EUROCAT - Epidemiological studies

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(on behalf of Professor Helen Dolk, Eurocat Project Leader)

Eurocat

European Surveillance of Congenital Anomalies

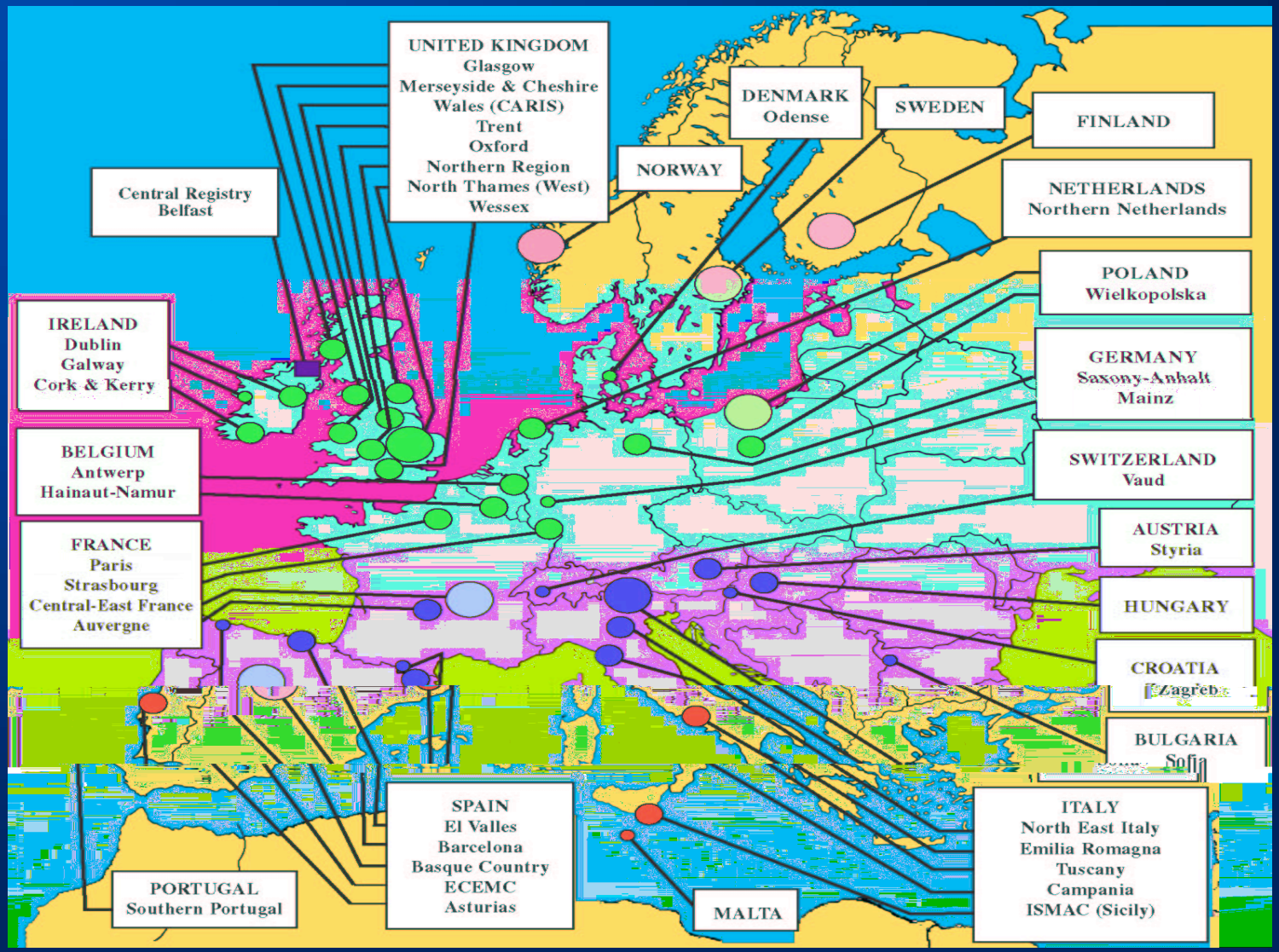
Funded by the Public Health Programme of the European Commission

WHO Collaborating Centre for the Epidemiological Surveillance of Congenital Anomalies

What is EUROCAT?

- European network of population-based registries for the epidemiologic surveillance of congenital anomalies.
- Started in 1979
- More than 1 million births surveyed per year in Europe
- 39 registries in 19 countries
- 25% of European birth population covered
- High quality multiple source registries, ascertaining terminations of pregnancy as well as births.

Map of Registries



Full Member

Associate Member

< 10,000 births per year

10,000 – 40,000 births per year

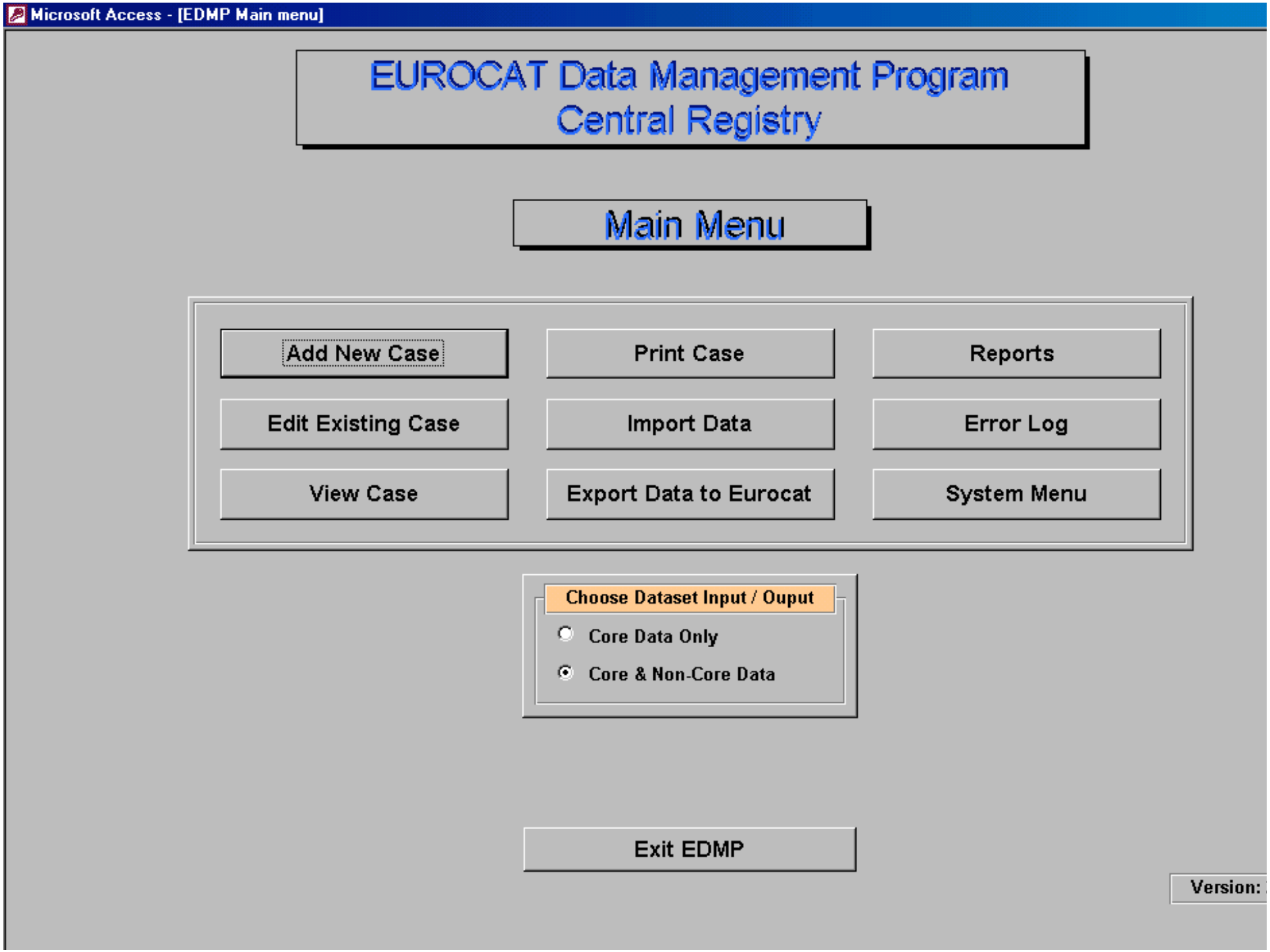
> 40,000 births per year

EUROCAT Objectives

- Provide essential epidemiologic information on congenital anomalies in Europe
- Co-ordinate the establishment of new registries throughout Europe collecting comparable, standardised data
- Co-ordinate the detection and response to clusters and early warning of teratogenic exposures

EUROCAT Objectives cont.

- evaluate the effectiveness of primary prevention
- assess the impact of developments in prenatal screening
- provide an information and resource centre and ready collaborative research network to address the causes and prevention of congenital anomalies and the treatment, care and outcome of affected individuals


Microsoft Access - [EDMP Main menu]
EUROCAT Data Management Program
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Add New Case
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Reports
Edit Existing Case
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Error Log
View Case
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Core & Non-Core Data
Exit EDMP
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Address http://www.biomedicalweb.biz/eurocat/search.cgi

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Selection Criteria

Table:

- A1: Total number of cases, number of cases by type of birth (liveborn, fetal death, induced abortion), and total prevalence rate per 10,000 birth congenital anomaly subgroups in *selected registries* (registries combined), *selected time period* (available for 28 full member registries)
- A5: *Selected congenital anomaly:* Total number of cases, number of cases by type of birth (liveborn, fetal death, induced abortion), population and total prevalence per 10,000 births per year and per registry in *selected registries*, *selected time period* (available for 32 registries)
- B3: *Selected congenital anomaly:* Total number of cases, number of cases by type of birth (liveborn, fetal death, induced abortion): total, birth livebirth prevalence rates per 10,000 births, per registry, in *selected registries*, *selected time period* (available for 32 registries)
- F1: *Selected congenital anomaly:* Line graph of *total*, *birth* and *livebirth* prevalence rate per 10,000 births per year, in *selected registries*, *selec period*

(NB: Italicised type indicates that choice is available from an option menu).

Date From: (eg. 1997)

Date To:

Click Here to view table and definitions

Continue

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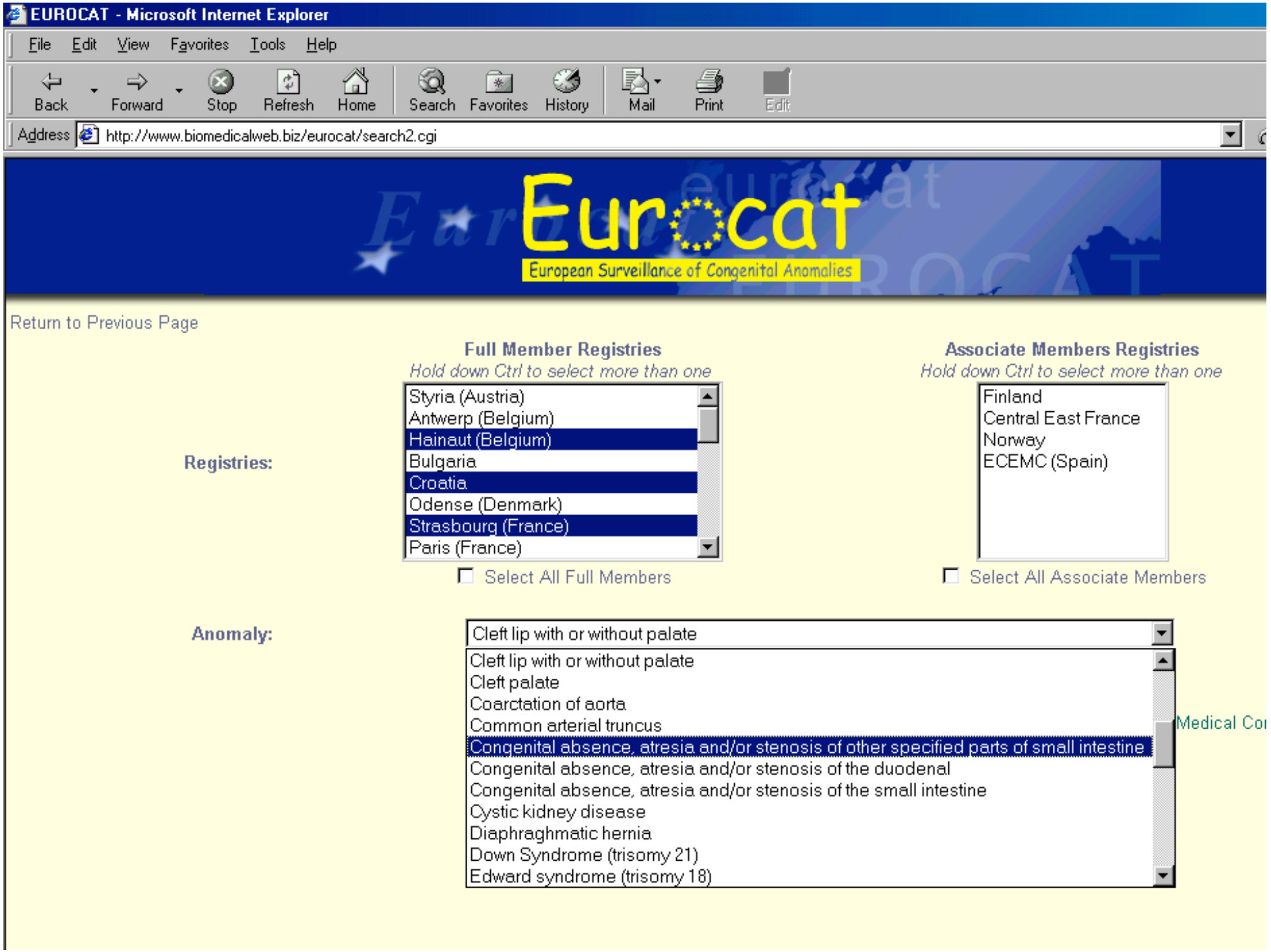
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Full Member Registries
Hold down Ctrl to select more than one
Styria (Austria)
Antwerp (Belgium)
Hainaut (Belgium)
Bulgaria
Croatia
Odense (Denmark)
Strasbourg (France)
Paris (France)
Select All Full Members
Associate Members Registries
Hold down Ctrl to select more than one
Finland
Central East France
Norway
ECEMC (Spain)
Select All Associate Members
Registries:
Anomaly:
Cleft lip with or without palate
Cleft lip with or without palate
Cleft palate
Coarctation of aorta
Common arterial truncus
Congenital absence, atresia and/or stenosis of other specified parts of small intestine
Congenital absence, atresia and/or stenosis of the duodenal
Congenital absence, atresia and/or stenosis of the small intestine
Cystic kidney disease
Diaphraghmatic hernia
Down Syndrome (trisomy 21)
Edward syndrome (trisomy 18)
Medical Co

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(B3) - Cleft lip with or without palate (prevalence per 10,000 births) for the following registries: Galway, Dublin, Mersey, North Thames (West), Glasgow, '
From 1980 - 1999

Registry	LB N	FD N	IA N	LB+FD+IA N	LB Rate	LB+FD Rate	LB+FD+IA Rate
Dublin (Ireland)	347	20	0	367	8.31	8.73	8.73
Galway (Ireland)	31	5	0	36	5.44	6.28	6.28
Mersey (UK: England)	110	2	5	117	6.56	6.64	6.94
North Thames (West) (UK: England)	338	19	74	431	7.14	7.55	9.11
Glasgow (UK: Scotland)	191	13	22	226	7.49	7.96	8.81
Wales (UK: Wales)	61	1	10	72	6.25	6.32	7.34
Total (full member registries):	**1078**	**60**	**111**	**1249**	**7.34**	**7.72**	**8.47**

LB = Live Births
FD = Fetal Deaths / Still Births from 20 weeks gestation
IA = Induced Abortions following prenatal diagnosis

For total live birth rates where the live birth denominator is not available, the denominator has been substituted by the total number of births (live births + stil births). This applies to the following registries: North Thames (West)

Description Of Anomaly	ICD9	ICD10	Comments
Clefting of the upper lip with or without clefting of the maxillary alveolar process and hard and soft palate	7491, 7492	Q36-Q37	

Why European collaboration?

- Pooling of data
- Comparison of data
- Common response to public health questions
- Sharing of expertise and resources

EUROCAT Special Reports and Coding Guides 2005-2006

- EUROCAT (2005) EUROCAT Special Report: Prevention of Neural Tube Defects by Periconceptional Folic Acid Supplementation in Europe. EUROCAT Central Registry, University of Ulster. (www.eurocat/ulster.ac.uk/pubdata.Folic-Acid.html)

- EUROCAT (2005), "EUROCAT Special Report: Prenatal Screening Policies in Europe". EUROCAT Central Registry, University of Ulster. (www.eurocat.ulster.ac.uk/pdf/Special-Report-Prenatal-Diagnosis.pdf)

- EUROCAT (2005), "EUROCAT Guide 1.3: Instruction for the Registration of Congenital Anomalies", EUROCAT Central Registry, University of Ulster. (www.eurocat.ulster.ac.uk/pubdata/Guide%201.3.html)

- EUROCAT (2005), "EUROCAT Guide 6: definition and Coding of Syndromes", *EUROCAT Central Registry*, University of Ulster. (www.eurocat.ulster.ac.uk/pdf/Ester/EUROCAT%20Guide%206%20Version%203.pdf)

A full list of EUROCAT publications and links to Reports can be found on:
www. eurocat.ulster.ac.uk/pubdata/publist.html

EUROCAT Publications

8. ……
9. Garne E, Loane, M, Dolk H et al (2005), "Prenatal Diagnosis of Severe Structural Congenital Malformations in Europe", *Ultrasound Obstet Gynecol*, Vol 25, pp 6-11.
10. International database of Craniofacial Anomalies (IDCFA) (2005), www.who.int/genomics/anomalies/idcfa_overview.pdf.
11. Loane M, Dolk H, Bradbory I et al (submitted for publication), "Increasing Prevalence of Gastrochisis in europe 1980-2002: A Phenomenon Restricted to Younger Mothers?"
12. Meijer WM, Cornel MC, Dolk H et al (2006), "The Potential of the European network of Congenital Anomaly Registers (EUROCAT) for Drug Safety Surveillance: A Descriptive Study", *Pharmacoepidemiology and Drug Safety*, Vol 15, pp 675-682.
13. Morris JK, de Vigan C, Mutton De et al (2005), "Risk of a Down Syndrome Live Birth in Women of 45 Years of Age and Older", *Prenatal Diagnosis*, Vol 25, pp 275-278.
14. Wellesley D, Bpyd P, Dolk H et al (2005), "An Aetiological Classification of Birth Defects for Epidemiological Research", *Journal of Medical Genetics*, Vol 42, No 1, pp 54-57
15. …….

EUROCAT News

- Further funding has been obtained from the European Commission for the period September 2007 to August 2010

- Prevalence data updated to 2006 on website.

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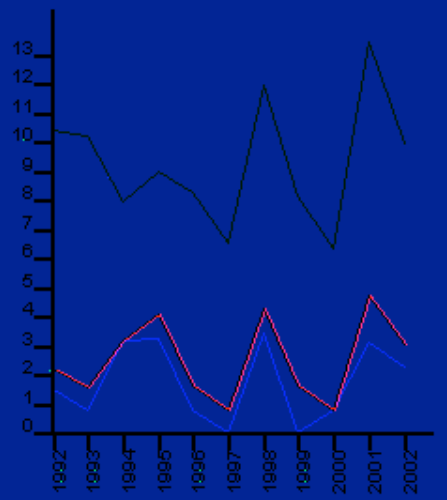
om 1990 - 2002

(F1) - Neural Tube Defects (total, birth and livebirth prevalence per 10,000 births) for the following registries: Barcelona, Fr

The graphs on this page require the Java2 runtime environment.
Click here if you cannot see the graph below

LEGEND
Total Prevalence
Birth Prevalence
Live Birth Prevalence

Barcelona (Spain)



Source : EUROCAT Website Database: http://www.eurocat.ulster.ac.uk/pubdata/tables.html (data uploaded 17/11/2004)

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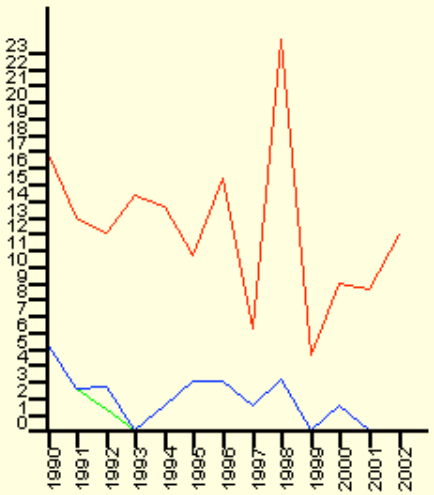
(F1) - Neural Tube Defects (total, birth and livebirth prevalence per 10,000 births) for the following registries: Basque Country, Asturias, Barcelona, **From** 1990 - 2002

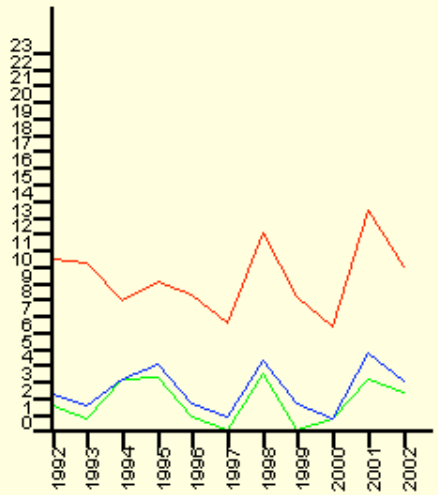
The graphs on this page require the Java2 runtime environment.
Click here if you cannot see the graph below

LEGEND
Total Prevalence
Birth Prevalence
Live Birth Prevalence

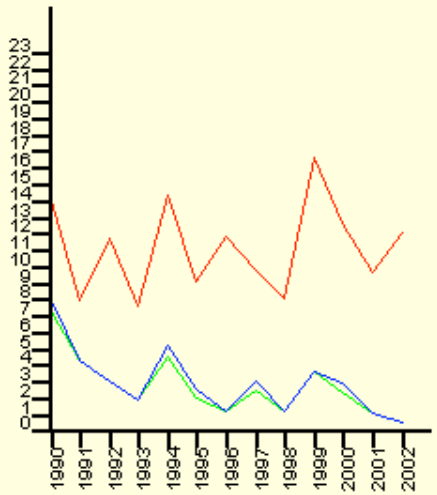
Asturias (Spain)



Barcelona (Spain)



Basque Country (Spain)

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Confidentiality

EUROCAT Guide 1.3

Prevalence Rates

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Guide 1.3 - Instructions for the Registration and Surveillance of Congenital Anomalies

Guide 1.3 - Instructions for the registration and Surveillance of Congenital Anomalies

Annex Documents

EUROCAT Guide 6: Definition and Coding of Syndromes

ICD10-BPA Extension Codes

EUROCAT activity on rare congenital anomalies

- routine collection, registration, analysis
- ad-hoc studies on rare

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Rare Diseases Task Force

Rare Diseases Task Force

ADOPTED AND FINALISED: Commission Proposal for a New Health and Consumer Strategy and Programme

German

French

English

Useful Links

Rare Diseases Task Force	www.rdtf.org
DG Sanco Rare Diseases Section	http://www.europa.eu.int/comm/health/ph_threats/non_com/rare_diseases_en.htm
Orphanews Newsletter of the RDTF	www.orpha.net
Rare Diseases Spain	http://repier.retics.net/repier/home.aspx
Orphanet Journal of Rare Diseases	www.ojrd.com

ACTIVITIES ON RARE CONGENITAL ANOMALIES: FIVE EXAMPLES

1. Epidemiology of rare syndromes in Europe
2. Registration and surveillance of Sentinel Phenotypes
3. Study of Gastroschisis
4. Survey of confidentiality and consent issues in EUROCAT registries
5. Folic acid and congenital anomalies

EPIDEMIOLOGY OF RARE SYNDROMES IN EUROPE

Main objectives are to:

- produce prevalence rates and descriptive epidemiology data on 9 rare malformation syndromes recognisable at birth
- assess the possible impact of prenatal diagnosis on the prevalence rates
- look for possible regional differences regarding the time of diagnosis of selected syndromes

EPIDEMIOLOGY OF RARE SYNDROMES IN EUROPE

cont..

- study type of birth (TOP, SB, LB) and survival
- describe clinical presentation and associated malformations in relation to “pure” or “minimal diagnostic criteria” definition of selected syndromes in non-Mendelian conditions
- look into geographic and time distribution for possible trends and clusters
- investigate the possible teratogenic exposures

EPIDEMIOLOGY OF RARE SYNDROMES IN EUROPE

cont …

- assess the accuracy of the diagnosis in registries of congenital malformations
- determine the role of medical geneticists in local registries in the diagnosing of syndrome cases
- evaluate the process of coding to improve the coding system

EPIDEMIOLOGY OF RARE SYNDROMES IN EUROPE

Syndrome	Reference	Prevalence (*)
Fraser	*Martinez-Frias et al 1998*	4.3
Cornelia de Lange	*Beck et al 1976*	6.0
Holt-Oram	*Elek et al 1991*	9.5
Fryns	*Ayme et al 1989*	7.0
Goldenhar	*Gorlin et al 1990*	18.0
	Morrison et al 1992	22.0
Meckel-Gruber	*Salonen and Norio 1984*	11.1
	Martinez-Frias et al 1994	8.0
Ellis van Creveld	*Mahony 1994*	7.0
Beckwith-Wiedemann	*Hamel et al 1981*	66.7
Treacher-Collins	*Jahrsdoerfer et al 1995*	20.0

(*) per 10,000 births

Descriptive epidemiology of Cornelia de Lange syndrome in Europe

Barisic I, Tokic V, Loane M, Bianchi F, Calzolari E, Garne E, Wellesley D, Dolk H; EUROCAT WG, Am J Med Genet A. 2008

Based on 23 years of epidemiologic monitoring (8,558,346 births in the 1980-2002 period), we found the prevalence of the classical form of CdLS to be 12.4/10,000 and estimated the overall CdLS prevalence at 16-22/10,000.

- live born 91.5%
- fetal deaths 2.8%
- termination of pregnancy 5.7%

Descriptive epidemiology of Cornelia de Lange syndrome in Europe

The most frequent associated congenital anomalies were:

- limb defects (73.1%)
- congenital heart defects (45.6%)
- central nervous system malformations (40.2%)
- cleft palate (21.7%)

Descriptive epidemiology of Cornelia de Lange syndrome in Europe

- In the last 11 years, as much as 68% of cases with major malformations were not detected by routine prenatal US
- Live born infants have a high first week survival (91.4%)
- All patients were sporadic
- Maternal and paternal age did not seem to be risk factors
- Almost 70% born after the 37th week of gestation weighed ≤ 2,500 g.
- Low birth weight correlated with a more severe phenotype.
- Severe limb defects were significantly more often present in males.

THE PREVALENCE AND SURVEILLANCE OF "SENTINEL PHENOTYPES"

- Surveillance of "sentinel phenotypes" has been proposed as a way of monitoring the rate of new mutations in a population

  (*WHO, 1985 &1988; Rutstein,D.D.et al.)*

- For a successful monitoring, SP should be well defined and diagnosed prenatally or soon after birth. Since information is not available to verify familial inheritance for each case, syndromes can be chosen which are always or usually due to new mutations, including those lethal in early life where familial inheritance is not possible.

THE PREVALENCE AND SURVEILLANCE OF "SENTINEL PHENOTYPES"

The EUROCAT subcommittee on Multiple Malformations recommends five syndromes, caused by new mutations (rather than familial inheritance) in more than 90% of cases.

• Achondroplasia	1.3 - 15.0	per 100,00 births
• Thanatophoric dysplasia	0.7 - 3.8	"
• Osteogenesis imperfecta	3.6 - 4.0	"
• Campomelic dysplasia	0.5	"
• Apert Syndrome	0.7	"

Study of Gastroschisis

Gastroschisis is a rare abdominal wall anomaly which has been increasing in prevalence in Europe and worldwide.

It is well established that young maternal age is a strong risk factor for this anomaly.
Smoking, recreational drug use and some therapeutic drugs are also risk factors.

A working group for investigating trends in prevalence by maternal age has been activated and a paper is in press.

Study of Gastroschisis

We analysed 936 cases of gastroschisis from 25 population-based registries in 15 European countries, 1980-2002.

The maternal age standardised prevalence rose

from 0.54 per 10,000 in 1980-84

to 2.12 per 10,000 in 2000-2002

Study of Gastroschisis

The relative risk for mothers <20 years of age 1995-2002 was 7.0 [95% C I 5.6, 8.7]

There were geographical differences within Europe, with higher rates in the UK and lower rates in Italy, after adjusting for maternal age

Study of Gastroschisis

After standardising for regional variation, our results showed that the increase in risk over time was the same for mothers of all ages.

These findings indicate that the phenomenon of increasing gastroschisis prevalence is not restricted to younger mothers only.

Survey of confidentiality and consent issues in EUROCAT registries

The EUROCAT survey was published in BMJ, 2005.

It was also presented to the Network of Competent Authorities, 5-6 July 2005 in Luxembourg and the Rare Diseases Task Force.

Registries collecting personal medical data must, under EC Directive 95/46/EC, obtain consent for the processing of such data, unless national law or a national supervisory body allows for an exemption. Member states have not always taken advantage of the ability to exempt health care or disease registries.

Survey of confidentiality and consent issues in EUROCAT registries

EUROCAT experience indicates that opt-in consent poses a serious threat to the operation of congenital anomaly registries.

The debate about informed consent has eclipsed more relevant consideration of procedures to maintain confidentiality of data or ensure the ethical operation of registries.

EUROCAT actvities on FOLIC ACID

Annual survey in member countries of policy changes regarding:

- *periconceptional FA supplementation*
- *health education initiatives undertaken*
- *available data on FA uptake*
- *analysis of available data on protective effect for other congenital anomalies*

EUROCAT actvities on FOLIC ACID

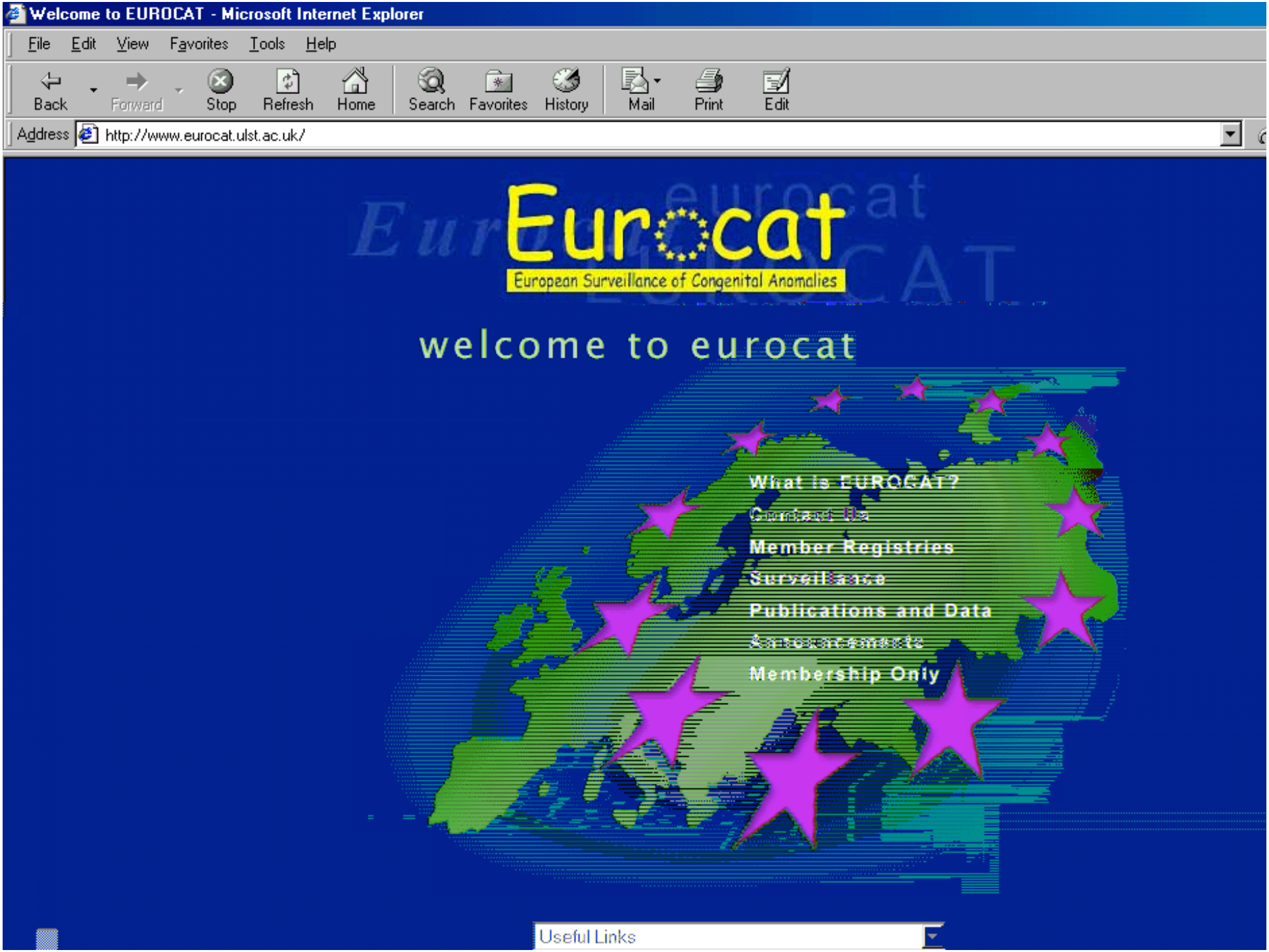
The 2007 update documents policy changes in a few countries, especially Italy, and the extremely slow progress in fortification of food with FA.

Although fortification has been advised in a few countries, it has not yet been implemented.

This report is on the EUROCAT website.

EUROCAT continues to advocate the recommendations from the earlier report.

Country representatives supply information on policy and practice changes periodically.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