001-2002-2003-2004	70.226	27	105	18	10	160	82,5	22,78	19,39	26,60
Denmark-Odense	2001-2002-2003	15.768	10	16	9	2	37	70,3	23,47	16,53	32,34
Japan JAOG	2001-2002-2003	270.656	177	368	82	17	644	84,6	23,79	21,99	25,71
Bolivia	2001-2002	13.588	7	23	5	0	35	85,7	25,76	17,95	35,82
Germany-Mainz	2001-2002-2003	9.443	5	12	10	0	27	63,0	28,59	18,85	41,60
TOTAL		6.541.765	2.041	4.176	2.887	554	9.658	64,4	14,76	14,47	15,06

* provisional data
** includes Wielkopolska registry

2.3. Multiple Congenital Anomalies (MCA), 2003

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, ten programmes participated in the annual monitoring of MCA (Table 1), which evaluated birth outcomes that occurred in 2003. Collectively, the ten programmes provided information on 1,910 cases ascertained among nearly 670,000 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 993 cases of two or more major unrelated defects of unknown etiology (Table 1). These 993 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 developed 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=0.01 cutoff of the appropriate Poisson distribution. In the analysis we focused mainly on combinations of major defects.

Findings

The overall rate of MCA cases (2 or more unrelated defects of unknown etiology) was 14.9 per 10,000 births (Table 1), with variations that are expected among programmes.

Two programmes showed noticeable differences between 2002 and 2003 rates, with a decrease for Canada British Columbia and an increase for Finland.

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 excess cases observed in 2003; this number will be positive when more cases than expected were observed, and negative when less cases were observed. The table is sorted by these excess numbers of cases. Finally, we noted which rate variations fell outside Poisson expectations (*p<0.05; **p<0.01; ***p<0.001).

Overall, there were nearly 250 more defect occurrences in this period (sum of excess cases) than expected from the baseline. Among the 48 defect groups, 32 (67%) showed an O/E ratio greater than 1. Seven of these reached statistical significance (p<0.001), namely, congenital heart defects, anorectal atresia, hypospadias, other severe craniofacial defects, other ear anomalies, neck anomalies, and vessel anomalies (including SUA).

Three of them, congenital heart defects, anorectal atresia, and other ear anomalies, also surfaced in the evaluation of both two- and three-defect combinations (p<0.01). Vessel anomalies and other craniofacial defects only appeared in excess among the two-defect combinations (p<0.01).

Among the 10 outstanding 2-defect combinations, one showed less observed than expected cases (cleft lip +/- palate and deformations) and another, with 3 cases, had not been previously reported (vessel anomalies + other urinary tract defects). Three combinations showed an excess that was significant at a p<0.001 level, and 2 of these (anencephaly + limb reduction defect and oral clefts + limb reduction defect) suggested disruptions with or without

evidence of amniotic bands.
Among the 5 outstanding 3-defect combinations, one, with 3 cases, had not been previously reported (other ear anomaly + congenital heart defect + broncho-pulmonary defect).
Another 3-defect combination (microcephaly + oral clefts + CHD), and where chromosomes had not been analyzed, could suggest a chromosome anomaly.
Three 3-defect combinations presented anal atresia and severe genital defects, mostly ambiguous or absent genitalia, and could therefore suggest an underlying cloaca. In one of these combinations, the third associated defect was spina bifida, reminding the often-mentioned OEIS association, even without exstrophy.
In the second combination, the third significantly associated defect was microtia, and three of its cases also showed amelia, hypoplasia of fingers and talipes.
In the third combination, the third outstanding defect was a transverse upper and/or lower limb defect, from complete amelia to hand/foot or finger/toe amputations. In one case, fetal attachment to placenta was mentioned.
The remaining associations with a significant excess did not seem to fit into any recognizable pattern, and no increase of the patterns attributable to selected known teratogens were identified.

Conclusions
The results shown in the present report seem to indicate an excess of anomalies suggesting disruptive events, including cases suggesting LBWC and disruption by amniotic bands. The fact that body wall defects did not appear among the present statistically significant combinations might indicate that such cases would rather be recognized as complexes and would therefore not be included as true multiples.

Table 1: Cases and rates of MCA by programme and type, 2003.

PROGRAMME	Births	Total cases Reported	known etiology (syndromes)	Major defects Unrelated<2	2 or +	Rate
Canada British Columbia	40566	87	28	45	14	3.5
Finland	56808	292	131	19	142	25.0
France Central East	104895	180	32	29	119	11.3
France Paris	38300	60	5	3	52	13.6
Israel IBDMS	18603	28	0	4	24	12.9
Italy IMER	27412	42	2	14	16	12.8
Mexico RYVEMCE	30312	50	2	5	43	14.1
Japan JAOG	84644	538	182	224	132	15.6
South America ECLAMC	214245	519	72	63	384	17.9
Usa Atlanta	52237	114	41	6	67	12.8
TOTAL	**668022**	**1910**	**495**	**412**	**993**	**14.9**

Table 2: Occurrence of component defects in MCA patterns and comparison with baseline, 2003.

			Rate		
Defect group	**Observed**	**Expected**	**Ratio**	**Excess**	**Poisson**
Congenital heart defect	413	336.6	1.2	76.4	***
Anorectal atresia	143	100.0	1.4	43.0	***
Hypospadias	73	50.1	1.5	22.9	***
Other brain defect	88	67.4	1.3	20.6	*
Cleft lip+/-palate	109	93.1	1.2	15.9	
Other severe craniofacial defect	35	19.4	1.8	15.6	***
Other ear anomaly	22	8.1	2.7	13.9	***
Renal a/dysgenesis	67	55.3	1.2	11.7	
Neck anomaly	22	11.7	1.9	10.3	***
Limb reduction defect	29	19.2	1.5	9.8	*
An-microtia	56	47.0	1.2	9.0	
Omphalocele	53	44.4	1.2	8.6	
Spina Bifida	43	34.6	1.2	8.4	
Holoprosencephaly	20	12.7	1.6	7.3	*
Limb reduction defect, preaxial	35	28.0	1.2	7.0	
Vessel anomalies (incl. SUA)	7	1.0	7.3	6.0	***
Other axial skeleton defect	95	89.1	1.1	5.9	
Polydactyly	83	78.0	1.1	5.0	
Other urinary tract defect	126	121.4	1.0	4.7	
Encephalocele	23	19.0	1.2	4.0	
Microcephaly	43	39.4	1.1	3.6	
Gut malrotation	14	10.9	1.3	3.1	
Situs inversus	13	10.2	1.3	2.8	
Duodenal atresia	16	14.0	1.1	2.0	
Teratoma, sirenomelia	7	5.2	1.4	1.8	
A/polysplenia	13	11.3	1.1	1.7	
Craniostenosis	11	9.4	1.2	1.6	
Anencephaly	15	13.6	1.1	1.4	
Cleft palate (incl P Robin)	70	68.9	1.0	1.1	
Diaphragmatic hernia	41	40.1	1.0	0.9	
Limb reduction defect, other types	30	29.6	1.0	0.4	
Ring constriction or fibrotic band	0	0.0		0.0	
Other small intestine atresia	12	12.3	1.0	-0.3	
Choanal atresia	11	12.1	0.9	-1.1	
Cystic kidney	34	35.3	1.0	-1.3	
Syndactyly	27	28.8	0.9	-1.8	
Laryngeo-tracheal defect	4	6.0	0.7	-2.0	
Esophageal atresia	75	77.4	1.0	-2.4	
Gastroschisis	13	15.9	0.8	-2.9	
Bladder extrophy/epispadias	7	10.4	0.7	-3.4	
Other small intestinal atresias	33	36.5	0.9	-3.5	
Lumbo-sacral axial skeleton defect	3	6.9	0.4	-3.9	
Severe genitalia defect	52	57.8	0.9	-5.8	
An-microphtalmia	23	29.4	0.8	-6.4	
Other eye anomaly	22	28.4	0.8	-6.4	
Broncho-pulmonary defect (incl lung hypoplasia)	31	37.8	0.8	-6.8	
Hydrocephaly	73	83.1	0.9	-10.1	
Deformation (incl club foot, hip dislocation)	106	126.7	0.8	-20.7	

*** p<0.001
** p<0.01
* p<0.05

Table 3: Two-defect combinations among MCA cases, 2003.

Defect Combination	Observed	Expected	O/E
Anencephaly + Limb reduction defect	3	0.2	15.8
Spina bifida + Anorectal atresia	12	4.4	2.7
Microtia + Cleft palate	14	4.6	3.0
Microtia + Anorectal atresia	9	3.0	3.0
Other ear anomaly + Congenital heart defect	10	2.8	3.5
Cleft lip +/- palate + Limb reduction defect	8	1.3	5.9
Cleft lip +/- palate + deformation (incl. club foot, hip dislocation)	4	14.6	0.3
Other severe craniofacial defect + polydactyly	10	2.8	3.5
Anorectal atresia + Congenital heart defect	37	22.7	1.6
Vessel anomaly (incl. SUA) + Other urinary tract defect	3	0.0	-
Congenital heart defect + Renal a-dysgenesis	32	17.3	1.8

Table 4: Three-defect combinations among MCA cases, 2003.

Defect Combination	Observed	Expected	O/E
Spina bifida + Anorectal atresia + Severe genitalia defect	4	0.6	6.9
Microtia + Anorectal atresia + Severe genitalia defect	4	0.2	20.0
Other ear anomalies + Congenital heart defects + Broncho-pulmonary defect (incl. lung hypoplasia)	3	0	-
Microcephaly + Cleft lip +/- palate + Congenital heart defect	4	0.4	10.5
Anorectal atresia + Severe genitalia defect + Limb reduction defect	4	0.4	10.5

2.4. Prenatal Diagnosis and Down Syndrome, 2003

Guido Cocchi (Italy: IMER)
Silvia Gualdi (Italy: IMER)

Introduction

Aim of the survey is to assess the variability in time and in the Programme the use and the spread of the prenatal diagnostic techniques and analyse 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.

2003 Data

During 2003, 16 programmes (two programmes lost data : England-Wales and Italy: North-East, while for the first time Moscow-region was able to send data) provided data on 1645 DS newborns, 933 of them (56.7%) were prenatally diagnosed and terminated (Table 1).

The total number of births under surveillance in 2003 was 781,461.

The percentage of terminations of pregnancy (ToP) ranged from the lowest values in Moscow region (7.6 %), Canada:Alberta (20.0%) and USA:Atlanta (24.4%) and, to the highest in France: Paris and Central-East that reached 88.5% and 77.1% respectively and Italy:Tuscany with 75.% (Table 2). Other Registries show percentages of terminations over 60%: Australia:Victoria (68.2%), Czech Republic (65.9%), France:Strasbourg (65.0%), Italy:BDRCam (61.7%) and Germany: Saxony-Anhalt (60.9%).

In the European registries that provided a data set of 11 years (1993-2003), 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, 58.7% in 2002 and 68.9% in 2003. The increased rate for 2003 is related to the lack of data of England and Wales.

The comparison of the rate of ToP in 2003, between European Countries and non-European Countries (i.e. Australia:Victoria, Canada:Alberta and USA:Atlanta) is significantly different (63.2% vs 44.6% , $c2 = 38.04$ $p< 0.001$).

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). On the contrary in the higher maternal age classes: i.e. over 35 years (38-39 and >= 40) the percentage of terminations is higher.

Overall, the proportion of DS pregnancies which were terminated among women at higher risk (≥35 years old), was over 90% in two out of the three France Registries: Paris and Central-East (92.7% and 93.1% respectively). In the Italian Registry of Tuscany and Germany: Saxony-Anhalt the percentage of terminations overcome the 80% (80.6% and 88.9% respectively). Percentages of ToPs less than 40% were observed in Israel IBDMS (27.3%), Canada:Alberta (29.2%) and USA:Atlanta (33.3%). The lowest percentage of ToPs in mothers aged 35 and over, was observed in Moscow region (16.7%) (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 2003 (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 in the majority of the 13 programmes that can provide the rates for all the 11 year period: Czech Republic, all three registries of France (Central-East, Paris and Strasbourg) and all three Italian registries (BDRCam, IMER and Tuscany) (Table 6). These are the programmes that showed the highest rate of ToPs 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 ToPs were lowest i.e Canada:Alberta and USA:Atlanta. Canada:Alberta registry shows a significant increasing in the years. Controversial data are showed by Finland, Germany:Saxony.Anhalt registries where despite quite a high rate of ToP (49.3% and 60.9% respectively see Table 2) it is possible to observe high rates of prevalence at birth, i.e 12.32 per 10.000 in Finland, but not in Germany:Saxony.Anhalt .

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	2003
AUSTRALIA	X	X	X	X	X	X				X	X
CANADA: ALBERTA					X	X	X	X	X	X	X
CZECH REPUBLIC	X	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	X
FRANCE:Central-East	X	X	X	X	X	X	X	X	X	X	X
FRANCE: PARIS	X	X	X	X	X	X	X	X	X	X	X
FRANCE: STRASB	X	X	X	X	X	X	X	X	X	X	X
GERMANY: Sax. -Anh.								X	X	X	X
ISRAEL: IBDMS	X	X	X	X	X	X	X	X	X	X	X
ITALY: BDRCam	X	X	X	X	X	X	X	X	X	X	X
ITALY: IMER	X	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	X
MOSCOW REGION											X
NORTHERN NETHER	X	X	X	X	X	X	X	X	X	X	X
SWEDEN								X	X	X	X
USA: ATLANTA	X	X	X	X	X	X	X	X	X	X	X

Table 2. Percentage (%) of terminations (TOP) among the total number of cases recorded in 2003

Monitoring Program	Maternal Age (years)					
	<= 29	30 – 34	35 – 37	38 – 39	>= 40	Total
Australia	29.4	61.9	68.0	83.8	68.3	68.2
Canada Alberta	0	21.1	22.2	20.0	40.0	20.0
Czech Republic	46.4	77.8	77.8	88.2	72.2	65.9
Finland	27.6	45.0	42.3	54.5	68.3	49.3
France Central East	80.5	90.9	90.3	84.6	86.5	77.1
France: Paris	88.9	71.4	91.4	89.7	95.6	88.5
France Strasbourg	66.7	50.0	62.5	100	75.0	65.0
Germany: Sax.-Anh.	28.6	57.1	100	66.6	100	60.9
Israel IBDMS	42.9	100	100	0	16.7	42.9
Italy BDRCam	40.0	54.5	68.2	71.4	76.5	61.7
Italy IMER	16.7	66.7	72.2	28.6	71.4	59.3
Italy Tuscany	0	50.0	100	66.7	75.0	75.0
Moscow region	0	0	0	16.7	28.6	7.6
Northern Netherlands	25.0	28.6	50.0	75.0	66.7	45.5
Sweden	22.4	27.7	48.3	52.3	69.8	43.2
USA Atlanta	19.4	11.1	33.3	50.0	17.6	24.4

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	21.1	73.2	19.4	72.2
Canada Alberta	14.6	29.2	62.0	87.5
Czech Republic	7.5	79.0	18.4	87.9
Finland	19.6	57.3	34.1	79.8
France Central East	17.9	93.1	7.4	54.2
France Paris	28.6	92.7	7.3	99.7
France Strasbourg	15.5	69.2	19.2	62.3
Germany: Saxony-Anhalt	11.0	88.9	5.3	48.0
Israel IBDMS	16.0	27.3	26.8	39.6
Italy BDRCam	17.6	71.7	14.2	50.3
Italy IMER	25.6	64.1	20.2	56.3
Italy Tuscany	27.2	80.6	9.4	48.2
Moscow region	6.3	16.7	73.0	87.6
Northern Netherlands	19.9	63.6	10.1	27.6
Sweden	19.6	56.8	34.3	79.3
USA Atlanta	16.1	33.3	41.6	60.6

* estimated

Table 4 . Down Syndrome techniques of prenatal diagnosis (number of cases) registered in 2003 by maternal age classe.

Monitoring Program	<35				35-39				>39				Tot*			
	CVS	AC	CC	UK	CVS	AC	CC	UK	CVS	AC	CC	UK	CVS	AC	CC	UK
Australia	8	17	0	6	23	15	0	5	17	7	0	4	48	39	0	15
Canada Alberta	0	4	0	0	0	5	0	1	2	6	0	0	2	15	0	1
Czech Republic	0	67	0	0	1	35	0	0	1	12	0	0	2	114	0	0
Finland	7	10	0	0	9	14	0	0	12	16	0	0	28	40	0	0
France Central East	9	55	0	9	7	34	1	8	10	32	0	3	26	124	1	21
France Paris	13	21	1	1	17	41	0	0	10	33	0	0	41	95	1	1
France Strasbourg	2	2	0	0	1	5	0	0	3	0	0	0	6	7	0	0
Germany:Sax-Anha	1	5	0	8	0	5	0	1	0	3	0	0	1	13	0	9
Israel IBDMS	1	5	0	0	0	3	0	0	0	0	0	0	1	8	0	0
Italy BDRCam	0	10	0	0	0	25	0	0	1	12	0	0	1	47	0	2
Italy IMER	1	5	0	1	3	11	0	1	3	6	0	1	7	22	0	3
Italy Tuscany	0	4	0	4	0	13	0	2	2	13	0	5	2	30	0	11
Moscow region	0	0	0	0	0	0	1	0	1	0	3	0	1	0	4	0
Northern Netherl.	2	1	0	0	2	1	0	2	1	0	0	1	5	2	0	3
USA Atlanta	0	7	0	0	3	9	0	1	1	1	0	0	4	17	0	1
Total	**44**	**213**	**1**	**29**	**66**	**216**	**2**	**21**	**64**	**141**	**3**	**14**	**175**	**573**	**6**	**67**

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	<=34			>=35		
	CVS	AC	Total	CVS	AC	Total
Australia	13.38±1.06	16.63±2.06	15.54±2.36	13.15±1.55	16.43±2.40	14.30±2.44
Canada Alberta	-	18.75±0.50	18.75±0.50	14.00±0.00	18.36±0.67	18.00±1.41
Czech Republic	-	19.99±2.00	19.99±2.00	20.50±0.71	19.33±1.76	19.38±1.75
Finland	16.29±1.25	17.60±0.84	17.06±1.20	13.33±1.43	17.83±1.68	15.98±2.73
France Central East	15.13±1.89	19.95±3.09	19.21±3.41	15.33±1.91	19.67±2.64	18.58±3.09
France Paris	13.92±1.66	22.57±4.23	19.26±5.48	13.96±1.00	19.97±3.73	18.32±4.19
France Strasbourg	14.50±2.12	21.00±1.41	17.75±4.03	16.50±1.91	20.60±2.97	18.78±3.23
Germany: Sax-Anha	14.00±0.00	19.25±4.57	18.20±4.60	-	18.88±0.83	18.88±0.83
Israel IBDMS	23.00±0.00	23.80±2.39	23.67±2.16	-	22.33±0.58	22.33±0.98
Italy BDRCam	-	20.44±2.40	20.44±2.40	13.00±0.00	20.55±1.82	20.32±2.21
Italy IMER	12.00±0.00	18.00±3.00	17.00±3.63	14.17±1.47	18.94±0.90	17.70±2.38
Italy Tuscany	-	18.25±1.26	18.25±1.26	13.00±2.83	18.92±0.91	18.48±1.89
Moscow region	-	-	-	12.00±0.00	25.25±0.96	22.60±5.98
Northern Netherl.	17.00±0.00	20.00±0.00	18.00±1.73	13.67±0.58	22.00±0.00	15.75±4.19
USA Atlanta	-	20.33±0.58	20.33±0.58	-	19.33±3.27	19.33±3.27

Table 6. Prevalence at birth (x 10,000) in the years of DS in the 13 programs participating in the survey for all the years.

Programme	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003
Canada Alberta	11.45	11.07	13.15	8.49	11.14	14.02	11.56	14.65	15.2	12.71	19.2
Czech Republic	7.52	7.67	7.26	5.51	5.06	6.72	6.57	5.37	5.51	5.37	6.38
Finland	13.21	12.83	12.94	10.33	10.07	11.33	10.04	11.76	14.18	14.16	12.32
France Central East	10.98	10.43	8.91	9.47	9.01	6.83	4.86	5.83	5.85	5.51	4.86
France Paris	10.61	9.19	7.05	9.67	7.78	10.48	5.24	7.87	7.79	6.20	4.69
France Strasbourg	16.75	17.87	24.04	17.44	27.95	2.20	4.34	5.62	2.23	2.96	5.18
Germany Saxony Anhalt	5.79	6.33	7.43	7.86	8.33	13.65	6.09	6.38	8.26	9.08	5.30
Israel IBDMS	5.06	5.03	6.32	4.87	9.13	3.28	6.01	4.74	6.15	4.75	6.45
Italy BDRCam	10.94	7.63	10.01	9.22	6.74	8.73	6.33	2.99	6.83	5.42	5.17
Italy IMER	8.97	9.27	10.24	7.97	7.27	9.36	9.58	6.47	6.33	6.15	8.11
Italy Tuscany	11.83	9.80	11.42	6.91	7.34	6.28	6.14	4.90	5.70	3.76	4.00
Northern Netherlands	9.86	5.74	9.38	13.74	11.91	10.03	8.43	6.35	9.32	13.31	5.99
USA Atlanta	12.02	13.81	10.93	11.98	10.49	11.46	12.00	11.08	13.25	12:56	13.01

2.5 Study Protocols

2.5.1 Malformations and Drug Exposure (MADRE):

Post-marketing surveillance of medications in pregnancy: A 15-year international collaborative study by birth defect registries of the International Clearinghouse for Birth Defects Surveillance and Research (ICBDSR)

Study Protocol, Version 3, March 28, 2006

Abbreviations

- Centre = Central Office of the International Clearinghouse for Birth Defects Surveillance and Research, previously known as International Centre on Birth Defects
- ICBDSR = International Clearinghouse for Birth Defects Surveillance and Research, previously known as International Clearinghouse for Birth Defects Monitoring Systems
- PD = Programme Director of a Registry Member of the ICBDSR
- PI = Principal Investigator of the Study

Title

Post-marketing surveillance of medications in pregnancy: A 15-year international collaborative study by birth defect registries of the International Clearinghouse (ICBDSR)

Authorship

- Coordination: Lorenzo D Botto (principal investigator), Alessandra Lisi (statistical analysis), Elisabeth Robert, Marian Bakker and Pierpaolo Mastroiacovo (coordination, review)
- Program directors PDs or collaborator(s) who provide data, and actively interact with coordinating staff by contributing to protocol, data interpretation, and report writing. One author per registry strongly encouraged.
- The name "Clearinghouse" will be part of authorship, and other participants will be recognized in the acknowledgements (see below)

Acknowledgments

Centre Staff, program directors or program staff who provide data and contribute to the aims of the study.

Rationale

- Post-marketing surveillance of adverse drug

effects is an essential public health function.
- Surveillance of teratogenic effects in particular is challenging because of the rarity of individual malformations (surveillance for all malformations as a group is useless in most cases)
- The Clearinghouse has been conducting post-marketing surveillance for teratogenic effects of medications for over 15 years, and currently has a cumulated database of around 16,000 cases of malformations exposed to a drug in the first trimester of pregnancy.
- This database can be evaluated in different ways
  - To detect specific malformation-medication association as signals of specific potential teratogenic effects
  - To systematically scan the relation between each medication and the complete series of malformation, creating a "risk-safety profile" for commonly used or medically important medications
- These two approaches are complementary and both types of information can be helpful to medical and public health professionals.
- This information is best viewed as exploratory. Incomplete information, measurement error (biasing OR's towards the null), and potential biases can lead to both false positive and false negative findings. Nevertheless, if thoughtfully used and interpreted, such surveillance can generate information and hypotheses to be replicated in this system or in other setting.
- The Clearinghouse database provides a window into this pressing issue and leverages its large population, systematic ascertainment, and diversity of populations.

Objectives
- To describe the general characteristic of the database, and the data collecting methods used by the registries.
- To present the methods of analysis
- To present the risk-safety profile of selected drugs, as examples of results : paracetamol, pregnene-4-derivatives, peripheral vasodilators (2-amino-1-phenylethanol derivatives), valproic acid and insulins (as proxy of maternal diabetes)

Data Request
- Information to evaluate the data collecting methods used by the registries
- New data submission not required
- Study will use data currently available in MADRE Database

Methods
- Participating registries: registries with more than 100 cases in the MADRE Database
- Subjects: cases of malformations (among liveborn infants, stillbirths, terminations of pregnancy) reported as having been exposed to a medication during the first trimester of pregnancy
- Time period: the longest available.

Definitions
- Isolated malformation: malformation or a sequence, with or without minor malformations
- Associated malformation: malformation or a sequence that occurs with other major malformations (or sequences)
- Minor malformation: according to the ICBDSR list
- Sequence: according to the ICBDSR list

Malformation coding
- Coding system developed in the Clearinghouse for coding multi-malformed infants

Study Design
- Exposed – only, case – only design
- To screen for potential teratogenicity the MADRE data is assessed with an "exposed-only, case-only" design. The study population consists of cases (infants or terminations of pregnancy with birth defects) all of which were exposed to some medication during the first trimester of pregnancy. Medications are cross-tabulated against birth defects.
- In the simplest approach, for each combination of medication and malformation, a two-by-two table is constructed and evaluated using an odds ratio, stratified by registry and year of pregnancy outcome. In this table, a case is a subject (infant or fetus) if it has the malformation in question and a control otherwise (really an affected control because it has other defects). A subject is defined as exposed if the mother used during the first trimester the medication under study, and unexposed otherwise (although exposed to other medications).
- If medications and malformations are not specifically associated, then they should be randomly distributed in the sample, otherwise deviations from this distribution are signalled by increased odds ratios for the corresponding tables.
- Analysis of such deviations and corresponding odds ratios is used to screen for associations that deserve further study.

Analysis
- Descriptive
  - frequency of 52 malformations by register
  - frequency of 10 most frequent medications by register and number of drugs reported per case per register
- Statistical analysis
  - Odds ratios and corresponding 99% confidence intervals (99% CI are used to control for multiple comparisons)
  - Odds ratio adjusted by program and year of pregnancy outcome
  - Subgroup analysis by type of malformation (isolated and associated) and by type of treatment (monotherapies, polytherapies)
  - Second step analysis after removing cases that showed a significant association with a medication
- Risk – safety analysis
  - Odds ratios (OR's) adjusted by year of pregnancy outcome and reporting program
  - For 3 of the 10 most common medications and for 2 selected other medications of teratologic interest, graph with OR for each of 52 malformations
  - Subgroups risk – safety profile
  - Second step risk – safety profile

Data security and confidentiality
- Rules for confidentiality and data security adopted by ICBD (available at the ICBD internal web-site) will be strictly applied. Concerns and suggestions from PD will be discussed and addressed.

Timeline
- Protocol and data analysis example circulated by February 15
- Comments received by February 28
- New protocol by March 31
- Paper first draft April 30
- Comments received by May 21
- Paper revised and submitted to a peer-reviewed Journal June 15

2.5.2 Very Rare Defects (VRD)

Study Protocol, Version 1.4, March 31, 2006

Abbreviations
- Centre = Central Office of the International Clearinghouse for Birth Defects Surveillance and Research, previously known as International Centre on Birth Defects
- ICBDSR = International Clearinghouse for Birth Defects Surveillance and Research, previously known as International Clearinghouse for Birth Defects Monitoring Systems
- PD = Programme Director of a Registry Member of the ICBDSR
- PI = Principal Investigator of the Study
- VRD = very rare defect

Pro – memoria
As agreed, since the participation to this study is quite wide, it was decided to produce 9 papers. The first paper will be based on a general descriptive study dealing only with prevalence and a few characteristics, the 2nd -9th paper will evaluate each malformation by more in-depth analysis and will use a case – control approach to describe possible risk factors.
The present protocol is concerning the first paper.
The PI will be Csaba Siffel.
Next paper PIs:
- Cyclopia – Iêda M Orioli (IO), Brasil
- Sirenomelia – Iêda M Orioli (IO), Brasil
- Conjoined twins – Osvaldo Mutchinick (OM), Mexico
- Amelia – Rongwei Ye (RY), China
- Bladder exstrophy – Csaba Siffel (CS), USA
- Cloaca exstrophy – Marcia Feldkamp (MF), USA
- Acardius-acephalus – Lorenzo Botto (LB), USA
- Phocomelia – Song Li (SL), China

Title (first paper)
Descriptive epidemiology of very rare birth defects

Authorship
Csaba Siffel (PI), Eduardo E Castilla, Pierpaolo Mastroiacovo, PDs or his/her collaborator(s) who are able to provide data, interact with the PI to reach study aim by commenting on the project

protocol and the drafts of the papers, and suggest interpretation of results.
Maximum 1 author per register for the paper on general description. Exceptions can be decided by the PI where deemed appropriate. PIs of case-control approach can choose one or two additional author(s) from their registry/site.

Acknowledgments
Centre Staff, any PDs or his/her collaborator(s) who are able to provide data and interact with the PI.

Rationale
Basic epidemiologic knowledge of birth defects is concentrated on the more common defects. Less known is the epidemiology of very rare defects. The understanding of the epidemiology of rare defects could shed light to a better understanding of basic dysmorphogenetic mechanisms also, as it occurred with phocomelia after the thalidomide induced epidemic. A very rare defect can be defined as a defect with an incidence of 1 out of 20,000 pregnancies or less.

Objectives
The purpose of this study is to describe the basic epidemiologic characteristics of the following defects

1. Acardius
2. Amelia, complete
3. Phocomelia (true!)
4. Bladder exstrophy
5. Cloaca exstrophy
6. Conjoined twins
7. Cyclopia
8. Sirenomelia

Definition and epidemiology

The following short descriptions of specific defects are considered as a general guideline. PIs of more specific analysis on the individual defects will provide more details.

Acardius

Definition: Anomaly of monozygotic twins in which one twin has an absent, rudimentary, or non-functioning heart. The unaffected co-twin supports the circulation of the acardiac twin. It has been observed in multiple births. Acardia is also referred to as TRAP (Twin Reversed Arterial Perfusion) sequence, which reflects one of the theories suggested for pathogenetic mechanisms. It is associated with monochorionic placentation. It can be classified as:

- Acardius acephalus – Most frequent (60-75% of acardiac cases) type. Head is absent, trunk and limbs are developed more or less
- Acardius acormus – Only fetal head develops
- Acardius amorphous (or anideus) – About 20% of acardiac cases. Irregular skin-covered mass of bone, muscle, fat, and connective tissue. No external form can be distinguished.
- Acardius anceps (or paracephalus) – Head poorly formed, trunk and limbs well developed.
- Acardius mylacephalus – Amorphus mass with some limb (one or more) development.

ICD-9 BPA code: part of 759.89
ICD-10 code: part of Q89.7

Tips for extracting cases: since no specific code is available, the original diagnosis in the appropriate codes must be checked. Acardius may be found not only in the general code 759.89 or Q89.7, but also in the codes

- 759.49 or Q89.4 (unspecified conjoined twins),
- 759.9 or Q89.9 (congenital malformation, unspecified).
- 746.88 or Q 24.8 (other specified anomalies of heart
- 746.99 or Q24.9 (anomaly of heart, unspecified),
- 747.9 or Q28.9 (unspecified anomalies of circulatory system).

Be aware that a wrong code like

- 740.01 (acrania) could have been used for coding acephalus.

Prevalence: 1:35,000 births

References:

- Human Malformations and Related Anomalies, 2nd Edition, Edited by Stevenson and Hall, Oxford University Press, 2006, pp. 1394-1396.
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- Napolitani FD, Schreiber I. The acardiac monster. A review of the world literature and presentation of 2 cases. Am J Obstet Gynecol. 1960; 80:582-9.
- Van Allen MI, Smith DW, Shepard TH. Twin reversed arterial perfusion (TRAP) sequence: a study of 14 twin pregnancies with acardius. Semin Perinatol. 1983;7(4):285-93.

Amelia, complete

Definition: Complete absence of one or more limbs (exclusive of girdle).

ICD-9 BPA code: 755.20, 755.30, 755.40
ICD-10 code: Q71.0, Q72.0, Q73.0

Prevalence: 1:70,000-250,000 births

Arrest of formation of the primordium in the very early stages of embryo development has been suggested, as well as disruption of normal development due to teratogenic exposure, mechanical, or vascular accidents. Cases with genetic linkage have been reported.

References:

- Everett et al.: Amelia, near total. http://www.thefetus.net
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Phocomelia (true)

Definition: A congenital malformation in which the hands or feet (normal, almost normal, or malformed) are attached to abbreviated arms and legs. The word phocomelia, introduced by Saint Hilaire on 1832, combines phoco- (seal) and melia (limb) to designate a limb like a seal's flipper. Frantz and O'Rahilly classified phocomelia into 3 anatomic types:

(a) complete = absence of all limb bones proximal to the hand or foot, which attaches directly to the trunk;
(b) proximal = absence of the proximal limb bones (humerus or femur) so that the forearm or leg, with the hand of foot attaches to the trunk
(c) distal = absence of distal limb bones (radius and ulna, or tibia and fibula) so that the hand or foot attaches to the humerus or femur. This type can be distinguished in
   - Radial
   - Ulnar
   - Radio-ulnar

In the present study "true" phocomelia includes only the complete type.

A recent study confirmed that phocomelia is not an intercalary defect.
Intercalary defects encompass a large range of defects where the distal part of a limb is present (normal, almost normal, or malformed) while the proximal part is absent or very hypoplastic or malformed

ICD-9 BPA code: 755.21, 755.31, 755.41
ICD-10 code: Q71.1, Q72.1, Q73.1

Prevalence: no recent data available

Phocomelia could be a consequence of exposure to thalidomide. In some cases it may be genetic (as in the Roberts tetraphocomelia syndrome).

References:

- Castilla et al.: Thalidomide, a current teratogen in South America. Teratology 1996; 54(6):273-7.
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- Frantz DH, O'Rahilly R. Ulnar hemimelia. Artif Limbs. 1971; 15(2):25-35.
- Geoffroy Saint-Hillaire I. Histoire generale et particuliere des anomalies de 1'organisation chez l'homme et les animaux (A comprehensive detailed historical approach to human and animal teratology). Paris: Bailliere, 1832-1836. 3 vols.

Bladder exstrophy

Definition: "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." (ICBDSR Annual Report)
Other characteristics include: protrusion of the posterior vesical wall, low-set umbilicus, incomplete descent of testes, short penis pointing upwards in males or cleft clitoris in females. Bladder exstrophy could be part of the OEIS complex (Omphalocele, Exstrophy of the bladder, Imperforate anus, Spinal defects).

ICD-9 BPA code: 753.5
ICD-10 code: Q64.1

Prevalence: 1:25,000-30,000 births
Male to female ratio: 2.3:1

Most cases are sporadic. Familial recurrence risk is 1%. Affected individuals have a 500 times greater risk to have an affected offspring with bladder exstrophy.

References:

- Boyadjiev SA, Dodson JL, Radford CL, Ashrafi GH, Beaty TH, Mathews RI, Broman KW, Gearhart JP. Clinical and molecular characterization of the bladder exstrophy-epispadias complex: analysis of 232 families. BJU Int. 2004; 94(9):1337-43.
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- Human Malformations and Related Anomalies, 2nd Edition, Edited by Stevenson and Hall, Oxford University Press, 2006, pp. 1232-1234.
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- Kallen K, Castilla EE, Robert E, Mastroiacovo P, Kallen B. OEIS complex--a population study. Am J Med Genet 2000; 92(1):62-8.

Cloaca exstrophy

Definition: Complex malformation in which there is an involvement of the urinary and intestinal tract. It represents the most severe manifestation of the epispadias-exstrophy spectrum of ventral body wall defects. Major diagnostic criteria include intestinal epithelium between the hemibladders, phallic separation with epispadias in males, pubic arch separation in females. The distal ileum opens to the surface. The anorectal region is absent. Bicornuated uterus and vagina duplex is more frequent among females.
Cloacal exstrophy is more commonly seen with omphalocele, spinal defects, single umbilical artery, hip dislocation, colon duplication, heart defects.

ICD-9 BPA code: 751.55, may be also in 756.79
ICD-10 code: Q43.7

Prevalence: 1:200,000-250,000 births
Male to female ratio: Higher proportion of males (?)

Etiology is unknown. It is more frequent among monozygotic twins. Most cases are sporadic but familial cases have been observed.

References:

- Birth Defects Encyclopedia, Edited by Buyse, Blackwell Scientific Publications, 1990, pp. 648-649.
- Human Malformations and Related Anomalies, 2nd Edition, Edited by Stevenson and Hall, Oxford University Press, 2006, pp. 1232-1234.
- Jeffs RD. Exstrophy, epispadias, and cloacal and urogenital sinus abnormalities. Pediatr Clin North Am. 1987 Oct;34(5):1233-57.
- Martinez-Frias ML, Bermejo E, Rodriguez-Pinilla E, Frias JL. Exstrophy of the cloaca and exstrophy of the bladder: two different expressions of a primary developmental field defect. Am J Med Genet. 2001; 99(4):261-9.

Conjoined twins

Definition: Conjoined twins result of a defect during the embryologic process of monozygotic twinning. Several classifications of cases have been suggested. Twins may be attached laterally or longitudinally. Among conjoined twins, 70-75% are thoracopaghus, 20% pygopagus, 6% ischiopagus, and 2% craniopagus. Many of the defects observed in conjoined twins are associated with the union site. Other more frequently associated, anatomically unrelated malformations include neural tube defects,

omphalocele, and orofacial clefts.

ICD-9 BPA code: 759.4
- 759.40 Dicephalus (two heads)
- 759.41 Craniopagus (head joined twins)
- 759.42 Thoracopagus (thorax joined twins)
- 759.43 Xiphopagus (xiphoid and pelvis joined twins)
- 759.44 Pygopagus (buttock joined twins)
- 759.48 Other specified conjoined twins
- 759.49 Unspecified conjoined twins

ICD-10 code: Q89.4

Prevalence: 1: 50,000 births
Male to female ratio: Higher proportion of females

Various theories have been proposed for the etiology and formation of conjoined twins. Whether they are formed by fission or fusion is not clear. Some recent publications support the fusion theory.

References:

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Cyclopia

Definition: Cyclopia (a single midline eye) is a severe malformation resulting from maldevelopment of the embryonic forebrain. It consists of a single midline orbit that can be anophthalmic, monophthalmic or contain synophthalmic ocular structures. Brain malformations, fusion of the optic vesicles, eyelids and lacrimal structures may occur. A proboscis, representing remnants of nasal structures, is usually present and located above the eye. Orofacial clefts, polydactyly, sirenomelia, hernias and spina bifida may be associated with it.
Holoprosencephaly is strongly correlated with facial anomalies ranging from cyclopia to a small forehead with hypotelorism. It has been suggested that cyclopia is part of the holoprosencephaly / cyclopia, / synophthalmos spectrum, and some developmental genes mutations, such as sonic hedgehog (SHH) and SIX3 have been reported in patients with holoprosencephaly and /or cyclopia.

Exclusion: Other type of holoprosencephaly, especially ethmocephaly, in which proboscis separates the severely hypoteloric eyes, and cebocephaly, in which a small, flattened nose with a single nostril is situated below hypoplastic and hypoteloric eyes should not be considered as a classic cyclopia (?). Synophthalmia (fusion of the eyes) is a distinct ocular malformation, as well.

ICD-9 BPA code: may be part of 742.26, included in 759.80
ICD-10 code: may be part of Q04.2, included in Q87.0

Tips for extracting cases: since no specific code is available for cyclopia, the original diagnosis in the appropriate codes must be checked. Cyclopia may be found in:
743.8 or Q15.8 or 743.9 or Q15.9 (other specified or unspecified anomalies of eye)

Prevalence: 1:23,000 births
Male to female ratio: Proportion of females is higher (?)

Etiologically heterogeneous, autosomal recessive and chromosomal etiologies have been described. Several teratogenic factors, including maternal diseases and cytomegalovirus infections have been suggested. Affected fetuses are usually aborted during the third trimester of pregnancy.

References:

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- Howard RO. Chromosomal abnormalities associated with cyclopia and synophthalmia. Trans Am Ophthalmol Soc. 1977; 75:505-38.
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- Human Malformations and Related Anomalies, 2nd Edition, Edited by Stevenson and Hall, Oxford University Press, 2006, pp. 302-303; 528-546.

- Kallen B, Castilla EE, Lancaster PA, Mutchinick O, Knudsen LB, Martinez-Frias ML, Mastroiacovo P, Robert E. The cyclops and the mermaid: an epidemiological study of two types of rare malformation. J Med Genet. 1992; 29(1):30-5.
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- Yamada S, Uwabe C, Fujii S, Shiota K. Phenotypic variability in human embryonic holoprosencephaly in the Kyoto Collection. Birth Defects Res A Clin Mol Teratol. 2004; 70(8):495-508.

Sirenomelia

Definition: A limb malformation affecting the lower limbs, which are fused with varying degrees. The real name should be symmelia. Long bones could be missing or present. Sirenomelia, also called mermaid malformation, has been classified into seven types based on osseous findings:

- Type I – all bones of thigh and lower leg present and unfused
- Type II – fused fibulae
- Type III – fibulae absent
- Type IV – partially fused femora and fused fibulae
- Type V – partially fused femora
- Type VI – fused femora and fused tibiae
- Type VII – fused femora and absent tibiae

Sirenomelia can be classified based on the type of leg and foot defects involved:

- Symelius (two feet) – legs almost perfectly united and terminating in a double foot with soles on the anterior surfaces
- Uromelus (one foot) – incompletely united legs ending in an incomplete single foot with the sole on the anterior surface
- Sirenomelus (no foot) – incomplete union of legs with absence of a distinct foot.

Genitourinary and gastrointestinal malformations are almost always present. Skeletal malformations and lung hypoplasia due to oligohydramnios are common findings. Cardiovascular malformations have been observed in one-fourth of cases with sirenomelia.

Exclusion: Caudal regression syndrome and Currarino syndrome. Caudal regression syndrome is a congenital heterogeneous constellation of caudal anomalies that include agenesis of the spinal column with varying degrees, anorectal malformations, genitourinary anomalies, and pulmonary hypoplasia. It has been associated with maternal diabetes. The combination of a particular form of hemisacrum, anorectal malformations, and presacral mass (teratoma, anterior meningocele, rectal duplication, or a combination thereof) constitutes Currarino syndrome. Previous reports indicated that mutation of HLXB9 gene could cause Currarino syndrome.

ICD-9 BPA code: part of 759.84
ICD-10 code: part of Q87.2

Tips for extracting cases: since no specific code is available for sirenomelia, the original diagnosis in the appropriate codes must be checked. Sirenomelia may be found in:
755.38 or 755.39 (other or unspecified reduction deformities of lower limb

Prevalence: 1:32,000 births
Male to female ratio: Proportion of males is higher (?)

Etiology is unknown. Maternal diabetes has been suggested but findings are inconclusive. It is more frequent among monozygotic twins.

References:

- Adra A, Cordero D, Mejides A, Yasin S, Salman F, O'Sullivan MJ. Caudal regression syndrome: etiopathogenesis, prenatal diagnosis, and perinatal management. Obstet Gynecol Surv. 1994; 49(7):508-16.
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- Valenzano M, Paoletti R, Rossi A, Farinini D, Garlaschi G, Fulcheri E. Sirenomelia. Pathological features, antenatal ultrasonographic clues, and a review of current embryogenic theories. Hum Reprod Update 1999; 5(1):82-6.

Notes for ICD codes
Two of the defects, sirenomelia and cyclopia do not have a specific ICD code.

Methods

Pro – memoria
All the information requested should be sent together (for cases and controls), although the complete project study planned to use some information first, in the descriptive study and other thereafter in each more deep study for each defect. For each case-control study a study protocol will be prepared and distributed in due time.
Participating registries: all registries have been invited to participate in this study.

Study subjects: all subjects (terminated fetuses or infants) with one of the VRDs isolated or with any associated malformation registered. Cases with any potential diagnosis of the above listed 8 malformations will be identified by registries participating in the study. All defects codes and written descriptions will be reviewed to validate a case according to the malformation definition.

Time period: the longest available.

Information needed: case by case information. Please see ***Appendix*** here below for variables requested. ***Please note that the compulsory information is limited*** (**only those in bold and blue**), ***the rest is limited to when available***..
More information will be provided more wide will be the analysis, especially of risk factors

Controls
1. Normal (if available): four (4) newborns (stillborns or liveborns) randomly selected from the appropriate file matched with the case by date of mother's last menstrual period. All the information given for the case must be given for the controls
2. Malformed: four (4) fetuses from termination of pregnancy or newborns (stillborns or liveborns) randomly selected from the same cases file matched with the case by date of mother's last menstrual period. All the information given for the case must be given for the controls, including the malformation description or code(s).

All registries that want to participate to the case-control study should send the malformed controls, those who have also normal controls should send both normal and malformed controls.

Descriptive analysis
We will describe each malformation of interest including a literature review, and estimate the worldwide prevalence of the malformation with selected basic characteristics such as pregnancy outcome, sex, birth weight, gestational age, twinning proportion.
In addition to that, using the available diagnostic information, subtypes of malformation of interest will be determined and phenotypically characterized by a clinical expert in a centralized way. If necessary, further information will be requested from local registries. This will enable us to look for phenotypic differences and do analysis

by phenotype. Cases with associated defect(s) will be classified as isolated (one major defect only), multiple (two or more major unrelated defects), and syndromic.

Data security and confidentiality
Rules for confidentiality and data security adopted by ICBD will strictly be applied. Concerns from individual PDs will be discussed.

APPENDIX

Information requested, only those in bold and blue are compulsory.
Anyway, please consider the possibility to give the maximum number of information

Variable	Suggested abbreviation	Content	Note
Variable Identification number	**ID**	**Any**	
Defect	**DEF**	**Character (ICD 9 or 10 or any other system code). Do not use dots.**	**Must be one of the very rare defect under study**
Defect laterality (only for amelia and phocomelia)	LAT	1=Upper right 2=Upper left 3=Lower right 4=Lower left Combination codes for others (e.g.: 12 = upper bilateral, 23=upper left and lower right, 1234=quadrimelic)	
Description of the defect	DEF DESCR	**Verbatim description, if available.** Copies of the original clinical record (without personal identifiers) are **welcomed. Photographs are GREATLY welcomed**	
Associated defects	ASSO-1	**Character (ICD 9 or 10 or any other system code). Do not use dots**	
	ASSO-2	**Character (ICD 9 or 10 or any other system code). Do not use dots**	
	ASSO-3	**Character (ICD 9 or 10 or any other system code). Do not use dots**	
	ASSO-4	**Character (ICD 9 or 10 or any other system code). Do not use dots**	
	ASSO-5	**Character (ICD 9 or 10 or any other system code). Do not use dots**	
	ASSO-6	**Character (ICD 9 or 10 or any other system code). Do not use dots**	
	ASSO-7	**Character (ICD 9 or 10 or any other system code). Do not use dots**	
	ASSO-8	**Character (ICD 9 or 10 or any other system code). Do not use dots**	Add more variables as needed
Summary diagnosis	SUMDIAG	Verbatim description, if available. (For example: Trisomy 13, etc)	
Time of the defect diagnosis	DIAG	Character 1=Prenatal < 20 weeks 2=Prenatal 20-24 weeks 3= Prenatal 24 – term 4=At birth	

Variable	Suggested abbreviation	Content	Note
Cytogenetic analysis	**CYTO**	**Character 0=NO 1=YES 9=Unknown**	
Karyotype	**KARYO**	**Character**	**If known**
Other genetic analysis	GENET	Character 0=NO 1=YES 9=Unknown	
Other genetic analysis description	GENETDESC	Character, any length	
Pregnancy Outcome	**OUTCOME**	**Character 1=Livebirth (LB) 2=Stillbirth (SB) 3=Termination of pregnancy (TOP) 4= Spontaneous abortion 9=Unknown**	**You can use your code. Give the key**
Sex	**SEX**	**Character M=Male F=Female I=Indeterminate sex U=Unknown**	**You can use your code. Give the key**
Plurality	PLURAL	Character 1=Singleton 2=Twin 3=Triplet etc 9=Unknown	You can use your code. Give the key
Sex of co-twin	CO-TWIN	Character M=Male F=Female I=Indeterminate sex U=Unknown	You can use your code. Give the key
Malformation in co-twin	CO-TW-MALF	Character (ICD 9 or 10 or any other system code). Do not use dots.	
Day of birth or termination	DOB	Number, 2 digits (dd)	Can be missed for confidentiality purposes
Month of birth or termination	MOB	Number, 2 digits (mm)	Can be missed for confidentiality purposes.
Year of birth or termination	**YOB**	**Number, 4 digits (yyyy)**	
Last menstrual period	**LMP**	**Day-month-year (ddmmyyyy)**	
Gestational age	**GA**	**Number, 2 digits (99 unknown)**	
Birth weight	**BW**	**Number, 4 digits (9999 unknown)**	

Variable	Suggested abbreviation	Content	Note
Maternal age	MATAGE	Number, 2 digits (99 unknown)	
Paternal age	PATAGE	Number, 2 digits (99 unknown)	
Parity	PARA	Number, 2 digits (99 unknown) Number of previous stillbirths + previous livebirths	
Gravidity	GRAVY	Number, 2 digits (99 unknown) Number of previous stillbirths + previous livebirths + spontaneous abortions + termination of pregnancies	
Previous spontaneous abortions	SPAB	Number, 2 digits (99 unknown) Number of previous spontaneous abortions	
Previous induced abortions	INDAB	Number, 2 digits (99 unknown) Number of previous induced abortions	
Previous births/abortions with a birth defect	PRA	Character (ICD 9 or 10 or any other system code). Do not use dots	
Consanguinity	CONS	Character 0=NO 1=YES 9=Unknown	You can use your code. Give the key
Drugs intake during first trimester, except folic acid or other vitamins	DRUG_1	Character, 1st ATC code (7 digits; no dots) OR the name of pharmacological substance	Four drugs are here; if more than 4 drugs, use additional columns
Drugs intake during first trimester, except folic acid or other vitamins	DRUG_2	Character, 2nd ATC code (7 digits; no dots) OR the name of pharmacological substance	Four drugs are here; if more than 4 drugs, use additional columns
Drugs intake during first trimester, except folic acid or other vitamins	DRUG_3	Character, 3rd ATC code (7 digits; no dots) OR the name of pharmacological substance	Four drugs are here; if more than 4 drugs, use additional columns
Drugs intake during first trimester, except folic acid or other vitamins	DRUG_4	Character, 4th ATC code (7 digits; no dots) OR the name of pharmacological substance	Four drugs are here; if more than 4 drugs, use additional columns
Folic acid, during the periconceptional period	FA	Character 0=NO 1=YES 9=Unknown	Periconceptional period: -1 month to + 2 months from ETC
Other vitamins, other than folic acid during the periconceptional period	VITAMIN	Character 0=NO 1=YES 9=Unknown	Periconceptional period: -1 month to + 2 months from ETC

Variable	Suggested abbreviation	Content	Note
Fever during first trimester of pregnancy	FEV	Character 0=NO 1=YES 9=Unknown	
Smoking during first trimester	SMOK	Character 0=NO 1=YES (any number of cigarettes) 9=Unknown	
Diabetes	DIAB	Character 0=NO 1=YES (pre-gestational diabetes) 9=Unknown	
Epilepsy	EPIL	Character 0= NO 1=YES (epilepsy in treatment, must be present in the DRUG field the ATC codes) 2=YES (epilepsy not in treatment) 9=Unknown	
Any other chronic condition	OTHCHRON	Character, free, verbatim	
Fertility problem	FERT	Character 0=NO 1=YES (pre-gestational diabetes) 9=Unknown	Please specify on notes. Drugs used to induce pregnancy should be given the DRUG field
Maternal education	MATED	Number, 2 digits (99 unknown) Number of school years	
Maternal working activity	MATWA	Character, any length, any code, give the key. If not coded, verbatim.	Be as precise as you can if you give the verbatim
Notes	NOTES	Character, any length	Give any useful information to interpret the data.

2.5.3 Geographical variation of common malformations

Study Protocol, Version 2.1, November 18, 2005

Abbreviations
- Centre = Central Office of the International Clearinghouse for Birth Defects Surveillance and Research, previously known as International Centre on Birth Defects
- ICBDSR = International Clearinghouse for Birth Defects Surveillance and Research, previously known as International Clearinghouse for Birth Defects Monitoring Systems
- PD = Programme Director of a Registry Member of the ICBDSR
- PI = Principal Investigator of the Study

Title
Geographical variation of common malformations

Principal investigator
Alessandra Lisi under the supervision of the CC Director.

Authorship
PI, CC Director, any PD or his/her collaborator sending the complete set of information required (see "How to participate" section), commenting the drafts of the paper, suggesting interpretation of results.

Acknowledgments
CC Staff , any PD or his/her collaborator able to provide data and interact with the PI.

Study Rationale
Considering that ICBDSR is a collaborative effort among 44 registries it is possible to investigate the geographical variation of congenital malformations. The study of geographical variation is becoming increasingly important for the evaluation of prevention programs and identification of causes of birth defects. ICBDSR has collected data on various malformations since 1974 using a standard definition. Annual data on prevalence of a number of malformations are available at the ICBDSR Centre, used and published for the Annual Report.

Objectives
The purpose of the present study is to explore the geographical variation of total (pregnancy terminations + births) prevalence rates of 22 malformations among registries who are members of the ICBDSR and explore the causes of it.

Methods
Registries considered for this study are those registries with

(a) complete data on births and terminations of pregnancies (ToPs) if permitted
(b) Data for the full five-year period or at least 100,000 births during some period between 1999-2003
(c) no variation more than 10-15% in the number of births per year (a higher variation may occur in presence of significant changes in population structure)
(d) registry annual rates stable in the considered period (_ = 0.20)

The stable "total rate" for the available years will be considered for the analysis.

<u>Twenty-two malformations will be included in the study:</u>

1. Anencephaly
2. Spina bifida
3. Arhinencephaly / Holoprosencephaly
4. Hydrocephaly
5. Transposition of great vessels
6. Tetralogy of Fallot
7. Hypoplastic left heart syndrome
8. Coarctation of aorta
9. Cleft palate without cleft lip
10. Cleft lip with or without cleft palate
11. Oesophageal atresia / stenosis with or without fistula
12. Small intestine atresia / stenosis
13. Anorectal atresia / stenosis
14. Hypospadias (all types)

14bis Hypospadias severe types only

15. Renal agenesis
16. Cystic kidney
17. Polydactyly, preaxial
18. Limb reduction defects
19. Diaphragmatic hernia
20. Omphalocele
21. Gastroschisis
22. Down syndrome (standardized rates)

Down syndrome will be studied only for those registries which report the number of cases and births per maternal age classes in the considered period. In fact Down syndrome standardized rates will be analyzed.

Eligible registries for this specific study:

3 registries where TOPs are not permitted and data are available for the full period 1999-2003
- **Ireland Dublin**
- **Malta**
- **United Arab Emirates**

1 registry where TOPs are not permitted, data are available for the 1999-2003 period but the considered period is 2001-2003 where no significant changes in number of births are present
- **South America ECLAMC**

1 registry where TOPs are not permitted and the considered period is 2001-2002 because it is the available period with at least 100,000 births
- **Costa Rica**

18 registries where TOPs are permitted and data are available for the period 1999-2003
- **Canada Alberta**
- **USA Atlanta**
- **USA Texas**
- **Finland**
- **Norway**
- **Northern Netherlands**
- **Hungary**
- **France Paris**
- **France Strasbourg**
- **France Central East**
- **Italy North East**
- **Italy IMER**
- **Italy Tuscany**
- **Italy BDRCAM**
- **Israel IBDMS**
- **Australia VBDR**
- **Australia WABDR**
- **Slovak Republic**

1 registry where data on TOPs are available for the period 1999-2003 but the considered period is 2000-2003 because of significant changes in population structure in the previous years
- **Germany Saxony Anhalt**

2 registries where data on TOPs are available for 4 years with at least 100,000 births, respectively 2000-2003 and 1999-2002
- **Sweden**
- **England and Wales**

1 registry where data are available for 3 years 2001-2003 but the considered period is 2002-2003 with at least 100,000 births because of significant changes in population structure in the previous years
- **Russia Moscow Region**

Non eligible registries: 14 registries do not fulfil the criteria for participation in this specific study

- Canada National, Canada British Columbia, Spain ECEMC, Japan JAOG, New Zealand, South Africa SABDSS, China Beijing, China CBDMN because TOPs are not registered in those countries although they are permitted.
- Chile Maule because data are available only for 2 years and births or less than 100,000
- Italy ISMAC and Cuba because TOPs have been reported only for two years and births are less than 100,000
- Ukraine because TOPs are reported only for 2 malformations
- Czech Republic because TOPs are not reported for all considered malformations
- Mexico RYVEMCE because of high variation in the number of annual births

Registries not submitting regular surveillance data:
Australia National and US California have not submitted data in the last years.
USA Utah and Wales joined the organization only few months ago.

Source of data: data published in the annual report

Time period: the last five, four, three or two years available according to the above-mentioned reasons.

Registry's description and self-evaluation of registration completeness:
To evaluate the main reasons of rates variability the following aspects will be considered:
- Coverage basis (population, hospital; national, regional)
- Institutional status (e.g.: voluntary research project, governmental compulsory project)
- Sources of ascertainment (single or multiple),
- Age limit for registration
- PD evaluation of completeness of registration among ToPs by malformation (or group) and by year (to be requested)
- PD evaluation of completeness of registration among births by malformation (or group) and by year (to be requested).

Statistical analysis
The crude cumulative rates of each malformation in each register will be used.
We will use point prevalence rates and their 95% confidence intervals as well as chi-square test for heterogeneity among participating registries for each malformation to identify variations in

prevalence. We will use the methodological characteristics of each register and the evaluation given by PD on the registration completeness to explain variations

Results

To interpret geographical variations the final results of the study will include:

- Table with the main characteristics of the participating registries
- Table with the prevalence's rank by register
- Graphs with each register's malformation prevalence with 95% CI by malformation
- Correlation between malformation and latitude (restricted to European registries)
- Correlations among specific malformations
- Summary of comments (the results obtained will be sent to each PD for comments)

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, Statewide	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	Hospital discharge	500 grams
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	2 years	22 weeks or 500 grams
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	Hospital based-National	1980	72 hours	20 weeks or 500 grams
New Zealand	Population-based National	1979	No limit	20 weeks or 400 grams
Northern Netherlands	Population-based Regional	1993	Up to 15 years	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
Slovak Republic	Population-based Regional	2003	1 year	Non-viable fetuses, 28 weeks or >1000 grams
South Africa: SABDSS	Hospital-based	1992	Hospital discharge (usually 4 days)	Stillbirths not recored
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	28 days	500 grams
United Arab Emirates	Hospital-based Regional	1995	7 days	23 weeks
USA: Atlanta	Population-based Regional	1974	6 years	20 weeks
USA: Texas	Population-base Regional	2004	1 year	Before 1999: 20 weeks. Since 1999: All stillbirths with documented birth defects included

4.1 Deviations from the ICBDSR 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					35					
Australia: WABDR				42					11										28		35	44				45
Canada: Alberta		2			2	7	8		11\12							25					35					2
Canada: British Columbia	1	2	4	6	2	7	8	10	11\12	13	15		18\19			25	25\26	27	28	30	35	37		2	2	2
Canada: National	1	1\2		6	2				11\12	14			18	21	23	25	26		28	31	35		40	2	2	2
China: Beijing																					35					
China: CBDMN	1	2		6	2	7	9		12				18			25		27	28	31	35	37		2	2	2
Costa Rica: CREC				6			9		11\12								26	27	28	31	35			2	2	2
Czech Republic																25					35					
England and Wales																										
Finland	1	2			2		8		11							25		27		32		37		2	2	2
France: Central East																25										2
France: Paris																25										
France: Strasbourg		2			2		9						18\19			25			28\29	30\33						
Germany: Saxony-Anhalt					2	7	9	10					18\19			25		27		32		37				2
Hungary	1	2			2		9									25	26				35	38\39		2	2	2
Ireland: Dublin		2			2				11				18\19			25	26				35			2	2	2
Israel: IBDMS							8									25				33						
Italy: BDRCAM																								2	2	2
Italy: IMER																25					35					
Italy: ISMAC																25										
Italy: North East			5		2					13	15	17	18\20	22					29		35					2
Italy: Tuscany							8																			
Japan: JAOG		2			2															31						
Malta		2			2		9		11									27		31	35	37		2	2	2
Mexico: RYVEMCE	1	2			2				11\12				18					27	28	30	35	37		2	2	2
New Zealand					2											25	26							2	2	2
Northern Netherlands															24	25					35					
Norway																25				34						
Russia: Moscow region		2					9			13	15		18			25				31	36					2
South Africa: SABDSS	1	2			2				11\12							25		27		31	35	37		2	2	2
South America: ECLAMC																25										
Spain: ECEMC		2			2													27				37				2
Sweden		2			2				11							25			28	32						2
Ukraine		2\3		6	2	7	9				16							27						2	2	2
United Arab Emirates		2			2	7	8	10	11				18						28/29	31						
USA: Atlanta									12		16															

4 ICBDSR 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 = stenosis 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 = genital ambiguity and absent genitalia included
28 = unilateral defects included
29 = severely dysplastic kidneys excluded
30 = single cyst included
31 = all kind of cystic kidney included
32 = all cystic kidneys are included except for single renal cysts
33 = AR polycystic kidney excluded
34 = some autosomalrecessive polycystyc kidneys are not excluded
35 = any type of polydactyly included
36 = polysyndactyly preaxial excluded
37 = any hypoplasia of skeletal limb structures included except branchydactyly and hypoplasia as part of skeletal dysplasia
38 = any hypoplasia of skeletal structures included
39 = sirenomalia included
40 = 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

Address for further information:
Dr Jane Halliday PhD, Epidemiologist, Birth Defects Register, Perinatal Data Collection Unit, 7/589 Collins St, Melbourne 3000

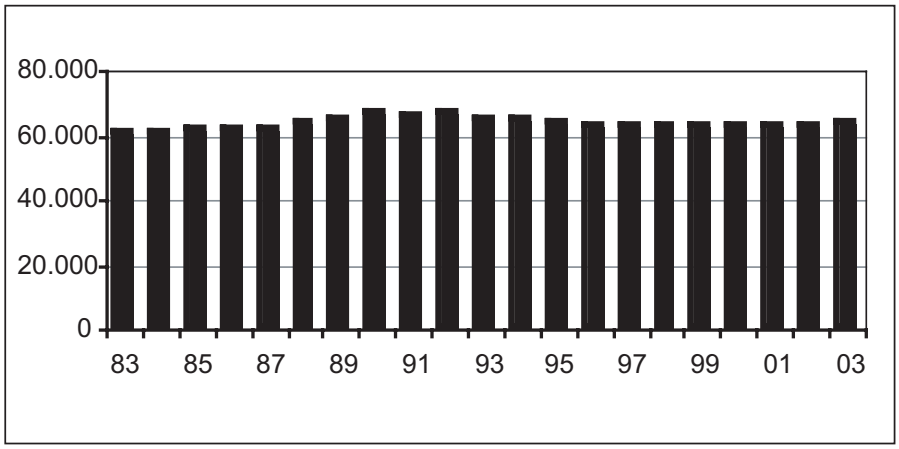
Phone: 61-3-96162729

E-mail: jane.halliday@dhs.vic.gov.au

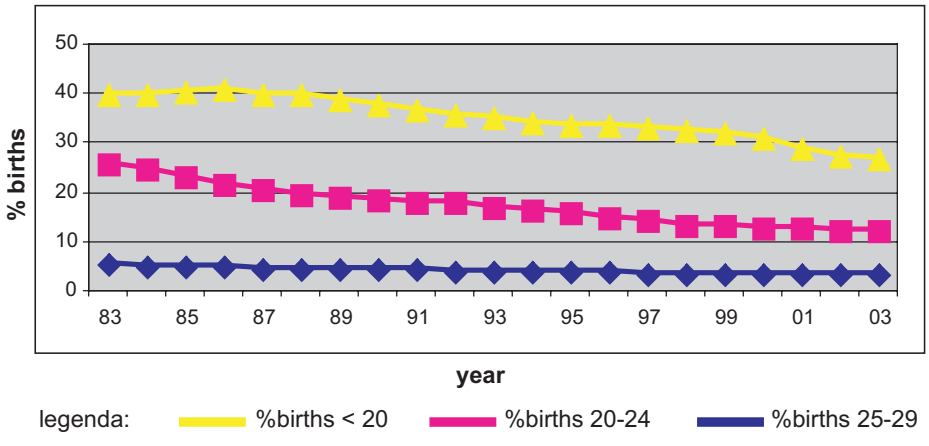
Website: http://www.dhs.vic.gov.au/phd/perinatal

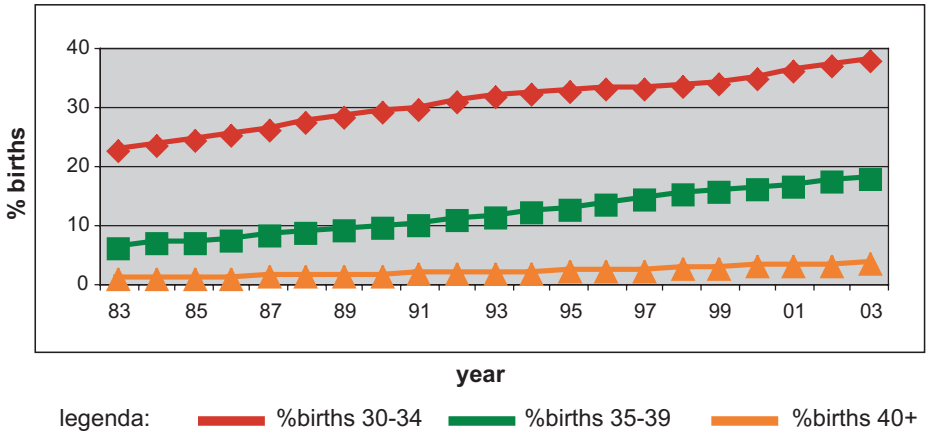
Australia: VBDR

Total births by year



Percentage of births by maternal age





Australia: VBDR, 2003

Live births (LB)	63018
Stillbirths (SB)	533
Total births	63551
Number of terminations of pregnancy (ToP) for birth defects	339

Birth Defects	Number of cases			Rates*10.000
	LB	SB	ToP	Total rate
Anencephaly	4	3	30	5.79
Spina bifida	8	12	14	5.32
Encephalocele	2	3	5	1.57
Microcephaly	8	1	1	1.57
Arhinencephaly / Holoprosencephaly	5	5	2	1.88
Hydrocephaly	36	16	14	10.33
Anophthalmos	2	1	1	0.63
Microphthalmos	1	1	0	0.31
Unspecified Anophthalmos / Microphthalmos	0	0	0	---
Anotia	1	0	1	0.31
Microtia	2	0	0	0.31
Unspecified Anotia / Microtia	0	0	0	---
Transposition of great vessels	27	2	0	4.54
Tetralogy of Fallot	24	2	1	4.23
Hypoplastic left heart syndrome	16	2	5	3.60
Coarctation of aorta	25	0	1	4.07
Choanal atresia, bilateral**	8	0	0	1.25
Cleft palate without cleft lip	62	4	2	10.64
Cleft lip with or without cleft palate	54	9	4	10.49
Oesophageal atresia / stenosis with or without fistula	19	1	0	3.13
Small intestine atresia / stenosis	19	1	0	3.13
Anorectal atresia / stenosis	24	1	2	4.23
Undescended testis (36 weeks of gestation or later)***	177	0	0	27.70
Hypospadias	179	0	0	28.02
Epispadias	4	0	0	0.63
Indeterminate sex	9	1	0	1.57
Renal agenesis	32	9	6	7.36
Cystic kidney	26	6	1	5.17
Bladder exstrophy	4	0	0	0.63
Polydactyly, preaxial****	54	4	0	9.08
Total Limb reduction defects (include unspecified)	21	2	2	3.91
Transverse	nr	nr	nr	nr
Preaxial	nr	nr	nr	nr
Postaxial	nr	nr	nr	nr
Intercalary	nr	nr	nr	nr
Mixed	nr	nr	nr	nr
Unspecified	nr	nr	nr	---
Diaphragmatic hernia	15	3	3	3.29
Omphalocele	7	2	12	3.29
Gastroschisis	10	2	1	2.03
Unspecified Omphalocele / Gastroschisis	2	0	0	---
Prune belly sequence	0	0	0	0.00
Trisomy 13	3	3	11	2.66
Trisomy 18	10	8	39	8.92
Down syndrome, all ages (include age unknown)	49	5	116	26.61
<20	1	0	0	5.47
20-24	2	1	1	5.32
25-29	7	1	4	7.12
30-34	16	0	26	17.53
35-39	11	2	43	49.67
40-44	12	1	26	181.82
45+	0	0	2	243.90
unspecified	0	0	14	---

** Choanal atresia, includes any, not just bilateral
*** UDT includes from 37 weeks gestation
**** Polydactyly includes any, not just preaxial
nr = not reported

Australia: VBDR, Previous years rates 1983 - 2003

Birth prevalence rates: (LB+SB+TOP) * 10,000

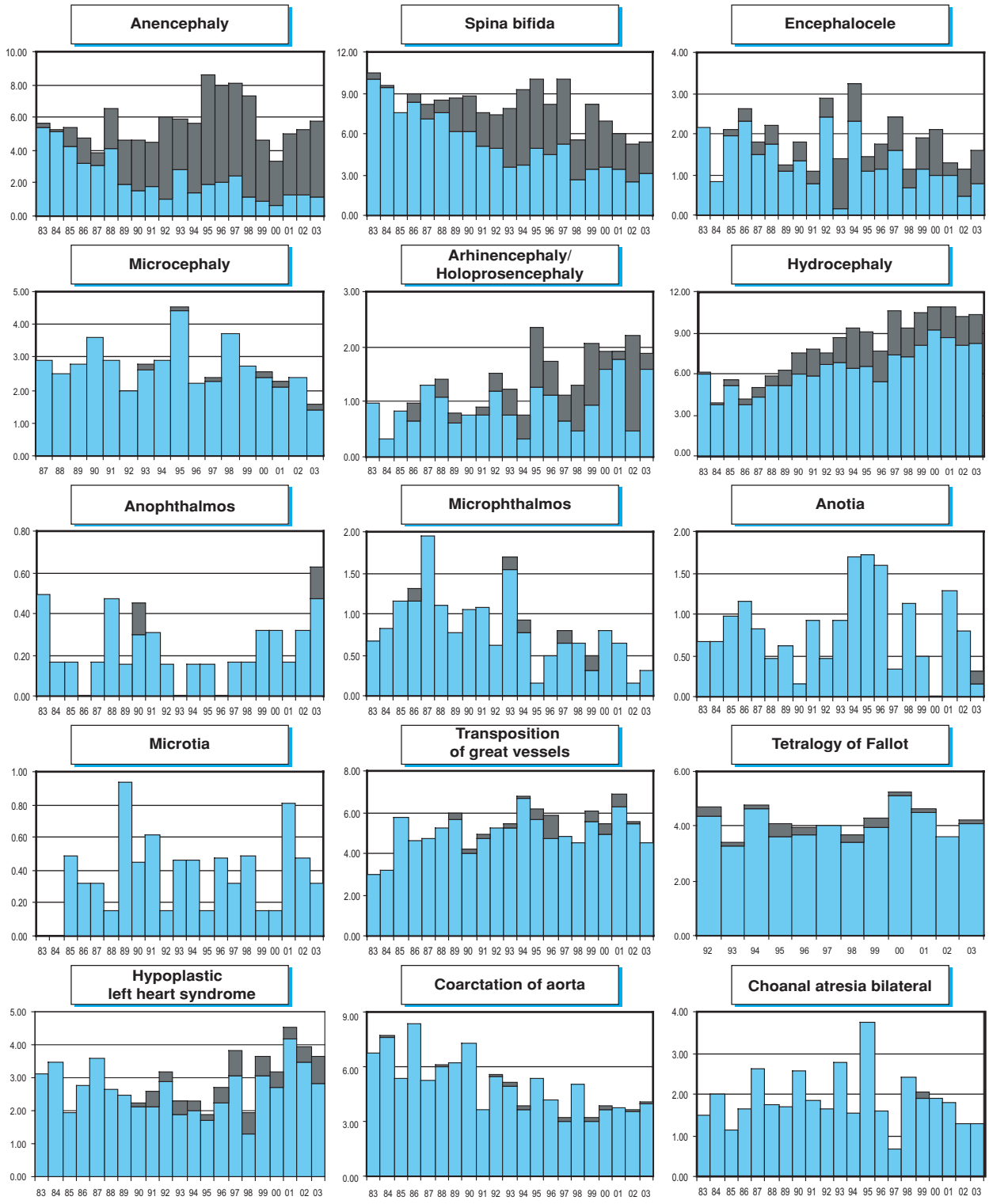
	1974-78	1979-83*	1984-88	1989-93	1994-98	1999-03
Births		**60,628**	**308,411**	**327,424**	**315,999**	**314,022**
Anencephaly		5.61	5.19	5.13	7.50	4.81
Spina bifida		10.39	8.53	8.03	8.58	6.31
Encephalocele		2.14	1.91	1.68	1.99	1.59
Microcephaly		nr	2.71*	2.81	3.16	2.29
Arhinencephaly / Holoprosencephaly		0.99	0.97	1.04	1.46	2.01
Hydrocephaly		6.10	4.93	7.54	9.21	10.57
Anophthalmos		0.49	0.19	0.21	0.13	0.35
Microphthalmos		0.66	1.26	1.04	0.60	0.48
Unspecified Anophthalmos / Microphthalmos		----	----	----	----	----
Anotia		0.66	0.81	0.61	1.30	0.57
Microtia		0.00	0.26	0.52	0.38	0.38
Unspecified Anotia / Microtia		----	----	----	----	----
Transposition of great vessels		2.97	4.67	5.13	5.63	5.70
Tetralogy of Fallot		nr	nr	4.04*	4.11	4.43
Hypoplastic left heart syndrome		3.13	2.89	2.57	2.53	3.79
Coarctation of aorta		6.76	6.55	5.59	4.30	3.69
Choanal atresia, bilateral		1.48	1.82	2.11	1.99	1.66
Cleft palate without cleft lip		7.92	7.94	6.57	8.07	8.92
Cleft lip with or without cleft palate		10.89	10.64	10.17	10.16	10.64
Oesophageal atresia / stenosis with or without fistula		3.30	3.66	3.66	3.99	2.80
Small intestine atresia / stenosis		1.32	2.53	2.75	2.50	3.50
Anorectal atresia / stenosis		2.97	3.50	4.15	5.28	3.85
Undescended testis (36 weeks of gestation or later)		nr	nr	46.32*	46.99	41.11
Hypospadias		nr	nr	32.58*	34.40	32.83
Epispadias		0.16	0.29	0.37	0.44	0.61
Indeterminate sex		1.48	1.82	2.93	2.12	1.56
Renal agenesis		4.12	4.96	4.52	6.80	6.85
Cystic kidney		2.80	3.31	4.80	6.39	6.85
Bladder exstrophy		0.66	0.39	0.21	0.51	0.57
Polydactyly, preaxial		6.76	7.85	9.62	10.38	9.90
Total Limb reduction defects (include unspecified)		7.09	5.74	6.35	6.93	5.48
Transverse		nr	nr	nr	nr	nr
Preaxial		nr	nr	nr	nr	nr
Postaxial		nr	nr	nr	nr	nr
Intercalary		nr	nr	nr	nr	nr
Mixed		nr	nr	nr	nr	nr
Unspecified		---	---	---	---	---
Diaphragmatic hernia		2.80	2.66	3.08	3.54	2.96
Omphalocele		1.15	2.17	2.35	2.97	2.74
Gastroschisis		0.49	0.91	1.77	1.96	2.64
Unspecified Omphalocele / Gastroschisis		---	---	---	---	---
Prune belly sequence		0.16	0.26	0.21	0.32	0.06
Trisomy 13		0.82	1.04	1.37	1.90	2.39
Trisomy 18		1.15	2.11	3.05	4.91	5.67
Down syndrome, all ages (include age unknown)		11.38	14.49	16.77	20.63	26.91
<20		6.30	7.33	8.45	5.56	5.11
20-24		5.83	7.47	8.56	7.92	7.78
25-29		7.90	8.86	8.41	7.75	10.46
30-34		13.87	15.59	15.73	15.55	18.99
35-39		34.81	46.25	45.80	50.87	54.48
40-44		121.46	114.49	120.51	181.22	187.53
45+		256.41	74.07	289.02	464.14	313.39
unspecified		---	---	---	---	---

* data include less than 5 years

nr= not reported

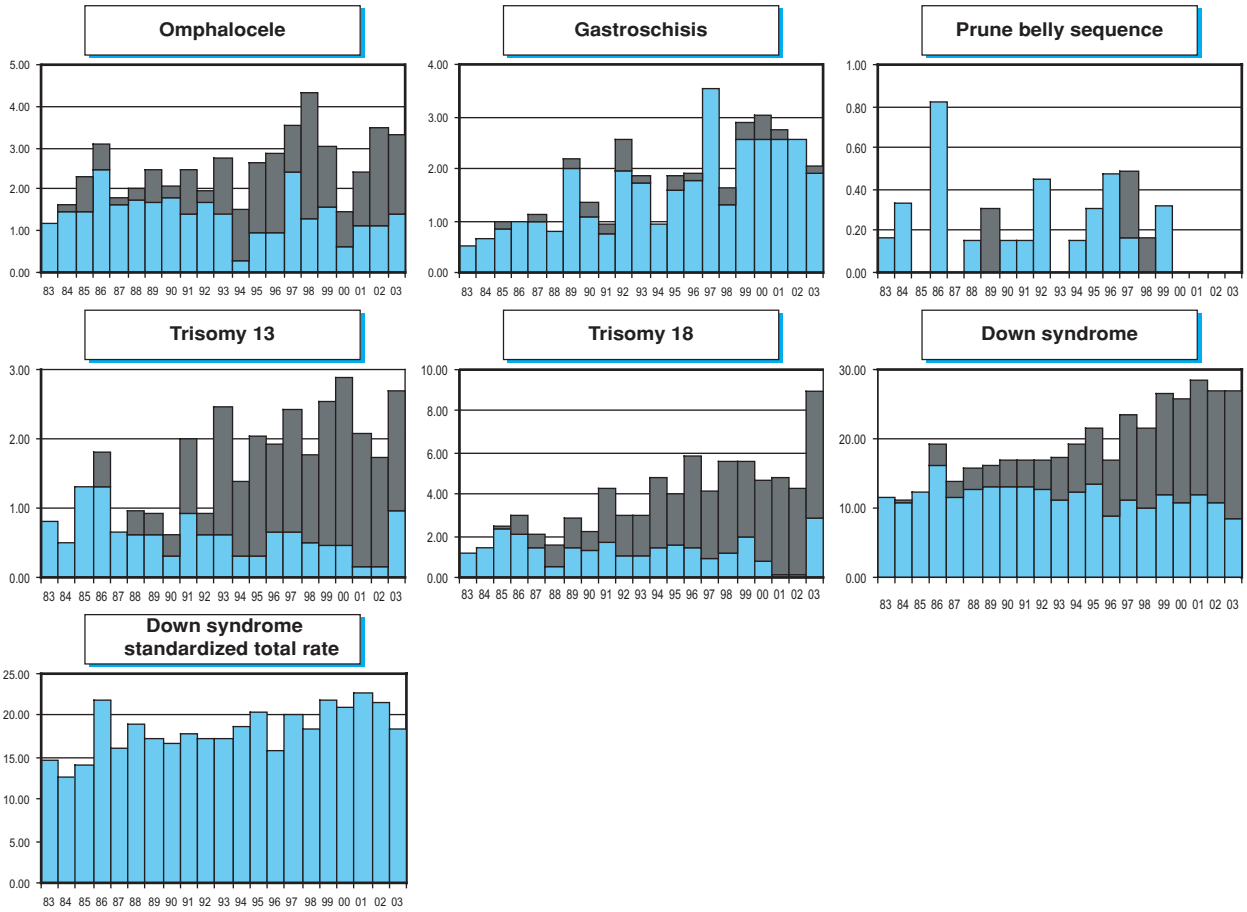
Australia: VBDR

'Time trends 1983-2003 (Birth prevalence rates per 10,000)



Note: L+S rates, ToP rates

Note: L+S rates, ToP rates



Note: L+S rates, ToP rates

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 programs.

Size and coverage
Population-based in the state of Western Australia. 25,000 birth a year, ~6% reported with a birth defect. Birth defects diagnosed prenatally and up to the age of 6 years, in stillbirths, terminations of pregnancy and livebirths 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 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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Women's and Children's Health Service
PO Box 134
SUBIACO 6904
Western Australia

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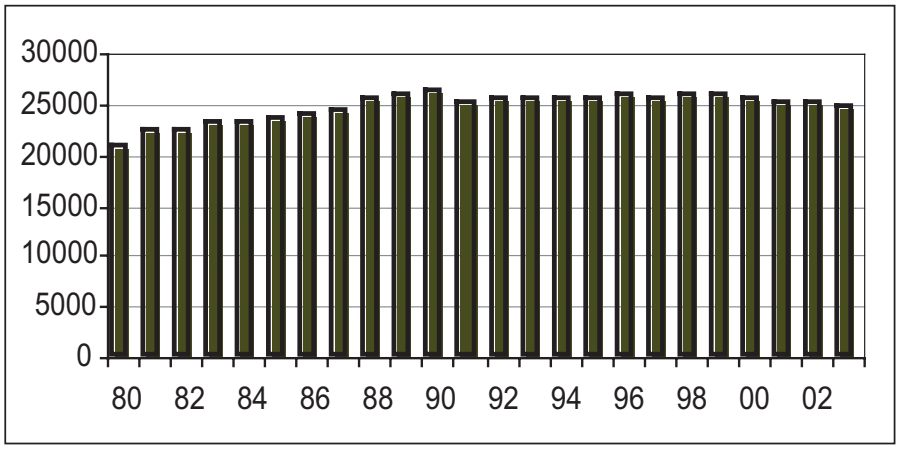
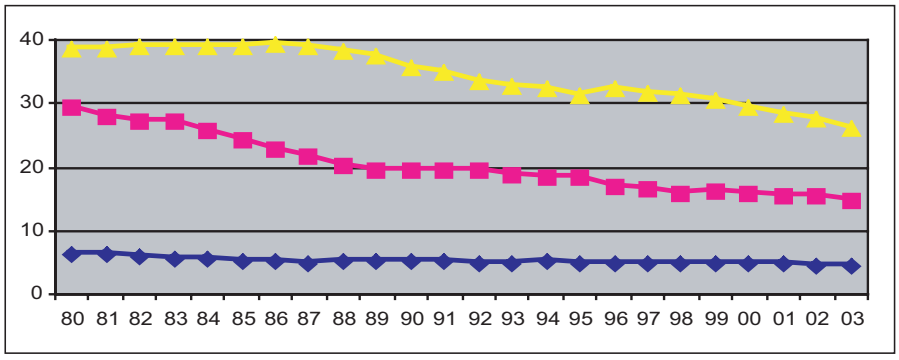
Australia: WABDR

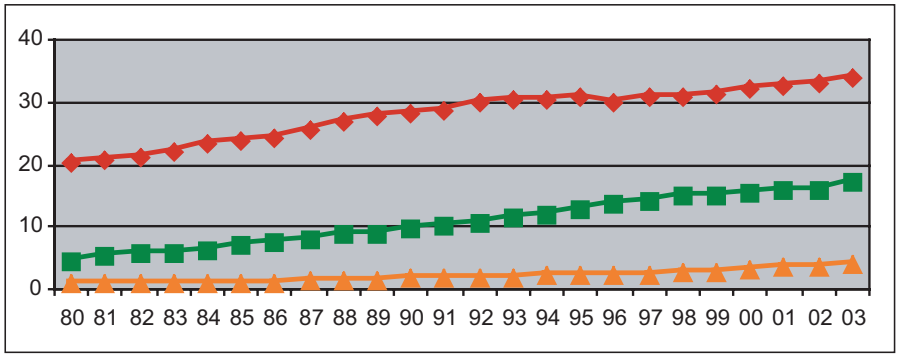
Total births by year



Percentage of births by maternal age



legenda: %births < 20 %births 20-24 %births 25-29



legenda: %births 30-34 %births 35-39 %births 40+

Australia: WABDR, 2003

Live births (LB)	24508
Stillbirths (SB)	184
Total births	24692
Number of terminations of pregnancy (ToP) for birth defects	165

Birth Defects	Number of cases			Rates*10.000
	LB	SB	ToP	Total rate
Anencephaly	2	0	8	4.02
Spina bifida	3	0	10	5.23
Encephalocele	0	1	1	0.80
Microcephaly	3	0	1	1.61
Arhinencephaly / Holoprosencephaly	0	0	4	1.61
Hydrocephaly	8	0	9	6.84
Anophthalmos	0	0	0	0.00
Microphthalmos	3	0	1	1.61
Unspecified Anophthalmos / Microphthalmos	0	0	0	---
Anotia	1	0	0	0.40
Microtia	1	0	0	0.40
Unspecified Anotia / Microtia	0	0	0	---
Transposition of great vessels	6	1	7	5.63
Tetralogy of Fallot	6	0	3	3.62
Hypoplastic left heart syndrome	0	0	2	0.80
Coarctation of aorta	15	2	5	8.85
Choanal atresia, bilateral	0	0	0	0.00
Cleft palate without cleft lip	29	0	1	12.07
Cleft lip with or without cleft palate	31	2	3	14.48
Oesophageal atresia / stenosis with or without fistula	6	0	3	3.62
Small intestine atresia / stenosis	9	0	3	4.83
Anorectal atresia / stenosis	10	0	4	5.63
Undescended testis (36 weeks of gestation or later)	40	0	0	16.09
Hypospadias	66	0	1	26.95
Epispadias	0	0	0	0.00
Indeterminate sex	0	0	0	0.00
Renal agenesis	4	0	6	4.02
Cystic kidney	13	1	9	9.25
Bladder exstrophy	0	0	0	0.00
Polydactyly, preaxial	18	0	8	10.46
Total Limb reduction defects (include unspecified)	3	1	5	3.62
Transverse	nr	nr	nr	nr
Preaxial	nr	nr	nr	nr
Postaxial	nr	nr	nr	nr
Intercalary	nr	nr	nr	nr
Mixed	nr	nr	nr	nr
Unspecified	nr	nr	nr	---
Diaphragmatic hernia	4	2	2	3.22
Omphalocele	5	3	10	7.24
Gastroschisis	9	1	4	5.63
Unspecified Omphalocele / Gastroschisis	0	0	0	---
Prune belly sequence	0	0	0	0.00
Trisomy 13	0	0	10	4.02
Trisomy 18	4	2	16	8.85
Down syndrome, all ages (include age unknown)	19	2	34	22.13
<20	0	0	0	0.00
20-24	3	0	0	8.28
25-29	1	0	2	4.63
30-34	5	1	5	13.19
35-39	5	0	17	51.70
40-44	3	1	10	156.77
45+	2	0	0	434.78
unspecified	0	0	0	---

nr= not reported

Australia: WABDR, Previous years rates 1980 - 2003

Birth prevalence rates: (LB+SB+TOP) * 10,000

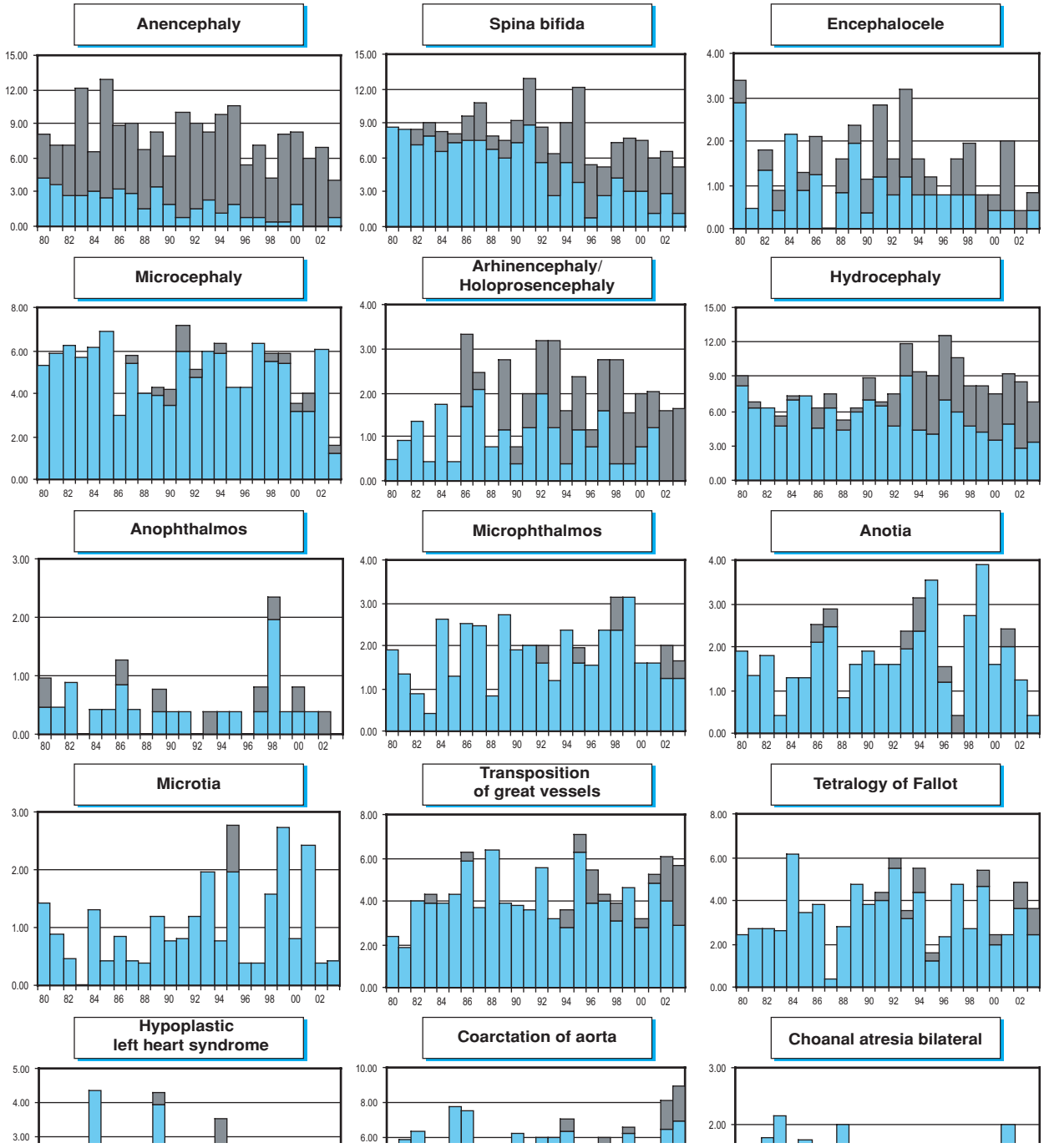
	1974-78	1979-83*	1984-88	1989-93	1994-98	1999-03
Births		**88,499**	**119,571**	**127,229**	**127,395**	**125,410**
Anencephaly		8.70	8.78	8.33	7.46	6.70
Spina bifida		8.70	8.95	8.88	7.85	6.62
Encephalocele		1.58	1.42	2.20	1.41	0.96
Microcephaly		5.76	5.10	5.34	5.42	4.23
Arhinencephaly / Holoprosencephaly		0.79	1.76	2.36	2.12	1.75
Hydrocephaly		6.89	6.69	8.25	9.97	8.05
Anophthalmos		0.56	0.50	0.39	0.78	0.40
Microphthalmos		1.13	1.92	1.96	2.28	1.99
Unspecified Anophthalmos / Microphthalmos		---	---	---	---	---
Anotia		1.36	1.76	1.81	2.28	1.91
Microtia		0.68	0.67	1.18	1.18	1.36
Unspecified Anotia / Microtia		---	---	---	---	---
Transposition of great vessels		3.16	4.93	4.01	4.87	4.94
Tetralogy of Fallot		2.60	3.26	4.48	3.38	3.75
Hypoplastic left heart syndrome		1.58	1.76	2.75	2.12	1.44
Coarctation of aorta		4.75	5.44	5.58	5.10	6.94
Choanal atresia, bilateral		1.36	1.51	0.94	0.63	0.88
Cleft palate without cleft lip		8.14	8.28	11.48	10.75	12.20
Cleft lip with or without cleft palate		11.86	13.72	10.37	12.56	12.52
Oesophageal atresia / stenosis with or without fistula		3.05	3.60	2.52	3.45	3.59
Small intestine atresia / stenosis		3.16	2.68	2.52	2.28	3.51
Anorectal atresia / stenosis		5.88	4.35	7.23	5.81	6.46
Undescended testis (36 weeks of gestation or later)		64.07	65.99	69.95	56.67	40.91
Hypospadias		26.33	30.02	32.15	37.13	34.61
Epispadias		0.34	0.33	0.24	0.08	0.16
Indeterminate sex		0.00	0.33	0.47	0.24	0.24
Renal agenesis		4.07	3.26	4.48	4.63	5.10
Cystic kidney		2.82	3.35	6.84	7.93	8.85
Bladder exstrophy		0.23	0.17	0.24	0.71	0.32
Polydactyly, preaxial		9.27	10.70	9.59	12.40	10.13
Total Limb reduction defects (include unspecified)		4.41	3.85	5.97	6.44	8.21
Transverse		nr	nr	nr	nr	nr
Preaxial		nr	nr	nr	nr	nr
Postaxial		nr	nr	nr	nr	nr
Intercalary		nr	nr	nr	nr	nr
Mixed		nr	nr	nr	nr	nr
Unspecified		---	---	---	---	---
Diaphragmatic hernia		3.50	2.34	3.07	3.45	3.67
Omphalocele		1.24	3.26	3.30	3.77	4.23
Gastroschisis		1.36	1.76	2.52	3.85	3.67
Unspecified Omphalocele / Gastroschisis		---	---	---	---	---
Prune belly sequence		0.56	0.67	0.55	0.39	0.08
Trisomy 13		0.68	1.09	1.34	1.73	2.71
Trisomy 18		1.58	1.67	3.54	5.02	7.34
Down syndrome, all ages (include age unknown)		11.41	15.14	16.74	18.92	24.16
<20		3.78	8.15	6.26	6.56	13.86
20-24		5.66	4.40	9.37	5.02	7.22
25-29		9.03	7.98	8.57	8.90	11.80
30-34		12.91	14.53	17.64	16.45	18.69
35-39		44.31	51.80	37.19	43.51	46.36
40-44		79.05	282.03	153.04	166.61	152.63
45+		625.00	491.80	410.96	291.97	558.38
unspecified		---	---	---	---	---

* data include less than 5 years

nr= not reported

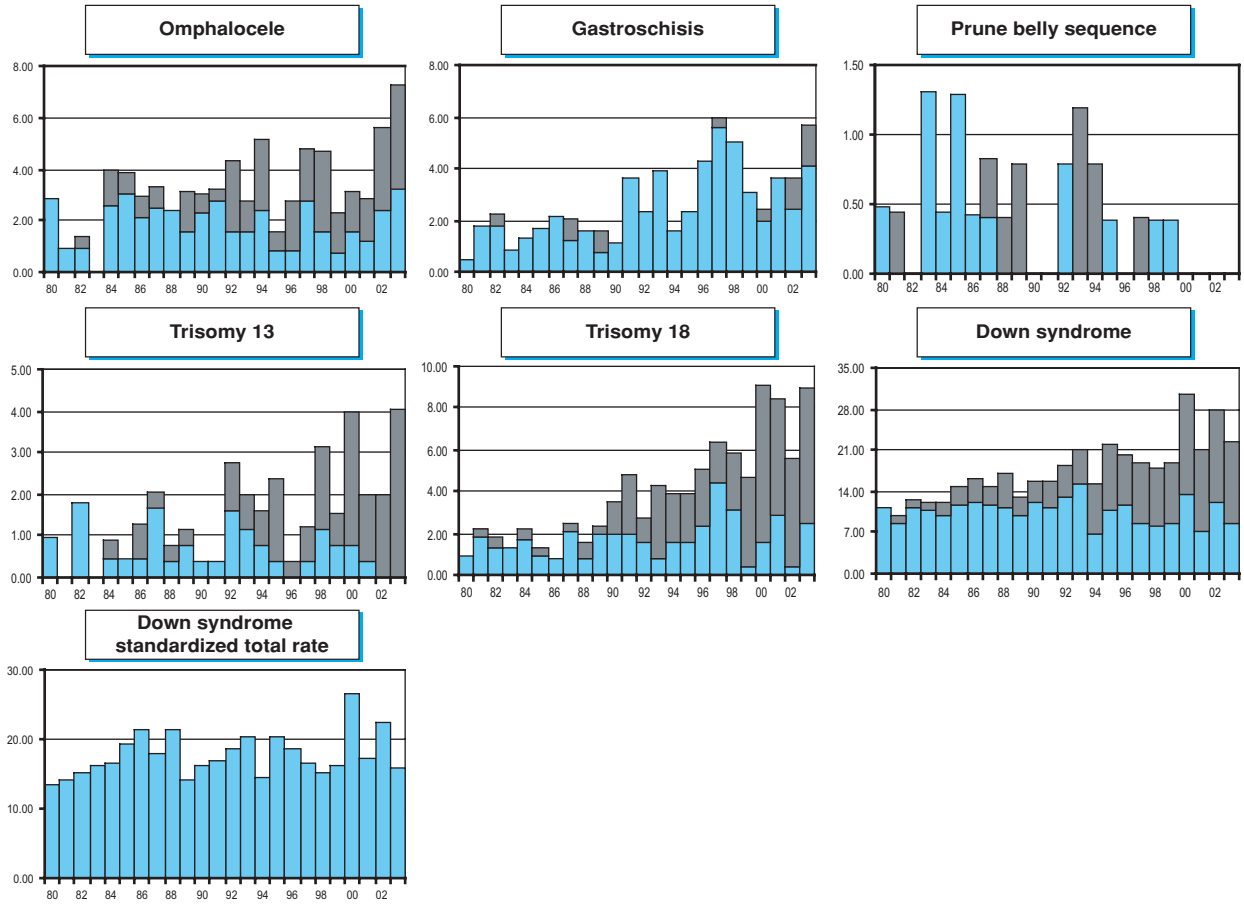
Australia: WABDR

'Time trends 1980-2003 (Birth prevalence rates per 10,000)



Note: L+S rates, ToP rates

Note: L+S rates, ToP rates



Note: L+S rates, ToP rates

Canada: Alberta

Alberta Congenital Anomalies Surveillance System

History:
The 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.

Size and coverage:
All live and stillbirths in the province are covered which at present comprises about 40,000 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:
The Alberta Government Health Information Act (2001) allows the collection and use of individual identifying information for purposes of Public Health Surveillance.
Reporting is voluntary. The system is run by members of the Department of Medical Genetics, Alberta Children's Hospital/University of Calgary reporting to Alberta Vital Statistics and 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 registrations, 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 speciality clinics, such as medical genetics and cytogenetics laboratories.

Exposure information:
None is routinely.
Background information:
Linkage studies are possible with other statistical data from Alberta Health.

Address for further information:
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Dept. Medical Genetics
Alberta Children's Hospital
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Calgary, Alberta Canada T2T 5C7

Phone: 1-403-943-7370
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Barbara Sibbald - Manager

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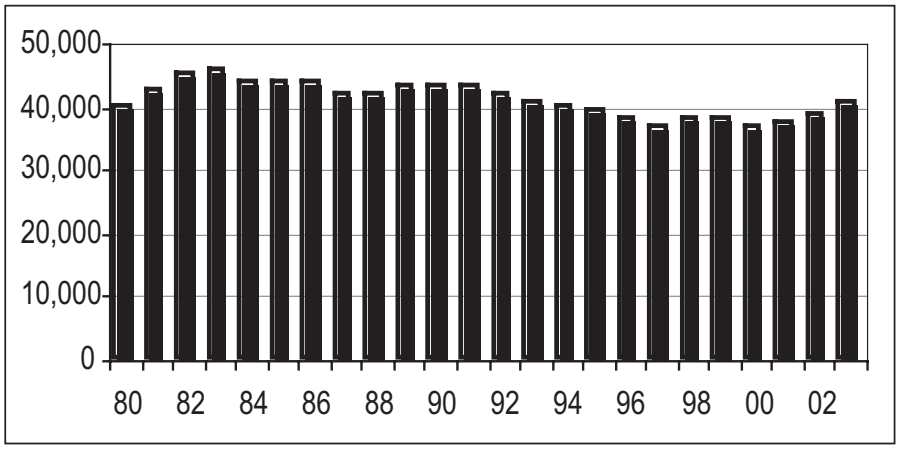
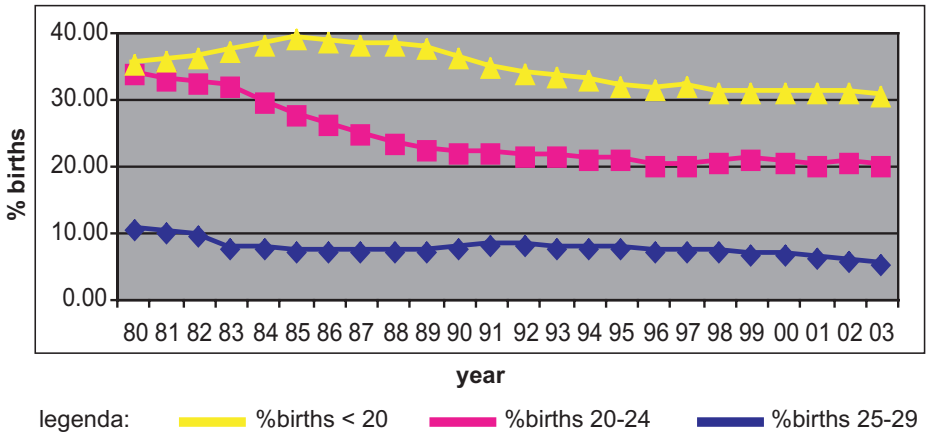
Canada: Alberta

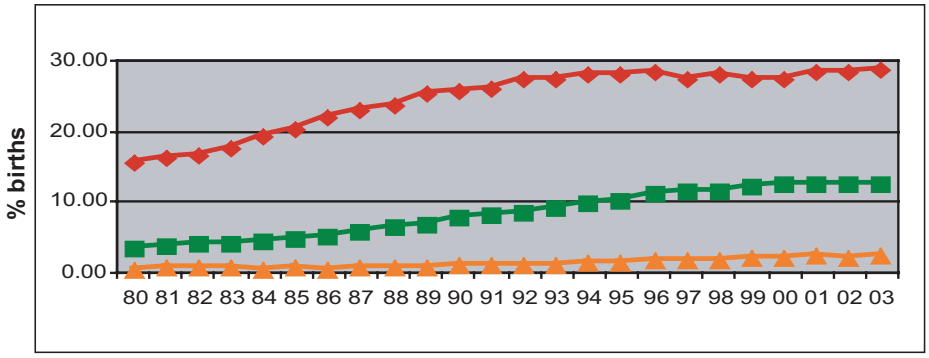
Total births by year



Percentage of births by maternal age



legenda: %births < 20 %births 20-24 %births 25-29



legenda: %births 30-34 %births 35-39 %births 40+

Canada: Alberta, 2003

Live births (LB)	39870
Stillbirths (SB)	272
Total births	40142
Number of terminations of pregnancy (ToP) for birth defects	85

Birth Defects	Number of cases			Rates*10.000
	LB	SB	ToP	Total rate
Anencephaly	4	5	3	2.98
Spina bifida	7	3	4	3.48
Encephalocele	2	1	2	1.24
Microcephaly	16	2	0	4.47
Arhinencephaly / Holoprosencephaly	4	0	3	1.74
Hydrocephaly	18	3	1	5.47
Anophthalmos	1	0	0	0.25
Microphthalmos	1	0	0	0.25
Unspecified Anophthalmos / Microphthalmos	0	0	0	---
Anotia	2	0	1	0.75
Microtia	4	0	0	0.99
Unspecified Anotia / Microtia	0	0	0	---
Transposition of great vessels	14	3	0	4.23
Tetralogy of Fallot	8	0	0	1.99
Hypoplastic left heart syndrome	6	0	1	1.74
Coarctation of aorta	12	0	0	2.98
Choanal atresia, bilateral	1	1	1	0.75
Cleft palate without cleft lip	23	1	0	5.97
Cleft lip with or without cleft palate	41	3	5	12.18
Oesophageal atresia / stenosis with or without fistula	5	1	0	1.49
Small intestine atresia / stenosis	2	0	0	0.50
Anorectal atresia / stenosis	16	8	2	6.46
Undescended testis (36 weeks of gestation or later)	114	0	0	28.34
Hypospadias	86	2	1	22.12
Epispadias	2	0	0	0.50
Indeterminate sex	1	1	2	0.99
Renal agenesis	11	5	3	4.72
Cystic kidney	37	4	2	10.69
Bladder exstrophy	2	0	0	0.50
Polydactyly, preaxial	55	1	2	14.42
Total Limb reduction defects (include unspecified)	32	7	10	12.18
Transverse	nr	nr	nr	nr
Preaxial	nr	nr	nr	nr
Postaxial	nr	nr	nr	nr
Intercalary	nr	nr	nr	nr
Mixed	nr	nr	nr	nr
Unspecified	nr	nr	nr	nr
Diaphragmatic hernia	10	1	2	3.23
Omphalocele	3	5	3	2.73
Gastroschisis	11	2	0	3.23
Unspecified Omphalocele / Gastroschisis	3	1	1	---
Prune belly sequence	2	0	0	0.50
Trisomy 13	4	1	3	1.99
Trisomy 18	2	3	7	2.98
Down syndrome, all ages (include age unknown)	65	7	18	22.37
<20	4	0	0	18.81
20-24	7	0	0	8.72
25-29	12	0	0	9.75
30-34	13	2	4	16.58
35-39	17	5	6	56.55
40-44	11	0	8	196.28
45+	1	0	0	227.27
unspecified	0	0	0	---

nr = not reported

Canada: Alberta, Previous years rates 1980 - 2003

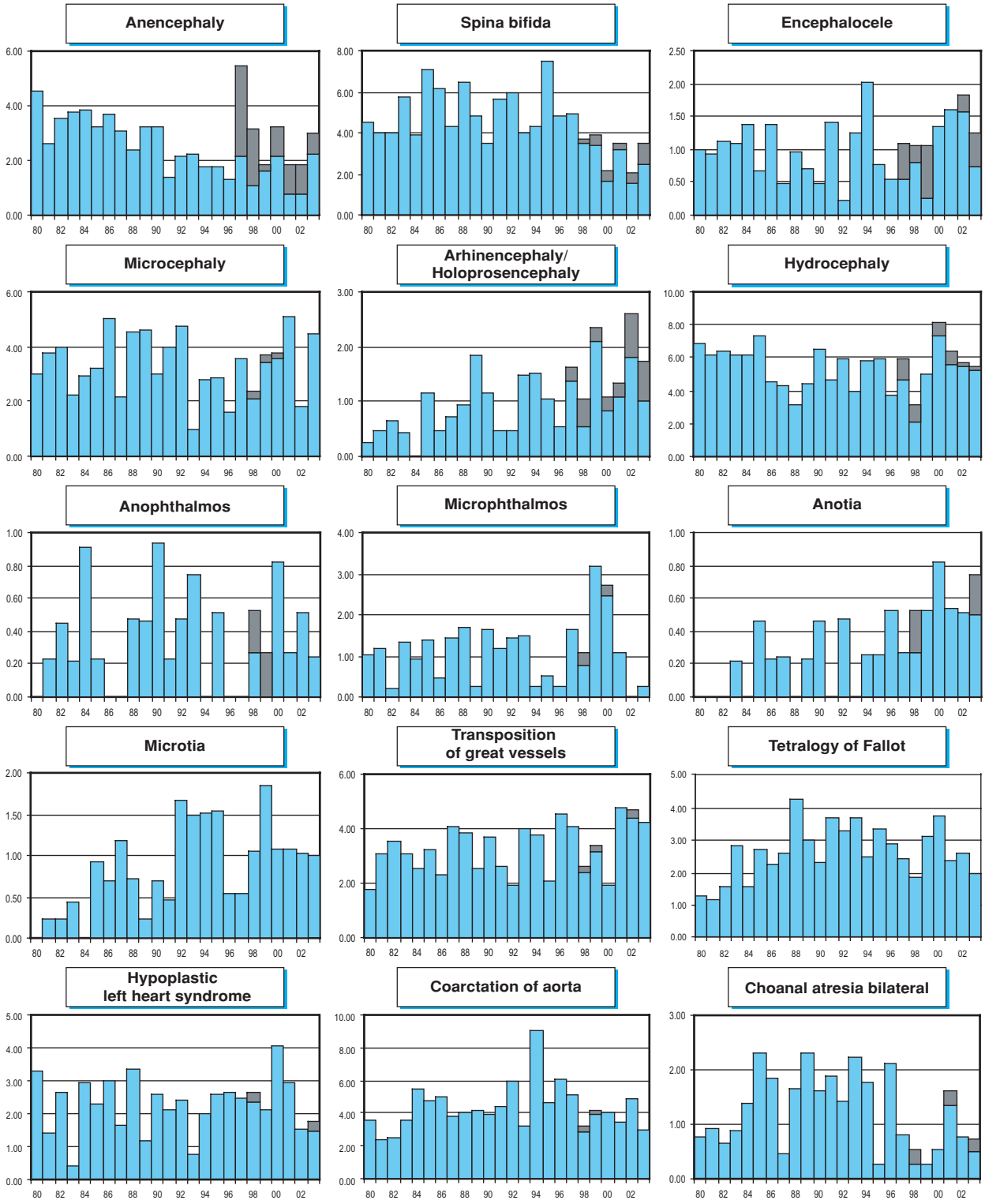
Birth prevalence rates: (LB+SB) * 10,000 until 1996
Birth prevalence rates: (LB+SB+TOP) * 10,000 since 1997

	1974-78	1979-83*	1984-88	1989-93	1994-98	1999-03
Births		**172,486**	**214,908**	**210,900**	**190,820**	**190,998**
Anencephaly		3.59	3.26	2.47	2.67	2.36
Spina bifida		4.58	5.58	4.79	5.03	3.04
Encephalocele		1.04	0.98	0.81	1.10	1.41
Microcephaly		3.25	3.58	3.51	2.62	3.77
Arhinencephaly / Holoprosencephaly		0.46	0.65	1.09	1.15	1.83
Hydrocephaly		6.38	5.12	5.12	4.93	6.13
Anophthalmos		0.23	0.33	0.57	0.21	0.42
Microphthalmos		0.93	1.16	1.19	0.73	1.41
Unspecified Anophthalmos / Microphthalmos		---	---	---	---	---
Anotia		0.06	0.19	0.24	0.37	0.63
Microtia		0.23	0.70	0.90	1.05	1.20
Unspecified Anotia / Microtia		---	---	---	---	---
Transposition of great vessels		2.90	3.16	2.94	3.41	3.82
Tetralogy of Fallot		1.74	2.70	3.22	2.62	2.77
Hypoplastic left heart syndrome		1.91	2.65	1.80	2.46	2.46
Coarctation of aorta		2.96	4.65	4.36	5.66	3.93
Choanal atresia, bilateral		0.81	1.54	1.90	1.10	0.79
Cleft palate without cleft lip		6.32	7.12	7.78	8.12	8.38
Cleft lip with or without cleft palate		10.15	11.68	11.95	12.21	11.83
Oesophageal atresia / stenosis with or without fistula		2.61	3.12	2.56	2.25	2.15
Small intestine atresia / stenosis		0.75	0.88	1.38	1.52	1.94
Anorectal atresia / stenosis		3.19	4.47	5.31	5.14	6.65
Undescended testis (36 weeks of gestation or later)		26.67	26.52	29.92	23.58	24.29
Hypospadias		17.16	22.52	24.85	18.60	19.79
Epispadias		0.64	0.23	0.43	0.37	0.63
Indeterminate sex		0.35	0.56	1.14	0.73	1.26
Renal agenesis		3.01	4.28	5.41	4.30	6.18
Cystic kidney		2.09	3.35	5.22	4.77	7.49
Bladder exstrophy		0.46	0.14	0.33	0.26	0.42
Polydactyly, preaxial		9.62	12.24	16.60	13.26	14.24
Total Limb reduction defects (include unspecified)		5.86	8.00	10.81	9.33	12.15
Transverse		nr	nr	nr	nr	nr
Preaxial		nr	nr	nr	nr	nr
Postaxial		nr	nr	nr	nr	nr
Intercalary		nr	nr	nr	nr	nr
Mixed		nr	nr	nr	nr	nr
Unspecified		---	---	---	---	---
Diaphragmatic hernia		3.25	3.44	2.66	2.52	4.50
Omphalocele		1.68	2.09	2.09	2.20	2.30
Gastroschisis		1.51	1.44	1.42	2.46	3.04
Unspecified Omphalocele / Gastroschisis		---	---	---	---	---
Prune belly sequence		0.58	0.23	0.24	0.31	0.31
Trisomy 13		0.81	0.74	1.19	1.26	1.68
Trisomy 18		1.28	1.86	2.04	3.35	4.35
Down syndrome, all ages (include age unknown)		9.33	9.17	11.10	13.26	18.74
<20		nr	5.40*	4.92	4.98	10.19
20-24		nr	4.14*	7.80	5.37	4.63
25-29		nr	6.56*	6.74	7.90	10.37
30-34		nr	11.35*	13.73	12.95	16.29
35-39		nr	36.95*	24.81	36.31	47.36
40-44		nr	111.52*	93.99	108.92	159.08
45+		nr	0.00*	375.00	246.91	196.08
unspecified		---	---	---	---	---

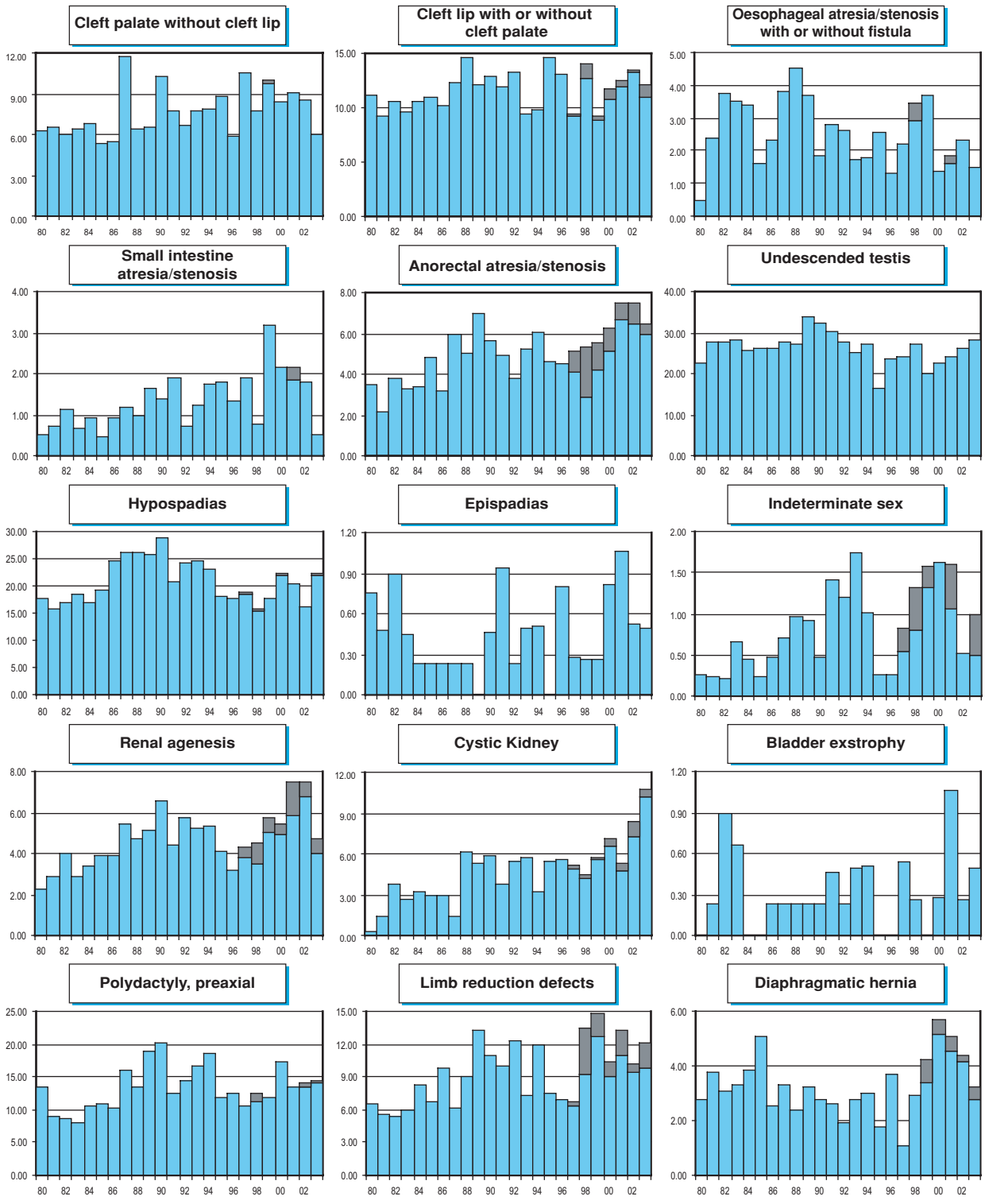
* data include less than 5 years
nr= not reported

Canada: Alberta

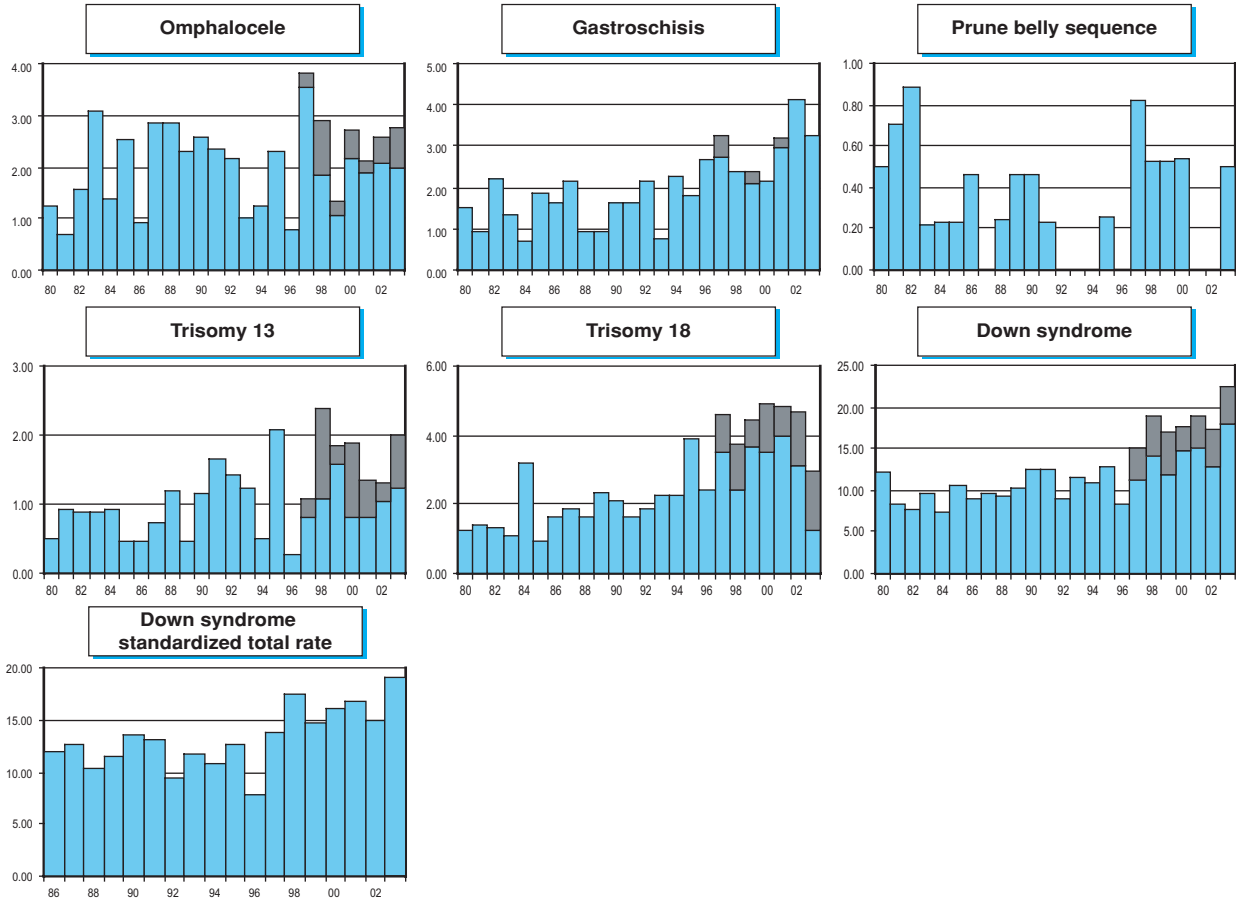
'Time trends 1980-2003 (Birth prevalence rates per 10,000)



Note: L+S rates, ToP rates



Note: L+S rates, ToP rates



Note: L+S rates, ToP rates

Canada: British Columbia

British Columbia Health Status Registry (BCHSR)
Congenital Anomalies Surveillance Program

History:
The programme was established in 1952 as the Crippled Children's Registry. Until 1959 the programme had an age limit of 21, but this was removed in 1960 and the name was change to the Registry for Handicapped Children and Adults and included all familial conditions and congenital malformations. In 1975, the Registry's name was changed to the Health Surveillance Registry as risk registers for amniocentesis, rubella, hyaline membrane disease, and fetal alcohol syndrome were added. In 1991, the Royal Commission Report on Health Care and Costs contained a recommendation that Vital Statistics should develop and maintain a registry of individuals with disabilities to assist in the development of long-range plans and to monitor the changing needs of the population. Subsequently, in September 1992, amendments to the Health Act established the legislative mandate and responsibilities for the HSR. The Registry's current name, Health Status Registry, was acquired in 1992. In order to refocus the Registry's emphasis on children, the criteria for registration of individuals with long-term physical, mental and/or emotional problems was restricted to persons under the age of 20 years old, however registration of persons with genetic conditions was not age limited. For the periods of 1973 to 2002, there were total 106,172 congenital anomaly cases registered with 152,838 diagnoses.

Size and coverage
The registry covers all births in the province approximately 45,000 births annually including stillbirths with at least 20 weeks gestation or birth weight 500 grams or more .

Legislation and funding
In 1992, amendments to the Health Act established the legislative mandate and responsibilities for the British Columbia Health Status Registry(BCHSR). Funding comes from the British Columbia Vital Statistics Agency.

Sources of ascertainment
Sources include: Notice of Live and Stillbirth, Death registrations, Hospital Admission/Discharge Abstracts, BC Children's Hospital, Sunnyhill Hospital, UBC and Victoria General Medical Genetics Clinics, Child Development Centres, Health Regions, the Asante Centre for Fetal Alcohol Syndrome.

Exposure information
Information on complications of pregnancy, labour or delivery is available on Vital Statistics birth registrations and environmental/occupational and drug/alcohol/smoking lifestyle related information can be obtained from the death registrations for the deceased.

Background information
The registry data are regularly matched to Vital Statistics birth registrations to obtain birth particulars of the registrants and maternal/paternal information, and also matched to death registrations to get the date of death and causes of death if the registered person was deceased. The Registry is now ready to collect and to register the medically terminated pregnancies due to congenital anomalies in the province.

Addresses and staff
Ron Danderfer, Assistant Deputy Minister, Knowledge Management and Technology, BC Ministry of Health, 7-1, 1515 Blanshard Street, Victoria, BC, V8W3C8, Canada

Phone: 1-250-952-2563

Fax: 1-250-952-1827

E-mail: mailto:ron.danderfer@gov.bc.ca

Soo-Hong Uh, Consultant, BC Health Status Registry, KMT Division, BC Ministry ofHealth, 7-1, 1515 Blanshard Street, Victoria, BC, V8W3C8, Canada

Phone: 1-250-217-1346

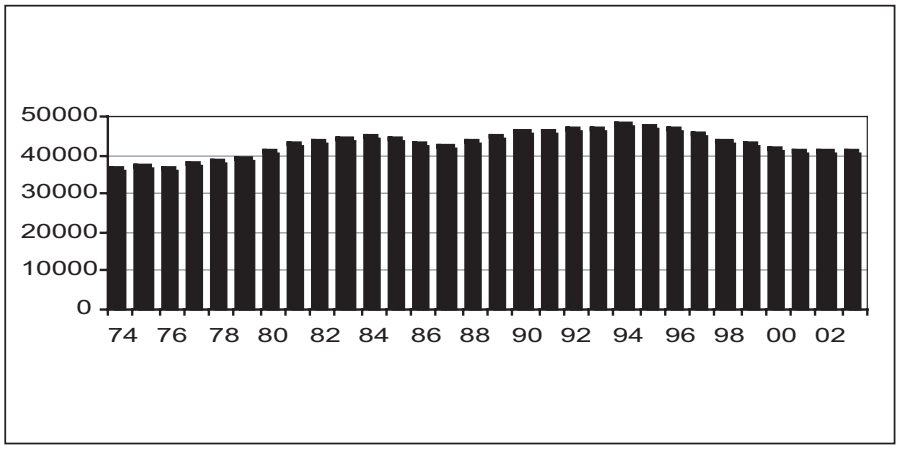
Fax: 1-250-952-1827

E-mail: soohong.uh@gov.bc.ca

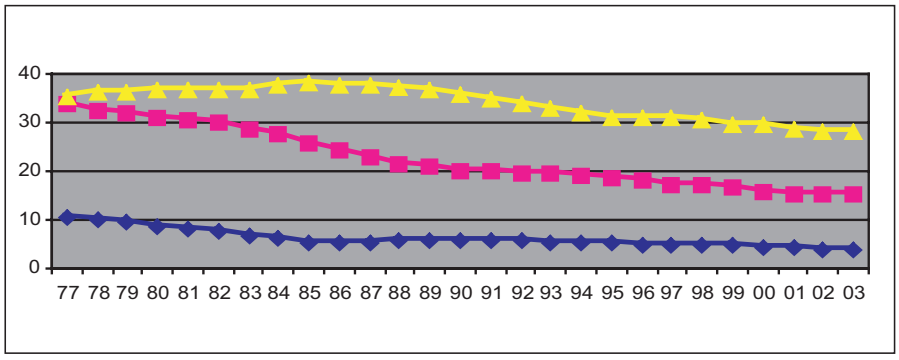
Web site:
http://www.vs.gov.bc.ca/stats/hsr/index.html

Canada: British Columbia

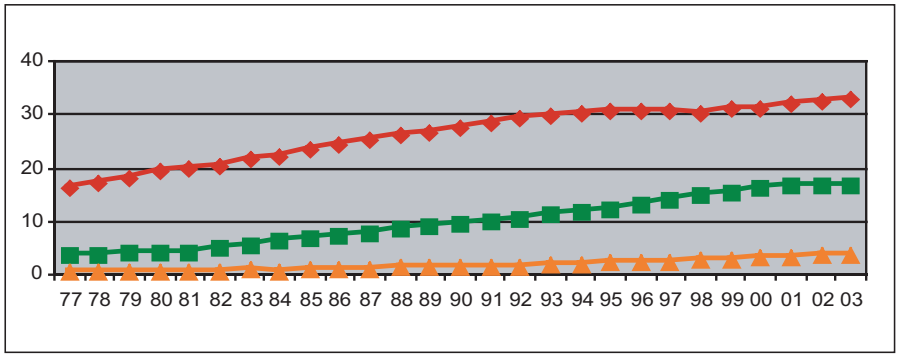
Total births by year



Percentage of births by maternal age



legenda: %births < 20 %births 20-24 %births 25-29



legenda: %births 30-34 %births 35-39 %births 40+

Canada: British Columbia. 2003

Live births (LB)	40282
Stillbirths (SB)	284
Total births	40566
Number of terminations of pregnancy (ToP) for birth defects	nr

Birth Defects	Number of cases			Rates*10.000
	LB	SB	ToP	Total rate
Anencephaly	0	4	nr	0.99
Spina bifida	10	2	nr	2.96
Encephalocele	2	1	nr	0.74
Microcephaly	13	1	nr	3.45
Arhinencephaly / Holoprosencephaly	15	10	nr	6.16
Hydrocephaly	4	8	nr	2.96
Anophthalmos	1	0	nr	0.25
Microphthalmos	0	0	nr	0.00
Unspecified Anophthalmos / Microphthalmos	0	0	nr	---
Anotia	2	0	nr	0.49
Microtia	0	0	nr	0.00
Unspecified Anotia / Microtia	3	0	nr	---
Transposition of great vessels	10	0	nr	2.47
Tetralogy of Fallot	10	0	nr	2.47
Hypoplastic left heart syndrome	2	3	nr	1.23
Coarctation of aorta	13	0	nr	3.20
Choanal atresia, bilateral	10	0	nr	2.47
Cleft palate without cleft lip	19	0	nr	4.68
Cleft lip with or without cleft palate	18	0	nr	4.44
Oesophageal atresia / stenosis with or without fistula	10	0	nr	2.47
Small intestine atresia / stenosis	12	0	nr	2.96
Anorectal atresia / stenosis	14	2	nr	3.94
Undescended testis (36 weeks of gestation or later)	38	1	nr	9.61
Hypospadias	37	0	nr	9.12
Epispadias	2	0	nr	0.49
Indeterminate sex	0	0	nr	0.00
Renal agenesis	0	0	nr	0.00
Cystic kidney	0	0	nr	0.00
Bladder exstrophy	0	0	nr	0.00
Polydactyly, preaxial	21	1	nr	5.42
Total Limb reduction defects (include unspecified)	6	1	nr	1.73
Transverse	nr	nr	nr	nr
Preaxial	nr	nr	nr	nr
Postaxial	nr	nr	nr	nr
Intercalary	nr	nr	nr	nr
Mixed	nr	nr	nr	nr
Unspecified	nr	nr	nr	---
Diaphragmatic hernia	8	1	nr	2.22
Omphalocele	4	4	nr	1.97
Gastroschisis	9	3	nr	2.96
Unspecified Omphalocele / Gastroschisis	3	0	nr	---
Prune belly sequence	0	0	nr	0.00
Trisomy 13	3	3	nr	1.48
Trisomy 18	5	7	nr	2.96
Down syndrome, all ages (include age unknown)	42	25	nr	16.52
<20	0	0	nr	0.00
20-24	2	0	nr	3.28
25-29	9	2	nr	9.71
30-34	4	7	nr	8.21
35-39	13	12	nr	36.57
40-44	8	4	nr	88.30
45+	0	0	nr	0.00
unspecified	6	0	nr	---

nr = not reported

Canada: British Columbia, Previous years rates 1974 - 2003

Birth prevalence rates: (LB+SB) * 10,000

	1974-78	1979-83	1984-88	1989-93	1994-98	1999-03
Births	**183,301**	**207,831**	**214,734**	**227,782**	**228,312**	**204,256**
Anencephaly	6.55	4.38	3.26	2.06	1.62	1.86
Spina bifida	11.02	8.23	7.68	7.46	5.21	4.06
Encephalocele	1.64	1.64	1.30	2.06	0.88	0.64
Microcephaly	4.96	5.97	6.38	7.42	8.94	5.78
Arhinencephaly / Holoprosencephaly	1.64	3.08	5.17	3.64	4.64	8.86
Hydrocephaly	10.58	9.72	6.47	6.59	6.35	4.65
Anophthalmos	0.38	0.53	0.47	0.40	0.31	0.20
Microphthalmos	1.69	1.64	1.54	1.62	1.80	1.37
Unspecified Anophthalmos / Microphthalmos	---	---	---	---	---	---
Anotia	3.06	2.41	3.31	2.24	2.45	0.98
Microtia	35.08	55.09	63.61	34.95	14.59	2.94
Unspecified Anotia / Microtia	---	---	---	---	---	---
Transposition of great vessels	4.64	4.67	4.56	4.70	5.83	3.72
Tetralogy of Fallot	5.18	5.00	6.15	5.14	4.56	4.41
Hypoplastic left heart syndrome	2.07	2.94	2.28	2.68	3.11	2.89
Coarctation of aorta	5.46	8.13	6.29	5.97	7.10	4.94
Choanal atresia, bilateral	1.25	1.78	1.96	1.67	2.10	2.59
Cleft palate without cleft lip	11.02	10.92	11.83	14.00	11.91	8.62
Cleft lip with or without cleft palate	14.08	15.06	14.67	14.79	13.40	10.48
Oesophageal atresia / stenosis with or without fistula	2.95	4.14	3.35	3.07	3.77	2.99
Small intestine atresia / stenosis	2.07	3.32	3.73	3.07	4.16	4.01
Anorectal atresia / stenosis	4.86	4.67	4.42	5.40	5.08	5.24
Undescended testis (36 weeks of gestation or later)	73.70	73.33	71.53	70.99	57.33	39.90
Hypospadias	27.33	31.85	31.76	38.24	35.65	25.02
Epispadias	0.00	0.00	0.05	0.00	0.00	0.29
Indeterminate sex	1.09	1.30	1.12	0.83	1.45	0.49
Renal agenesis	5.02	5.77	7.13	6.80	5.69	3.23
Cystic kidney	3.33	4.14	5.82	6.10	6.88	2.89
Bladder exstrophy	0.38	0.43	0.65	0.44	0.35	0.39
Polydactyly, preaxial	23.19	22.09	20.58	23.40	20.67	15.57
Total Limb reduction defects (include unspecified)	10.64	8.71	8.29	6.45	6.66	3.67
Transverse	nr	nr	nr	nr	nr	nr
Preaxial	nr	nr	nr	nr	nr	nr
Postaxial	nr	nr	nr	nr	nr	nr
Intercalary	nr	nr	nr	nr	nr	nr
Mixed	nr	nr	nr	nr	nr	nr
Unspecified	---	---	---	---	---	---
Diaphragmatic hernia	4.96	3.99	3.26	3.95	4.82	3.08
Omphalocele	0.00	0.00	0.05	0.00	0.18	1.66
Gastroschisis	0.00	0.00	0.05	0.00	0.18	3.43
Unspecified Omphalocele / Gastroschisis	---	---	---	---	---	---
Prune belly sequence	0.00	0.00	0.05	0.00	0.04	0.10
Trisomy 13	0.65	0.63	1.07	1.01	1.40	1.42
Trisomy 18	1.20	2.12	2.19	1.76	3.28	4.01
Down syndrome, all ages (include age unknown)	12.27	14.05	13.83	15.85	17.48	17.14
<20	3.92*	8.32	7.54	10.95	10.31	8.09
20-24	6.47*	5.39	7.05	8.81	8.03	7.83
25-29	7.14*	8.41	6.45	6.19	11.10	10.23
30-34	17.72*	14.34	14.61	15.36	14.71	12.77
35-39	25.95*	36.84	18.99	22.08	28.68	30.57
40-44	171.99*	87.57	85.62	57.29	82.17	62.77
45+	322.58*	178.57	156.25	310.08	560.34	69.69
unspecified	---	---	---	---	---	---

* data include less than 5 years

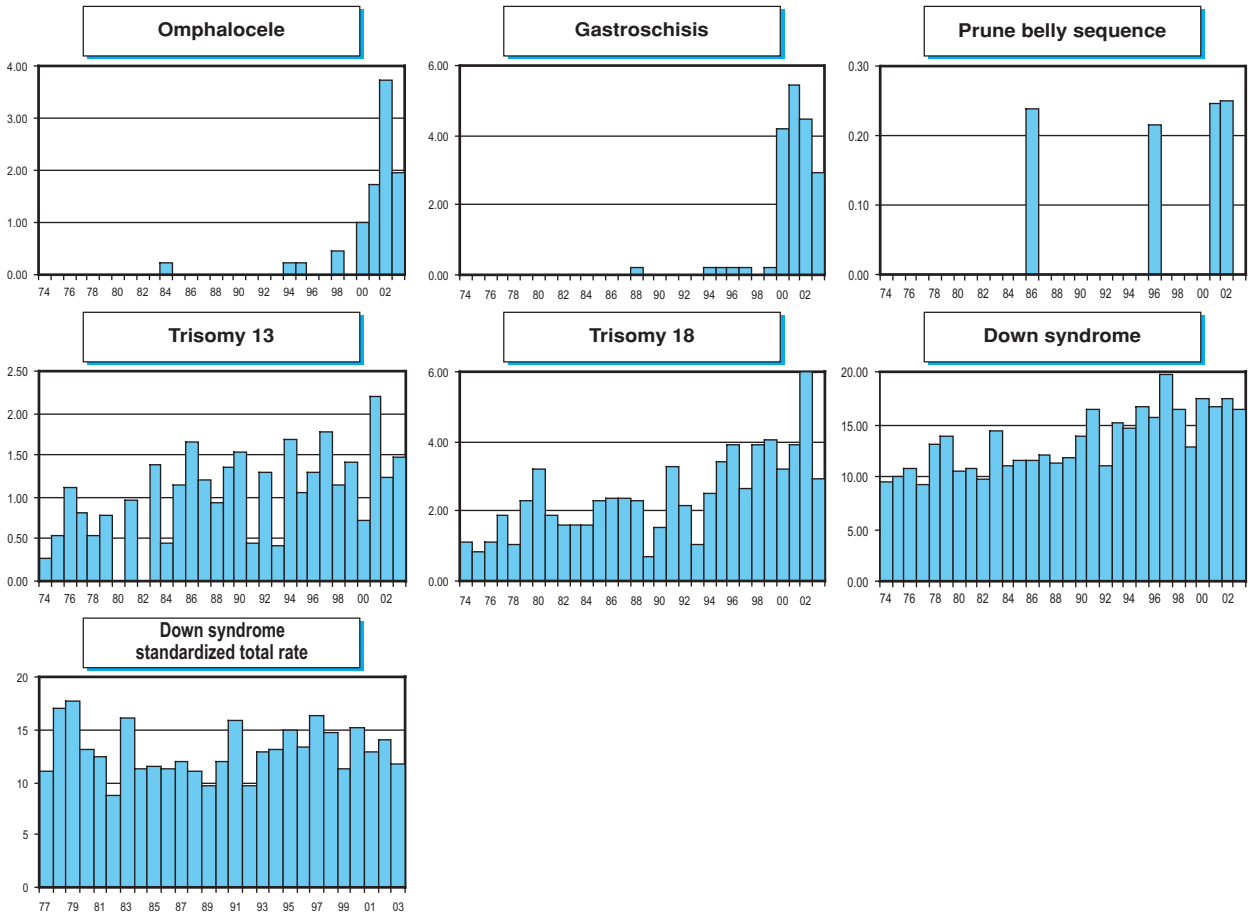
nr = not reported

Canada: British Columbia

Time trends 1974-2003 (Birth prevalence rates per 10,000)

Note: L+S rates

Note: L+S rates



Note: L+S rates

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 a 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 included 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 partcipating 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 statisticals units.

Address 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 Maule: RRMC-SSM, 2003

Live births (LB)	12359
Stillbirths (SB)	73
Total births	12432
Number of terminations of pregnancy (ToP) for birth defects	not permitted

Birth Defects	Number of cases			Rates*10.000
	LB	SB	ToP	Total rate
Anencephaly	2	5		5.63
Spina bifida	4	1		4.02
Encephalocele	0	0		0.00
Microcephaly	0	0		0.00
Arhinencephaly / Holoprosencephaly	0	1		0.80
Hydrocephaly	3	0		2.41
Anophthalmos	1	0		0.80
Microphthalmos	0	0		0.00
Unspecified Anophthalmos / Microphthalmos	0	0		---
Anotia	1	1		1.61
Microtia	3	0		2.41
Unspecified Anotia / Microtia	0	0		---
Transposition of great vessels	3	0		2.41
Tetralogy of Fallot	0	0		0.00
Hypoplastic left heart syndrome	1	0		0.80
Coarctation of aorta	0	0		0.00
Choanal atresia, bilateral	3	0		2.41
Cleft palate without cleft lip	10	0		8.04
Cleft lip with or without cleft palate	19	1		16.09
Oesophageal atresia / stenosis with or without fistula	0	0		0.00
Small intestine atresia / stenosis	0	0		0.00
Anorectal atresia / stenosis	4	0		3.22
Undescended testis (36 weeks of gestation or later)	10	0		8.04
Hypospadias	11	0		8.85
Epispadias	0	0		0.00
Indeterminate sex	1	0		0.80
Renal agenesis	2	0		1.61
Cystic kidney	0	0		0.00
Bladder exstrophy	0	0		0.00
Polydactyly, preaxial	5	0		4.02
Total Limb reduction defects (include unspecified)	0	0		0.00
Transverse	0	0		0.00
Preaxial	0	0		0.00
Postaxial	0	0		0.00
Intercalary	0	0		0.00
Mixed	0	0		0.00
Unspecified	0	0		---
Diaphragmatic hernia	0	1		0.80
Omphalocele	1	0		0.80
Gastroschisis	2	0		1.61
Unspecified Omphalocele / Gastroschisis	0	0		---
Prune belly sequence	0	0		0.00
Trisomy 13	4	1		4.02
Trisomy 18	0	0		0.00
Down syndrome, all ages (include age unknown)	21	0		16.89
<20	1	0		4.42
20-24	0	0		0.00
25-29	3	0		10.54
30-34	2	0		8.67
35-39	7	0		47.65
40-44	7	0		174.13
45+	1	0		588.24
unspecified	0	0		---

China: BDSS-Beijing

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.

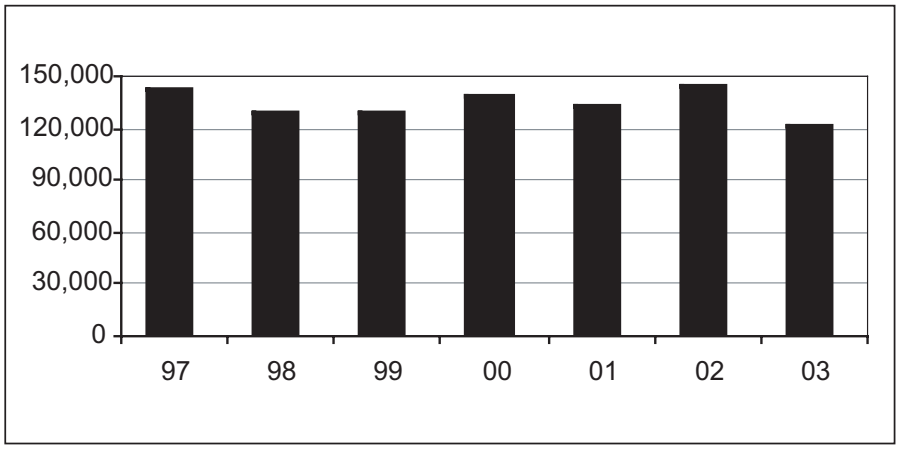
Phone: 86-10-62091138

Fax: 86-10-62091141

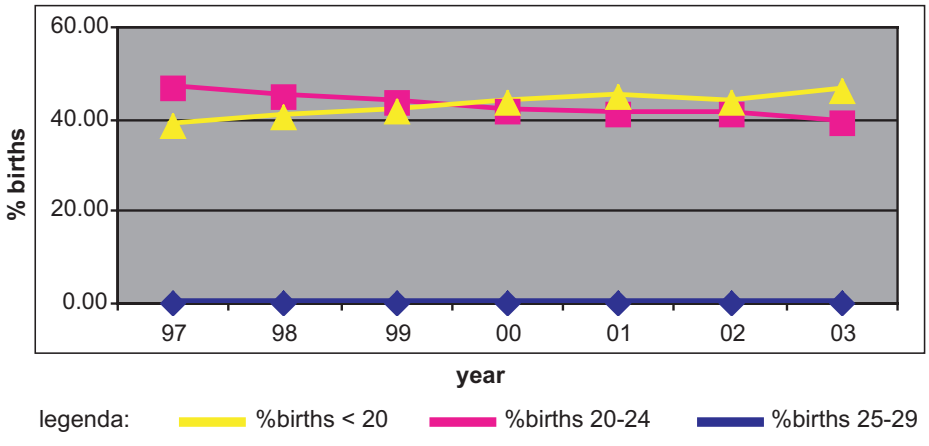
E-mail: lzh@public.bta.net.cn

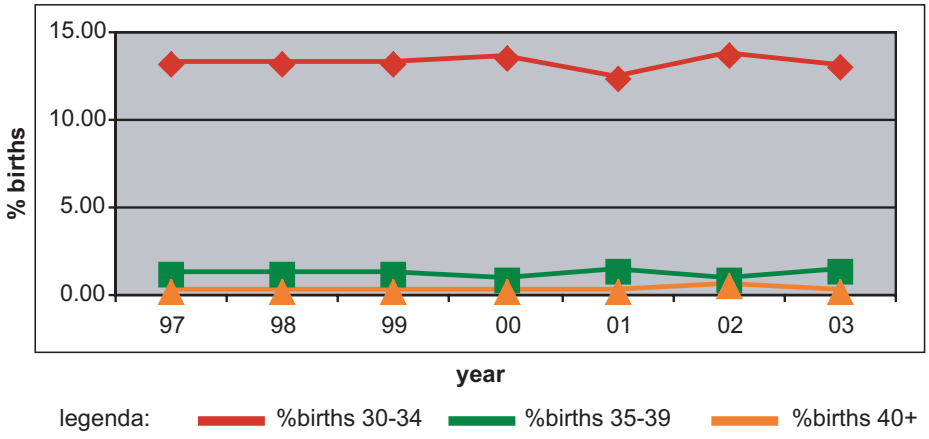
China: BDSS-Beijing

Total births by year



Percentage of births by maternal age





China: Beijing, 2003

Live births (LB)	119011
Stillbirths (SB)	462
Total births	119473
Number of terminations of pregnancy (ToP) for birth defects	nr

Birth Defects	Number of cases			Rates*10.000
	LB	SB	ToP	Total rate
Anencephaly	0	29	nr	2.43
Spina bifida	7	18	nr	2.09
Encephalocele	0	12	nr	1.00
Microcephaly	4	3	nr	0.59
Arhinencephaly / Holoprosencephaly	1	4	nr	0.42
Hydrocephaly	7	49	nr	4.69
Anophthalmos	1	1	nr	0.17
Microphthalmos	1	0	nr	0.08
Unspecified Anophthalmos / Microphthalmos	0	0	nr	---
Anotia	0	0	nr	0.00
Microtia	19	1	nr	1.67
Unspecified Anotia / Microtia	0	0	nr	---
Transposition of great vessels	nr	nr	nr	nr
Tetralogy of Fallot	nr	nr	nr	nr
Hypoplastic left heart syndrome	nr	nr	nr	nr
Coarctation of aorta	nr	nr	nr	nr
Choanal atresia, bilateral	nr	nr	nr	nr
Cleft palate without cleft lip	25	1	nr	2.18
Cleft lip with or without cleft palate	104	33	nr	11.47
Oesophageal atresia / stenosis with or without fistula	nr	nr	nr	nr
Small intestine atresia / stenosis	nr	nr	nr	nr
Anorectal atresia / stenosis	15	3	nr	1.51
Undescended testis (36 weeks of gestation or later)	4	0	nr	0.33
Hypospadias	18	0	nr	1.51
Epispadias	0	0	nr	0.00
Indeterminate sex	4	5	nr	0.75
Renal agenesis	nr	nr	nr	nr
Cystic kidney	nr	nr	nr	nr
Bladder exstrophy	0	0	nr	0.00
Polydactyly, preaxial	65	0	nr	5.44
Total Limb reduction defects (include unspecified)	23	8	nr	2.59
Transverse	20	3	nr	1.93
Preaxial	1	5	nr	0.50
Postaxial	0	0	nr	0.00
Intercalary	2	0	nr	0.17
Mixed	0	0	nr	0.00
Unspecified	0	0	nr	---
Diaphragmatic hernia	nr	nr	nr	nr
Omphalocele	2	5	nr	0.59
Gastroschisis	3	15	nr	1.51
Unspecified Omphalocele / Gastroschisis	0	0	nr	0.00
Prune belly sequence	0	6	nr	0.50
Trisomy 13	nr	nr	nr	nr
Trisomy 18	nr	nr	nr	nr
Down syndrome, all ages (include age unknown)	nr	nr	nr	nr
<20	nr	nr	nr	nr
20-24	nr	nr	nr	nr
25-29	nr	nr	nr	nr
30-34	nr	nr	nr	nr
35-39	nr	nr	nr	nr
40-44	nr	nr	nr	nr
45+	nr	nr	nr	nr
unspecified	nr	nr	nr	---

nr= not reported

China: Beijing, Previous years rates 1997 - 2003

Prevalence rates: (LB+SB) * 10,000

	1974-78	1979-83	1984-88	1989-93	1994-98*	1999-03
Births					**267,071**	**654,230**
Anencephaly					3.22	3.38
Spina bifida					3.00	2.66
Encephalocele					1.27	1.28
Microcephaly					0.34	0.41
Arhinencephaly / Holoprosencephaly					0.34	0.49
Hydrocephaly					6.18	4.88
Anophthalmos					0.15	0.11
Microphthalmos					0.11	0.14
Unspecified Anophthalmos / Microphthalmos					---	---
Anotia				0.07	0.17	
Microtia					2.85	2.34
Unspecified Anotia / Microtia					---	---
Transposition of great vessels					nr	nr
Tetralogy of Fallot					nr	nr
Hypoplastic left heart syndrome					nr	nr
Coarctation of aorta					nr	nr
Choanal atresia, bilateral					nr	nr
Cleft palate without cleft lip					3.03	2.55
Cleft lip with or without cleft palate					12.17	10.65
Oesophageal atresia / stenosis with or without fistula					nr	nr
Small intestine atresia / stenosis					nr	nr
Anorectal atresia / stenosis					1.68	1.60
Undescended testis (36 weeks of gestation or later)					0.30	0.21
Hypospadias					1.42	1.22
Epispadias					0.00	0.02
Indeterminate sex					1.12	1.09
Renal agenesis					nr	nr
Cystic kidney					nr	nr
Bladder exstrophy					0.07	0.02
Polydactyly, preaxial					6.74	6.27
Total Limb reduction defects (include unspecified)					2.13	2.58
Transverse					0.94*	1.88
Preaxial					0.24*	0.35
Postaxial					0.00*	0.00
Intercalary					0.08*	0.03
Mixed					0.00*	0.03
Unspecified					---	---
Diaphragmatic hernia					nr	nr
Omphalocele					1.27	0.84
Gastroschisis					1.39	1.99
Unspecified Omphalocele / Gastroschisis					---	---
Prune belly sequence					1.91	0.86
Trisomy 13					nr	nr
Trisomy 18					nr	nr
Down syndrome, all ages (include age unknown)					nr	nr
<20					nr	nr
20-24					nr	nr
25-29					nr	nr
30-34					nr	nr
35-39					nr	nr
40-44					nr	nr
45+					nr	nr
unspecified					---	---

* data include less than 5 years

nr= not reported

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.

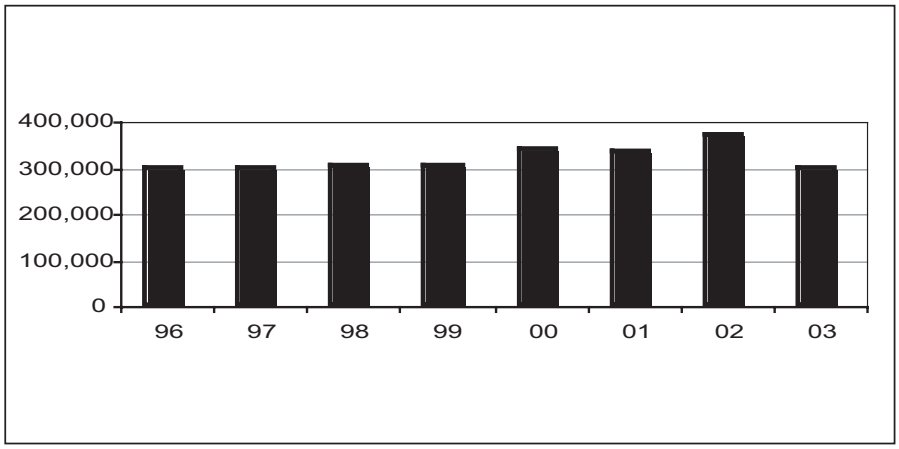
Phone: 86-28-5501363

Fax: 86-28-5501363

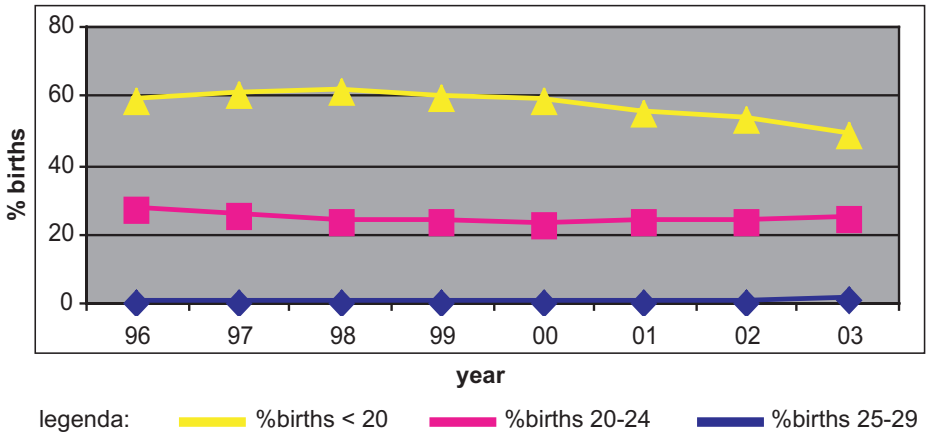
E-mail: cnbdms@mail.sc.cninfo.net

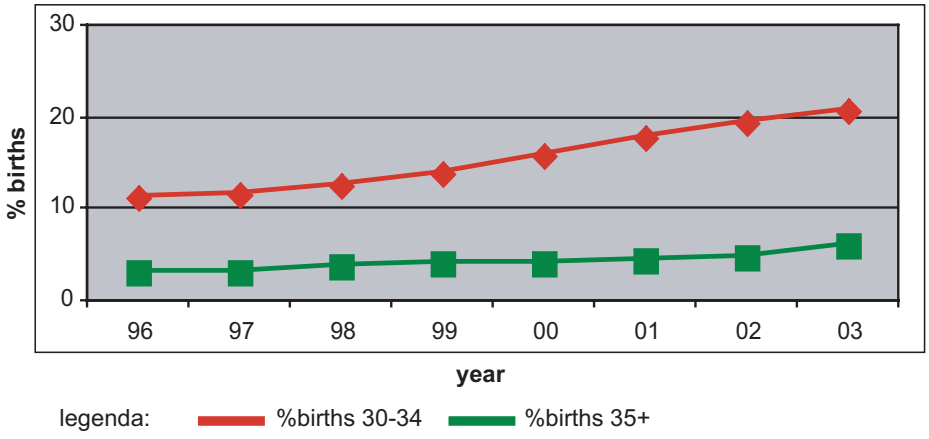
China: CBDMN

Total births by year



Percentage of births by maternal age





China: CBDMN, 2003

Live births (LB)	294553
Stillbirths (SB)	2926
Total births	297479
Number of terminations of pregnancy (ToP) for birth defects	nr

Birth Defects	Number of cases			Rates*10.000
	LB	SB	ToP	Total rate
Anencephaly	18	108	nr	4.24
Spina bifida	91	114	nr	6.89
Encephalocele	22	23	nr	1.51
Microcephaly	4	3	nr	0.24
Arhinencephaly / Holoprosencephaly	nr	nr	nr	nr
Hydrocephaly	35	182	nr	7.29
Total Anophthalmos / Microphthalmos (include unspecified)	7	3	nr	0.34
Anophthalmos	nr	nr	nr	nr
Microphthalmos	nr	nr	nr	nr
Total Anotia / Microtia (include unspecified)	92	8	nr	3.36
Anotia	nr	nr	nr	nr
Microtia	nr	nr	nr	nr
Transposition of great vessels	nr	nr	nr	nr
Tetralogy of Fallot	nr	nr	nr	nr
Hypoplastic left heart syndrome	nr	nr	nr	nr
Coarctation of aorta	nr	nr	nr	nr
Choanal atresia, bilateral	nr	nr	nr	nr
Cleft palate without cleft lip	75	4	nr	2.66
Cleft lip with or without cleft palate	379	86	nr	15.63
Oesophageal atresia / stenosis with or without fistula	18	7	nr	0.84
Small intestine atresia / stenosis	nr	nr	nr	nr
Anorectal atresia / stenosis	85	16	nr	3.40
Undescended testis (36 weeks of gestation or later)	45	3	nr	1.61
Hypospadias	141	5	nr	4.91
Epispadias	nr	nr	nr	nr
Indeterminate sex	nr	nr	nr	nr
Renal agenesis	2	11	nr	0.44
Cystic kidney	17	29	nr	1.55
Bladder exstrophy	3	0	nr	0.10
Polydactyly, unspecified	404	19	nr	14.22
Total Limb reduction defects (include unspecified)	119	49	nr	5.65
Transverse	nr	nr	nr	nr
Preaxial	nr	nr	nr	nr
Postaxial	nr	nr	nr	nr
Intercalary	nr	nr	nr	nr
Mixed	nr	nr	nr	nr
Unspecified	nr	nr	nr	---
Diaphragmatic hernia	11	8	nr	0.64
Omphalocele	32	15	nr	1.58
Gastroschisis	47	54	nr	3.40
Unspecified Omphalocele / Gastroschisis	0	0	nr	---
Prune belly sequence	nr	nr	nr	nr
Trisomy 13	3	0	nr	0.10
Trisomy 18	1	0	nr	0.03
Down syndrome, all ages (include age unknown)	69	6	nr	2.52
<20	0	0	nr	0.00
20-24	8	0	nr	1.10
25-29	30	3	nr	2.29
30-34	15	0	nr	2.44
35+	15	3	nr	10.13
unspecified	1	0	nr	---

nr = not reported

China: CBDMN, Previous years rates 1996 - 2003

Prevalence rates: (LB+SB) * 10,000

	1974-78	1979-83	1984-88	1989-93	1994-98*	1999-03
Births					**893,559**	**1,641,568**
Anencephaly					5.69	4.08
Spina bifida					7.64	7.08
Encephalocele					2.10	1.54
Microcephaly					0.16	0.28
Arhinencephaly / Holoprosencephaly					nr	nr
Hydrocephaly					6.47	6.89
Total Anophthalmos / Microphthalmos (include unspecified)					0.46	0.31
Anophthalmos					nr	nr
Microphthalmos					nr	nr
Total Anotia / Microtia (include unspecified)					2.98	3.03
Anotia					nr	nr
Microtia					nr	nr
Transposition of great vessels					nr	nr
Tetralogy of Fallot					nr	nr
Hypoplastic left heart syndrome					nr	nr
Coarctation of aorta					nr	nr
Choanal atresia, bilateral					nr	nr
Cleft palate without cleft lip					2.24	2.52
Cleft lip with or without cleft palate					13.78	14.22
Oesophageal atresia / stenosis with or without fistula					0.62	0.87
Small intestine atresia / stenosis					nr	nr
Anorectal atresia / stenosis					2.76	3.11
Undescended testis (36 weeks of gestation or later)					0.51	0.89
Hypospadias					2.99	4.54
Epispadias					nr	nr
Indeterminate sex					1.06	1.22
Renal agenesis					0.21	0.31
Cystic kidney					0.65	1.15
Bladder exstrophy					0.09	0.10
Polydactyly, preaxial					nr	12.99
Total Limb reduction defects (include unspecified)					5.01	5.68
Transverse					nr	nr
Preaxial					nr	nr
Postaxial					nr	nr
Intercalary					nr	nr
Mixed					nr	nr
Unspecified					---	---
Diaphragmatic hernia					0.53	0.53
Total Abdominal wall defects (include unspecified)					3.96	4.29
Omphalocele					1.25	1.52
Gastroschisis					2.71	2.77
Unspecified Omphalocele / Gastrschisis					---	---
Prune belly sequence					nr	nr
Trisomy 13					nr	0.06
Trisomy 18					nr	0.08
Down syndrome, all ages (include age unknown)					1.61	2.34
<20					0.00	5.59
20-24					0.99	1.26
25-29					1.23	1.92
30-34					2.31	2.73
35+					9.45	11.19
unspecified					---	---

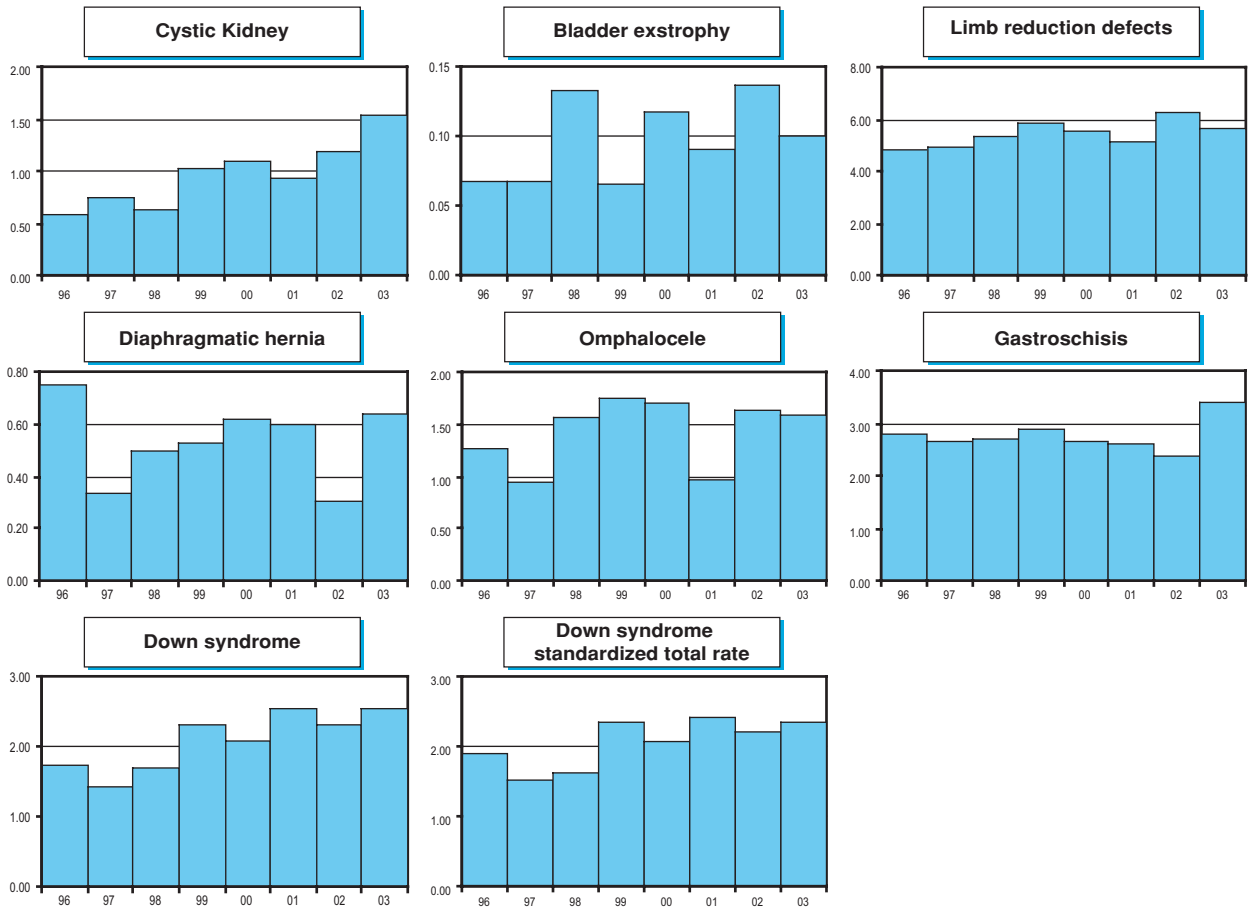
* data include less than 5 years

nr = not reported

China: CBDMN

Time trends 1996-2003 (Birth prevalence rates per 10,000)

Note: L+S rates



Note: L+S rates

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.

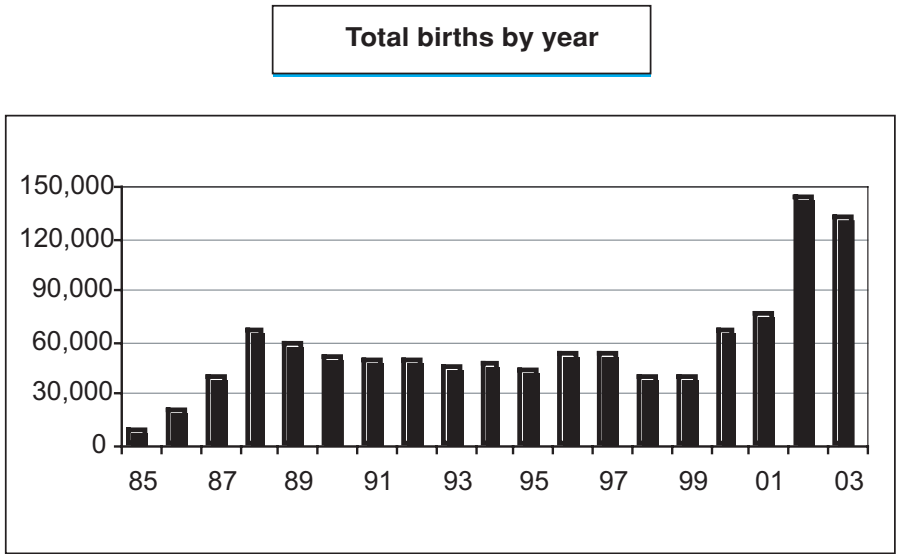
Exposure information
The mother of each reported infant and the mother of a control infant, the next non ,alformed infant born at the hospital with the same sex as the proband are interviewedon various exposures, including drug usage and parental occupation.

Background information
Total number of birth 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
Maria Teresa Pérez Mateo, Recumac. Centro Nacional De Genética Medica. ISCM-Habana. Victoria de Girón, C.P. 16000 Ciudad de la Habana. Cuba.

E-mail: mauro@infomed.sld.cu

Cuba: RECUMAC



Cuba: RECUMAC, 2003

Live births (LB)	129819
Stillbirths (SB)	1672
Total births	131491
Number of terminations of pregnancy (ToP) for birth defects	522

Birth Defects	Number of cases			Rates*10.000
	LB	SB	ToP	Total rate
Anencephaly	0	0	56	4.24
Spina bifida	10	4	43	4.32
Encephalocele	2	0	2	0.30
Microcephaly	1	0	0	0.08
Arhinencephaly / Holoprosencephaly	1	0	1	0.15
Hydrocephaly	16	2	43	4.62
Anophthalmos	1	0	0	0.08
Microphthalmos	2	0	1	0.23
Unspecified Anophthalmos / Microphthalmos	0	0	0	---
Anotia	2	0	0	0.15
Microtia	14	0	0	1.06
Unspecified Anotia / Microtia	0	0	0	---
Transposition of great vessels	18	1	4	1.74
Tetralogy of Fallot	8	2	10	1.52
Hypoplastic left heart syndrome	2	1	3	0.45
Coarctation of aorta	3	0	2	0.38
Choanal atresia, bilateral	1	0	1	0.15
Cleft palate without cleft lip	15	0	2	1.29
Cleft lip with or without cleft palate	48	0	12	4.55
Oesophageal atresia / stenosis with or without fistula	20	1	8	2.20
Small intestine atresia / stenosis	12	0	8	1.52
Anorectal atresia / stenosis	10	0	0	0.76
Undescended testis (36 weeks of gestation or later)	41	0	0	3.11
Hypospadias	89	0	0	6.74
Epispadias	0	0	0	0.00
Indeterminate sex	3	0	0	0.23
Renal agenesis	3	2	7	0.91
Cystic kidney	9	0	14	1.74
Bladder exstrophy	1	0	0	0.08
Polydactyly, preaxial	9	0	0	0.68
Total Limb reduction defects (include unspecified)	17	0	10	2.05
Transverse	7	0	0	0.53
Preaxial	0	0	0	0.00
Postaxial	0	0	0	0.00
Intercalary	0	0	0	0.00
Mixed	0	0	0	0.00
Unspecified	10	0	10	---
Diaphragmatic hernia	2	0	13	1.14
Omphalocele	5	0	15	1.52
Gastroschisis	3	1	12	1.21
Unspecified Omphalocele / Gastroschisis	0	0	11	---
Prune belly sequence	0	0	0	0.00
Trisomy 13	2	0	7	0.68
Trisomy 18	2	0	5	0.53
Down syndrome, all ages (include age unknown)	95	0	21	8.79
<20	4	0	0	nr
20-24	16	0	0	nr
25-29	19	0	0	nr
30-34	16	0	0	nr
35-39	18	0	0	nr
40-44	10	0	0	nr
45+	2	0	0	nr
unspecified	10	0	21	---

nr = not reported

Cuba: RECUMAC, Previous years rates 1985 - 2003

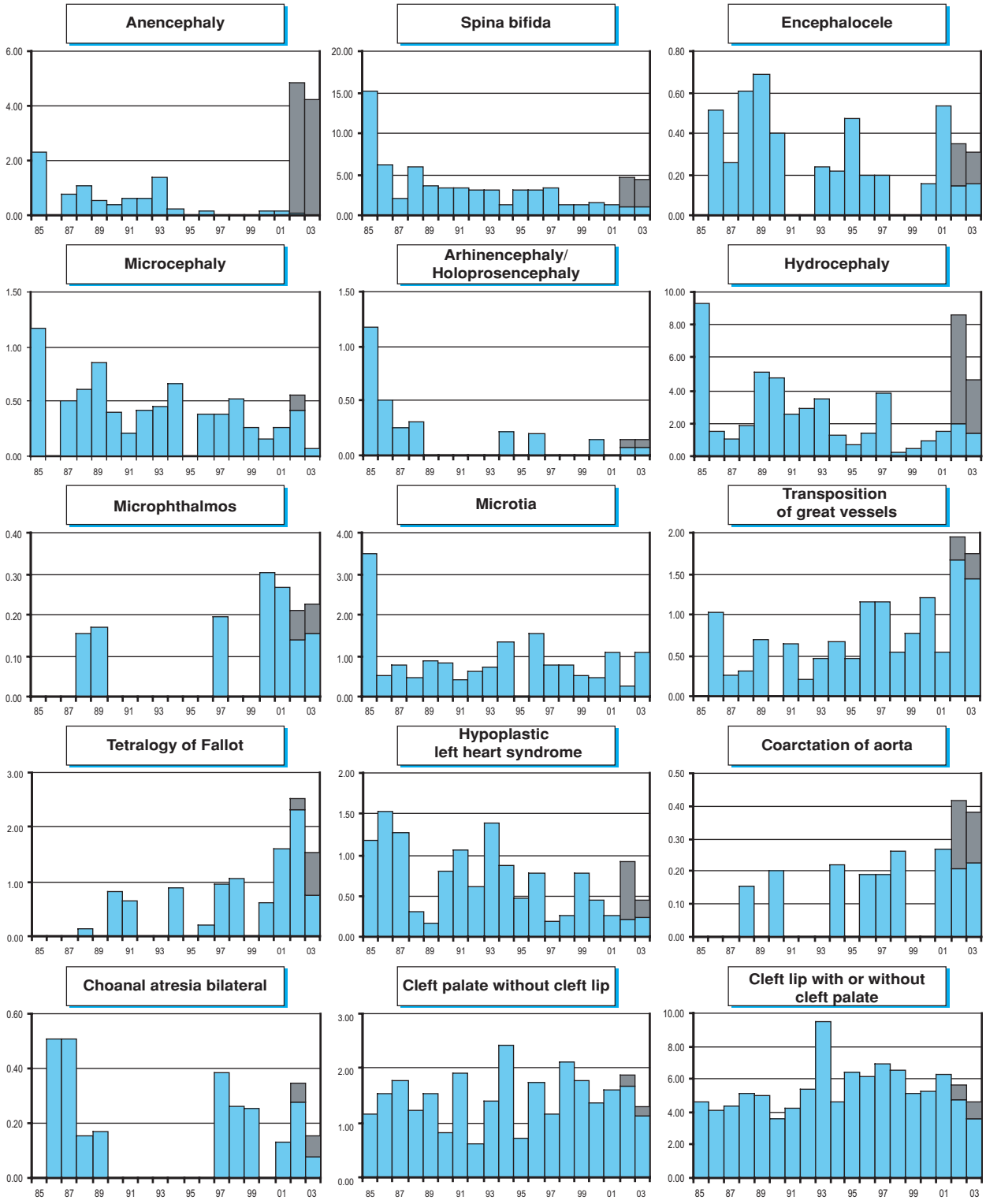
Prevalence rates: (LB+SB) * 10,000 until 2001
Prevalence rates: (LB+SB+TOP) * 10,000 since 2002

	1974-78	1979-83	1984-88*	1989-93	1994-98	1999-03
Births			**132,887**	**247,658**	**230,039**	**454,218**
Anencephaly			0.90	0.69	0.09	2.80
Spina bifida			5.42	3.27	2.48	3.30
Encephalocele			0.45	0.28	0.22	0.31
Microcephaly			0.53	0.48	0.39	0.29
Arhinencephaly / Holoprosencephaly			0.38	0.00	0.09	0.11
Hydrocephaly			2.03	3.84	1.61	4.49
Anophthalmos			0.00	0.08	0.00	0.09
Microphthalmos			0.08	0.04	0.04	0.22
Unspecified Anophthalmos / Microphthalmos			---	---	---	---
Anotia			0.00	0.00	0.04	0.09
Microtia			0.75	0.69	0.91	0.68
Unspecified Anotia / Microtia			---	---	---	---
Transposition of great vessels			0.38	0.40	0.83	1.45
Tetralogy of Fallot			0.08	0.28	0.61	1.59
Hypoplastic left heart syndrome			0.83	0.77	0.52	0.59
Coarctation of aorta			0.08	0.04	0.17	0.29
Choanal atresia, bilateral			0.30	0.04	0.13	0.20
Cleft palate without cleft lip			1.43	1.25	1.61	1.59
Cleft lip with or without cleft palate			4.74	5.41	6.13	5.35
Oesophageal atresia / stenosis with or without fistula			0.90	1.53	1.96	2.33
Small intestine atresia / stenosis			0.98	0.61	0.74	1.19
Anorectal atresia / stenosis			1.28	1.45	1.17	1.39
Undescended testis (36 weeks of gestation or later)			5.79	2.38	4.56	2.51
Hypospadias			13.39	15.55	10.61	7.77
Epispadias			0.23	0.32	0.13	0.09
Indeterminate sex			0.23	0.16	0.17	0.35
Renal agenesis			0.68	0.32	0.35	0.66
Cystic kidney			1.05	1.25	0.52	1.61
Bladder exstrophy			0.23	0.12	0.22	0.13
Polydactyly, preaxial			0.15	0.16	0.30	0.75
Total Limb reduction defects (include unspecified)			3.16	2.54	2.48	2.44
Transverse			1.20	0.97	0.74	0.57
Preaxial			nr	nr	nr	nr
Postaxial			nr	nr	nr	nr
Intercalary			nr	nr	nr	nr
Mixed			nr	nr	nr	nr
Unspecified			---	---	---	---
Diaphragmatic hernia			1.96	1.17	1.43	1.63
Omphalocele			0.75	0.73	0.39	1.14
Gastroschisis			0.45	0.32	0.48	1.63
Unspecified Omphalocele / Gastroschisis			---	---	---	---
Prune belly sequence			0.15	0.12	0.00	0.00
Trisomy 13			0.30	0.61	0.39	0.68
Trisomy 18			0.15	0.20	0.35	0.42
Down syndrome, all ages (include age unknown)			8.73	7.87	7.09	8.72
<20			nr	nr	nr	nr
20-24			nr	nr	nr	nr
25-29			nr	nr	nr	nr
30-34			nr	nr	nr	nr
35-39			nr	nr	nr	nr
40-44			nr	nr	nr	nr
45+			nr	nr	nr	nr
unspecified			---	---	---	---

* data include less than 5 years
nr = not reported

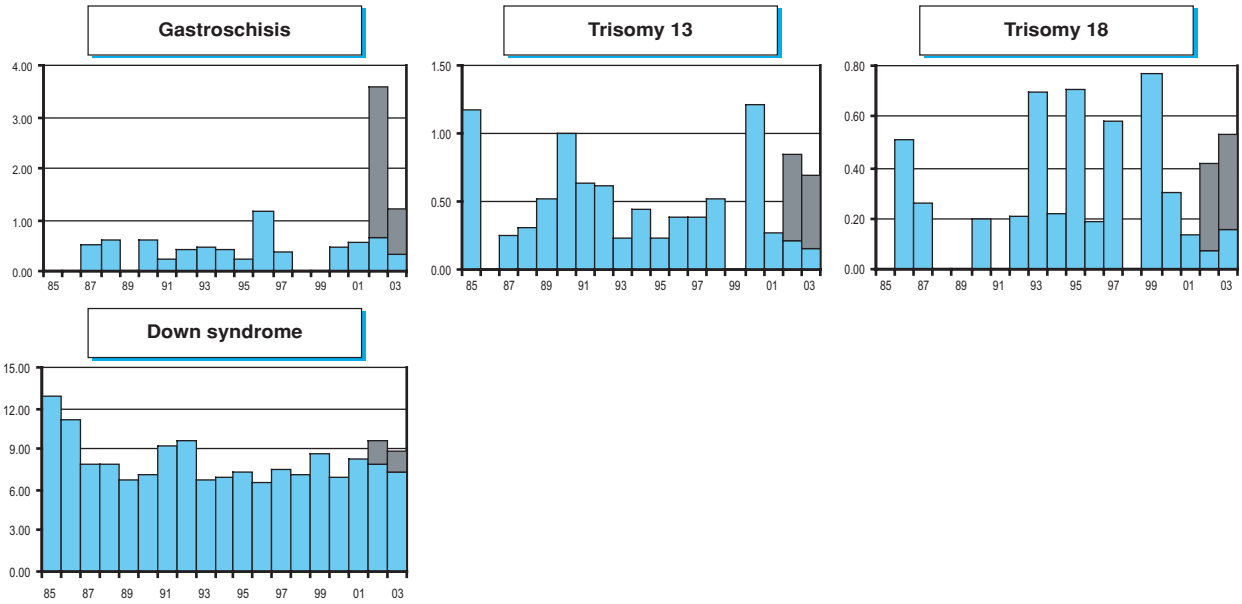
Cuba: RECUMAC

'Time trends 1985-2003 (Birth prevalence rates per 10,000)



Note: L+S rates, ToP rates

Note: L+S rates, ToP rates



Note: L+S rates, ToP rates

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.

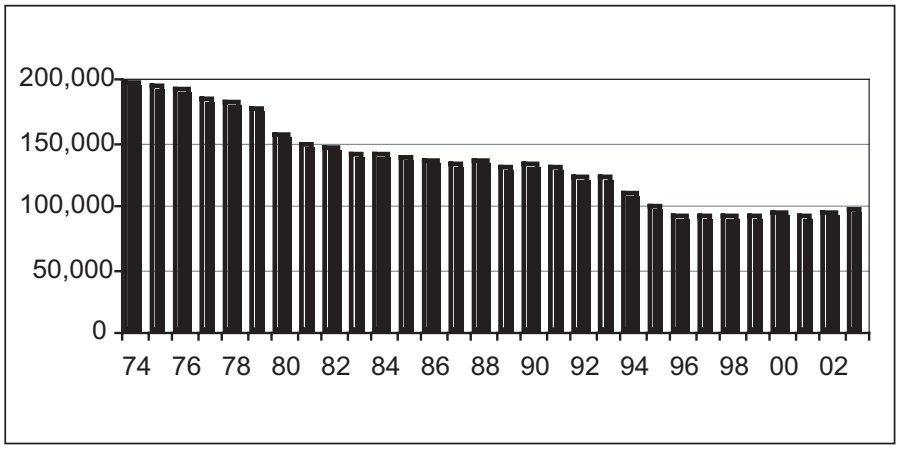
Background information:
Information's on all births are available in the Institute of Health Information and Statistics of the Czech Republic.

Address for further information:
Antonin Sipek, Department of Population Teratology, Institute for Care of Mother and Child, Podolske nabrezi 157, 147 10, Prague 4, Czech Republic.

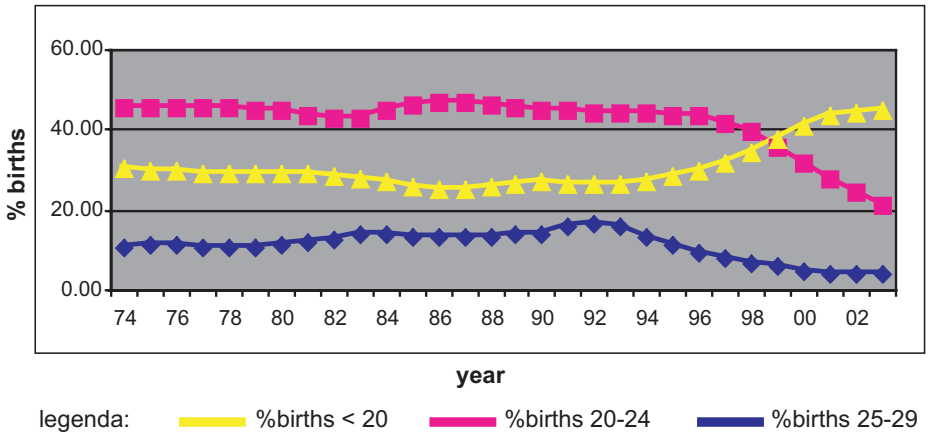
e-mail: antoninsipek@seznam.cz

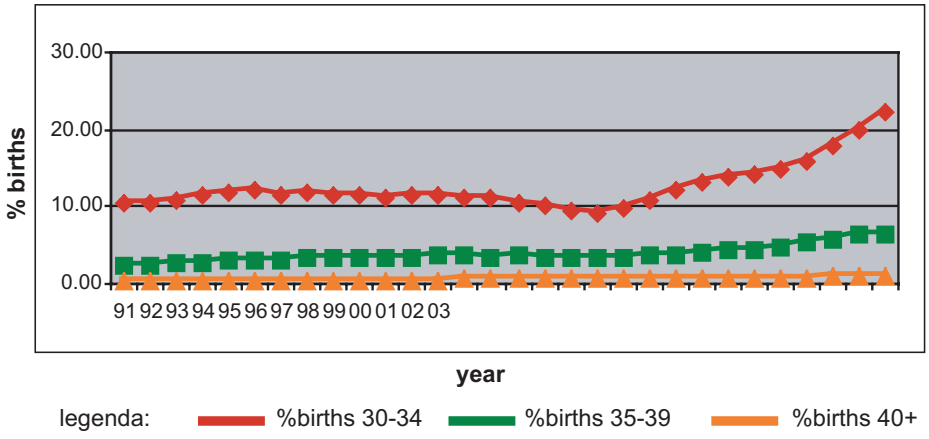
Czech Republic

Total births by year



Percentage of births by maternal age





Czech Republic, 2003

Live births (LB)	93721
Stillbirths (SB)	272
Total births	93993
Number of terminations of pregnancy (ToP) for birth defects	560

Birth Defects	Number of cases			Rates*10.000
	LB	SB	ToP	Total rate
Anencephaly	3	0	26	3.07
Spina bifida	17	1	26	4.65
Encephalocele	3	0	6	0.95
Microcephaly	14	0	1	1.59
Arhinencephaly / Holoprosencephaly	0	0	0	0.00
Hydrocephaly	33	4	17	5.71
Anophthalmos	0	0	nr	0.00
Microphthalmos	4	0	nr	0.43
Unspecified Anophthalmos / Microphthalmos	0	0	nr	---
Anotia	3	0	nr	0.32
Microtia	3	0	nr	0.32
Unspecified Anotia / Microtia	0	0	nr	---
Transposition of great vessels	36	0	7	4.55
Tetralogy of Fallot	27	0	6	3.49
Hypoplastic left heart syndrome	15	0	23	4.02
Coarctation of aorta	41	0	9	5.29
Choanal atresia, bilateral	0	0	nr	0.00
Cleft palate without cleft lip	72	2	nr	7.87
Cleft lip with or without cleft palate	91	0	13	11.00
Oesophageal atresia / stenosis with or without fistula	21	1	0	2.33
Small intestine atresia / stenosis	29	0	0	3.07
Anorectal atresia / stenosis	24	0	0	2.54
Undescended testis (36 weeks of gestation or later)	251	0	nr	26.70
Hypospadias	296	0	nr	31.49
Epispadias	5	0	nr	0.53
Indeterminate sex	5	0	nr	0.53
Renal agenesis	53	1	14	7.19
Cystic kidney	47	2	6	5.82
Bladder exstrophy	0	0	0	0.00
Polydactyly, preaxial	151	0	nr	16.07
Total Limb reduction defects (include unspecified)	49	0	8	6.03
Transverse	nr	nr	nr	nr
Preaxial	nr	nr	nr	nr
Postaxial	nr	nr	nr	nr
Intercalary	nr	nr	nr	nr
Mixed	nr	nr	nr	nr
Unspecified	nr	nr	nr	---
Diaphragmatic hernia	23	0	8	3.28
Omphalocele	16	0	17	3.49
Gastroschisis	5	0	23	2.96
Unspecified Omphalocele / Gastroschisis	0	0	0	---
Prune belly sequence	0	0	0	0.00
Trisomy 13	9	0	12	2.22
Trisomy 18	9	1	34	4.65
Down syndrome, all ages (include age unknown)	59	1	116	18.61
<20	5	0	0	13.19
20-24	11	0	5	8.00
25-29	20	1	27	11.37
30-34	10	0	35	21.43
35-39	8	0	36	72.54
40-44	5	0	11	161.29
45+	0	0	2	416.67
unspecified	0	0	0	---

nr = not reported

Czech Republic, Previous years rates 1974 - 2003

Birth prevalence rates: (LB+SB) * 10,000
Birth prevalence rates: (LB+SB+TOP) * 10,000 in different periods according to the malformation

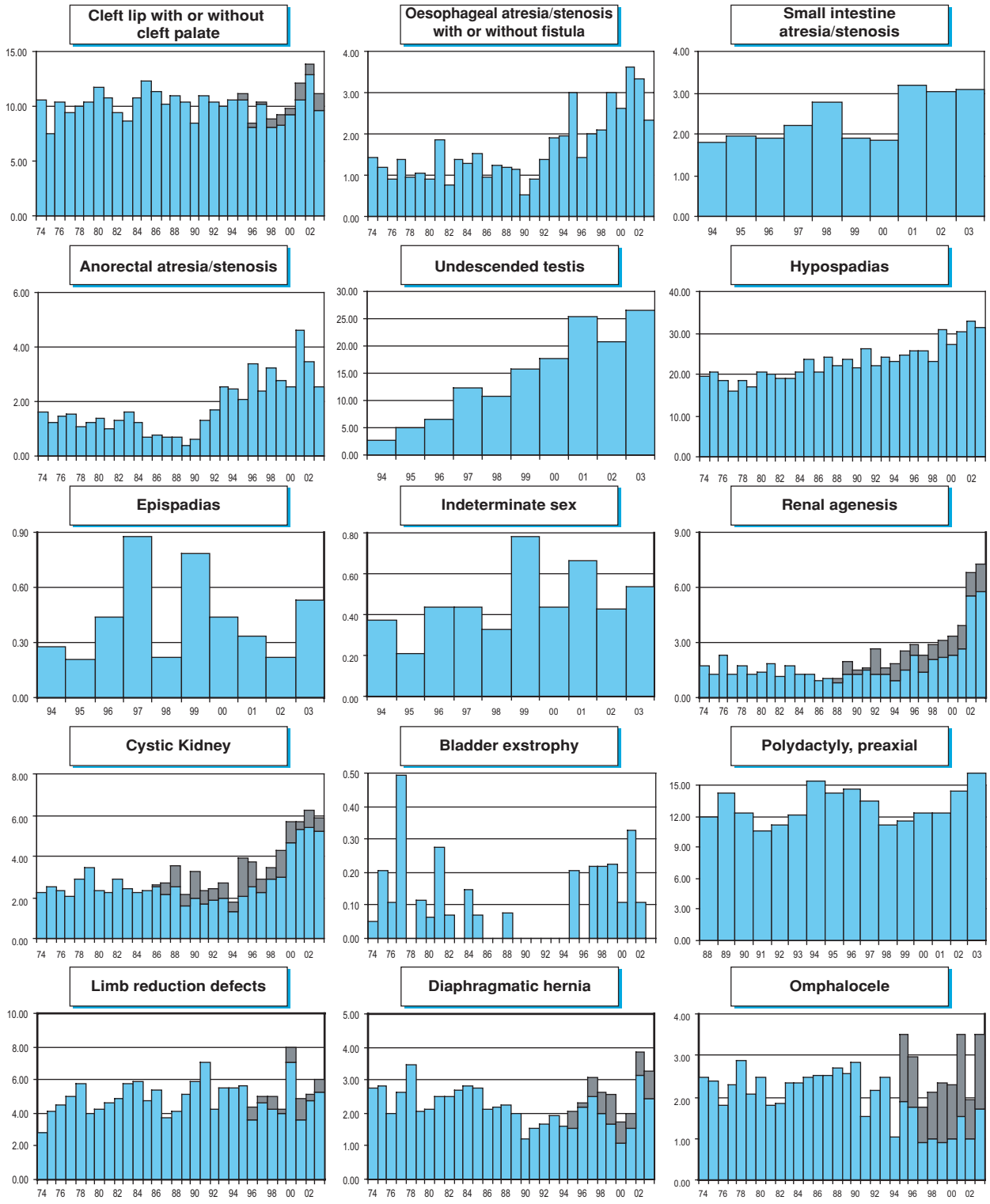
	1974-78	1979-83	1984-88	1989-93	1994-98	1999-03
Births	**939,701**	**753,577**	**672,724**	**632,059**	**475,780**	**458,961**
Anencephaly	3.16	3.30	2.65	3.77	2.94	2.77
Spina bifida	3.96	4.02	3.63	3.81	4.16	4.05
Encephalocele	0.48	0.69	0.61	1.15	0.78	0.89
Microcephaly	1.02	1.15	0.88	0.79	0.90	1.26
Arhinencephaly / Holoprosencephaly	nr	nr	nr	nr	0.14*	0.20
Hydrocephaly	2.16	2.89	3.11	5.40	4.20	4.82
Anophthalmos	nr	nr	nr	nr	0.11*	0.04
Microphthalmos	nr	nr	nr	nr	0.22*	0.33
Unspecified Anophthalmos / Microphthalmos	---	---	---	---	---	---
Anotia	nr	nr	nr	nr	1.21*	0.76
Microtia	nr	nr	nr	nr	0.11*	0.41
Unspecified Anotia / Microtia	---	---	---	---	---	---
Transposition of great vessels	2.83	2.22	1.72	1.08	2.63	4.16
Tetralogy of Fallot	nr	nr	nr	nr	2.63	3.38
Hypoplastic left heart syndrome	0.52	0.61	0.83	0.54	2.14	2.81
Coarctation of aorta	nr	nr	nr	nr	3.68	4.62
Choanal atresia, bilateral	nr	nr	nr	nr	0.36	0.15
Cleft palate without cleft lip	5.64	6.60	6.14	5.22	6.37	7.43
Cleft lip with or without cleft palate	9.53	10.20	11.15	10.03	9.90	11.24
Oesophageal atresia / stenosis with or without fistula	1.17	1.18	1.25	1.17	2.10	2.99
Small intestine atresia / stenosis	nr	nr	nr	nr	2.10	2.61
Anorectal atresia / stenosis	1.37	1.30	0.80	1.30	2.69	3.18
Undescended testis (36 weeks of gestation or later)	nr	nr	nr	nr	7.31	21.31
Hypospadias	18.58	19.02	22.12	23.57	24.40	30.46
Epispadias	nr	nr	nr	nr	0.40	0.46
Indeterminate sex	nr	nr	nr	nr	0.36	0.57
Renal agenesis	1.68	1.49	1.13	1.85	2.48	4.92
Cystic kidney	2.41	2.68	2.68	2.58	3.11	5.56
Bladder exstrophy	0.17	0.11	0.06	0.00	0.16*	0.15
Polydactyly, preaxial	nr	nr	12.01*	12.09	13.85	13.38
Total Limb reduction defects (include unspecified)	4.41	4.67	4.77	5.57	5.09	5.66
Transverse	nr	nr	nr	nr	nr	nr
Preaxial	nr	nr	nr	nr	nr	nr
Postaxial	nr	nr	nr	nr	nr	nr
Intercalary	nr	nr	nr	nr	nr	nr
Mixed	nr	nr	nr	nr	nr	nr
Unspecified	---	---	---	---	---	---
Diaphragmatic hernia	2.71	2.36	2.44	1.66	2.31	2.70
Omphalocele	2.36	2.10	2.51	2.31	2.25	2.72
Gastroschisis	0.96	1.33	1.37	0.59	2.59	2.92
Unspecified Omphalocele / Gastroschisis	0.00	0.00	0.00	0.00	0.02	0.00
Prune belly sequence	nr	nr	nr	nr	nr	0.00*
Trisomy 13	nr	nr	nr	nr	0.86	1.48
Trisomy 18	nr	nr	nr	nr	2.67	3.90
Down syndrome, all ages (include age unknown)	8.27	8.47	8.16	9.71	13.72	16.36
<20	5.32	3.74	5.29	4.74	5.20	8.46
20-24	5.31	5.11	4.46	3.33	7.85	8.39
25-29	8.14	7.81	7.99	5.71	9.97	10.64
30-34	12.35	9.44	8.23	9.75	18.13	20.31
35-39	34.69	30.12	28.70	35.11	55.41	59.23
40-44	114.24	127.89	60.49	137.18	247.16	186.53
45+	147.78	458.02	0.00	782.61	672.27	584.80
unspecified	---	---	---	---	---	---

* data include less than 5 years
nr= not reported

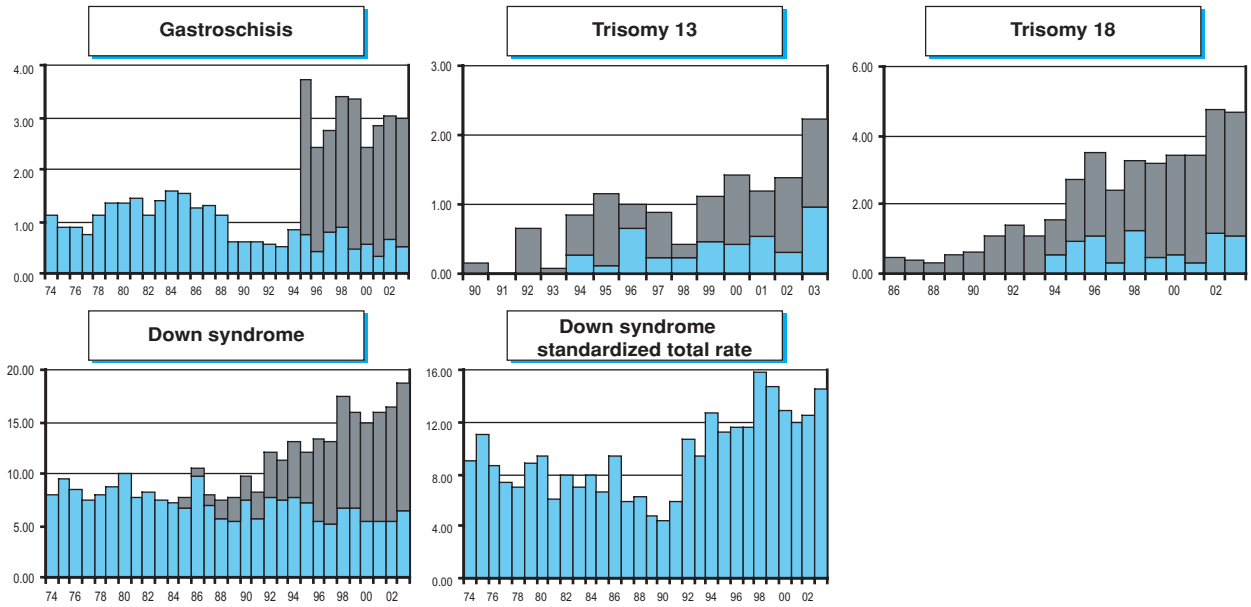
Czech Republic

'Time trends 1974-2003 (Birth prevalence rates per 10,000)

Note: L+S rates, ToP rates



Note: L+S rates, ToP rates



Note: L+S rates, ToP rates

England and Wales

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 625,000 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 by means of a paper form (the SD56 form). This form contains a written description of the anomaly and details of the birth, along with some demographic information about the parents. In areas covered by local congenital anomaly registers this information is supplemented by other reports from neonatal intensive care units, special care baby units etc.

It has long been recognised, however, that there is under reporting in NCAS. Therefore NCAS has embarked on an on-going programme of improving the level of reporting to the system. Since 1998, local congenital anomaly registers have begun to provide data to NCAS in each of the years detailed below:

1998	CARIS (Wales)
1999	East Midlands & South Yorkshire Congenital Anomaly Register
2000	North Thames (West) Congenital Malformation Register
2000	Merseyside and Cheshire Congenital Anomaly Survey
2002	Wessex Clinical Genetics Service
2002	Congenital Anomaly Register for Oxfordshire, Berkshire & Buckinghamshire (Oxfordshire only prior to 2004)
2003	Northern Congenital Abnormality Survey
2003	South West Congenital Anomaly Register

In 2003, congenital anomaly notifications are now received for all births in Wales and 42 per cent of births in England. For areas for which NCAS relies solely on SD56 notification forms recording is likely to be less complete.

Exposure information:
Parents' occupation is known.

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

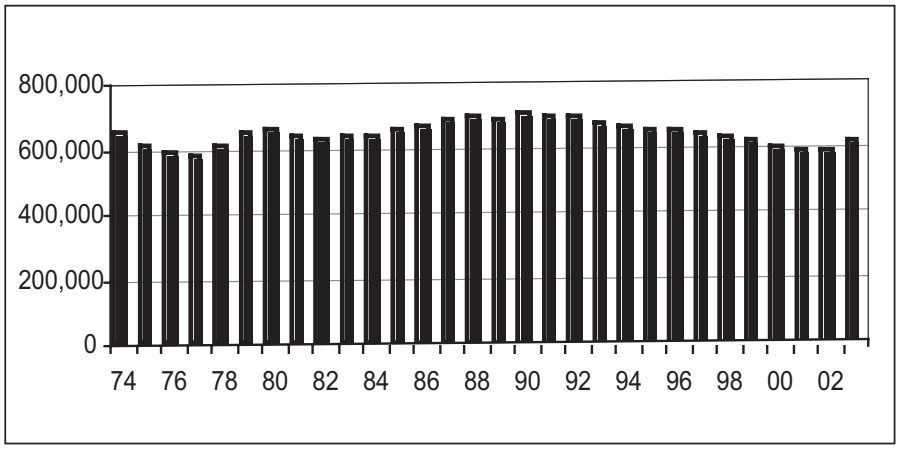
Phone: 44-20-7533 5205

Fax: 44-20-7533 5635

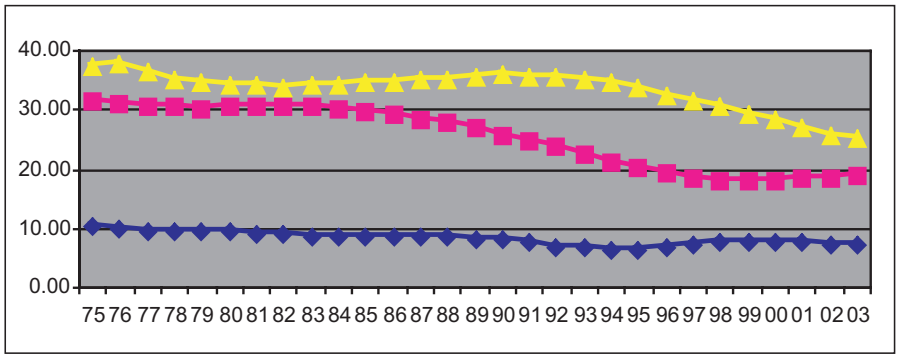
E-mail: nirupa.dattani@ons.gov.uk

England and Wales

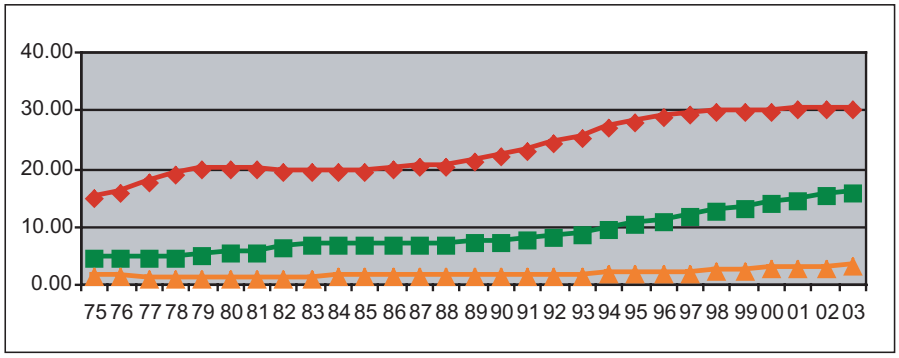
Total births by year



Percentage of births by maternal age



legenda: %births < 20 %births 20-24 %births 25-29



legenda: %births 30-34 %births 35-39 %births 40+

England and Wales, 2003

Live births (LB)	621251
Stillbirths (SB)	3565
Total births	624816
Number of terminations of pregnancy (ToP) for birth defects	1941

Birth Defects	Number of cases			Rates*10.000
	LB	SB	ToP	Total rate
Anencephaly	17	16	nr	0.53
Spina bifida	57	23	nr	1.28
Encephalocele	9	0	nr	0.14
Microcephaly	27	5	nr	0.51
Arhinencephaly / Holoprosencephaly	1	8	nr	0.14
Hydrocephaly	56	17	nr	1.17
Anophthalmos	3	0	nr	0.05
Microphthalmos	8	0	nr	0.13
Unspecified Anophthalmos / Microphthalmos	0	0	nr	---
Anotia	15	1	nr	0.26
Microtia	2	0	nr	0.03
Unspecified Anotia / Microtia	0	0	nr	---
Transposition of great vessels	67	2	nr	1.10
Tetralogy of Fallot	61	7	nr	1.09
Hypoplastic left heart syndrome	59	5	nr	1.02
Coarctation of aorta	84	1	nr	1.36
Choanal atresia, bilateral	15	0	nr	0.24
Cleft palate without cleft lip	170	5	nr	2.80
Cleft lip with or without cleft palate	339	10	nr	5.59
Oesophageal atresia / stenosis with or without fistula	60	1	nr	0.98
Small intestine atresia / stenosis	58	6	nr	1.02
Anorectal atresia / stenosis	79	3	nr	1.31
Undescended testis (36 weeks of gestation or later)	21	0	nr	0.34
Hypospadias	456	1	nr	7.31
Epispadias	13	0	nr	0.21
Indeterminate sex	30	7	nr	0.59
Renal agenesis	69	10	nr	1.26
Cystic kidney	141	14	nr	2.48
Bladder exstrophy	6	0	nr	0.10
Polydactyly, preaxial	38	0	nr	0.61
Total Limb reduction defects (include unspecified)	171	18	nr	3.02
Transverse	83	6	nr	1.42
Preaxial	11	1	nr	0.19
Postaxial	1	0	nr	0.02
Intercalary	44	7	nr	0.82
Mixed	16	2	nr	0.29
Unspecified	16	2	nr	---
Diaphragmatic hernia	69	8	nr	1.23
Omphalocele	48	7	nr	0.88
Gastroschisis	129	2	nr	2.10
Unspecified Omphalocele / Gastroschisis	30	3	nr	---
Prune belly sequence	5	0	nr	0.08
Trisomy 13	10	2	nr	0.19
Trisomy 18	23	27	nr	0.80
Down syndrome, all ages (include age unknown)	350	24	nr	5.99
<20	5	1	nr	1.35
20-24	33	3	nr	3.07
25-29	48	2	nr	3.17
30-34	95	4	nr	5.26
35-39	102	13	nr	11.75
40-44	52	1	nr	28.89
45+	4	0	nr	45.35
unspecified	11	0	nr	---

nr = not reported

England and Wales, Previous years rates 1974 - 2003

Birth prevalence rates: (LB+SB) * 10,000 until 1993
Birth prevalence rates: (LB+SB+TOP) * 10,000 since 1994

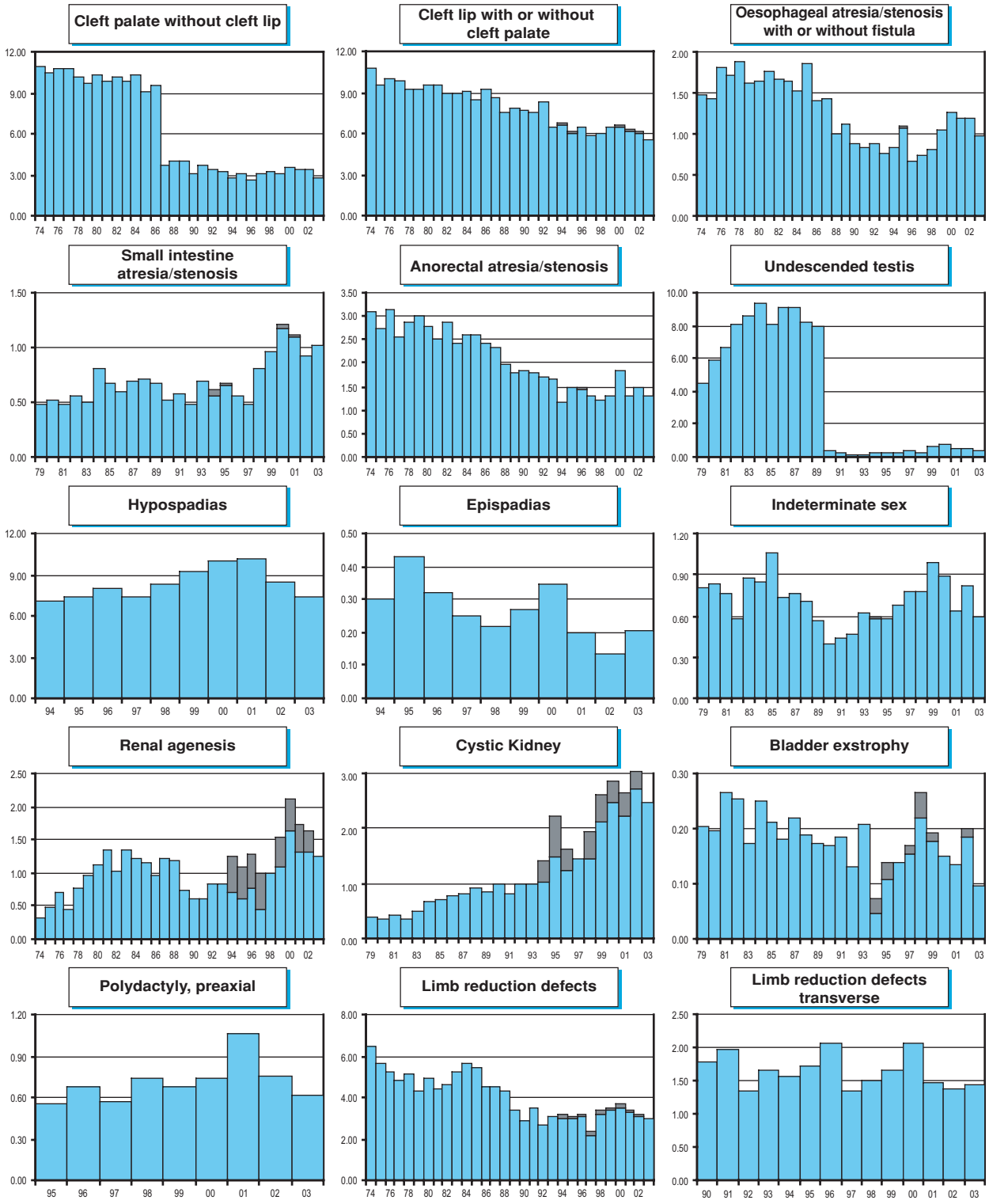
	1974-78	1979-83	1984-88	1989-93	1994-98	1999-03
Births	**3,020,261**	**3,203,053**	**3,345,100**	**3,471,115**	**3,257,122**	**3,053,767**
Anencephaly	11.13	4.15	0.82	0.37	2.88	2.40
Spina bifida	16.18	10.02	4.11	1.49	2.93	2.70
Encephalocele	2.34	1.11	0.55	0.27	0.53	0.49
Microcephaly	nr	1.21	0.79	0.42	0.55	0.67
Arhinencephaly / Holoprosencephaly	nr	0.07	0.13	0.13	0.44	0.47
Hydrocephaly	9.73	6.42	3.07	1.28	2.21	1.89
Anophthalmos	nr	0.25	0.22	0.13	0.13	0.06
Microphthalmos	nr	0.17	0.16	0.13	0.21	0.21
Unspecified Anophthalmos / Microphthalmos	---	---	---	---	---	---
Anotia	nr	nr	nr	nr	0.20*	0.20
Microtia	nr	nr	nr	nr	0.04*	0.06
Unspecified Anotia / Microtia	---	---	---	---	---	---
Transposition of great vessels	0.37	0.49	0.57	0.50	0.51	1.06
Tetralogy of Fallot	nr	nr	nr	0.29	0.45	1.10
Hypoplastic left heart syndrome		0.17	0.27	0.20	0.77	1.06
Coarctation of aorta	nr	nr	nr	0.31	0.40	1.20
Choanal atresia, bilateral	nr	0.20	0.25	0.15	0.11	0.19
Cleft palate without cleft lip	10.63	9.97	7.23	3.47	2.97	3.26
Cleft lip with or without cleft palate	9.91	9.24	8.56	7.55	6.28	6.21
Oesophageal atresia / stenosis with or without fistula	1.66	1.66	1.44	0.90	0.82	1.13
Small intestine atresia / stenosis	nr	0.51	0.70	0.59	0.63	1.04
Anorectal atresia / stenosis	2.88	2.71	2.38	1.76	1.32	1.45
Undescended testis (36 weeks of gestation or later)	nr	6.74	8.74	1.78	0.25	0.54
Hypospadias	nr	nr	nr	nr	7.64	9.01
Epispadias	nr	nr	nr	0.00*	0.30	0.23
Indeterminate sex	nr	0.77	0.82	0.50	0.68	0.79
Renal agenesis	0.54	1.17	1.15	0.73	1.12	1.66
Cystic kidney	nr	0.41	0.77	0.93	1.73	2.73
Bladder exstrophy	nr	0.22	0.21	0.17	0.16	0.15
Polydactyly, preaxial	nr	nr	nr	nr	0.63*	0.76
Total Limb reduction defects (include unspecified)	5.47	4.69	4.90	3.10	3.02	3.35
Transverse	nr	nr	nr	1.70*	1.64	1.59
Preaxial	nr	nr	nr	0.22*	0.19	0.22
Postaxial	nr	nr	nr	0.13*	0.13	0.10
Intercalary	nr	nr	nr	0.55*	0.45	0.82
Mixed	nr	nr	nr	0.17*	0.18	0.21
Unspecified	---	---	---	---	---	---
Diaphragmatic hernia	nr	1.35	1.52	1.18	1.07	1.46
Omphalocele	nr	nr	nr	2.20	1.14	1.18
Gastroschisis	nr	nr	nr	1.36*	1.60	2.05
Unspecified Omphalocele / Gastroschisis	---	---	---	---	---	---
Prune belly sequence	nr	nr	nr	nr	0.06*	0.07
Trisomy 13	nr	0.14	0.22	0.24	0.66	0.83
Trisomy 18	nr	0.46	0.70	0.52	1.69	2.17
Down syndrome, all ages (include age unknown)	6.99	7.61	6.81	6.63	10.54	11.00
<20	nr	nr	4.70*	3.06	4.45	4.22
20-24	nr	nr	3.99*	3.80	4.41	4.16
25-29	nr	nr	4.30*	4.47	5.01	5.06
30-34	nr	nr	7.71*	7.36	9.14	8.89
35-39	nr	nr	18.25*	18.35	28.63	24.61
40-44	nr	nr	39.34*	45.51	98.51	77.48
45+	nr	nr	56.66*	89.11	182.14	118.89
unspecified	---	---	---	---	---	---

* data include less than 5 years
nr = not reported

England and Wales

Time trends 1974-2003 (Birth prevalence rates per 10,000)

Note: L+S rates, ToP rates



Note: L+S rates, ToP rates

Note: L+S rates, ToP rates

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 ICBDSR 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 57,000 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 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 interviews 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

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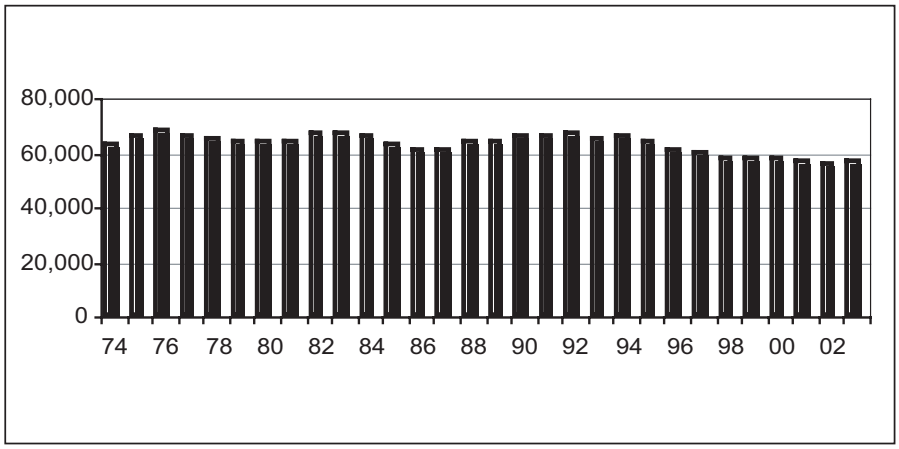
Fax: +358-9-39672459

E-mail: annukka.ritvanen@stakes.fi

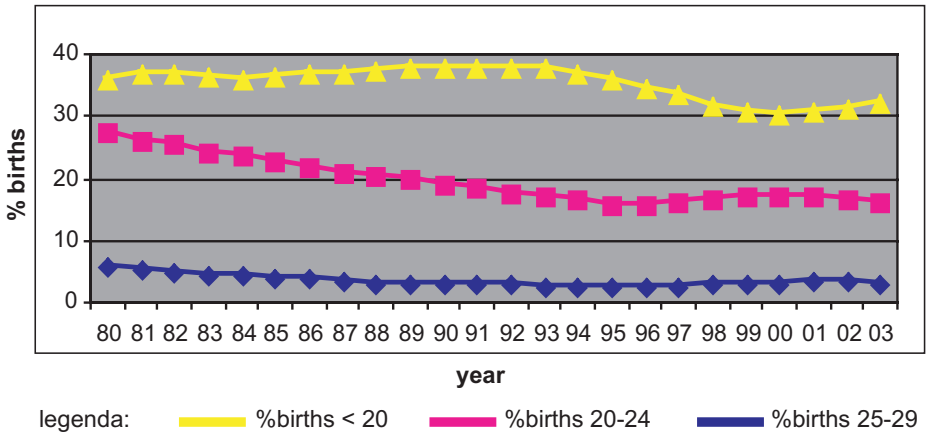
Website: http://www.stakes.fi/

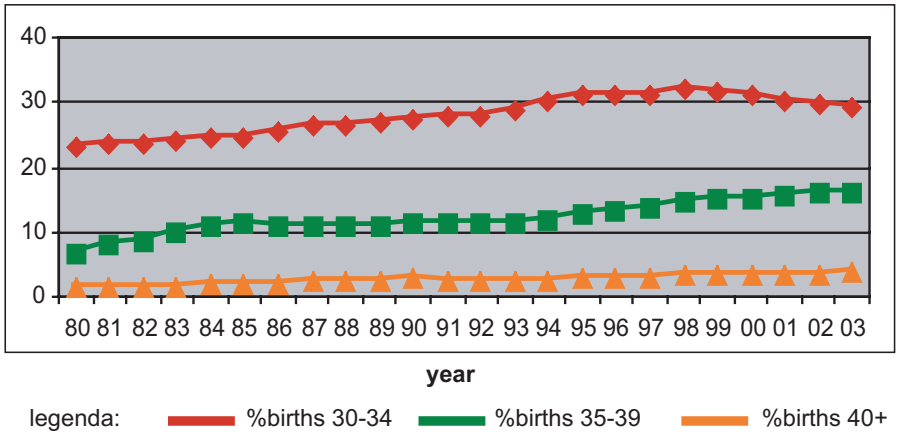
Finland

Total births by year



Percentage of births by maternal age





Finland, 2003

Live births (LB)	56630
Stillbirths (SB)	178
Total births	56808
Number of terminations of pregnancy (ToP) for birth defects	290

Birth Defects	Number of cases			Rates*10.000
	LB	SB	ToP	Total rate
Anencephaly	1	0	21	3.85
Spina bifida	22	1	8	5.43
Encephalocele	2	0	8	1.75
Microcephaly	7	0	1	1.40
Arhinencephaly / Holoprosencephaly	4	0	2	1.05
Hydrocephaly	17	2	12	5.43
Anophthalmos	0	0	1	0.18
Microphthalmos	12	0	1	2.28
Unspecified Anophthalmos / Microphthalmos	0	0	0	---
Anotia	nr	nr	nr	nr
Microtia	nr	nr	nr	nr
Unspecified Anotia / Microtia	nr	nr	nr	nr
Transposition of great vessels	14	0	1	2.63
Tetralogy of Fallot	16	2	1	3.33
Hypoplastic left heart syndrome	15	3	4	3.85
Coarctation of aorta	41	1	5	8.23
Choanal atresia, bilateral	3	0	0	0.53
Cleft palate without cleft lip	74	1	2	13.49
Cleft lip with or without cleft palate	55	2	6	11.03
Oesophageal atresia / stenosis with or without fistula	14	2	1	2.98
Small intestine atresia / stenosis	5	0	0	0.88
Anorectal atresia / stenosis	23	1	5	5.08
Undescended testis (36 weeks of gestation or later)	nr	nr	nr	nr
Hypospadias	92	0	1	16.29
Epispadias	4	0	0	0.70
Indeterminate sex	6	1	4	1.93
Renal agenesis	3	0	6	1.58
Cystic kidney	29	0	14	7.53
Bladder exstrophy	5	0	0	0.88
Polydactyly, preaxial	19	0	1	3.50
Total Limb reduction defects (include unspecified)	34	4	9	8.23
Transverse	nr	nr	nr	nr
Preaxial	nr	nr	nr	nr
Postaxial	nr	nr	nr	nr
Intercalary	nr	nr	nr	nr
Mixed	nr	nr	nr	nr
Unspecified	nr	nr	nr	---
Diaphragmatic hernia	9	0	4	2.28
Omphalocele	17	1	20	6.66
Gastroschisis	11	3	10	4.20
Unspecified omphalocele/gastroschisis	0	0	1	---
Prune belly sequence	0	0	1	0.18
Trisomy 13	4	0	8	2.10
Trisomy 18	11	9	19	6.83
Down syndrome, all ages (include age unknown)	67	3	68	24.17
<20	2	0	1	18.35
20-24	3	0	4	7.62
25-29	16	0	3	10.38
30-34	11	0	9	12.10
35-39	24	1	23	52.97
40-44	8	2	25	171.48
45+	3	0	3	576.92
unspecified	0	0	0	---

nr = not reported

Finland, Previous years rates 1974 - 2003

Prevalence rates: (LB+SB) * 10,000 until 1992
Prevalence rates: (LB+SB+TOP) * 10,000 since 1993

	1974-78	1979-83	1984-88	1989-93	1994-98	1999-03
Births	**326,546**	**324,285**	**313,035**	**327,309**	**306,727**	**283,724**
Anencephaly	2.66	2.07	1.09	1.16	2.97	3.10
Spina bifida	1.99	2.37	1.88	3.42	4.89	4.37
Encephalocele	nr	0.45*	0.64	0.79	1.50	1.80
Microcephaly	nr	nr	nr	2.46*	2.28	1.69
Arhinencephaly / Holoprosencephaly	nr	nr	nr	1.38*	1.37	1.20
Hydrocephaly	1.84	2.28	2.17	2.78	7.47	5.96
Anophthalmos	nr	nr	nr	0.46*	0.52	0.46
Microphthalmos	nr	nr	nr	2.00*	1.70	1.73
Unspecified Anophthalmos / Microphthalmos	---	---	---	---	---	---
Anotia	nr	nr	nr	nr	nr	nr
Microtia	nr	nr	nr	nr	nr	nr
Unspecified Anotia / Microtia	---	---	---	---	---	---
Transposition of great vessels	nr	nr	1.25*	2.14	4.21	3.74
Tetralogy of Fallot	nr	nr	nr	2.46*	3.10	3.74
Hypoplastic left heart syndrome	nr	nr	2.06*	2.14	3.20	4.26
Coarctation of aorta	nr	nr	nr	8.45*	8.87	10.22
Choanal atresia, bilateral	nr	nr	nr	0.77*	1.01	0.85
Cleft palate without cleft lip	7.75	10.18	12.17	12.16	14.35	12.94
Cleft lip with or without cleft palate	7.38	8.11	8.59	8.98	11.51	11.07
Oesophageal atresia / stenosis with or without fistula	1.22	1.08	2.14	1.96	3.81	3.77
Small intestine atresia / stenosis	nr	nr	nr	1.23*	1.17	1.06
Anorectal atresia / stenosis	1.32	0.77	2.11	3.18	5.41	4.90
Undescended testis (36 weeks of gestation or later)	nr	nr	nr	nr	nr	nr
Hypospadias	nr	nr	nr	18.13*	14.21	14.49
Epispadias	nr	nr	nr	0.15*	0.29	0.39
Indeterminate sex	nr	nr	nr	0.92*	0.88	1.94
Renal agenesis	nr	nr	1.25	1.68	2.09	1.27
Cystic kidney	nr	nr	nr	5.53*	6.19	7.44
Bladder exstrophy	nr	nr	nr	0.61*	0.46	0.70
Polydactyly, preaxial	nr	nr	nr	5.22*	4.27	4.16
Total Limb reduction defects (include unspecified)	4.13	4.41	3.93	5.16	7.24	7.33
Transverse	nr	nr	nr	nr	nr	nr
Preaxial	nr	nr	nr	nr	nr	nr
Postaxial	nr	nr	nr	nr	nr	nr
Intercalary	nr	nr	nr	nr	nr	nr
Mixed	nr	nr	nr	nr	nr	nr
Unspecified	---	---	---	---	---	---
Diaphragmatic hernia	nr	0.74*	0.70	1.62	2.45	2.68
Omphalocele	0.78*	1.17	1.34	1.92	3.88	4.93
Gastroschisis	nr	nr	0.54	1.16	2.25	3.21
Unspecified Omphalocele / Gastroschisis	---	---	---	---	---	---
Prune belly sequence	nr	nr	nr	0.31*	0.33	0.21
Trisomy 13	nr	nr	nr	1.69*	2.38	1.90
Trisomy 18	nr	nr	nr	5.22*	5.61	6.49
Down syndrome, all ages (include age unknown)	5.88	8.45	9.01	13.75	23.28	24.04
<20	nr	nr	nr	7.53*	12.98	8.37
20-24	nr	nr	nr	8.31*	6.51	7.16
25-29	nr	nr	nr	8.58*	11.55	9.57
30-34	nr	nr	nr	17.27*	18.18	15.99
35-39	nr	nr	nr	38.70*	54.81	54.66
40-44	nr	nr	nr	119.75*	171.50	171.53
45+	nr	nr	nr	420.17*	294.12	399.20
unspecified	---	---	---	---	---	---

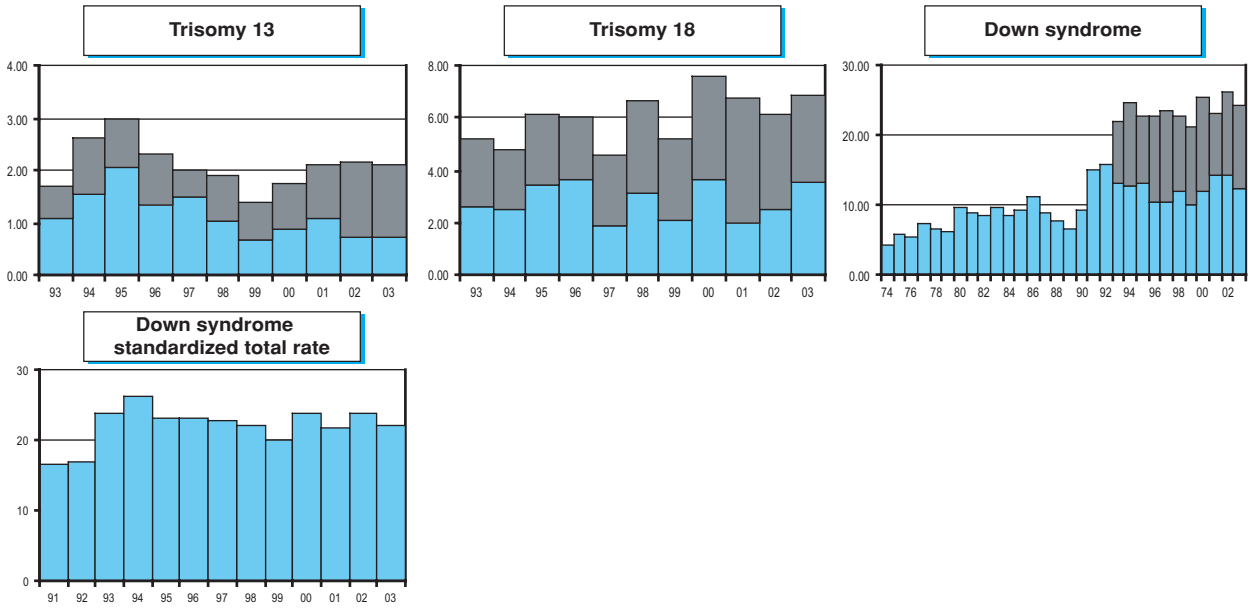
* data include less than 5 years
nr = not reported

Finland

'Time trends 1974-2003 (Birth prevalence rates per 10,000)

Note: L+S rates, ToP rates

Note: L+S rates, ToP rates



Note: L+S rates, ToP rates

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.

Address for further information:
Elisabeth Robert-Gnansia, Institute Européen des Génomutations, 86 Rue Edmond Locard, F-69005 Lyon, France.

Phone: 33-4-78258210

Fax: 33-4-78366182

E-mail: elisabeth.robert@ieg.asso.fr

Website: http://www.ieg.asso.fr

Contact for the Auvergne registry:
Christine Francannet, CEMC Auvergne, BP31, 63401 Chamalieres Cedex, France

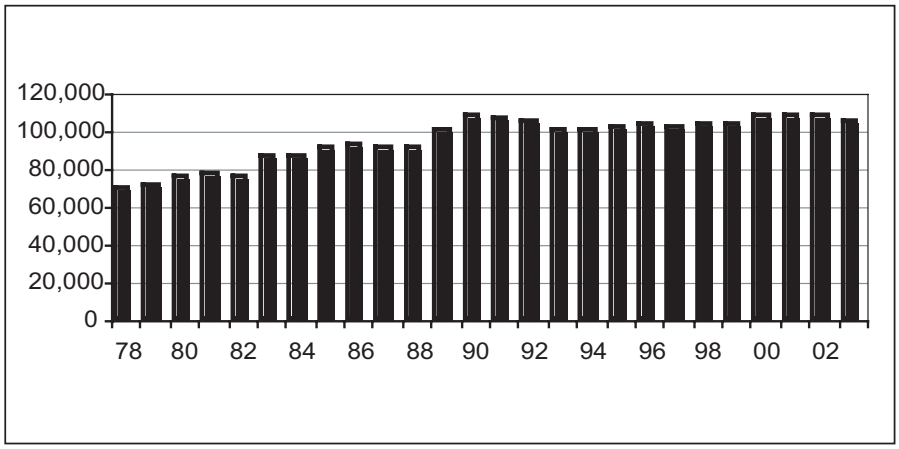
Phone: 33-4-73750001

Fax: 33-4-73750010

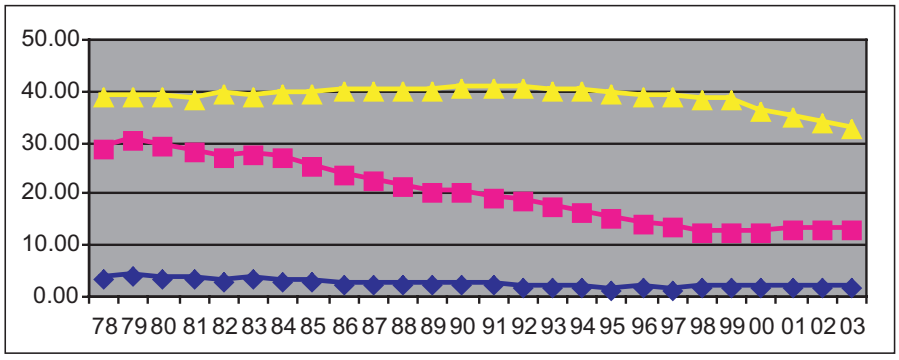
E-mail: cfrancannet@chu-clermontferrand.fr

France: Central-East

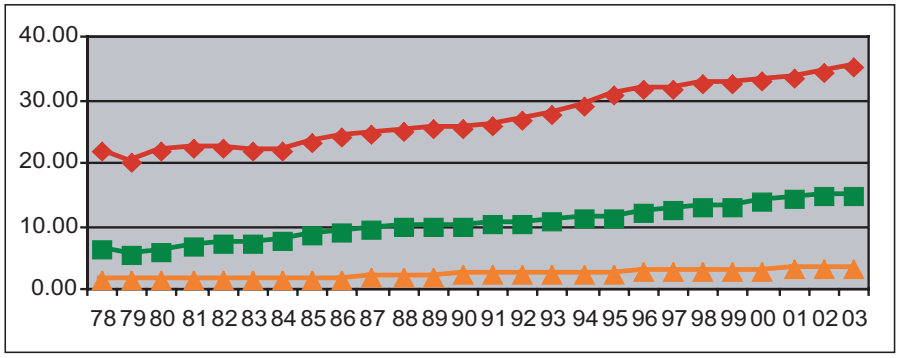
Total births by year



Percentage of births by maternal age



legenda: %births < 20 %births 20-24 %births 25-29



legenda: %births 30-34 %births 35-39 %births 40+

France: Central East, 2003

Live births (LB)	104037
Stillbirths (SB)	858
Total births	104895
Number of terminations of pregnancy (ToP) for birth defects	552

Birth Defects	Number of cases			Rates*10.000
	LB	SB	ToP	Total rate
Anencephaly	0	0	18	1.71
Spina bifida	7	1	35	4.08
Encephalocele	5	1	24	2.85
Microcephaly	15	0	10	2.37
Arhinencephaly / Holoprosencephaly	1	0	12	1.23
Hydrocephaly	27	0	53	7.59
Anophthalmos	2	0	2	0.38
Microphthalmos	5	0	7	1.14
Unspecified Anophthalmos / Microphthalmos	0	0	0	---
Anotia	4	0	0	0.38
Microtia	3	0	1	0.38
Unspecified Anotia / Microtia	0	0	0	---
Transposition of great vessels	24	0	5	2.75
Tetralogy of Fallot	18	0	4	2.09
Hypoplastic left heart syndrome	9	0	19	2.66
Coarctation of aorta	20	0	0	1.90
Choanal atresia, bilateral	14	0	2	1.52
Cleft palate without cleft lip	57	0	2	5.60
Cleft lip with or without cleft palate	58	2	16	7.21
Oesophageal atresia / stenosis with or without fistula	26	1	2	2.75
Small intestine atresia / stenosis	33	0	3	3.41
Anorectal atresia / stenosis	26	1	9	3.41
Undescended testis (36 weeks of gestation or later)	nr	nr	nr	nr
Hypospadias	132	0	8	13.28
Epispadias	0	0	0	0.00
Indeterminate sex	4	0	2	0.57
Renal agenesis	2	0	15	1.61
Cystic kidney	30	0	23	5.03
Bladder exstrophy	1	0	0	0.09
Polydactyly, preaxial	13	0	2	1.42
Total Limb reduction defects (include unspecified)	26	0	13	3.70
Transverse	17	0	6	2.18
Preaxial	4	0	2	0.57
Postaxial	4	0	2	0.57
Intercalary	0	0	2	0.19
Mixed	0	0	1	0.09
Unspecified Limb reduction defects	1	0	0	---
Diaphragmatic hernia	19	2	9	2.85
Omphalocele	7	2	8	1.61
Gastroschisis	8	0	7	1.42
Unspecified Omphalocele / Gastroschisis	0	0	0	---
Prune belly sequence	0	0	2	0.19
Trisomy 13	0	1	19	1.90
Trisomy 18	1	1	37	3.70
Down syndrome, all ages (include age unknown)	49	2	172	21.15
<20	0	0	0	0.00
20-24	3	0	6	6.60
25-29	5	0	27	9.39
30-34	4	0	40	11.98
35-39	6	1	50	36.97
40-44	5	0	41	143.44
45+	1	1	4	335.20
unspecified	25	0	4	---

nr = not reported

France: Central East, Previous years rates 1978 - 2003

Birth prevalence rates: (LB+SB) * 10,000 until 1993
Birth prevalence rates: (LB+SB+TOP) * 10,000 since 1994

	1974-78*	1979-83	1984-88	1989-93	1994-98	1999-03
Total deliveries	**68,778**	**385,294**	**451,173**	**517,564**	**509,840**	**530,612**
Anencephaly	1.02	0.91	0.60	0.19	1.80	1.70
Spina bifida	5.23	3.61	2.93	2.14	3.96	3.68
Encephalocele	0.73	0.78	0.73	1.24	1.49	1.83
Microcephaly	1.45	1.95	2.28	2.01	1.84	1.96
Arhinencephaly / Holoprosencephaly	0.58	0.34	0.62	1.22	1.47	1.15
Hydrocephaly	1.31	2.28	3.13	2.94	4.75	6.03
Anophthalmos	0.15	0.21	0.13	0.21	0.22	0.13
Microphthalmos	1.45	0.75	1.15	1.16	1.27	1.02
Unspecified Anophthalmos / Microphthalmos	---	---	---	---	---	---
Anotia	0.15	0.31	0.44	0.33	0.47	0.38
Microtia	0.15	0.21	0.31	0.21	0.63	0.36
Unspecified Anotia / Microtia	---	---	---	---	---	---
Transposition of great vessels	2.62	3.22	3.24	3.40	3.31	3.03
Tetralogy of Fallot	1.45	2.13	2.39	2.28	2.29	2.28
Hypoplastic left heart syndrome	1.02	1.71	2.08	2.11	2.84	2.81
Coarctation of aorta	1.74	2.39	2.70	2.90	2.69	1.70
Choanal atresia, bilateral	0.73	0.62	0.86	0.62	0.78	1.02
Cleft palate without cleft lip	4.51	4.52	4.94	5.14	6.96	5.69
Cleft lip with or without cleft palate	7.42	6.75	6.10	6.78	8.20	7.11
Oesophageal atresia / stenosis with or without fistula	1.16	2.18	2.79	2.92	3.28	2.85
Small intestine atresia / stenosis	2.33	1.19	1.93	1.82	2.41	2.75
Anorectal atresia / stenosis	2.47	2.39	3.44	2.92	3.90	3.77
Undescended testis (36 weeks of gestation or later)	nr	nr	nr	nr	nr	nr
Hypospadias	nr	6.41	8.13	10.01	10.81	12.34
Epispadias	0.29	0.16	0.22	0.25	0.20	0.19
Indeterminate sex	0.73	0.75	0.73	0.66	0.76	0.47
Renal agenesis	0.29	0.75	0.64	0.46	1.47	1.43
Cystic kidney	0.00	1.06	1.99	2.98	4.55	4.66
Bladder exstrophy	0.29	0.13	0.35	0.31	0.37	0.30
Polydactyly, preaxial	0.87	0.80	1.15	1.70	2.29	1.70
Total Limb reduction defects (include unspecified)	3.63	4.70	3.99	4.33	5.43	4.45
Transverse	2.18	2.31	2.13	2.57	2.53	2.19
Preaxial	0.44	0.73	0.71	0.56	0.71	1.04
Postaxial	0.44	0.23	0.29	0.50	0.33	0.45
Intercalary	0.15	0.60	0.42	0.46	0.47	0.34
Mixed	0.29	0.67	0.42	0.23	0.27	0.34
Unspecified	---	---	---	---	---	---
Diaphragmatic hernia	2.62	2.49	2.53	2.34	3.24	2.53
Omphalocele	1.02	1.04	1.20	1.16	2.39	2.24
Gastroschisis	0.15	0.70	0.89	1.18	1.24	1.38
Unspecified Omphalocele / Gastroschisis	---	---	---	---	---	---
Prune belly sequence	0.29	0.18	0.22	0.44	0.61	0.19
Trisomy 13	0.29	0.55	0.75	1.20	1.49	1.88
Trisomy 18	0.87	0.86	1.62	2.53	3.67	4.30
Down syndrome, all ages (include age unknown)	13.96	10.80	11.19	11.98	19.69	20.66
<20	8.47	6.18	5.47	4.76	9.63	7.26
20-24	8.12	7.04	5.07	6.52	7.31	7.98
25-29	6.01	5.16	7.15	5.44	7.92	8.56
30-34	11.40	10.87	10.15	8.70	14.33	12.56
35-39	32.50	26.88	26.37	24.22	45.31	43.81
40-44	173.27	75.01	57.54	65.09	154.89	134.76
45+	0.00	141.84	160.18	215.44	287.08	210.67
unspecified	---	---	---	---	---	---

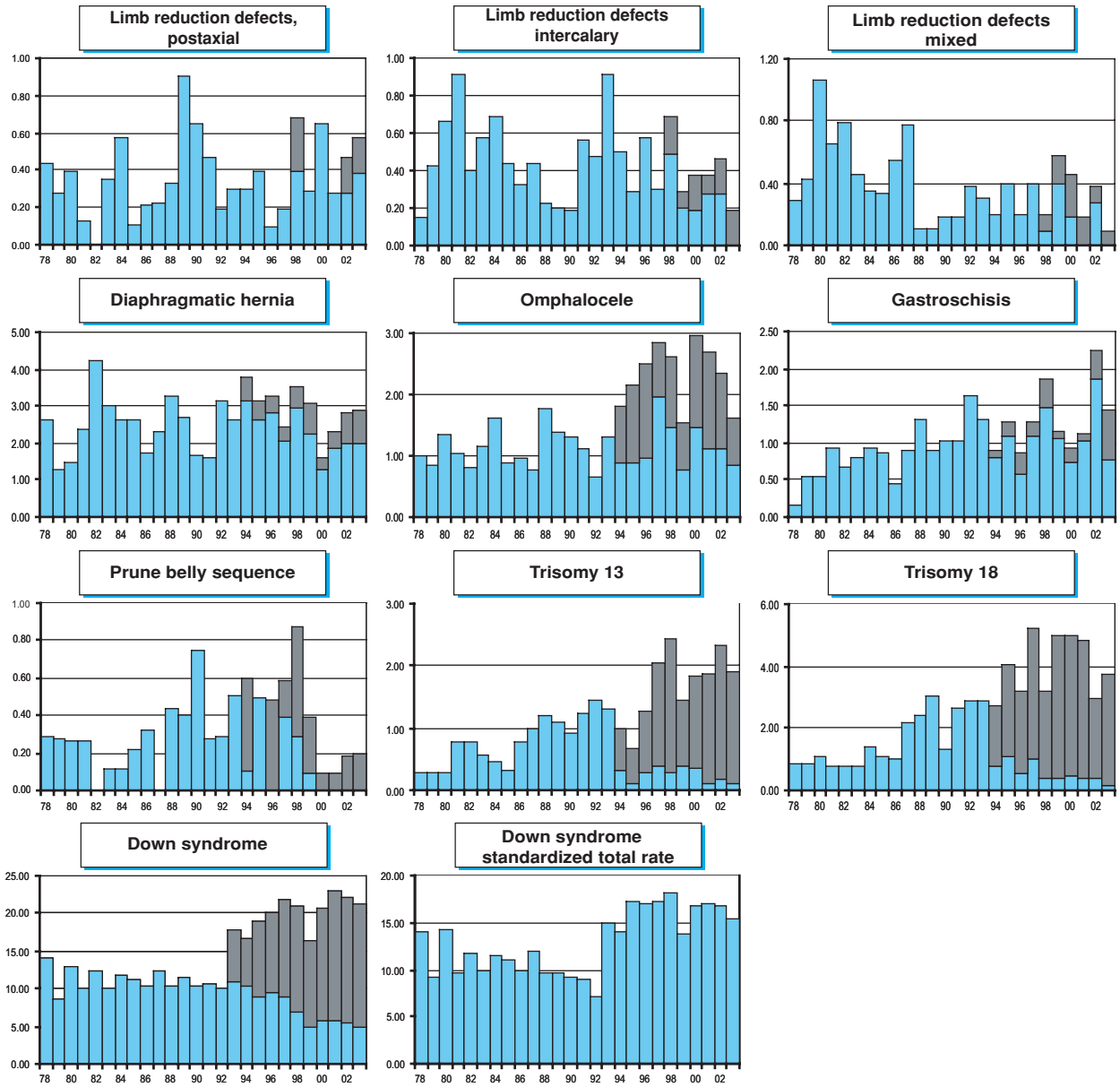
* data include less than 5 years
nr = not reported

France: Central-East

'Time trends 1978-2003 (Birth prevalence rates per 10,000)

Note: L+S rates, ToP rates

Note: L+S rates, ToP rates



Note: L+S rates, ToP rates

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)

Address for further information:
Catherine De Vigan, INSERM U149, 16 av P Vaillant-Couturier, 94807 Villejuif Cedex, France.

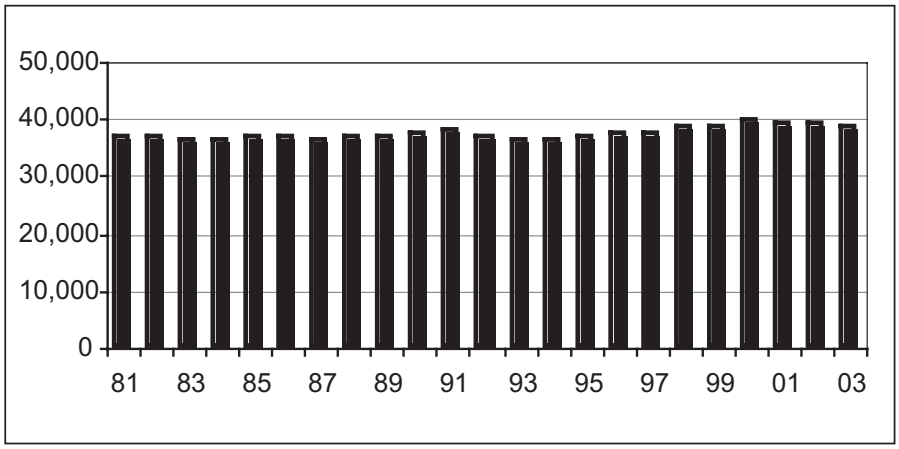
Phone: 33-1-45595009

Fax: 33-1-45595089

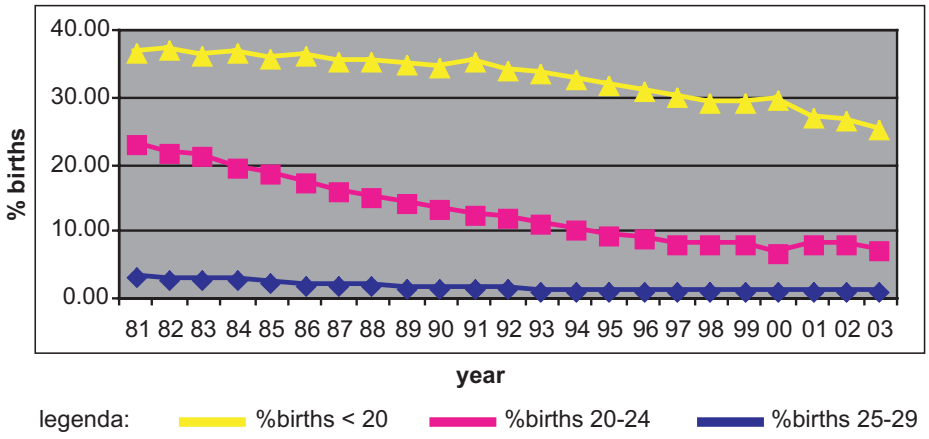
E-mail: devigan@vjf.inserm.fr

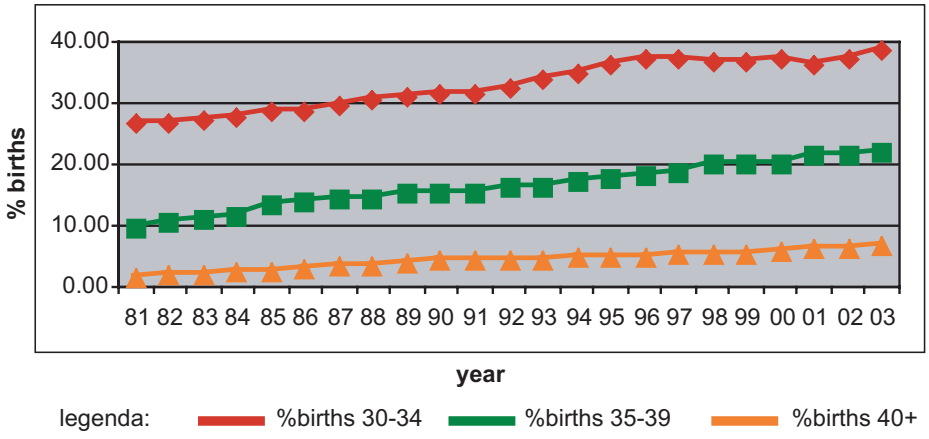
France: Paris

Total births by year



Percentage of births by maternal age





France: Paris, 2003

Live births (LB)	37802
Stillbirths (SB)	498
Total births	38300
Number of terminations of pregnancy (ToP) for birth defects	501

Birth Defects	Number of cases			Rates*10.000
	LB	SB	ToP	Total rate
Anencephaly	1	0	26	6.96
Spina bifida	4	0	17	5.41
Encephalocele	1	0	6	1.80
Microcephaly	5	0	8	3.35
Arhinencephaly / Holoprosencephaly	2	0	13	3.87
Hydrocephaly	33	2	32	17.27
Anophthalmos	0	0	0	0.00
Microphthalmos	0	0	2	0.52
Unspecified Anophthalmos / Microphthalmos	0	0	0	---
Anotia	1	0	0	0.26
Microtia	2	0	0	0.52
Unspecified Anotia / Microtia	0	0	0	---
Transposition of great vessels	12	0	2	3.61
Tetralogy of Fallot	12	1	1	3.61
Hypoplastic left heart syndrome	6	1	11	4.64
Coarctation of aorta	10	0	0	2.58
Choanal atresia, bilateral	1	1	0	0.52
Cleft palate without cleft lip	14	1	3	4.64
Cleft lip with or without cleft palate	26	0	9	9.02
Oesophageal atresia / stenosis with or without fistula	11	0	5	4.12
Small intestine atresia / stenosis	18	1	2	5.41
Anorectal atresia / stenosis	10	0	6	4.12
Undescended testis (36 weeks of gestation or later)	nr	nr	nr	nr
Hypospadias	55	0	5	15.46
Epispadias	2	0	0	0.52
Indeterminate sex	1	1	1	0.77
Renal agenesis	2	2	3	1.80
Cystic kidney	33	0	9	10.82
Bladder exstrophy	1	0	1	0.52
Polydactyly, preaxial	4	0	0	1.03
Total Limb reduction defects (include unspecified)	11	3	22	9.28
Transverse	5	3	11	4.90
Preaxial	2	0	6	2.06
Postaxial	3	0	2	1.29
Intercalary	1	0	1	0.52
Mixed	0	0	1	0.26
Unspecified	0	0	1	---
Diaphragmatic hernia	16	0	6	5.67
Omphalocele	10	1	12	5.93
Gastroschisis	9	0	1	2.58
Unspecified Omphalocele / Gastroschisis	0	0	3	---
Prune belly sequence	0	0	1	0.26
Trisomy 13	2	0	17	4.90
Trisomy 18	2	1	49	13.40
Down syndrome, all ages (include age unknown)	18	0	138	40.21
<20	0	0	1	34.01
20-24	1	0	0	3.60
25-29	1	0	15	16.79
30-34	8	0	20	18.92
35-39	6	0	58	75.61
40-44	1	0	37	157.55
45+	1	0	6	434.78
Unspecified	0	0	1	---

nr = not reported

France: Paris, Previous years rates 1981 - 2003

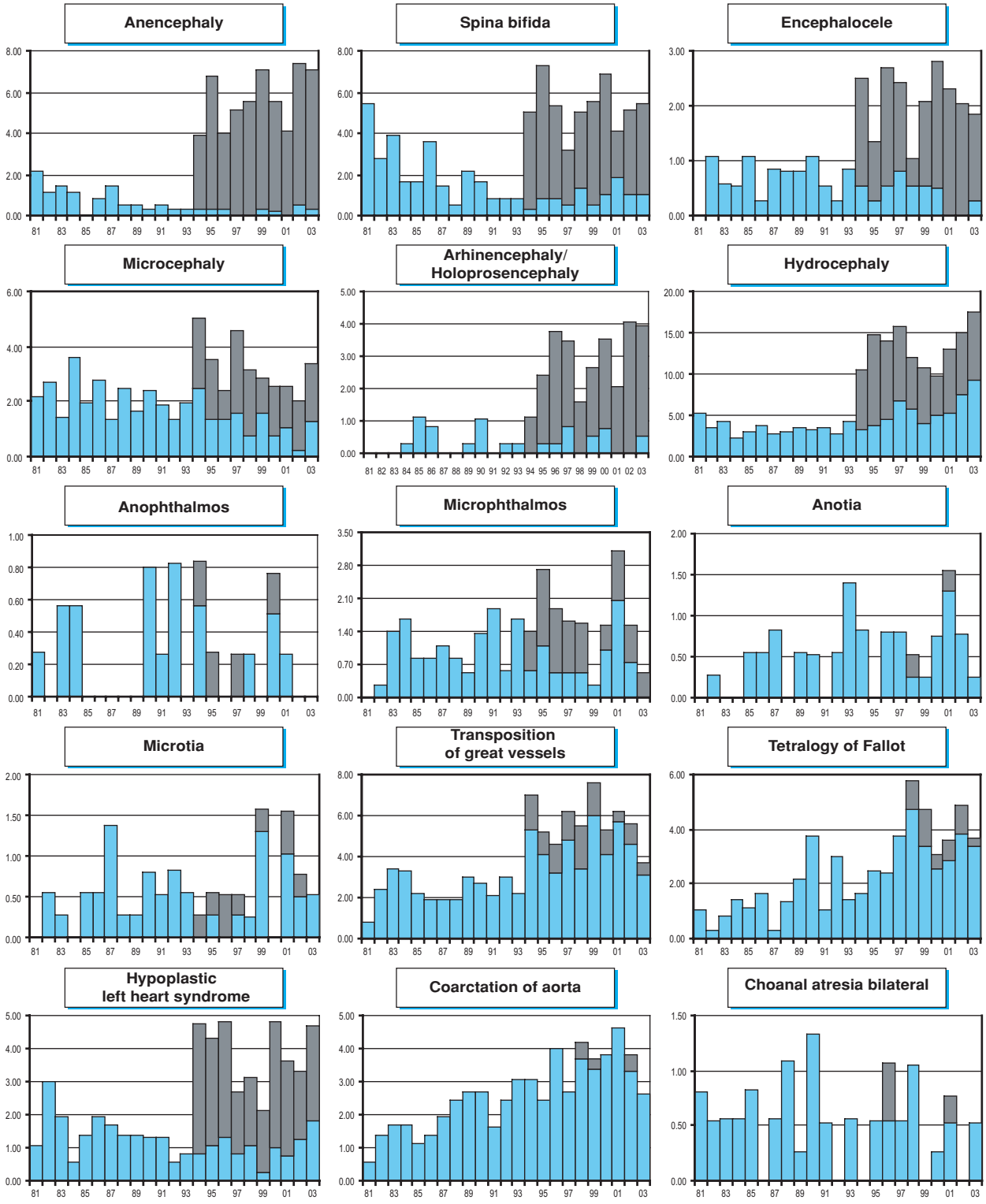
Birth prevalence rates: (LB+SB) * 10,000 until 1993
Birth prevalence rates: (LB+SB+TOP) * 10,000 since 1994 (Cleft palate and Cleft lip with or without cleft palate since 1981)

	1974-78	1979-83*	1984-88	1989-93	1994-98	1999-03
Births		**109,441**	**181,574**	**183,997**	**185,471**	**193,818**
Anencephaly		1.55	0.77	0.38	5.07	6.24
Spina bifida		4.02	1.76	1.25	5.18	5.42
Encephalocele		0.55	0.72	0.71	1.99	2.22
Microcephaly		2.10	2.42	1.85	3.72	2.68
Arhinencephaly / Holoprosencephaly		0.00	0.44	0.38	2.48	3.25
Hydrocephaly		4.29	2.97	3.42	13.43	13.16
Anophthalmos		0.27	0.11	0.38	0.32	0.21
Microphthalmos		0.55	1.05	1.20	1.83	1.39
Unspecified Anophthalmos / Microphthalmos		---	---	---	---	---
Anotia		0.09	0.39	0.60	0.59	0.72
Microtia		0.27	0.55	0.60	0.43	0.88
Unspecified Anotia / Microtia		---	---	---	---	---
Transposition of great vessels		2.19	2.26	2.61	5.66	5.68
Tetralogy of Fallot		0.73	1.16	2.28	3.24	3.97
Hypoplastic left heart syndrome		2.01	1.38	1.09	3.94	3.71
Coarctation of aorta		1.19	1.71	2.50	3.29	3.71
Choanal atresia, bilateral		0.64	0.61	0.54	0.65	0.31
Cleft palate without cleft lip		4.11	3.86	5.65	6.36	6.91
Cleft lip with or without cleft palate		6.40	6.99	8.97	9.97	7.95
Oesophageal atresia / stenosis with or without fistula		2.10	2.37	3.59	3.77	4.39
Small intestine atresia / stenosis		0.18	0.94	1.52	2.48	2.94
Anorectal atresia / stenosis		3.20	2.26	2.93	3.61	3.66
Undescended testis (36 weeks of gestation or later)		7.86	11.84	11.90	8.14	6.24*
Hypospadias		10.96	9.75	14.40	12.19	12.95
Epispadias		0.00	0.61	0.49	0.43	0.26
Indeterminate sex		1.92	0.94	1.30	1.35	1.34
Renal agenesis		0.91	1.16	0.49	3.50	2.58
Cystic kidney		1.01	3.30	3.70	9.06	10.89
Bladder exstrophy		0.27	0.33	0.27	0.92	0.36
Polydactyly, preaxial		0.46	0.94	1.36	2.37	1.55
Total Limb reduction defects (include unspecified)		nr	nr	nr	5.88*	8.77
Transverse		nr	nr	nr	2.14*	5.06
Preaxial		nr	nr	nr	0.53*	1.60
Postaxial		nr	nr	nr	0.33*	0.77
Intercalary		nr	nr	nr	0.47*	0.52
Mixed		nr	nr	nr	0.20*	0.62
Unspecified		---	---	---	---	---
Diaphragmatic hernia		2.10	2.86	2.88	5.61	5.31
Omphalocele		1.55	1.82	1.74	4.58	6.24
Gastroschisis		0.18	0.72	2.01	2.53	3.41
Unspecified Omphalocele / Gastroschisis		---	---	---	---	---
Prune belly sequence		0.00	0.22	0.00	0.16	0.10
Trisomy 13		0.46	0.44	0.60	3.07	4.54
Trisomy 18		1.46	1.05	1.09	7.76	11.61
Down syndrome, all ages (include age unknown)		11.24	12.12	15.00	33.48	37.15
<20		9.78	14.20	8.20	6.20	17.23
20-24		6.70	6.43	6.92	14.06	9.56
25-29		6.76	6.32	7.74	13.36	13.57
30-34		10.54	12.58	13.95	20.57	20.42
35-39		23.16	27.73	27.58	58.26	60.55
40-44		53.79	33.15	55.46	194.07	189.14
45+		363.64	76.92	143.27	373.83	336.70
unspecified		---	---	---	---	---

* data include less than 5 years
nr = not reported

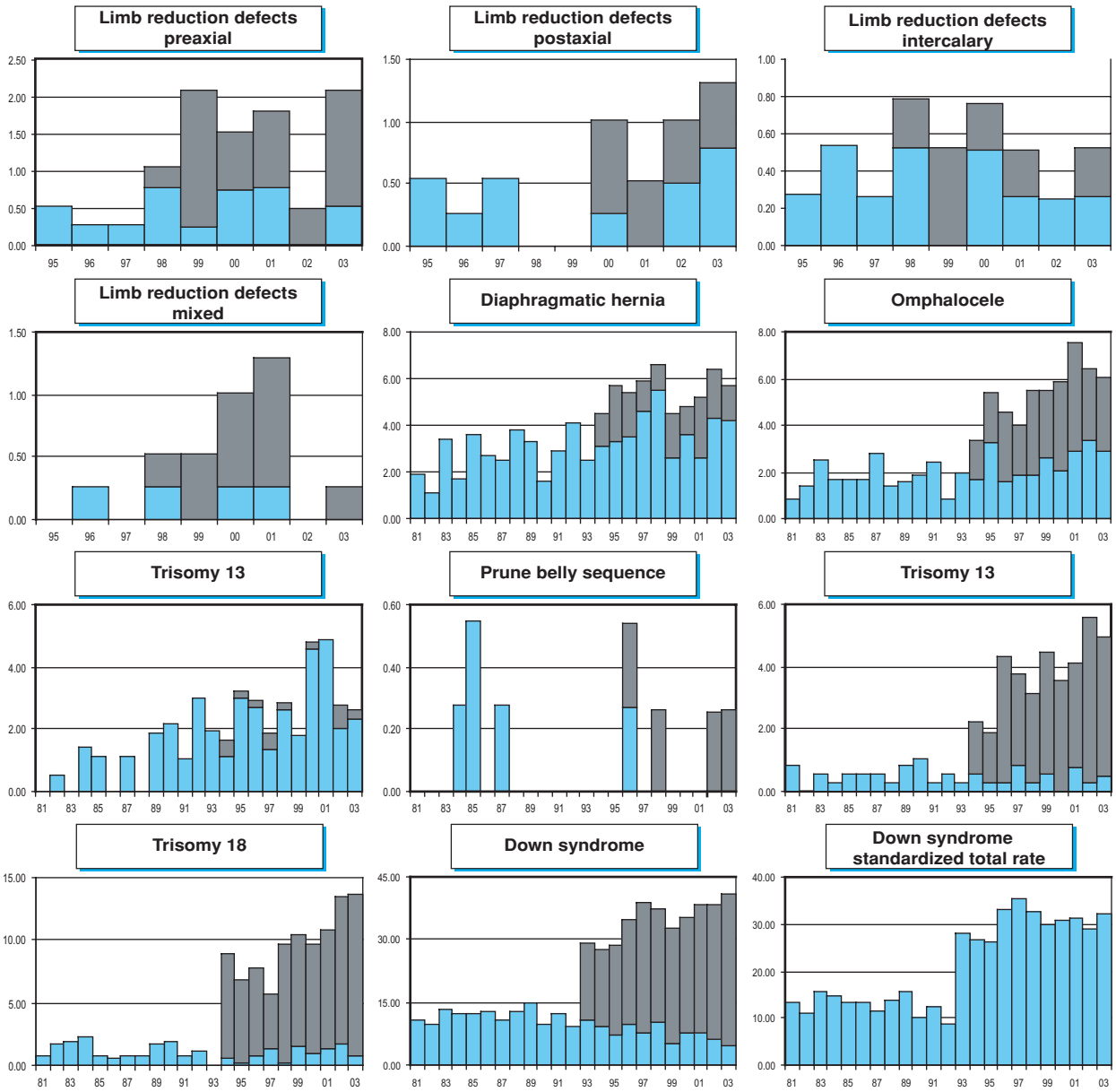
France: Paris

'Time trends 1981-2003 (Birth prevalence rates per 10,000)



Note: L+S rates, ToP rates

Note: L+S rates, ToP rates



Note: L+S rates, ToP rates

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.

Address for further information:
Claude Stoll,Genetique Medicale Faculte de Medecine,11,rue Humann,67085 Strasbourg cedex, France

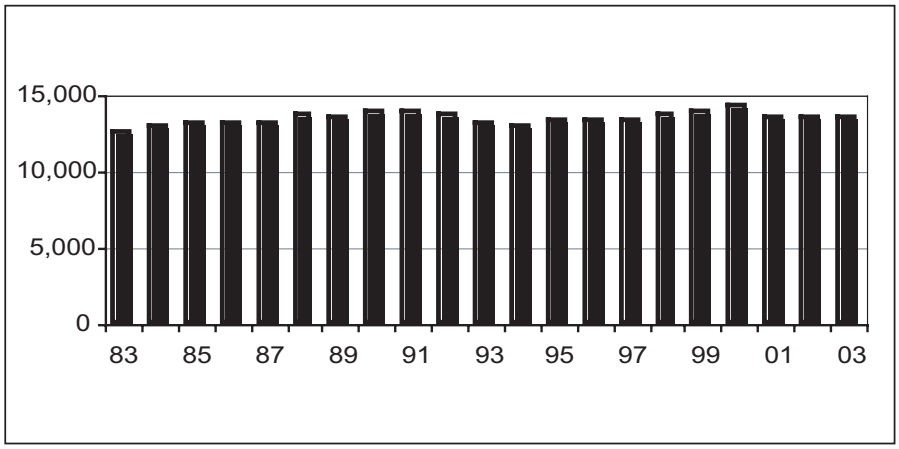
Phone: 33-3-90243207

Fax: 33-3-90243179

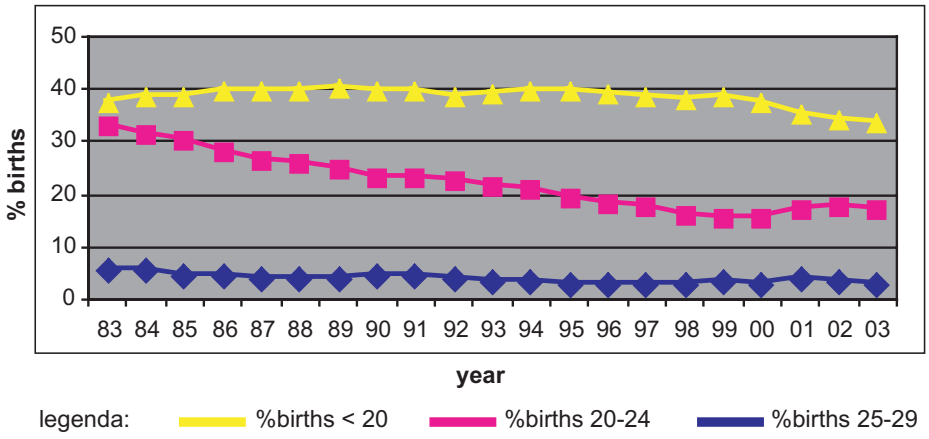
E-mail: Claude.Stoll@medecine.u-strasbg.fr

France: Strasbourg

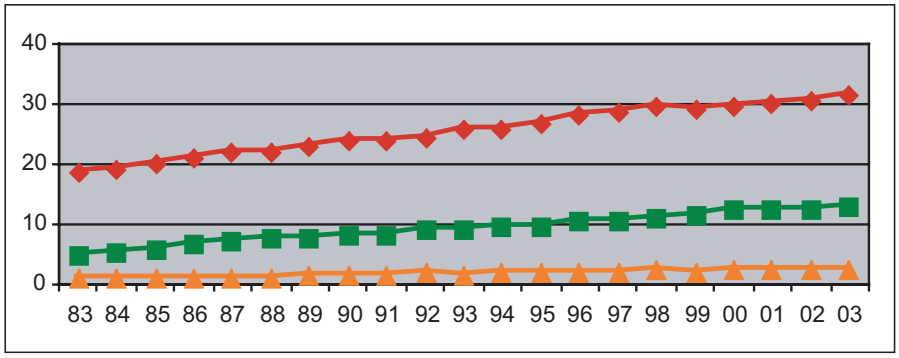
Total births by year



Percentage of births by maternal age



legenda: %births < 20 %births 20-24 %births 25-29



legenda: %births 30-34 %births 35-39 %births 40+

France: Strasbourg, 2003

Live births (LB)	13390
Stillbirths (SB)	105
Total births	13495
Number of terminations of pregnancy (ToP) for birth defects	99

Birth Defects	Number of cases			Rates*10.000
	LB	SB	ToP	Total rate
Anencephaly	0	0	11	8.09
Spina bifida	1	0	5	4.41
Encephalocele	0	0	3	2.21
Microcephaly	1	0	0	0.74
Arhinencephaly / Holoprosencephaly	0	0	8	5.88
Hydrocephaly	0	0	4	2.94
Anophthalmos	0	0	0	0.00
Microphthalmos	1	0	0	0.74
Unspecified Anophthalmos / Microphthalmos	0	0	0	---
Anotia	0	0	1	0.74
Microtia	3	0	0	2.21
Unspecified Anotia / Microtia	0	0	0	---
Transposition of great vessels	1	0	1	1.47
Tetralogy of Fallot	3	0	4	5.15
Hypoplastic left heart syndrome	0	0	4	2.94
Coarctation of aorta	4	0	0	2.94
Choanal atresia, bilateral	1	0	0	0.74
Cleft palate without cleft lip	6	0	2	5.88
Cleft lip with or without cleft palate	19	0	7	19.13
Oesophageal atresia / stenosis with or without fistula	5	0	1	4.41
Small intestine atresia / stenosis	1	0	0	0.74
Anorectal atresia / stenosis	3	0	5	5.88
Undescended testis (36 weeks of gestation or later)	nr	nr	nr	nr
Hypospadias	34	0	0	25.01
Epispadias	0	0	0	0.00
Indeterminate sex	3	0	0	2.21
Renal agenesis	5	0	3	5.88
Cystic kidney	6	0	1	5.15
Bladder exstrophy	2	0	0	1.47
Polydactyly, preaxial	1	0	1	1.47
Total Limb reduction defects (include unspecified)	4	0	5	6.62
Transverse	1	0	2	2.21
Preaxial	0	0	2	1.47
Postaxial	1	0	0	0.74
Intercalary	0	0	0	0.00
Mixed	2	0	1	2.21
Unspecified	0	0	0	---
Diaphragmatic hernia	6	0	2	5.88
Omphalocele	1	0	6	5.15
Gastroschisis	2	0	0	1.47
Unspecified Omphalocele / Gastroschisis	0	0	4	---
Prune belly sequence	0	0	2	1.47
Trisomy 13	0	0	7	5.15
Trisomy 18	0	0	13	9.56
Down syndrome, all ages (include age unknown)	7	0	13	14.71
<20	0	0	0	0.00
20-24	0	0	1	4.38
25-29	1	0	1	4.43
30-34	2	0	2	9.43
35-39	3	0	6	51.22
40-44	1	0	3	122.32
45+	0	0	0	0.00
unspecified	0	0	0	---

nr = not reported

France: Strasbourg, Previous years rates 1983 - 2003

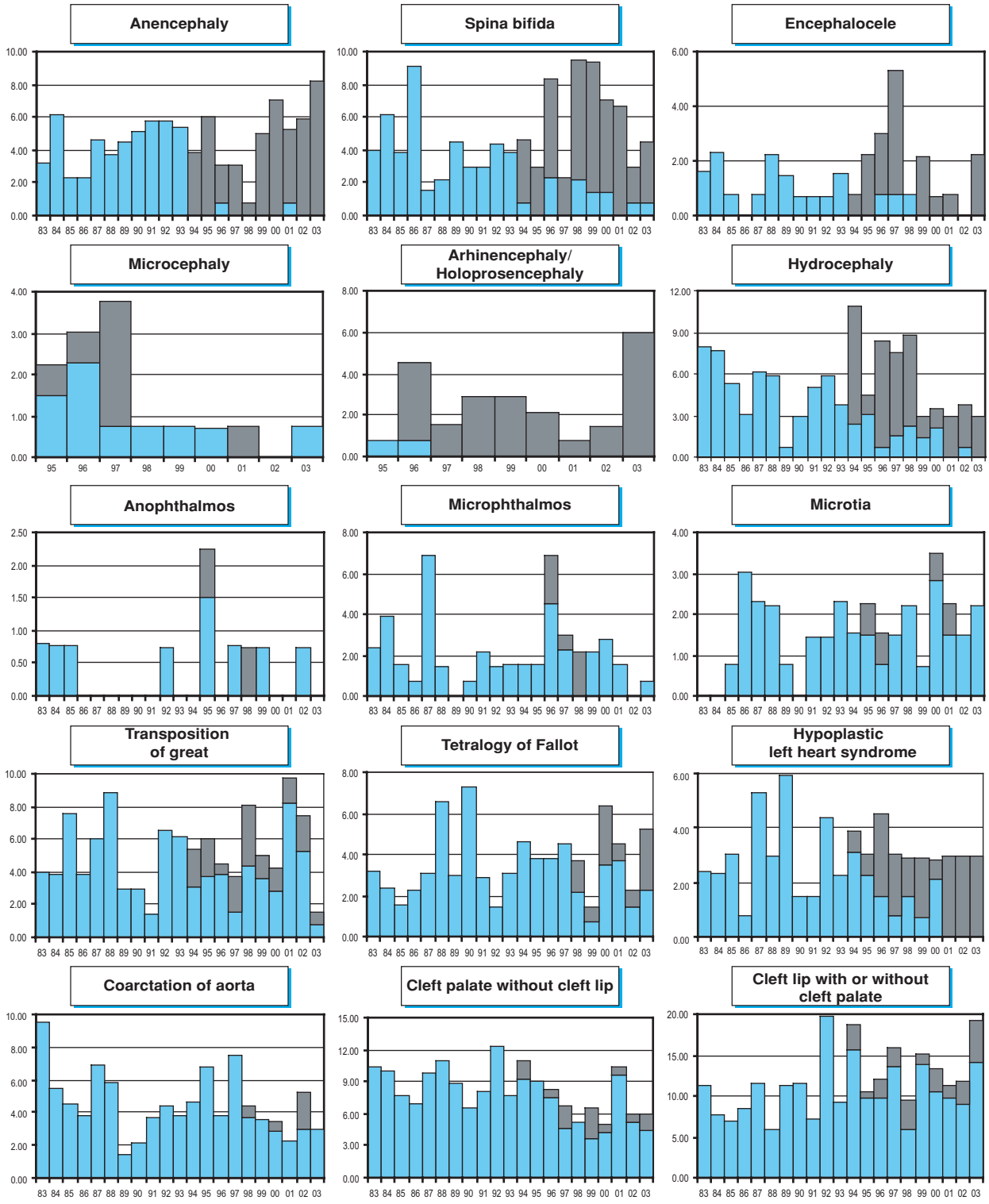
Birth prevalence rates: (LB+SB) * 10,000 until 1993
Birth prevalence rates: (LB+SB+TOP) * 10,000 since 1994

	1974-78	1979-83*	1984-88	1989-93	1994-98	1999-03
Births		**12,526**	**65,979**	**67,849**	**66,261**	**68,447**
Anencephaly		3.19	3.79	5.31	3.32	6.28
Spina bifida		3.99	4.55	3.68	5.58	6.14
Encephalocele		1.60	1.21	1.03	2.41	1.17
Microcephaly		nr	nr	nr	2.43*	0.58
Arhinencephaly / Holoprosencephaly		nr	nr	nr	2.43*	2.63
Hydrocephaly		7.98	5.61	3.68	8.00	3.21
Anophthalmos		0.80	0.30	0.15	0.75	0.29
Microphthalmos		2.40	2.88	1.18	3.02	1.46
Unspecified Anophthalmos / Microphthalmos		---	---	---	---	---
Anotia		0.00	0.30	0.00	0.91	0.15
Microtia		0.00	1.67	1.18	1.81	2.05
Unspecified Anotia / Microtia		---	---	---	---	---
Transposition of great vessels		3.99	6.06	3.98	5.58	5.55
Tetralogy of Fallot		3.19	3.18	3.54	4.07	3.94
Hypoplastic left heart syndrome		2.40	2.88	3.10	3.47	2.92
Coarctation of aorta		9.58	5.30	3.10	5.43	3.51
Choanal atresia, bilateral		nr	nr	nr	0.00*	0.44
Cleft palate without cleft lip		10.38	9.09	8.70	8.00	6.72
Cleft lip with or without cleft palate		11.18	8.03	11.79	13.28	14.17
Oesophageal atresia / stenosis with or without fistula		2.40	2.12	2.95	2.41	4.38
Small intestine atresia / stenosis		nr	nr	nr	2.43*	1.90
Anorectal atresia / stenosis		5.59	4.55	6.04	6.19	5.11
Undescended testis (36 weeks of gestation or later)		nr	nr	nr	1.52*	nr
Hypospadias		12.77	21.98	26.09	23.09	23.08
Epispadias		nr	nr	nr	0.25*	0.15
Indeterminate sex		nr	nr	nr	0.19*	0.88
Renal agenesis		nr	nr	nr	3.32	8.77
Cystic kidney		nr	nr	nr	8.62*	8.04
Bladder exstrophy		nr	nr	nr	0.56*	0.44
Polydactyly, preaxial		nr	nr	nr	3.93*	4.68
Total Limb reduction defects (include unspecified)		6.39	6.06	7.37	11.92	7.74
Transverse		5.59	4.24	3.98	5.13	4.24
Preaxial		0.80	1.36	1.92	1.81	0.73
Postaxial		0.00	0.15	0.74	0.30	0.58
Intercalary		0.00	0.00	0.29	1.06	0.29
Mixed		0.00	0.30	0.44	0.60	1.31
Unspecified		---	---	---	---	---
Diaphragmatic hernia		2.40	4.09	4.86	4.23	4.97
Omphalocele		3.19	2.88	3.68	4.83	3.36
Gastroschisis		0.80	1.97	1.92	3.02	1.90
Unspecified Omphalocele / Gastroschisis		---	---	---	---	---
Prune belly sequence		nr	nr	nr	0.56*	0.73
Trisomy 13		nr	nr	nr	1.87*	2.19
Trisomy 18		nr	nr	nr	3.18*	6.57
Down syndrome, all ages (include age unknown)		7.98	13.49	20.93	32.30	20.60
<20		0.00	17.16	11.26	15.68	9.38
20-24		7.24	7.50	11.62	9.08	12.39
25-29		6.43	6.98	11.24	12.81	6.55
30-34		13.06	11.71	18.37	25.02	13.14
35-39		15.97	53.25	60.22	120.64	63.00
40-44		0.00	207.61	260.26	317.85	118.89
45+		0.00	270.27	238.10	0.00	0.00
unspecified		---	---	---	---	---

* data include less than 5 years
nr = not reported

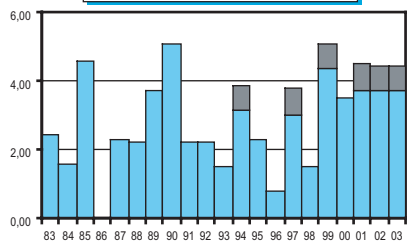
France: Strasbourg

'Time trends 1983-2003 (Birth prevalence rates per 10,000)

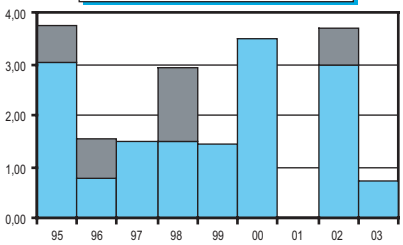


Note: L+S rates, ToP rates

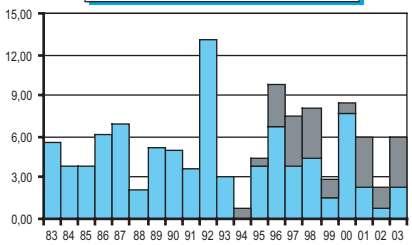
Oesophageal atresia/stenosis with or without fistula



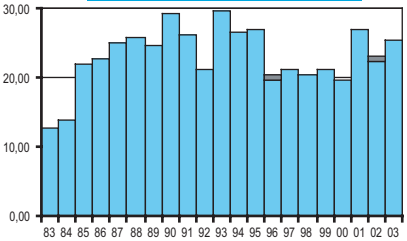
Small intestine atresia/stenosis



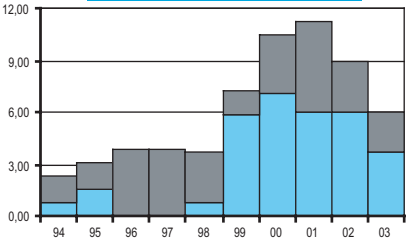
Anorectal atresia/stenosis



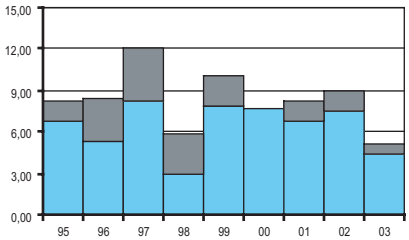
Hypospadias



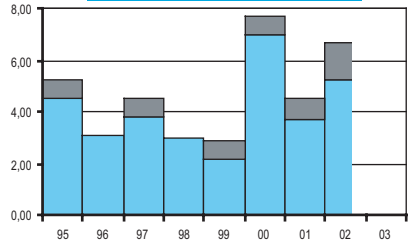
Renal agenesis



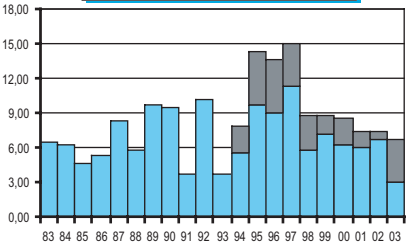
Cystic Kidney



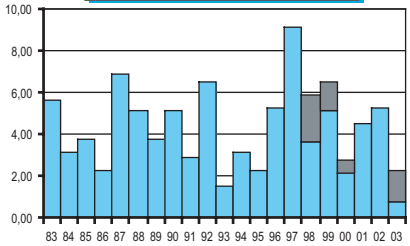
Polydactyly, preaxial



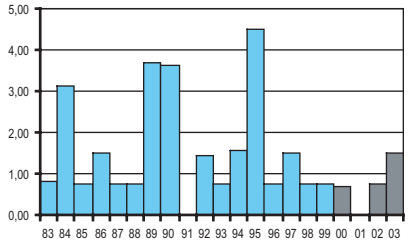
Limb reduction defects



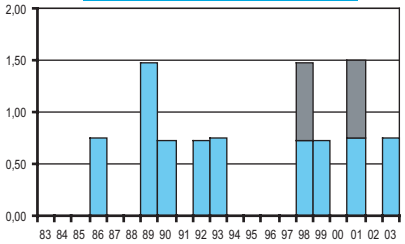
Limb reduction defects transverse



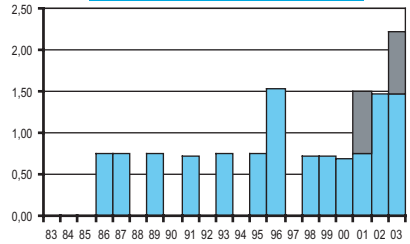
Limb reduction defects preaxial



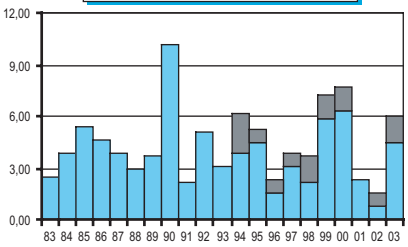
Limb reduction defects postaxial



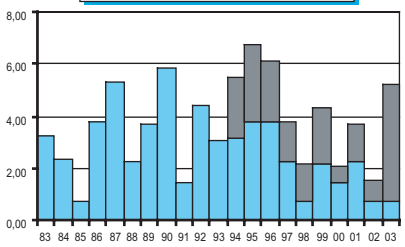
Limb reduction defects mixed



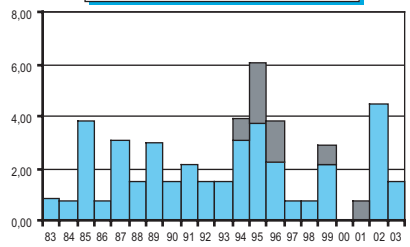
Diaphragmatic hernia



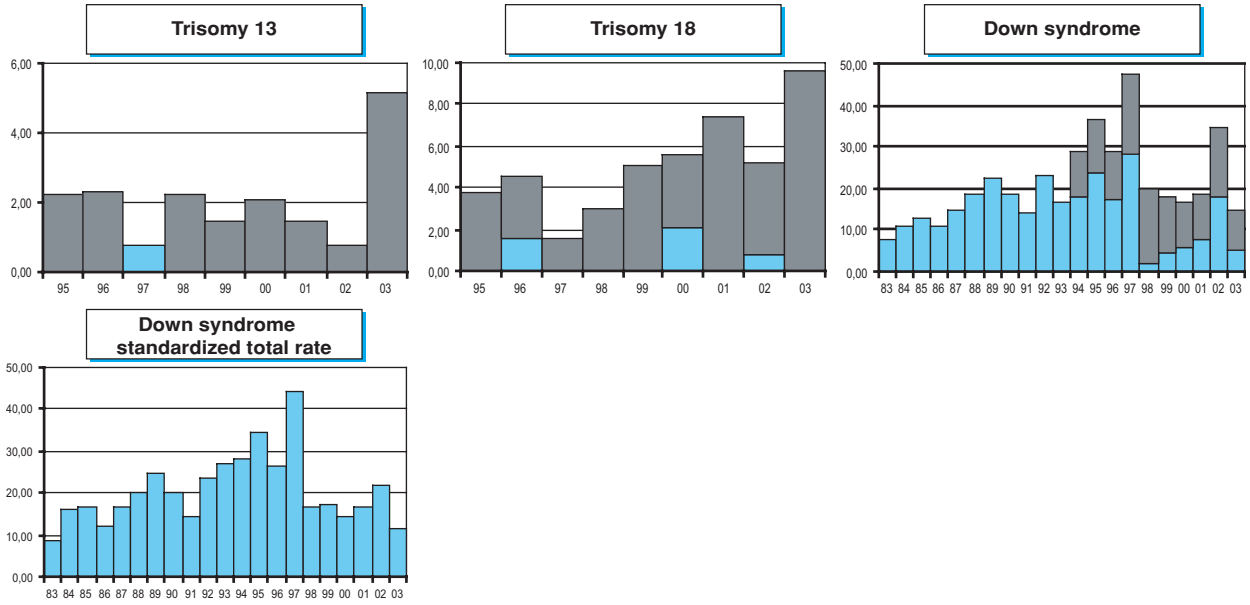
Omphalocele



Gastroschisis



Note: L+S rates, ToP rates



Note: L+S rates, ToP rates

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 2.49 million inhabitants (31.12.2004) and annual births at a rate of about 17 500 children (2004).
The survey system is multi-centric and based on population.

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 Labour, Women, Health and Social Security of the Federal State of Saxony-Anhalt.
The Malformation Monitoring is working in order of Ministry of Labour, Women, Health and Social Security of the Federal State of Saxony-Anhalt.

Sources of ascertainment
The co-operation partner are:
- 32 obstetrics departments
- 29 children hospitals
- 10 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 information
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).

Addresses and staff
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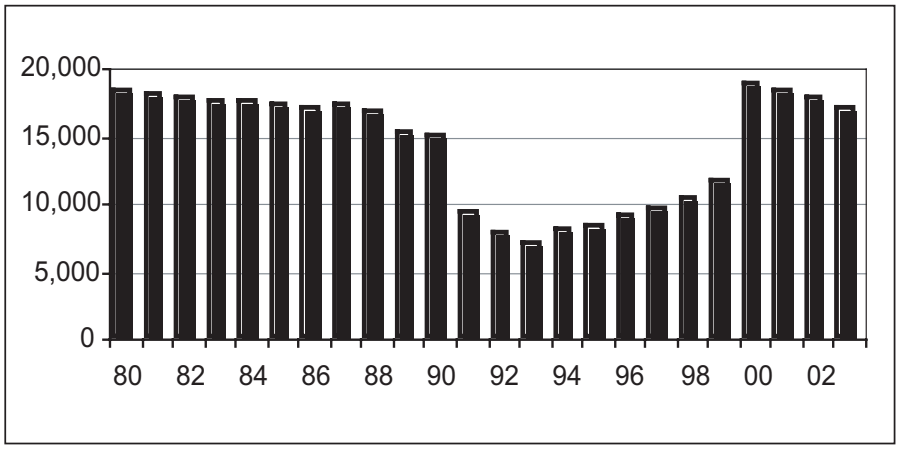
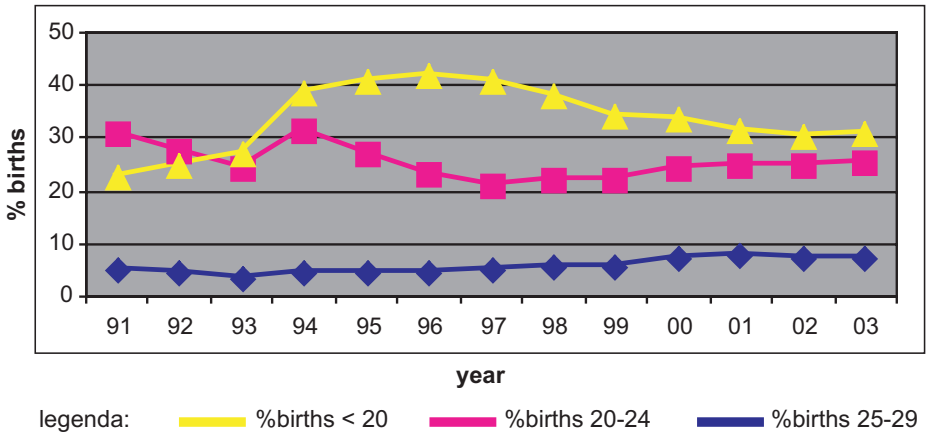
http://www.med.uni-magdeburg.de/fme/zkh/mz/

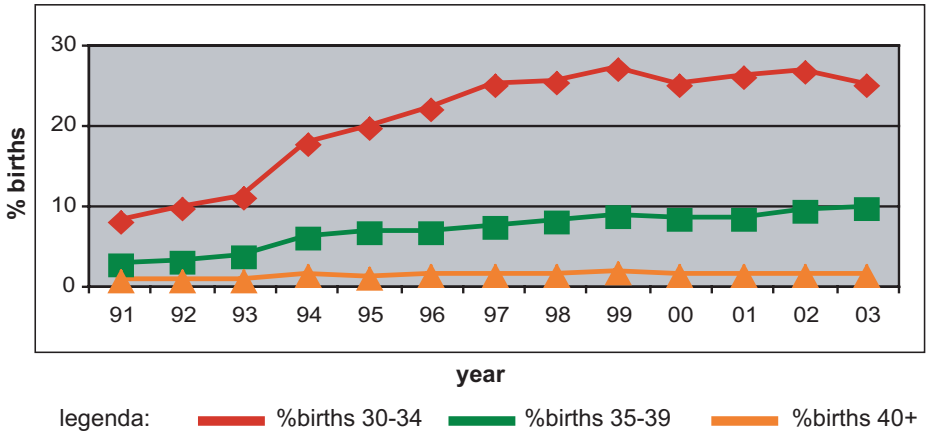
Germany: Saxony-Anhalt

Total births by year



Percentage of births by maternal age





Germany: Saxony Anhalt, 2003

Live births (LB)	16889
Stillbirths (SB)	87
Total births	16976
Number of terminations of pregnancy (ToP) for birth defects	83

Birth Defects	Number of cases			Rates*10.000
	LB	SB	ToP	Total rate
Anencephaly	0	0	9	5.28
Spina bifida	3	1	5	5.28
Encephalocele	0	0	4	2.34
Microcephaly	30	0	1	18.17
Arhinencephaly / Holoprosencephaly	0	0	4	2.34
Hydrocephaly	3	1	3	4.10
Anophthalmos	0	0	0	0.00
Microphthalmos	1	0	0	0.59
Unspecified Anophthalmos / Microphthalmos	0	0	0	---
Anotia	0	0	0	0.00
Microtia	3	0	0	1.76
Unspecified Anotia / Microtia	0	0	0	---
Transposition of great vessels	11	0	3	8.21
Tetralogy of Fallot	3	1	0	2.34
Hypoplastic left heart syndrome	0	0	2	1.17
Coarctation of aorta	3	0	2	2.93
Choanal atresia, bilateral	1	0	0	0.59
Cleft palate without cleft lip	22	0	3	14.66
Cleft lip with or without cleft palate	8	1	1	5.86
Oesophageal atresia / stenosis with or without fistula	3	0	1	2.34
Small intestine atresia / stenosis	3	0	0	1.76
Anorectal atresia / stenosis	0	0	0	0.00
Undescended testis (36 weeks of gestation or later)	26	0	0	15.24
Hypospadias	12	0	1	7.62
Epispadias	1	0	0	0.59
Indeterminate sex	0	0	0	0.00
Renal agenesis (Potter)	0	0	6	3.52
Cystic kidney	13	1	1	8.79
Bladder exstrophy	0	0	0	0.00
Polydactyly, preaxial	2	0	1	1.76
Total Limb reduction defects (include unspecified)	10	1	5	9.38
Transverse	2	1	2	2.93
Preaxial	1	0	1	1.17
Postaxial	0	0	0	0.00
Intercalary	0	0	1	0.59
Mixed	4	0	0	2.34
Unspecified	3	0	1	---
Diaphragmatic hernia	3	0	2	2.93
Omphalocele	1	0	4	2.93
Gastroschisis	1	1	2	2.34
Unspecified Omphalocele / Gastroschisis	0	0	0	---
Prune belly sequence	0	0	0	0.00
Trisomy 13	0	0	2	1.17
Trisomy 18	2	0	4	3.52
Down syndrome, all ages (include age unknown)	9	0	14	13.48
<20	1	0	0	7.97
20-24	2	0	1	7.02
25-29	2	0	1	5.74
30-34	3	0	4	16.39
35-39	1	0	5	36.83
40-44	0	0	3	127.12
45+	0	0	0	0.00
unspecified	0	0	0	---

Germany: Saxony Anhalt, Previous years rates 1980 - 2003

Prevalence rates: (LB+SB+TOP) * 10,000

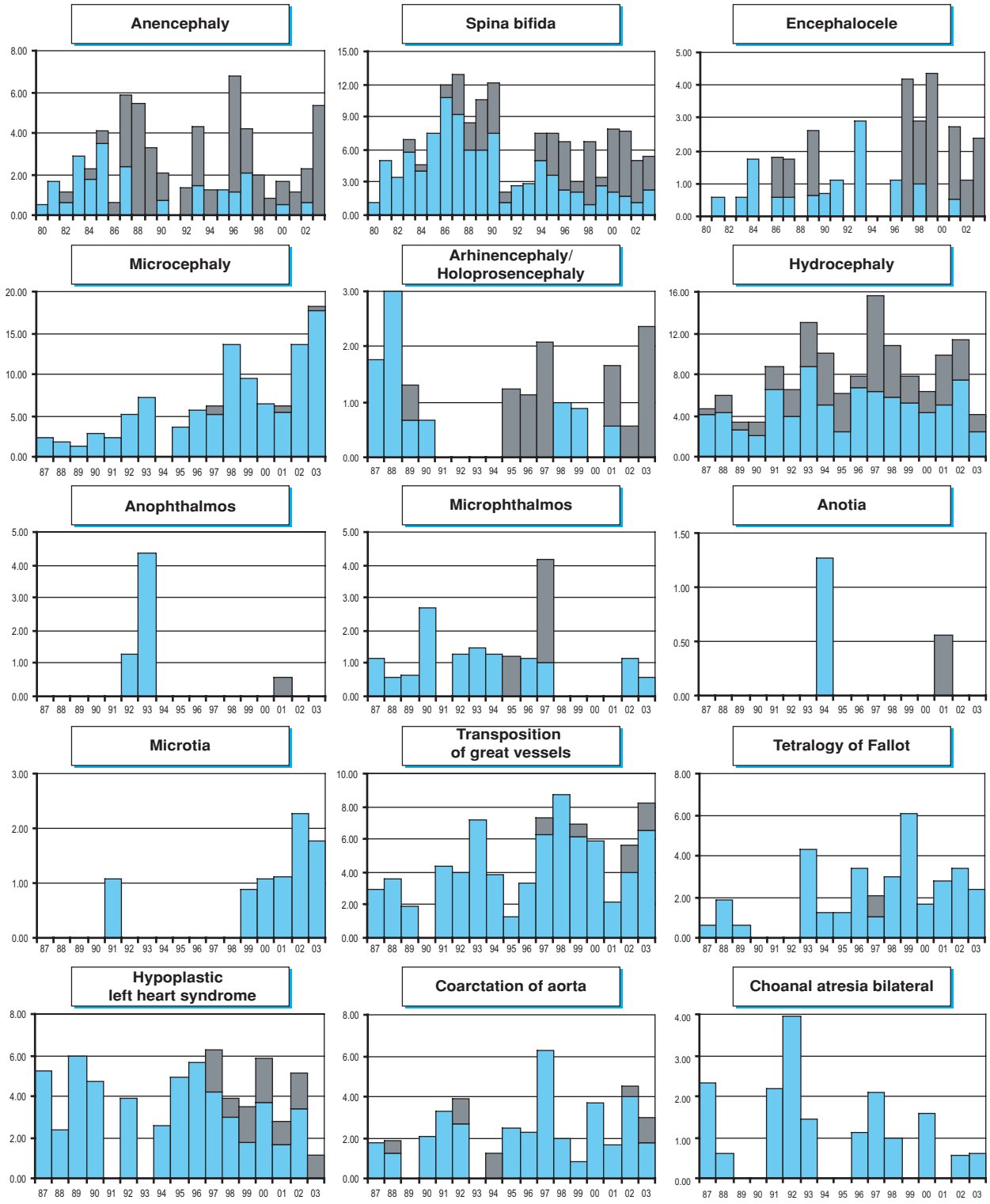
	1974-78	1979-83*	1984-88	1989-93	1994-98	1999-03
Births		**71,127**	**85,154**	**53,635**	**44,758**	**83,096**
Anencephaly		1.55	3.64	2.24	3.13	2.29
Spina bifida		4.08	9.04	7.46	6.26	6.14
Encephalocele		0.28	1.06	1.49	1.79	1.93
Microcephaly		nr	2.07*	3.17	6.26	10.71
Arhinencephaly / Holoprosencephaly		nr	2.37*	0.56	1.12	1.08
Hydrocephaly		nr	5.33*	5.97	10.28	7.94
Anophthalmos		nr	0.00*	0.75	0.00	0.12
Microphthalmos		nr	0.89*	1.31	1.56	0.36
Unspecified Anophthalmos / Microphthalmos		---	---	---	---	---
Anotia		nr	0.00*	0.00	0.22	0.12
Microtia		nr	0.00*	0.19	0.00	1.44
Unspecified Anotia / Microtia		---	---	---	---	---
Transposition of great vessels		nr	3.26*	2.80	5.14	5.66
Tetralogy of Fallot		nr	1.18*	0.75	2.23	3.01
Hypoplastic left heart syndrome		nr	3.85*	3.54	4.69	3.73
Coarctation of aorta		nr	1.78*	1.68	2.90	2.89
Choanal atresia, bilateral		nr	1.48*	1.12	0.89	0.60
Cleft palate without cleft lip		nr	4.14*	5.97	7.15	11.43
Cleft lip with or without cleft palate		nr	13.61*	13.42	16.09	14.44
Oesophageal atresia / stenosis with or without fistula		nr	2.66*	2.61	2.68	2.65
Small intestine atresia / stenosis		nr	0.89*	2.61	1.34	2.29
Anorectal atresia / stenosis		nr	2.96*	3.92	2.23	2.77
Undescended testis (36 weeks of gestation or later)		nr	10.36*	18.64	12.96	9.87
Hypospadias		nr	12.73*	17.53	16.76	10.23
Epispadias		nr	0.30*	0.37	0.67	0.24
Indeterminate sex		nr	0.89*	0.00	0.45	0.96
Renal agenesis		nr	2.37*	0.75	2.68	2.41
Cystic kidney		nr	2.37*	1.68	5.14	4.57
Bladder exstrophy		nr	0.59*	0.56	0.67	0.00
Polydactyly, preaxial		nr	0.00*	0.93	4.02	4.09
Total Limb reduction defects (include unspecified)		nr	3.26*	7.46	6.70	8.18
Transverse		nr	nr	nr	nr	3.35*
Preaxial		nr	nr	nr	nr	0.42*
Postaxial		nr	nr	nr	nr	0.00*
Intercalary		nr	nr	nr	nr	1.54*
Mixed		nr	nr	nr	nr	1.68*
Unspecified		---	---	---	---	---
Diaphragmatic hernia		nr	1.78*	1.49	0.67	2.65
Omphalocele		nr	5.62*	3.73	2.23	2.89
Gastroschisis		nr	1.18*	1.86	3.35	2.77
Unspecified Omphalocele / Gastroschisis		---	---	---	---	---
Prune belly sequence		nr	0.00*	0.75	0.89	0.84
Trisomy 13		0.28	0.35	0.56	2.23	0.96
Trisomy 18		1.12	0.70	0.75	1.56	2.65
Down syndrome, all ages (include age unknown)		8.72	7.99	10.44	15.19	16.25
<20		nr	nr	nr	nr	5.72*
20-24		nr	nr	nr	nr	6.20*
25-29		nr	nr	nr	nr	9.74*
30-34		nr	nr	nr	nr	13.07*
35-39		nr	nr	nr	nr	55.01*
40-44		nr	nr	nr	nr	142.86*
45+		nr	nr	nr	nr	512.82*
unspecified		---	---	---	---	---

* data include less than 5 years

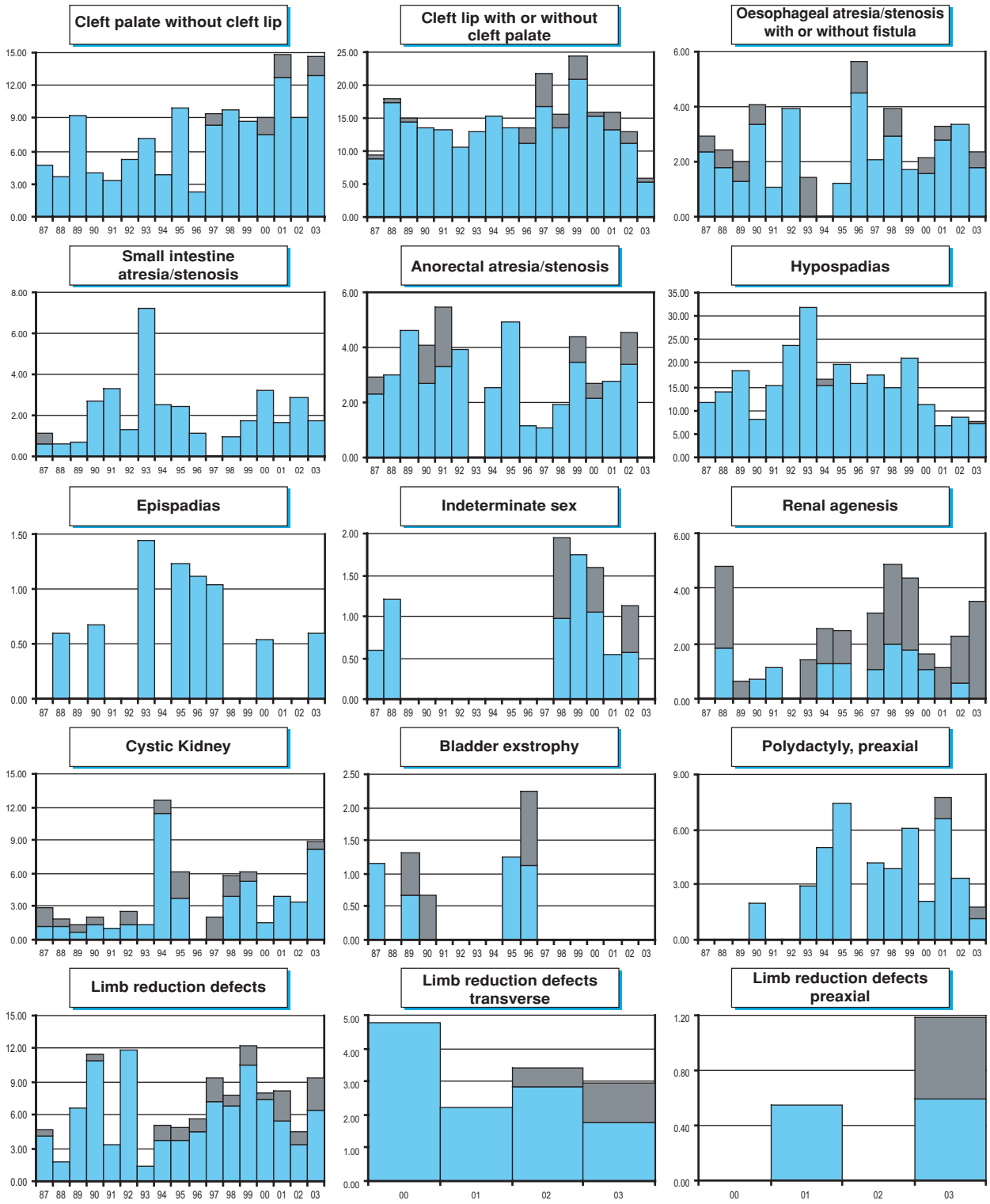
nr = not reported

Germany: Saxony Anhalt

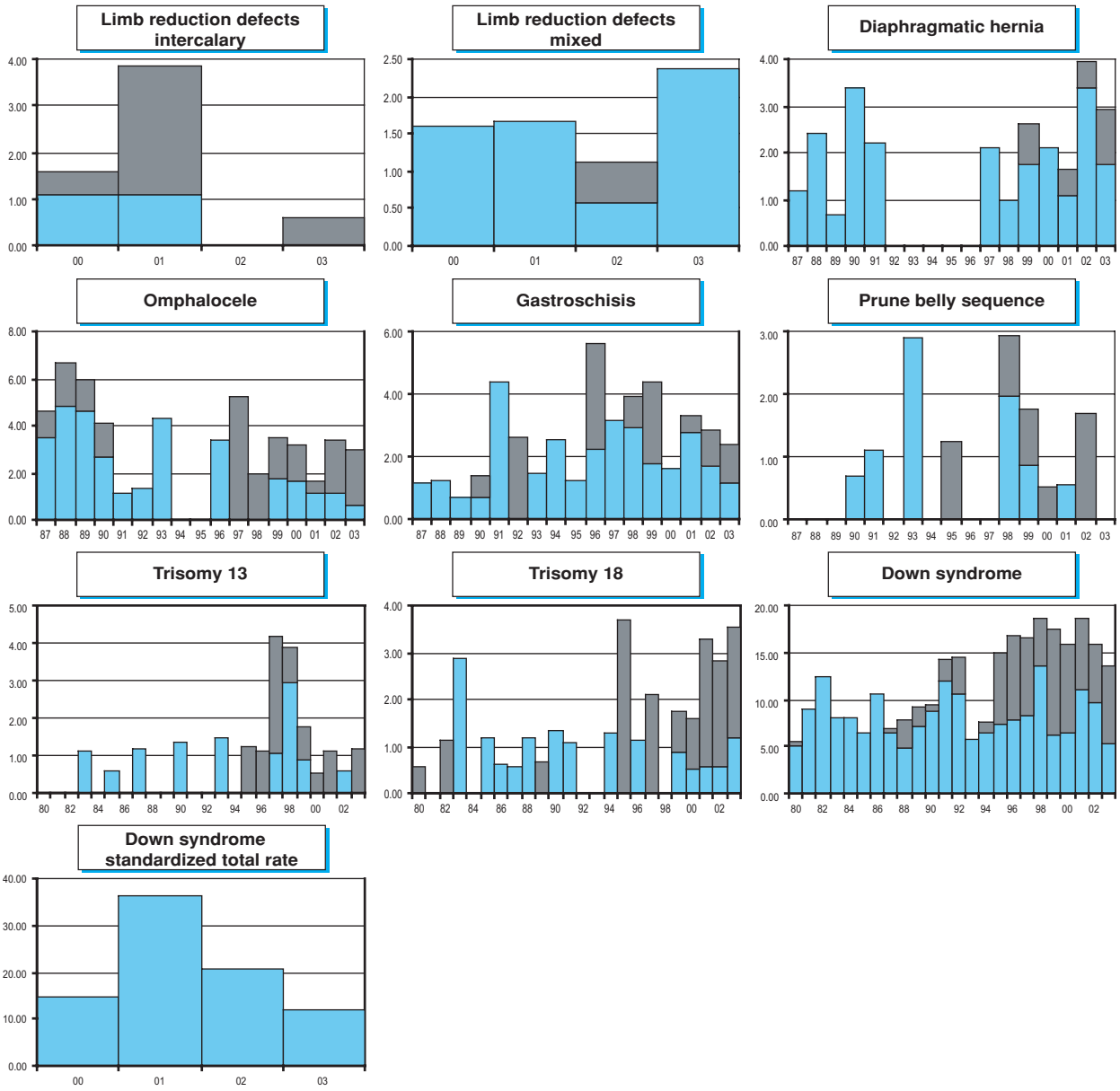
'Time trends 1980-2003 (Birth prevalence rates per 10,000)



Note: L+S rates, ToP rates



Note: L+S rates, ToP rates



Note: L+S rates, ToP rates

Hungary
Hungarian Congenital Abnormality Registry

History:
Centralized registration of congenital abnormalities began in Hungary in 1962, and came under our coordination 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. In 2003 the case-control system was interrupted due to temporary problems of the legislative background. Therefore, exposure information has not been collected since that year. Our expectation is that the formal system will be restarted in 2005.

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

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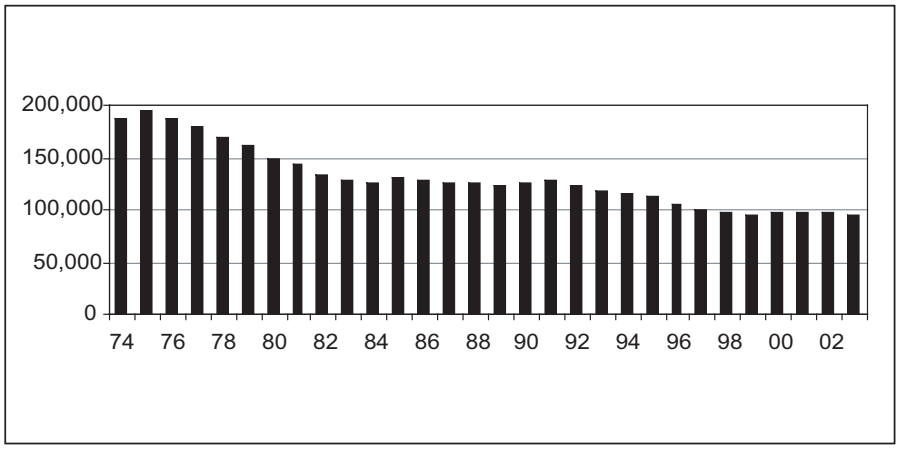
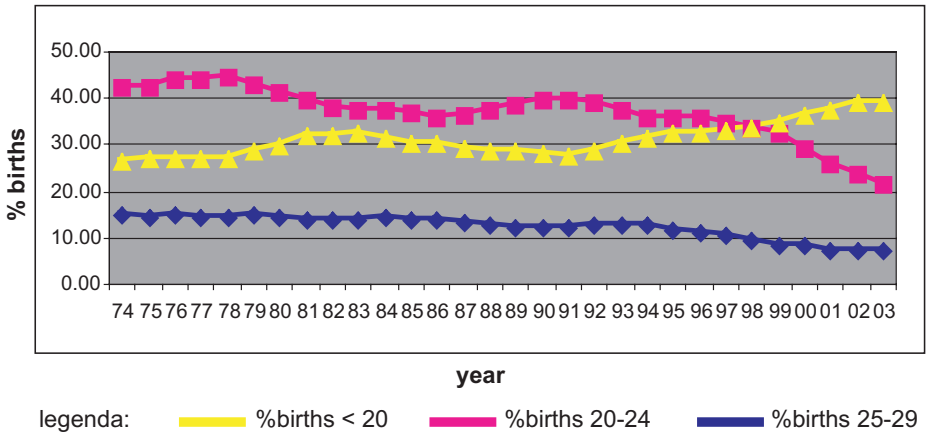
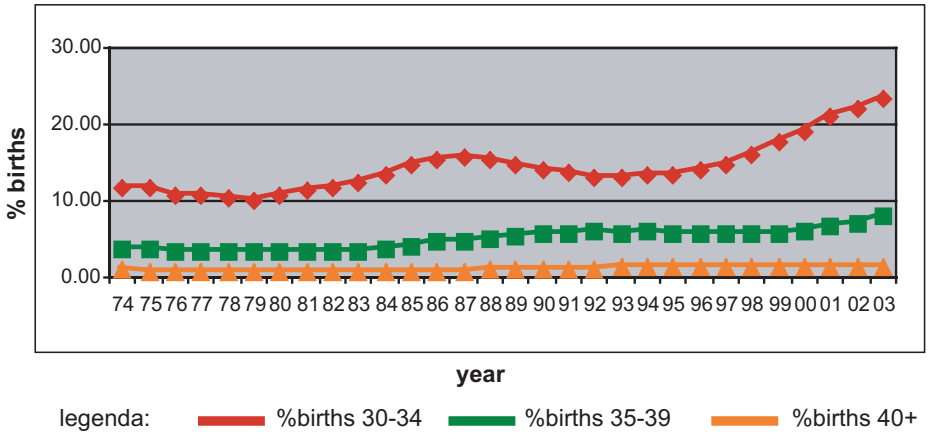
Hungary

Total births by year



Percentage of births by maternal age





Hungary, 2003

Live births (LB)	94647
Stillbirths (SB)	530
Total births	95177
Number of terminations of pregnancy (ToP) for birth defects	208

Birth Defects	Number of cases			Rates*10.000
	LB	SB	ToP	Total rate
Anencephaly	1	0	12	1.36
Spina bifida	11	0	20	3.25
Encephalocele	4	0	0	0.42
Microcephaly	3	0	1	0.42
Arhinencephaly / Holoprosencephaly	6	0	2	0.84
Hydrocephaly	19	0	14	3.46
Anophthalmos	2	0	0	0.21
Microphthalmos	1	0	0	0.10
Unspecified Anophthalmos / Microphthalmos	0	0	0	---
Anotia	4	0	0	0.42
Microtia	2	0	0	0.21
Unspecified Anotia / Microtia	0	0	0	---
Transposition of great vessels	8	0	1	0.94
Tetralogy of Fallot	26	0	1	2.83
Hypoplastic left heart syndrome	5	0	1	0.63
Coarctation of aorta	16	0	0	1.68
Choanal atresia, bilateral	1	0	0	0.10
Cleft palate without cleft lip	34	0	0	3.56
Cleft lip with or without cleft palate	62	0	0	6.50
Oesophageal atresia / stenosis with or without fistula	10	0	2	1.26
Small intestine atresia / stenosis	12	0	0	1.26
Anorectal atresia / stenosis	14	0	0	1.47
Undescended testis (36 weeks of gestation or later)	103	0	0	10.80
Hypospadias	211	0	0	22.12
Epispadias	nr	nr	nr	nr
Indeterminate sex	6	0	0	0.63
Renal agenesis	2	0	0	0.21
Cystic kidney	21	0	2	2.41
Bladder exstrophy	3	0	0	0.31
Polydactyly, preaxial	64	0	0	6.71
Total Limb reduction defects (include unspecified)	23	0	0	2.41
Transverse	nr	nr	nr	nr
Preaxial	nr	nr	nr	nr
Postaxial	nr	nr	nr	nr
Intercalary	nr	nr	nr	nr
Mixed	nr	nr	nr	nr
Unspecified	nr	nr	nr	---
Diaphragmatic hernia	4	0	0	0.42
Omphalocele	5	0	7	1.26
Gastroschisis	2	0	5	0.73
Unspecified Omphalocele / Gastroschisis	0	0	0	---
Prune belly sequence	0	0	0	0.00
Trisomy 13	0	0	4	0.42
Trisomy 18	3	0	9	1.26
Down syndrome, all ages (include age unknown)	93	0	35	13.42
<20	4	0	1	7.52
20-24	16	0	3	9.37
25-29	24	0	6	8.06
30-34	24	0	4	12.64
35-39	15	0	8	30.60
40+	9	0	13	160.47
unspecified	1	0	0	---

NOTE1: Epispadias included in Hypospadias
NOTE2: Only isolated birth defects are reported

nr = not reported

Hungary, Previous years rates 1974 - 2003

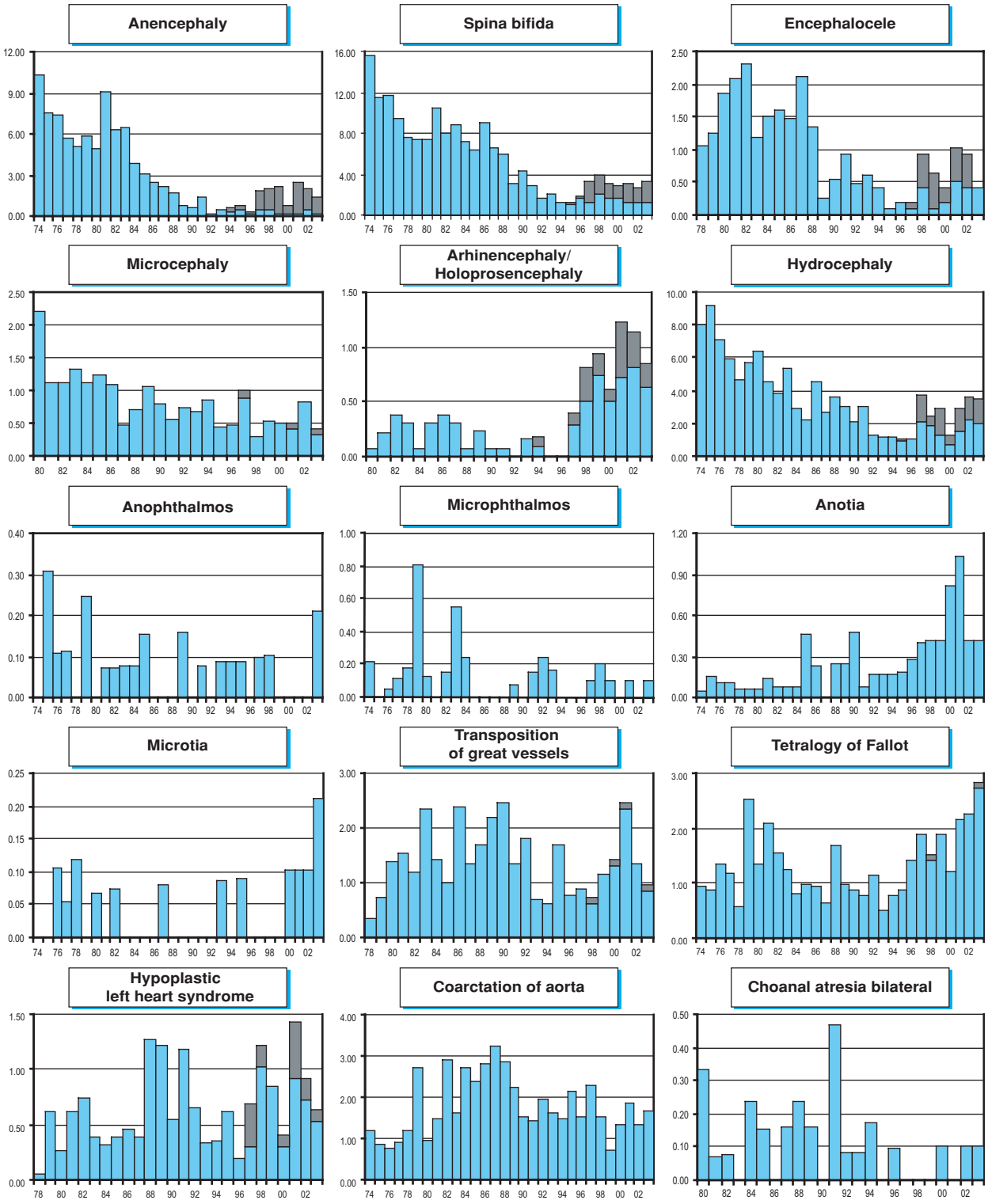
Birth prevalence rates: (LB+SB) * 10,000 until 1993
Birth prevalence rates: (LB+SB+TOP) * 10,000 since 1994

	1974-78	1979-83	1984-88	1989-93	1994-98	1999-03
Births	**919,396**	**718,307**	**637,980**	**617,808**	**532,809**	**483,352**
Anencephaly	7.29	6.47	2.66	0.71	1.09	1.74
Spina bifida	11.20	8.35	7.04	2.78	2.21	3.02
Encephalocele	1.06*	1.73	1.61	0.57	0.36	0.68
Microcephaly	nr	1.46*	0.92	0.76	0.62	0.56
Arhinencephaly / Holoprosencephaly	nr	0.23*	0.24	0.11	0.26	0.95
Hydrocephaly	7.06	5.21	3.18	2.10	1.86	2.83
Anophthalmos	0.11	0.10	0.05	0.06	0.08	0.04
Microphthalmos	0.11	0.33	0.05	0.13	0.06	0.06
Unspecified Anophthalmos / Microphthalmos	---	---	---	---	---	---
Anotia	0.10	0.08	0.20	0.23	0.28	0.62
Microtia	0.05	0.03	0.02	0.02	0.02	0.10
Unspecified Anotia / Microtia	---	---	---	---	---	---
Transposition of great vessels	0.35*	1.41	1.57	1.70	0.94	1.47
Tetralogy of Fallot	0.99	1.78	1.00	0.86	1.28	2.07
Hypoplastic left heart syndrome	0.06*	0.53	0.56	0.79	0.60	0.85
Coarctation of aorta	0.97	1.94	2.79	1.75	1.78	1.39
Choanal atresia, bilateral	nr	0.13*	0.16	0.16	0.06	0.06
Cleft palate without cleft lip	3.62	4.61	4.00	3.67	2.70	3.17
Cleft lip with or without cleft palate	10.96	11.54	9.47	9.40	6.46	6.85
Oesophageal atresia / stenosis with or without fistula	2.09*	1.80	1.63	1.60	0.98	0.99
Small intestine atresia / stenosis	nr	1.46*	1.29	1.13	0.60	0.77
Anorectal atresia / stenosis	2.42*	2.14	2.13	1.62	0.90	0.93
Undescended testis (36 weeks of gestation or later)	nr	16.91*	17.54	14.99	12.57	10.51
Hypospadias	17.56	16.86	21.40	21.50	19.13	21.85
Epispadias	nr	nr	nr	nr	nr	
Indeterminate sex	nr	0.22*	0.36	0.31	0.13	0.29
Renal agenesis	1.06*	1.28	0.89	1.05	0.13	0.21
Cystic kidney	nr	0.00*	0.11	0.52	1.03	2.01
Bladder exstrophy	nr	0.34*	0.49	0.08	0.04	0.10
Polydactyly, preaxial	nr	0.90*	1.82	1.46	3.62	7.94
Total Limb reduction defects (include unspecified)	nr	4.34*	4.26	3.08	2.95	2.88
Transverse	nr	nr	nr	nr	nr	nr
Preaxial	nr	nr	nr	nr	nr	nr
Postaxial	nr	nr	nr	nr	nr	nr
Intercalary	nr	nr	nr	nr	nr	nr
Mixed	nr	nr	nr	nr	nr	nr
Unspecified	---	---	---	---	---	---
Diaphragmatic hernia	2.08	2.17	2.07	1.99	0.94	0.35
Omphalocele	nr	2.44*	1.43	0.83	0.79	0.99
Gastroschisis	nr	0.65*	0.50	0.55	0.49	0.83
Unspecified Omphalocele / Gastroschisis	---	---	---	---	---	---
Prune belly sequence	nr	nr	nr	nr	0.09	0.00
Trisomy 13	nr	0.11*	0.25	0.19	0.24	0.43
Trisomy 18	nr	0.23*	0.25	0.34	0.43	1.22
Down syndrome, all ages (include age unknown)	9.00	8.59	7.70	8.82	6.53	13.26
<20	nr	1.65*	1.39	2.23	1.54	5.45
20-24	nr	1.11*	2.83	2.67	2.19	6.74
25-29	nr	3.43*	4.04	3.58	2.13	8.48
30-34	nr	5.37*	4.95	4.84	4.61	11.99
35-39	nr	6.77*	14.41	24.29	11.27	37.10
40+	nr	67.81*	50.52	98.32	61.03	165.98
unspecified	---	---	---	---	---	---

* data include less than 5 years
nr= not reported

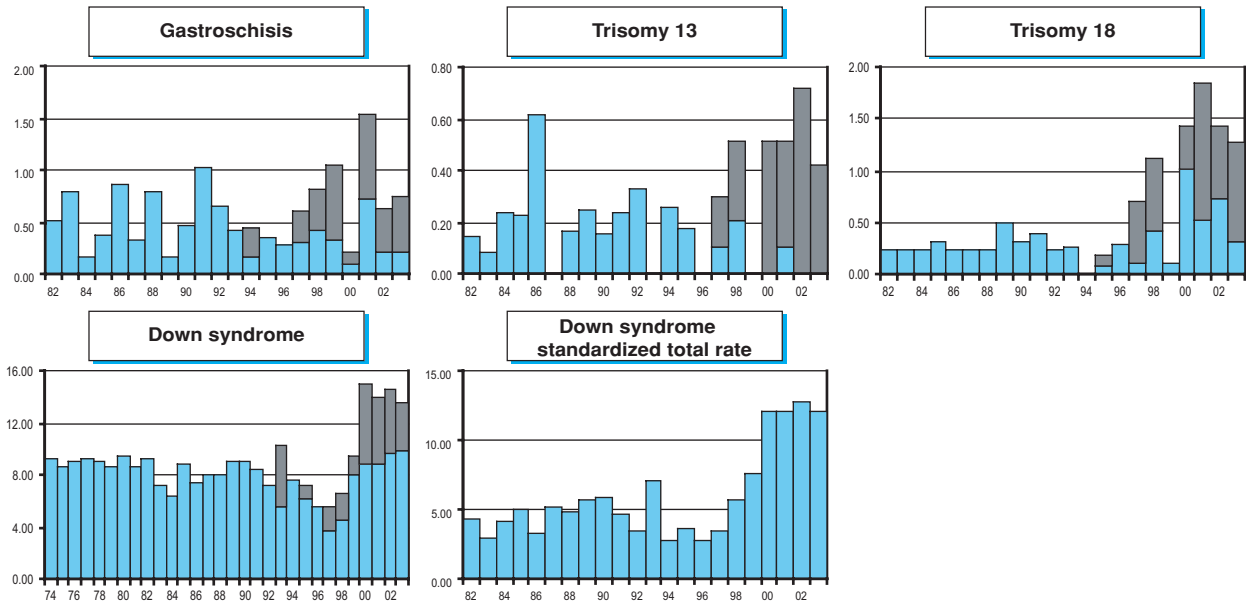
Hungary

'Time trends 1974-2003 (Birth prevalence rates per 10,000)



Note: L+S rates, ToP rates

Note: L+S rates, ToP rates



Note: L+S rates, ToP rates

Ireland: Dublin
Dublin EUROCAT Registry

History:
The Registry began in September 1979 and joined EUROCAT at the same time. Joined International Clearinghouse 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 (22,000 births) of all births in Ireland occur in this region.

Legislation and funding
The Registry is located within the Public Health Department of the Health Service Executive-Eastern Region. Staffing includes a full time co-ordinator/nurse researcher and a part time secretary plus a part-time public health specialist. Funding is provided by the Department of Health through the Health Service Executive. There is a Steering Committee comprised of 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 included. Termination of pregnancy is not legal in Ireland.

Addresses and staff

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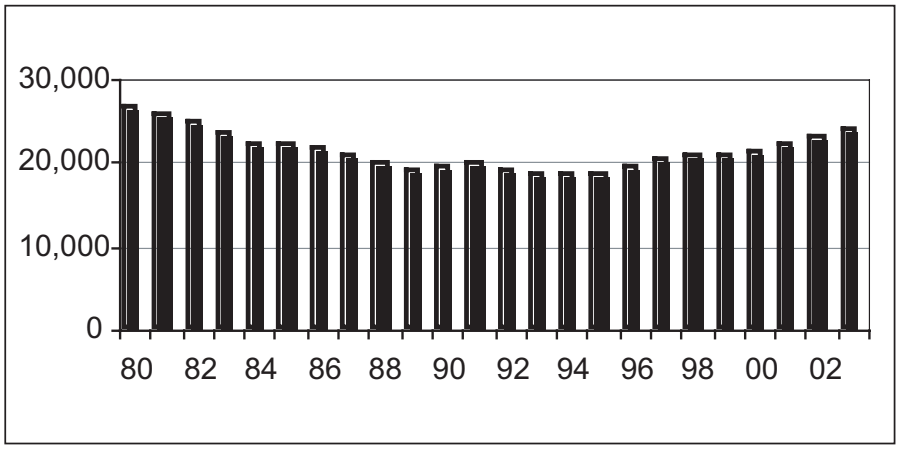
Fax: 353-1-6353745

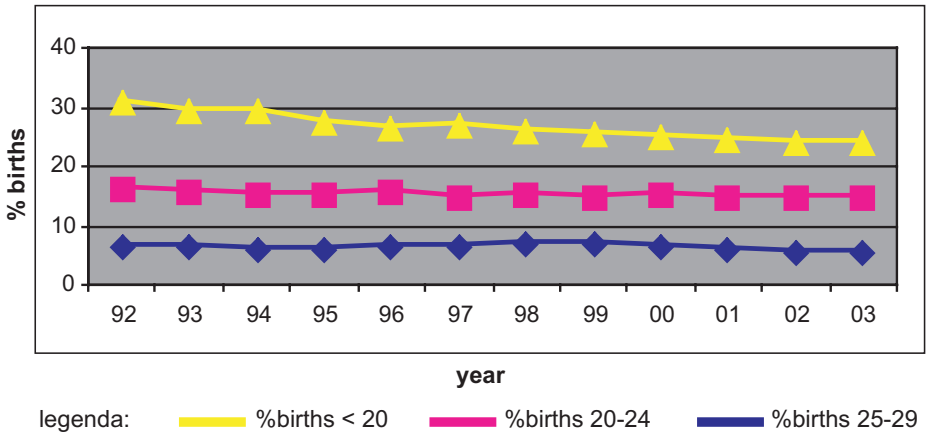
E-mail: virginia.delaney@mailf.hse.ie

Ireland: Dublin

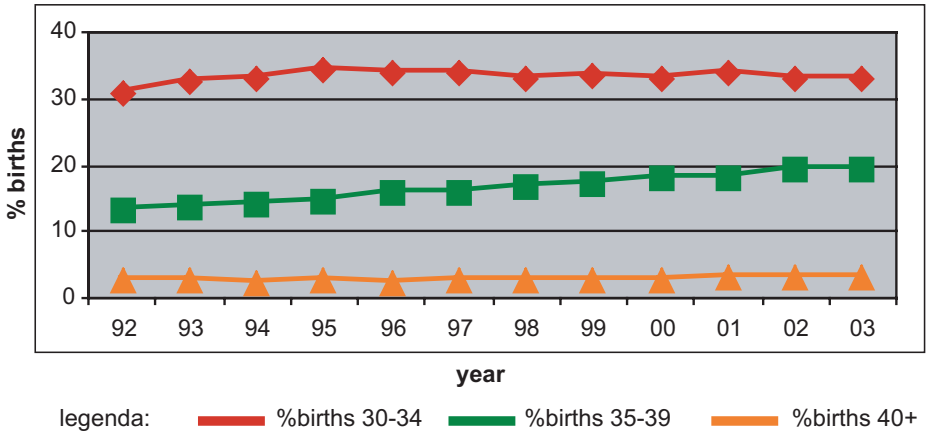
Total births by year



Percentage of births by maternal age



legenda: %births < 20 %births 20-24 %births 25-29



legenda: %births 30-34 %births 35-39 %births 40+

Ireland: Dublin, 2003

Live births (LB)	23500*
Stillbirths (SB)	130*
Total births	23630*
Number of terminations of pregnancy (ToP) for birth defects	not permitted

Birth Defects	Number of cases			Rates*10.000
	LB	SB	ToP	Total rate
Anencephaly	4	1		2.12
Spina bifida	8	0		3.39
Encephalocele	1	0		0.42
Microcephaly	5	0		2.12
Arhinencephaly / Holoprosencephaly	1	1		0.85
Hydrocephaly	1	1		0.85
Anophthalmos	nr	nr		nr
Microphthalmos	nr	nr		nr
Unspecified Anophthalmos / Microphthalmos	nr	nr		---
Anotia	nr	nr		nr
Microtia	nr	nr		nr
Unspecified Anotia / Microtia	nr	nr		---
Transposition of great vessels	9	0		3.81
Tetralogy of Fallot	3	0		1.27
Hypoplastic left heart syndrome	6	0		2.54
Coarctation of aorta	22	1		9.73
Choanal atresia, bilateral	1	0		0.42
Cleft palate without cleft lip	17	0		7.19
Cleft lip with or without cleft palate	10	1		4.66
Oesophageal atresia / stenosis with or without fistula	4	2		2.54
Small intestine atresia / stenosis	6	0		2.54
Anorectal atresia / stenosis	5	0		2.12
Undescended testis (36 weeks of gestation or later)	nr	nr		nr
Hypospadias	23	0		9.73
Epispadias	nr	nr		nr
Indeterminate sex	1	0		0.42
Renal agenesis	8	0		3.39
Cystic kidney	4	1		2.12
Bladder exstrophy	nr	nr		nr
Polydactyly, preaxial	17	0		7.19
Total Limb reduction defects (include unspecified)	8	1		3.81
Transverse	nr	nr		nr
Preaxial	nr	nr		nr
Postaxial	nr	nr		nr
Intercalary	nr	nr		nr
Mixed	nr	nr		nr
Unspecified	nr	nr		---
Diaphragmatic hernia	6	0		2.54
Omphalocele	7	3		4.23
Gastroschisis	5	0		2.12
Unspecified Omphalocele / Gastroschisis	0	0		---
Prune belly sequence	nr	nr		nr
Trisomy 13	2	2		1.69
Trisomy 18	7	4		4.66
Down syndrome, all ages (include age unknown)	35	2		15.66
<20	1	0		7.88
20-24	1	0		2.87
25-29	3	0		5.31
30-34	9	1		12.91
35-39	15	1		35.04
40-44	6	0		80.86
45+	0	0		0.00
unspecified	0	0		---

* = estimated
nr = not reported

Ireland: Dublin, Previous years rates 1980 - 2003

Birth prevalence rates: (LB+SB) * 10,000

	1974-78	1979-83*	1984-88	1989-93	1994-98	1999-03
Births		**99,297**	**105,916**	**94,974**	**96,865**	**110,162**
Anencephaly		16.11	9.25	5.90	3.30	3.27
Spina bifida		13.49	13.31	6.63	5.06	4.72
Encephalocele		3.02	1.23	2.53	1.86	0.91
Microcephaly		3.83	3.30	3.16	5.27	3.36
Arhinencephaly / Holoprosencephaly		0.40	0.19	0.53	1.03	1.18
Hydrocephaly		nr	nr	nr	2.49*	1.91
Anophthalmos		0.30	0.09	0.21	0.83	0.15*
Microphthalmos		0.40	1.23	1.16	2.79	1.06*
Unspecified Anophthalmos / Microphthalmos		---	---	---	---	---
Anotia		nr	nr	nr	nr	nr
Microtia		nr	nr	nr	nr	nr
Unspecified Anotia / Microtia		---	---	---	---	---
Transposition of great vessels		nr	nr	nr	5.32*	4.63
Tetralogy of Fallot		2.62	2.83	2.95	3.82	2.45
Hypoplastic left heart syndrome		2.42	1.89	2.42	1.45	2.63
Coarctation of aorta		4.33	6.80	4.84	6.71	6.45
Choanal atresia, bilateral		0.40	0.47	0.84	1.96	1.18
Cleft palate without cleft lip		7.86	6.51	7.27	8.78	7.99
Cleft lip with or without cleft palate		10.17	8.21	8.00	9.19	7.99
Oesophageal atresia / stenosis with or without fistula		3.93	3.40	3.47	3.61	2.36
Small intestine atresia / stenosis		2.42	3.02	2.53	1.96	2.36
Anorectal atresia / stenosis		3.42	3.78	3.05	2.68	2.18
Undescended testis (36 weeks of gestation or later)		nr	nr	nr	nr	0.00*
Hypospadias		14.20	11.90	12.85	16.31	15.07
Epispadias		nr	nr	nr	nr	0.00*
Indeterminate sex		0.20	0.09	0.21	0.52	0.09
Renal agenesis		4.63	4.91	4.74	3.82	3.18
Cystic kidney		2.82	3.12	2.53	5.16	2.54
Bladder exstrophy		nr	nr	nr	0.83*	0.66*
Polydactyly, preaxial		5.64	6.89	5.90	5.68	9.17
Total Limb reduction defects (include unspecified)		4.33	3.21	4.42	4.65	3.90
Transverse		nr	nr	nr	nr	nr
Preaxial		nr	nr	nr	nr	nr
Postaxial		nr	nr	nr	nr	nr
Intercalary		nr	nr	nr	nr	nr
Mixed		nr	nr	nr	nr	nr
Unspecified		---	---	---	---	---
Diaphragmatic hernia		3.12	3.40	5.16	4.34	4.27
Omphalocele		2.42	2.45	1.79	2.89	3.72
Gastroschisis		0.20	0.57	0.74	1.55	2.72
Unspecified Omphalocele / Gastroschisis		0.00	0.00	0.00	0.00	0.00
Prune belly sequence		0.10	0.28	0.32	0.72	0.00*
Trisomy 13		1.21	0.76	1.05	2.17	3.00
Trisomy 18		2.42	1.70	2.95	3.61	4.27
Down syndrome, all ages (include age unknown)		18.23	19.45	19.48	22.51	20.61
<20		nr	nr	21.17*	10.11	4.60
20-24		nr	nr	11.95*	8.20	5.52
25-29		nr	nr	9.78*	9.92	7.06
30-34		nr	nr	13.64*	19.37	15.60
35-39		nr	nr	40.37*	46.77	46.75
40-44		nr	nr	215.52*	151.58	128.69
45+		nr	nr	1282.05*	531.91	306.12
unspecified		---	---	---	---	---

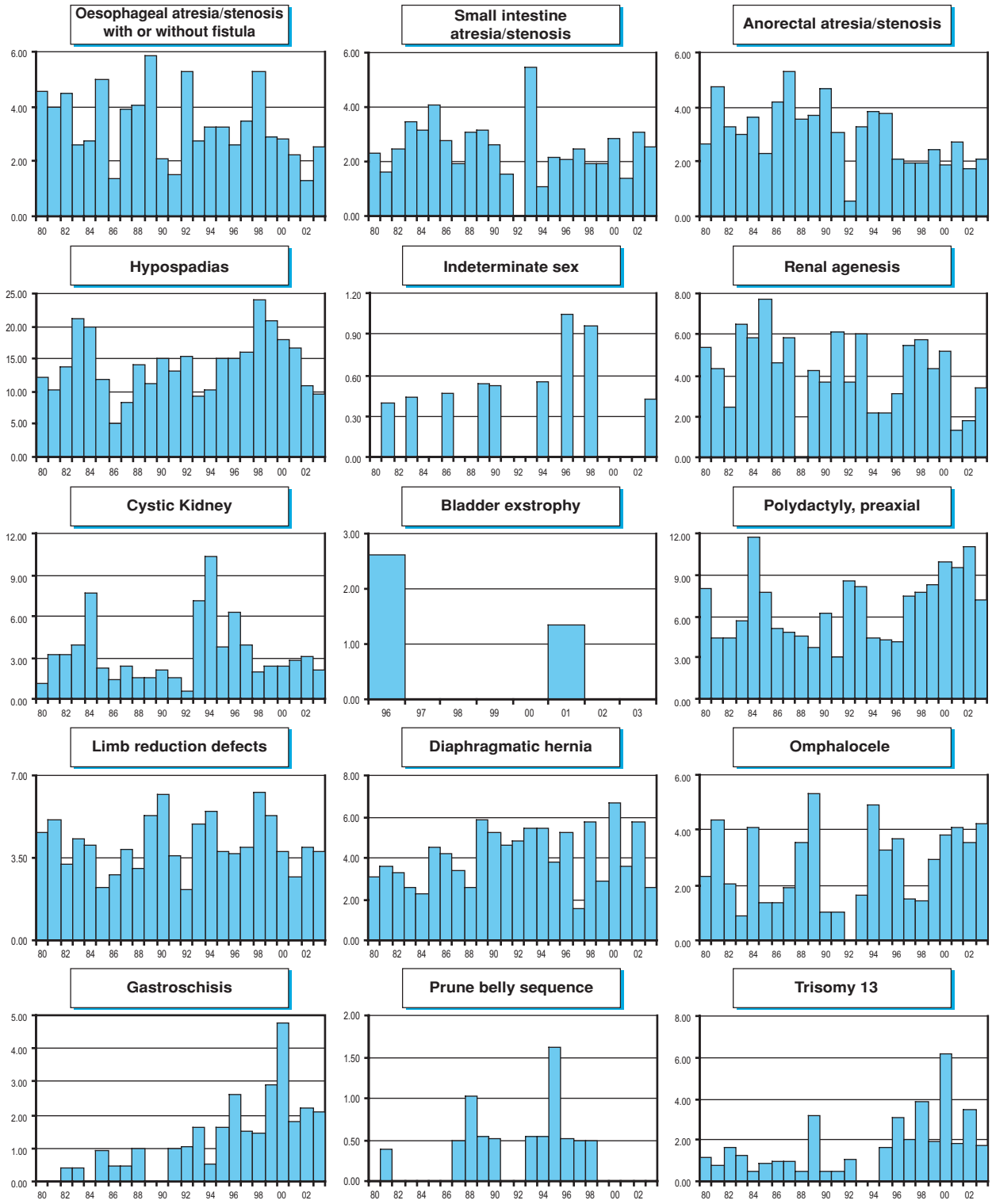
* data include less than 5 years

nr = not reported

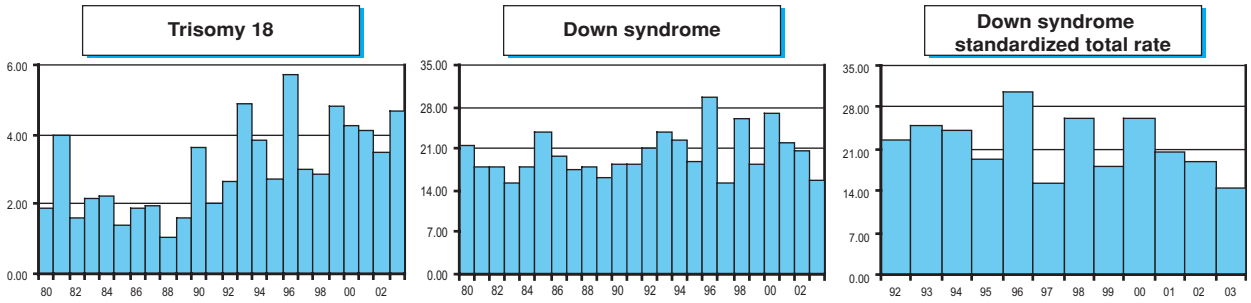
Ireland: Dublin

Time trends 1980-2003 (Birth prevalence rates per 10,000)

Note: L+S rates



Note: L+S rates



Note: L+S rates

Israel: IBDSP

Israel Birth Defects Surveillance Program

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 four hospitals located in the central and south regions of the country, with more than 37.000 annual births (more than 25% of all births in Israel). Stillbirths of 20 weeks gestation or more and 500 gm or more are included. The registry of termination 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 four included hospitals are: Rabin Medical Center, Beilinson Campus, Petah Tikva; Kaplan Hospital, Rehovot (Prof. A. Shinwell); Lis Medical Center, Tel Aviv (Prof. Mimouni, Prof. Dolberg); Soroka Medical Center, Beer-Sheva (Dr. D. Landau, Prof. E. Zmora). The first three hospitals are affiliated with Sackler Faculty of Medicine, Tel Aviv University. The fourth hospital is affiliated with Ben-Gurion University of the Negev, Beer-Sheva.

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
Prof. Paul Merlob Department of Neonatology Rabin Medical Center Beilinson Campus 49100 Petah Tikva, Israel

Dr. Daniela Landau Department of Neonatology Soroka Medical Center Beer Sheva, Israel

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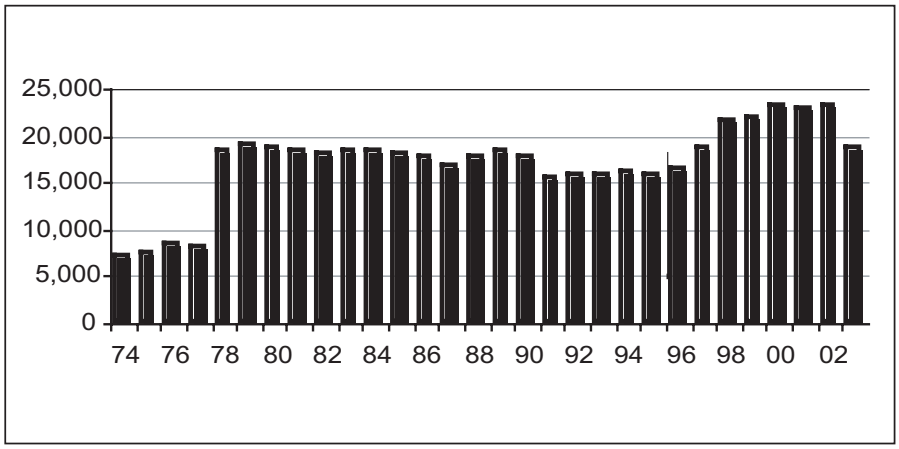
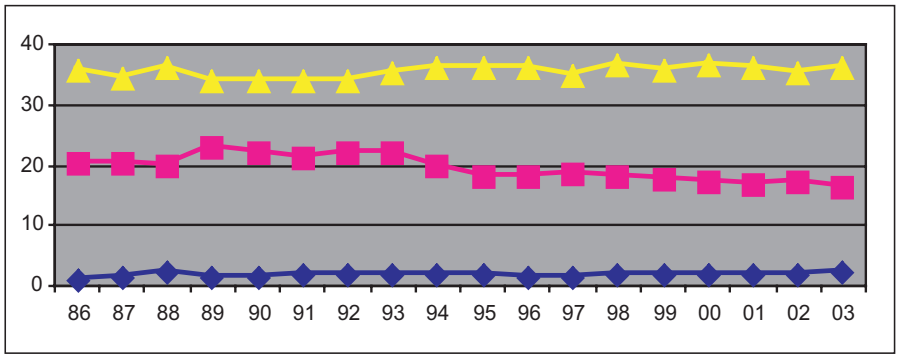
Israel: IBDSP

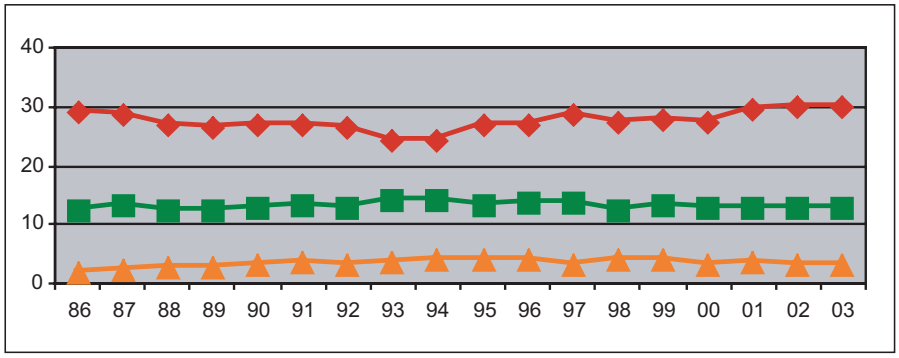
Total births by year



Percentage of births by maternal age



legenda: %births < 20 %births 20-24 %births 25-29



legenda: %births 30-34 %births 35-39 %births 40+

Israel: IBDSP, 2003

Live births (LB)	18449
Stillbirths (SB)	154
Total births	18603
Number of terminations of pregnancy (ToP) for birth defects	28

Birth Defects	Number of cases			Rates*10.000
	LB	SB	ToP	Total rate
Anencephaly	1	0	0	0.54
Spina bifida	2	0	0	1.07
Encephalocele	0	0	0	0.00
Microcephaly	12	0	0	6.44
Arhinencephaly / Holoprosencephaly	0	0	0	0.00
Hydrocephaly	8	0	5	6.98
Anophthalmos	0	0	0	0.00
Microphthalmos	1	0	0	0.54
Unspecified Anophthalmos / Microphthalmos	0	0	0	---
Anotia	0	0	0	0.00
Microtia	3	0	0	1.61
Unspecified Anotia / Microtia	0	0	0	---
Transposition of great vessels	11	0	1	6.44
Tetralogy of Fallot	8	0	2	5.37
Hypoplastic left heart syndrome	3	0	1	2.15
Coarctation of aorta	7	0	2	4.83
Choanal atresia, bilateral	0	0	0	0.00
Cleft palate without cleft lip	4	0	0	2.15
Cleft lip with or without cleft palate	9	0	1	5.37
Oesophageal atresia / stenosis with or without fistula	5	0	0	2.68
Small intestine atresia / stenosis	1	0	0	0.54
Anorectal atresia / stenosis	6	0	0	3.22
Undescended testis (36 weeks of gestation or later)	nr	nr	nr	nr
Hypospadias	74	0	2	40.79
Epispadias	2	0	0	1.07
Indeterminate sex	nr	nr	nr	nr
Renal agenesis	2	0	0	1.07
Cystic kidney*	6	0	0	3.22
Bladder exstrophy	1	0	0	0.54
Polydactyly, preaxial	3	0	0	1.61
Total Limb reduction defects (include unspecified)	5	0	0	2.68
Transverse	2	0	0	1.07
Preaxial	2	0	0	1.07
Postaxial	0	0	0	0.00
Intercalary	0	0	0	0.00
Mixed	1	0	0	0.54
Unspecified	0	0	0	---
Diaphragmatic hernia	2	0	2	2.15
Omphalocele	3	0	0	1.61
Gastroschisis	2	0	0	1.07
Unspecified Omphalocele / Gastroschisis	0	0	0	0.00
Prune belly sequence	0	0	0	0.00
Trisomy 13	0	0	0	0.00
Trisomy 18	7	0	0	3.76
Down syndrome, all ages (include age unknown)	12	0	9	11.27
<20	0	0	0	0.00
20-24	1	0	0	3.34
25-29	3	0	3	8.99
30-34	0	0	3	5.36
35-39	3	0	2	20.90
40-44	5	0	1	111.73
45+	0	0	0	0.00
unspecified	0	0	0	---

*= all multicystic
nr = not reported

Israel: IBDSP, Previous years rates 1974 - 2003

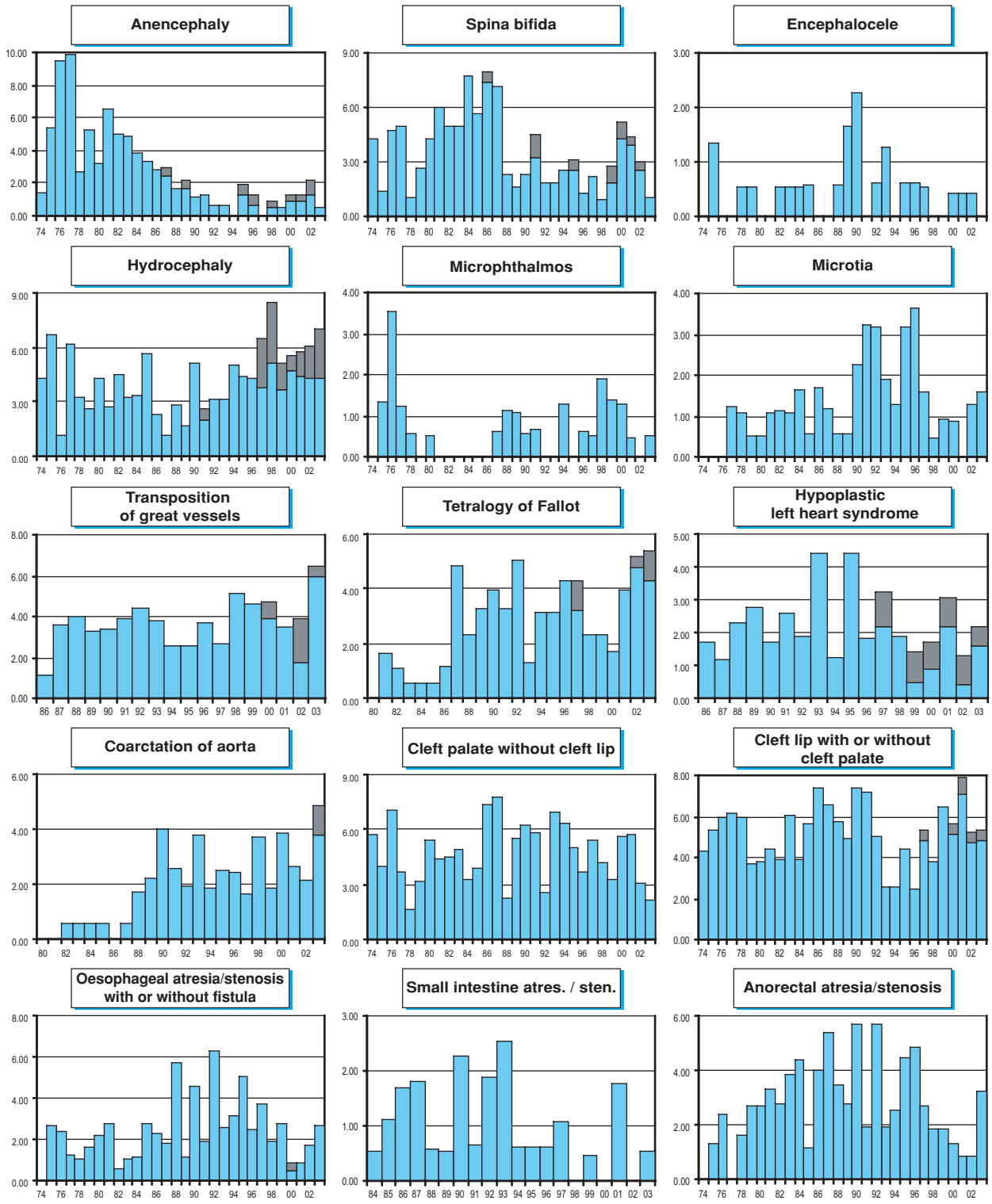
Birth prevalence rates: (LB+SB) * 10,000 until 1985
Birth prevalence rates: (LB+SB+TOP) * 10,000 since 1986

	1974-78	1979-83	1984-88	1989-93	1994-98	1999-03
Births	**49,485**	**91,919**	**87,670**	**82,748**	**88,101**	**109,335**
Anencephaly	5.25	5.00	2.97	1.21	0.79	1.19
Spina bifida	2.83	4.57	6.16	2.42	1.93	3.38
Encephalocele	0.40	0.33	0.34	1.21	0.34	0.27
Microcephaly	nr	nr	nr	nr	nr	2.84
Arhinencephaly / Holoprosencephaly	nr	nr	0.23	0.48	0.00	0.00
Hydrocephaly	4.04	3.48	3.08	3.14	5.90	5.85
Anophthalmos	0.00	0.00	0.00	0.00	0.00	0.18
Microphthalmos	1.21	0.11	0.34	0.48	0.91	0.73
Unspecified Anophthalmos / Microphthalmos	---	---	---	---	---	---
Anotia	0.00	0.00	0.00	0.00	0.11	0.00
Microtia	0.61	0.87	1.14	2.18	1.93	0.91
Unspecified Anotia / Microtia	---	---	---	---	---	---
Transposition of great vessels	nr	nr	2.90*	3.75	3.41	4.57
Tetralogy of Fallot	nr	0.82*	1.83	3.38	3.41	3.66
Hypoplastic left heart syndrome	nr	nr	1.74*	2.66	2.50	1.92
Coarctation of aorta	nr	0.27*	0.68	2.90	2.50	3.02
Choanal atresia, bilateral	nr	nr	0.34	0.24	0.11	0.18
Cleft palate without cleft lip	3.84	4.46	4.90	5.44	4.88	4.02
Cleft lip with or without cleft palate	5.66	4.35	5.82	5.44	3.75	6.13
Oesophageal atresia / stenosis with or without fistula	1.41	1.63	2.74	3.26	3.18	1.74
Small intestine atresia / stenosis	nr	nr	1.14	1.57	0.57	0.55
Anorectal atresia / stenosis	1.21	3.05	3.65	3.63	3.18	1.55
Undescended testis (36 weeks of gestation or later)	nr	nr	nr	nr	nr	nr
Hypospadias	31.73	26.87	28.29	42.42	33.94	40.33
Epispadias	0.20	0.00	0.11	0.24	0.00	0.46
Indeterminate sex	nr	nr	nr	nr	nr	0.00*
Renal agenesis	nr	nr	0.97*	0.73	0.57	0.37
Cystic kidney	0.81	0.54	1.14	1.21	1.14	2.47
Bladder exstrophy	0.20	0.22	0.57	0.48	0.23	0.27
Polydactyly, preaxial	0.20	0.65	0.34	0.36	1.14	1.01
Total Limb reduction defects (include unspecified)	3.84	2.61	3.08	3.14	2.04	1.37
Transverse	nr	0.28*	1.03	1.81	0.68	0.55
Preaxial	nr	0.55*	0.80	0.12	0.79	0.46
Postaxial	nr	0.83*	0.11	0.36	0.34	0.09
Intercalary	nr	0.00*	0.57	0.24	0.00	0.18
Mixed	nr	0.55*	0.57	0.60	0.23	0.09
Unspecified	---	---	---	---	---	---
Diaphragmatic hernia	2.18*	2.39	2.05	3.02	1.59	1.65
Omphalocele	1.82	2.28	1.37	1.09	0.45	0.91
Gastroschisis	0.00*	0.22	0.80	0.00	0.11	0.46
Unspecified Omphalocele / Gastroschisis	---	---	---	---	---	---
Prune belly sequence	0.40	0.33	0.00	0.12	0.11	0.09
Trisomy 13	nr	nr	0.34	0.60	0.45	0.37
Trisomy 18	nr	nr	0.57	0.60	0.91	1.74
Down syndrome, all ages (include age unknown)	11.72	9.25	12.78	8.58	7.04	10.52
<20	nr	nr	nr	0.00*	0.00	4.99
20-24	nr	nr	nr	0.00*	1.84	2.69
25-29	nr	nr	nr	2.48*	4.12	6.36
30-34	nr	nr	nr	7.42*	5.90	8.23
35-39	nr	nr	nr	19.16*	12.75	21.97
40-44	nr	nr	nr	41.67*	46.24	70.79
45+	nr	nr	nr	90.91*	82.64	133.33
unspecified	---	---	---	---	---	---

* data include less than 5 years
nr= not reported

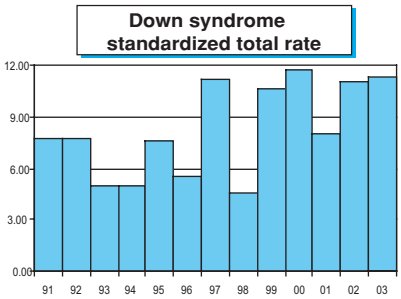
Israel: IBDSP

'Time trends 1974-2003 (Birth prevalence rates per 10,000)



Note: L+S rates, ToP rates

Note: L+S rates, ToP rates



Note: L+S rates, ToP rates

Italy: BDRCam
Birth Defects Registry of Campania

History:
The Registry started in 1991 and 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 60.000 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 each source: pediatric cardiologist, pediatric surgeon, ultrasonographyst, pathologist, cytogeneticist and son.

Exposure information
For each malformed infant reported, informations are given on maternal illness before and during pregnancy, and certain exposures, including maternal drug usage and habitual exposures as smoke and alcool and son. Beginning from 2002 the same informations are available but only partially on induced abortions.

Background information
Background informations are given on maternal place, parental age, occupation, and educational. Beginning from 2002 the same informations are available on controls.

Addresses and staff

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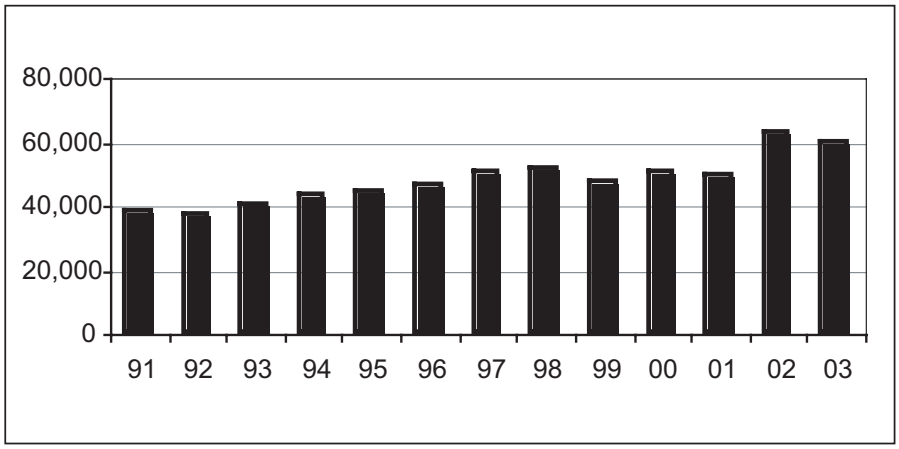
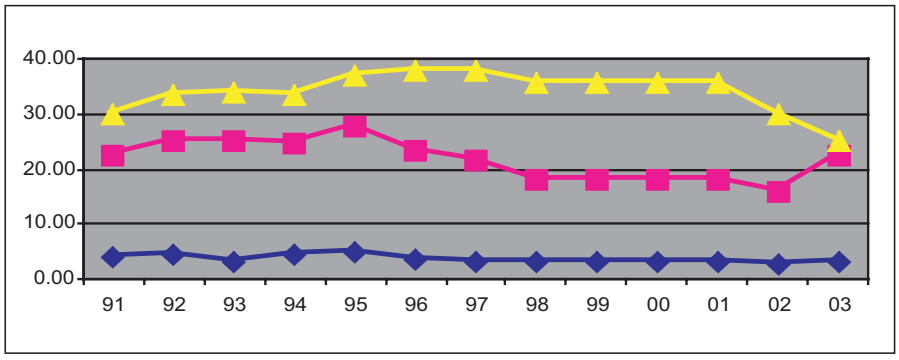
Italy: BDRCam

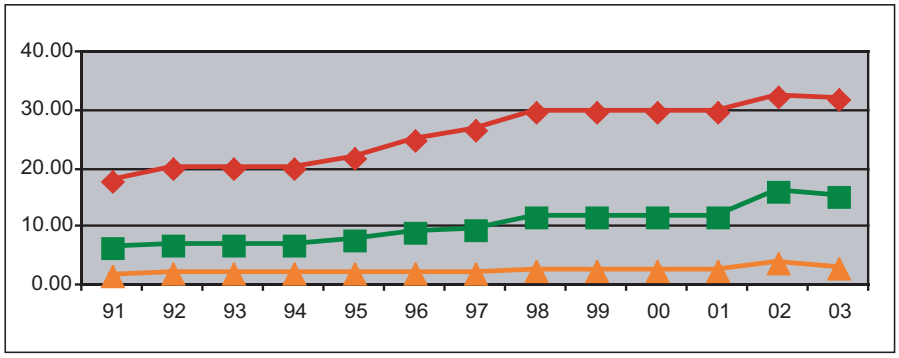
Total births by year



Percentage of births by maternal age



legenda: %births < 20 %births 20-24 %births 25-29



legenda: %births 30-34 %births 35-39 %births 40+

Italy: BDRCAM, 2003

Live births (LB)	59739
Stillbirths (SB)	139
Total births	59878
Number of terminations of pregnancy (ToP) for birth defects	241

Birth Defects	Number of cases			Rates*10.000
	LB	SB	ToP	Total rate
Anencephaly	3	0	20	3.83
Spina bifida	4	0	14	2.99
Encephalocele	0	0	5	0.83
Microcephaly	2	0	1	0.50
Arhinencephaly / Holoprosencephaly	2	0	3	0.83
Hydrocephaly	2	0	31	5.49
Anophthalmos	0	0	1	0.17
Microphthalmos	1	0	6	1.16
Unspecified Anophthalmos / Microphthalmos	0	0	0	---
Anotia	3	0	0	0.50
Microtia	0	0	1	0.17
Unspecified Anotia / Microtia	0	0	0	---
Transposition of great vessels	4	0	4	1.33
Tetralogy of Fallot	12	0	4	2.66
Hypoplastic left heart syndrome	2	0	11	2.16
Coarctation of aorta	5	0	3	1.33
Choanal atresia, bilateral	1	0	0	0.17
Cleft palate without cleft lip	17	0	3	3.33
Cleft lip with or without cleft palate	22	0	8	4.99
Oesophageal atresia / stenosis with or without fistula	9	0	3	2.00
Small intestine atresia / stenosis	5	0	2	1.16
Anorectal atresia / stenosis	6	0	3	1.50
Undescended testis (36 weeks of gestation or later)	nr	nr	nr	nr
Hypospadias*	29	0	0	4.82
Epispadias	0	0	0	0.00
Indeterminate sex	5	0	3	1.33
Renal agenesis	18	0	7	4.16
Cystic kidney	8	0	3	1.83
Bladder exstrophy	0	0	0	0.00
Polydactyly, preaxial	12	0	3	2.50
Total Limb reduction defects (include unspecified)	15	0	7	3.66
Transverse	13	0	1	2.33
Preaxial	1	0	1	0.33
Postaxial	1	0	3	0.67
Intercalary	0	0	2	0.33
Mixed	0	0	0	0.00
Unspecified	0	0	0	---
Diaphragmatic hernia	10	0	3	2.16
Omphalocele	4	0	14	2.99
Gastroschisis	0	0	6	1.00
Unspecified Omphalocele / Gastroschisis	1	0	0	---
Prune belly sequence	0	0	0	0.00
Trisomy 13	0	1	2	0.50
Trisomy 18	3	0	8	1.83
Down syndrome, all ages (include age unknown)	31	0	50	13.47
<20	1	0	0	5.22
20-24	0	0	2	1.49
25-29	5	0	2	4.66
30-34	5	0	6	5.79
35-39	11	0	25	40.51
40-44	2	0	10	76.58
45+	2	0	3	406.50
unspecified	5	0	2	---

* excluded glandular hypospadias
nr = not reported

Italy: BDRCAM, Previous years rates 1991 - 2003

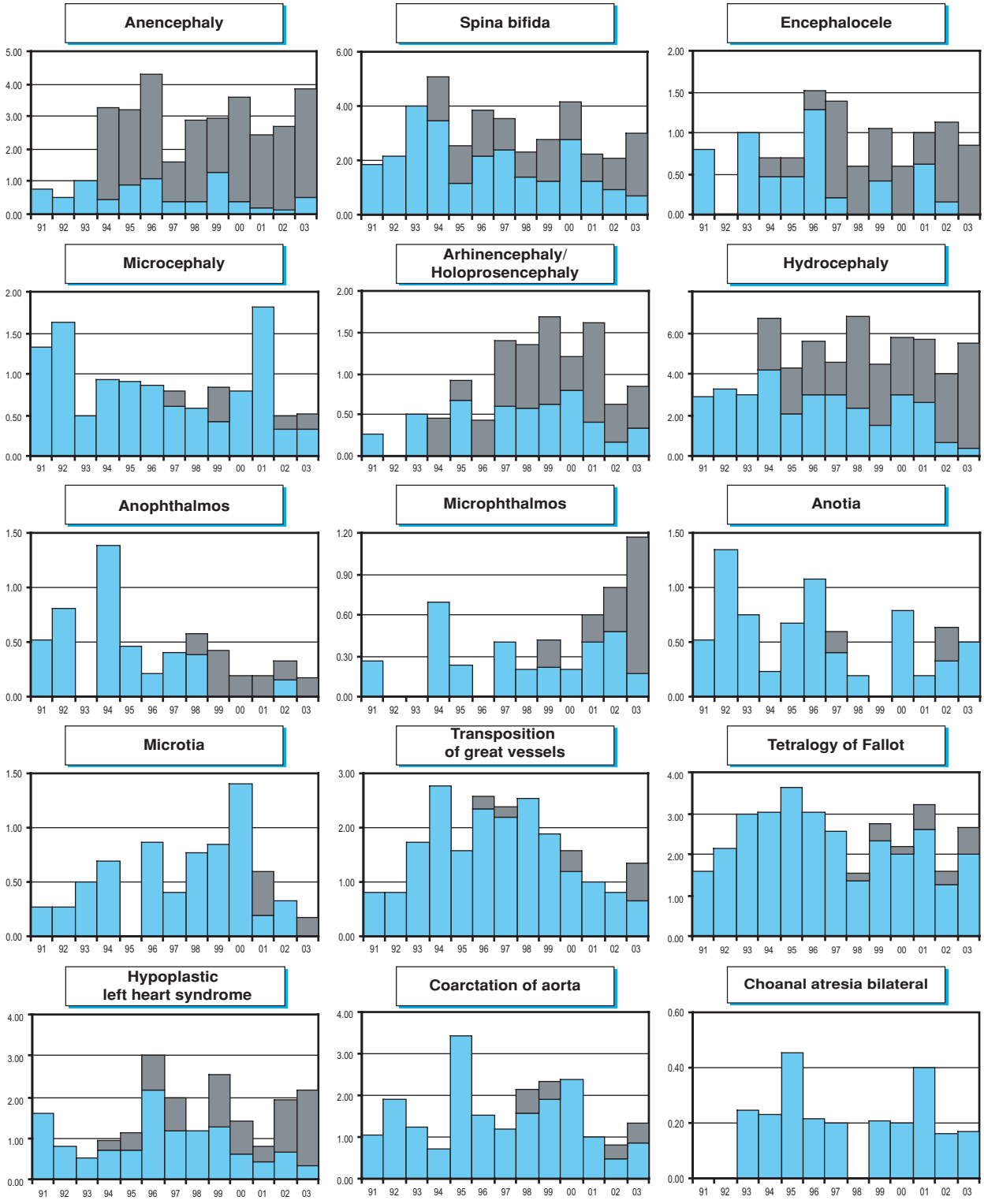
Birth prevalence rates: (LB+SB) * 10,000 until 1993
Birth prevalence rates: (LB+SB+TOP) * 10,000 since 1994

	1974-78	1979-83	1984-88	1989-93*	1994-98	1999-03
Births				**115,294**	**235,872**	**269,868**
Anencephaly				0.78	3.01	3.11
Spina bifida				2.69	3.43	2.82
Encephalocele				0.61	0.98	0.93
Microcephaly				1.13	0.81	0.85
Arhinencephaly / Holoprosencephaly				0.26	0.93	1.15
Hydrocephaly				3.04	5.60	5.04
Anophthalmos				0.43	0.59	0.26
Microphthalmos				0.09	0.30	0.67
Unspecified Anophthalmos / Microphthalmos				---	---	---
Anotia				0.87	0.55	0.44
Microtia				0.35	0.55	0.63
Unspecified Anotia / Microtia				---	---	---
Transposition of great vessels				1.13	2.37	1.30
Tetralogy of Fallot				2.26	2.71	2.45
Hypoplastic left heart syndrome				0.95	1.65	1.78
Coarctation of aorta				1.39	1.78	1.52
Choanal atresia, bilateral				0.09	0.21	0.22
Cleft palate without cleft lip				4.42	4.45	4.48
Cleft lip with or without cleft palate				5.72	7.42	6.00
Oesophageal atresia / stenosis with or without fistula				2.26	2.12	1.93
Small intestine atresia / stenosis				2.17	1.99	1.63
Anorectal atresia / stenosis				2.60	3.26	2.67
Undescended testis (36 weeks of gestation or later)				nr	nr	nr
Hypospadias				3.21	3.18	5.41
Epispadias				0.17	0.30	0.11
Indeterminate sex				0.26	0.59	0.85
Renal agenesis				1.04	3.05	3.89
Cystic kidney				1.39	2.71	2.04
Bladder exstrophy				0.17	0.30	0.07
Polydactyly, preaxial				1.73	1.87	1.52
Total Limb reduction defects (include unspecified)				5.29	5.05	4.52
Transverse				3.90	2.67	2.78
Preaxial				0.69	0.76	0.85
Postaxial				0.17	0.55	0.41
Intercalary				0.26	0.51	0.37
Mixed				0.26	0.13	0.04
Unspecified				---	---	---
Diaphragmatic hernia				1.30	2.37	2.63
Omphalocele				1.13	1.99	2.04
Gastroschisis				0.17	0.68	0.67
Unspecified Omphalocele / Gastroschisis				---	---	---
Prune belly sequence				0.00	0.13*	0.06*
Trisomy 13				0.78	0.68	0.67
Trisomy 18				0.35	1.87	1.67
Down syndrome, all ages (include age unknown)				12.14	13.35	12.27
<20				6.89	3.37	3.63
20-24				6.46	5.20	2.21
25-29				9.11	5.14	5.80
30-34				12.29	12.39	6.64
35-39				37.23	33.91	27.61
40-44				50.51	145.75	92.47
45+				256.41	198.02	206.19
unspecified				---	---	---

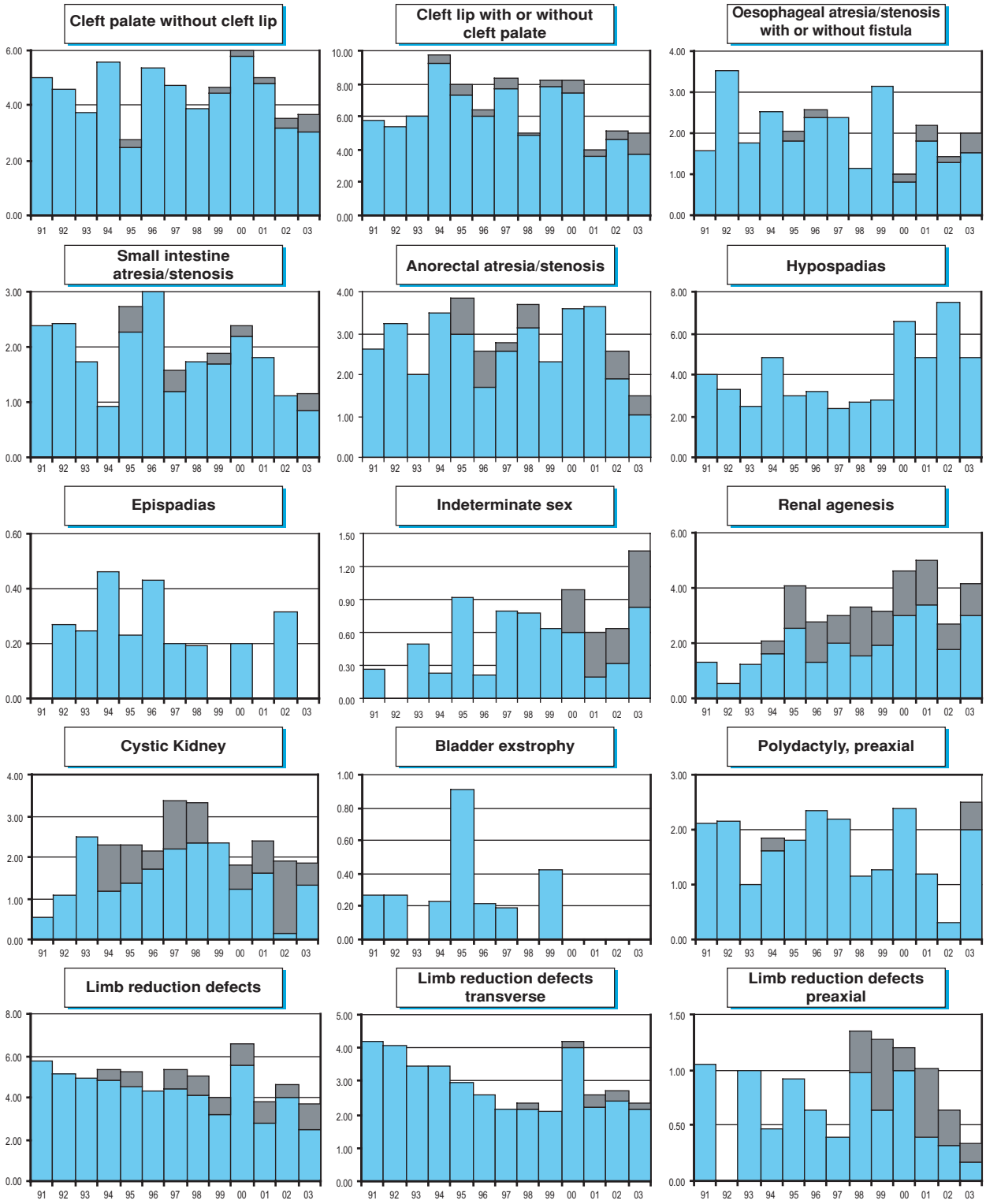
* data include less than 5 years
nr = not reported

Italy: BDRCam

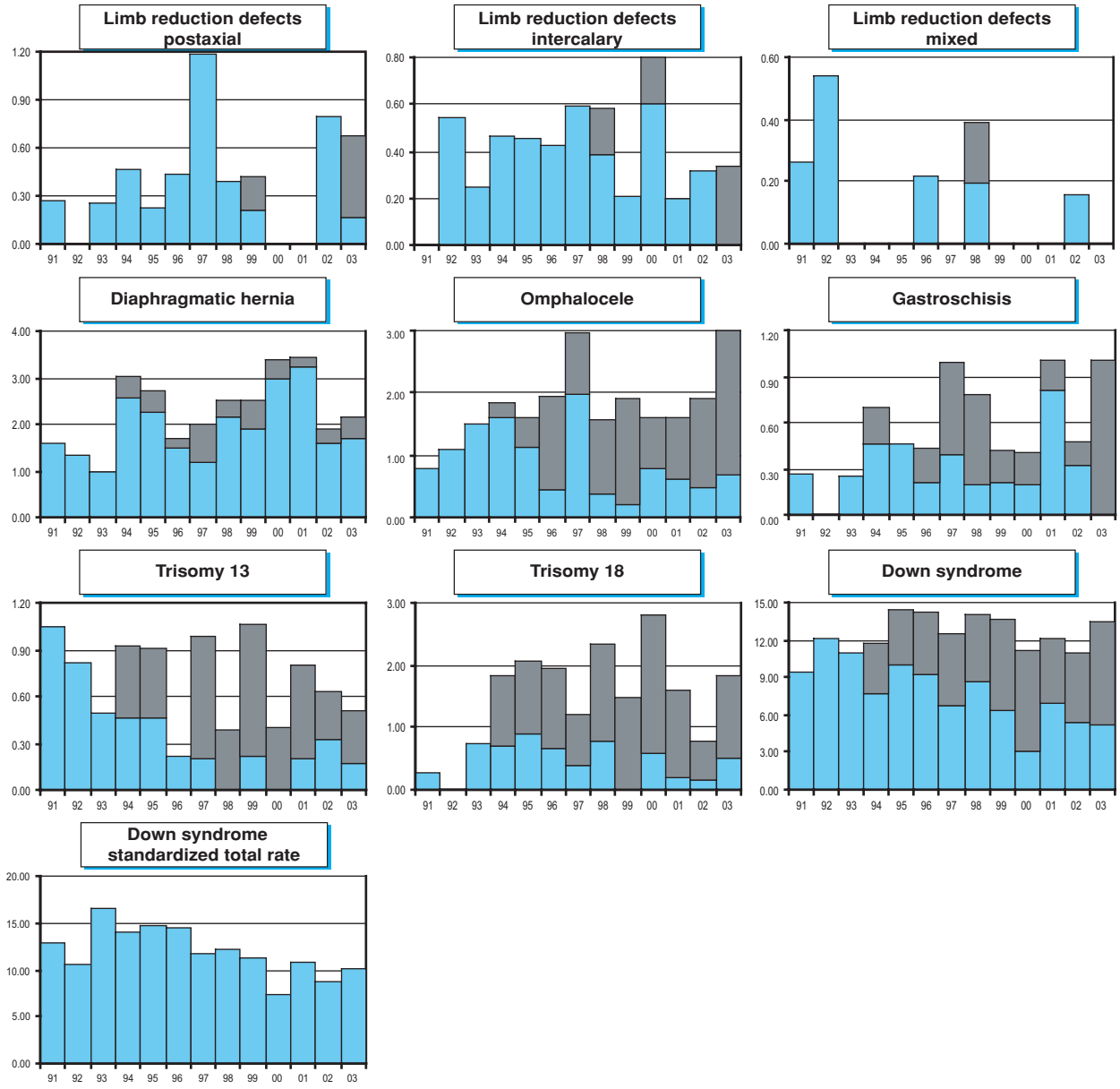
'Time trends 1991-2003 (Birth prevalence rates per 10,000)



Note: L+S rates, ToP rates



Note: L+S rates, ToP rates



Note: L+S rates, ToP rates

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.

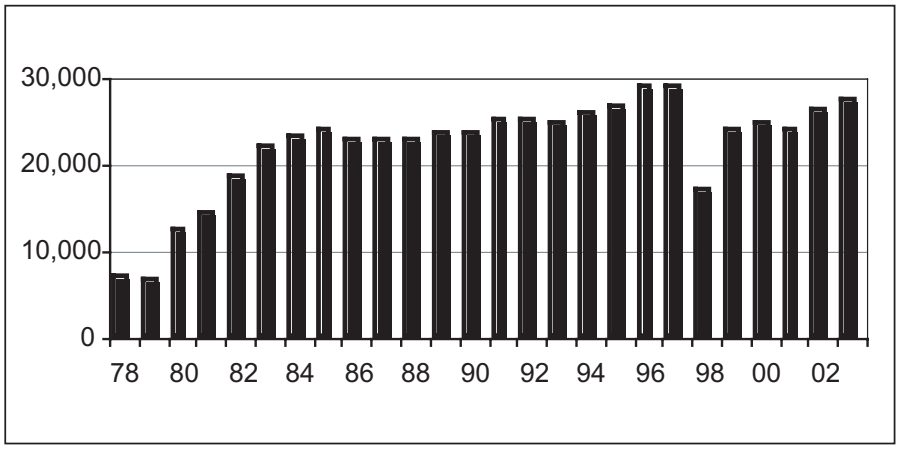
Phone: 39-051-342754 / 6363654

Fax: 39-051-342754

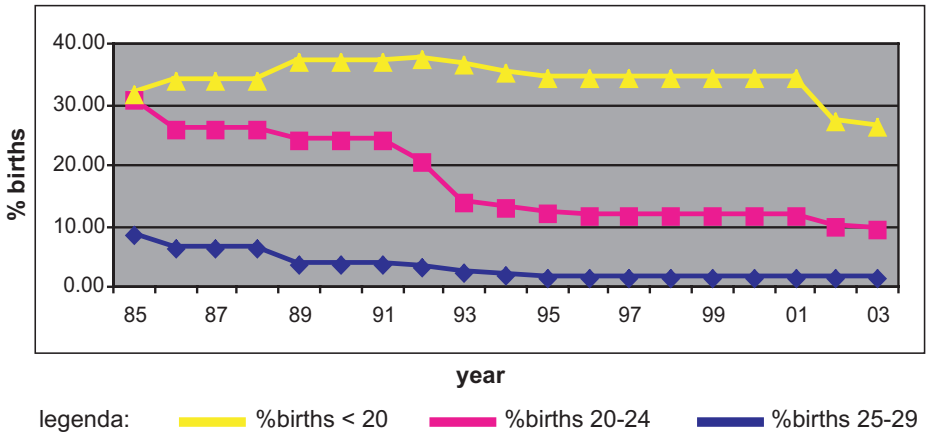
E-mail: cocchi@med.unibo.it

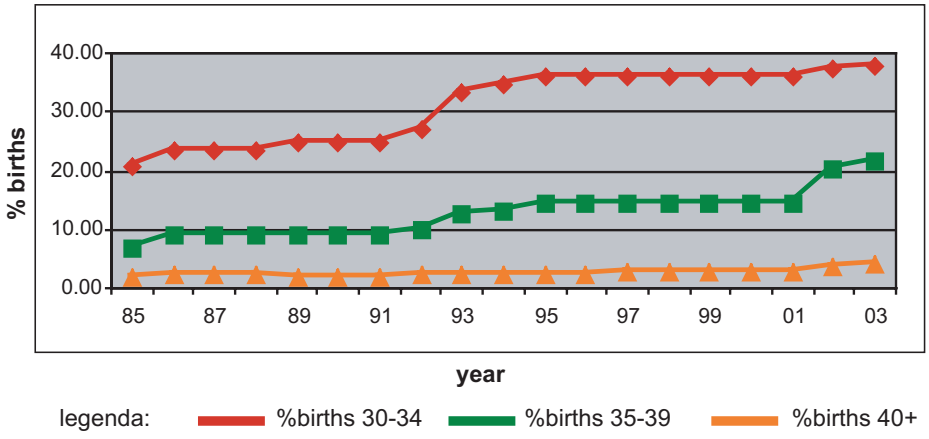
Italy: IMER

Total births by year



Percentage of births by maternal age





Italy: IMER, 2003

Live births (LB)	27324
Stillbirths (SB)	88
Total births	27412
Number of terminations of pregnancy (ToP) for birth defects	162

Birth Defects	Number of cases			Rates*10.000
	LB	SB	ToP	Total rate
Anencephaly	1	0	7	2.90
Spina bifida	3	0	10	4.71
Encephalocele	0	0	1	0.36
Microcephaly	2	0	2	1.45
Arhinencephaly / Holoprosencephaly	1	0	2	1.09
Hydrocephaly	9	1	12	7.98
Anophthalmos	1	0	1	0.73
Microphthalmos	1	0	1	0.73
Unspecified Anophthalmos / Microphthalmos	0	0	0	---
Anotia	3	0	0	1.09
Microtia	4	0	0	1.45
Unspecified Anotia / Microtia	0	0	0	---
Transposition of great vessels	12	0	3	5.44
Tetralogy of Fallot	9	0	0	3.26
Hypoplastic left heart syndrome	5	0	0	1.81
Coarctation of aorta	7	0	0	2.54
Choanal atresia, bilateral	1	0	1	0.73
Cleft palate without cleft lip	12	0	0	4.35
Cleft lip with or without cleft palate	16	0	2	6.53
Oesophageal atresia / stenosis with or without fistula	10	0	2	4.35
Small intestine atresia / stenosis	5	0	1	2.18
Anorectal atresia / stenosis	8	1	1	3.63
Undescended testis (36 weeks of gestation or later)	nr	nr	nr	nr
Hypospadias	53	0	0	19.22
Epispadias	0	0	0	0.00
Indeterminate sex	1	0	0	0.36
Renal agenesis	6	0	4	3.63
Cystic kidney	9	0	3	4.35
Bladder exstrophy	0	0	0	0.00
Polydactyly, preaxial	5	0	0	1.81
Total Limb reduction defects (include unspecified)	10	0	4	5.08
Transverse	4	0	nr	1.46
Preaxial	1	0	nr	0.36
Postaxial	4	0	nr	1.46
Intercalary	1	0	nr	0.36
Mixed	0	0	nr	0.00
Unspecified	0	0	nr	---
Diaphragmatic hernia	6	0	1	2.54
Omphalocele	4	1	9	5.08
Gastroschisis	1	0	2	1.09
Unspecified Omphalocele / Gastroschisis	0	0	0	---
Prune belly sequence	0	0	1	0.36
Trisomy 13	1	0	6	2.54
Trisomy 18	5	0	12	6.17
Down syndrome, all ages (include age unknown)*	22	0	32	19.58
<20	0	0	0	0.00
20-24	3	0	0	11.93
25-29	2	0	1	4.17
30-34	3	0	6	8.72
35-39	10	0	15	42.41
40-44	4	0	10	127.16
45+	0	0	0	0.00
unspecified	0	0	0	---

*= excluding ToP in women not residening in Emilia-Romagna
nr= not reported

Italy: IMER, Previous years rates 1978 - 2003

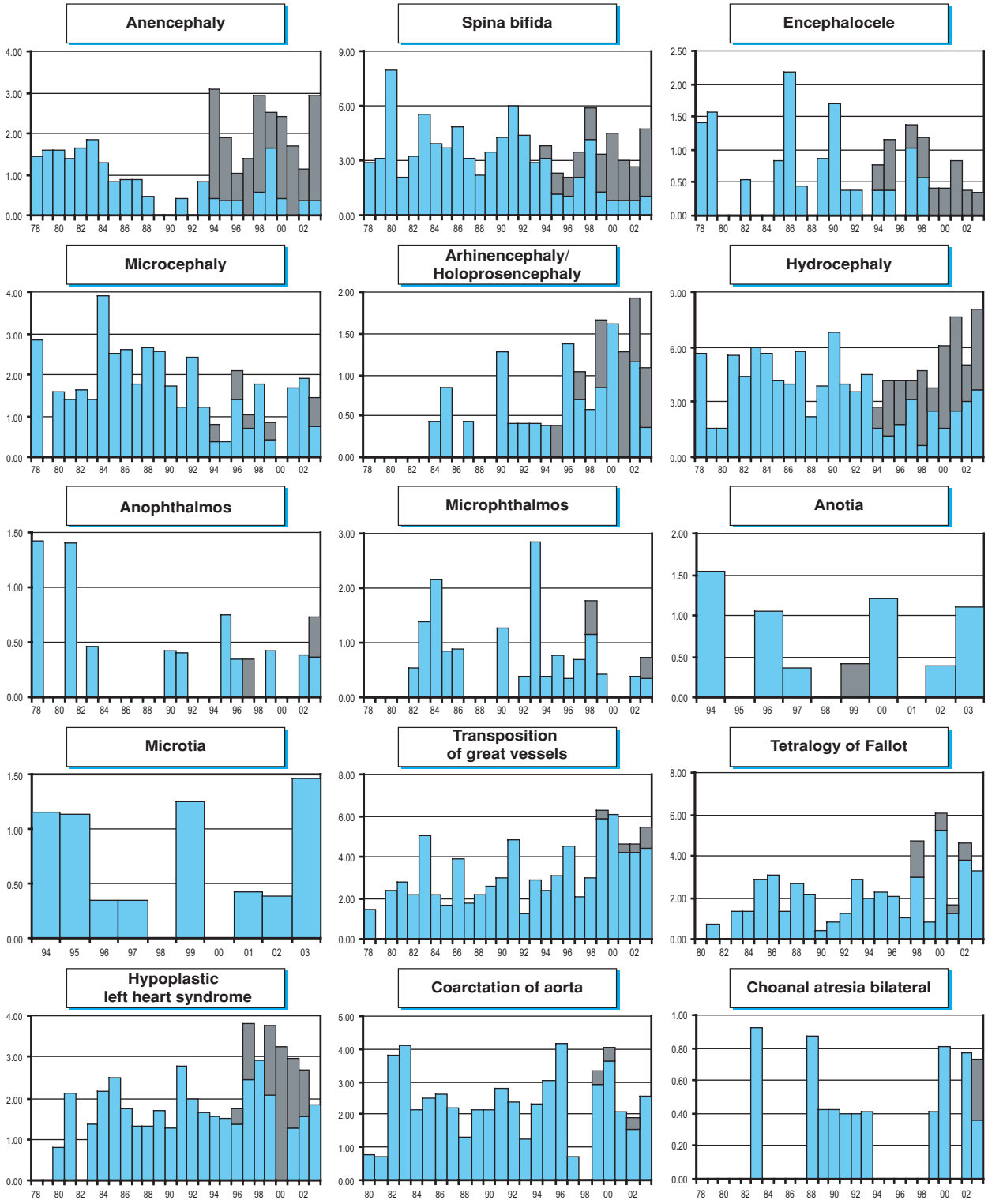
Birth prevalence rates: (LB+SB) * 10,000 until 1993
Birth prevalence rates: (LB+SB+TOP) * 10,000 since 1994

	1974-78*	1979-83	1984-88	1989-93	1994-98	1999-03
Births	**7,042**	**73,287**	**115,574**	**121,629**	**127,071**	**125,807**
Anencephaly	1.42	1.64	0.87	0.25	1.97	2.15
Spina bifida	2.84	4.50	3.55	4.19	3.31	3.66
Encephalocele	1.42	0.27	0.69	0.66	0.87	0.48
Microcephaly	2.84	1.36	2.68	1.81	1.18	1.19
Arhinencephaly / Holoprosencephaly	0.00	0.00	0.35	0.49	0.79	1.51
Hydrocephaly	5.68	4.37	4.33	4.52	3.93	6.12
Anophthalmos	1.42	0.41	0.00	0.16	0.31	0.32
Microphthalmos	0.00	0.55	0.78	0.90	0.71	0.32
Unspecified Anophthalmos / Microphthalmos	---	---	---	---	---	---
Anotia	nr	nr	nr	nr	0.63	0.64
Microtia	nr	nr	nr	nr	0.63	0.72
Unspecified Anotia / Microtia	---	---	---	---	---	---
Transposition of great vessels	1.42	3.00	2.34	2.88	2.99	5.41
Tetralogy of Fallot	nr	0.60*	2.25	1.48	2.20	3.34
Hypoplastic left heart syndrome	0.00	0.96	1.82	1.89	2.28	2.86
Coarctation of aorta	nr	2.69*	2.16	2.14	2.20	2.78
Choanal atresia, bilateral	0.00	0.27	0.17	0.41	0.00	0.56
Cleft palate without cleft lip	2.84	4.91	5.88	5.92	4.25	4.29
Cleft lip with or without cleft palate	5.68	6.55	7.79	6.25	6.53	5.48
Oesophageal atresia / stenosis with or without fistula	7.10	3.00	3.72	3.95	3.46	3.50
Small intestine atresia / stenosis	0.00	2.18	3.20	3.78	3.23	2.31
Anorectal atresia / stenosis	0.00	3.00	2.86	3.45	2.12	3.42
Undescended testis (36 weeks of gestation or later)	nr	nr	nr	nr	nr	nr
Hypospadias	9.94	19.92	21.11	17.76	16.71*	17.01
Epispadias	nr	nr	nr	nr	0.00*	0.00
Indeterminate sex	nr	nr	nr	nr	0.20*	0.32
Renal agenesis	4.26	1.50	1.21	1.89	2.05	4.05
Cystic kidney	1.42	0.27	1.04	0.16	2.83	3.82
Bladder exstrophy	1.42	0.41	0.78	0.08	0.16	0.24
Polydactyly, preaxial	8.52	9.69	8.13	8.55	3.15	2.54
Total Limb reduction defects (include unspecified)	nr	nr	5.63*	5.59	4.09	4.21
Transverse	nr	nr	3.35*	2.96	1.89	1.75
Preaxial	nr	nr	0.54*	0.90	0.94	0.56
Postaxial	nr	nr	0.76*	0.49	0.24	0.79
Intercalary	nr	nr	0.43*	0.82	0.39	0.64
Mixed	nr	nr	0.22*	0.41	0.24	0.08
Unspecified	---	---	---	---	---	---
Diaphragmatic hernia	0.00	1.23	2.16	2.71	2.68	3.42
Omphalocele	2.84	1.50	1.99	2.06	1.34	2.78
Gastroschisis	0.00	0.82	0.87	1.07	0.47	0.87
Unspecified Omphalocele / Gastroschisis	---	---	---	---	---	---
Prune belly sequence	0.00	0.27	0.52	0.25	0.31	0.32
Trisomy 13	0.00	1.77	0.78	0.66	1.02	1.51
Trisomy 18	1.42	1.09	0.95	0.90	1.81	4.37
Down syndrome, all ages (include age unknown)	21.30	13.51	13.50	12.91	19.52	17.96
<20	nr	nr	1.60*	7.67	5.74	12.19
20-24	nr	nr	5.97*	4.27	8.65	8.25
25-29	nr	nr	11.45*	8.03	8.22	4.87
30-34	nr	nr	11.96*	16.91	12.10	14.08
35-39	nr	nr	37.79*	30.35	44.98	34.13
40-44	nr	nr	75.71*	58.93	188.49	114.24
45+	nr	nr	59.88*	80.65	133.33	220.59
unspecified	---	---	---	---	---	---

* data include less than 5 years
nr = not reported

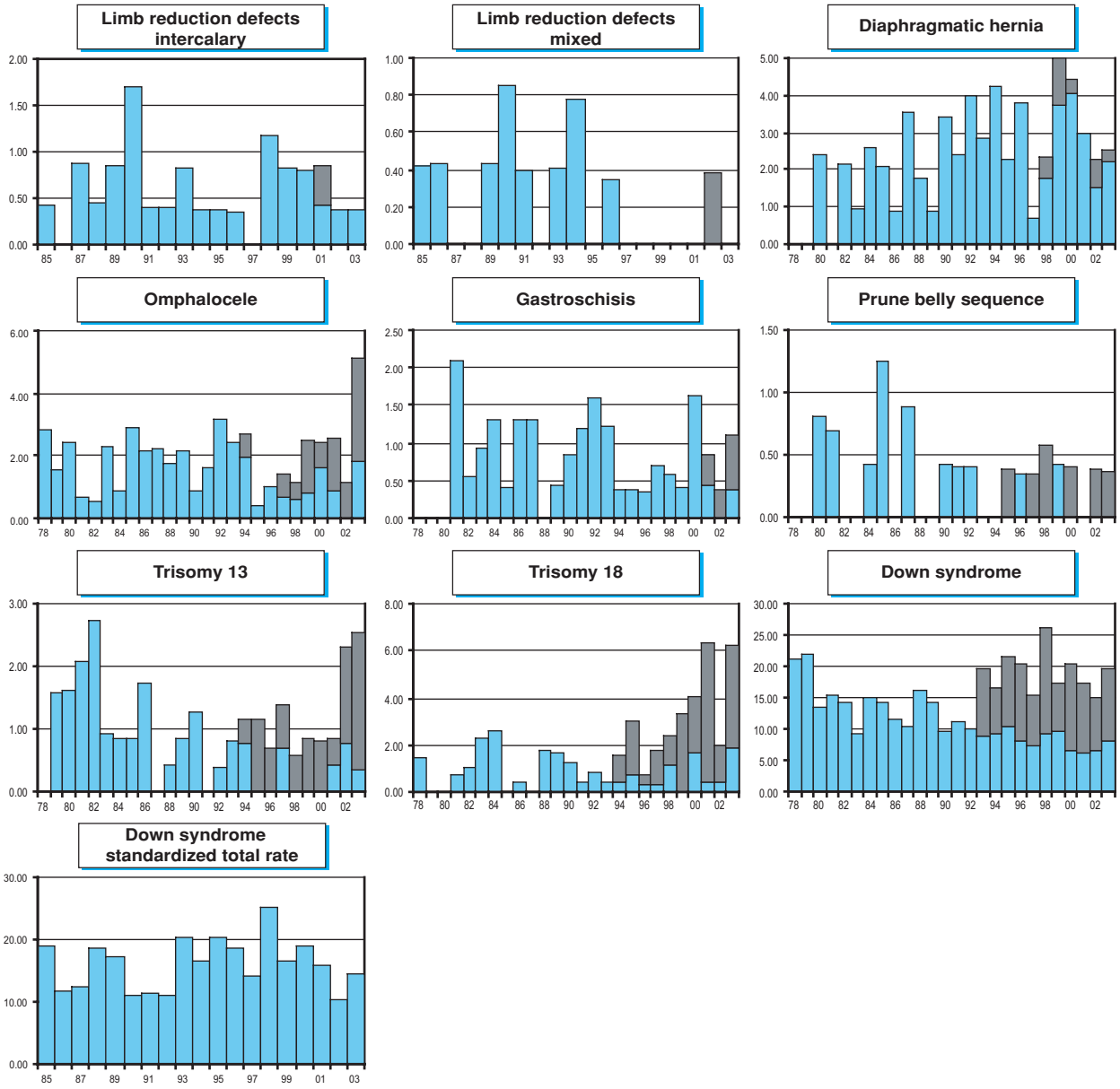
Italy: IMER

Time trends 1978-2003 (Birth prevalence rates per 10,000)



Note: L+S rates, ToP rates

Note: L+S rates, ToP rates



Note: L+S rates, ToP rates

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
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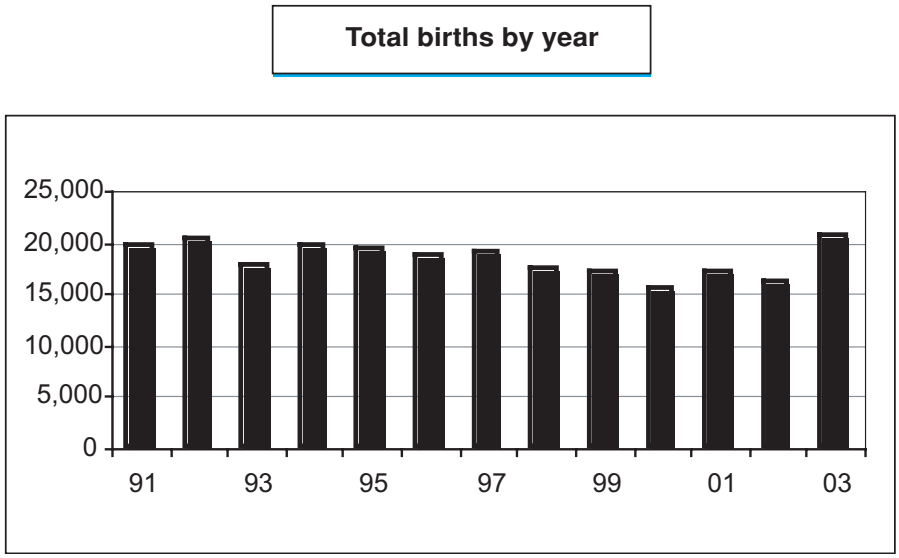
Centro di Consulenza Genetica e di Teratologia della Riproduzione Dipartimento Materno Infantile
ARNAS Garibaldi-Nesima Via Palermo 636
95122 Catania, Italy

Phone: +39/095.7595384

Fax: +39/095.7595140

E-mail: sebastiano.bianca@tiscali.it

Italy: ISMAC


Total births by year
25,000
20,000
15,000
10,000
5,000
0
91
93
95
97
99
01
03

Italy: ISMAC, 2003

Live births (LB)	20450
Stillbirths (SB)	0
Total births	20450
Number of terminations of pregnancy (ToP) for birth defects	nr

Birth Defects	Number of cases			Rates*10.000
	LB	SB	ToP	Total rate
Anencephaly	0	0	nr	0.00
Spina bifida	4	0	nr	1.96
Encephalocele	0	0	nr	0.00
Microcephaly	0	0	nr	0.00
Arhinencephaly / Holoprosencephaly	0	0	nr	0.00
Hydrocephaly	2	0	nr	0.98
Anophthalmos	0	0	nr	0.00
Microphthalmos	1	0	nr	0.49
Unspecified Anophthalmos / Microphthalmos	0	0	nr	---
Anotia	2	0	nr	0.98
Microtia	1	0	nr	0.49
Unspecified Anotia / Microtia	0	0	nr	---
Transposition of great vessels	2	0	nr	0.98
Tetralogy of Fallot	1	0	nr	0.49
Hypoplastic left heart syndrome	0	0	nr	0.00
Coarctation of aorta	2	0	nr	0.98
Choanal atresia, bilateral	2	0	nr	0.98
Cleft palate without cleft lip	8	0	nr	3.91
Cleft lip with or without cleft palate	5	0	nr	2.44
Oesophageal atresia / stenosis with or without fistula	4	0	nr	1.96
Small intestine atresia / stenosis	1	0	nr	0.49
Anorectal atresia / stenosis	0	0	nr	0.00
Undescended testis (36 weeks of gestation or later)	25	0	nr	12.22
Hypospadias	26	0	nr	12.71
Epispadias	0	0	nr	0.00
Indeterminate sex	0	0	nr	0.00
Renal agenesis	2	0	nr	0.98
Cystic kidney	4	0	nr	1.96
Bladder exstrophy	0	0	nr	0.00
Polydactyly, preaxial	4	0	nr	1.96
Total Limb reduction defects (include unspecified)	4	0	nr	1.96
Transverse	4	0	nr	1.96
Preaxial	0	0	nr	0.00
Postaxial	0	0	nr	0.00
Intercalary	0	0	nr	0.00
Mixed	0	0	nr	0.00
Unspecified	0	0	nr	---
Diaphragmatic hernia	2	0	nr	0.98
Omphalocele	0	0	nr	0.00
Gastroschisis	0	0	nr	0.00
Unspecified Omphalocele / Gastroschisis	0	0	nr	---
Prune belly sequence	0	0	nr	0.00
Trisomy 13	1	0	nr	0.49
Trisomy 18	1	0	nr	0.49
Down syndrome, all ages (include age unknown)	14	0	nr	6.85
<20	0	0	nr	nr
20-24	2	0	nr	nr
25-29	2	0	nr	nr
30-34	5	0	nr	nr
35-39	1	0	nr	nr
40-44	3	0	nr	nr
45+	1	0	nr	nr
unspecified	0	0	nr	---

nr = not reported

Italy: ISMAC, Previous years rates 1991 - 2003

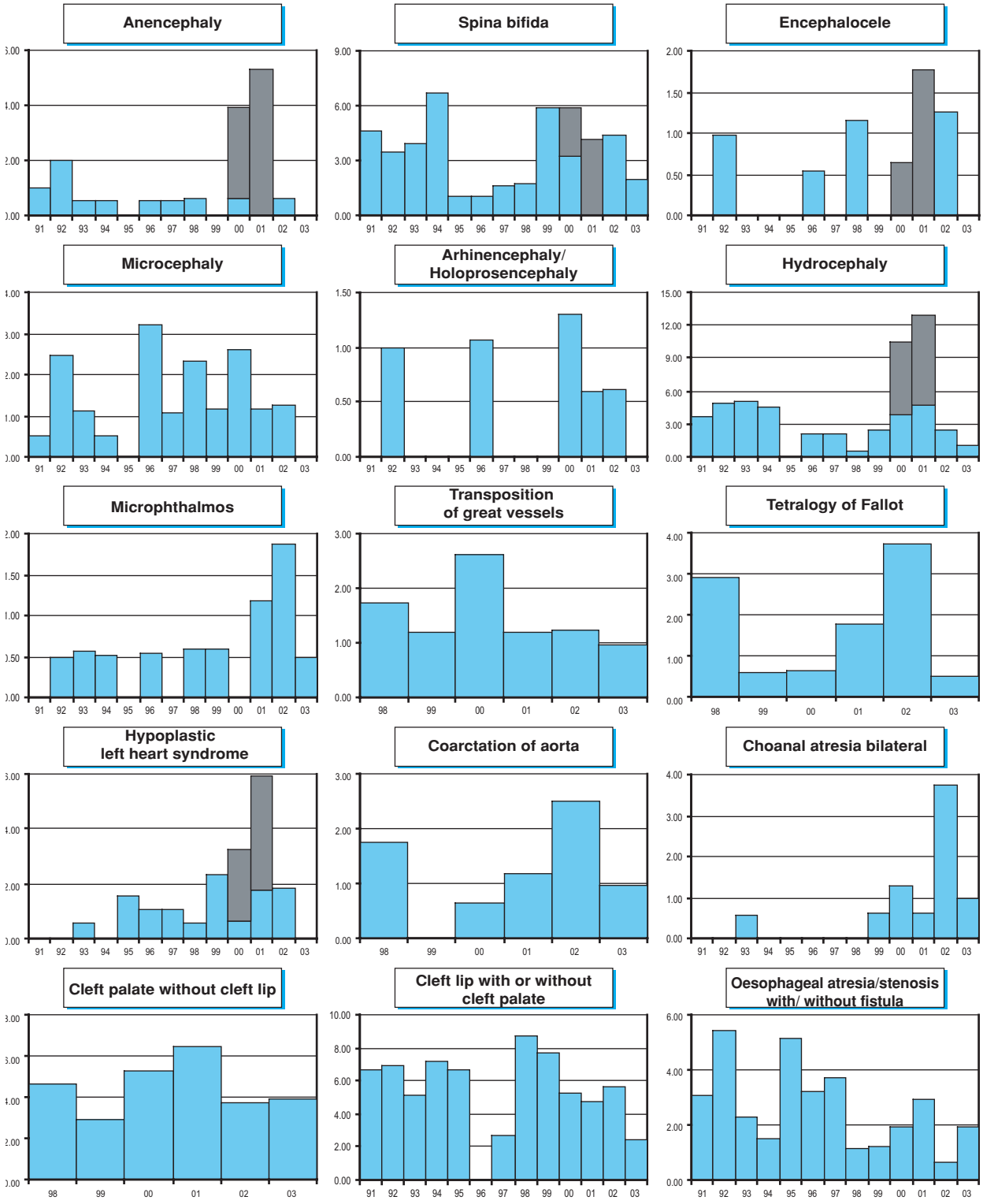
Birth prevalence rates: (LB+SB) * 10,000
Birth prevalence rates: (LB+SB+TOP) * 10,000 only for 2000-2001

	1974-78	1979-83	1984-88	1989-93*	1994-98	1999-03
Births				**57,328**	**93,661**	**85,718**
Anencephaly				1.22	0.43	1.87
Spina bifida				4.01	2.46	4.32
Encephalocele				0.35	0.32	0.70
Microcephaly				1.40	1.39	1.17
Arhinencephaly / Holoprosencephaly				0.35	0.21	0.47
Hydrocephaly				4.54	1.92	5.60
Anophthalmos				0.00	0.21	0.23
Microphthalmos				0.35	0.32	0.82
Unspecified Anophthalmos / Microphthalmos				----	----	----
Anotia				nr	0.58*	0.58
Microtia				nr	0.00*	0.47
Unspecified Anotia / Microtia				----	----	----
Transposition of great vessels				2.97	3.95	1.40
Tetralogy of Fallot					2.90*	1.40
Hypoplastic left heart syndrome				0.17	0.85	2.57
Coarctation of aorta				nr	1.74*	1.05
Choanal atresia, bilateral				0.17	0.00*	1.40
Cleft palate without cleft lip				5.76	4.48	4.43
Cleft lip with or without cleft palate				6.28	7.05	5.02
Oesophageal atresia / stenosis with or without fistula				3.66	2.99	1.75
Small intestine atresia / stenosis				6.28	4.59	2.10
Anorectal atresia / stenosis				3.66	2.35	1.98
Undescended testis (36 weeks of gestation or later)				4.88	8.33	17.62
Hypospadias				nr	14.61*	22.87
Epispadias				0.00	0.00*	0.58
Indeterminate sex				0.52	0.21	0.70
Renal agenesis				0.00	2.24	0.93
Cystic kidney				0.35	1.28	2.92
Bladder exstrophy				0.17	0.40*	0.35
Polydactyly, preaxial				0.17	0.80*	3.03
Total Limb reduction defects (include unspecified)				3.66	2.46	3.73
Transverse				nr	1.16*	3.27
Preaxial				nr	0.00*	0.00
Postaxial				nr	1.16*	0.00
Intercalary				nr	0.00*	0.00
Mixed				nr	0.00*	0.00
Unspecified				----	----	----
Diaphragmatic hernia				1.92	1.71	2.10
Omphalocele				2.09	1.28	1.40
Gastroschisis				1.22	0.53	2.22
Unspecified Omphalocele / Gastroschisis				----	----	----
Prune belly sequence				0.00	0.13*	0.00
Trisomy 13				0.17	0.40*	1.75
Trisomy 18				0.52	0.43	1.52
Down syndrome, all ages (include age unknown)				13.43	11.53	12.13
<20				nr	nr	nr
20-24				nr	nr	nr
25-29				nr	nr	nr
30-34				nr	nr	nr
35-39				nr	nr	nr
40-44				nr	nr	nr
45+				nr	nr	nr
unspecified				----	----	----

* data include less than 5 years
nr = not reported

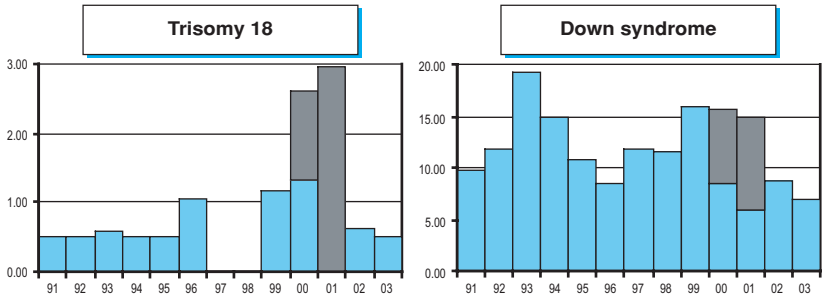
Italy: ISMAC

'Time trends 1991-2003 (Birth prevalence rates per 10,000)



Note: L+S rates, ToP rates

Note: L+S rates, ToP rates



Note: L+S rates, ToP rates

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

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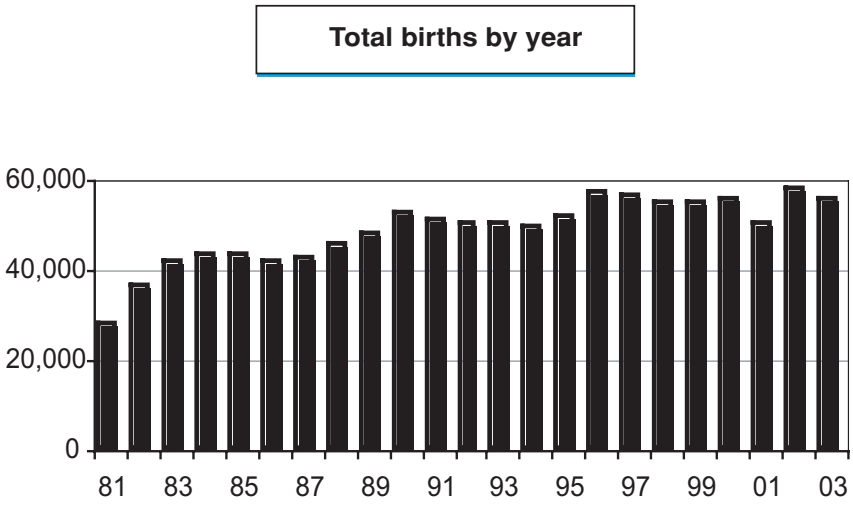
Fax: +39 049 8211425

E-mail: romano.tenconi@unipd.it

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

Italy: North East



Italy: North East, 2003

Live births (LB)	55268
Stillbirths (SB)	147
Total births	55415
Number of terminations of pregnancy (ToP) for birth defects	125

Birth Defects	Number of cases			Rates*10.000
	LB	SB	ToP	Total rate
Anencephaly	2	0	5	1.26
Spina bifida	6	0	8	2.52
Encephalocele	1	0	1	0.36
Microcephaly	7	0	0	1.26
Arhinencephaly / Holoprosencephaly	1	0	4	0.90
Hydrocephaly	3	0	8	1.98
Anophthalmos	2	0	0	0.36
Microphthalmos	0	0	1	0.18
Unspecified Anophthalmos / Microphthalmos	0	0	0	---
Anotia	1	0	0	0.18
Microtia	2	0	1	0.54
Unspecified Anotia / Microtia	0	0	0	---
Transposition of great vessels	4	0	0	0.72
Tetralogy of Fallot	12	0	0	2.16
Hypoplastic left heart syndrome	2	0	1	0.54
Coarctation of aorta	4	0	0	0.72
Choanal atresia, bilateral	1	0	0	0.18
Cleft palate without cleft lip	16	0	4	3.60
Cleft lip with or without cleft palate	25	0	2	4.86
Oesophageal atresia / stenosis with or without fistula	15	0	0	2.70
Small intestine atresia / stenosis	5	0	0	0.90
Anorectal atresia / stenosis	6	0	1	1.26
Undescended testis (36 weeks of gestation or later)	nr	nr	nr	nr
Hypospadias	27	0	0	4.86
Epispadias	0	0	0	0.00
Indeterminate sex	nr	nr	nr	nr
Renal agenesis	1	0	0	0.18
Cystic kidney	3	0	1	0.72
Bladder exstrophy	1	0	0	0.18
Polydactyly, preaxial	9	0	0	1.62
Total Limb reduction defects (include unspecified)	9	0	6	2.70
Transverse	6	0	2	1.44
Preaxial	0	0	1	0.18
Postaxial	0	0	0	0.00
Intercalary	1	0	0	0.18
Mixed	2	0	3	0.90
Unspecified	0	0	0	---
Diaphragmatic hernia	8	0	0	1.44
Omphalocele	4	0	2	1.08
Gastroschisis	2	0	3	0.90
Unspecified Omphalocele / Gastroschisis	0	0	0	---
Prune belly sequence	1	0	0	0.18
Trisomy 13	1	0	5	1.08
Trisomy 18	3	2	6	1.98
Down syndrome, all ages (include age unknown)	47	0	34	14.58
<20	1	0	0	nr
20-24	1	0	0	nr
25-29	3	0	1	nr
30-34	12	0	2	nr
35-39	11	0	14	nr
40-44	5	0	16	nr
45+	4	0	1	nr
unspecified	10	0	0	---

nr = not reported

Italy: North East, Previous years rates 1981 - 2003

Birth prevalence rates: (LB+SB) * 10,000 until 1995
Birth prevalence rates: (LB+SB+TOP) * 10,000 since 1996

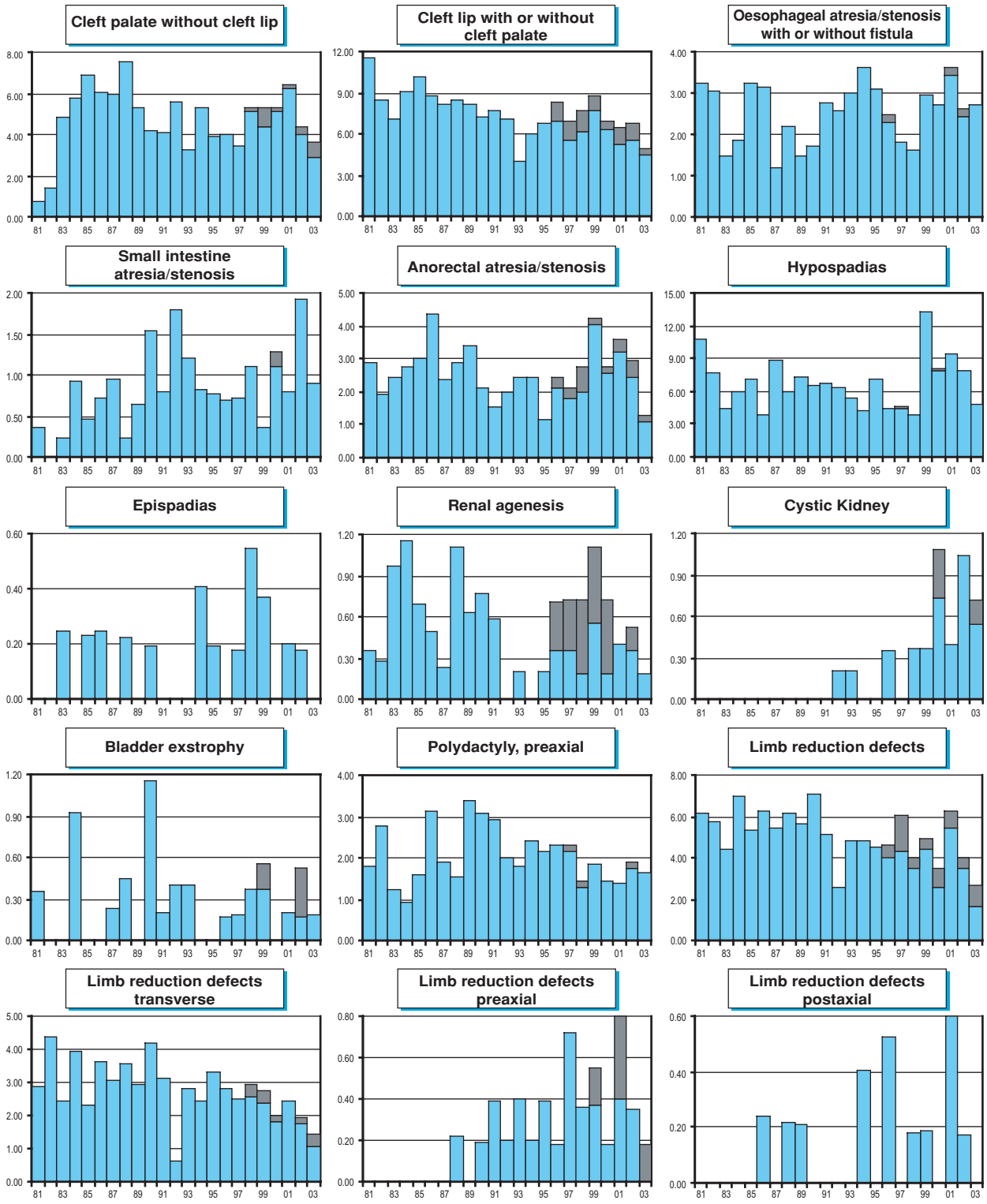
	1974-78	1979-83*	1984-88	1989-93	1994-98	1999-03
Births		**105,224**	**215,223**	**250,888**	**268,645**	**272,107**
Anencephaly		2.00	1.35	0.40	1.45	1.51
Spina bifida		3.90	3.39	2.23	2.90	2.61
Encephalocele		1.14	0.56	0.36	0.56	0.59
Microcephaly		0.48	0.33	0.28	0.67	1.43
Arhinencephaly / Holoprosencephaly		0.10	0.05	0.00	0.34	0.62
Hydrocephaly		1.05	1.30	1.12	2.79	3.01
Anophthalmos		0.19	0.74	0.16	0.22	0.18
Microphthalmos		0.00	0.00	0.36	0.78	0.59
Unspecified Anophthalmos / Microphthalmos		---	---	---	---	---
Anotia		0.19	0.14	0.20	0.22	0.15
Microtia		2.76	2.00	1.51	1.97	1.14
Unspecified Anotia / Microtia		---	---	---	---	---
Transposition of great vessels		0.00	0.05	0.52	1.64	1.51
Tetralogy of Fallot		0.00	0.46	1.04	2.35	2.83
Hypoplastic left heart syndrome		0.00	0.00	0.56	1.75	0.74
Coarctation of aorta		0.00	0.05	0.88	0.97	2.17
Choanal atresia, bilateral		0.00	0.28	0.28	0.48	0.74
Cleft palate without cleft lip		2.57	6.46	4.46	4.36	4.96
Cleft lip with or without cleft palate		8.74	8.87	6.86	7.18	6.76
Oesophageal atresia / stenosis with or without fistula		2.47	2.32	2.31	2.49	2.90
Small intestine atresia / stenosis		0.19	0.65	1.20	0.82	1.07
Anorectal atresia / stenosis		2.38	3.07	2.27	2.20	2.94
Undescended testis (36 weeks of gestation or later)		nr	nr	nr	nr	nr
Hypospadias		7.22	6.37	6.46	4.84	8.64
Epispadias		0.10	0.14	0.04	0.26	0.15
Indeterminate sex		nr	nr	nr	nr	nr
Renal agenesis		0.57	0.74	0.44	0.48	0.59
Cystic kidney		0.00	0.00	0.08	0.15	0.74
Bladder exstrophy		0.10	0.33	0.44	0.15	0.29
Polydactyly, preaxial		1.90	1.81	2.63	2.12	1.65
Total Limb reduction defects (include unspecified)		5.32	6.04	5.06	4.80	4.23
Transverse		3.23	3.30	2.75	2.79	2.09
Preaxial		0.00	0.05	0.24	0.37	0.40
Postaxial		0.00	0.09	0.04	0.22	0.18
Intercalary		0.67	0.60	0.72	0.26	0.51
Mixed		1.43	2.00	1.32	0.67	1.03
Unspecified		---	---	---	---	---
Diaphragmatic hernia		0.29	0.65	0.24	0.11	1.54
Omphalocele		1.43	1.21	0.88	0.97	0.96
Gastroschisis		0.95	0.65	0.36	0.26	0.62
Unspecified Omphalocele / Gastroschisis		---	---	---	---	---
Prune belly sequence		0.10	0.00	0.00	0.04	0.11
Trisomy 13		0.67	0.88	0.36	0.48	1.29
Trisomy 18		0.86	1.25	0.92	0.93	2.54
Down syndrome, all ages (include age unknown)		14.35	14.64	13.71	16.86	16.94
<20		nr	nr	nr	nr	nr
20-24		nr	nr	nr	nr	nr
25-29		nr	nr	nr	nr	nr
30-34		nr	nr	nr	nr	nr
35-39		nr	nr	nr	nr	nr
40-44		nr	nr	nr	nr	nr
45+		nr	nr	nr	nr	nr
unspecified		---	---	---	---	---

* data include less than 5 years
nr = not reported

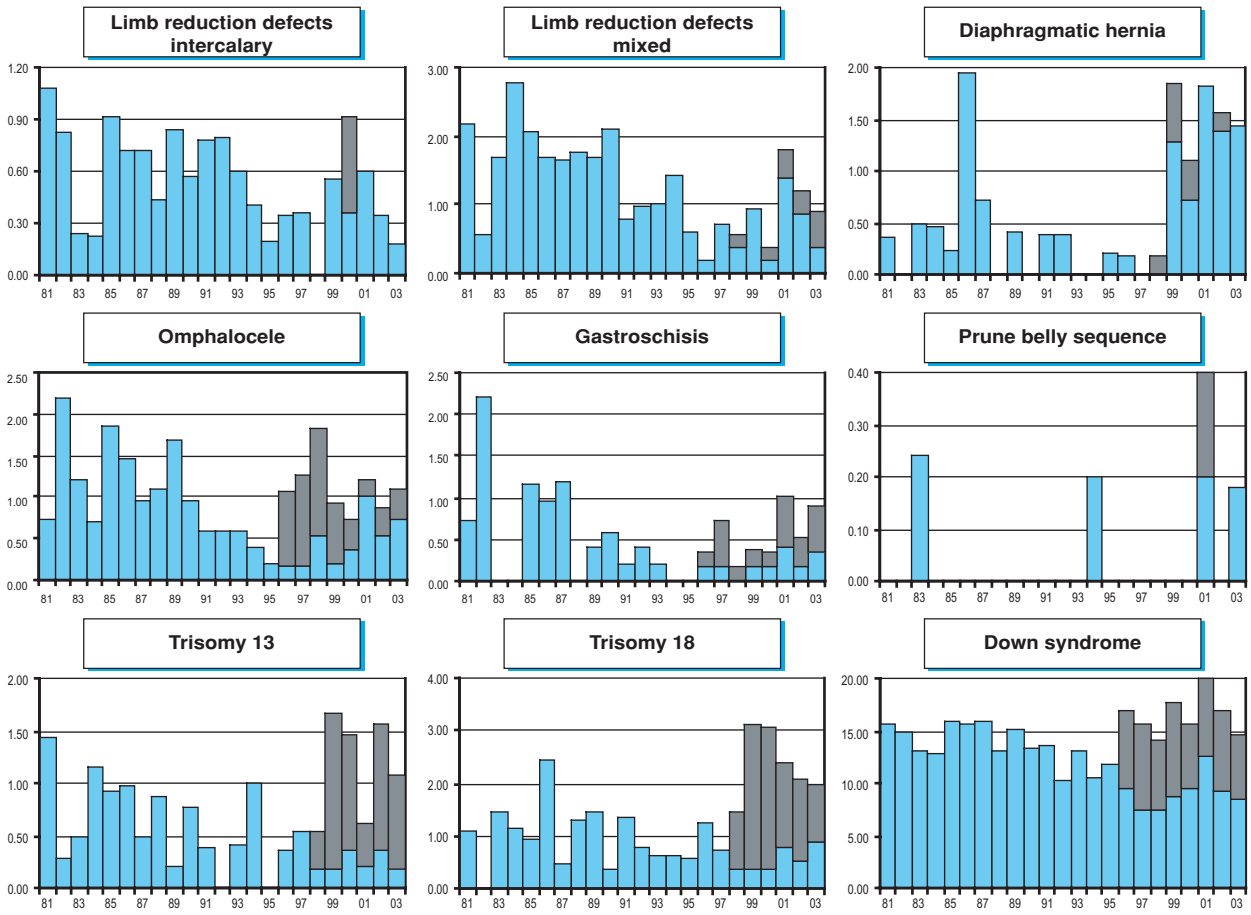
Italy: North East

'Time trends 1981-2003 (Birth prevalence rates per 10,000)

Note: L+S rates, ToP rates



Note: L+S rates, ToP rates



Note: L+S rates, ToP rates

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.

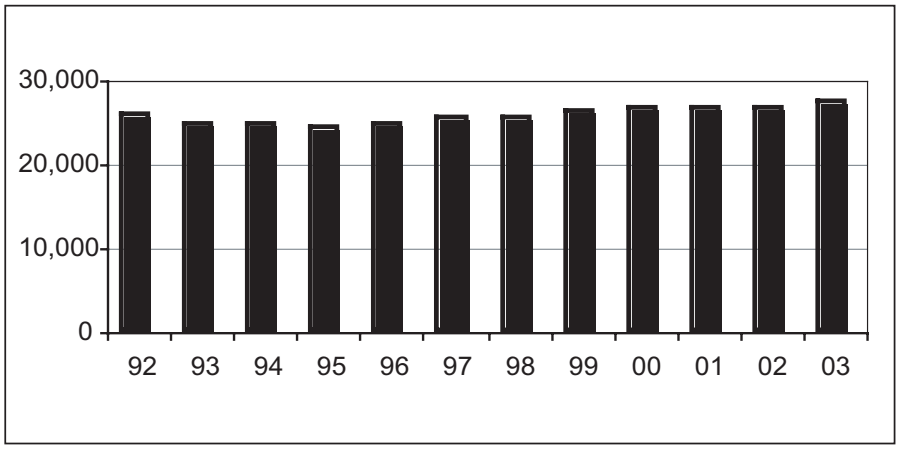
Phone: 39-050-3152100

Fax: 39-050 3152095

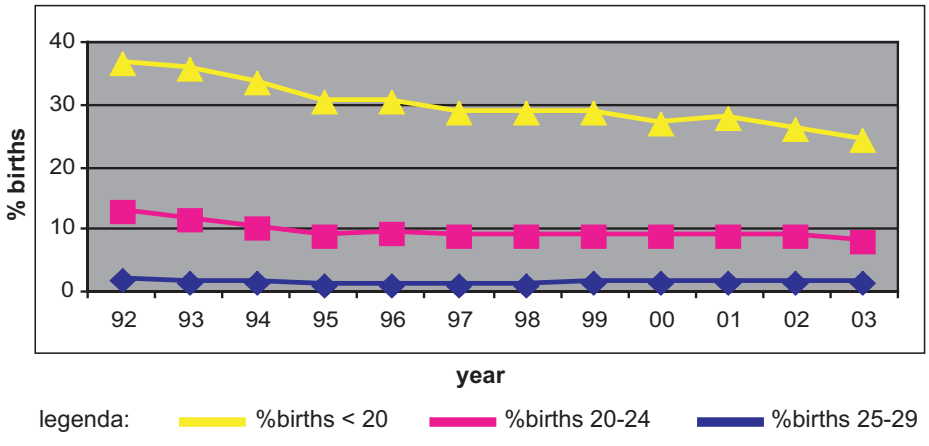
E-mail: fabrizio.bianchi@ifc.cnr.it

Italy: Tuscany

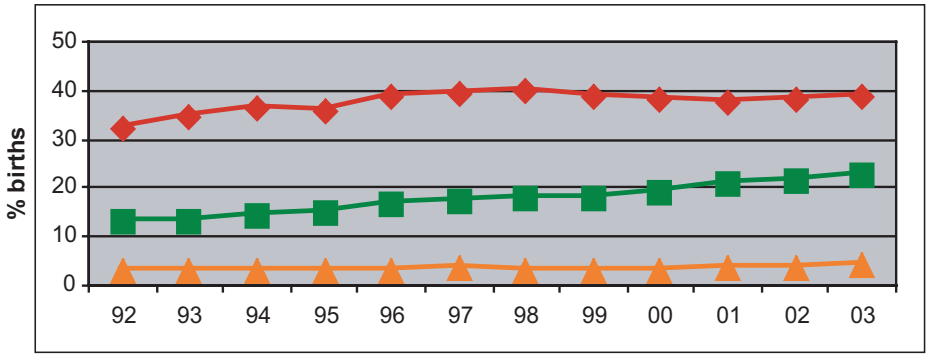
Total births by year



Percentage of births by maternal age



legenda: %births < 20 %births 20-24 %births 25-29



legenda: %births 30-34 %births 35-39 %births 40+

Italy: Tuscany, 2003

Live births (LB)	27378
Stillbirths (SB)	111
Total births	27489
Number of terminations of pregnancy (ToP) for birth defects	92

Birth Defects	Number of cases			Rates*10.000
	LB	SB	ToP	Total rate
Anencephaly	0	0	4	1.45
Spina bifida	2	1	5	2.90
Encephalocele	0	0	0	0.00
Microcephaly	4	0	0	1.45
Arhinencephaly / Holoprosencephaly	0	0	2	0.73
Hydrocephaly	12	1	10	8.34
Anophthalmos	0	0	0	0.00
Microphthalmos	3	0	0	1.09
Unspecified Anphthalmos / Microphthalmos	0	0	0	---
Anotia	3	0	0	1.09
Microtia	2	0	0	0.73
Unspecified Anotia / Microtia	0	0	0	---
Transposition of great vessels	10	1	0	3.99
Tetralogy of Fallot	5	0	2	2.54
Hypoplastic left heart syndrome	3	0	2	1.81
Coarctation of aorta	4	0	0	1.45
Choanal atresia, bilateral	2	0	0	0.73
Cleft palate without cleft lip	16	0	0	5.80
Cleft lip with or without cleft palate	13	1	3	6.16
Oesophageal atresia / stenosis with or without fistula	6	0	0	2.18
Small intestine atresia / stenosis	8	0	0	2.90
Anorectal atresia / stenosis	6	1	1	2.90
Undescended testis (36 weeks of gestation or later)	41	0	0	14.87
Hypospadias	19	0	0	6.89
Epispadias	0	0	0	0.00
Indeterminate sex	3	0	0	1.09
Renal agenesis	1	0	2	1.09
Cystic kidney	12	1	1	5.08
Bladder exstrophy	1	0	0	0.36
Polydactyly, preaxial	3	0	0	1.09
Total Limb reduction defects (include unspecified)	10	2	3	5.44
Transverse	7	1	2	3.63
Preaxial	2	0	1	1.09
Postaxial	0	0	0	0.00
Intercalary	1	1	0	0.73
Mixed	0	0	0	0.00
Unspecified	0	0	0	---
Diaphragmatic hernia	5	1	0	2.18
Omphalocele	2	3	1	2.18
Gastroschisis	1	0	1	0.73
Unspecied Omphalocele / Gastroschisis	0	0	0	---
Prune belly sequence	0	0	0	0.00
Trisomy 13	1	0	1	0.73
Trisomy 18	1	0	6	2.54
Down syndrome, all ages (include age unknown)	10	1	33	15.95
<20	0	0	0	0.00
20-24	0	0	0	0.00
25-29	0	0	0	0.00
30-34	4	0	4	7.47
35-39	2	0	14	25.35
40-44	3	1	15	165.65
45+	1	0	0	263.16
unspecified	0	0	0	---

Italy: Tuscany, Previous years rates 1992 - 2003

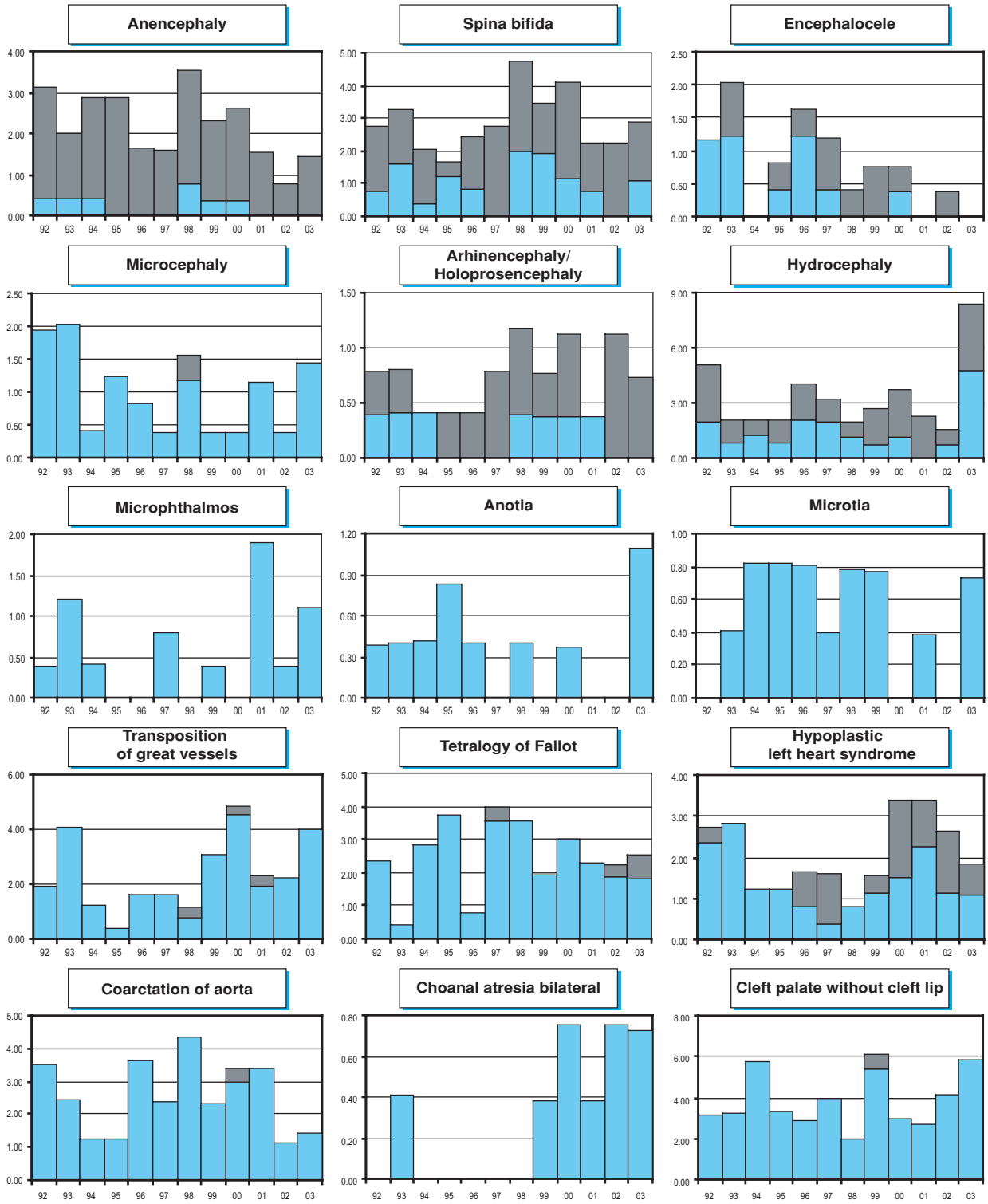
	1974-78	1979-83	1984-88	1989-93*	1994-98	1999-03
Births				**50,357**	**124,065**	**133,141**
Anencephaly				2.58	2.50	1.73
Spina bifida				2.98	2.74	3.00
Encephalocele				1.59	0.81	0.38
Microcephaly				1.99	0.89	0.75
Arhinencephaly / Holoprosencephaly				0.79	0.64	0.83
Hydrocephaly				3.57	2.66	3.76
Anophthalmos				0.00	0.08	0.23
Microphthalmos				0.79	0.24	0.75
Unspecified Anophthalmos / Microphthalmos				---	---	---
Anotia				0.40	0.40	0.30
Microtia				0.20	0.73	0.38
Unspecified Anotia / Microtia				---	---	---
Transposition of great vessels				2.98	1.21	3.30
Tetralogy of Fallot				1.39	2.98	2.40
Hypoplastic left heart syndrome				2.78	1.29	2.55
Coarctation of aorta				2.98	2.58	2.33
Choanal atresia, bilateral				0.20	0.00	0.60
Cleft palate without cleft lip				3.18	3.55	4.36
Cleft lip with or without cleft palate				10.13	5.32	6.91
Oesophageal atresia / stenosis with or without fistula				2.18	2.58	2.25
Small intestine atresia / stenosis				0.99	0.73	1.05
Anorectal atresia / stenosis				1.19	1.69	3.00
Undescended testis (36 weeks of gestation or later)				2.78	5.24	11.49
Hypospadias				6.16	3.47	6.16
Epispadias				0.20	0.32	0.15
Indeterminate sex				0.20	1.05	0.60
Renal agenesis				1.79	1.77	0.83
Cystic kidney				2.38	3.87	3.83
Bladder exstrophy				0.60	0.16	0.23
Polydactyly, preaxial				0.99	0.81	1.35
Total Limb reduction defects (include unspecified)				5.36	4.67	6.16
Transverse				nr	0.79*	4.06
Preaxial				nr	0.00*	0.68
Postaxial				nr	0.79*	0.23
Intercalary				nr	1.96*	0.45
Mixed				nr	0.79*	0.30
Unspecified				---	---	---
Diaphragmatic hernia				1.39	1.53	2.10
Omphalocele				2.38	1.29	1.95
Gastroschisis				0.79	0.16	0.53
Unspecified Omphalocele / Gastroschisis				---	---	---
Prune belly sequence				0.20	0.16	0.00
Trisomy 13				0.40	0.73	0.98
Trisomy 18				2.58	3.39	2.55
Down syndrome, all ages (include age unknown)				12.31	16.60	16.00
<20				0.00	0.00	0.00
20-24				1.64	9.65	4.35
25-29				9.37	8.27	4.52
30-34				8.92	13.16	10.76
35-39				30.36	29.45	23.74
40-44				47.39	107.47	145.56
45+				235.29	88.50	103.09
unspecified				---	---	---

* data include less than 5 years

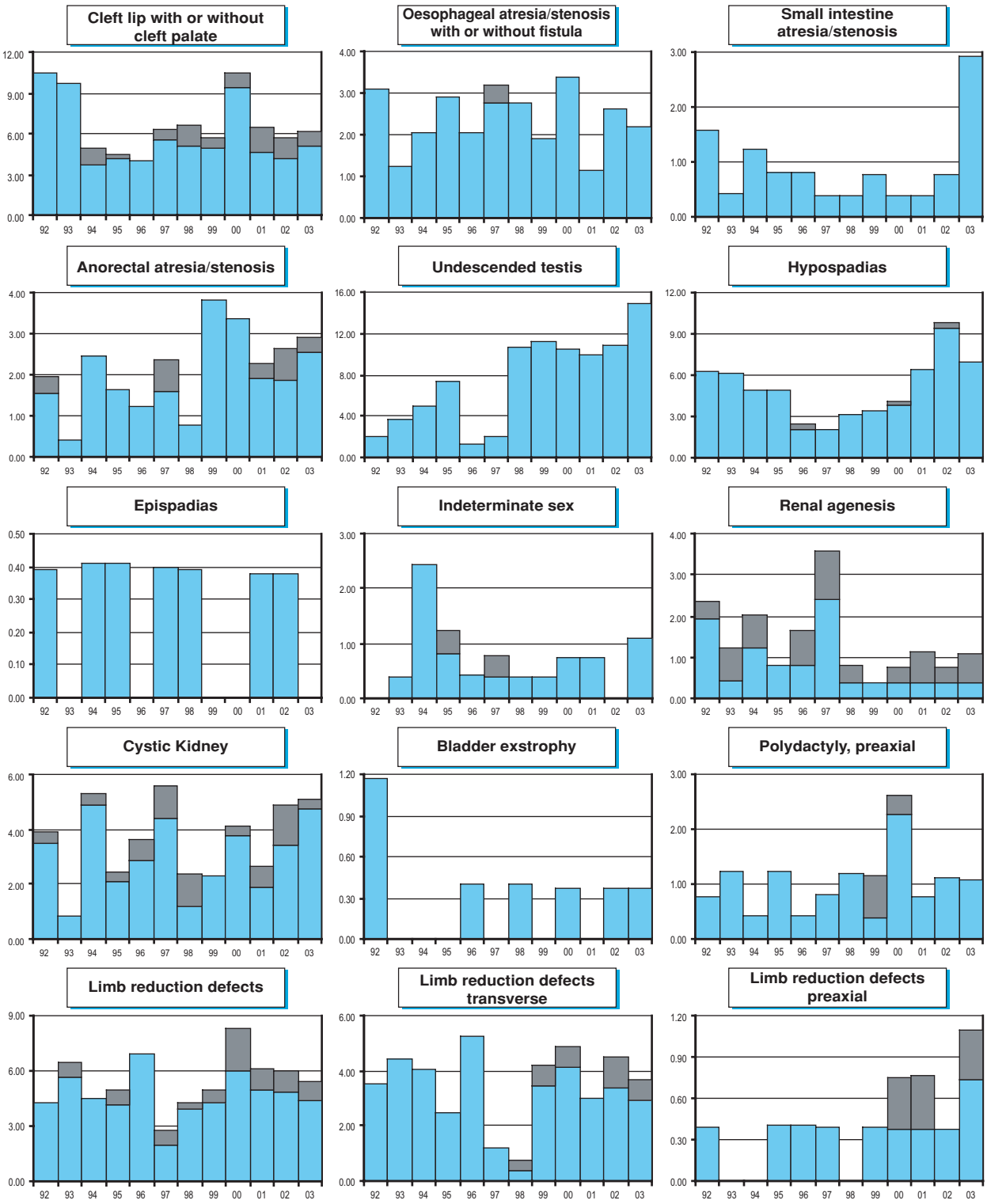
nr = not reported

Italy: Tuscany

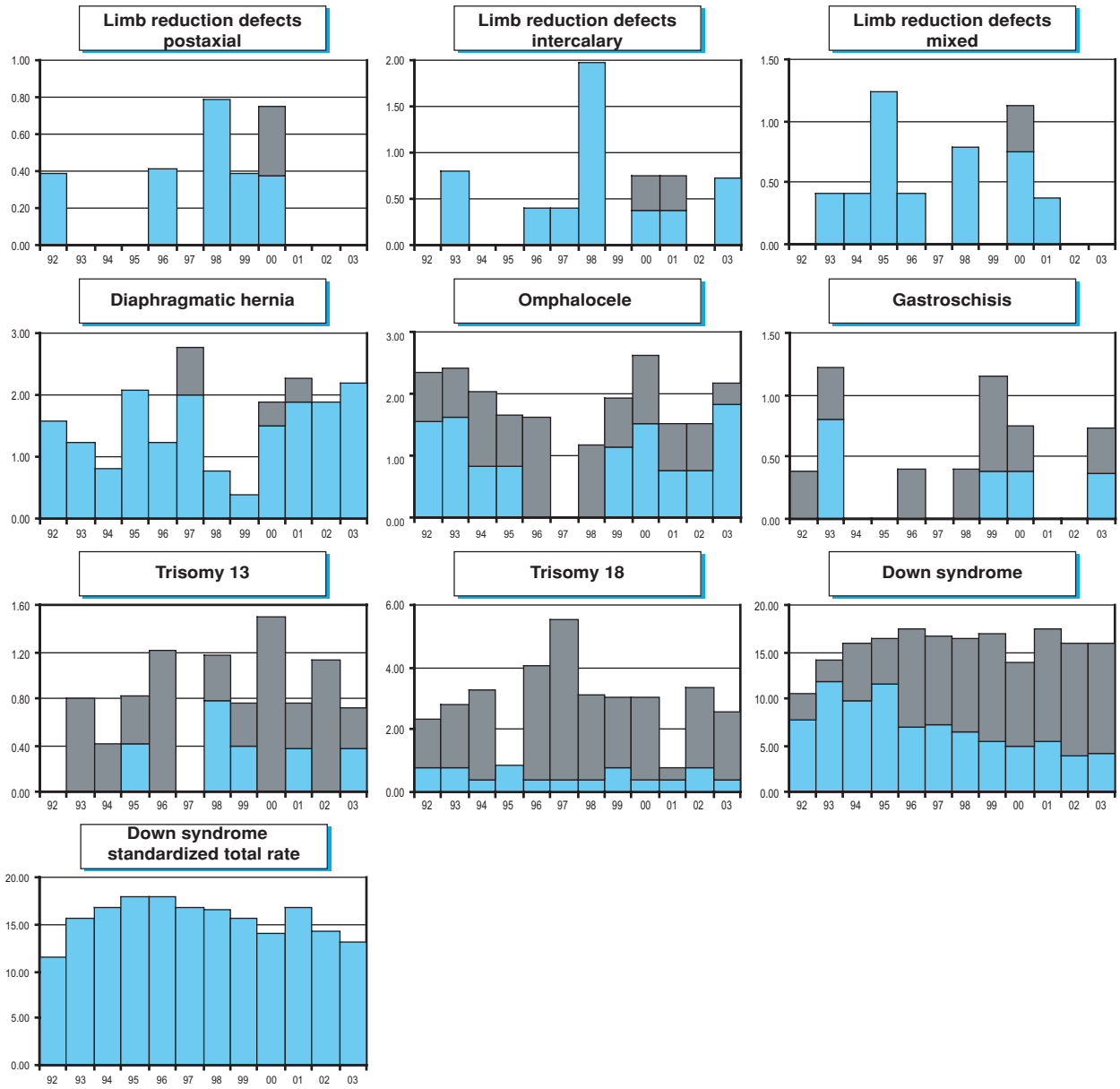
Time trends 1992-2003 (Birth prevalence rates per 10,000)



Note: L+S rates, ToP rates



Note: L+S rates, ToP rates



Note: L+S rates, ToP rates

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

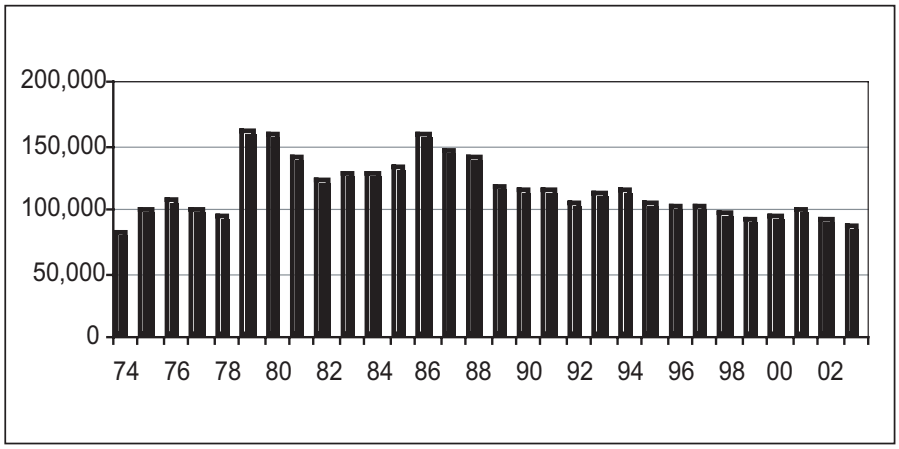
Phone: 81-45-2533668

Fax: 81-45-2533668

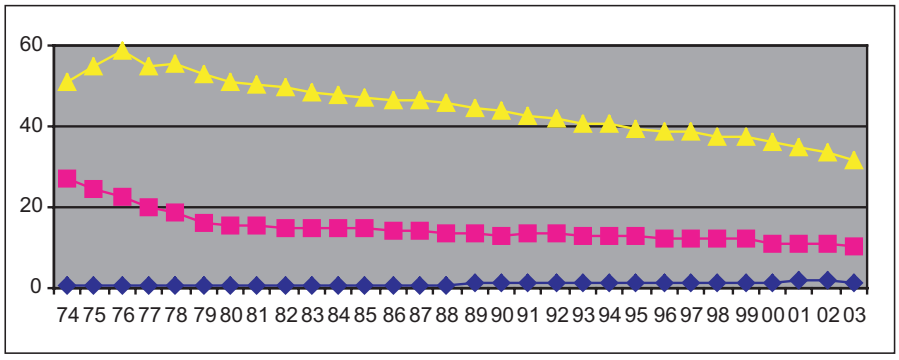
E-mail: fuhira@hamakko.or.jp

Japan: JAOG

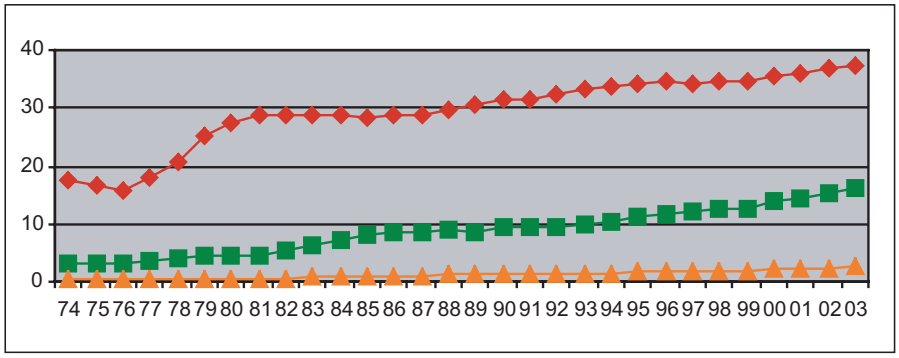
Total births by year



Percentage of births by maternal age



legenda: %births < 20 %births 20-24 %births 25-29



legenda: %births 30-34 %births 35-39 %births 40+

Japan: JAOG, 2003

Live births (LB)	84019
Stillbirths (SB)	625
Total births	84644
Number of terminations of pregnancy (ToP) for birth defects	nr

Birth Defects	Number of cases			Rates*10.000
	LB	SB	ToP	Total rate
Anencephaly	4	5	nr	1.06
Spina bifida	48	4	nr	6.14
Encephalocele	6	2	nr	0.95
Microcephaly	9	2	nr	1.30
Arhinencephaly / Holoprosencephaly	7	3	nr	1.18
Hydrocephaly	72	12	nr	9.92
Anophthalmos	0	2	nr	0.24
Microphthalmos	1	0	nr	0.12
Unspecified Anophthalmos / Microphthalmos	nr	nr	nr	nr
Anotia	nr	nr	nr	nr
Microtia	8	2	nr	1.18
Unspecified Anotia / Microtia	nr	nr	nr	nr
Transposition of great vessels	40	1	nr	4.84
Tetralogy of Fallot	40	1	nr	4.84
Hypoplastic left heart syndrome	27	4	nr	3.66
Coarctation of aorta	21	0	nr	2.48
Choanal atresia, bilateral	nr	nr	nr	nr
Cleft palate without cleft lip	27	1	nr	3.31
Cleft lip with or without cleft palate	148	10	nr	18.67
Oesophageal atresia / stenosis with or without fistula	32	3	nr	4.13
Small intestine atresia / stenosis	63	4	nr	7.92
Anorectal atresia / stenosis	45	4	nr	5.79
Undescended testis (36 weeks of gestation or later)	nr	nr	nr	nr
Hypospadias	37	1	nr	4.49
Epispadias	nr	nr	nr	nr
Indeterminate sex	nr	nr	nr	nr
Renal agenesis	18	2	nr	2.36
Cystic kidney	49	2	nr	6.03
Bladder exstrophy	3	0	nr	0.35
Polydactyly, preaxial	60	1	nr	7.21
Total Limb reduction defects (include unspecified)	25	3	nr	3.31
Transverse	2	0	nr	0.24
Preaxial	5	1	nr	0.71
Postaxial	1	0	nr	0.12
Intercalary	9	0	nr	1.06
Mixed	4	0	nr	0.47
Unspecified	4	2	nr	---
Diaphragmatic hernia	56	7	nr	7.44
Omphalocele	26	7	nr	3.90
Gastroschisis	24	3	nr	3.19
Unspecified Omphalocele / Gastroschisis	3	1	nr	---
Prune belly sequence	0	0	nr	0.00
Trisomy 13	3	2	nr	0.59
Trisomy 18	41	28	nr	8.15
Down syndrome, all ages (include age unknown)	82	5	nr	10.28
<20	1	0	nr	7.63
20-24	4	0	nr	4.49
25-29	10	0	nr	3.76
30-34	30	3	nr	10.42
35-39	29	0	nr	20.97
40+	8	2	nr	42.77
unspecified	0	0	nr	---

nr = not reported

Japan: JAOG, Previous years rates 1974 - 2003

Prevalence rates: (LB+SB) * 10,000

	1974-78	1979-83	1984-88	1989-93	1994-98	1999-03
Births	**470,634**	**702,082**	**695,332**	**555,726**	**506,077**	**452,752**
Anencephaly	8.67	9.64	7.48	4.55	2.45	1.33
Spina bifida	1.72	2.48	2.95	3.51	3.58	5.12
Encephalocele	1.02	1.11	1.27	1.01	1.03	0.77
Microcephaly	0.81	1.25	1.08	1.60	1.24	1.46
Arhinencephaly / Holoprosencephaly	nr	nr	nr	nr	0.89*	1.19
Hydrocephaly	2.66	3.60	4.95	7.25	6.74	7.93
Anophthalmos	0.72	0.95	0.63	0.49	0.18	0.22
Microphthalmos	0.55	0.64	0.55	0.52	0.55	0.40
Unspecified Anophthalmos / Microphthalmos	---	---	---	---	---	---
Anotia	nr	nr	nr	nr	nr	nr
Microtia	1.04	1.18	0.98	1.17	1.38	1.24
Unspecified Anotia / Microtia	---	---	---	---	---	---
Transposition of great vessels	nr	nr	nr	nr	1.86*	3.05
Tetralogy of Fallot	nr	nr	nr	nr	2.22*	3.60
Hypoplastic left heart syndrome	nr	nr	nr	nr	1.45*	2.16
Coarctation of aorta	nr	nr	nr	nr	1.34*	2.39
Choanal atresia, bilateral	nr	nr	nr	nr	nr	nr
Cleft palate without cleft lip	12.86	10.30	5.02	5.69	4.47	4.00
Cleft lip with or without cleft palate	14.92	13.06	14.05	15.12	16.34	18.40
Oesophageal atresia / stenosis with or without fistula	0.75*	1.18	1.45	2.03	2.63	3.98
Small intestine atresia / stenosis	nr	nr	nr	nr	3.98*	5.74
Anorectal atresia / stenosis	4.04	3.90	3.87	4.34	4.15	5.17
Undescended testis (36 weeks of gestation or later)	nr	nr	nr	nr	nr	0.00*
Hypospadias	1.61	2.19	2.36	2.90	2.96	3.98
Epispadias	nr	nr	nr	nr	nr	nr
Indeterminate sex	nr	nr	nr	nr	nr	nr
Renal agenesis	nr	nr	nr	1.40	1.34	2.12
Cystic kidney	nr	nr	nr	nr	2.28*	4.40
Bladder exstrophy	0.10*	0.20	0.14	0.14	0.14	0.27
Polydactyly, preaxial	nr	nr	nr	6.21	6.26	6.36
Total Limb reduction defects (include unspecified)	nr	nr	nr	3.24*	3.46	3.29
Transverse	nr	nr	nr	0.45*	0.36	0.29
Preaxial	nr	nr	nr	0.45*	0.55	0.66
Postaxial	nr	nr	nr	0.09*	0.34	0.27
Intercalary	nr	nr	nr	1.62*	1.21	0.88
Mixed	nr	nr	nr	0.27*	0.63	0.73
Unspecified	---	---	---	---	---	---
Diaphragmatic hernia	nr	nr	nr	2.75	3.30	6.10
Omphalocele	0.98	1.38	2.33	3.19	3.44	3.27
Gastroschisis	1.21	0.81	1.06	1.64	1.62	2.52
Unspecified Omphalocele / Gastroschisis	---	---	---	---	---	---
Prune belly sequence	nr	nr	nr	nr	0.05*	0.02
Trisomy 13	nr	nr	nr	nr	0.77	0.97
Trisomy 18	nr	nr	nr	nr	3.18	6.60
Down syndrome, all ages (include age unknown)	2.79*	4.87	5.25	6.26	7.96	8.97
<20	nr	nr	nr	0.00*	3.49	7.24
20-24	nr	nr	nr	0.68*	3.80	2.20
25-29	nr	nr	nr	3.96*	4.87	4.99
30-34	nr	nr	nr	5.68*	7.56	7.97
35-39	nr	nr	nr	17.01*	18.02	19.11
40+	nr	nr	nr	53.86*	52.71	52.86
unspecified	---	---	---	---	---	---

* data include less than 5 years

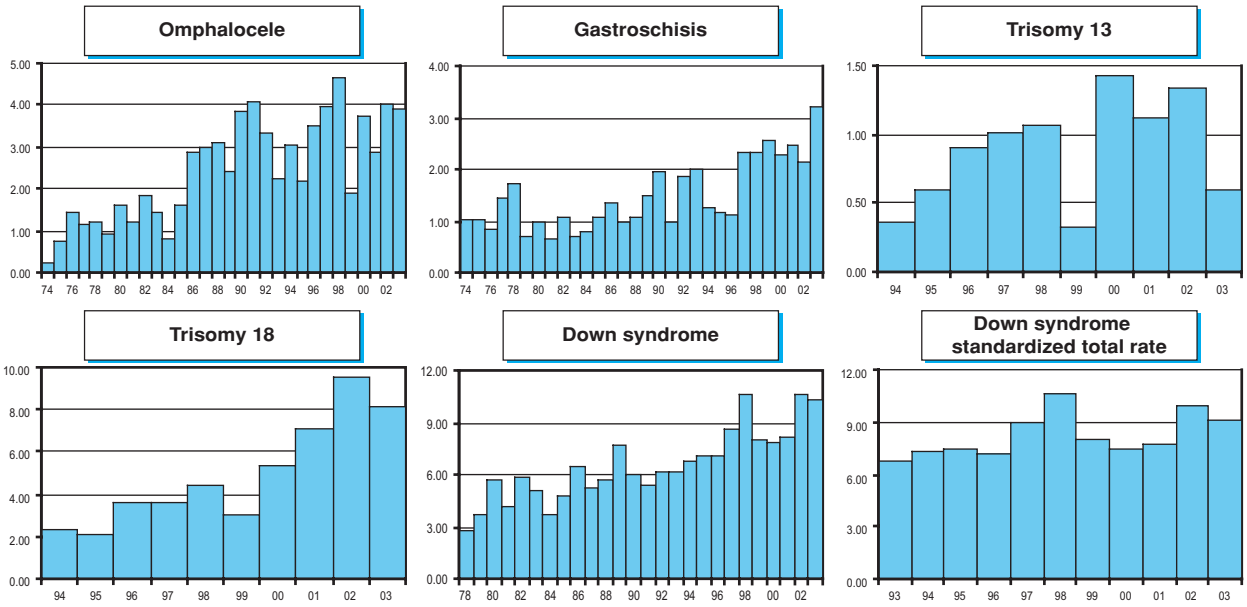
nr = not reported

Japan: JAOG

Time trends 1974-2003 (Birth prevalence rates per 10,000)

Note: L+S rates

Note: L+S rates



Note: L+S rates

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).

Address for further information:
Miriam Gatt, Malta Congenital Anomalies Registry, Department of Health Information, 95 Guardamangia Hill, Guardamangia MSD 08, Malta

Tel: 356-21234915

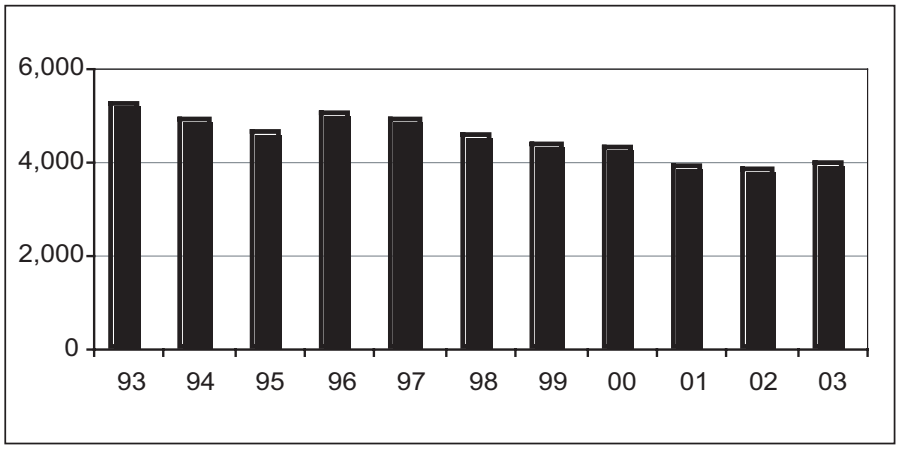
Fax: 356-21235910

E-mail: miriam.gatt@gov.mt

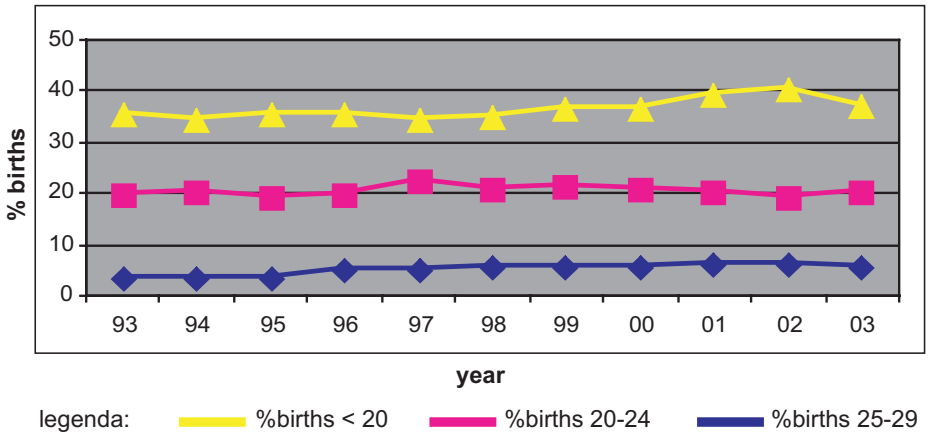
Website:
http://www.sahha.gov.mt/pages.aspx?page=90

Malta

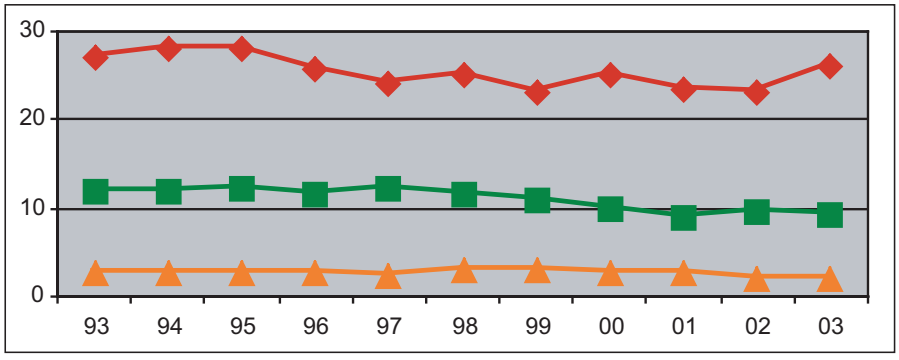
Total births by year



Percentage of births by maternal age



legenda: %births < 20 %births 20-24 %births 25-29



legenda: %births 30-34 %births 35-39 %births 40+

Malta, 2003

Live births (LB)	3902
Stillbirths (SB)	18
Total births	3920
Number of terminations of pregnancy (ToP) for birth defects	not permitted

Birth Defects	Number of cases			Rates*10.000
	LB	SB	ToP	Total rate
Anencephaly	0	0		0.00
Spina bifida	3	0		7.65
Encephalocele	0	0		0.00
Microcephaly	1	1		5.10
Arhinencephaly / Holoprosencephaly	0	0		0.00
Hydrocephaly	0	0		0.00
Anophthalmos	0	0		0.00
Microphthalmos	0	0		0.00
Unspecified Anophthalmos / Microphthalmos	0	0		---
Anotia	0	0		0.00
Microtia	0	0		0.00
Unspecified Anotia / Microtia	0	0		---
Transposition of great vessels	0	0		0.00
Tetralogy of Fallot	1	0		2.55
Hypoplastic left heart syndrome	2	0		5.10
Coarctation of aorta	0	0		0.00
Choanal atresia, bilateral	0	0		0.00
Cleft palate without cleft lip	0	0		0.00
Cleft lip with or without cleft palate	2	1		7.65
Oesophageal atresia / stenosis with or without fistula	1	0		2.55
Small intestine atresia / stenosis	1	0		2.55
Anorectal atresia / stenosis	0	1		2.55
Undescended testis (36 weeks of gestation or later)	nr	nr		nr
Hypospadias	2	0		5.10
Epispadias	0	0		0.00
Indeterminate sex	0	0		0.00
Renal agenesis	2	0		5.10
Cystic kidney	1	0		2.55
Bladder exstrophy	0	0		0.00
Polydactyly, total	6	0		15.31
Total Limb reduction defects (include unspecified)	0	2		5.10
Transverse	nr	nr		nr
Preaxial	nr	nr		nr
Postaxial	nr	nr		nr
Intercalary	nr	nr		nr
Mixed	nr	nr		nr
Unspecified	nr	nr		---
Diaphragmatic hernia	0	0		0.00
Omphalocele	0	0		0.00
Gastroschisis	0	0		0.00
Unspecified Omphalocele / Gastroschisis	0	0		---
Prune belly sequence	0	0		0.00
Trisomy 13	0	0		0.00
Trisomy 18	4	0		10.20
Down syndrome, all ages (include age unknown)	6	0		15.31
<20	0	0		0.00
20-24	0	0		0.00
25-29	0	0		0.00
30-34	4	0		39.14
35-39	2	0		54.95
40-44	0	0		0.00
45+	0	0		0.00
unspecified	0	0		---

nr = not reported

Malta, Previous years rates 1993 - 2003

Birth prevalence rates: (LB+SB) * 10,000

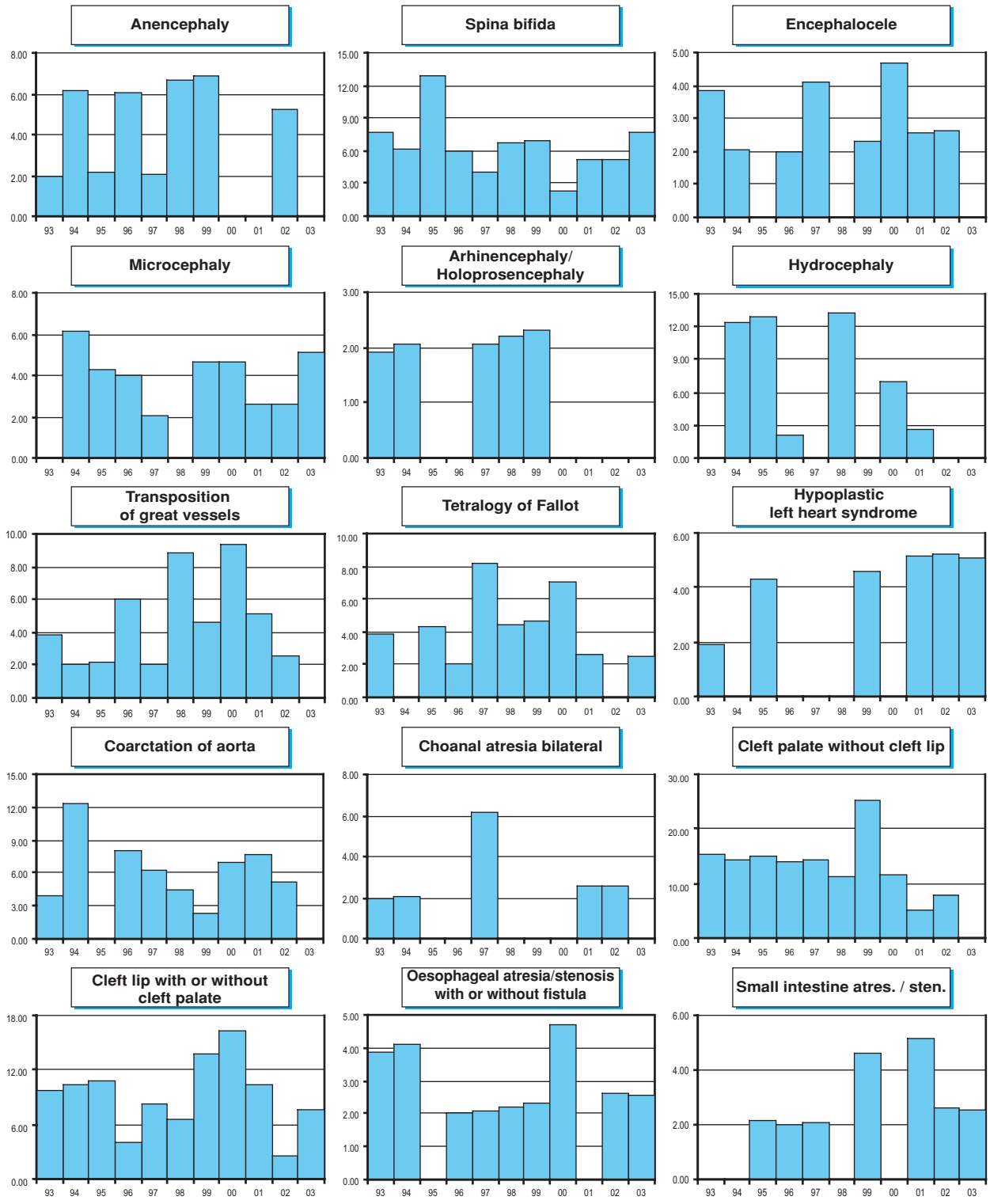
	1974-78	1979-83	1984-88	1989-93*	1994-98	1999-03
Births				**5,172**	**23,849**	**20,240**
Anencephaly				1.93	4.61	2.47
Spina bifida				7.73	7.13	5.43
Encephalocele				3.87	1.68	2.47
Microcephaly				0.00	3.35	3.95
Arhinencephaly / Holoprosencephaly				1.93	1.26	0.49
Hydrocephaly				0.00	7.97	1.98
Anophthalmos				0.00	0.42	0.00
Microphthalmos				0.00	1.26	0.99
Unspecified Anophthalmos / Microphthalmos				---	---	---
Anotia				0.00	0.00	0.00
Microtia				0.00	0.00	0.00
Unspecified Anotia / Microtia				---	---	---
Transposition of great vessels				3.87	4.19	4.45
Tetralogy of Fallot				3.87	3.77	3.46
Hypoplastic left heart syndrome				1.93	0.84	3.95
Coarctation of aorta				3.87	6.29	4.45
Choanal atresia, bilateral				1.93	1.68	0.99
Cleft palate without cleft lip				15.47	13.84	10.38
Cleft lip with or without cleft palate				9.67	7.97	10.38
Oesophageal atresia / stenosis with or without fistula				3.87	2.10	2.47
Small intestine atresia / stenosis				0.00	1.26	2.96
Anorectal atresia / stenosis				3.87	4.19	4.94
Undescended testis (36 weeks of gestation or later)				nr	nr	nr
Hypospadias				21.27	10.90	21.25
Epispadias				1.93	1.26	0.00
Indeterminate sex				1.93	0.84	0.99
Renal agenesis				0.00	1.68	1.48
Cystic kidney				1.93	5.03	1.98
Bladder exstrophy				0.00	0.00	0.00
Polydactyly, preaxial				15.47	15.51	16.80
Total Limb reduction defects (include unspecified)				5.80	5.45	7.41
Transverse				nr	nr	nr
Preaxial				nr	nr	nr
Postaxial				nr	nr	nr
Intercalary				nr	nr	nr
Mixed				nr	nr	nr
Unspecified				---	---	---
Diaphragmatic hernia				1.93	6.71	4.45
Omphalocele				1.93	2.94	0.99
Gastroschisis				3.87	0.42	0.99
Unspecified Omphalocele / Gastroschisis				---	---	---
Prune belly sequence				1.93	0.42	0.00
Trisomy 13				0.00	0.00	0.49
Trisomy 18				0.00	3.77	3.95
Down syndrome, all ages (include age unknown)				29.00	13.84	21.74
<20				0.00	0.00	17.09
20-24				0.00	0.00	0.00
25-29				5.45	3.61	10.47
30-34				21.57	17.64	24.58
35-39				114.19	46.20	65.82
40-44				312.50	83.19	182.93
45+				0.00	312.50	0.00
unspecified				---	---	---

* data include less than 5 years

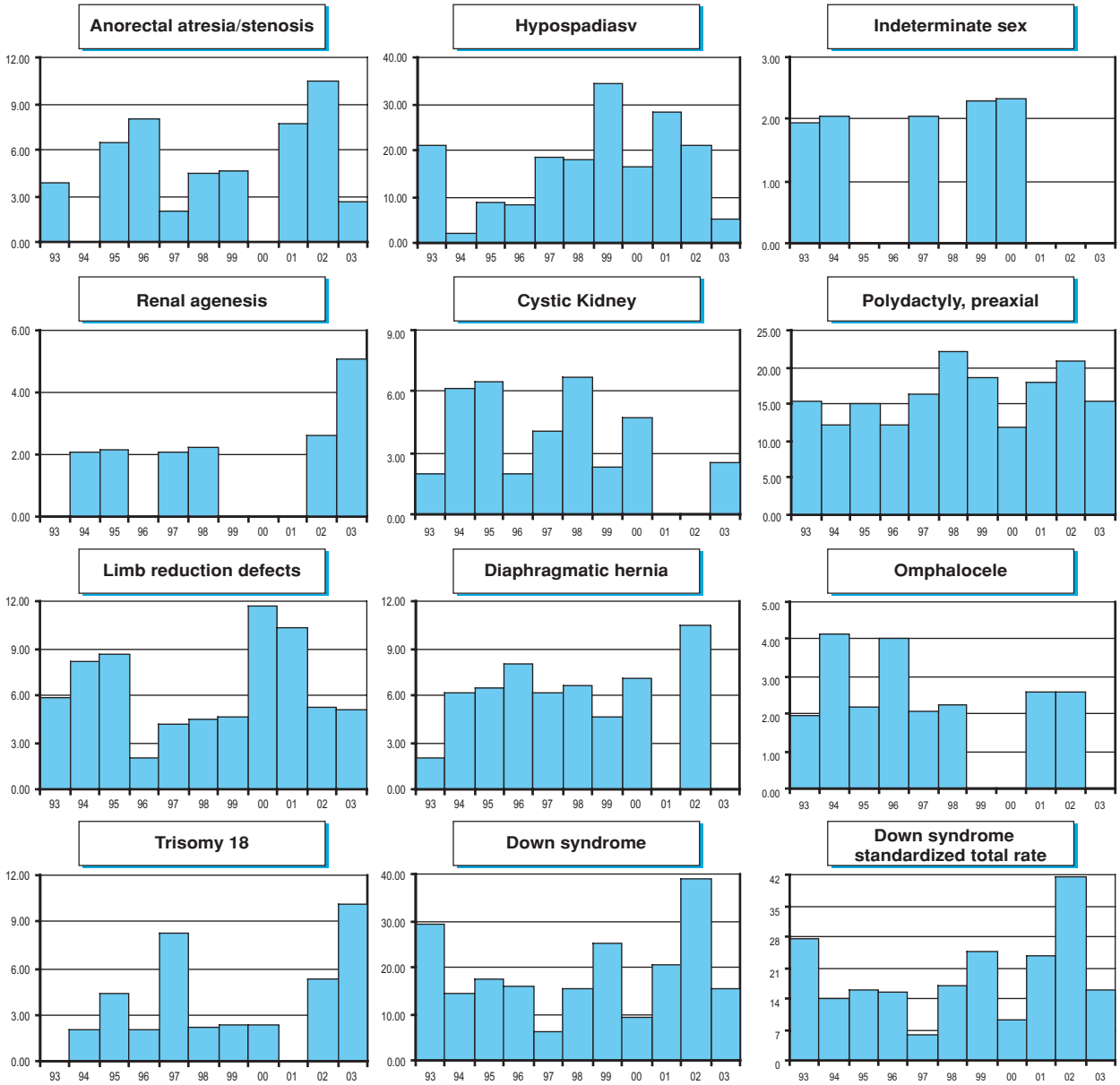
nr = not reported

Malta

'Time trends 1993-2003 (Birth prevalence rates per 10,000)



Note: L+S rates



Note: L+S rates

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 ICB-DMS 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.

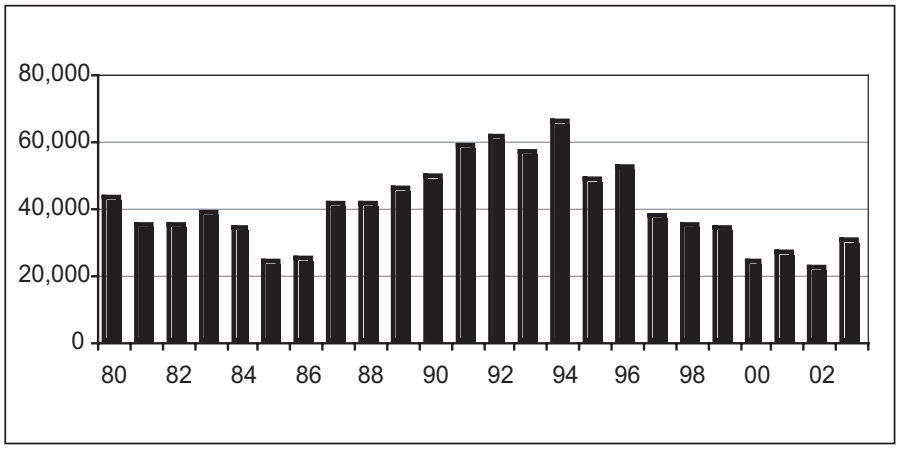
Phone: 52 5 5731200/ 52-5-5730611, 52-5-5737333 (ext 2426, 2425)

Fax: 52 5 6556138

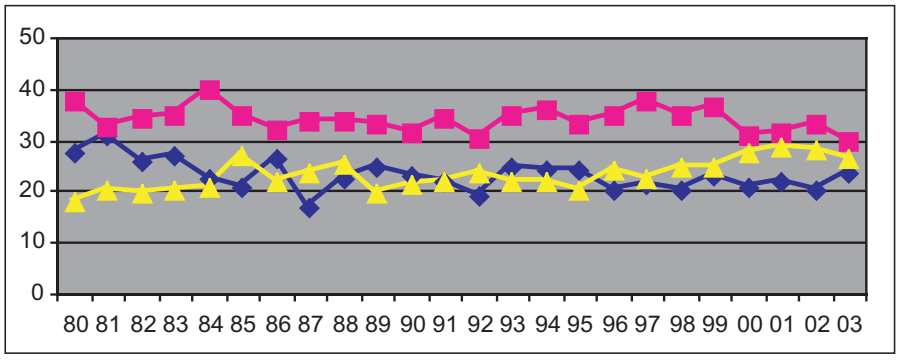
E-mail: osvaldo@servidor.unam.mx

Mexico: RYVEMCE

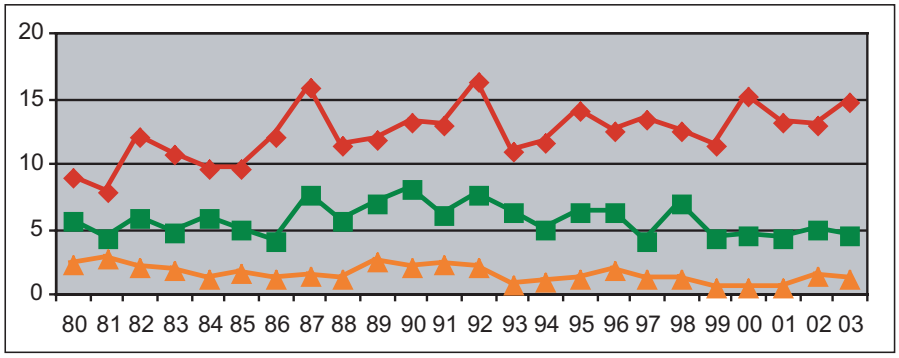
Total births by year



Percentage of births by maternal age



legenda: %births < 20 %births 20-24 %births 25-29



legenda: %births 30-34 %births 35-39 %births 40+

Mexico: RYVEMCE, 2003

Live births (LB)	29943
Stillbirths (SB)	369
Total births	30312
Number of terminations of pregnancy (ToP) for birth defects	not permitted

Birth Defects	Number of cases			Rates*10.000
	LB	SB	ToP	Total rate
Anencephaly	9	15		7.92
Spina bifida	23	3		8.58
Encephalocele	5	0		1.65
Microcephaly	5	2		2.31
Arhinencephaly / Holoprosencephaly	4	0		1.32
Hydrocephaly	12	2		4.62
Total Anophthalmos / Microphthalmos (include unspecified)	6	0		1.98
Anophthalmos	nr	nr		nr
Microphthalmos	nr	nr		nr
Total Anotia / Microtia (include unspecified)	22	1		7.59
Anotia	nr	nr		nr
Microtia	nr	nr		nr
Transposition of great vessels	1	0		0.33
Tetralogy of Fallot	nr	nr		nr
Hypoplastic left heart syndrome	1	0		0.33
Coarctation of aorta	nr	nr		nr
Choanal atresia, bilateral	2	0		0.66
Cleft palate without cleft lip	9	0		2.97
Cleft lip with or without cleft palate	40	2		13.86
Oesophageal atresia / stenosis with or without fistula	10	0		3.30
Small intestine atresia / stenosis	9	0		2.97
Anorectal atresia / stenosis	20	2		7.26
Undescended testis (36 weeks of gestation or later)	nr	nr		nr
Hypospadias	15	0		4.95
Epispadias	nr	nr		nr
Indeterminate sex	9	4		4.29
Renal agenesis	1	0		0.33
Cystic kidney	5	2		2.31
Bladder exstrophy	0	0		0.00
Polydactyly, preaxial	43	1		14.52
Total Limb reduction defects (include unspecified)	19	1		6.60
Transverse	8	0		2.64
Preaxial	4	1		1.65
Postaxial	0	0		0.00
Intercalary	1	0		0.33
Mixed	6	0		1.98
Unspecified	0	0		---
Diaphragmatic hernia	4	1		1.65
Total Abdominal wall defects (include unspecified)	nr	nr		nr
Omphalocele	7	2		2.97
Gastroschisis	13	2		4.95
Prune belly sequence	2	1		0.99
Trisomy 13	1	0		0.33
Trisomy 18	2	0		0.66
Down syndrome, all ages (include age unknown)	32	0		10.56
<20	4	0		5.59
20-24	7	0		7.82
25-29	4	0		5.01
30-34	11	0		24.57
35-39	5	0		37.37
40-44	1	0		27.78
45+	0	0		---

nr = not reported

Mexico: RYVEMCE, Previous years rates 1980 - 2003

Prevalence rates: (LB+SB) * 10,000

	1974-78	1979-83*	1984-88	1989-93	1994-98	1999-03
Births		**149,631**	**163,986**	**269,895**	**238,101**	**134,951**
Anencephaly		18.51	18.29	17.90	15.33	8.74
Spina bifida		14.37	17.32	17.97	13.99	10.74
Encephalocele		3.21	3.17	2.33	2.60	1.78
Microcephaly		2.34	3.05	1.82	1.72	2.07
Arhinencephaly / Holoprosencephaly		nr	nr	nr	0.13	1.11
Hydrocephaly		6.28	4.15	5.89	5.71	6.67
Total Anophthalmos / Microphthalmos (include unspecified)		2.47	2.01	1.70	1.39	1.70
Anophthalmos		nr	nr	nr	nr	nr
Microphthalmos		nr	nr	nr	nr	nr
Unspecified Anophthalmos / Microphthalmos		---	---	---	---	---
Total Anotia / Microtia (include unspecified)		6.75	5.98	7.00	6.13	7.48
Anotia		nr	nr	nr	nr	nr
Microtia		nr	nr	nr	nr	nr
Unspecified Anotia / Microtia		---	---	---	---	---
Transposition of great vessels		nr	nr	nr	0.12*	0.37
Tetralogy of Fallot		nr	nr	nr	nr	nr
Hypoplastic left heart syndrome		nr	nr	nr	0.00*	0.15
Coarctation of aorta		nr	nr	nr	nr	nr
Choanal atresia, bilateral		0.27	0.18	0.48	0.42	0.22
Cleft palate without cleft lip		3.54	3.17	3.93	2.98	2.45
Cleft lip with or without cleft palate		12.90	12.74	12.38	12.43	13.93
Oesophageal atresia / stenosis with or without fistula		1.34	1.40	2.59	1.97	2.30
Small intestine atresia / stenosis		0.74	0.67	1.15	1.51	1.78
Anorectal atresia / stenosis		3.94	4.21	5.11	4.75	4.89
Undescended testis (36 weeks of gestation or later)		nr	nr	nr	nr	nr
Hypospadias		4.28	3.90	4.93	4.41	3.33
Epispadias		nr	nr	nr	nr	nr
Indeterminate sex		1.67	2.01	2.22	2.48	2.74
Renal agenesis		nr	nr	nr	0.55	0.52
Cystic kidney		0.20	0.55	0.70	0.88	1.93
Bladder exstrophy		0.33	0.55	0.52	0.34	0.37
Polydactyly, preaxial		11.70	13.11	13.12	12.37*	13.63
Total Limb reduction defects (include unspecified)		6.55	5.92	6.19	5.46	6.00
Transverse		3.14	3.11	3.11	3.91	3.11
Preaxial		0.79	1.34	1.37	0.46	1.04
Postaxial		0.00	0.18	0.41	0.34	0.22
Intercalary		0.26	0.12	0.37	0.34	0.44
Mixed		2.10	0.79	0.67	0.34	1.11
Unspecified		---	---	---	---	---
Diaphragmatic hernia		0.53	0.67	1.04	1.05	1.11
Total Abdominal wall defects (include unspecified)		4.61	3.60	4.56	4.83	6.21*
Omphalocele		1.67	1.46	1.45	1.93	2.07
Gastroschisis		1.60	1.22	1.82	2.86	4.37
Unspecified Omphalocele / Gastroschisis		---	---	---	---	---
Prune belly sequence		1.34	0.91	1.30	0.55	0.96
Trisomy 13		0.40	0.24	0.19	0.13	0.37
Trisomy 18		0.67	0.55	0.41	0.25	0.22
Down syndrome, all ages (include age unknown)		12.70	13.17	13.89	12.73	11.28*
<20		7.44	10.00	8.23	6.98	7.68
20-24		5.52	5.77	6.78	7.02	5.49
25-29		7.86	7.43	10.19	8.58	7.73
30-34		15.69	15.32	15.91	13.32	17.76
35-39		55.31	46.10	40.94	50.65	43.99
40-44		112.36	186.47	153.85	167.36	154.00
45+		206.19	258.62*	103.63	184.62*	nr
unspecified		---	---	---	---	---

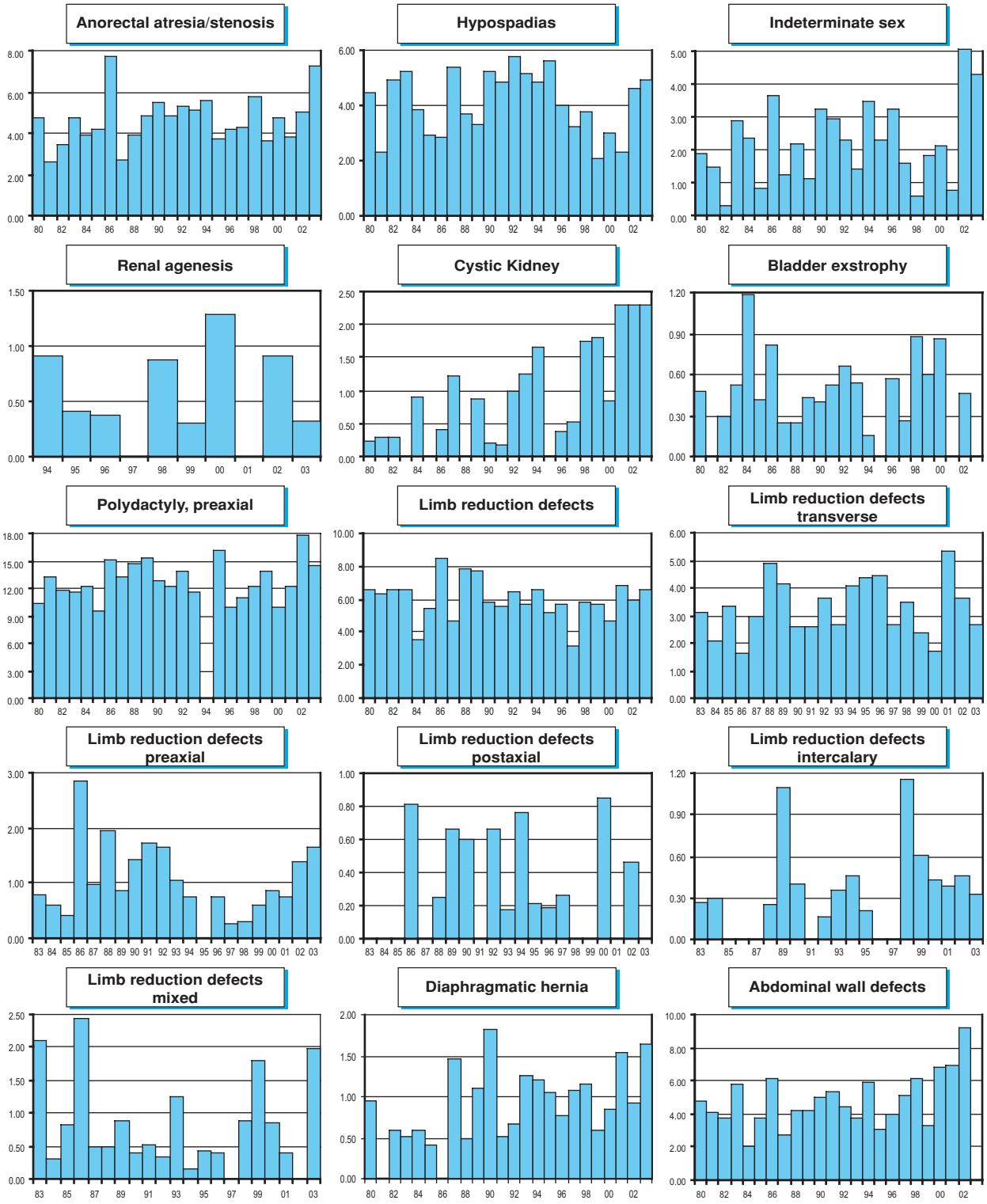
* data include less than 5 years

nr = not reported

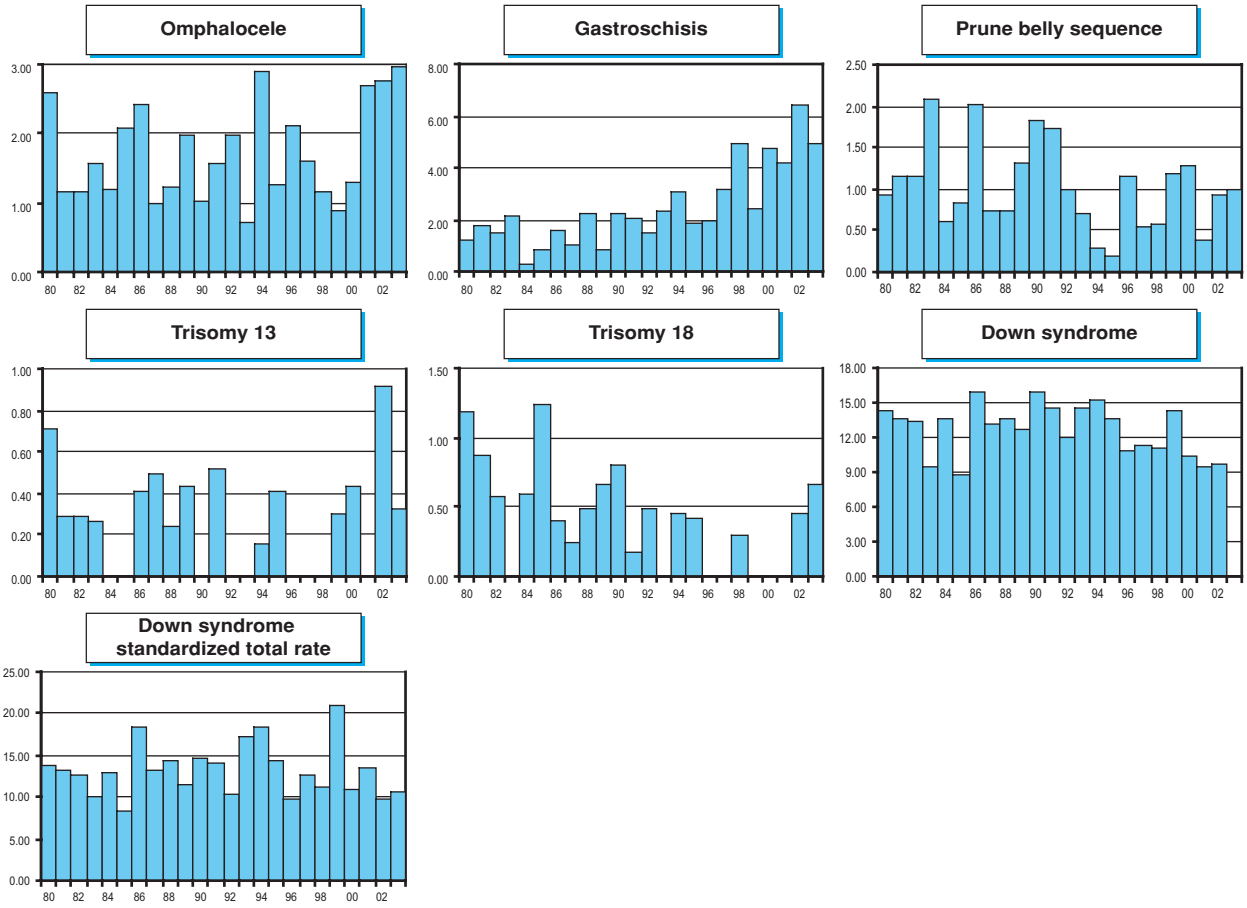
Mexico: RYVEMCE

'Time trends 1980-2003 (Birth prevalence rates per 10,000)

Note: L+S rates



Note: L+S rates



Note: L+S rates

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.

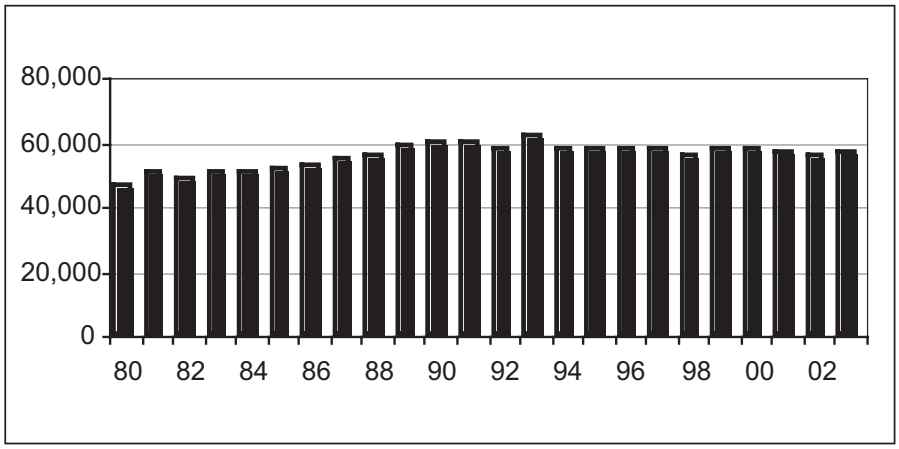
Phone: 64-4-495-4379

Fax: 64-4-495-4401

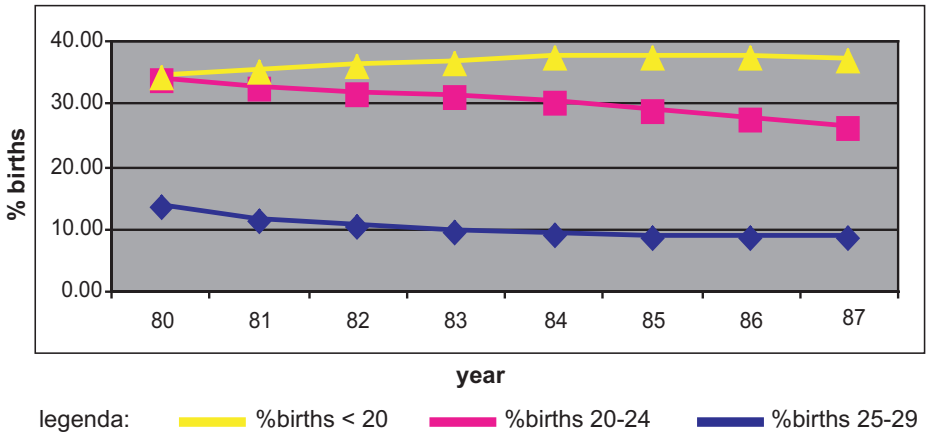
E-mail: barry_borman@moh,govt.nz

New Zealand

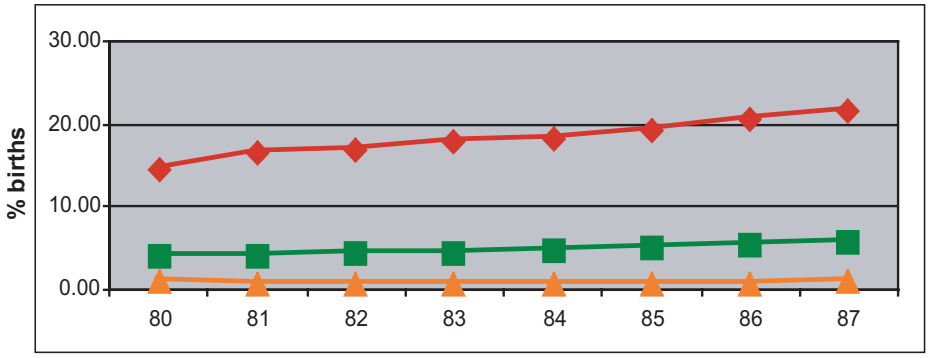
Total births by year



Percentage of births by maternal age



legenda: %births < 20 %births 20-24 %births 25-29



legenda: %births 30-34 %births 35-39 %births 40+

New Zealand, 2003

Live births (LB)	56134
Stillbirths (SB)	346
Total births	56480
Number of terminations of pregnancy (ToP) for birth defects	nr

Birth Defects	Number of cases			Rates*10.000
	LB	SB	ToP	Total rate
Anencephaly	1	nr	nr	0.18
Spina bifida	8	nr	nr	1.42
Encephalocele	2	nr	nr	0.35
Microcephaly	15	nr	nr	2.66
Arhinencephaly / Holoprosencephaly	nr	nr	nr	nr
Hydrocephaly	18	nr	nr	3.19
Anophthalmos	0	nr	nr	0.00
Microphthalmos	6	nr	nr	1.06
Unspecified Anophthalmos / Microphthalmos	0	nr	nr	---
Anotia	nr	nr	nr	nr
Microtia	nr	nr	nr	nr
Unspecified Anotia / Microtia	nr	nr	nr	---
Transposition of great vessels	27	nr	nr	4.78
Tetralogy of Fallot	25	nr	nr	4.43
Hypoplastic left heart syndrome	4	nr	nr	0.71
Coarctation of aorta	21	nr	nr	3.72
Choanal atresia, bilateral	6	nr	nr	1.06
Cleft palate without cleft lip	60	nr	nr	10.62
Cleft lip with or without cleft palate	40	nr	nr	7.08
Oesophageal atresia / stenosis with or without fistula	10	nr	nr	1.77
Small intestine atresia / stenosis	11	nr	nr	1.95
Anorectal atresia / stenosis	13	nr	nr	2.30
Undescended testis	445	nr	nr	78.79
Hypospadias & epispadias	182	nr	nr	32.22
Epispadias	nr	nr	nr	nr
Indeterminate sex	5	nr	nr	0.89
Renal agenesis	19	nr	nr	3.36
Cystic kidney	37	nr	nr	6.55
Bladder exstrophy	1	nr	nr	0.18
Polydactyly	60	nr	nr	10.62
Total Limb reduction defects (include unspecified)	18	nr	nr	3.19
Transverse	nr	nr	nr	nr
Preaxial	nr	nr	nr	nr
Postaxial	nr	nr	nr	nr
Intercalary	nr	nr	nr	nr
Mixed	nr	nr	nr	nr
Unspecified	nr	nr	nr	---
Diaphragmatic hernia	18	nr	nr	3.19
Omphalocele	nr	nr	nr	nr
Gastroschisis	nr	nr	nr	nr
Unspecified Omphalocele / Gastroschisis	nr	nr	nr	---
Prune belly sequence	nr	nr	nr	nr
Trisomy 13	1	nr	nr	0.18
Trisomy 18	6	nr	nr	1.06
Down syndrome, all ages (include age unknown)	53	nr	nr	9.38
<20	nr	nr	nr	nr
20-24	nr	nr	nr	nr
25-29	nr	nr	nr	nr
30-34	nr	nr	nr	nr
35-39	nr	nr	nr	nr
40-44	nr	nr	nr	nr
45+	nr	nr	nr	nr
unspecified	nr	nr	nr	---

nr = not reported

New Zealand, Previous years rates 1980 - 2003

Birth prevalence rates: (LB+SB) * 10,000

	1974-78	1979-83*	1984-88	1989-93	1994-98	1999-03
Births		**194,693**	**263,305**	**296,449**	**285,914**	**282,403**
Anencephaly		5.86	2.92	1.05	0.52	0.32
Spina bifida		11.30	7.79	3.88	3.57	2.23
Encephalocele		0.79	0.68	nr	0.35*	0.35
Microcephaly		nr	nr	nr	2.64*	2.90
Arhinencephaly / Holoprosencephaly		nr	nr	nr	nr	nr
Hydrocephaly		4.67	3.46	2.63	3.32	3.86
Anophthalmos		nr	nr	nr	0.00*	0.04
Microphthalmos		nr	nr	nr	0.59*	0.92
Unspecified Anophthalmos / Microphthalmos		---	---	---	---	---
Anotia		nr	nr	nr	nr	nr
Microtia		nr	nr	nr	nr	nr
Unspecified Anotia / Microtia		---	---	---	---	---
Transposition of great vessels		nr	0.55	nr	5.10*	4.96
Tetralogy of Fallot		nr	nr	nr	4.68*	4.14
Hypoplastic left heart syndrome		nr	0.82*		1.49*	1.13
Coarctation of aorta		nr	nr	nr	2.52*	2.90
Choanal atresia, bilateral		nr	nr	nr	0.70*	1.35
Cleft palate without cleft lip		6.11	7.60	5.46	6.54	10.16
Cleft lip with or without cleft palate		8.68	8.70	5.16	4.72	4.96
Oesophageal atresia / stenosis with or without fistula		1.75	1.94	2.02	2.45	1.42
Small intestine atresia / stenosis		nr	nr	nr	1.70*	1.90*
Anorectal atresia / stenosis		2.57	2.43	2.53	2.62	2.41
Undescended testis (36 weeks of gestation or later)		nr	nr	nr	58.10*	77.30
Hypospadias		12.89	13.79	11.77	18.63*	29.60
Epispadias		nr	nr	nr	nr	nr
Indeterminate sex		nr	nr	nr	0.53*	0.57
Renal agenesis		nr	0.34	nr	3.80*	3.01
Cystic kidney		nr	nr	nr	6.21*	5.77
Bladder exstrophy		nr	nr	nr	0.43*	0.32
Polydactyly, preaxial		nr	nr	nr	5.99*	10.47*
Total Limb reduction defects (include unspecified)		4.01	3.04	2.73	2.27	2.76
Transverse		nr	nr	nr	nr	nr
Preaxial		nr	nr	nr	nr	nr
Postaxial		nr	nr	nr	nr	nr
Intercalary		nr	nr	nr	nr	nr
Mixed		nr	nr	nr	nr	nr
Unspecified		---	---	---	---	---
Diaphragmatic hernia		0.99	1.60	nr	2.34*	2.62
Omphalocele		2.49	1.90	2.06	2.44*	nr
Gastroschisis		0.00	0.65	nr	nr	nr
Unspecified Omphalocele / Gastroschisis		---	---	---	---	---
Prune belly sequence		nr	nr	nr	nr	nr
Trisomy 13		nr	nr	nr	0.59*	0.28
Trisomy 18		nr	nr	nr	0.94*	1.27
Down syndrome, all ages (include age unknown)		8.22	9.68	9.49*	9.90	12.07
<20		4.20	7.29*	nr	nr	nr
20-24		4.64	3.76*	nr	nr	nr
25-29		7.99	9.04*	nr	nr	nr
30-34		10.00	9.11*	nr	nr	nr
35-39		29.63	34.94*	nr	nr	nr
40-44		60.98	221.38*	nr	nr	nr
45+		82.64	219.78*	nr	nr	nr
unspecified		---	---	---	---	---

* data include less than 5 years

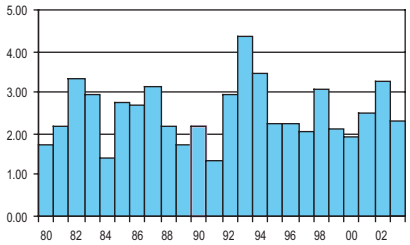
nr= not reported

New Zealand

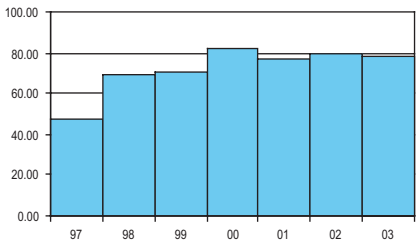
Time trends 1980-2003 (Birth prevalence rates per 10,000)

Note: L+S rates

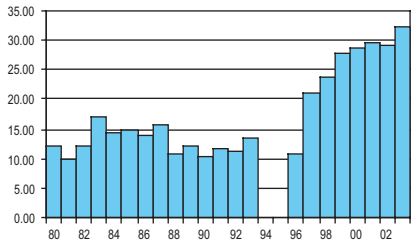
Anorectal atresia/stenosis



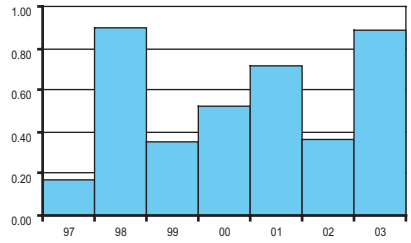
Undescended Testis



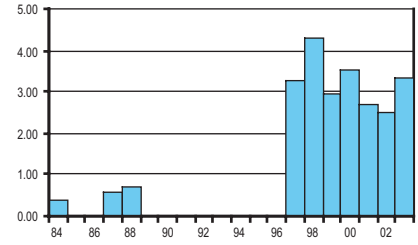
Hypospedies



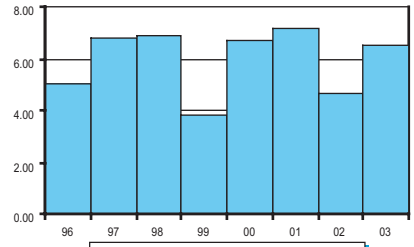
Indeterminate sex



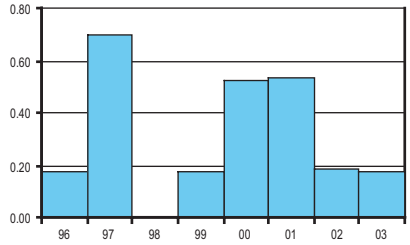
Renal agenesis



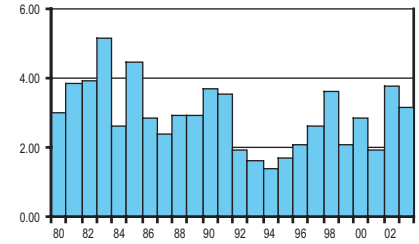
Cystic Kidney



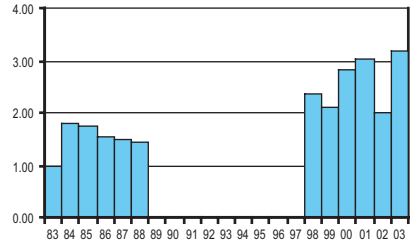
Bladder exstrophy



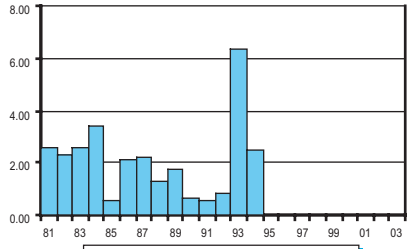
Limb reduction defects



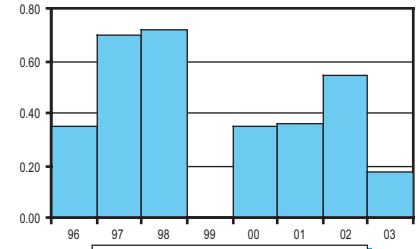
Diaphragmatic hernia



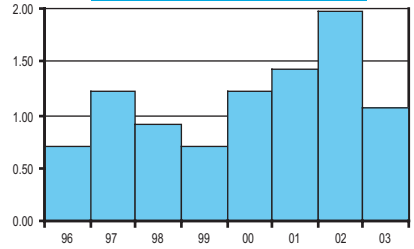
Omphalocele



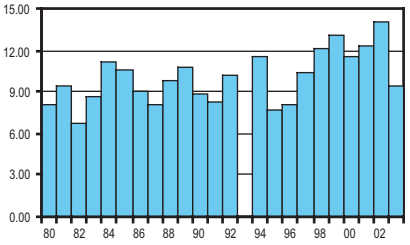
Trisomy 13



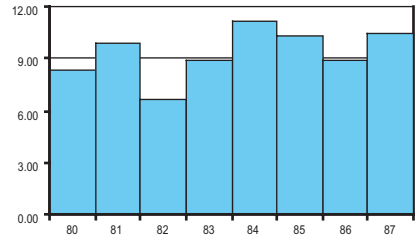
Trisomy 18



Down Syndrome



Down syndrome standardized total rete



Note: L+S rates

Northern Netherlands

EUROCAT Registration Northern Netherlands

History:
The programme started in 1981, and became a Clearinghouse member in 1993.

Size and coverage
In the beginning the programme covered 7,500 births annually in the province of Groningen and northern Drenthe. Coverage was gradually increased to 19,000 births annually in the provinces Groningen, Friesland and Drenthe from 1989 onwards. Home deliveries (35% 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 State University of Groningen.

Sources of ascertainment
The physician reporting the child is asked to fill out questions on parental drug use and other exposures. Furthermore, 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. to the registry on a voluntary basis. Informed consent of the parents is needed. Obstetricians, pediatricians, clinical geneticist, surgeons, general practitioners, midwives, well-baby clinics, pathologists and the national obstetric registry send information to the registry. Registry personnel is actively involved in data collection. No age limits are applied.

Exposure information
Questions on parental drug use, maternal and paternal occupation, diseases etc. are present at the standard notification form. The general practitioner is asked to complete this information in cases where the physician reporting the child did not fill in these questions.

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

Addresses and Staff

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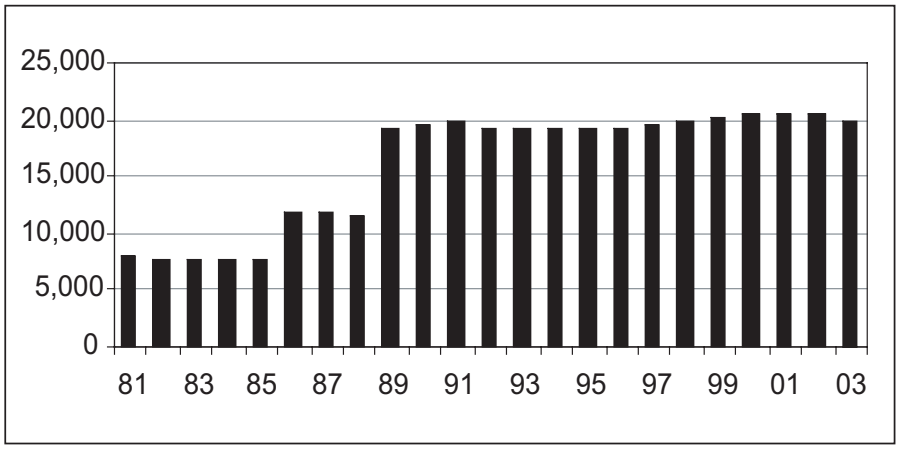
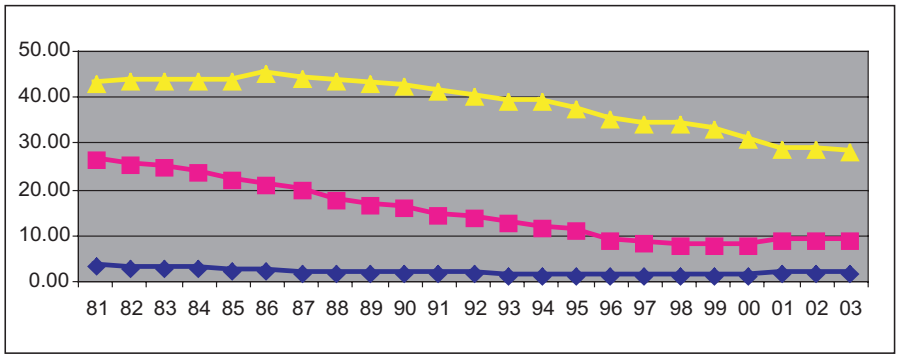
Website: www.eurocatnederland.nl

Northern Netherlands

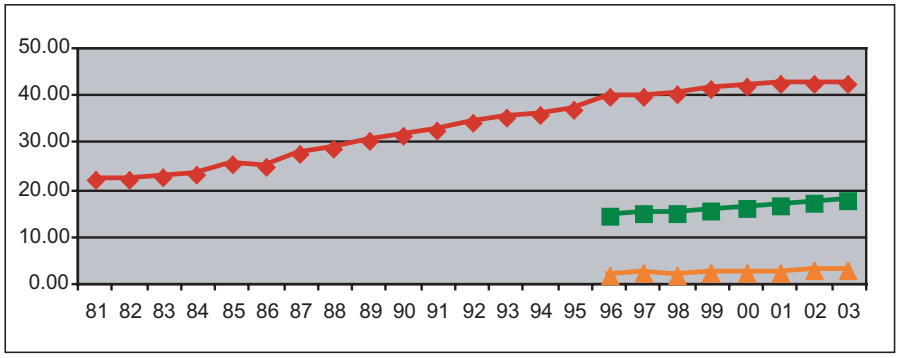
Total births by year



Percentage of births by maternal age



legenda: %births < 20 %births 20-24 %births 25-29



legenda: %births 30-34 %births 35-39 %births 40+

Northern Netherlands, 2003

Live births (LB)	19886
Stillbirths (SB)	119
Total births	20005
Number of terminations of pregnancy (ToP) for birth defects	30

Birth Defects	Number of cases			Rates*10.000
	LB	SB	ToP	Total rate
Anencephaly	2	1	1	2.00
Spina bifida	4	0	1	2.50
Encephalocele	0	0	0	0.00
Microcephaly	1	2	0	1.50
Arhinencephaly / Holoprosencephaly	1	1	0	1.00
Hydrocephaly	4	2	1	3.49
Anophthalmos	0	0	0	0.00
Microphthalmos	0	0	0	0.00
Unspecified Anophthalmos / Microphthalmos	0	0	0	---
Anotia	4	0	0	2.00
Microtia	2	0	0	1.00
Unspecified Anotia / Microtia	0	0	0	---
Transposition of great vessels	0	0	0	0.00
Tetralogy of Fallot	6	0	0	2.99
Hypoplastic left heart syndrome	1	0	1	1.00
Coarctation of aorta	10	0	1	5.49
Choanal atresia, bilateral	0	0	0	0.00
Cleft palate without cleft lip	14	0	2	7.99
Cleft lip with or without cleft palate	30	2	0	15.97
Oesophageal atresia / stenosis with or without fistula	12	0	1	6.49
Small intestine atresia / stenosis	3	0	1	2.00
Anorectal atresia / stenosis	0	0	0	0.00
Undescended testis (36 weeks of gestation or later)	1	0	0	0.50
Hypospadias	25	0	1	12.98
Epispadias	1	0	0	0.50
Indeterminate sex	2	1	0	1.50
Renal agenesis	3	0	2	2.50
Cystic kidney	5	0	0	2.50
Bladder exstrophy	2	0	0	1.00
Polydactyly, preaxial	0	0	0	0.00
Total Limb reduction defects (include unspecified)	11	2	1	6.99
Transverse	4	1	0	2.50
Preaxial	3	0	1	2.00
Postaxial	1	1	0	1.00
Intercalary	0	0	0	0.00
Mixed	0	0	0	0.00
Unspecified	3	0	0	---
Diaphragmatic hernia	2	0	0	1.00
Omphalocele	3	0	2	2.50
Gastroschisis	2	0	0	1.00
Unspecified Omphalocele / Gastroschisis	0	0	0	---
Prune belly sequence	0	0	0	0.00
Trisomy 13	1	1	0	1.00
Trisomy 18	3	2	5	4.99
Down syndrome, all ages (include age unknown)	12	0	10	10.98
<20	0	0	0	0.00
20-24	2	0	1	17.13
25-29	1	0	0	1.79
30-34	5	0	2	8.31
35-39	3	0	5	22.92
40-44	1	0	2	62.24
45+	0	0	0	0.00
unspecified	0	0	0	---

Northern Netherlands, Previous years rates 1981 - 2003

Prevalence rates: (LB+SB+TOP) * 10,000

	1974-78	1979-83*	1984-88	1989-93	1994-98	1999-03
Births		**23,150**	**50,729**	**97,108**	**97,054**	**101,617**
Anencephaly		6.48	5.91	2.16	3.30	2.66
Spina bifida		5.18	6.11	7.72	5.46	4.03
Encephalocele		2.16	1.38	1.13	0.62	0.49
Microcephaly		4.75	4.53	3.60	4.02	3.25
Arhinencephaly / Holoprosencephaly		1.30	1.58	0.51	0.72	1.38
Hydrocephaly		3.46	3.15	3.60	3.40	4.03
Anophthalmos		0.00	0.20	0.51	0.21	0.30
Microphthalmos		1.73	1.18	1.96	1.75	0.59
Unspecified Anophthalmos / Microphthalmos		---	---	---	---	---
Anotia		3.02	1.18	0.82	0.93	1.08
Microtia		0.86	0.59	1.13	0.82	0.98
Unspecified Anotia / Microtia		---	---	---	---	---
Transposition of great vessels		2.59	3.35	3.60	5.05	2.95
Tetralogy of Fallot		5.62	3.35	3.81	2.47	2.66
Hypoplastic left heart syndrome		3.46	2.17	2.37	2.27	2.36
Coarctation of aorta		6.91	4.93	5.35	5.46	3.84
Choanal atresia, bilateral		1.30	0.20	0.41	0.52	0.30
Cleft palate without cleft lip		9.50	6.11	7.41	6.29	7.38
Cleft lip with or without cleft palate		15.98	15.57	14.01	15.87	14.27
Oesophageal atresia / stenosis with or without fistula		3.02	2.96	2.47	4.02	3.74
Small intestine atresia / stenosis		3.02	3.15	2.37	2.37	2.16
Anorectal atresia / stenosis		2.16	3.75	2.78	3.50	2.46
Undescended testis (36 weeks of gestation or later)		2.16	1.97	1.65	1.34	1.57
Hypospadias		19.44	9.07	10.19	12.67	13.97
Epispadias		0.00	0.79	0.41	0.62	0.39
Indeterminate sex		0.00	0.39	0.21	0.52	0.39
Renal agenesis		2.59	5.52	4.02	4.43	4.72
Cystic kidney		1.30	4.14	4.94	4.95	2.95
Bladder exstrophy		0.00	0.20	0.31	0.10	0.30
Polydactyly, preaxial		1.73	1.58	1.96	1.96	1.77
Total Limb reduction defects (include unspecified)		7.78	4.73	6.69	5.67	6.40
Transverse		6.05	2.56	3.81	3.61	3.54
Preaxial		1.30	0.59	0.93	0.62	0.89
Postaxial		0.43	1.18	1.24	1.24	1.28
Intercalary		0.00	0.00	0.31	0.10	0.10
Mixed		0.00	0.39	0.41	0.10	0.30
Unspecified		---	---	---	---	---
Diaphragmatic hernia		1.73	3.35	2.16	3.92	1.48
Omphalocele		1.30	1.97	2.99	2.78	1.87
Gastroschisis		1.30	0.79	0.51	0.72	1.08
Unspecified Omphalocele / Gastroschisis		---	---	---	---	---
Prune belly sequence		0.43	0.20	0.51	0.21	0.39
Trisomy 13		0.43	0.99	1.44	0.93	0.98
Trisomy 18		2.59	2.37	1.85	3.19	3.64
Down syndrome, all ages (include age unknown)		9.94	15.97	13.59	15.35	14.76
<20		0.00	0.00	0.00	0.00	0.00
20-24		10.19	5.73	9.20	6.54	4.74
25-29		3.99	13.53	8.02	6.04	8.93
30-34		9.69	12.81	12.91	13.14	9.18
35-39		nr	nr	nr	43.91*	31.73
40-44		nr	nr	nr	113.64*	98.80
45+		nr	nr	nr	0.00*	243.90
unspecified		---	---	---	---	---

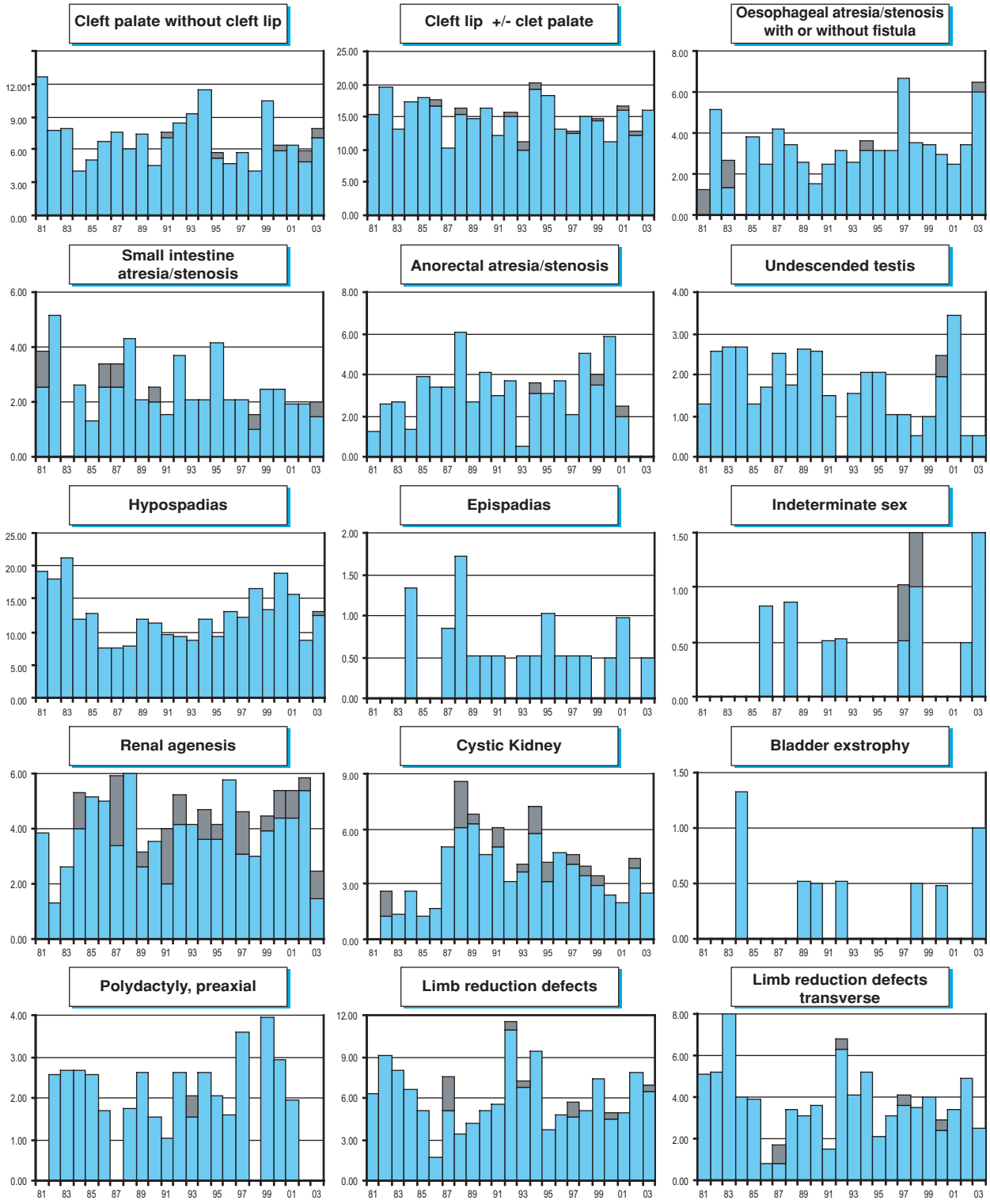
* data include less than 5 years

nr = not reported

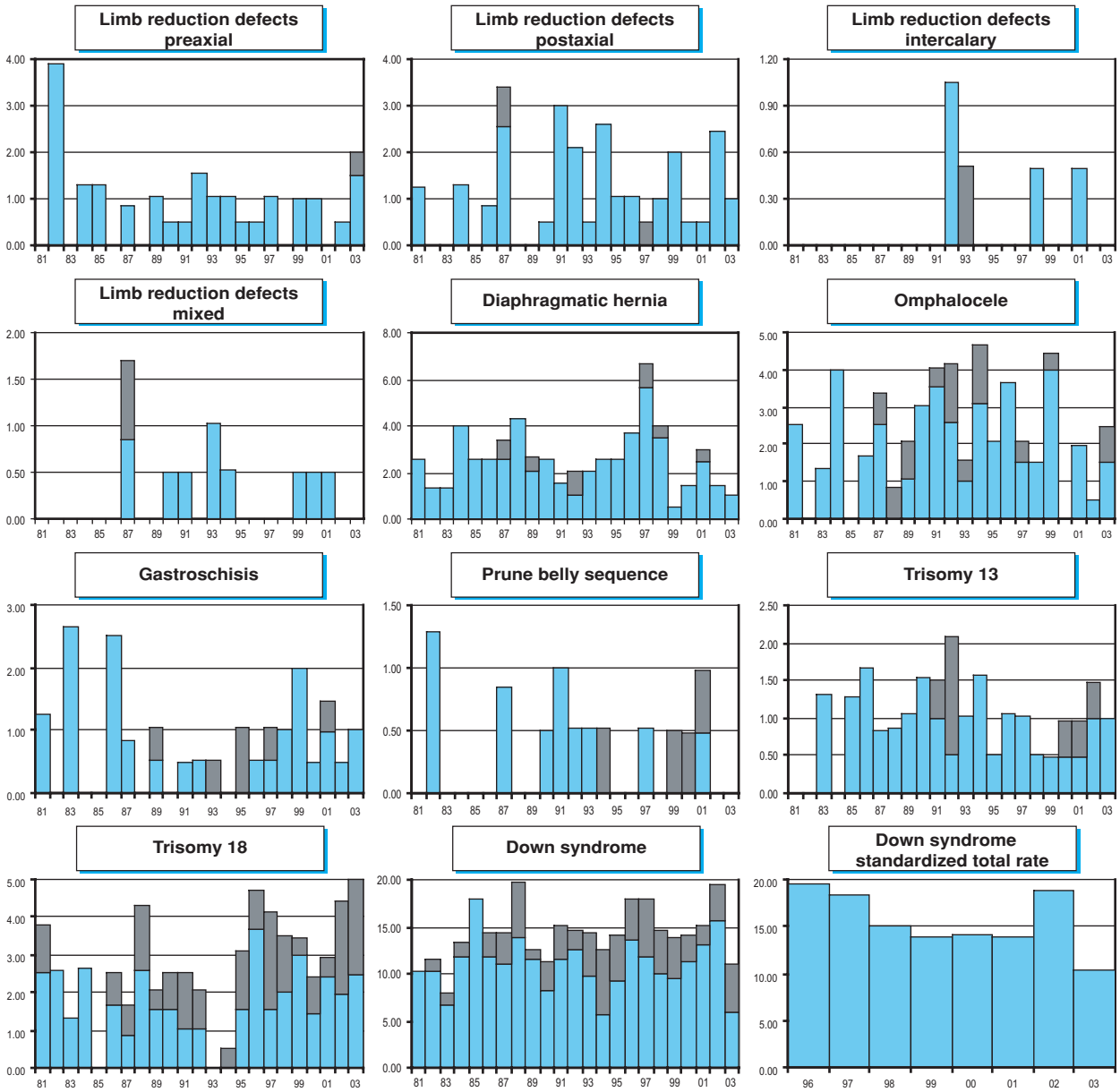
Northern Netherlands

'Time trends 1981-2003 (Birth prevalence rates per 10,000)

Note: L+S rates, ToP rates



Note: L+S rates, ToP rates



Note: L+S rates, ToP rates

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 12 weeks or more gestation are included.

Legislation and funding
The programme is run and funded by the governmental Norwegian Institute of Public Health in cooperation with the University of Bergen. Reporting is compulsory.

Sources of ascertainment
The registry is based on the medical notification of births from the delivery units and since 1999 also on reports from the neonatal units, gynaecological units (induced abortions) and IVF units (in vitro fertilization).

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

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

Addresses and Staff

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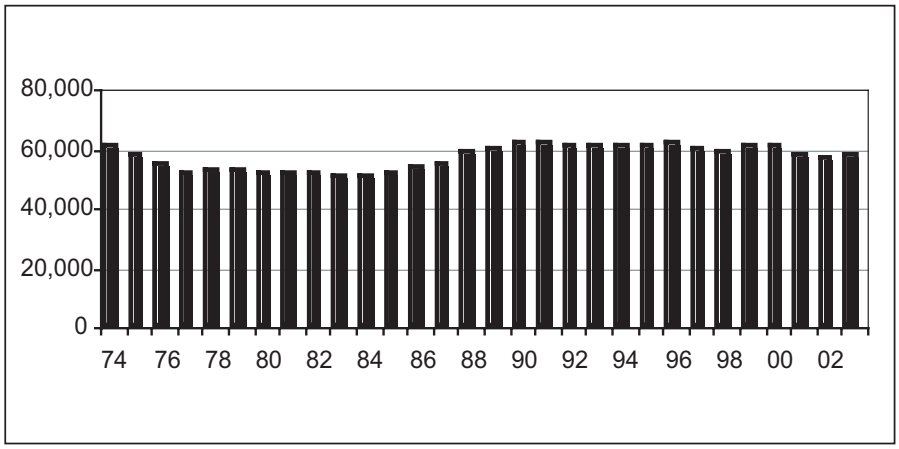
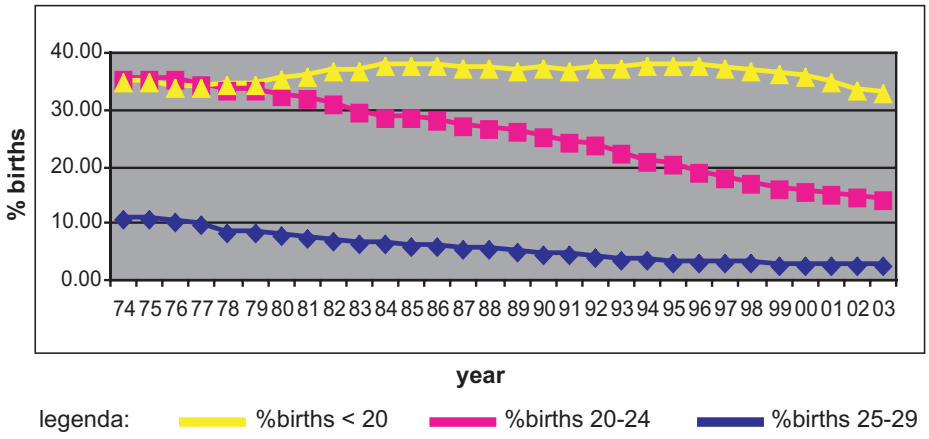
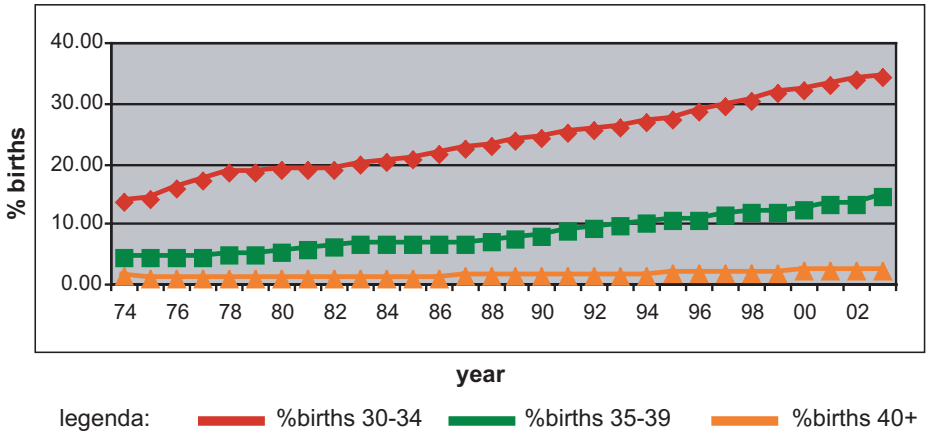
Norway

Total births by year



Percentage of births by maternal age





Norway, 2003

Live births (LB)	56989
Stillbirths (SB)	387
Total births	57376
Number of terminations of pregnancy (ToP) for birth defects	180

Birth Defects	Number of cases			Rates*10.000
	LB	SB	ToP	Total rate
Anencephaly	2	1	33	6.25
Spina bifida	17	0	10	4.69
Encephalocele	4	2	2	1.39
Microcephaly	5	1	1	1.22
Arhinencephaly / Holoprosencephaly	2	0	3	0.87
Hydrocephaly	24	0	16	6.95
Anophthalmos	0	0	0	0.00
Microphthalmos	2	1	0	0.52
Unspecified Anophthalmos / Microphthalmos	0	0	0	---
Anotia	1	0	0	0.17
Microtia	3	0	0	0.52
Unspecified Anotia / Microtia	nr	nr	nr	---
Transposition of great vessels	19	0	0	3.30
Tetralogy of Fallot	21	0	0	3.65
Hypoplastic left heart syndrome	10	1	7	3.13
Coarctation of aorta	7	0	0	1.22
Choanal atresia, bilateral	4	0	0	0.69
Cleft palate without cleft lip	30	0	0	5.21
Cleft lip with or without cleft palate	82	1	0	14.42
Oesophageal atresia / stenosis with or without fistula	9	0	1	1.74
Small intestine atresia / stenosis	4	0	0	0.69
Anorectal atresia / stenosis	15	0	0	2.61
Undescended testis (36 weeks of gestation or later)	174	0	0	30.23
Hypospadias	105	0	0	18.24
Epispadias	0	0	0	0.00
Indeterminate sex	3	1	0	0.69
Renal agenesis	0	0	1	0.17
Cystic kidney	24	1	8	5.73
Bladder exstrophy	2	0	0	0.35
Polydactyly, preaxial	47	0	0	8.17
Total Limb reduction defects (include unspecified)	26	0	3	5.04
Transverse	13	0	0	2.26
Preaxial	2	0	2	0.69
Postaxial	1	0	0	0.17
Intercalary	0	0	0	0.00
Mixed	12	0	1	2.26
Unspecified	0	0	0	---
Diaphragmatic hernia	12	2	3	2.95
Omphalocele	8	1	7	2.78
Gastroschisis	15	0	0	2.61
Unspecified Omphalocele/Gastroschisis	1	0	0	---
Prune belly sequence	7	0	1	1.39
Trisomy 13	3	1	1	0.87
Trisomy 18	6	0	2	1.39
Down syndrome, all ages (include age unknown)	73	6	29	18.76
<20	1	0	0	7.85
20-24	6	0	0	7.36
25-29	11	0	2	6.95
30-34	23	1	5	14.69
35-39	23	3	15	49.88
40-44	9	2	5	128.10
45+	0	0	2	377.36
unspecified	0	0	0	---

nr = not reported

Norway, Previous years rates 1974 - 2003

Birth prevalence rates: (LB+SB) * 10,000 until 1993
Birth prevalence rates: (LB+SB+TOP) * 10,000 since 1994

	1974-78	1979-83	1984-88	1989-93	1994-98	1999-03
Births	**275,304**	**256,698**	**267,316**	**303,808**	**300,662**	**291,947**
Anencephaly	4.00	3.86	2.32	1.42	3.03	5.04
Spina bifida	5.19	5.26	4.75	3.98	4.96	5.17
Encephalocele	0.44	0.74	0.52	0.53	0.67	0.99
Microcephaly	0.76	0.47	0.71	0.53	0.73	0.62
Arhinencephaly / Holoprosencephaly	0.04	0.23	0.34	0.56	1.00	0.69
Hydrocephaly	3.78	3.93	3.89	3.09	3.06	5.31
Anophthalmos	0.00	0.16	0.11	0.16	0.03	0.07
Microphthalmos	0.15	0.23	0.22	0.39	0.17	0.27
Unspecified Anophthalmos / Microphthalmos	---	---	---	---	---	---
Anotia	0.15	0.16	0.26	0.07	0.27	0.24
Microtia	nr	nr	1.39*	0.82	0.27	0.55
Unspecified Anotia / Microtia	---	---	---	---	---	---
Transposition of great vessels	0.33	0.78	1.08	2.11	1.76	3.53
Tetralogy of Fallot	0.15	0.19	0.45	1.05	1.23	2.95
Hypoplastic left heart syndrome	nr	nr	0.53*	1.48	1.93	3.08
Coarctation of aorta	nr	0.47	0.49	0.95	0.86	2.16
Choanal atresia, bilateral	0.18	0.31	0.71	0.49	0.43	0.62
Cleft palate without cleft lip	4.58	4.83	5.65	5.53	5.45	5.93
Cleft lip with or without cleft palate	14.06	14.53	13.88	13.07	13.87	12.95
Oesophageal atresia / stenosis with or without fistula	2.18	1.68	1.95	2.57	1.70	2.88
Small intestine atresia / stenosis	0.87	1.17	0.90	1.58	1.63	0.86
Anorectal atresia / stenosis	1.60	1.79	2.13	2.76	1.86	2.60
Undescended testis (36 weeks of gestation or later)	18.31	14.69	15.08	18.30	15.07	26.03
Hypospadias	12.39	13.48	16.68	15.47	14.47	16.68
Epispadias	0.25	0.31	0.45	0.23	0.33	0.27
Indeterminate sex	2.11	3.78	3.67	4.74	8.88	0.58
Renal agenesis	0.15	0.62	1.01	1.58	1.53	1.16
Cystic kidney	0.51	0.70	1.50	2.40	2.53	5.04
Bladder exstrophy	0.22	0.39	0.41	0.23	0.37	0.31
Polydactyly, preaxial	nr	nr	nr	nr	nr	8.19
Total Limb reduction defects (include unspecified)	7.92	7.48	7.89	6.45	6.85	4.28
Transverse	nr	nr	nr	3.42	3.43	2.02
Preaxial	nr	nr	nr	0.79	0.33	0.55
Postaxial	nr	nr	nr	0.69	0.43	0.10
Intercalary	nr	nr	nr	0.26	0.57	0.10
Mixed	nr	nr	nr	0.49	0.90	1.64
Unspecified	---	---	---	---	---	---
Diaphragmatic hernia	1.78	2.38	2.47	2.34	3.09	2.47
Omphalocele	2.51	1.83	2.13	1.88	2.26	2.43
Gastroschisis	1.23	1.32	1.95	1.94	2.93	2.67
Unspecified Omphalocele / Gastroschisis	---	---	---	---	---	---
Prune belly sequence	nr	nr	nr	nr	nr	1.23
Trisomy 13	nr	nr	nr	nr	nr	0.75
Trisomy 18	nr	nr	nr	nr	nr	1.13
Down syndrome, all ages (include age unknown)	9.44	10.40	10.85	10.47	11.47	16.27
<20	1.46	4.85	4.67	1.60	3.41	8.26
20-24	5.98	7.05	6.91	5.97	3.69	5.45
25-29	8.14	7.10	5.80	7.13	5.98	8.86
30-34	10.26	12.53	14.96	11.80	10.56	14.26
35-39	33.91	35.53	36.95	25.06	33.15	41.10
40-44	128.11	104.22	63.85	82.90	108.54	94.71
45+	182.93	94.34	294.12	416.67	138.89	328.64
unspecified	---	---	---	---	---	---

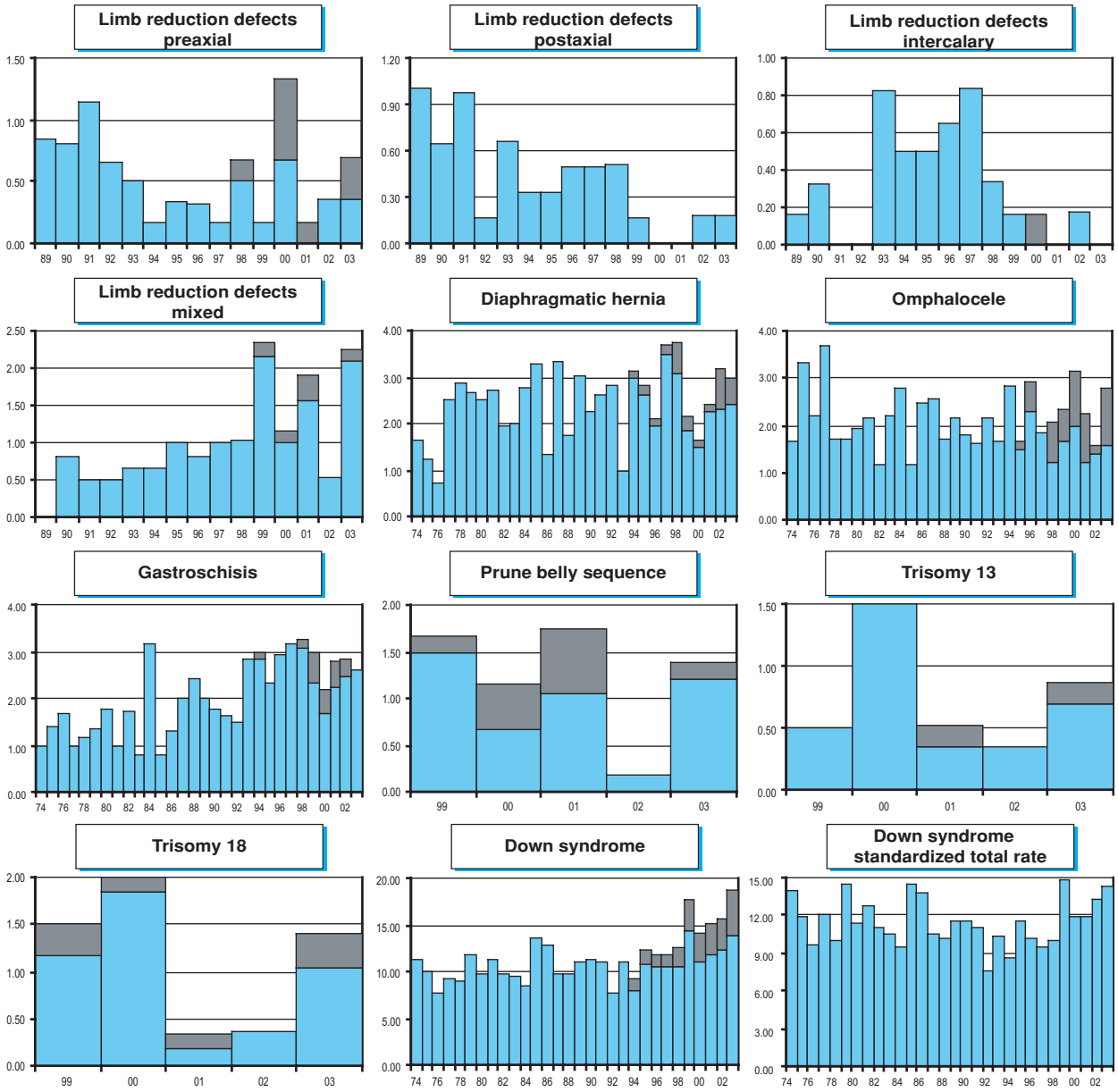
* data include less than 5 years
nr = not reported

Norway

'Time trends 1974-2003 (Birth prevalence rates per 10,000)

Note: L+S rates, ToP rates

Note: L+S rates, ToP rates



Note: L+S rates, ToP rates

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.
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: MRRCM, 2003

Live births (LB)	53751
Stillbirths (SB)	350
Total births	54101
Number of terminations of pregnancy (ToP) for birth defects	130

Birth Defects	Number of cases			Rates*10.000
	LB	SB	ToP	Total rate
Anencephaly	0	0	12	2.21
Spina bifida	14	1	4	3.50
Encephalocele	1	0	0	0.18
Microcephaly	5	0	1	1.11
Arhinencephaly / Holoprosencephaly	0	0	0	0.00
Hydrocephaly	19	4	10	6.09
Anophthalmos	1	0	0	0.18
Microphthalmos	0	0	0	0.00
Unspecified Anophthalmos / Microphthalmos	0	0	0	---
Anotia	0	0	0	0.00
Microtia	0	0	0	0.00
Unspecified Anotia / Microtia	5	0	0	---
Transposition of great vessels	10	0	1	2.03
Tetralogy of Fallot	5	0	0	0.92
Hypoplastic left heart syndrome	2	0	3	0.92
Coarctation of aorta	1	0	0	0.18
Choanal atresia, bilateral	4	0	0	0.74
Cleft palate without cleft lip	28	0	0	5.16
Cleft lip with or without cleft palate	41	0	0	7.56
Oesophageal atresia / stenosis with or without fistula	5	0	0	0.92
Small intestine atresia / stenosis	1	2	0	0.55
Anorectal atresia / stenosis	15	0	0	2.77
Undescended testis (36 weeks of gestation or later)	119	0	0	21.94
Hypospadias	72	0	0	13.28
Epispadias	1	0	0	0.18
Indeterminate sex	2	0	0	0.37
Renal agenesis	1	0	4	0.92
Cystic kidney	5	0	1	1.11
Bladder exstrophy	3	0	0	0.55
Polydactyly, preaxial	9	0	0	1.66
Total Limb reduction defects (include unspecified)	13	0	1	2.58
Transverse	3	0	1	0.74
Preaxial	2	0	0	0.37
Postaxial	2	0	0	0.37
Intercalary	0	0	0	0.00
Mixed	6	0	0	1.11
Unspecified	0	0	0	---
Diaphragmatic hernia	11	0	1	2.21
Omphalocele	8	0	2	1.84
Gastroschisis	6	0	6	2.21
Unspecified Omphalocele / Gastroschisis	26	0	0	---
Prune belly sequence	0	0	0	0.00
Trisomy 13	0	0	1	0.18
Trisomy 18	1	0	0	0.18
Down syndrome, all ages (include age unknown)	61	0	5	12.17
<20	4	0	0	6.14
20-24	14	0	0	6.73
25-29	4	0	0	2.61
30-34	14	0	0	17.55
35-39	15	0	1	56.86
40-44	6	0	3	152.80
45+	4	0	1	1851.85
unspecified	0	0	0	---

Slovak Republic

Congenital Malformations Monitoring Program of the Slovak Republic

History:
In Slovakia the collection of reports from delivery units and processing of data performs the Institution of Health Information and Statistics (IHIS). The obligation of reporting all groups of congenital malformations results from valid legislation norms. Reporting of congenital malformations began in 1964 year.
The programme of Slovak Teratological Information Center (STIC) was established in 2003 year and consists in cooperation of the Slovak Medical University, IHIS and the Center of Medical Genetics. Research collaboration began from 1995 year, under the responsibility of Elena Szabova.

Size and coverage
The registry covers all births in the area approximately 55.000 births annually according to the announcements of birth defects from delivery units.
The detail informations about cases of CM are collected in the Center of Medical Genetics, Bratislava from western regions of Slovakia (cca 15.000 births) by Eva Veghova, or under the running research projects at the Slovak Medical University.

Legislation and funding
Reporting is compulsory. Analysis of data is supported by grant projects.

Sources of ascertainment
Reports are received from delivery units, neonatal, pediatric clinics, or departments of clinical genetics.

Exposure Information
Detail information on maternal and paternal occupation, drug use, etc. are collected by interviews of case´s and control´s mothers only according to research projects.

Backround information
Some background information is available from the general population statistics.

Address for further Information

Elena Szabova, Programme Director Slovak Medical University Limbova 12 833 03 Bratislava, Slovak Republic

Phone: 00421 2 59369241

E-mail: elena.szabova@szu.sk

Contact for the Slovak Teratologic Information Center (STIC):

Elena Szabova

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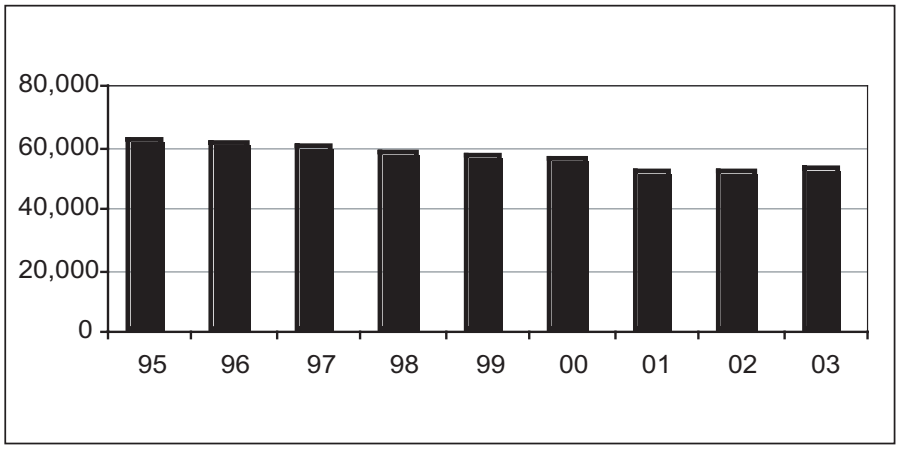
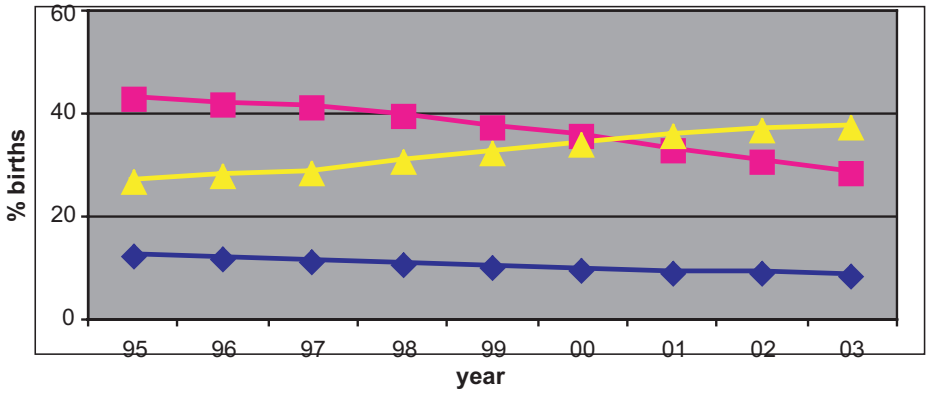
Phone: 00421 2 59369379

Slovak Republic

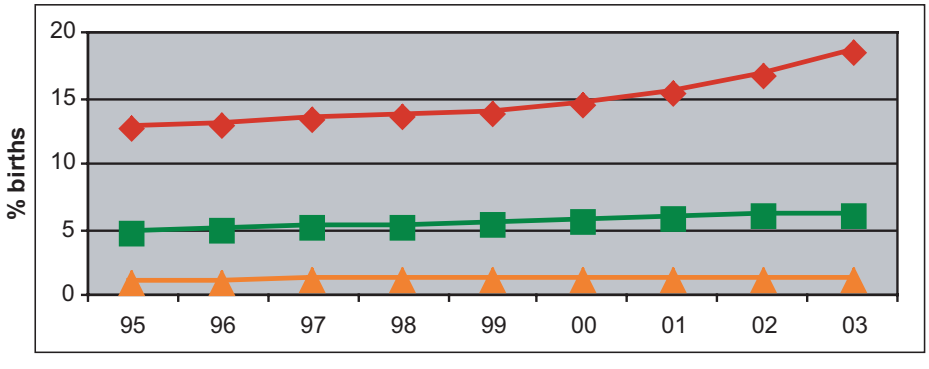
Total births by year



Percentage of births by maternal age



legenda: %births < 20 %births 20-24 %births 25-29



legenda: %births 30-34 %births 35-39 %births 40+

Slovak Republic, 2003

Live births (LB)	51713
Stillbirths (SB)	217
Total births	51930
Number of terminations of pregnancy (ToP) for birth defects	41

Birth Defects	Number of cases			Rates*10.000
	LB	SB	ToP	Total rate
Anencephaly	1	1	0	0.38
Spina bifida	11	0	1	2.31
Encephalocele	5	0	3	1.54
Microcephaly	6	1	0	1.35
Arhinencephaly / Holoprosencephaly	1	0	1	0.38
Hydrocephaly	17	4	1	4.23
Anophthalmos	0	0	0	0.00
Microphthalmos	3	0	0	0.58
Unspecified Anophthalmos / Microphthalmos	0	0	0	---
Anotia	1	0	0	0.19
Microtia	0	0	0	0.00
Unspecified Anotia / Microtia	0	0	0	---
Transposition of great vessels	10	0	0	1.92
Tetralogy of Fallot	9	0	0	1.73
Hypoplastic left heart syndrome	10	0	0	1.92
Coarctation of aorta	6	1	0	1.35
Choanal atresia, bilateral	0	0	0	0.00
Cleft palate without cleft lip	25	0	1	5.00
Cleft lip with or without cleft palate	62	0	0	11.93
Oesophageal atresia / stenosis with or without fistula	4	0	0	0.77
Small intestine atresia / stenosis	12	0	0	2.31
Anorectal atresia / stenosis	14	0	0	2.69
Undescended testis (36 weeks of gestation or later)	37	1	0	7.31
Hypospadias	114	1	0	22.13
Epispadias	1	0	0	0.19
Indeterminate sex	0	0	0	0.00
Renal agenesis	32	0	1	6.35
Cystic kidney	11	0	0	2.12
Bladder exstrophy	1	0	0	0.19
Polydactyly, preaxial	17	0	0	3.27
Total Limb reduction defects (include unspecified)	25	0	0	4.81
Transverse	nr	nr	nr	nr
Preaxial	nr	nr	nr	nr
Postaxial	nr	nr	nr	nr
Intercalary	nr	nr	nr	nr
Mixed	nr	nr	nr	nr
Unspecified	nr	nr	nr	---
Diaphragmatic hernia	10	0	0	1.92
Omphalocele	3	0	0	0.58
Gastroschisis	7	0	1	1.54
Unspecified Omphalocele / Gastroschisis	0	0	0	---
Prune belly sequence	3	0	0	0.58
Trisomy 13	2	0	0	0.38
Trisomy 18	3	0	1	0.77
Down syndrome, all ages (include age unknown)	63	0	7	13.47
<20	2	0	0	4.57
20-24	7	0	1	5.44
25-29	10	0	2	6.18
30-34	20	0	0	20.80
35-39	16	0	4	62.99
40-44	7	0	0	115.70
45+	1	0	0	370.37
unspecified	0	0	0	---

Note: data ToP are not quite exact because of not all reporting cases by gynecologists
nr = not reported

Slovak Republic, Previous years rates 1995 - 2003

Birth prevalence rates: (LB+SB+TOP) * 10,000

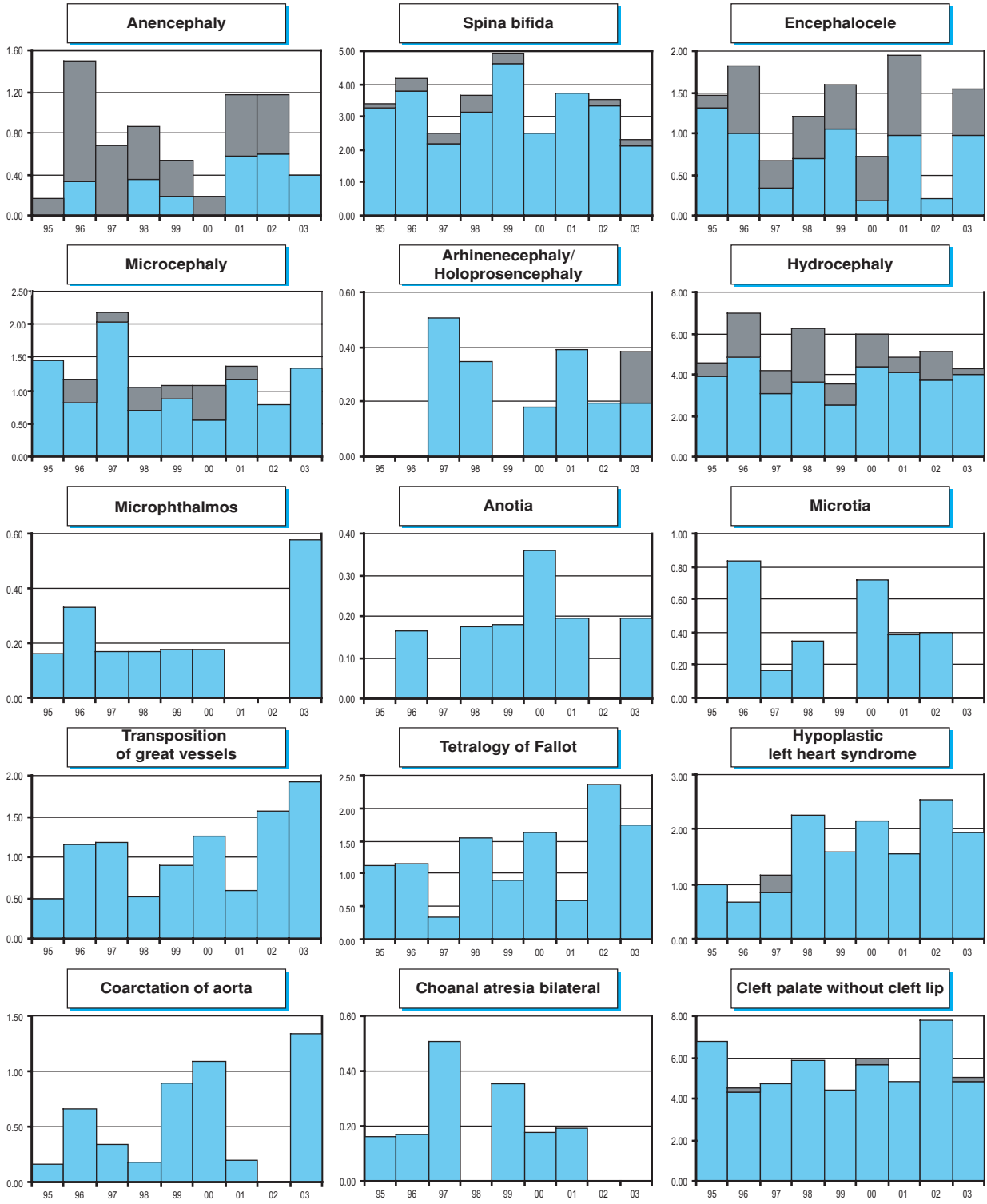
	1974-78	1979-83	1984-88	1989-93	1994-98*	1999-03
Births					**239,250**	**266,156**
Anencephaly					0.79	0.68
Spina bifida					3.43	3.42
Encephalocele					1.30	1.20
Microcephaly					1.46	1.13
Arhinencephaly / Holoprosencephaly					0.21	0.23
Hydrocephaly					5.48	4.73
Anophthalmos					0.04	0.08
Microphthalmos					0.21	0.19
Unspecified Anophthalmos / Microphthalmos					---	---
Anotia					0.08	0.19
Microtia					0.33	0.30
Unspecified Anotia / Microtia					---	---
Transposition of great vessels					0.84	1.24
Tetralogy of Fallot					1.04	1.43
Hypoplastic left heart syndrome					1.25	1.95
Coarctation of aorta					0.33	0.71
Choanal atresia, bilateral					0.21	0.15
Cleft palate without cleft lip					5.48	5.60
Cleft lip with or without cleft palate					10.07	10.82
Oesophageal atresia / stenosis with or without fistula					0.88	1.50
Small intestine atresia / stenosis					1.46	1.80
Anorectal atresia / stenosis					1.34	2.89
Undescended testis (36 weeks of gestation or later)					5.85	7.78
Hypospadias					23.78	22.28
Epispadias					0.17	0.19
Indeterminate sex					0.50	0.38
Renal agenesis					2.05	5.30
Cystic kidney					0.84	1.43
Bladder exstrophy					0.08	0.23
Polydactyly, preaxial					1.34	3.27
Total Limb reduction defects (include unspecified)					3.76	3.49
Transverse					nr	nr
Preaxial					nr	nr
Postaxial					nr	nr
Intercalary					nr	nr
Mixed					nr	nr
Unspecified					---	---
Diaphragmatic hernia					1.25	1.58
Omphalocele					0.63	0.60
Gastroschisis					0.79	1.16
Unspecified Omphalocele / Gastroschisis					---	---
Prune belly sequence					0.00	0.15
Trisomy 13					0.08	0.56
Trisomy 18					0.21	0.45
Down syndrome, all ages (include age unknown)					8.86	10.75
<20					5.86	6.92
20-24					6.17	4.88
25-29					6.20	7.29
30-34					12.81	12.67
35-39					31.43	45.78
40-44					59.57	107.24
45+					208.33	252.10
unspecified					---	---

* data include less than 5 years

nr = not reported

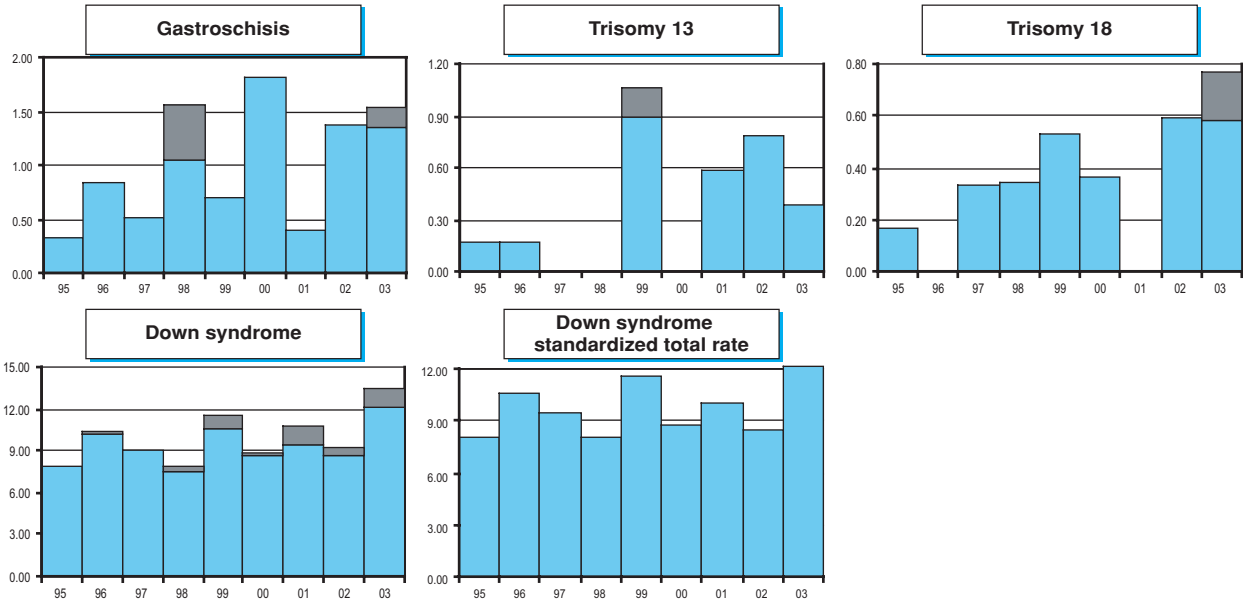
Slovak Republic

'Time trends 1995-2003 (Birth prevalence rates per 10,000)



Note: L+S rates, ToP rates

Note: L+S rates, ToP rates



Note: L+S rates, ToP rates

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.

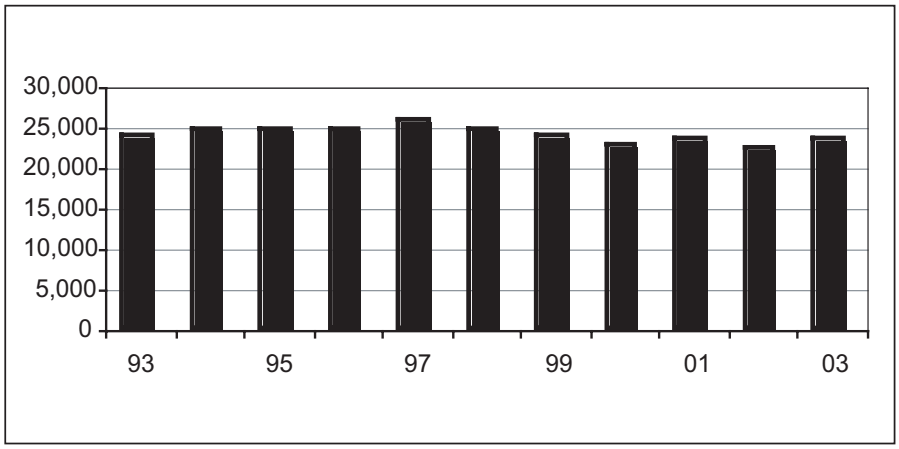
Phone: 27-21-4066275

Fax: 27-21-4066163

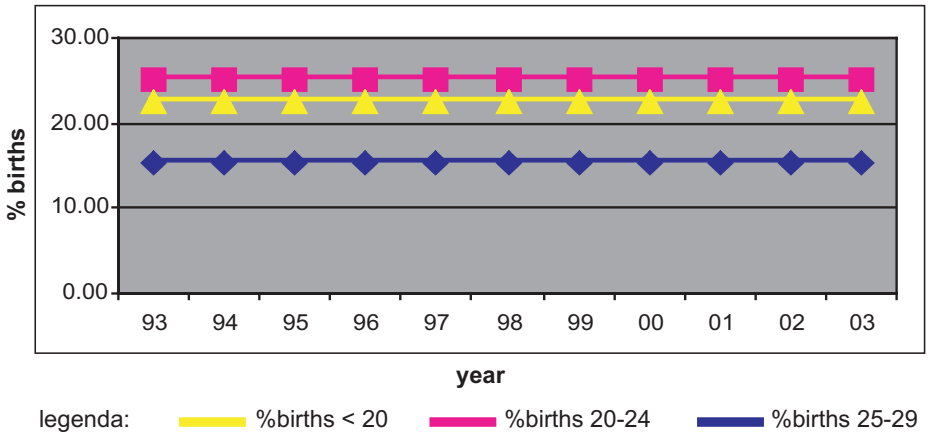
Email: rauf@phfm.uct.ac.za
db@phfm.uct.ac.za

South Africa: SABDSS

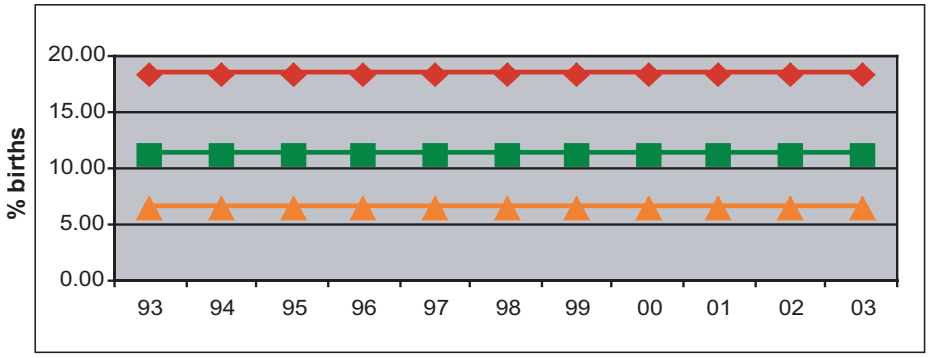
Total births by year



Percentage of births by maternal age



legenda: %births < 20 %births 20-24 %births 25-29



legenda: %births 30-34 %births 35-39 %births 40+

South Africa: SABDSS, 2003

Live births (LB)	23440
Stillbirths (SB)	nr
Total births	23440
Number of terminations of pregnancy (ToP) for birth defects	nr

Birth Defects	Number of cases			Rates*10.000
	LB	SB	ToP	Total rate
Anencephaly	8	nr	nr	3.41
Spina bifida	15	nr	nr	6.40
Encephalocele	3	nr	nr	1.28
Microcephaly	nr	nr	nr	nr
Arhinencephaly / Holoprosencephaly	3	nr	nr	1.28
Hydrocephaly	8	nr	nr	3.41
Anophthalmos	nr	nr	nr	nr
Microphthalmos	nr	nr	nr	nr
Unspecified Anophthalmos / Microphthalmos	nr	nr	nr	---
Anotia	nr	nr	nr	nr
Microtia	nr	nr	nr	nr
Unspecified Anotia / Microtia	nr	nr	nr	---
Transposition of great vessels	1	nr	nr	0.43
Tetralogy of Fallot	nr	nr	nr	nr
Hypoplastic left heart syndrome	nr	nr	nr	nr
Coarctation of aorta	nr	nr	nr	nr
Choanal atresia, bilateral	10	nr	nr	4.27
Cleft palate without cleft lip	6	nr	nr	2.56
Cleft lip with or without cleft palate	8	nr	nr	3.41
Oesophageal atresia / stenosis with or without fistula	3	nr	nr	1.28
Small intestine atresia / stenosis	3	nr	nr	1.28
Anorectal atresia / stenosis	19	nr	nr	8.11
Undescended testis (36 weeks of gestation or later)	3	nr	nr	1.28
Hypospadias	2	nr	nr	0.85
Epispadias	nr	nr	nr	nr
Indeterminate sex	1	nr	nr	0.43
Renal agenesis	2	nr	nr	0.85
Cystic kidney	1	nr	nr	0.43
Bladder exstrophy	1	nr	nr	0.43
Polydactyly, preaxial	nr	nr	nr	nr
Total Limb reduction defects (include unspecified)	1	nr	nr	0.43
Transverse	nr	nr	nr	nr
Preaxial	nr	nr	nr	nr
Postaxial	nr	nr	nr	nr
Intercalary	nr	nr	nr	nr
Mixed	nr	nr	nr	nr
Unspecified	nr	nr	nr	---
Diaphragmatic hernia	5	nr	nr	2.13
Omphalocele	11	nr	nr	4.69
Gastroschisis	4	nr	nr	1.71
Unspecified Omphalocele / Gastroschisis	0	nr	nr	---
Prune belly sequence	nr	nr	nr	nr
Trisomy 13	nr	nr	nr	nr
Trisomy 18	nr	nr	nr	nr
Down syndrome, all ages (include age unknown)	28	nr	nr	11.95
<20	4	nr	nr	11.05
20-24	1	nr	nr	1.71
25-29	7	nr	nr	13.29
30-34	1	nr	nr	2.32
35-39	4	nr	nr	15.33
40-44	4	nr	nr	35.40
45+	1	nr	nr	26.67
unspecified	6	nr	nr	---

nr = not reported

South Africa: SABDSS, Previous years rates 1993 - 2003

Birth prevalence rates: (LB) * 10,000

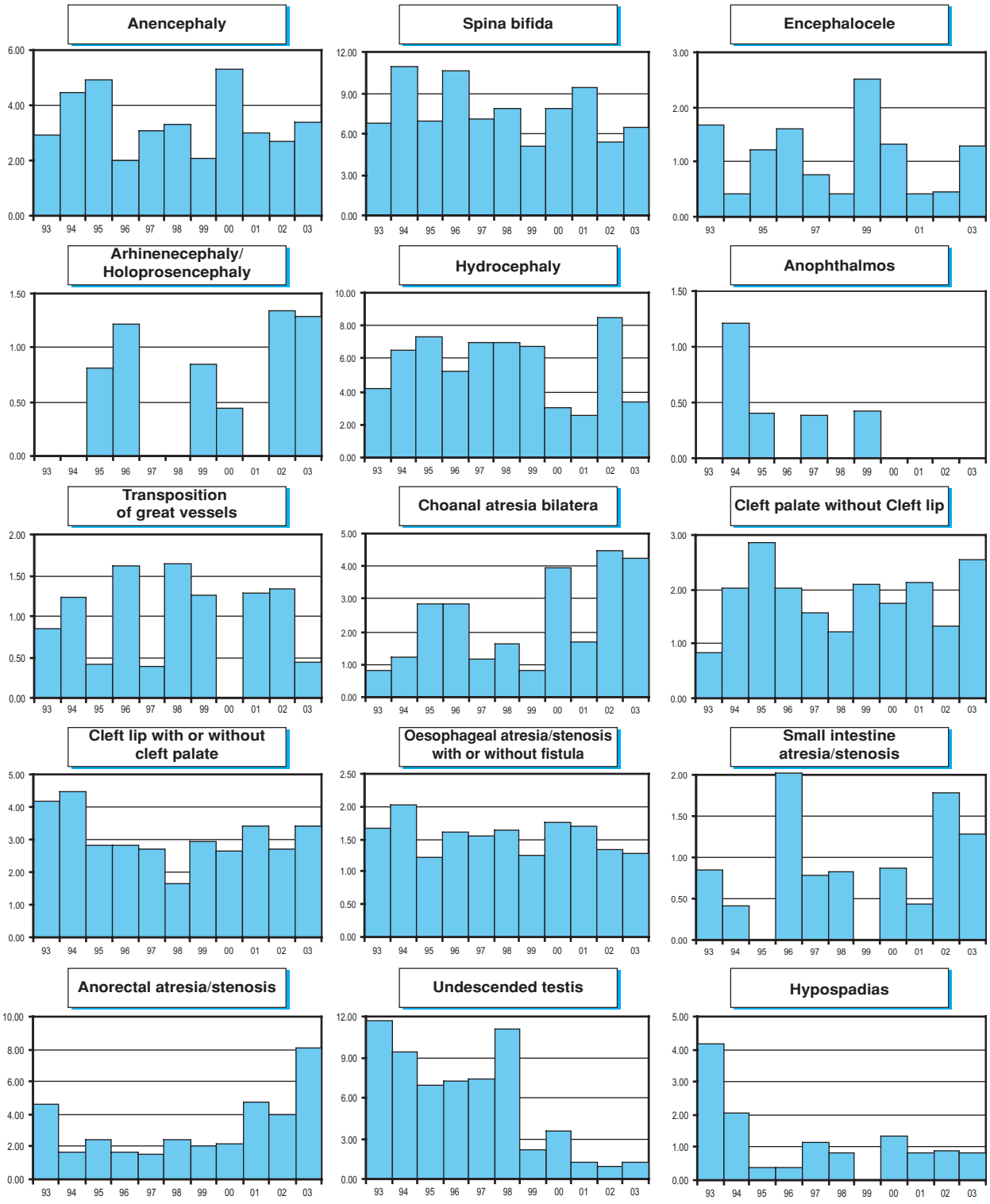
	1974-78	1979-83	1984-88	1989-93*	1994-98	1999-03
Total livebirths				**23,857**	**123,986**	**115,815**
Anencephaly				2.93	3.55	3.28
Spina bifida				6.71	8.63	6.82
Encephalocele				1.68	0.89	1.21
Microcephaly				nr	nr	nr
Arhinencephaly / Holoprosencephaly				0.00	0.40	0.78
Hydrocephaly				4.19	6.61	4.84
Anophthalmos				0.00	0.40	0.11
Microphthalmos				nr	nr	nr
Unspecified Anophthalmos / Microphthalmos				---	---	---
Anotia				nr	nr	nr
Microtia				nr	nr	nr
Unspecified Anotia / Microtia				---	---	---
Transposition of great vessels				0.84	1.05	0.86
Tetralogy of Fallot				nr	nr	nr
Hypoplastic left heart syndrome				nr	nr	nr
Coarctation of aorta				nr	nr	nr
Choanal atresia, bilateral				0.84	1.94	3.02
Cleft palate without cleft lip				0.84	1.94	1.99
Cleft lip with or without cleft palate				4.19	2.90	3.02
Oesophageal atresia / stenosis with or without fistula				1.68	1.61	1.47
Small intestine atresia / stenosis				0.84	0.81	0.86
Anorectal atresia / stenosis				4.61	1.94	4.23
Undescended testis (36 weeks of gestation or later)				11.74	8.39	1.81
Hypospadias				4.19	0.97	0.78
Epispadias				nr	nr	nr
Indeterminate sex				1.26	1.37	0.43
Renal agenesis				0.42	0.89	0.69
Cystic kidney				1.68	0.40	0.26
Bladder exstrophy				0.00	0.32	0.60
Polydactyly, preaxial				nr	nr	nr
Total Limb reduction defects (include unspecified)				4.19	4.36	1.47
Transverse				nr	nr	nr
Preaxial				nr	nr	nr
Postaxial				nr	nr	nr
Intercalary				nr	nr	nr
Mixed				nr	nr	nr
Unspecified				---	---	---
Diaphragmatic hernia				2.51	0.89	1.21
Omphalocele				1.26	2.02	4.23
Gastroschisis				0.84	1.29	1.64
Unspecified Omphalocele / Gastroschisis				---	---	---
Prune belly sequence				nr	nr	nr
Trisomy 13				nr	nr	nr
Trisomy 18				nr	nr	nr
Down syndrome, all ages (include age unknown)				8.38	8.95	8.98
<20				5.43	3.65	5.03
20-24				1.68	4.19	2.07
25-29				7.46	5.38	5.76
30-34				4.56	11.40	5.63
35-39				11.30	16.67	14.74
40-44				52.17	25.10	28.66
45+				26.18	10.08	26.98
unspecified				---	---	---

* data include less than 5 years

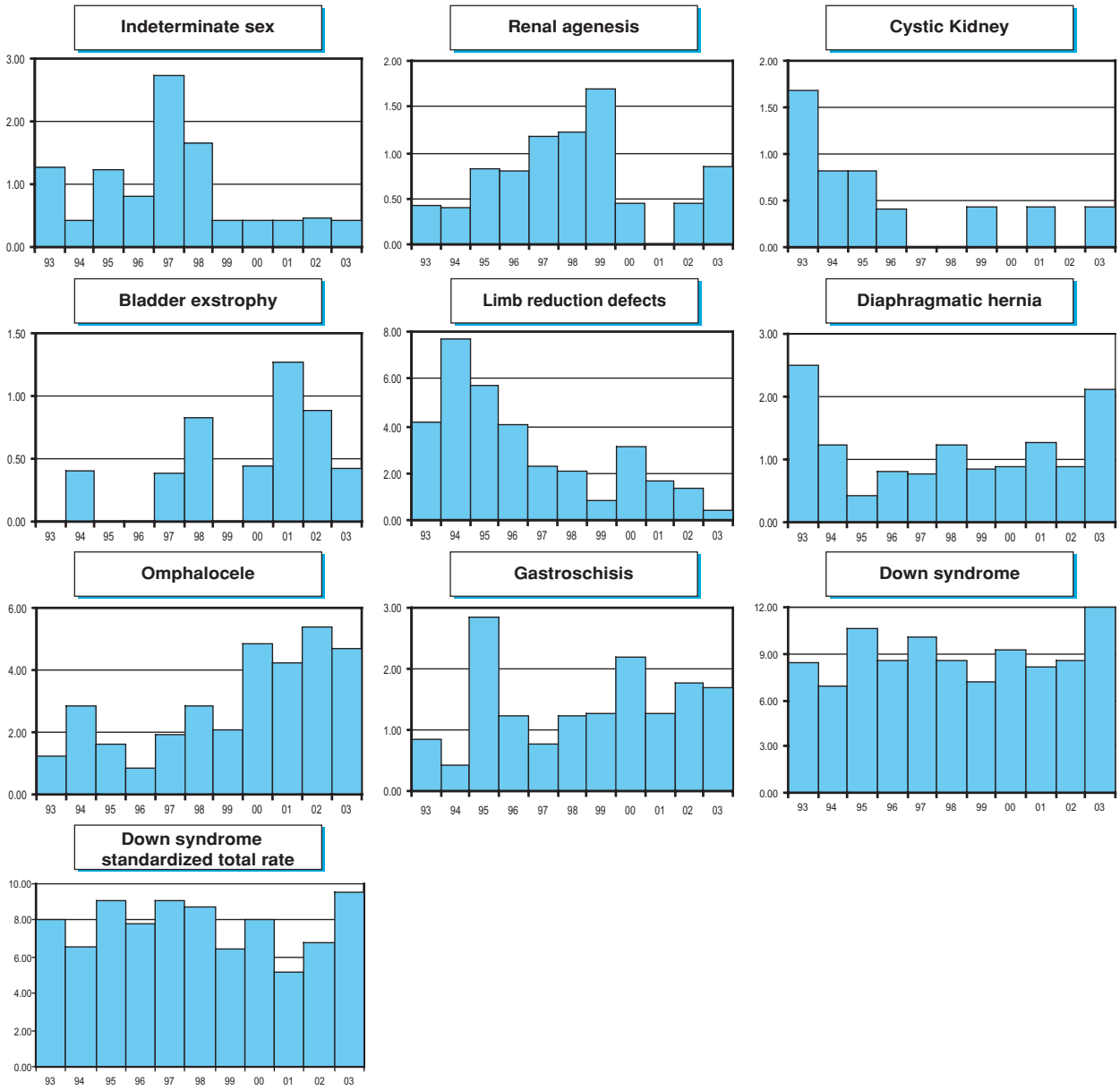
nr = not reported

South Africa: SABDSS

'Time trends 1993-2003 (Birth prevalence rates per 10,000)



Note: L+S rates



Note: L+S rates

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.

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Phone: 55-21-25984358

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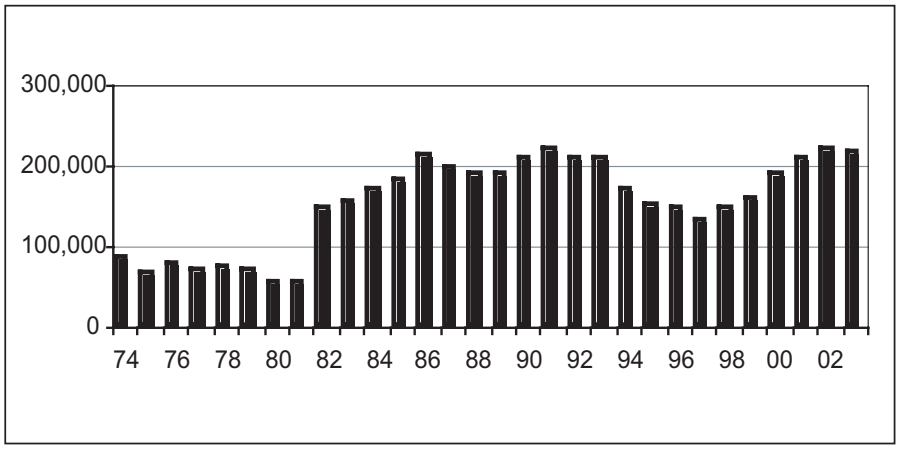
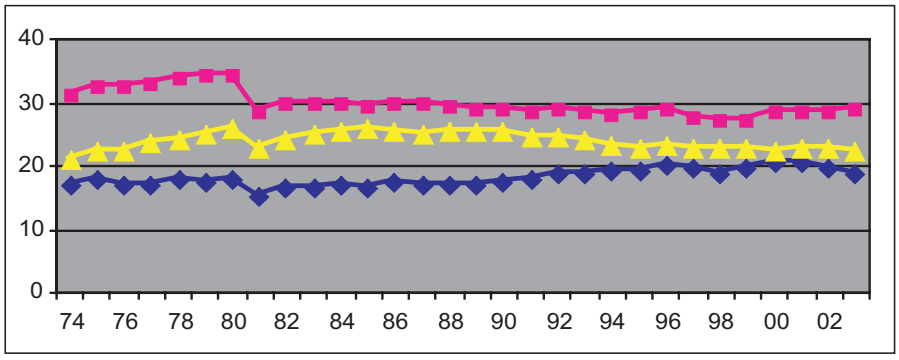
E-mail: castilla@centroin.com.br

South America: ECLAMC

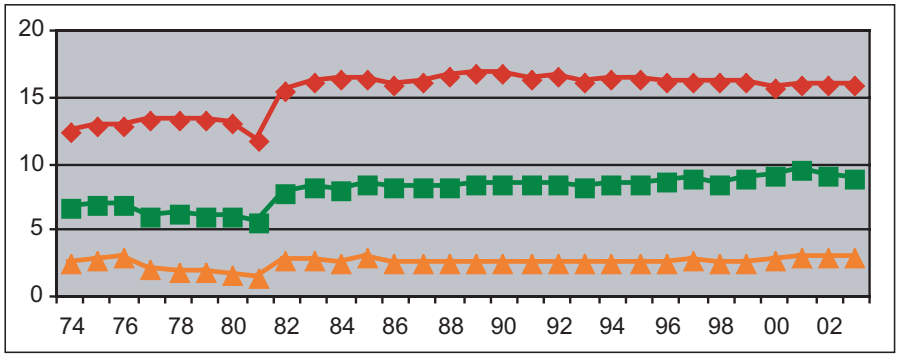
Total births by year



Percentage of births by maternal age



legenda: %births < 20 %births 20-24 %births 25-29



legenda: %births 30-34 %births 35-39 %births 40+

South America: ECLAMC, 2003

Live births (LB)	211607
Stillbirths (SB)	2638
Total births	214245
Number of terminations of pregnancy (ToP) for birth defects	not permitted

Birth Defects	Number of cases			Rates*10.000
	LB	SB	ToP	Total rate
Anencephaly	68	83		7.05
Spina bifida	215	9		10.46
Encephalocele	45	11		2.61
Microcephaly	89	3		4.29
Arhinencephaly / Holoprosencephaly	31	5		1.68
Hydrocephaly	242	23		12.37
Anophthalmos	10	5		0.70
Microphthalmos	24	4		1.31
Unspecified Anophthalmos / Microphthalmos	0	0		---
Anotia	6	2		0.37
Microtia	112	4		5.41
Unspecified Anotia / Microtia	0	0		---
Transposition of great vessels	31	1		1.49
Tetralogy of Fallot	37	0		1.73
Hypoplastic left heart syndrome	28	1		1.35
Coarctation of aorta	14	0		0.65
Choanal atresia, bilateral	6	0		0.28
Cleft palate without cleft lip	82	6		4.11
Cleft lip with or without cleft palate	273	20		13.68
Oesophageal atresia / stenosis with or without fistula	76	4		3.73
Small intestine atresia / stenosis	62	1		2.94
Anorectal atresia / stenosis	110	11		5.65
Undescended testis (36 weeks of gestation or later)	138	1		6.49
Hypospadias	108	0		5.04
Epispadias	4	0		0.19
Indeterminate sex	44	10		2.52
Renal agenesis	38	7		2.10
Cystic kidney	64	13		3.59
Bladder exstrophy	7	1		0.37
Polydactyly, preaxial	84	2		4.01
Total Limb reduction defects (include unspecified)	131	23		7.19
Transverse	76	11		4.06
Preaxial	25	6		1.45
Postaxial	7	2		0.42
Intercalary	9	1		0.47
Mixed	10	2		0.56
Unspecified	4	1		---
Diaphragmatic hernia	76	7		3.87
Omphalocele	62	17		3.69
Gastroschisis	69	4		3.41
Unspecified Omphalocele / Gastroschisis	23	5		---
Prune belly sequence	8	3		0.51
Trisomy 13	14	4		0.84
Trisomy 18	35	7		1.96
Down syndrome, all ages (include age unknown)	386	6		18.30
<20	28	0		6.95
20-24	52	0		8.45
25-29	55	0		11.46
30-34	51	0		15.03
35-39	104	3		56.63
40-44	82	2		151.41
45+	14	1		397.88
unspecified	0	0		---

South America: ECLAMC, Previous years rates 1974 - 2003

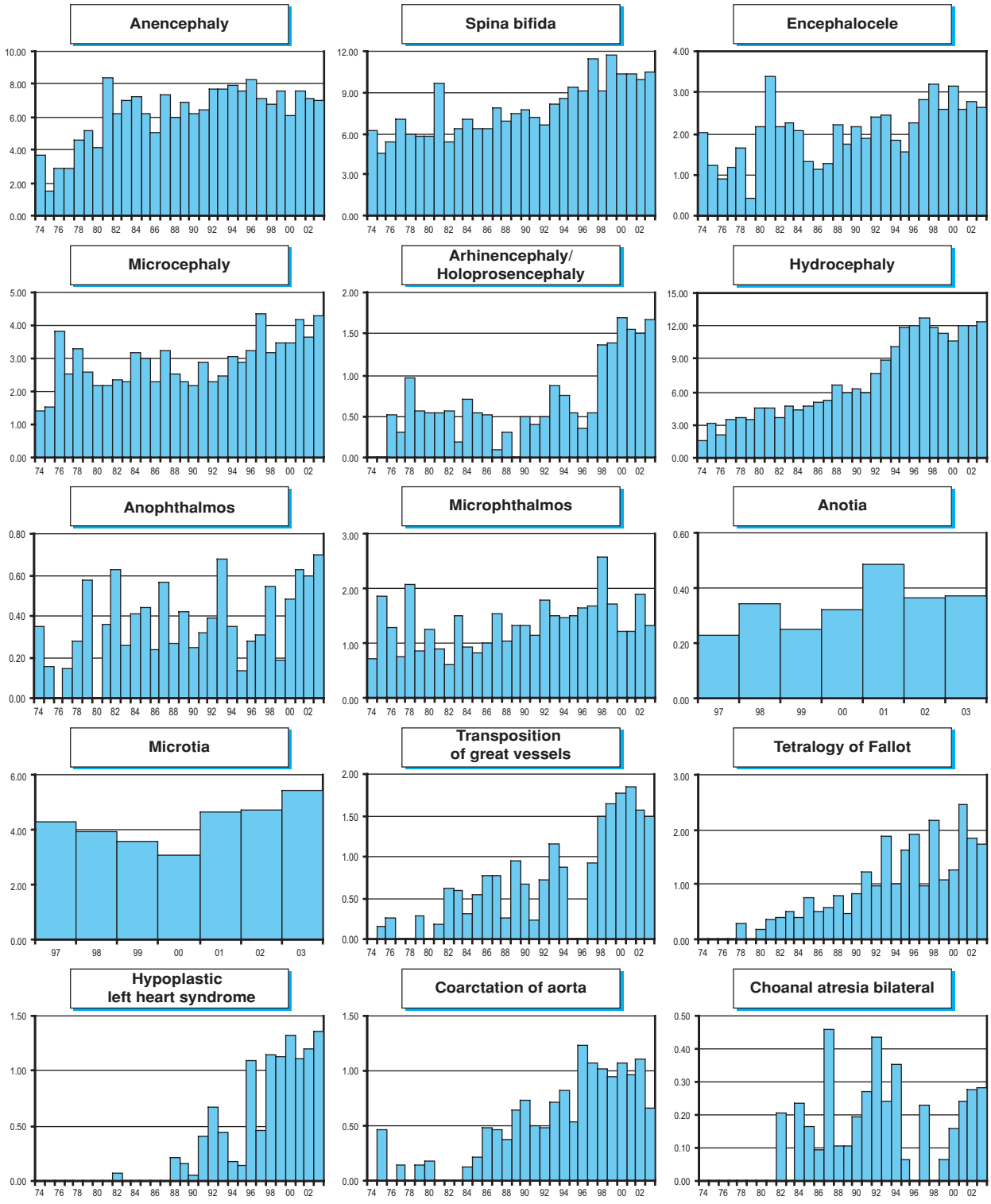
Prevalence rates: (LB+SB) * 10,000

	1974-78	1979-83	1984-88	1989-93	1994-98	1999-03
Births	**368,640**	**479,280**	**948,406**	**1,031,139**	**742,650**	**986,382**
Anencephaly	3.15	6.34	6.32	7.01	7.57	7.09
Spina bifida	5.83	6.26	6.89	7.45	9.44	10.50
Encephalocele	1.41	2.09	1.58	2.14	2.30	2.75
Microcephaly	2.52	2.32	2.84	2.43	3.31	3.82
Arhinencephaly / Holoprosencephaly	0.35	0.44	0.43	0.46	0.71	1.57
Hydrocephaly	2.77	4.13	5.22	6.96	11.65	11.71
Anophthalmos	0.19	0.40	0.38	0.41	0.32	0.54
Microphthalmos	1.30	1.04	1.08	1.41	1.76	1.46
Unspecified Anophthalmos / Microphthalmos	---	---	---	---	---	---
Anotia	nr	nr	nr	nr	0.29*	0.36
Microtia	nr	nr	nr	nr	4.09*	4.36
Unspecified Anotia / Microtia	nr	nr	nr	nr	0.04*	0.08
Transposition of great vessels	0.08	0.44	0.54	0.74	0.82*	1.65
Tetralogy of Fallot	0.05	0.35	0.61	1.09	1.54	1.71
Hypoplastic left heart syndrome	0.00	0.02	0.04	0.35	0.59	1.23
Coarctation of aorta	0.11	0.04	0.34	0.61	0.93	0.94
Choanal atresia, bilateral	0.00	0.06	0.21	0.25	0.13	0.21
Cleft palate without cleft lip	3.36	3.30	3.22	3.62	3.90	4.61
Cleft lip with or without cleft palate	11.01	10.56	10.90	10.18	12.00	13.43
Oesophageal atresia / stenosis with or without fistula	2.01	2.36	2.57	2.89	3.23	3.65
Small intestine atresia / stenosis	0.43	1.52	1.47	1.75	1.87	2.85
Anorectal atresia / stenosis	2.60	3.86	3.48	4.41	4.74	5.57
Undescended testis (36 weeks of gestation or later)	1.41	2.84	4.59	4.60	5.10	6.56
Hypospadias	3.69	4.01	4.56	4.06	5.00	5.16
Epispadias	0.16	0.25	0.33	0.36	0.19	0.21
Indeterminate sex	1.00	1.96	2.17	1.76	1.71	2.24
Renal agenesis	0.43	0.63	0.76	1.52	2.06	2.37
Cystic kidney	0.62	0.79	1.49	1.84	3.39	4.28
Bladder exstrophy	0.14	0.19	0.28	0.23	0.38	0.34
Polydactyly, preaxial	3.09	2.15	2.44	2.73	2.85	3.69
Total Limb reduction defects (include unspecified)	4.10	5.57	4.83	5.23	6.19	6.60
Transverse	2.03	2.61	2.69	2.62	3.11	3.52
Preaxial	0.62	1.13	0.98	0.99	1.48	1.54
Postaxial	0.24	0.58	0.24	0.46	0.38	0.41
Intercalary	0.57	0.63	0.35	0.48	0.47	0.46
Mixed	0.52	0.54	0.44	0.58	0.61	0.46
Unspecified	---	---	---	---	---	---
Diaphragmatic hernia	0.57	1.44	1.52	1.99	3.39	3.93
Omphalocele	1.06	1.90	2.22	2.35	3.10	3.35
Gastroschisis	0.05	0.31	0.67	0.93	2.37	3.03
Unspecified Omphalocele / Gastroschisis	---	---	---	---	---	---
Prune belly sequence	0.03	0.46	0.66	0.75	1.10	1.09
Trisomy 13	0.16	0.38	0.53	0.46	0.89	0.90
Trisomy 18	0.27	0.54	0.98	0.90	1.64	2.15
Down syndrome, all ages (include age unknown)	14.38	14.90	15.03	15.49	17.77	19.11
<20	7.38	7.20	6.72	6.79	8.08	7.11
20-24	7.32	7.18	6.45	7.84	8.33	9.56
25-29	7.24	7.90	7.32	8.34	9.68	10.18
30-34	12.49	17.08	15.56	15.36	16.48	17.01
35-39	56.73	47.71	43.27	45.90	50.73	55.80
40-44	152.66	149.92	155.47	140.61	181.56	167.56
45+	260.99	299.79	274.29	253.44	303.29	387.17
unspecified	---	---	---	---	---	---

* data include less than 5 years

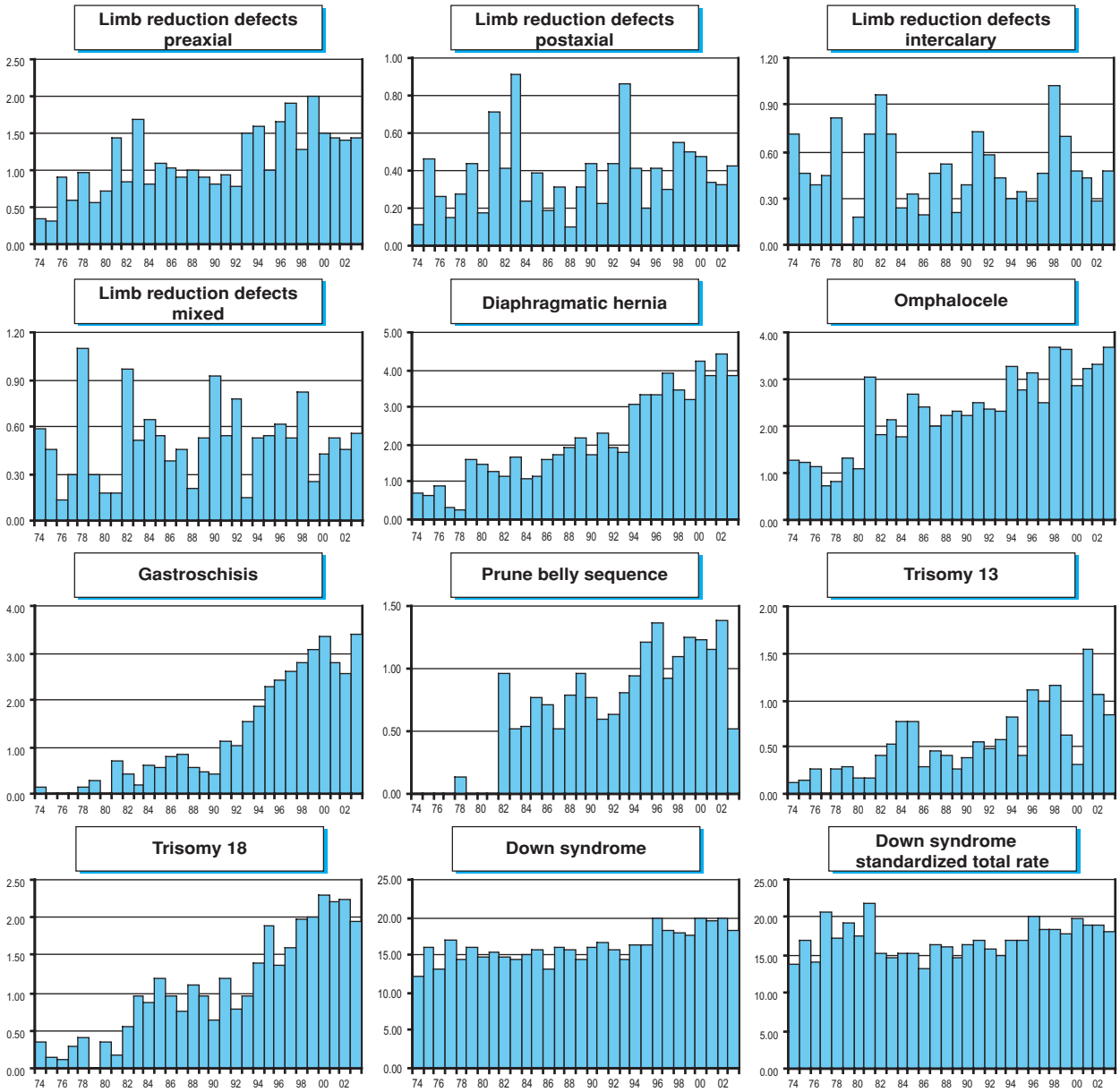
South America: ECLAMC

'Time trends 1974-2003 (Birth prevalence rates per 10,000)



Note: L+S rates

Note: L+S rates



Note: L+S rates

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 activity is organized in a multidisciplinary way through the following three main lines of coordinated activity:

1) Registry and Surveillance of the frequencies of the different congenital defects (whether major or minor), and epidemiological analysis.
2) Clinical and cytogenetic study of the malformed infants of the Registry. In this group, the ECEMC has organized a bank of biological samples of the malformed infants, for further molecular analyses.
3) Clinical Teratology analyses. Into this group, there are 2 Teratogen Information Services since 1991, one for the general population and another one for physicians.

Size and coverage: Reports are obtained from hospitals (77 at present) distributed all over Spain. The annual number of births surveyed surpasses 100,000, representing 23.4% of all births in Spain. 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. It is organized as a non-governmental organisation (NGO) which completes its financial aspects partially by the Spanish Administration and, partially, by other NGOs.

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 by the collaborating physicians 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, whether professional or accidental) within the first three days after delivery.

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

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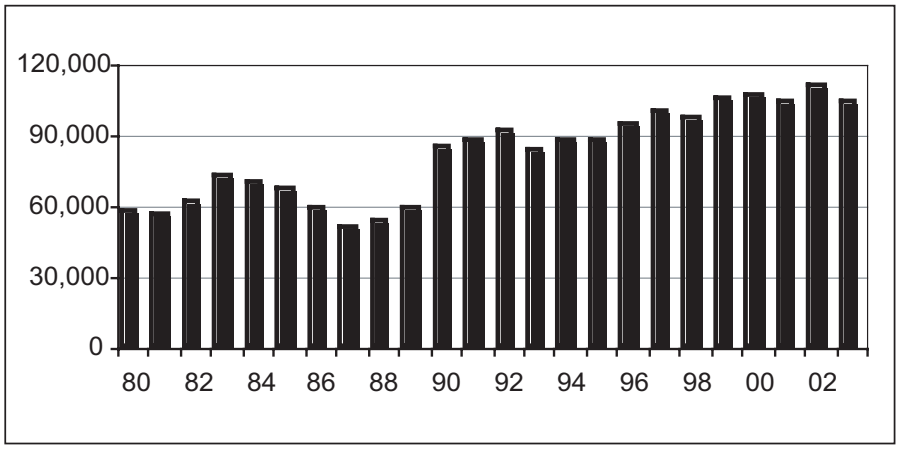
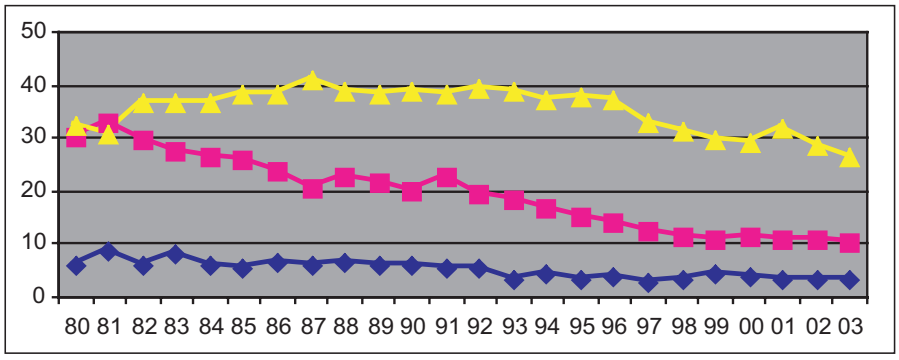
David Prieto Professor of Biostatistics at the Department of Health Sciences Universidad de Alcalá de Henares. Madrid
E-mail: davidprieto55@hotmail.com

Spain: ECEMC

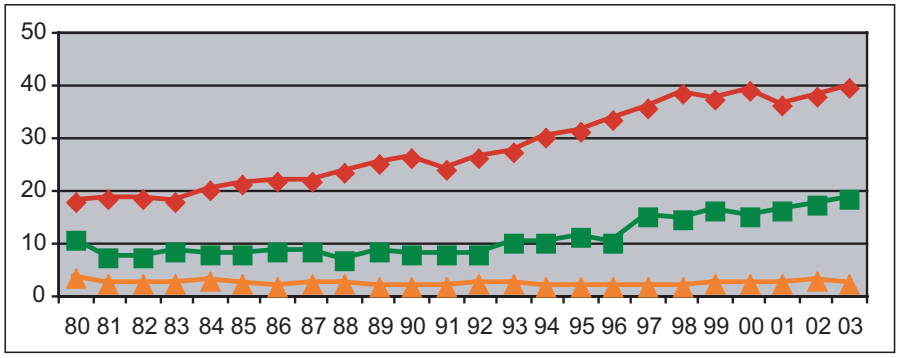
Total births by year



Percentage of births by maternal age



legenda: %births < 20 %births 20-24 %births 25-29



legenda: %births 30-34 %births 35-39 %births 40+

Spain: ECEMC, 2003

Live births (LB)	102647
Stillbirths (SB)	441
Total births	103088
Number of terminations of pregnancy (ToP) for birth defects	nr

Birth Defects	Number of cases			Rates*10.000
	LB	SB	ToP	Total rate
Anencephaly	1	1	nr	0.19
Spina bifida	10	1	nr	1.07
Encephalocele	0	0	nr	0.00
Microcephaly	8	0	nr	0.78
Arhinencephaly / Holoprosencephaly	1	2	nr	0.29
Hydrocephaly	11	1	nr	1.16
Anophthalmos	0	0	nr	0.00
Microphthalmos	5	1	nr	0.58
Unspecified Anophthalmos / Microphthalmos	0	0	nr	---
Anotia	2	0	nr	0.19
Microtia	13	0	nr	1.26
Unspecified Anotia / Microtia	0	0	nr	---
Transposition of great vessels	13	0	nr	1.26
Tetralogy of Fallot	10	0	nr	0.97
Hypoplastic left heart syndrome	5	0	nr	0.49
Coarctation of aorta	6	0	nr	0.58
Choanal atresia, bilateral	1	0	nr	0.10
Cleft palate without cleft lip	42	1	nr	4.17
Cleft lip with or without cleft palate	38	0	nr	3.69
Oesophageal atresia / stenosis with or without fistula	26	0	nr	2.52
Small intestine atresia / stenosis	6	0	nr	0.58
Anorectal atresia / stenosis	15	1	nr	1.55
Undescended testis (36 weeks of gestation or later)	20	0	nr	1.94
Hypospadias	15	1	nr	1.55
Epispadias	0	0	nr	0.00
Indeterminate sex	6	0	nr	0.58
Renal agenesis	1	0	nr	0.10
Cystic kidney	13	1	nr	1.36
Bladder exstrophy	1	0	nr	0.10
Polydactyly, preaxial	15	0	nr	1.46
Total Limb reduction defects (include unspecified)	47	3	nr	4.85
Transverse	17	1	nr	1.75
Preaxial	7	0	nr	0.68
Postaxial	0	0	nr	0.00
Intercalary	3	1	nr	0.39
Mixed	8	1	nr	0.87
Unspecified	12	0	nr	---
Diaphragmatic hernia	6	0	nr	0.58
Omphalocele	8	0	nr	0.78
Gastroschisis	4	0	nr	0.39
Unspecified Omphalocele / Gastroschisis	1	0	nr	---
Prune belly sequence	2	0	nr	0.19
Trisomy 13	4	0	nr	0.39
Trisomy 18	11	0	nr	1.07
Down syndrome, all ages (include age unknown)	78	0	nr	7.57
<20	2	0	nr	6.45
20-24	4	0	nr	3.75
25-29	10	0	nr	3.68
30-34	30	0	nr	7.33
35-39	23	0	nr	12.05
40-44	8	0	nr	39.72
45+	1	0	nr	100.00
unspecified	0	0	nr	---

nr= not reported

Spain: ECEMC, Previous years rates 1980 - 2003

Prevalence rates: (LB+SB) * 10,000

	1974-78	1979-83*	1984-88	1989-93	1994-98	1999-03
Births		**246,157**	**298,215**	**405,665**	**464,090**	**527,616**
Anencephaly		4.59	3.55	1.21	0.80	0.15
Spina bifida		4.22	4.93	3.82	2.48	1.38
Encephalocele		1.30	0.60	1.01	0.39	0.11
Microcephaly		2.11	2.11	2.29	1.77	1.23
Arhinencephaly / Holoprosencephaly		0.41	0.54	0.57	0.54	0.25
Hydrocephaly		2.60	2.58	2.71	2.82	1.86
Anophthalmos		1.83	1.98	1.87	1.40	0.11
Microphthalmos		1.91	1.98	1.65	1.62	0.91
Unspecified Anophthalmos / Microphthalmos		---	---	---	---	---
Anotia		1.91	1.94	1.55	1.42	0.09
Microtia		0.65	0.77	1.33	1.42	1.52
Unspecified Anotia / Microtia		---	---	---	---	---
Transposition of great vessels		0.16	0.23	1.06	1.19	1.10
Tetralogy of Fallot		0.45	0.47	1.13	0.84	1.04
Hypoplastic left heart syndrome		0.41	0.30	0.79	0.90	0.32
Coarctation of aorta		0.16	0.30	0.27	0.22	0.66
Choanal atresia, bilateral		5.48	3.99	5.30	4.01	0.13
Cleft palate without cleft lip		5.69	5.57	5.69	4.85	3.83
Cleft lip with or without cleft palate		2.27	1.78	2.24	1.85	3.58
Oesophageal atresia / stenosis with or without fistula		0.49	0.54	0.62	0.32	1.78
Small intestine atresia / stenosis		2.60	2.38	2.05	2.07	0.59
Anorectal atresia / stenosis		1.83	2.38	2.64	2.80	2.05
Undescended testis (36 weeks of gestation or later)		2.72	2.58	2.10	1.53	2.43
Hypospadias		0.28	0.13	0.25	0.06	2.22
Epispadias		0.81	1.11	0.94	0.58	0.09
Indeterminate sex		0.61	0.84	0.71	0.56	0.63
Renal agenesis		1.26	1.24	1.77	1.72	0.09
Cystic kidney		0.20	0.30	0.30	0.30	1.42
Bladder exstrophy		2.40	2.65	3.35	2.59	0.17
Polydactyly, preaxial		7.56	6.40	7.07	5.99	1.95
Total Limb reduction defects (include unspecified)		3.13	2.82	2.74	2.26	4.81
Transverse		1.26	1.04	1.04	0.65	1.97
Preaxial		0.12	0.20	0.15	0.24	0.61
Postaxial		0.61	0.27	0.59	0.26	0.13
Intercalary		1.18	1.01	1.18	1.03	0.30
Mixed		2.64	2.31	2.12	1.83	0.97
Unspecified		---	---	---	---	---
Diaphragmatic hernia		2.92	2.15	1.75	1.40	0.78
Omphalocele		0.61	0.40	0.42	0.37	0.63
Gastroschisis		0.49	0.60	0.59	0.32	0.38
Unspecified Omphalocele / Gastroschisis		---	---	---	---	---
Prune belly sequence		0.32	0.47	0.37	0.60	0.11
Trisomy 13		0.77	1.17	1.08	0.69	0.34
Trisomy 18		14.34	15.66	12.82	11.27	0.66
Down syndrome, all ages (include age unknown)		6.86	7.68	10.76	1.23	8.51
<20		7.37	6.13	4.97	4.52	2.22
20-24		6.17	8.22	7.28	6.34	5.33
25-29		10.16	14.16	14.88	11.22	5.15
30-34		46.30	45.10	35.93	28.06	7.60
35-39		146.04	180.66	72.78	59.45	13.67
40-44		126.94	284.28	239.04	368.10*	46.84
45+		nr	nr	nr	nr	143.54
unspecified		---	---	---	---	---

* data include less than 5 years

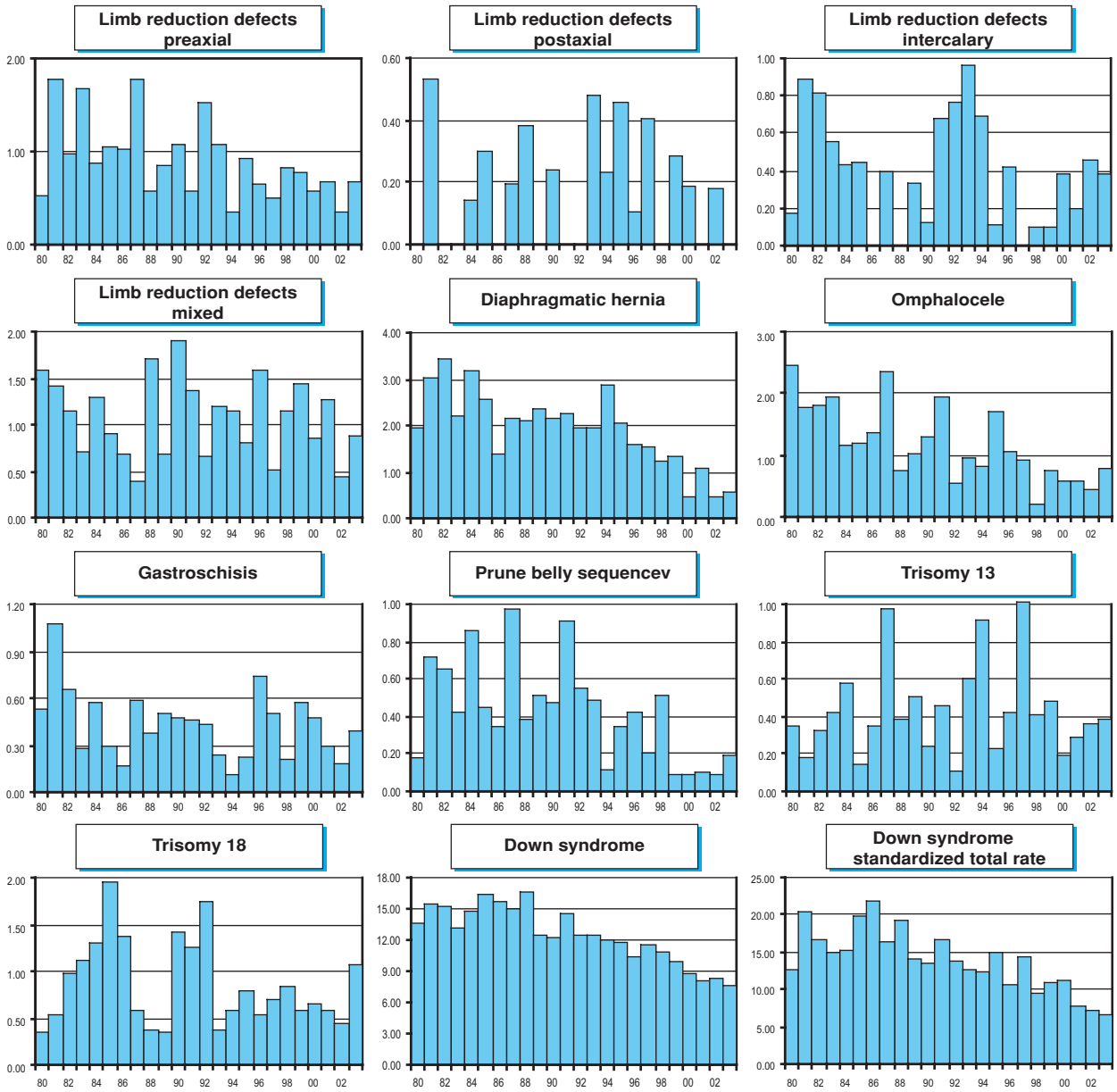
nr = not reported

Spain: ECEMC

'Time trends 1980-2003 (Birth prevalence rates per 10,000)

Note: L+S rates

Note: L+S rates



Note: L+S rates

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.

Address for further information:
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Fax: +46-8-55553327

E-mail: birgitta.ollars@socialstyrelsen.se

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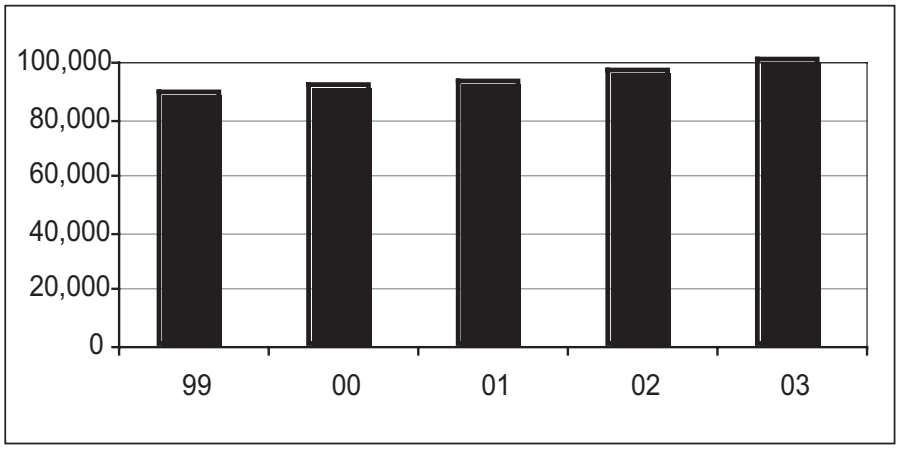
Fax: +46-18-554025

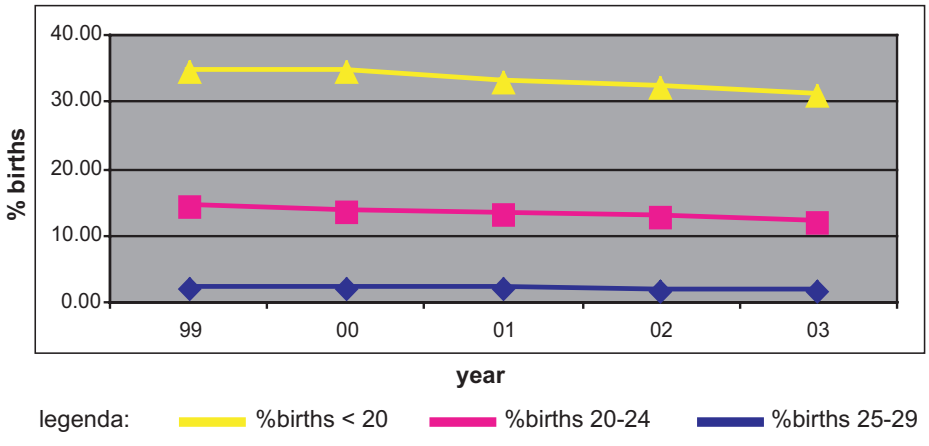
E-mail: goran.anneren@genpat.uu.se

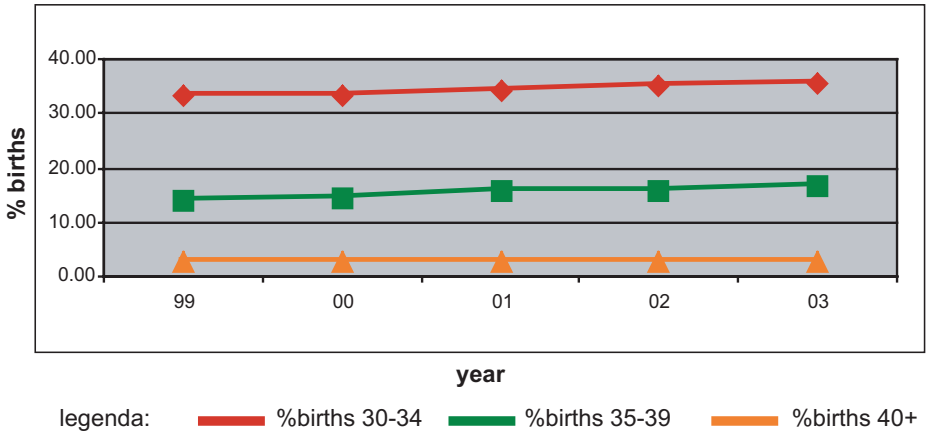
Sweden

Total births by year



Percentage of births by maternal age





Sweden, 2003

Live births (LB)	99157
Stillbirths (SB)	359
Total births	99516
Number of terminations of pregnancy (ToP) for birth defects	419

Birth Defects	Number of cases			Rates*10.000
	LB	SB	ToP	Total rate
Anencephaly	0	1	34	3.50
Spina bifida	22	0	17	3.90
Encephalocele	4	1	5	1.00
Microcephaly	2	0	0	0.20
Arhinencephaly / Holoprosencephaly	5	0	3	0.80
Hydrocephaly	12	0	19	3.10
Anophthalmos	1	0	0	0.10
Microphthalmos	6	0	0	0.60
Unspecified Anophthalmos / Microphthalmos	0	0	0	---
Anotia	8	0	0	0.80
Microtia	0	0	0	0.00
Unspecified Anotia / Microtia	0	0	0	---
Transposition of great vessels	28	0	1	2.90
Tetralogy of Fallot	24	0	1	2.50
Hypoplastic left heart syndrome	20	1	7	2.80
Coarctation of aorta	61	0	3	6.40
Choanal atresia, bilateral	7	1	0	0.80
Cleft palate without cleft lip	35	1	3	3.90
Cleft lip with or without cleft palate	89	2	9	10.01
Oesophageal atresia / stenosis with or without fistula	32	2	1	3.50
Small intestine atresia / stenosis	27	1	0	2.80
Anorectal atresia / stenosis	21	0	5	2.60
Undescended testis (36 weeks of gestation or later)	nr	nr	nr	nr
Hypospadias	193	0	0	19.31
Epispadias	2	0	1	0.30
Indeterminate sex	0	0	0	0.00
Renal agenesis	3	0	8	1.10
Cystic kidney	17	0	14	3.10
Bladder exstrophy	2	0	0	0.20
Polydactyly, preaxial	45	0	2	4.70
Total Limb reduction defects (include unspecified)	46	0	10	5.60
Transverse	32	0	7	3.90
Preaxial	2	0	0	0.20
Postaxial	4	0	0	0.40
Intercalary	2	0	1	0.30
Mixed	6	0	2	0.80
Unspecified	0	0	0	---
Diaphragmatic hernia	24	0	11	3.50
Omphalocele	5	1	14	2.00
Gastroschisis	20	1	5	2.60
Unspecified Omphalocele / Gastroschisis	0	0	0	---
Prune belly sequence	0	0	0	0.00
Trisomy 13	8	1	17	2.60
Trisomy 18	19	3	52	7.40
Down syndrome, all ages (include age unknown)	152	2	117	27.12
<20	2	0	0	12.53
20-24	8	0	2	8.32
25-29	28	0	9	12.00
30-34	47	0	18	18.28
35-39	50	1	51	61.07
40-44	15	1	35	180.98
45+	0	0	2	165.29
unspecified	2	0	0	---

nr = not reported

Sweden, Previous years rates 1999 - 2003

Prevalence rates: (LB+SB+TOP) * 10,000

	1974-78	1979-83	1984-88	1989-93	1994-98	1999-03
Births						**466,806**
Anencephaly						3.73
Spina bifida						4.88
Encephalocele						1.01
Microcephaly						0.32
Arhinencephaly / Holoprosencephaly						0.90
Hydrocephaly						3.17
Anophthalmos						0.17
Microphthalmos						0.39
Unspecified Anophthalmos / Microphthalmos						---
Anotia						0.96
Microtia						0.06
Unspecified Anotia / Microtia						---
Transposition of great vessels						3.36
Tetralogy of Fallot						2.48
Hypoplastic left heart syndrome						2.21
Coarctation of aorta						4.26
Choanal atresia, bilateral						0.66
Cleft palate without cleft lip						5.46
Cleft lip with or without cleft palate						10.05
Oesophageal atresia / stenosis with or without fistula						2.40
Small intestine atresia / stenosis						2.25
Anorectal atresia / stenosis						3.00
Undescended testis (36 weeks of gestation or later)						nr
Hypospadias						20.61
Epispadias						0.21
Indeterminate sex						0.26
Renal agenesis						1.95
Cystic kidney						3.00
Bladder exstrophy						0.24
Polydactyly, preaxial						4.24
Total Limb reduction defects (include unspecified)						5.06
Transverse						3.56
Preaxial						0.24
Postaxial						0.19
Intercalary						0.21
Mixed						0.86
Unspecified						---
Diaphragmatic hernia						2.74
Omphalocele						2.34
Gastroschisis						2.01
Unspecified Omphalocele / Gastroschisis						---
Prune belly sequence						0.09
Trisomy 13						2.08
Trisomy 18						5.96
Down syndrome, all ages (include age unknown)						24.16
<20						9.54
20-24						8.09
25-29						9.19
30-34						17.09
35-39						54.68
40-44						173.40
45+						400.00
unspecified						---

nr = not reported

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.

Address for further information:
Medical Director: Dr. Lyubov Yevtushok, UABDP, 2, Skovorody St., build.3., Room 209, Kiev-Mohyla Academy Ukraine 04070

Phone/fax: 38-036-262-3447

E-mail: bdrivne@bdp.rovno.ua

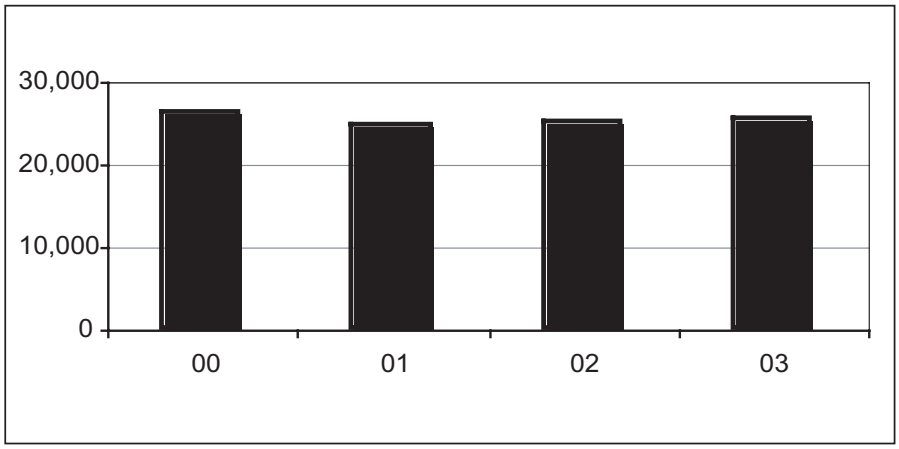
Director: Dr. Wladimir Wertelecki, Department of Medical Genetics, University of South Alabama, 307 University Blvd., CCCB, 274, Mobile, AL, USA 36688

Phone/Fax: 1-251-4607505

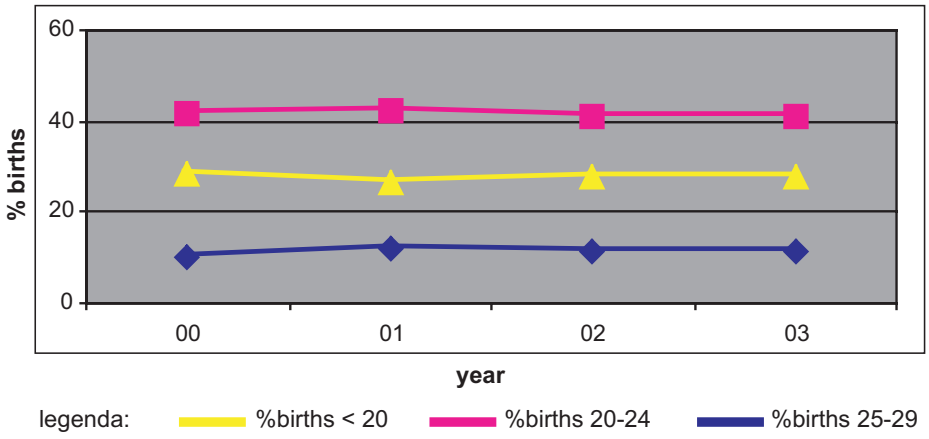
E-mail: wwertele@usouthal.edu

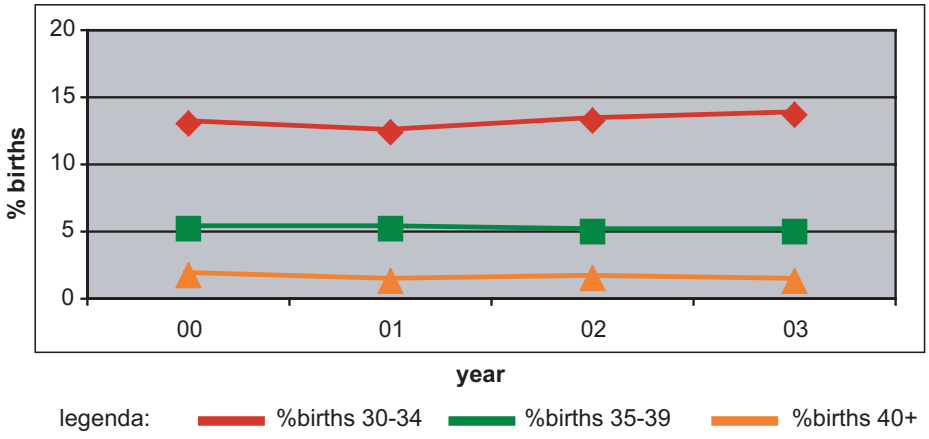
Ukraine: UABDP

Total births by year



Percentage of births by maternal age





Ukraine: UABDP, 2003

Live births (LB)	25319
Stillbirths (SB)	127
Total births	25446
Number of terminations of pregnancy (ToP) for birth defects (1)	nr

Birth Defects	Number of cases			Rates*10.000
	LB	SB	ToP	Total rate
Anencephaly	0	1	17	7.07
Spina bifida	19	1	15	13.75
Encephalocele	2	0	2	1.57
Microcephaly (2)	5	0	nr	1.96
Arhinencephaly / Holoprosencephaly	4	0	nr	1.57
Hydrocephaly	10	5	nr	5.89
Anophthalmos (2)	0	0	nr	0.00
Microphthalmos (2)	1	0	nr	0.39
Unspecified Anophthalmos / Microphthalmos	0	0	nr	---
Anotia	2	0	nr	0.79
Microtia	8	0	nr	3.14
Unspecified Anotia / Microtia	0	0	nr	---
Transposition of great vessels	5	0	nr	1.96
Tetralogy of Fallot	8	0	nr	3.14
Hypoplastic left heart syndrome	2	1	nr	1.18
Coarctation of aorta	6	1	nr	2.75
Choanal atresia, bilateral	0	0	nr	0.00
Cleft palate without cleft lip	9	0	nr	3.54
Cleft lip with or without cleft palate	24	0	nr	9.43
Oesophageal atresia / stenosis with or without fistula	2	0	nr	0.79
Small intestine atresia / stenosis	1	1	nr	0.79
Anorectal atresia / stenosis	9	0	nr	3.54
Undescended testis (36 weeks of gestation or later)	102	0	nr	40.08
Hypospadias (3)	8	0	nr	3.14
Epispadias	0	0	nr	0.00
Indeterminate sex	2	0	nr	0.79
Renal agenesis	1	1	nr	0.79
Cystic kidney	8	3	nr	4.32
Bladder exstrophy	3	0	nr	1.18
Polydactyly, preaxial	3	0	nr	1.18
Total Limb reduction defects (include unspecified)	5	0	nr	1.96
Transverse	4	0	nr	1.57
Preaxial	1	0	nr	0.39
Postaxial	0	0	nr	0.00
Intercalary	0	0	nr	0.00
Mixed	0	0	nr	0.00
Unspecified	0	0	nr	---
Diaphragmatic hernia	0	1	nr	0.39
Omphalocele	3	0	nr	1.18
Gastroschisis	3	0	nr	1.18
Unspecified Omphalocele / Gastroschisis	0	0	nr	---
Prune belly sequence	0	0	nr	0.00
Trisomy 13 (2)	0	0	nr	0.00
Trisomy 18 (2)	0	0	nr	0.00
Down syndrome, all ages (include age unknown) (2, 4)	26	0	nr	10.22
<20	1	0	nr	3.54
20-24	6	0	nr	5.77
25-29	8	0	nr	11.25
30-34	7	0	nr	20.11
35-39	3	0	nr	23.20
40-44	1	0	nr	31.65
45+	0	0	nr	0.00
unspecified	0	0	nr	---

(1) Number of terminations of pregnancy (ToP) for birth defects is not reported, except for NTD
(2) Clinical diagnosis only; with photodocumentation or measurements documented
(3) Includes penile, scrotal, and perineal hypospadias only
(4) 1 case of pregnancy termination with Down Syndrome fetus was registered whose mother was 38 years old and it was confirmed by amniocentesis

Ukraine: UABDP, Previous years rates 2000 - 2003

Prevalence rates: (LB+SB+TOP) * 10,000 (anencephaly-spina bifida-encephalocele)
Prevalence rates: (LB+SB) * 10,000 (all other malformations)

	1974-78	1979-83	1984-88	1989-93	1994-98	1999-03*
Births						**101,137**
Anencephaly						8.21
Spina bifida						10.88
Encephalocele						2.08
Microcephaly						2.67
Arhinencephaly / Holoprosencephaly						0.40
Hydrocephaly						6.03
Anophthalmos						0.10
Microphthalmos						1.09
Unspecified Anophthalmos / Microphthalmos						---
Anotia						0.40
Microtia						1.78
Unspecified Anotia / Microtia						---
Transposition of great vessels						3.56
Tetralogy of Fallot						2.27
Hypoplastic left heart syndrome						0.69
Coarctation of aorta						1.19
Choanal atresia, bilateral						0.00
Cleft palate without cleft lip						4.15
Cleft lip with or without cleft palate						9.39
Oesophageal atresia / stenosis with or without fistula						1.38
Small intestine atresia / stenosis						1.48
Anorectal atresia / stenosis						2.77
Undescended testis (36 weeks of gestation or later)						39.25
Hypospadias						3.46
Epispadias						0.40
Indeterminate sex						0.69
Renal agenesis						0.89
Cystic kidney						1.78
Bladder exstrophy						0.89
Polydactyly, preaxial						3.07
Total Limb reduction defects (include unspecified)						3.76
Transverse						2.08
Preaxial						0.49
Postaxial						0.30
Intercalary						0.30
Mixed						0.20
Unspecified						---
Diaphragmatic hernia						1.68
Omphalocele						1.29
Gastroschisis						1.09
Unspecified Omphalocele / Gastroschisis						---
Prune belly sequence						0.00
Trisomy 13						0.20
Trisomy 18						0.30
Down syndrome, all ages (include age unknown)						12.16
<20						7.97
20-24						6.69
25-29						9.98
30-34						18.88
35-39						28.77
40-44						92.99
45+						657.89
unspecified						---

* data include less than 5 years

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

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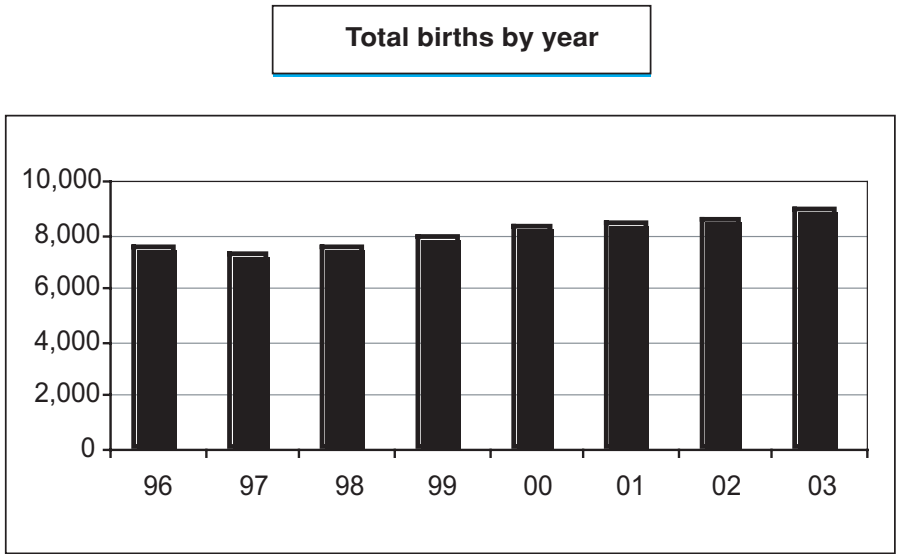
United Arab Emirates



United Arab Emirates, 2003

Live births (LB)	8724
Stillbirths (SB)	61
Total births	8785
Number of terminations of pregnancy (ToP) for birth defects	not permitted

Birth Defects	Number of cases			Rates*10.000
	LB	SB	ToP	Total rate
Anencephaly	1	0		1.14
Spina bifida	10	0		11.38
Encephalocele	1	0		1.14
Microcephaly	1	0		1.14
Arhinencephaly / Holoprosencephaly	1	0		1.14
Hydrocephaly	1	0		1.14
Anophthalmos	1	0		1.14
Microphthalmos	1	0		1.14
Unspecified Anophthalmos / Microphthalmos	0	0		---
Anotia	0	0		0.00
Microtia	1	0		1.14
Unspecified Anotia / Microtia	0	0		---
Transposition of great vessels	1	0		1.14
Tetralogy of Fallot	0	0		0.00
Hypoplastic left heart syndrome	2	0		2.28
Coarctation of aorta	1	0		1.14
Choanal atresia, bilateral	0	0		0.00
Cleft palate without cleft lip	1	0		1.14
Cleft lip with or without cleft palate	3	0		3.41
Oesophageal atresia / stenosis with or without fistula	2	0		2.28
Small intestine atresia / stenosis	2	0		2.28
Anorectal atresia / stenosis	5	0		5.69
Undescended testis (36 weeks of gestation or later)	nr	nr		nr
Hypospadias	nr	nr		nr
Epispadias	nr	nr		nr
Indeterminate sex	0	0		0.00
Renal agenesis	2	0		2.28
Cystic kidney	1	0		1.14
Bladder exstrophy	1	0		1.14
Polydactyly, preaxial	0	0		0.00
Total Limb reduction defects (include unspecified)	2	0		2.28
Transverse	1	0		1.14
Preaxial	1	0		1.14
Postaxial	0	0		0.00
Intercalary	0	0		0.00
Mixed	0	0		0.00
Unspecified	0	0		---
Diaphragmatic hernia	5	0		5.69
Omphalocele	3	0		3.41
Gastroschisis	0	0		0.00
Unspecified Omphalocele / Gastroschisis	0	0		---
Prune belly sequence	1	0		1.14
Trisomy 13	0	0		0.00
Trisomy 18	1	0		1.14
Down syndrome, all ages (include age unknown)	10	0		11.38
<20	0	0		nr
20-24	1	0		nr
25-29	1	0		nr
30-34	1	0		nr
35-39	2	0		nr
40-44	0	0		nr
45+	0	0		nr
unspecified	5	0		---

nr = not reported

United Arab Emirates, Previous years rates 1996 - 2003

Prevalence rates: (LB+SB) * 10,000

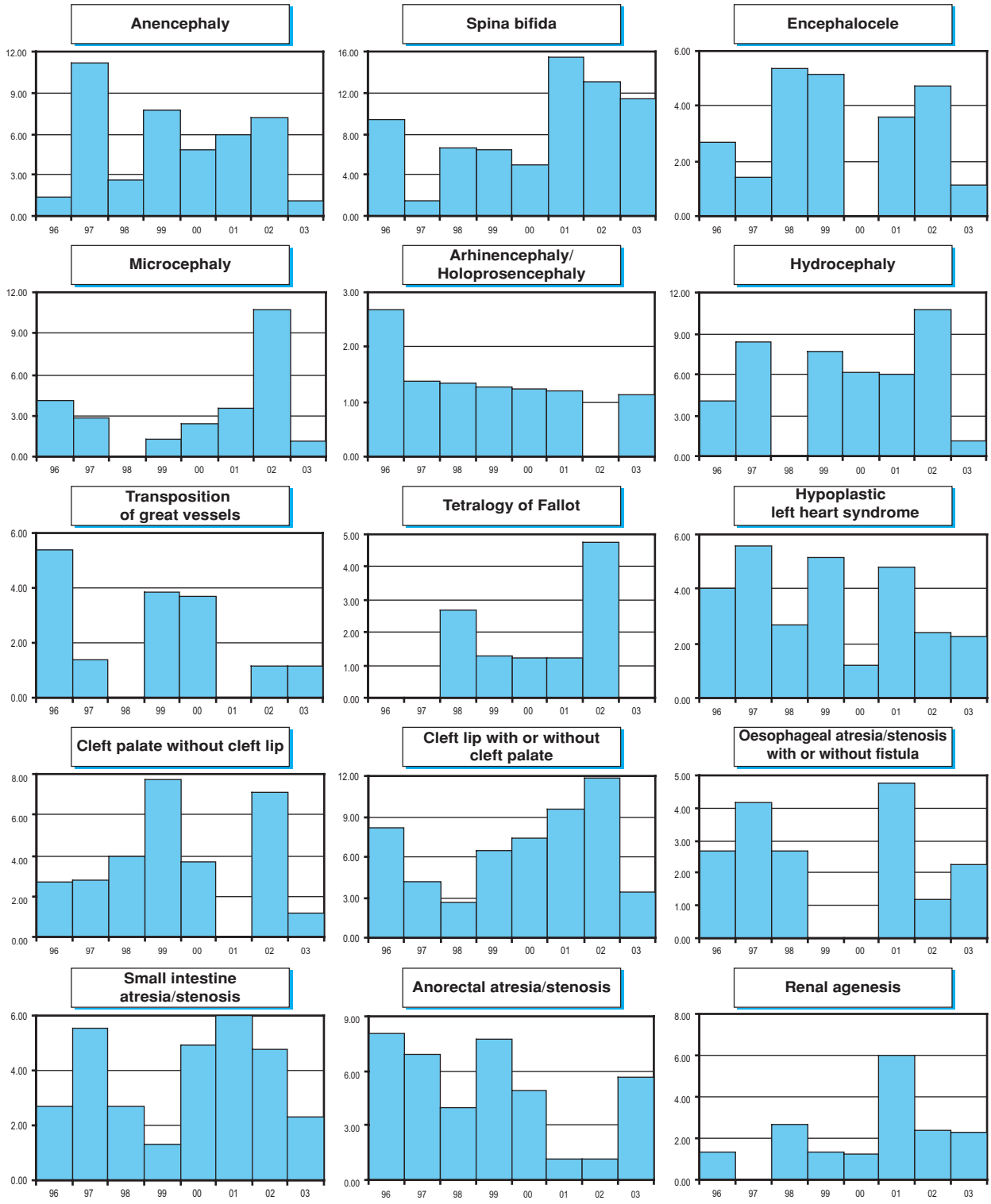
	1974-78	1979-83	1984-88	1989-93	1994-98*	1999-03
Births					**22,099**	**41,507**
Anencephaly					4.98	5.30
Spina bifida					5.88	10.36
Encephalocele					3.17	2.89
Microcephaly					2.26	3.85
Arhinencephaly / Holoprosencephaly					1.81	0.96
Hydrocephaly					4.07	6.26
Anophthalmos					0.00	0.72
Microphthalmos					0.00	0.24
Unspecified Anophthalmos / Microphthalmos					---	---
Anotia					0.00	0.00
Microtia					1.36	1.45
Unspecified Anotia / Microtia					---	---
Transposition of great vessels					2.26	1.93
Tetralogy of Fallot					2.67	1.69
Hypoplastic left heart syndrome					4.07	3.13
Coarctation of aorta					1.33	0.96
Choanal atresia, bilateral					0.91	0.72
Cleft palate without cleft lip					3.17	3.85
Cleft lip with or without cleft palate					4.98	7.71
Oesophageal atresia / stenosis with or without fistula					3.17	1.69
Small intestine atresia / stenosis					3.62	3.85
Anorectal atresia / stenosis					6.34	4.10
Undescended testis (36 weeks of gestation or later)					nr	nr
Hypospadias					nr	nr
Epispadias					nr	nr
Indeterminate sex					3.62	0.24
Renal agenesis					1.36	2.65
Cystic kidney					3.62	5.30
Bladder exstrophy					0.45	0.72
Polydactyly, preaxial					0.45	0.24
Total Limb reduction defects (include unspecified)					4.53	1.69
Transverse					0.00	0.96
Preaxial					2.67	0.48
Postaxial					1.33	0.00
Intercalary					0.00	0.00
Mixed					0.00	0.00
Unspecified					---	---
Diaphragmatic hernia					5.88	6.02
Omphalocele					1.36	2.65
Gastroschisis					0.45	0.96
Unspecified Omphalocele / Gastroschisis					---	---
Prune belly sequence					2.26	0.96
Trisomy 13					0.91	1.45
Trisomy 18					2.72	1.20
Down syndrome, all ages (include age unknown)					17.65	19.27
<20					nr	nr
20-24					nr	nr
25-29					nr	nr
30-34					nr	nr
35-39					nr	nr
40-44					nr	nr
45+					nr	nr
unspecified					---	---

* data include less than 5 years

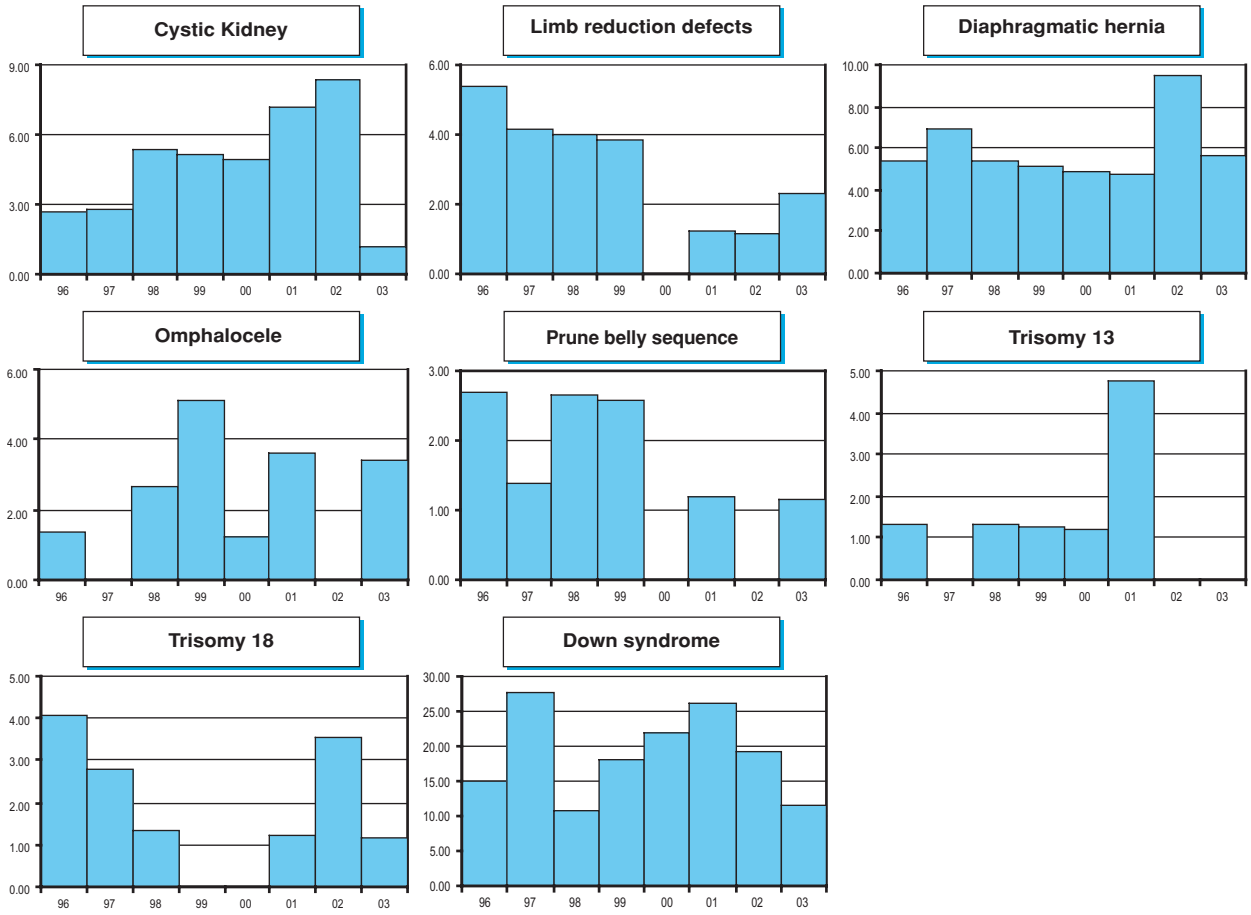
nr= not reeported

United Arab Emirates

'Time trends 1996-2003 (Birth prevalence rates per 10,000)



Note: L+S rates



Note: L+S rates

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. Live births and stillbirths of at least 20 weeks gestations are included. Elective terminations at any gestational age are included.

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, neonatal intensive care units, laboratories, prenatal diagnostic centers, and tertiary care centers 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:
Adolfo Correa / Csaba Siffel, Centers for Disease Control and Prevention, National Center on Birth Defects and Developmental Disabilities, Mailstop E-86, 1600 Clifton Road, Atlanta, GA 30333, USA

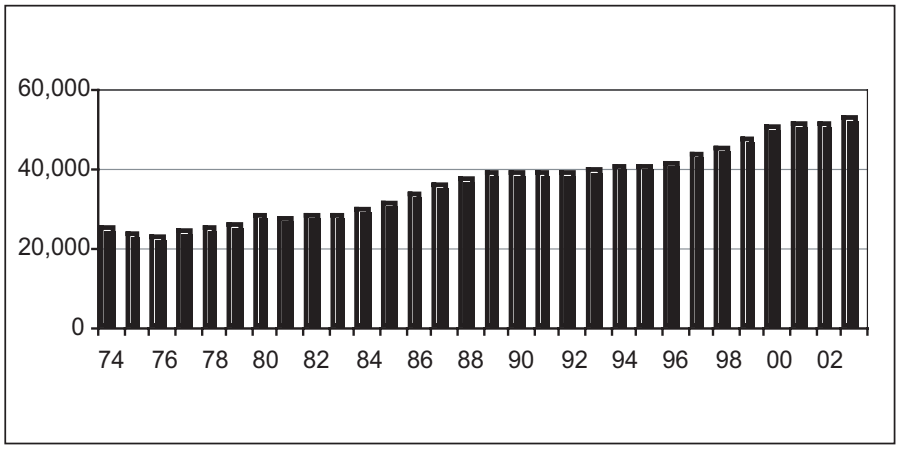
Phone: 1-404-498-4090

Fax: 1-404-498 3040

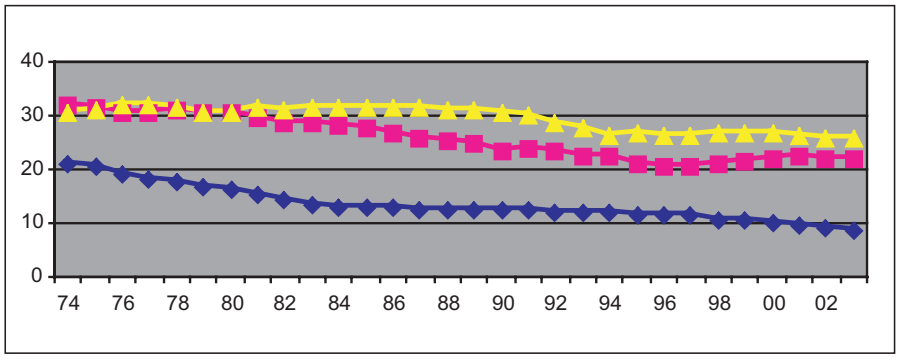
E-mail: ACorrea@cdc.gov; CSiffel@cdc.gov

USA: Atlanta

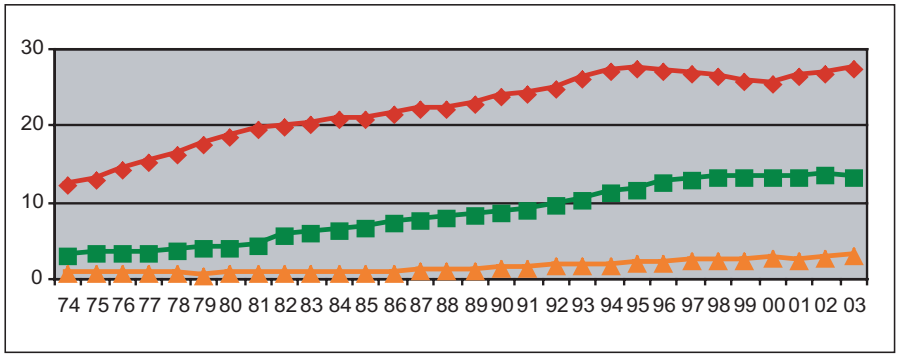
Total births by year



Percentage of births by maternal age



legenda: %births < 20 %births 20-24 %births 25-29



legenda: %births 30-34 %births 35-39 %births 40+

USA: Atlanta, 2003

Live births (LB)	51676
Stillbirths (SB)	561
Total births	52237
Number of terminations of pregnancy (ToP) for birth defects	nr

Birth Defects	Number of cases			Rates*10.000
	LB	SB	ToP	Total rate
Anencephaly	1	3	4	1.53
Spina bifida	12	1	7	3.83
Encephalocele	2	1	2	0.96
Microcephaly	14	0	0	2.68
Arhinencephaly / Holoprosencephaly	1	2	1	0.77
Hydrocephaly	16	0	0	3.06
Anophthalmos	0	0	0	0.00
Microphthalmos	6	0	0	1.15
Unspecified Anophthalmos / Microphthalmos	0	0	0	---
Anotia	2	0	0	0.38
Microtia	7	0	0	1.34
Unspecified Anotia / Microtia	0	0	0	---
Transposition of great vessels	23	0	0	4.40
Tetralogy of Fallot	17	0	0	3.25
Hypoplastic left heart syndrome	8	1	0	1.72
Coarctation of aorta	20	0	0	3.83
Choanal atresia, bilateral	2	0	0	0.38
Cleft palate without cleft lip	14	0	1	2.87
Cleft lip with or without cleft palate	31	1	0	6.13
Oesophageal atresia / stenosis with or without fistula	5	0	0	0.96
Small intestine atresia / stenosis	8	0	0	1.53
Anorectal atresia / stenosis	9	1	0	1.91
Undescended testis (36 weeks of gestation or later)	27	0	0	5.17
Hypospadias	27	0	0	5.17
Epispadias	4	0	0	0.77
Indeterminate sex	2	0	0	0.38
Renal agenesis	0	3	1	0.77
Cystic kidney	16	1	1	3.45
Bladder exstrophy	0	0	0	0.00
Polydactyly, preaxial	6	0	0	1.15
Total Limb reduction defects (include unspecified)	16	0	0	3.06
Transverse	14	0	0	2.68
Preaxial	1	0	0	0.19
Postaxial	1	0	0	0.19
Intercalary	0	0	0	0.00
Mixed	0	0	0	0.00
Unspecified	0	0	0	---
Diaphragmatic hernia	16	0	0	3.06
Omphalocele	6	1	1	1.53
Gastroschisis	12	1	0	2.49
Unspecified Omphalocele / Gastroschisis	0	0	0	---
Prune belly sequence	0	1	0	0.19
Trisomy 13	3	2	3	1.53
Trisomy 18	7	6	11	4.59
Down syndrome, all ages (include age unknown)	66	2	22	17.23
<20	4	0	0	8.81
20-24	8	0	2	8.71
25-29	5	0	2	5.20
30-34	15	1	2	12.57
35-39	20	1	13	49.45
40-44	14	0	3	115.10
45+	0	0	0	0.00
unspecified	0	0	0	---

USA: Atlanta, Previous years rates 1974 - 2003

Birth prevalence rates: (LB+SB+TOP) * 10,000

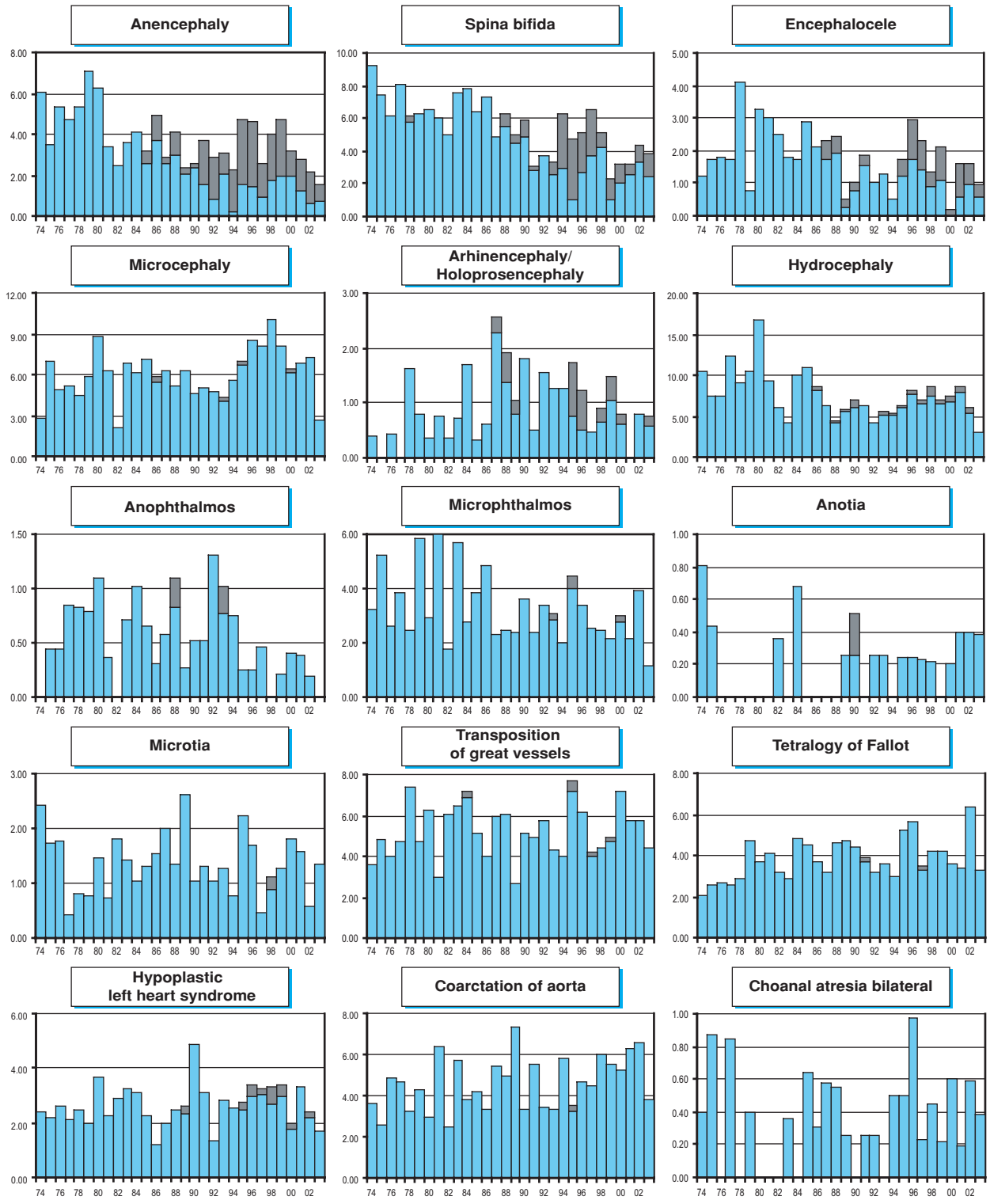
	1974-78	1979-83	1984-88	1989-93	1994-98	1999-03
Births	**118,381**	**135,541**	**164,677**	**192,408**	**208,832**	**250,560**
Anencephaly	4.98	4.50	3.83	2.91	3.64	2.83
Spina bifida	7.43	6.27	6.50	4.21	5.55	3.39
Encephalocele	2.11	2.29	2.31	1.14	1.77	1.28
Microcephaly	4.81	5.98	6.07	4.99	7.90	6.23
Arhinencephaly / Holoprosencephaly	0.51	0.59	1.46	1.25	1.10	0.76
Hydrocephaly	9.38	9.37	7.83	5.77	7.09	6.39
Anophthalmos	0.51	0.59	0.73	0.73	0.34	0.24
Microphthalmos	3.46	4.43	3.22	2.96	2.97	2.47
Unspecified Anophthalmos / Microphthalmos	---	---	---	---	---	---
Anotia	0.25	0.07	0.12	0.26	0.19	0.28
Microtia	1.44	1.25	1.46	1.46	1.25	1.32
Unspecified Anotia / Microtia	---	---	---	---	---	---
Transposition of great vessels	4.90	5.31	5.65	4.57	5.27	5.59
Tetralogy of Fallot	2.53	3.69	4.13	3.95	4.31	4.15
Hypoplastic left heart syndrome	2.37	2.80	2.19	2.96	3.06	2.55
Coarctation of aorta	3.80	4.35	4.37	4.57	4.88	5.47
Choanal atresia, bilateral	0.42	0.15	0.43	0.16	0.53	0.40
Cleft palate without cleft lip	7.52	4.50	5.22	5.09	5.03	5.83
Cleft lip with or without cleft palate	11.23	11.88	9.53	9.10	9.67	7.78
Oesophageal atresia / stenosis with or without fistula	2.45	2.43	2.31	2.29	2.06	2.00
Small intestine atresia / stenosis	1.77	1.55	1.58	1.66	1.58	2.00
Anorectal atresia / stenosis	4.81	3.62	4.07	3.79	3.74	3.07
Undescended testis (36 weeks of gestation or later)	nr	nr	nr	nr	nr	12.38*
Hypospadias	1.18	1.11	4.62	4.57	6.70	8.78
Epispadias	1.01	1.03	0.55	0.73	0.34	0.44
Indeterminate sex	2.20	2.14	1.21	1.20	1.29	1.44
Renal agenesis	1.86	1.92	1.58	1.30	1.39	0.88
Cystic kidney	2.37	2.58	4.01	4.94	5.46	5.79
Bladder exstrophy	0.51	0.30	0.18	0.31	0.19	0.12
Polydactyly, preaxial	1.77	1.99	2.67	2.75	3.02	2.08
Total Limb reduction defects (include unspecified)	6.50	4.50	4.49	4.78	6.46	5.67
Transverse	3.97	2.80	2.98	3.43	3.59	3.31
Preaxial	1.18	0.74	0.61	0.78	1.10	1.20
Postaxial	0.17	0.30	0.30	0.21	0.38	0.16
Intercalary	0.59	0.30	0.30	0.10	0.29	0.16
Mixed	0.08	0.37	0.24	0.16	0.77	0.68
Unspecified	---	---	---	---	---	---
Diaphragmatic hernia	2.87	2.07	2.73	2.60	2.01	2.83
Omphalocele	4.05	3.47	2.61	2.65	2.78	2.16
Gastroschisis	1.44	2.21	2.13	2.65	2.01	2.63
Unspecified Omphalocele / Gastroschisis	---	---	---	---	---	---
Prune belly sequence	0.68	0.59	0.49	0.31	0.24	0.44
Trisomy 13	1.01	1.18	1.82	1.25	1.72	1.88
Trisomy 18	0.59	1.48	2.31	2.29	3.88	4.67
Down syndrome, all ages (include age unknown)	8.45	11.36	9.47	11.43	17.62	17.44
<20	nr	8.01*	5.83	7.20	10.20	6.25
20-24	nr	7.45*	7.97	6.42	8.90	7.45
25-29	nr	8.17*	6.38	7.76	7.96	8.07
30-34	nr	17.83*	11.61	11.37	14.24	14.53
35-39	nr	22.25*	22.08	23.32	46.24	47.53
40-44	nr	103.99*	48.23	62.16	136.60	103.59
45+	nr	0.00*	0.00	547.95	59.52	227.27
unspecified	---	---	---	---	---	---

* data include less than 5 years

nr = not reported

USA: Atlanta

'Time trends 1974-2003 (Birth prevalence rates per 10,000)



Note: L+S rates, ToP rates

Note: L+S rates, ToP rates

Note: L+S rates, ToP rates

USA: Texas

Texas Birth Defects Epidemiology & Surveillance Branch (BDES)

History:
BDES was established in 1993 as the result of an unusual cluster of anencephaly cases that occurred in Brownsville, Texas. Epidemiologic investigations revealed a higher than expected rate of neural tube defects among children born to Hispanic mothers living in South Texas. In recognition that epidemiologic resources are routinely needed to investigate birth defects clusters, the Texas State Legislature passed the Texas Birth Defects Act in 1993, which authorized the establishment of BDES. Since 1994, BDES has maintained the Texas Birth Defects Registry, population-based birth defects surveillance system, which is now statewide. Through multiple sources of information, the Registry monitors all births in Texas, approximately 380,000 each year, and identifies cases of birth defects. Children identified through the Registry are referred to appropriate medical and community services. In 1996, the CDC-funded Texas Center for Birth Defects Research and Prevention was established under the auspices of BDES. The program is a full member of the ICBDMS.

Size and coverage
The program covers all deliveries to mothers residing in Texas (approximately 380,000 annually). Stillbirths and terminations of any gestational age are included. Cases diagnosed up to age one are included (up to any age for fetal alcohol syndrome).

Legislation and funding
Birth defects surveillance was mandated by the Texas Birth Defects Act in 1993, and is codified in the Texas health and safety Code Chapter 87. About one-half of funding for the birth defects registry is from state general revenue, 33% from federal Maternal Child health block grant funds, and 16% from the federal Preventive Health and Health Services Block grant.

Sources of ascertainment
Birth hospitals, birthing centres, lay midwives, hospitals where affected children are treated.

Exposure information
Limited information on maternal illnesses and conditions, limited information on maternal exposures such as medications.

Background information
Basic demographics, reproductive history, gestational age, delivery information.

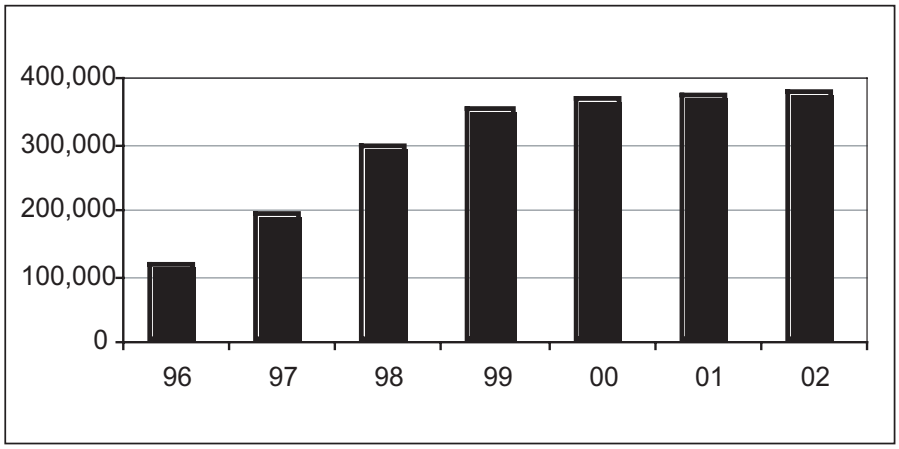
Address for further information
Mark A. Canfield, Ph.D.,Division Director Texas Birth Defects Monitoring Division Texas Department of Health, 1100 West 49th Street Austin, TX 78756-3180, USA

Phone: 512-458-7232

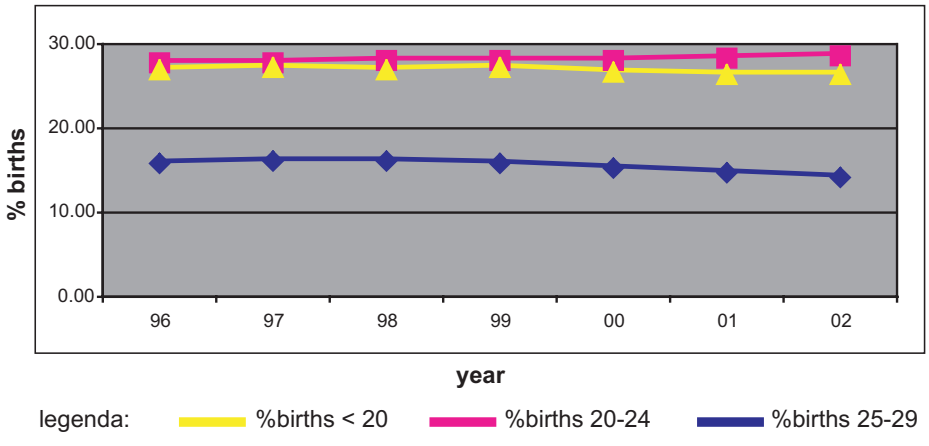
E-mail: mark.canfield@tdh.state.tx.us

USA: Texas

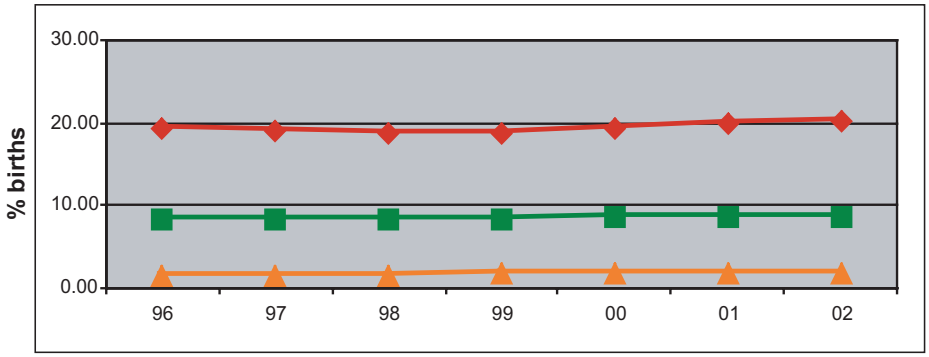
Total births by year



Percentage of births by maternal age



legenda: %births < 20 %births 20-24 %births 25-29



legenda: %births 30-34 %births 35-39 %births 40+

USA: Texas, 2003

Live births (LB)	372369
Stillbirths (SB)	2284
Total births	374653
Number of terminations of pregnancy (ToP) for birth defects	194

Birth Defects	Number of cases			Rates*10.000
	LB	SB	ToP	Total rate
Anencephaly	28	23	41	2.45
Spina bifida	91	3	2	2.56
Encephalocele	19	3	4	0.69
Microcephaly	232	4	0	6.30
Arhinencephaly / Holoprosencephaly	34	5	6	1.20
Hydrocephaly	182	6	10	5.28
Anophthalmos	10	0	1	0.29
Microphthalmos	89	3	0	2.45
Unspecified Anophthalmos / Microphthalmos	0	0	0	---
Anotia	8	0	1	0.24
Microtia	82	0	2	2.24
Unspecified Anotia / Microtia	0	0	0	---
Transposition of great vessels	140	3	0	3.81
Tetralogy of Fallot	118	1	0	3.17
Hypoplastic left heart syndrome	82	1	0	2.21
Coarctation of aorta	170	4	0	4.64
Choanal atresia, bilateral	44	0	0	1.17
Cleft palate without cleft lip	164	5	5	4.64
Cleft lip with or without cleft palate	351	7	3	9.63
Oesophageal atresia / stenosis with or without fistula	81	0	0	2.16
Small intestine atresia / stenosis	57	0	0	1.52
Anorectal atresia / stenosis	166	6	3	4.67
Undescended testis (36 weeks of gestation or later)	266	0	1	7.12
Hypospadias	554	0	3	14.86
Epispadias	16	0	0	0.43
Indeterminate sex	17	4	3	0.64
Renal agenesis	47	6	7	1.60
Cystic kidney	142	2	2	3.89
Bladder exstrophy	9	1	0	0.27
Polydactyly, preaxial	104	3	0	2.85
Total Limb reduction defects (include unspecified)	156	9	5	4.54
Transverse	85	4	2	2.43
Preaxial	30	1	1	0.85
Postaxial	10	0	0	0.27
Intercalary	7	0	1	0.21
Mixed	19	3	1	0.61
Unspecified	5	1	0	---
Diaphragmatic hernia	88	0	1	2.37
Omphalocele	53	9	8	1.87
Gastroschisis	122	14	4	3.73
Unspecified Omphalocele / Gastroschisis	8	2	0	---
Prune belly sequence	5	0	0	0.13
Trisomy 13	28	6	4	1.01
Trisomy 18	40	12	22	1.97
Down syndrome, all ages (include age unknown)	381	15	22	11.15
<20	32	0	0	5.99
20-24	50	0	1	4.74
25-29	39	1	0	4.05
30-34	64	2	4	9.28
35-39	73	4	6	25.54
40-44	55	5	7	101.53
45+	8	0	0	227.92
unspecified	60	3	4	---

USA: Texas, Previous years rates 1996 - 2002

Birth prevalence rates: (LB+SB+TOP) * 10,000

	1974-78	1979-83	1984-88	1989-93	1994-98*	1999-03*
Births					**595,992**	**1,458,775**
Anencephaly					3.31	2.76
Spina bifida					4.70	3.43
Encephalocele					1.11	0.88
Microcephaly					5.84	6.55
Arhinencephaly / Holoprosencephaly					1.48	1.19
Hydrocephaly					7.03	6.41
Anophthalmos					0.40	0.29
Microphthalmos					2.53	2.42
Unspecified Anophthalmos / Microphthalmos					---	---
Anotia					0.23	0.23
Microtia					2.32	2.52
Unspecified Anotia / Microtia					---	---
Transposition of great vessels					4.95	4.62
Tetralogy of Fallot					3.00	3.14
Hypoplastic left heart syndrome					2.25	2.02
Coarctation of aorta					5.00	4.30
Choanal atresia, bilateral					1.22	1.21
Cleft palate without cleft lip					5.74	5.55
Cleft lip with or without cleft palate					11.16	10.34
Oesophageal atresia / stenosis with or without fistula					2.25	2.08
Small intestine atresia / stenosis					1.83	1.65
Anorectal atresia / stenosis					4.09	4.65
Undescended testis (36 weeks of gestation or later)					7.11	8.31
Hypospadias					16.90	17.64
Epispadias					0.60	0.64
Indeterminate sex					1.54	1.20
Renal agenesis					2.16	1.89
Cystic kidney					4.31	4.30
Bladder exstrophy					0.22	0.20
Polydactyly, preaxial					2.87	2.92
Total Limb reduction defects (include unspecified)					5.45	5.24
Transverse					2.50	2.61
Preaxial					1.12	1.06
Postaxial					0.25	0.25
Intercalary					0.10	0.13
Mixed					1.28	1.02
Unspecified					---	---
Diaphragmatic hernia					2.35	2.65
Omphalocele					2.32	2.15
Gastroschisis					3.69	3.91
Unspecified Omphalocele / Gastroschisis					---	---
Prune belly sequence					0.22	0.25
Trisomy 13					1.12	1.19
Trisomy 18					2.47	2.15
Down syndrome, all ages (include age unknown)					11.76	12.39
<20					7.06	7.03
20-24					5.47	5.22
25-29					4.04	5.56
30-34					10.28	8.96
35-39					27.79	28.32
40-44					90.15	114.69
45+					113.31	191.80
unspecified					---	---

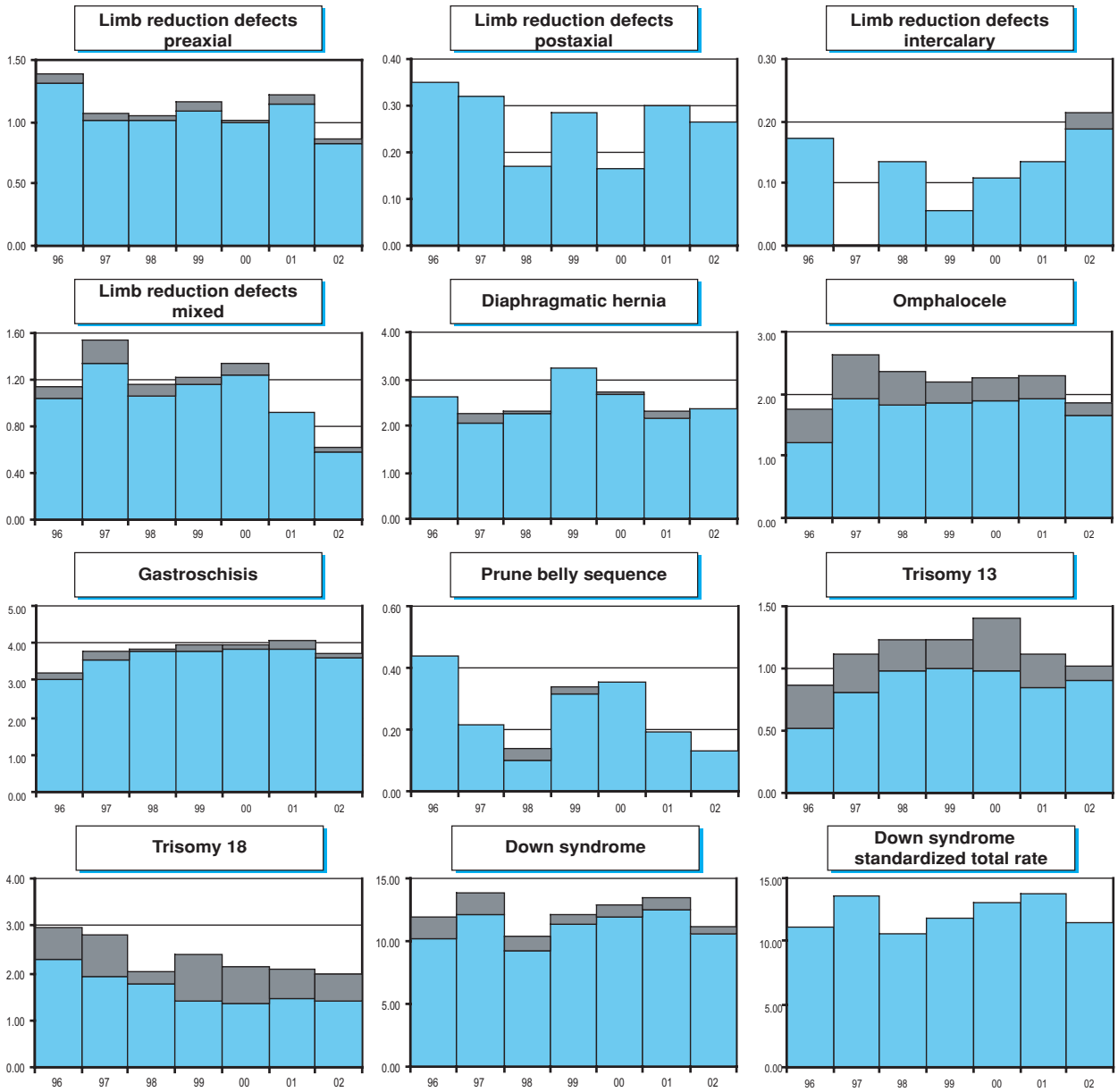
* data include less than 5 years

USA: Texas

'Time trends 1996-2003 (Birth prevalence rates per 10,000)

Note: L+S rates, ToP rates

Note: L+S rates, ToP rates



Note: L+S rates, ToP rates

5 Monitoring Systems

5.1 Monitoring Systems, not contributing with Annual Data: description of the registry

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

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

Canada: National

Canadian Congenital Anomalies Surveillance System/Network (CCASS/N)

History:
The Programme was started in 1966. It 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, capturing 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) were captured until 2000. Since 2001, all data provided by the Canadian Institute for Health Information (CIHI) include only a 30 days followup period.

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 the Public Health Agency of Canada. The Alberta Congenital Anomalies Surveillance System 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 to the central registry, 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 (CIHI) and Med-Echo. The Alberta Congenital Anomalies Surveillance System provides its own separate provincial data. All data sources had a one year follow-up period until 2000. Since 2001, all data provided by the Canadian Institute for Health Information (CIHI) only include a 30 days followup period.

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 (CIHI) and Med-Echo. The Alberta Congenital Anomalies Surveillance System provides its own background information. Interpretation of trends should be done cautiously, since 2001 an increasing percentage of records are being coded using ICD-10 CA and may cause discrepancies from the previously used ICD-9 coding. Also, the variation in the follow-up period, as mentioned previously, is another factor which may alter reporting of trends.

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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. 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.

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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.

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E-mail: jwy@cbdmp.org

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Papers can be obtained contacting authors.

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