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Oral Abstracts

Congenital anomalies and small for gestational age: is there a Relation?

A Vinkel-Hansen, E Garne, A-M Nybo Andersen

Background: Congenital anomalies and fetal growth restriction may share the same pathogenic factors. We aim to describe the proportion of intrauterine growth restriction measured as small for gestational age (SGA) among live and stillborn infants with congenital anomalies compared to the background population. **Methods**: Data from the EUROCAT congenital anomaly registry for Funen county is linked to the background population for the same geographical area. SGA is defined as birth weight falling below the 10^{th} percentile of the birth weight distribution for Danish births of a given sex in a given week of gestation in a given year. Due to a small reference group, SGA is only computed for gestational age $\geq$28 weeks. **Results**: Out of a total of 87,881 births, 2,074 had a major congenital anomaly giving a prevalence of 2.36% (2.26-2.46). For SGA infants, prevalence of congenital anomalies was 4.18% (3.79-4.61). Among infants with isolated structural anomalies, 15.9% were SGA at birth compared to 10.5% in the population. For infants with multiple anomalies or chromosomal anomaly, the proportion of SGA infants was 25.3% and 33.8% respectively. **Conclusions**: There is a statistically significant relation between major congenital anomalies and fetal growth restriction.

Role and modalities of thyroid function screening in children with Down syndrome: a prospective cohort study

G Poletti, A Rocca, GD Rana, A Cassio, G Cocchi

Background: Thyroid dysfunction occurs more frequently in children with Down syndrome than in the overall population. Therefore, strict thyroid function monitoring is deemed necessary. However, modalities to screen these subjects are not yet clearly defined. **Materials and Methods**: Thyroid function was prospectively evaluated in 100 children with Down syndrome. Thyroid function was assessed and monitored by dosing fT3, fT4, TSH, and autoantibodies such as anti – TG and anti – TPO. Data were analyzed using Fisher exact test and linear regression. **Results**: Congenital laboratory hypothyroidism was detected in four cases (4%). These patients were followed for 8.6 +/- 4.7 years. During the follow-up, three subjects developed hyperthyroidism (3%) and 24 hypothyroidism (24%). Positive autoantibodies were associated with a higher risk of developing hypothyroidism (p: 0.009 – OR: 0.14). In fact, subjects with autoantibodies were nine, six of whom developed severe hypothyroidism during the follow-up. Therapy was started at the median age of 2.8 years, but in four cases (16.5%) significantly earlier (at 3 months of life). The subclinical hypothyroidism was a condition tending to be self-limiting ($p < 0.01$, r: $-0,1$). **Conclusion**: According to our observations, thyroid function should be strictly monitored in children with Down syndrome, especially during the first year of life. Moreover, thyroid function should be monitored by dosing fT3, fT4, TSH and autoantibodies, because auto-antibodies positivity seems to be a good predictor of hypothyroidism appearance later on.

Fetal exposure to Montelukast and congenital anomalies

C Cavero-Carbonell, E Garne, A Vinkel-Hansen, MJ Rabanaque-Hernández, C Martos-Jiménez, O Zurriaga

Objective: To study differences in pregnancy outcomes between groups of Danish women whose pregnancy has ended between 1998-2009 according to their exposure to Montelukast. **Methods**: Cross-sectional observational study in Danish women, selecting live births and stillbirths (Birth Registry) and spontaneous abortions and induced terminations (Patient Registry). Montelukast exposure was obtained from the Prescription Registry (code R03DC03). The exposure period was from three months before the last menstrual period until the end of the first trimester. Four groups were studied: 1) women with prescription for Montelukast, 2) women with prescription for Montelukast and other anti-asthmatic drugs, 3) women with prescription for other anti-asthmatic drugs, 4) women without prescription for Montelukast or any other anti-asthmatic drugs. **Results**: A total of 754,300 singleton pregnancies ($>$ 12 weeks) were identified: 401 pregnancies in group 1, 426 pregnancies in group 2, 24,878 in group 3 and 728,595 in group 4. Risk of preterm birth and for maternal preeclampsia and gestational diabetes was increased for pregnancies exposed to Montelukast. No significant differences were found for the risk of congenital anomalies. Adjusted odds ratio for congenital anomalies was 1.41 (95% CI 0.86-2.33) for the group 1. 50 congenital anomalies were identified in 33 live births and three in induced terminations for groups 1 and 2. **Conclusions**: Women treated with Montelukast had a higher risk of preterm birth and maternal complications, but the higher risk of congenital anomalies was not found. Further analysis including more exposed pregnancies will be needed in order to determine a risk of specific congenital anomalies.

Maternal occupational exposure and oral clefts in offspring

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Background: Oral clefts are common congenital anomalies, but their aetiology is not fully understood. Previous studies found an association between maternal occupational exposures and oral clefts in the offspring, but results are inconsistent. **Methods**: This case-malformed control study used data from a population-based birth defects registry (EUROCAT) of children and fetuses born in the Northern Netherlands between 1997 and 2013. Cases were defined as non-syndromic oral clefts and malformed controls had chromosomal/syndromal defects. Maternal occupational exposure was estimated through linkage of mothers' occupation with a Job Exposure Matrix. A multivariate logistic regression was used to estimate the effect of occupational exposure. Odds ratios (ORs) were adjusted for the child's gender, maternal age at delivery, pre-pregnancy BMI, education level, smoking and alcohol use during pregnancy, positive family history for congenital anomalies and for concurrent exposures. **Results**: A total of 387 cases and 1,135 controls were included in this study. Prevalence of maternal occupational exposure in general was 43.9% and 41.0% among cases and controls, respectively. The highest aORs were found for fungicides and insecticides (aOR=1.7, 95% CI 0.8-3.5 and aOR=1.7 95% CI 0.8-3.3, respectively). Maternal occupational exposure to fungicides and insecticides adjusted for exposure to organic and mineral dust was associated with cleft palate in the offspring (aOR=4.2, 95% CI: 1.1-15.6 and aOR=3.9, 95% CI: 1.0-14.9). No other statistically significant associations were observed. **Conclusions**: Our findings suggest that maternal occupational exposure to fungicides and/or insecticides during the periconceptional period increases the risk of a cleft palate in the offspring.

Predictors of survival in children born with congenital diaphragmatic hernia: a registry-based study

Vieira R, Rankin J

Background: Congenital diaphragmatic hernia (CDH) is a severe congenital anomaly associated with high neonatal mortality. This study aims to evaluate the predictors for survival in infants born with CDH. **Methods**: A cohort study of prospectively collected data on all liveborn infants with CDH notified to the population-based UK Northern Congenital Abnormality Survey (NorCAS), and delivered between 01 Jan 1985 and 31 Dec 2003, matched to hospital and national mortality records to 29 Jan 2008. Survival to 20 years was estimated using Kaplan-Meier methods. Multiple logistic regression was used to identify overall predictors of mortality while Royston-Parmar survival models were used to examine predictors of survival at 1-week and 1-month within the children that died. **Results**: There were 246 CDH singleton infants notified to NorCAS during the study period, a total prevalence of 3.8 (95% CI: 3.3,4.3) CDH cases per 10,000 pregnancies. Of these, 18.3% resulted in termination of pregnancy, 7.3% in spontaneous fetal loss (miscarriage$\geq$20 weeks and stillbirth) and 74.4% in live births. Forty-seven percent of the live births resulted in death. Year of birth (per year; OR=0.88; 95% CI: 0.82, 0.95; $p<0.001$), birth weight (per 100g; OR=0.92; 95% CI: 0.86, 0.98; $p=0.007$), most deprived (compared to moderately deprived; OR=2.98; 95% CI: 1.28, 6.92; $p=0.01$), prenatal diagnosis (OR=5.0; 95% CI: 2.17, 11.4; $p<0.001$) and presence of other congenital anomalies (OR=5.3; 95% CI: 1.46, 18.7; $p=0.01$) were significant predictors of mortality. Within the children that died, year of birth (per year; Hazard Ratio (HR)=0.95; 95% CI: 0.91, 0.99; $p<0.001$) was the only significant predictor of survival at 1-week and 1-month. **Conclusions**: Identifying predictors of survival is important for prenatal counselling of parents whose pregnancy is affected by CDH and for health care planning for the future care needs of affected children.

Risk of recurrent congenital anomalies in successive pregnancies: a population-based register study in the North of England

SV Glinianaia, PWG Tennant, J Rankin

Background: There is limited information on the recurrence of sporadic congenital anomalies in successive pregnancies. We estimated the absolute and relative risks of recurrent congenital anomaly in the second pregnancy for mothers who experienced congenital anomaly in their first pregnancy. **Methods**: Data on 18,524 singleton pregnancies affected by major

congenital anomaly occurring in 872,500 singleton stillbirths, live births and terminations of pregnancy for fetal anomaly were obtained from the Northern Congenital Abnormality Survey for 1985-2010. Absolute risks (AR) and relative risks (RR) for recurrent anomaly in the second pregnancy were estimated by congenital anomaly group/subtype in the first pregnancy. **Results**: The estimated prevalences of congenital anomaly in first and second pregnancies were 276 (95% CI=270-281) and 163 (159-168) per 10,000 respectively. For women with a congenital anomaly in their first pregnancy, the AR of recurrent congenital anomaly in the second pregnancy was 378 (336-420) per 10,000, 2.4 (2.2-2.7, $p<0.0001$) times higher than for those with unaffected first pregnancies. For similar anomalies, the RR was substantially elevated [21.6 (18.1-25.1, $p<0.0001$)] while for dissimilar anomalies the RR was modest [1.2 (1.1-1.4, $p=0.007$)], though the ARs for both were around 2%. Lower socio-economic circumstances were associated with higher recurrence risk independent of maternal age. **Conclusions**: For most major congenital anomaly groups, absolute recurrence risks varied between 1 in 20 and 1 in 30. At pre-conception counselling, women whose first pregnancy was affected by a congenital anomaly may find it reassuring that despite high relative risks, the absolute recurrence risk is relatively low.

Modelling rates of disability: predicted population prevalence of spina bifida in children across England and Wales by 2020

K Best, SV Glinianaia, R Lingam, J Rankin

Background: Spina bifida is the commonest neural tube defect, occurring in 4.7 per 10,000 births in Europe, often resulting in permanent disability. We aimed to estimate the number of individuals aged <16 years with spina bifida in England & Wales in 2020. **Methods**: Cases of spina bifida born during 1985-2013 were identified from the Northern Congenital Abnormality Survey (NorCAS). Cases associated with chromosomal or structural anomalies were excluded. Poisson regression was performed to model temporal trends in the prevalence of spina bifida in the North of England until 2013. Using the UK Office for National Statistics projected population births, these models were extrapolated to estimate the number of cases born each year in England and Wales until 2020. Survival up to age 16 was estimated from a NorCAS dataset of livebirths in 1985-2003, and linked to death registrations in 2008.[1] The number of children aged <16 living with spina bifida in England and Wales was estimated by multiplying year-specific survival estimates by modelled case numbers. **Results**: There were 128 and 119 liveborn cases of spina bifida with and without hydrocephalus respectively during 1985-2013. For cases born in 2004, 78.1% (95% confidence interval (CI) 45.2-92.6%) and 94.9% (95% CI 69.8-99.2%) with and without hydrocephalus were predicted to be living by 2020. In 2020, an estimated 1929 children aged <16 will be living with spina bifida in England and Wales, of which 620 will also have hydrocephalus. **Conclusions**: Estimating the number of individuals living with spina bifida is important for health and social care planning.

Epidemiological surveillance of fetal diseases related to Zika virus, mainland France, 2016

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Background: The outbreak of Zika virus (ZIKV), transmitted by *Aedes mosquitoes,* reached the French Departments of the Americas in December 2015. Little known, this frequently asymptomatic infection which was deemed benign, may probably be responsible for severe fetopathies. This potential severity and the risk of transmission, from May to November, in the 30 Departments of mainland France, where the *Aedes albopictus* vector is present in 2016, has led to the implementation of specific surveillance. **Methods**: The surveillance is intended to guide prevention and control actions through: 1) the identification and description of imported cases; 2) the early detection of imported and autochthonous cases to initiate the appropriate vector control measures in the 30 Departments where *Aedes Albopictus* is present. A confirmed ZIKV infection is defined by positive RT-PCR for Zika or by positive Zika serology (IgM or seroconversion or fourfold increase of IgG confirmed by serum neutralization). The monitoring of anomalies identified in fetuses or newborns of ZIKV-infected pregnant women or women exposed to areas where the virus is present, is based on multidisciplinary prenatal diagnosis centers and their network of laboratories, obstetricians, sonographers and pediatricians. **Results**: As of 25 February 2016, 81 imported cases of Zika were recorded in mainland France including five pregnant women. **Conclusions**: Surveillance will contribute to the identification and the description of cases of fetal malformation identified in women infected by the Zika virus during their pregnancy.

Obtaining global estimates of the baseline birth prevalence of congenital malformations using EUROCAT data

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Background: The baseline birth prevalence (including termination of pregnancy, fetal death and livebirths) of many congenital malformations is determined by basic biological principles. Consequently, registry data from high income countries can be used to obtain average rates and generate estimates for countries globally with no or insufficient observational data. We describe the use of EUROCAT data to obtain these for "non-syndromic" congenital malformations (NSCM) whose primary causes have not been attributed to specific genetic or environmental factors. **Methods**: EUROCAT data on pregnancy outcomes of "non-genetic" malformations for the years 2000-2009 was downloaded by individual system group. As individuals with more than one malformation appear in multiple system groups, we undertook the

TABLE 1. *Baseline birth prevalence rates of isolated malformations in the absence of intervention from EUROCAT data 2000-09*

System group	EUROCAT non-syndromic/1,000	Per cent associated[a]	Births, isolated malformations/ 1,000	Multiple malfns/1,000
Baseline birth prevalence, non-syndromic malformations[b]	20.3		18.7	1.59
Neural Tube Defects	0.94	13.0	0.82	0.12
CNS not NTD	1.25	23.5	0.96	0.29
Eye	0.40	24.4	0.31	0.10
Ear, face and neck	0.34	38.1	0.21	0.13
Congenital heart defects	7.17	11.0	6.39	0.79
Respiratory	0.57	11.7	0.50	0.07
Oro-facial clefts	1.37	15.5	1.16	0.21
Digestive system	1.60	29.9	1.13	0.48
Abdominal wall defects	0.49	14.2	0.42	0.07
Urinary	3.15	10.7	2.82	0.34
Genital	2.04	12.8	1.78	0.26
Limb	4.20	11.0	3.75	0.46
Sum of system groups	23.5	14.1	20.3	3.32

[a]Based on data from Rittler et al (2008) and Garne (2011)

[b]includes affected livebirths, fetal deaths and terminations of pregnancy

following to estimate the rates for individuals with isolated and multiple malformations.

1. Calculation of average birth prevalence of NSCM and by system group.

2. Calculation of proportion of each system group isolated or associated with other types of malformation by system group.

3. Estimation of rates for individuals with multiple malformations.

4. Application of rates from steps 2 & 3 to obtain average birth prevalences of individuals with isolated or multiple malformations by system group.

Results: Table 1 shows the rates calculated for isolated and multiple malformations by system group.

Conclusions: EUROCAT data can be used to obtain rates for baseline birth prevalence of most congenital malformations. In the absence of local data, these rates can themselves provide a starting point for assessing disease burden and service implications. Processed further, they can also contribute to structured, systematic evidence-based public health policy development at the local level.

Codes matter: identifying complex congenital anomalies in England and Scotland

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Aim: We aimed to compare prevalence rates of complex congenital anomalies (CCAs) in the first two years of life in England and Scotland using two published CCA diagnosis code lists developed to identify children who will require high levels of healthcare attention. **Methods**: We used Scottish and English administrative population-based hospital data to extract hospital live births between 1998-2011, with two years of follow-up. We compared CCA prevalence using two CCA ICD-9/10 code lists developed in the UK (Hardelid et al.) and the US (Feudtner et al.). To assess required level of healthcare, we compared the proportion of children who had at least one re-admission to hospital in the first two years of life. **Results**: Rates of CCAs in England and Scotland were higher using the Hardelid codelist (2.8% for both countries) than the Feudtner codelist (1.8% and 1.5% respectively, table 1). CCA rates increased between 1997-2011: the increase was more notable with the Hardelid codelist (37.2% and 20.2%, in England and Scotland, respectively) than with the Feudtner codelist (35.6% and 13.0%). The proportion of children with more than one re-admission in 2011 was higher with Feudtner (75.7% in England and 84.8% in Scotland) than with Hardelid (73.9% and 72.0% in England and Scotland, respectively). **Conclusions**: Prevalence of CCAs and associated hospital use vary depending on use of CCA code list. The impact of coding methods for defining CCAs in administrative hospital records should be explored and externally validated when comparing prevalence of CCAs and associated hospital use between countries.

	England		
	Hardelid	**Feudtner**	**No CA**
Average prevalence CA	2.8%	1.8%	-
% Change 1998-2011	37.2%	35.6%	-
Proportion with +1 re-admission for children born in 1998	60.6%	63.6%	18.6%
Proportion with + re-admission for children born in 2011	73.9%	75.7%	30.0%
	Scotland		
	Hardelid	**Feudtner**	**No CA**
Average prevalence CA	2.8%	1.5%	-
% Change 1998-2011	20.2%	13.0%	-
Proportion with +1 re-admission for children born in 1998	76.6%	81.2%	24.0%
Proportion with + re-admission for children born in 2011	72.0%	84.8%	25.8%

Predictive performance of surgical severity scores for risk of infant mortality of newborns with congenital heart defects (CHD): a population-based survival analysis study (the EPICARD cohort study)

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Background: Whereas there is no global severity score for CHD, risk (RACHS-1) and/or complexity (Aristotle) scores exist for surgical cases. However, previous studies did not assess their performance in population-based data, did not look at timing of mortality, neither did they adequately assess the predictive ability of the proposed risk scores. Our objective was to assess the predictive performance of RACHS-1 and Aristotle basic scores using survival analysis of surgical data from a population-based cohort study. **Methods**: Data comprised 2348 newborns, of whom 501 had surgery, including 450 who had a curative procedure and the final study population of 443 newborns with complete data. Statistical analyses included Kaplan-Meyer curves and Cox models. Indices of model performance included Harrell's C, Gönen & Heller's K and Royston's R^2. Models were estimated using each score alone and together with other known predictors of infant mortality. **Results**: Overall, infant mortality of newborns who had curative surgery was 6.1%, (95% CI, 4.1–8.7). Risk of mortality increased substantially as RACHS-1 scores increased; hazard ratios were 1 (ref. category, scores 1-2), 1.7, 4.9 and 12.7 for scores 3, 4, and 5-6, respectively ($p< 0.001$); relation between mortality and Aristotle scores was much weaker and was not statistically significant. All indices of model performance were higher for RACHS-1 based models (e.g., Royston's R^2 0.30 vs. 0.06). **Conclusions**: The RACHS-1-based models had greater discrimination and higher explained variance than Aristotle-based models. Nonetheless, estimates of explained variance suggested substantial "unobserved" residual heterogeneity in the models based on these scores.

Developmental dysplasia of the hip (DDH) - screening and early outcome

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Background: Congenital developmental dysplasia of the hip (DDH) can be a precursor of adult hip disease. Management is dependent on age at diagnosis. Later diagnoses are more likely to necessitate surgical intervention, have poorer outcomes and increase the risk of a total hip replacement in young adulthood. Authors generally classify diagnosis after age three months as late diagnosis. Reported rates of DDH per 10,000 births vary widely for EUROCAT registries. Best practice on screening for DDH is not agreed with differing international recommendations. The outcome of screening for DDH is poorly documented. **Methods**: Cases of DDH registered between 2009-2013 on the Cork and Kerry Congenital Anomaly Register EUROCAT Registry were reviewed. **Results**: Between 2009 and 2013, there were 283 (0.69 per 10,000 live births) and 38 (0.39 per 10,000 live births) cases of DDH in Cork and Kerry respectively. Screening practice with respect to DDH was different in each county. Sixty-two per cent and 74% of Cork and Kerry cases respectively were diagnosed late (after three months). Late diagnosed infants were more likely to require surgical management with 7% and 16% of Cork and Kerry cases respectively requiring open surgery. **Conclusions**: Early outcome of DDH is influenced by screening practice with less invasive treatment possible with earlier diagnosis. Whether earlier treatment can prevent total hip replacement in young adulthood is unclear. Later outcome of screening for and treatment of DDH starts with case ascertainment and DDH case registration. A long term cohort study is recommended.

POSTER ABSTRACTS

Maternal obesity and the risk of congenital anomalies: use of BMI data from the IMER registry

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Background: Obesity is a risk factor for many chronic diseases and maternal obesity adversely impacts pregnancy outcome including congenital anomalies. The EUROCAT recommendations for the primary prevention of congenital anomalies, present an array of actions aimed at reducing risk factors like overweight and obesity. Body mass index (BMI) is a simple measure commonly used to classify overweight and obesity in adults. From 2013 the IMER registry and hospital birth records contained this variable allowing research. **Objective and Methods**: The aim of the study was to compare the BMI distribution in mothers of babies with congenital anomalies (IMER 2013), with the BMI distribution in the general population (report on births in 2013 in Emilia-Romagna). The relationship between BMI and associated factors in the general population was investigated. IMER data on 821 mothers were compared with the results of the analysis on 34,466 mothers in the general birth population. The variables analyzed included mother's age, smoking status, foreign citizenship, education level, multiparity, hypertension status, pre- and gestational diabetes. The study took into account the type of congenital anomaly, prenatal diagnosis,

preterm delivery and macrosomia. **Results**: Most mothers were of normal-weight (67,6%), with a mean BMI of 23.5 ± 4.7 kg/m^2. Compared to the frequencies in the general population, we observed a greater frequency of moderate-severe obesity (3.5% vs 2.4%) but this was not statistically significant, (p-values >0.05). BMI associated factors were consistent with those in the general population. There were higher overweight and obesity percentages for mothers with foreign citizenship, those ≥36 years old, low education level and smokers. A strong relationship between increase in BMI and the presence of hypertensive status and diabetes was confirmed. **Conclusion**: The analysis highlighted the increase in overweight and obesity with the rise in mothers' age, for low education level, for foreign and smoker mothers, and with concomitant hypertension status and diabetes. The numbers of high BMI mothers was small and the analysis will be repeated including 2014 data.

Impact of prenatal diagnosis of single Congenital Heart Defects (CHD) on termination of pregnancy for fetal anomalies (TOPFA): the IMER (Indagine sulle Malformazioni Congenite in Emilia-Romagna) experience

GD Rocca, M Rana, G Brighenti, G Poletti, A Astolfi, A Neville, G Cocchi

Background: Development and improvement of prenatal ultrasound imaging in the last decades allow a precision in prenatal diagnosis that may have an influence on TOPFA choice. We performed a retrospective cohort study using the IMER database, analyzing the impact of prenatal diagnosis of CHD reported in Emilia-Romagna from 2001 to 2012 on TOPFA choice. **Methods**: We collected all the reported cases of 12 types of CHD, including Coarctation of the Aorta (COA), Total Anomalous Pulmonary Venous Connection (TAPVC), Tetralogy of Fallot (TOF), Aortic Stenosis (AS), Hypoplastic Left Heart Syndrome (HLHS), Double Outlet Right Ventricle (DORV), Single Ventricle (SV), Tricuspid Valve Atresia (TVA), Persistent Truncus Arteriosus (PTA), focusing on prenatal US and related TOPFA. **Results**: 626 single CHD were reported in 12 years, 340 (54.3%) were prenatally detected by ultrasound of which 97 (28.5%) resulted in TOPFA. Of the TOPFAs, 45 (46.4%) were performed after a prenatal diagnosis of HLHS (p<0,01), 10 (10,3%) after a diagnosis of DORV and 10 (10,3%) after a diagnosis of TOF. Analyzing the outcomes by malformation 45 of 75 (60%) cases of HLHS were terminated, 9 of 16 (56.2%) cases of TVA, 10 of 24 (41,6%) cases of DORV, five of 12 (41.6%) cases of SV and five of 12 (41.6%) of PTA. **Conclusions**: HLHS is the main CHD that leads to TOPFA. A prenatal ultrasound diagnosis of TVA, DORV, SV and PTA also leads to a high number of TOPFAs.

The UK NHS Fetal Anomaly Screening Programme: is the target for serious cardiac anomalies being met?

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Background: The UK National Screening Committee (NSC) target for antenatal ultrasound detection of serious cardiac anomalies is 50%. Congenital Anomaly Registers (CARs) collect high-quality data on the affected cohort of antenatal screening programmes. Our aim was to estimate screening outcomes for four cardiac anomalies (hypoplastic left heart (HLH), transposition of the great arteries, tetralogy of Fallot (TOF), atrioventricular septal defect) using CAR data **Methods**: Cases of isolated anomaly in 2012 were identified from five regional population-based CARs covering 52 NHS Trusts and 31% of English births. Case classification included expert fetal cardiology input. Antenatal detection rates (DTRs) were generated for the screening test (screened population) and programme (eligible population). **Results**: 192 cases were identified from a cohort of 219,265 births; all cases were offered and accepted screening. Screening coverage (affected population) at 18^{+0}–20^{+6} weeks gestation was 70%; DTRs were 53% for the screening test, 37% for the programme. Programme DTRs varied significantly by CAR (16-52%) and individual cardiac anomaly; the DTR was highest for HLH (90%; 95%CI 75-97) and lowest for TOF (31%; 95%CI 20-46). **Conclusions**: The NSC target for detection of serious cardiac anomalies was met for the screening test, but not the programme. CARs have provided the first robust estimates of screening outcomes for cardiac anomalies. The National Congenital Anomaly and Rare Diseases Registration Service (NCARDRS),will support the routine analysis of DTRs for fetal anomalies and offer commissioners/clinicians evidence of geographical variation to enable further scrutiny, service improvement, and ensure women have access to a uniform screening programme

Assessment of screening for Down syndrome in Martinique from 2011 to 2013: a island location favoured

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Aim: The aim of this study is to evaluate the screening for trisomy 21 between 2011 and 2013 in Martinique French West Indies after the French decree of 23 June 2009. **Materials and Methods**: We used the prenatal data provided by accredited laboratories and the data from the Registry of Congenital French West Indies (REMALAN). **Results**: 85.9% of patients underwent screening: 60.5% on a combined calculation of risk (CRC), 14.6% on a sequential calculation of risk (CRS) and 10.8% on serum markers 2nd trimester (MST2). Overall 5.4% of the patients were placed in a risk group. During this period, 47 trisomy 21 were identified by the REMALAN with 38 (80.1%) detected prenatally: 24 of CRC, three on MST2 and 11 on signs of ultrasound at the 1st and 2nd trimester. The sensitivity of the CRC was 88% for a false positive rate of 3.87%. The overall sensitivity of screening (CRC, CRS and MST2) was 87% for a false positive rate of 5.21%. **Conclusion**: These data show that the coverage rate in Martinique is satisfactory and the screening for Down syndrome meets expectations.

Chromosomal anomalies: the experience of the Congenital Anomalies Registry of the Valencia Region

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Aim: The aim is to describe the temporal trend and distribution of chromosomal congenital anomalies in the Valencia Region (VR), in less than one year olds, during the period 2007-2011. **Methods**: Live births, stillbirths and termination of pregnancy due to fetal anomaly (TOPFA) between 2007-2011 with chromosomal congenital anomaly (Q90-Q99.9 codes of the 10th ICD10-BPA) were selected from the congenital anomaly population-based Registry of VR. The prevalence per 10,000 births for the chromosomal anomalies and for the different types of chromosomal syndromes with 95% confidence intervals were calculated. The analysis was performed by calculating prevalences and data were compared using Pearson Chi-squared test. **Results**: 895 cases were found, representing a prevalence of 33.5/10,000 births (95%CI: 31.0-35.9), highlighting five syndromes: Down's, Edward's, Patau, Turner and Klinefelter. Prevalence of chromosomal anomalies and Down's were stable over the period, except in 2010. Down's was the most frequent chromosomal anomaly (67.0%), and the most frequent pregnancy outcome was TOPFA (69.0%). Cardiac heart defects represented 70.3% of the associated congenital anomalies. Mothers of children with chromosomal anomalies were mainly Spanish (73.3%). The age group of mothers over 39 years had a higher prevalence (133.0/10,000 births). The Province of Castellón had the highest prevalence (39.1/10,000 births). **Conclusions**: The prevalence has remained stable over the five years, excluding the significant decline in 2010, for chromosomal anomalies detected and two of the major syndromes. Chromosomal anomalies are an important public health problem as they represent 15% of all congenital anomalies identified in the VR, coinciding with the European data.

A national approach to Marfan Syndrome in Spain

C Cavero-Carbonell, E Gras-Colomer, S Gimeno-Martos, L Páramo-Rodríguez, R Amorós, O Zurriaga

Background: Marfan syndrome (MFS) is a rare disease of connective tissue characterized by a variable combination of cardiovascular, musculoskeletal, ophthalmic and pulmonary manifestations. Apart from the support of patients' associations, there isn't a Spanish registry of patients with MFS. The objective is to identify the prevalence and incidence, determine the mortality distribution, study the quality of regional registries and analyze the mortality associated with aortic dissections in the MFS. **Methods**: A cross-sectional epidemiological study was performed in Spain during 2010-2012. Patients diagnosed with MFS included in the regional registries of rare diseases of the participating regions with ICD9-CM code 759.82 and/or ICD10 Q87.4 and/or ICD10-BPA were included in the study. Each Spanish region identified their cases, reviewed the clinical documentation and sent the database to the coordinating center (Valencia Region) who performed the global analysis. **Results**: 720 cases were included belonging to the 15 regions. The review of the clinical documentation confirmed the diagnosis in 91.0% of cases (prevalence: 0.16/10,000). The remaining 9.0% cases had other diseases, especially multiple malformation syndromes or Beals syndrome that is very similar to MFS. 22.0% of cases had surgery for aortic dissection and 5.5% died. **Conclusions**: The information provided by the

regional registry of rare diseases through the Spanish Rare Disease Registries Research Network (SpainRDR) provides an approximation to the real situation of the MFS in Spain. The study of the quality of these data will allow to offer in the future a better approximation without reviewing the clinical documentation.

Congenital heart diseases: antenatal diagnosis and impact of ethnicity. A fixed-cohort study in Trentino region (North-East of Italy)

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Background: Congenital heart disease (CHD) is the most common cause of congenital anomalies with a complex etiology including both genetic and environmental factors; 8‰ live births is generally accepted as the best approximation of incidence. The population of Trentino region (North-East of Italy) shows a broad range of minority ethnic groups. The aim of this study was to quantify antenatal diagnoses and to verify the impact of ethnic background on the CHD prevalence at birth. **Methods**: A retrospective fixed-cohort study was carried out. The prevalence of CHD types was assessed among live births over a period of four years (2009-2012). Identification of all patients was done through any ICD-9-CM code for CHD at birth. Mothers' and children's characteristics were collected from the Newborns Informative Flow, supplemented with information from the Hospital Discharges and Specialized Medical Examinations Databases. All cases were validated by a Geneticist utilizing EUROCAT criteria. **Results**: Among 20,774 births registered, we identified 139 cases of CHD, 6,7‰ (7.6‰ including also abortions). Birth proportion of the three main CHD subtypes observed was: Ventricular Septal Defect 44.6%, Atrial Septal Defect 17.9% and Patent Ductus Arteriosus 9.3%. 8.8% of newborns with CHD died after birth and 13.7% had an antenatal diagnosis. Table 1 shows CHD incidence rates by mother's ethnicity. **Conclusions**: Birth prevalence of CHD in Trentino Province is consistent with the worldwide trend. Ethnicity shows a greater impact, increasing the incidence rate from 5,6‰ to 10,8‰ and this may have long-term public health importance. In-depth assessments would be useful to better understand the factors associated with ethnicity.

TABLE 1. *CHD incidence rates by mother's ethnicity*

Country	Incidence rate at birth (‰ live births) – 2009-2012
Italy	5,6
Asia	13,6
Africa	10,9
Europe	8,4
South America	15,5
Total	6,7

Ellis van Creveld syndrome: European population - based study

I Barisic, LJ Boban, M Loane, E Garne, D Wellesley, E Calzolari, H Dolk, EUROCAT Working Group

Background: Ellis-van Creveld syndrome or chondroectodermal dysplasia (EVC, MIM 225500) is a rare autosomal recessive skeletal dysplasia characterized by short limbs and ribs, postaxial polydactyly, dysplastic nails and teeth and congenital heart defects. We present the largest population-based epidemiological study to date using data provided by the European Surveillance of Congenital Anomalies (EUROCAT) network of congenital anomaly registries. **Methods**: The study population consisted of 43 cases of EVC identified between January 1990 and December 2012 in 34 European registries. **Results**: The mean prevalence of EVC was 0.54 per 100 000 births. There were 26 (60.4%) terminations of pregnancy after prenatal diagnosis, two (4.6%) foetal deaths, and 15 (34.8%) live births. The most common anomaly was polydactyly (27; 87.1%). Congenital heart anomalies, mostly septal defects, were present in 20 (64.5%) cases. Most cases (85.7%) are suspected prenatally at 18.9 ± 4.3 (range 12-33) gestational weeks. The ultrasound examination usually reveals shortening of long bones, narrow thorax, hexadactyly and cardiac defects. Pregnancies are mainly (26/31, 83.8%) terminated at 20.1 ± 4.4 gestational weeks, reducing the number of live births to one third of the total prevalence rate (0.2 per 100 000 births, or 1 in 500 000). **Conclusions**: EVC is a very rare disease affecting 1 in 188,679 births. Early diagnosis is important for timely counselling of couples and multidisciplinary management of affected children. The study is part of the EUROCAT Joint Action funded by the EC, under the framework of EU Health Programme 2008-2013, Grant Agreement 20102204 (Executive Agency for Health & Consumers).

Beckwith Wiedemann syndrome in a European population

L Boban, I Barisic, M Loane, E Garne, D Wellesley, E Calzolari, Helen Dolk, EUROCAT Working group

Background: Beckwith Wiedemann syndrome (BWS, OMIM 130 650) is a rare overgrowth syndrome of complex etiology characterised by macrosomia, visceromegaly, abdominall wall defects, dysmorphic features, neonatal hypoglycemia and increased cancer risk. The aim of the study is to present prevalence of all birth outcomes, prenatal diagnosis, associated congenital malformations and other descriptive epidemiology characteristics of BWS in Europe. **Methods**: We analysed 294 BWS patients registered in the EUROCAT (European Surveillance of Congenital Anomalies) network in 1990-2012 among 15,988,003 births. The data on livebirths, stillbirths after 20 gestational weeks and terminations of pregnancy after prenatally detected severe anomalies were included in the study. **Results**: The estimated prevalence was 3.45 in 100 000 births. There were 270 (91.8%) live births, 11 (3.7%) stillbirths and 13 (4.4%) terminations of pregnancies. Most of the patients were suspected prenatally (112; 44.1%), 76 were discovered at birth (24.9%) and 66 (25.9%) were diagnosed in the first week of life or later. 210 out of 294 (71,4%) patients had one or more major congenital anomalies. The most frequent were abdominal wall defects (58.1%) and macroglossia (51.9%) followed by urogenital (32.8%), limb (21,4%), and cardiac (16.2%) anomalies. Eleven (4.1%) patients did not survive the first week of life. **Conclusions**: BWS is a rare disorder affecting 1 in 26 912 births. It is often associated with major congenital anomalies leading to relatively high prenatal diagnosis rate. Nevertheless, prenatal diagnosis has no significant impact on the livebirth prevalence.

Fetal trisomies and micro-rearrangements identified by Non Invasive Prenatal Testing (NIPT)

B Grisart, J-F Vanbellinghen, M Lienard, N Simonis, J Désir, Ch Verellen-Dumoulin

Background: Non Invasive Prenatal Testing (NIPT) is a new option in testing for genetic abnormalities during pregnancy. Currently-used fetal diagnostic tests such as amniocentesis or chorionic villus sampling are invasive procedures involving a risk of miscarriage (0,5 – 1%). By contrast, NIPT uses a simple blood test to collect cell-free fetal DNA (cfDNA) circulating in a mother's bloodstream and represents minimal risk to mother and fetus. Recent clinical trials suggest that tests may be up to 99% accurate in detecting more common chromosomal abnormalities, such as trisomy 21, 13 and 18. **Methods**: Method for non-invasive fetal aneuploidy detection (trisomy 13, 18, 21) involves counting chromosomes by mapping sequences generated via Massive Parallel Sequencing of cfDNA in maternal plasma. The number of reads produced per patient for this analysis is usually considered as low coverage sequencing: 7 to 25 millions reads depending on the sequencing platform used. In order to look in maternal plasma for the microdeletions or micro-duplications, we used the Wisecondor package (Straver et al., 2013; NAR). **Results**: We analyzed, during a period of 22 months, 2,857 maternal blood samples after 11 weeks of pregnancy to exclude trisomies 13, 18 and 21. We reported 40 T21, five T13 and five T18 (1,75%). Thirty-four rearrangements (1,19%), aneuploidies of other chromosomes not confirmed by invasive prenatal diagnosis, microdeletions and/or microduplications with a size above 10 Mb were also observed. Until now, no false negative test has been reported. **Conclusions**: NIPT is a reliable test to detect trisomy 21 early in pregnancy. Trisomy 13 and 18 are also easily diagnosed. Microdeletions and microduplications are also detected but they need to be interpreted with caution.

Prenatal diagnoses and postnatal outcome of major congenital malformations - A comparison of registry data with a selected study population

A Rissmann, L Neumann, S Henschen, A Köhn

Aim: This retrospective cohort study evaluates the rate of prenatal detected malformations within an active study cohort versus the routine birth defect registry data. **Methods**: Study period 2005 to 2010, covering 104,622 births in Saxony-Anhalt. **Results**: 234 cases (33.43%) of 700 prenatally examined pregnant women in the extra cohort (Stendal) and in 615 cases (57.53%) of 1,069 prenatally examined pregnant women in the remaining area of Saxony-Anhalt, at least one malformation was detected prenatally. This

corresponds to a percentage of 4.24% of all births in the district of Stendal compared to 0.62% of all births in the remaining population. Detection rate of congenital anomalies was variable for the different diagnosis groups of malformations. 76.0% of the prenatally diagnosed malformations (n=179) were postnatally confirmed within the study population and 23.50% (n=55) were not confirmed. In case of the population from the remaining districts of Saxony-Anhalt, the prenatally diagnosed malformations were confirmed postnatally in 54.72% of the cases (n=585) and in 45.28% (n=484) they were not confirmed. A positive predictive value of 0.76 was obtained for the study group in contrast to 0.55 of the registry group. **Conclusions**: Under extra study conditions registered data may be used to evaluate and improve the registries data quality.

Surveillance of congenital malformations in Calabria

GA De Biase, D Macchioni, AD Mignuoli, S Lopresti

Background: Congenital anomalies are errors of morphogenesis, determined in part by genetic factors. Their overall birth prevalence (diagnosed within the first week of life) is about 2-3%. This study aims to improve knowledge of congenital malformations in the region of Calabria in the year 2013 through the development of a formal procedure to connect and integrate different sources of information and create a single database. **Methods**: An algorithm was built that runs initially a search and identification of malformed cases from the analysis of the Hospital Discharge boards and then checks for the presence of the cases identified in the flows of the Certificate of attendance at birth and in the Regional Registry of Congenital malformations. **Results**: The integration of the flow of the Regional Registry of Congenital Malformations with other information flows, has led to the complete coverage of the birth centers of Calabria Region, a total of 16,282 births supervised. Cases with at least one ICD-9-CM code in the range 740-759 in hospital discharge records were 1,307, were excluded cases deemed "minor" in accordance with EUROCAT guidelines. The cases with congenital malformations "established" in the various streams were 449 (250 males and 199 females) with a birth prevalence at 27.6 per 1,000. **Conclusions**: Multiple detection of cases of malformation is necessary because the information of the individual streams cannot identify all cases. The recording and monitoring systems, to be complete must integrate with other existing epidemiological reality.

A review of notifiers to the Northern Congenital Abnormality Survey

L Phillips, J Rankin

Background: Disease registers play an essential role in healthcare planning and delivery. They provide high quality information to: inform patient care, improve public health, advance medical knowledge and support clinical practice. Local congenital anomaly registers have been established in a number of regions in Europe to meet local needs and to carry out audit and research. To ensure a high case ascertainment, congenital anomaly registers use multiple source notification. This study involved a review of notifiers to the Northern Congenital Abnormality Survey (NorCAS) during a 23 year period. **Methods**: Singleton, isolated cases of major congenital anomalies delivered between 1 Jan 1990 and 31 Dec 2013 were included. The data were categorised into anomaly groups according to EUROCAT guidelines. Descriptive analyses was conducted to describe notifiers to the register and any changes in notifiers over time. **Results**: A total of 12,879 cases were included. Between 1990 and 2001 medical specialists, paediatricians and geneticists were the primary notifiers; thereafter, a greater proportion of cases were notified by the fetal anomaly screening programme co-ordinators, geneticists and fetal assessment, increasing to 16%, 15% and 11% respectively. Medical specialists were the primary notifiers for congenital heart defects, geneticists for chromosomal defects and fetal assessment for the nervous, respiratory and digestive system anomalies. All relevant clinical specialties were represented. **Conclusions**: The NorCAS maintains a high case ascertainment through its close working relationship with the clinical network within the region. Despite this, continued engagement, review and action is needed to ensure case ascertainment is maximised.

Quality of life in children born with gastroschisis by self and parent report using KIDSCREEN-52 questionnaire: qualitative results

SV Glinianaia, J Jardine, H McConachie, ND Embleton, H Borrill, J Rankin

Background: There is little research on health-related quality of life (QoL) in children born with gastroschisis, in particular using self-report in young children. In this cross-sectional exploratory study of QoL, using the KIDSCREEN-52 questionnaire, we aimed to obtain both children's and parents' views on life aspects that are important for the child. **Methods**: Children born with gastroschisis (aged 8-11 years) were identified from the Northern Congenital Abnormality Survey. We analysed children's and parents' comments from open-ended questions in the individual interviews to obtain information on children's interests and what makes them happiest. **Results**: Ten children (median age 9.6, IQR=8.3-11.0) and eight parents participated in face-to-face interviews with the researcher. Most children reported being happy with the way they looked and some felt 'unique' and 'special' because of their scar. Among things that made them happiest, 'playing and being with friends and family' were mentioned most frequently. Parents reported that in addition to physical activity and relationship with peers and family, important dimensions for their child's QoL were parents' attention at home and being treated fairly, appearance related issues, and hobbies and interests. Parents felt that their children were thriving and had no health problems associated with their gastroschisis. **Conclusions**: Overall, separate interviews with children and parents revealed consistency in their views in relation to QoL dimensions of particular importance to the child. Both children and parents commented on the importance of being physically active and being outside playing with friends and family members, which was not limited by their condition.

Maternal body mass index and risk of congenital anomalies

TD Nhiwatiwa, N Heslehurst, J Rankin

Background: Previous studies suggest an association between maternal obesity (BMI $\geq$30.00 kg/m2) and congenital anomalies. The aim of this study is to investigate the relationship between overweight (BMI 25.00 – 29.99 kg/m2), obesity and congenital anomalies. **Methods**: Data on all singleton isolated cases of major congenital anomaly delivered from 01 January 2003 to 31 December 2013 were obtained from the Northern Congenital Abnormality Survey (NorCAS). The anomaly data were grouped in accordance with European Surveillance of Congenital Anomalies (EUROCAT) guidelines. Body mass index (BMI) was classified according to World Health Organisation (WHO) guidelines. BMI distribution for non-case data was modelled using previous data[1]. Relative risks (RR) and 95% confidence intervals (95% CI) were calculated. **Results**: Of the 9509 cases notified to NorCAS, 3434 were eligible for inclusion. Of these, 30.8% were congenital heart defects (CHD), 18.8% were chromosomal anomalies and 9.4% were nervous system anomalies. 715 women (20.8%) were obese, 947 (27.6%) overweight and 1641 (47.8%) were of recommended weight. Maternal obesity (RR 1.4, 95% CI= 19.5, 22.1, p=0.0000) and overweight (RR 1.2 95%, CI= 26.1, 29.1, p=0.0001) were associated with a significantly increased risk of congenital anomaly compared to mothers with recommended BMI (18.50-24.99 kg/m2). **Conclusions**: Findings are consistent with previous studies, as women who were obese were at increased risk of congenital anomaly. We also found that overweight women had a significantly larger risk. Women and health professionals should be made aware of these dangers and women supported pre-pregnancy to optimise their BMI.

Reference

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Epidemiology of oral facial clefts in North East Italy and the challenge for developing countries

A Cazzuffi, JA Neville, A Franchella

Background: The epidemiology of cleft lip (CL) with (CLP) or without cleft palate and isolated cleft palate (ICP) represents a challenge due to the complete lack of data in large areas of the word and incomplete data from the remaining areas. Recent research estimates an overall prevalence of CL+/-P as 9.92 per 10,000 births and prevalence in our geographic area (North-East-Italy) as 6/10,000. Prevalence of ICP is 1.3 to 25.3/10,000 depending on registries. Our hospital has treated patients with CLP since 1980 and is also involved in surgical missions to developing countries. **Methods**: We retrospectively reviewed medical case records and mission reports. Statistical analysis was performed to establish which variables are implicated in functional outcome (chi-squared and Mann-Whitney tests). **Results**: In a 35-year period, we treated 141 patients, 81 males, 60 females: 62 CP (43,9%), 28 CLP (19.8%), 25 CL (17.7%), 13 bilateral clefts (9.2%), eight primary velopharingeal insufficiency (VPI) and five submucosal CP. Unilateral CL were right in 26.9%, left in 73.1%. Incidence of non-isolated cleft (NIC) was 13.6% (19 patients), 12 (8.5%) patients presented with recognized

syndromes, 7 (4.9%) as multi-malformed cases (MMC) (Table 1). Incidence of post-surgical VPI was 5.8% influenced by an average older age at operation, not by surgical technique used for palate closure. Outcome in SC was not statistically worse. Over 200 patients were treated in developing countries, but complete data concerning the distribution of defects among this population are not available.

Conclusions: The distribution of gender and laterality of defect agrees with the current literature. A high prevalence of ICP and a relatively low incidence of NIC were observed among the studied population with no detection of musculoskeletal, brain or cardiovascular deformities (the most commonly associated anomalies). Efforts should be made to encourage registries to be set up in developing countries.

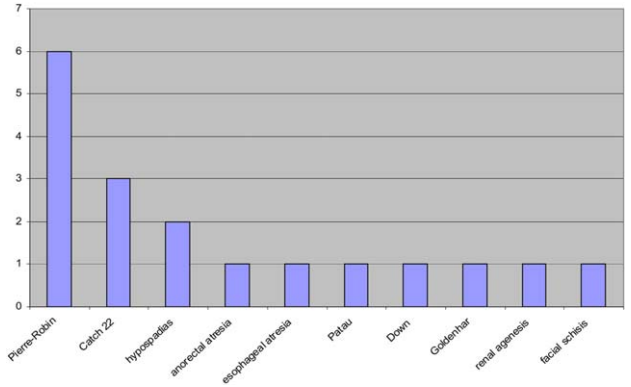

Table 1: Number of cases and type of associated congenital anomalies

Primary prevention of neural tube defects: data from the Portuguese national registry of congenital anomalies (RENAC)
P Braz, A Machado, C Matias Dias

Background: In Portugal folic acid supplementation is recommended to start at least 2-3 months before conception for primary prevention of Neural Tube Defects. The aim of this study was to evaluate, within gestations with at least one congenital anomaly, possible association between maternal socio-demographic factors and the use of folic acid. **Methods**: Using data from the Portuguese national registry of congenital anomalies, for the 2004-2013 period, the association between folic acid use during pregnancy and maternal characteristics was studied using the chi-square test. **Results**: Considering all reported cases with congenital anomaly, the use of folic acid before conception was reported by 12.7% (n = 1233) of the women; 47.8% (n = 4623) started supplementation during the 1st trimester, 7% (n = 680) did not take folic acid and 32.5% (3143) of the records had no information on folic acid use. Women with professions that require higher academic differentiation started the use of supplements before pregnancy ($p < 0.001$); women under 19 years old and with Arab ethnicity ($p < 0.001$) did not take folic acid. Mothers with a previous pregnancy reported less use of folic acid (11.5% versus 14.7%) than mothers without a previous pregnancy ($p < 0.001$). **Conclusions**: The results suggest some degree of association between maternal characteristics and use of folic acid. To increase the consumption of folic acid before pregnancy new measures are need to promote this primary prevention, among couples and health professionals. This study highlights some maternal characteristics and subgroups of mothers for who the measures should be reinforced.

Is there a relation between environmental exposure to teratogenic substances during pregnancy and congenital anomalies in the newborn? A pilot study in Portugal
A Machado, P Braz, J Santos, I Marques, C Matias Dias

Background: Maternal occupation as a proxy of environmental exposure has been consistently associated with specific congenital anomalies (CA) in the foetus and newborn. On the other hand, geographical location of the mother such as place of residence and place of work have not been used as proxy for environmental exposures during pregnancy. We designed a pilot study aiming to investigate the association between maternal place of residence and workplace during pregnancy and CA in Portugal. **Methods**: Cases and controls are identified in the maternity unit. Cases are all live births with at least one CA delivered in the Barreiro hospital located in a heavy industrial area near Lisboa. Controls are the two normal births following each case. Residents outside the study area, stillbirths and women who decline to participate or are incapable of giving consent are excluded. A health professional interviews the mothers using a questionnaire adapted from the registry form of the Portuguese national registry of CA and includes information on places during pregnancy (residence, workplace, leisure), and demographic characterization as place of birth, infant sex, weight, description of CA, age of mother, ethnicity, maternal birth place. Maternal health and obstetric history, education, smoking, alcohol, drugs and medication use is also collected as potential confounders. **Results**: The pilot study started in January 2016 and at the moment two cases and four controls have been recruited without refusals. The study will continue to be implemented and it is proposed to start in other hospital units during 2016.

Elevated congenital anomaly rates and incorporated cesium-137 in the Polissia region of Ukraine
W Wertelecki

Background: Investigations soon after the 1986 Chornobyl (Chernobyl in Russian) accident of exposed populations residing elsewhere in Europe led government and international agencies to conclude that exposures to cesium-137 (Cs-137) were not teratogenic. Our observations of elevated population rates of neural tube defects (NTD), microcephaly and microphthalmia (M/M) in the Rivne Province in Ukraine, which were among the highest in Europe, prompted this follow-up investigation inclusive of whole body counts (WBC) of Cs-137 among ambulatory patients and pregnant women residing in Polissia, the most polluted region in Rivne. **Methods**: Yearly (2000-2012) population rates of NTDs and M/M and WBC patterns of ambulatory patients (2001-2010) and pregnant women (2011-2013) in Polissia and non-Polissia regions of Rivne were analyzed. **Results**: The NTD and M/M population rates in Rivne remain elevated and are statistically significantly higher in Polissia than in non-Polissia. The WBCs among residents in Polissia are statistically significantly higher than among those from non-Polissia. **Conclusions**: NTD and M/M rates are highest in the Polissia region of Rivne and are among the highest in Europe. In Polissia, the WBCs of Cs-137 are above officially set permissible upper limits. The results are based on aggregate data of NTDs and M/Ms and average WBC values. Further investigations of causality of the high rates of NTDs and M/Ms are needed and urgent strengthening policies and implementations to reduce exposures to teratogens, in particular radioactive nuclides and alcohol, and consumption of folic acid supplements are indicated.

Spatial investigation of congenital malformations in Reunion Island (2008-2012)
M André, H Randrianaivo, B Bertaud-Nativel, V Herbreteau

Background: Reunion Island is a French territory located in the south-western Indian Ocean. The Reunion Registry of congenital malformations is in charge of monitoring cases. Overall prevalence (289 cases per 10,000 births) is close to the average reported by mainland French registries (315 cases). However, the prevalence of spina bifida is almost twice (10 cases per 10,000 births) the one reported in mainland France (5 cases). This study aims to describe the spatial distribution of different birth defects and identifying clusters. **Methods**: The analysis specifically tackles three groups being potentially related to environmental exposure. Each case recorded between 2008 and 2012 was geolocated according to its home address: 492 cases of congenital heart defects, 108 cases of cleft lip and palate and 69 cases of spina bifida. Four statistical methods were applied at different administrative scales: Standardized Prevalence Ratio (SPR), Hierarchical Cluster Analysis (HCA), Kulldorff method and Geographic epicenter method. **Results**: The resulting clusters differ depending on the method. Combining the observation at different administrative scales helps to identify the most affected areas for each pathology. **Conclusions**: These initial observations allow considering case-control studies to identify exposure factors in the most affected areas, including environmental, socio-economic and healthcare factors.

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