

# Selected Abstracts of the 1<sup>st</sup> Congress of joint European Neonatal Societies (jENS 2015) • Session “Epidemiology”

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## POSTER PRESENTATIONS

## ABS 1

### A PERFORMANCE INDICATOR FOR THE PROLONGATION OF GESTATIONAL AGE

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## INTRODUCTION

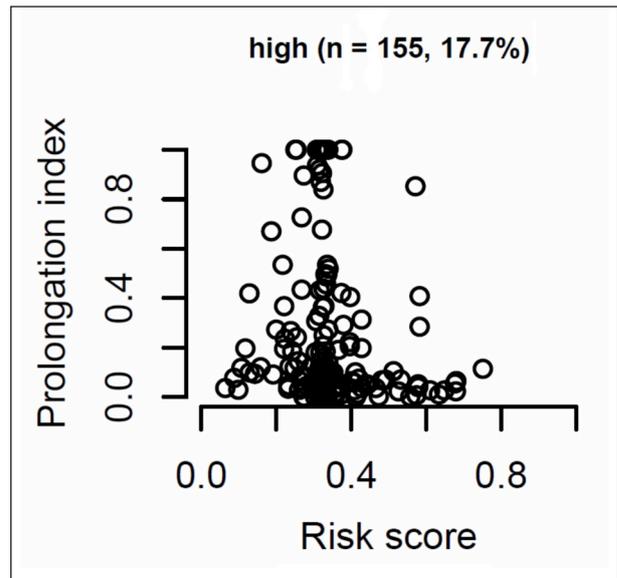
In Germany high level perinatal centers are classified in terms of annual number of VLBW treated neonates. Substantial financial support is granted for each neonate under 1,250 grams which has resulted in misrecording of birth weights and also in iatrogenic premature deliveries by caesarean section. In order to improve inter hospital comparisons for the sake of benchmarking an alternative performance indicator aimed at reflecting positive pregnancy outcome is proposed.

## PATIENTS AND METHODS

Routine data from the Bavarian Quality Assurance Programme were extracted from 1,345,123 pregnancies during 2001 and 2013. The mean duration of prenatal hospital stay is computed for each unit and its distribution stratified by a prematurity risk score as well as by degree of therapeutic in-hospital intervention. As a proviso all prenatal transfers are excluded from the analysis. Individual case records are selected from obstetric units at the extreme tails of the gestational age distribution are selected for further in depth analysis. These are matched with actual hospital records on a 5 percent sample basis.

## RESULTS

The results show expected increasing variance of gestational age as well as intensity of intervention with increasing VLBW risk score (**Fig. 1**). In terms of positive outcome the results break down into a two dimensional table of VLBW risk by intensity of intervention. In general high risk pregnancies



**Figure 1 (ABS 1).** Prolongation of gestational age and increasing VLBW score.

receive higher degrees of therapeutic intervention. However, a small proportion of units was identified in the low VLBW risk group but intensive care suggesting sudden unexpected and unforeseeable complications at term and conversely an even smaller proportion of units in the high VLBW risk group with little intervention. Units from the extreme tails of the gestational age distribution were selected from both of these subgroups to inspect individual case histories for possible determinants of success or failure.

## CONCLUSIONS

The data suggest that treatment response is in general closely related to perceived risk of premature delivery. A substantial proportion of units was identified, however, that consistently provided significantly lower levels of therapeutic intervention over the study period. Inspection of the case records revealed a significant bias of the catchment population in terms of social status. Further research is needed especially in the area of intervention prior to hospital admission.

## ABS 2

### LATE PRETERM NEONATES AND CAUSES OF ADMISSION TO THE NICU

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**AIM**

The aim of this study was to evaluate the clinical and demographic characteristics, the causes of admission of late preterm (LP) infants admitted to our neonatal intensive care unit (NICU).

**PATIENTS AND METHODS**

This retrospective study was conducted at our NICU, between January 2012 and December 2012. Neonates born at 34<sup>0/7</sup>-36<sup>6/7</sup> weeks of gestation and admitted to the NICU were included to the study. Neonates were evaluated in terms of the reasons for hospitalization, clinical and demographic characteristics and compared with term ones.

**RESULTS**

During the study period there were 17,690 births in our hospital; these included 13,975 (79%) term births, 1,981 (11.2%) LP births. The number of neonates admitted to the NICU was 2,844. The NICU admission rates for LP infants and term infants were 21.5% (n = 426) and 5.5% (n = 765), respectively. The mean gestational age of the LP and term neonates was 35.1 ± 0.8 and 38.5 ± 1.2 weeks, the mean birth weight was 2,384 ± 502 and 3,185 ± 593 g, respectively. The most common reason for hospitalization in both groups was respiratory distress (55.2%, n = 235 in the LP neonates, 52.3%, n = 400 in the term neonates). The mean duration of hospitalization was 8.2 ± 5.5 days in LP infants and 6.9 ± 5.2 days in term infants. Compared with term infants, LP infants had significantly higher rates of hypoglycemia (p = 0.014), polycythemia (p = 0.046), and feeding difficulty (p = 0.009).

**CONCLUSIONS**

LP infants who have not completed the physiological and metabolic aspects of maturation than term infants are at risk for many complications such as hypoglycemia, polycythemia and feeding difficulty. Therefore they should be monitored more closely for development of complications.

**ABS 3****INCIDENCE AND OUTCOMES OF METABOLIC DISORDERS IN VERY PRETERM INFANTS**

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**INTRODUCTION**

Infants' immaturity associated with preterm birth is the cause of frequent violations of early

postnatal metabolic adaptation. The development of carbohydrate homeostasis disorders, acid-base and glucose balances are associated with an increased risk of death and morbidity in this category of newborns. In a cohort study we evaluated the incidence and severity of major metabolic disorders (hypo- and hyperglycemia [HG], metabolic acidosis [MA]) in very low birth weight infants with respiratory distress depending on the degree of infant's immaturity and assessed the impact of these metabolic disorders on some important clinical outcomes.

**PATIENTS AND METHODS**

One hundred very low birth weight newborns (gestational age < 32 wks) with respiratory distress were enrolled into the study on the first day of life. Blood gases and blood glucose concentration were measured every day during 7 days. Interventions that were used to treat hyperglycaemia included reducing the rate of parenteral glucose infusion and administration of insulin (in the cases of blood glucose concentration > 10.0 mmol/l). Sodium bicarbonate (SB) was given to correct significant metabolic acidosis. The primary study outcome was the incidence of metabolic disorders. We also assessed potential association between the violation of blood glucose concentration, acid-base status and risk of death and the occurrence of intraventricular hemorrhage (IVH).

**RESULTS**

The incidence of MA (pH ≤ 7.22) was 48% (95% CI: 38.4 to 57.5), hypoglycemia (≤ 2.6 mmol/l) – 29% (95% CI: 23.2 to 34.7), HG ≥ 8.3 mmol/l – 56% (95% CI: 44.8 to 67.1) and > 13.9 mmol/l – 21% (95% CI: 16.8 to 25.1). Univariate analysis demonstrated that the incidence of HG and MA is inversely related to birth weight (R = -0.20 and R = -0.26 accordingly; p < 0.05). With decreasing of gestational age and birth weight duration of HG, insulin use, SB administration and incidence of IVH increased as well (p < 0.05). Infants with IVH experienced more days with HG (R = 0.20; p < 0.05) and MA (R = 0.21; p < 0.05) and had higher risk of death (R = 0.37; p < 0.05). Higher mortality was also associated with higher incidence (R = 0.42; p < 0.05) and duration (R = 0.38; p < 0.05) of metabolic disorders and the use of SB (R = 0.36; p < 0.05) and insulin (R = 0.42; p < 0.05).

**CONCLUSIONS**

Our data suggest that hyperglycemia and metabolic acidosis are associated with the development of IVH and increased mortality in premature infants. But it is still uncertain if the metabolic disorders per se or methods of their correction cause adverse results.

## ABS 4

## MATERNAL FACTORS INFLUENCE INFANT'S VITAMIN D STATUS

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## INTRODUCTION

Vitamin D regulates the expression of 3% of genome and has pronounced effects on ante- and postnatal development. The concentration of vitamin D in cord blood correlates closely with that in the maternal circulation. At northern latitudes with insufficient UVB-radiation from sun, main sources of vitamin D are food and supplements. The objective of this study was to define the main maternal determinants for cord blood 25-OHD concentration.

## PATIENTS AND METHODS

Altogether 584 mother-infant pairs of Caucasian origin were recruited between January 2013 and May 2014. Infants were born at term and with birth weight appropriate for gestational age (**Tab. 1**). The concentrations of 25-hydroxyvitamin D (25-OHD) in maternal first trimester serum sample and cord blood were analyzed. The maternal supplement use was obtained with questionnaire, and maternal diet during pregnancy was analyzed with a 22-item semiquantitative food frequency questionnaire (FFQ). Based on FFQ principal component analysis with Varimax rotation was used to formulate dietary patterns (DPs) with factor scores. The relationship between different factors and 25-OHD in cord blood was analyzed with linear regression.

## RESULTS

Mean (SD) maternal 25-OHD concentration was 89 (25) nmol/l, in cord blood 77 (25) nmol/l. Maternal 25-OHD associated with cord blood 25-OHD ( $\beta$  [95% CI]: 0.277 [0.258-0.460]) and alone explained 8% of the variation in cord blood 25-OHD. Maternal mean vitamin D intake from supplements was 16 (17)  $\mu$ g per day. Altogether

Table 1 (ABS 4). Maternal and infant characteristics.

Number of mother-infant pairs	584
Maternal age in years, mean $\pm$ SD	31.6 $\pm$ 4.2
Prepregnancy BMI, mean $\pm$ SD	23.3 $\pm$ 3.8
Duration of gestation in weeks, mean $\pm$ SD	40.2 $\pm$ 1.1
Birth weight z-score, mean $\pm$ SD	-0.22 (0.82)
Birth length z-score, mean $\pm$ SD	-0.18 (0.88)
Maternal education	
Higher education (Bachelor or Master level), %	75.9
Prepregnancy smoking status	
Yes, %	13.9
Season at birth	
Spring, %	43.8
Summer, %	21.1
Fall, %	16.6
Winter, %	18.5
Newborn sex	
Girls, %	51.5

five maternal DPs were extracted with eigenvalues over 1 and explained 46% of the total variation in diet. These DPs were interpreted as 'goodies and snacks', 'health conscious', 'meat', 'sandwich' and 'alcohol'. Of these, health conscious DP (0.103 [95% CI: 0.541-4.518] and sandwich DP (0.086 [0.110-4.093]) were associated with cord blood 25-OHD (although with marginal explanatory rate). In addition, vitamin D intake from supplements was a strong predictor for 25-OHD in cord blood (0.231 [0.221-0.451]), explaining 5% of the variation in cord blood 25-OHD.

## CONCLUSIONS

The overall maternal vitamin D status was sufficient, as only 1% were regarded as vitamin D deficient (< 50 nmol/l). Cord blood 25-OHD concentration is determined by maternal vitamin D status, vitamin D intake from supplements, health conscious DP rich with vegetables, fruits and fish; and sandwich DP rich with bread, cheese, vitamin D fortified dietary fats and milk products. The results emphasize the importance of vitamin D supplementation to pregnant women.

## ABS 5

## THE HIGH PREVALENCE OF VITAMIN D DEFICIENCY IN A LARGE NUMBER OF PREGNANT WOMEN AND RELATED FACTORS IN ANKARA, TURKEY

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## INTRODUCTION

Many studies show a high prevalence of vitamin D deficiency in pregnant women and consequently in neonates. We have some different data on vitamin D concentration in these risk groups for Turkey but we performed a large prospective study to evaluate vitamin D concentration in pregnant women in Ankara region.

## PATIENTS AND METHODS

We determined 25-hydroxy-vitamin D and parathormon concentration from blood samples taken before delivery from 1,088 pregnant women who gave birth in Zekai Tahir Burak Maternity Education and Research Hospital through June and October 2013. We collected data on nutrition, wearing habituals and sun exposure during pregnancy. We determined the vitamin D concentrations in pregnant women according to season of blood collection and use of nutrition supplements and checked the correlation with vitamin D levels.

## RESULTS

The mean vitamin D concentration in the summer group was  $20.4 \pm 9$  ng/mL, and in the autumn group  $8.4 \pm 6$  ng/mL ( $p < 0.001$ ). When we compare pregnant women according to vitamin D levels (group A 15 ng/ml), women who took nutrition supplements containing vitamin D ( $p = 0.001$ ), milk derived nutrition (cheese) more than average during pregnancy ( $p = 0.037$ ) had significantly higher vitamin D levels than those who did not. Multinomial logistic regression analysis revealed that, season OR 92.7 (36.4-236, 95% CI;  $p = 0.0001$ ), vitamin supplements use OR 2.5 (1.2-5.2, 95% CI;  $p = 0.014$ ), cheese consumption OR 1.2 (1.01-1.6, 95% CI;  $p = 0.038$ ) and body sun exposure more than face OR 6.04 (1.29-28.2, 95% CI;  $p = 0.22$ ) seemed to be independent risk factors for vitamin D deficiency.

## CONCLUSIONS

Vitamin D deficiency is very common in pregnant women in Turkey as well, especially in autumn-

winter season and in those women who do not take nutrition supplements containing vitamin D.

## ABS 6

### SNAPPE-II: A VALUABLE PREDICTOR OF ADVERSE OUTCOMES IN PREMATURITY

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## INTRODUCTION

Illness severity scores are important tools for quality of care evaluation, risk adjustment comparisons and management of resources. The Score for Neonatal Acute Physiology Perinatal Extension (SNAPPE-II) includes six clinical variables, as well as the Apgar score at 5 minutes, the birth weight and intrauterine growth restriction. SNAPPE-II has previously been shown to be a robust predictor of mortality in newborns. The aim of this study was to evaluate the ability of SNAPPE-II to predict other adverse outcomes, including bronchopulmonary dysplasia, necrotizing enterocolitis, severe peri-intraventricular hemorrhage and severe retinopathy, in preterm infants.

## PATIENTS AND METHODS

Retrospective study of all the newborns < 32 weeks, admitted to a NICU, from Jan 2008 to Dec 2014. SNAPPE-II score was calculated during the first 12 h of life. Bronchopulmonary dysplasia was defined as the need for oxygen supplementation at 36 postmenstrual weeks. Severe retinopathy of prematurity (ROP) was characterized as severely abnormal blood vessel growth or detached retina (stages  $\geq$  III). Severe peri-intraventricular hemorrhage was considered for grade  $\geq$  3, according to Volpe, or whenever periventricular hemorrhagic parenchymal infarction or post-hemorrhagic ventricular dilatation occurred. Data analysis was performed using Student's t test, calculating the area under the receiving operating characteristic curve (AUC) and calibrating the model with the Hosmer-Lemeshow methodology.

## RESULTS

During the last 7 years 624 neonates born < 32 weeks were admitted to our NICU. Of these, 238 were extremely low birth weight infants (38%) and 82 born < 26 weeks (13%). Mortality was 14%. Bronchopulmonary dysplasia was diagnosed in

21%, severe peri-intraventricular hemorrhage in 9%, necrotizing enterocolitis in 7% and severe ROP in 4%. The SNAPPE-II score was calculated in 97%. SNAPPE-II score was  $18 \pm 19$  for infants that survived and  $51 \pm 28$  for those who died ( $p < 0.0001$ ). This score was significantly associated with bronchopulmonary dysplasia, severe peri-intraventricular hemorrhage and severe ROP ( $p < 0.0001$  in all), but not with necrotizing enterocolitis. The SNAPPE-II AUC was 0.84 (95% CI: 0.80-0.89) for death, 0.74 (95% CI: 0.68-0.79) for bronchopulmonary dysplasia, 0.77 (95% CI: 0.71-0.82) for severe peri-intraventricular hemorrhage and 0.80 (95% CI: 0.70-0.90) for severe ROP.

#### CONCLUSIONS

The SNAPPE-II score is not only a valuable predictor of in-hospital mortality for infants born at gestations of less than 32 weeks, but it is also associated with adverse outcomes, namely with bronchopulmonary dysplasia, severe peri-intraventricular hemorrhage and severe ROP.

#### ABS 7

### THE ASSOCIATION BETWEEN MATERNAL AND FETAL 25OHD AND INFANT SIZE AND ADIPOSITY AT BIRTH, 6 MONTHS AND 2 YEARS OF AGE

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#### INTRODUCTION

While the effects of vitamin D in pregnancy and offspring bone health are well established, there remains a dearth of knowledge on the effect of maternal vitamin D status on offspring size and adiposity. The aim of this study was to examine the association of early and late pregnancy and fetal 25-hydroxyvitamin D (25OHD) on offspring size and on adiposity at birth, at 6 months and at 2 years of age in a cohort from the ROLO (Randomised cONtrol trial of LOw glycaemic index diet versus no dietary intervention to prevent recurrence of fetal macrosomia study).

#### PATIENTS AND METHODS

272 mother and infant pairs from the ROLO study were included in this analysis at 20 weeks gestation,

290 at 34 weeks gestation, 292 at birth, 160 at 6 months postpartum and 287 at 2 years postpartum. 25OHD was measured in mothers in early (13 weeks) and late (28 weeks) gestation, and in fetal umbilical cord blood samples at delivery.

#### RESULTS

According to Institute of Medicine 2011 Report, 30% in early pregnancy and 38% in late pregnancy were at risk of vitamin D deficiency (25OHD < 30 nmol/L). Birthweight was negatively associated with early pregnancy 25OHD ( $p = 0.004$ ) and with fetal 25OHD ( $p < 0.001$ ). Birth length when controlled for birth weight was not associated with early, late or fetal 25OHD. Neonatal sum of all skinfolds and

**Table 1 (ABS 7).** Multiple linear regression showing associations between 25OHD (independent variable) and offspring anthropometrics (dependent variables).

Variable	$\beta$	SE	P	F	R <sup>2</sup>
<b>Early pregnancy 25OHD (nmol/L)</b>					
Birthweight	-4.16	1.42	<b>0.004</b>	7.623	0.20
Birth length	-0.02	0.01	<b>0.023</b>	6.639	0.20
*Birth length	-0.01	0.01	0.123	9.512	0.29
2 year weight for age z score	-0.01	0.00	<b>0.041</b>	5.157	0.12
<b>Late pregnancy 25OHD (nmol/L)</b>					
Birthweight	-2.51	1.34	0.063	6.729	0.18
Birth length	-0.02	0.01	<b>0.028</b>	5.142	0.15
*Birth length	-0.01	0.01	0.117	9.650	0.29
<b>Fetal 25OHD (nmol/L)</b>					
Birthweight	-5.92	1.20	<b>&lt; 0.001</b>	10.198	0.29
Birth length	-0.02	0.01	<b>0.006</b>	5.180	0.20
*Birth length	-0.01	0.01	0.244	9.074	0.32
Birth subscapular SFT	-0.02	0.01	<b>&lt; 0.001</b>	3.534	0.24
Birth sum of subscapular SFT and triceps SFT	-0.08	0.02	<b>0.001</b>	2.093	0.12
Birth sum of SFT	-0.04	0.01	<b>&lt; 0.001</b>	2.501	0.16

SFT: skinfold thickness; R<sup>2</sup>: adjusted coefficient of multiple determination. Multiple linear regression models for dependent variables at birth were adjusted for season of pregnancy, maternal education, maternal BMI in early pregnancy, any supplement use during pregnancy, maternal smoking, offspring gender and gestational age. The association between birth length and 25OHD was also controlled for birthweight as indicated by the asterisk. Multiple linear regression models for dependent variables at 6 months and 2 years were adjusted for season of pregnancy, maternal education, birthweight, any supplement use during pregnancy, maternal smoking, offspring gender and age at assessment (weeks), and duration of breastfeeding.

sum of subscapular and triceps skinfolds, which are measures of overall adiposity, were negatively associated with fetal 25OHD (respectively,  $p < 0.001$ , and  $p = 0.001$ ). At 2 years of age there was a negative association between weight-for-age z-score and early pregnancy 25OHD ( $p = 0.041$ ) (**Tab. 1**).

#### CONCLUSIONS

Maternal and fetal 25OHD were negatively associated with offspring size and adiposity at birth, at 6 months, and 2 years of age in a cohort at risk of macrosomia in whom risk of vitamin D deficiency was high. Improvement of vitamin D status in pregnancy remains a public health concern.

#### ABS 8

##### IMPACT OF *EX UTERO* TRANSPORT, GENDER, AND ANTENATAL STEROIDS ON IN-HOSPITAL MORTALITY OF NEONATES IN HUNGARY: A RETROSPECTIVE COHORT STUDY

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#### INTRODUCTION

Infant mortality, which occurs in 4-7 per 1,000 live births in the Western world, has remained unchanged in the last several years. Preterm birth is the leading risk factor for infant death and initiatives to prevent preterm births have been deemed to be unsuccessful so far. Traditional risk factors for death such as gestational age and birth weight are well-described. However, the effect of other risk factors such as gender, methods of *ex utero* transport to neonatal intensive care units (NICU), and effectiveness of partial versus full antenatal corticosteroid regimens on overall survival have remained controversial.

#### PATIENTS AND METHODS

The goal of this retrospective, registry based, cohort study was to compare the effects of *ex utero* transport from 1) the same hospital, same building, 2) the same hospital, different building, 3) a different hospital in the same city, and 4) a different city on the in-hospital mortality of viable, preterm (23-36 weeks of gestation) infants born in Hungary between 2005-2010. Secondary objectives include the influence of antenatal steroid prophylaxis (none versus full dose, versus partial dose) and gender on in-hospital all-cause mortality. Cox proportional hazard models were used to evaluate the association between predictors of interest, confounders and mortality.

#### RESULTS

In total 15,393 patients were included in the study and 899 deaths were observed. *Ex utero* transport to another building in the same hospital increased the rate of mortality by 36% (HR 1.358, 95% CI 1.164-1.585,  $p = 0.0001$ ). The hazard ratio for transferring to another hospital in the same city was 2.338 (95% CI 1.795-3.044,  $p < 0.0001$ ) and transfer to a different city yielded a hazard ratio of 1.601 (95% CI 1.285-1.994,  $p < 0.0001$ ). The effect of antenatal steroids was evaluated in patients born between 23-32 weeks of gestation. A partial regimen of steroids did not result in a significant difference in mortality rate when compared to the full regimen, whereas neonates without steroids had an increased mortality rate of 68% (HR 1.679, 95% CI 1.424-1.979,  $p < 0.0001$ ). Male gender was associated with a 29% higher risk of death (HR 1.29, 95% CI 1.129-1.475,  $p = 0.0002$ ).

#### CONCLUSIONS

We found that all levels of *ex utero* transport were associated with increased mortality with rate ranging from 36 to 138%. Even partial steroid prophylaxis is beneficial in premature neonates and we also found evidence that male gender is associated with poorer survival. Our study yielded important results with implications for health care management with the ultimate goal to provide better care for future preterm infants.

#### ABS 9

##### PREVALENCE OF VITAMIN D DEFICIENCY IN MOTHERS AND THEIR NEWBORNS IN A TUNISIAN TERTIARY CARE HOSPITAL

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#### INTRODUCTION

Vitamin D deficiency has a high prevalence over the world. Pregnancy belongs to the traditional risk groups for vitamin D deficiency. The aims of this study were to assess vitamin D status in mothers and their newborns and to identify predictive factors of vitamin D deficiency.

## PATIENTS AND METHODS

Eighty seven healthy mothers and their newborns included in a cross sectional study from October to November 2012. Serum 25-hydroxyvitamin D (25OHD) levels were measured in mothers and newborns. For each mother and her newborn, data were obtained from their medical records. For mothers, daily intake of dietary calcium and vitamin D were calculated from a food frequency questionnaire.

## RESULTS

Vitamin D deficiency (serum 25OHD < 20 ng/ml) was found in 96.6% of the mothers and 97.7% of the neonates. Severe vitamin D deficiency (serum 25OHD < 12 ng/ml) was found in 87.4% and 89.7% of the mothers and of the neonates, respectively. No mother and no neonate had adequate vitamin D status. Mean maternal serum 25OHD was  $6.82 \pm 5.14$  ng/ml (3.6-23.77) and mean neonatal serum 25OHD was  $5.92 \pm 4.15$  ng/ml (3.6-22.28). Maternal serum 25OHD showed a strong positive correlation with neonatal serum 25OHD ( $r = 0.69$ ,  $p < 0.001$ ).

## CONCLUSIONS

Although conducted after the summer period, the study showed high prevalence of vitamin D deficiency among mothers and their neonates. Diet does not provide sufficient vitamin D. Vitamin D supplementation should be included in the prenatal care programs in Tunisia.

## ABS 10

### PLACENTAL GROWTH FACTOR AND ENDOTHELIAL CELL-SPECIFIC MOLECULE 1 LEVELS IN DISCORDANT AND CONCORDANT TWINS AND THEIR RELATIONSHIP WITH FETAL GROWTH

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## INTRODUCTION

Our aim was to determine whether fetal growth is related to placental growth factor (PGF) and endothelial cell-specific molecule 1 (ESM-1) in twins and to investigate correlation of cord blood PGF and ESM-1 levels with birth weight discordance in twins.

## PATIENTS AND METHODS

We studied 79 pairs, 158 infants with twin gestation.

## RESULTS

Eighteen of these 79 twin gestations (22%) were discordant. There was no correlation between birthweight and PGF&ESM-1 levels, but a positive correlation between PGF and ESM-1 levels,  $r = +0.51$ ,  $p = 0.001$ . There was a correlation between birthweight difference (delta birthweight) and difference between PGF levels (delta PGF) ( $r = +0.430$ ,  $p = 0.001$ ) but not ESM-1. When we divided infants into three group according to birthweight appropriateness for gestational age, there was a positive correlation through groups for PGF ( $r = +0.557$ ,  $p = 0.0005$ ) and slightly with ESM-1 ( $r = +0.324$ ,  $p = 0.001$ ).

## CONCLUSIONS

These results suggest that growth of twins exposed to the similar intrauterine environment may be due to variations in either growth factors like PGF, depending upon the genetic similarity and susceptibility. PGF levels have a strong relationship with birthweight differences and discordance in twins.

## ABS 11

### THERMOREGULATION IN VERY LOW BIRTHWEIGHT INFANTS: A SURVEY OF CURRENT PRACTICE IN 87 NICUs

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## INTRODUCTION

Thermoregulation of the newborn and preterm infant is an essential task in the neonatologist's daily routine. However, the optimal thermal environment for preterm infants is not known and evidence-based guidelines defining temperature targets and thermal management procedures are lacking. Our aim was to assess routine procedures and practices for temperature management in very low birthweight (VLBW) infants. We hypothesized, that temperature goals and thermal management practices would show considerable heterogeneity across the different institutions.

## PATIENTS AND METHODS

An online survey was sent to 149 level 1 neonatal intensive care units (NICUs) in Germany, Austria

and Switzerland. With a total of 20 questions, current practice of thermoregulation in very low birthweight infants with gestational age  $\leq 30$  weeks and birthweight  $\leq 1,500$  g was assessed. The neonates were categorized into three subgroups according to gestational age and birthweight.

#### RESULTS

The survey return rate was 58%. In 93% the reported target body temperature covered the value of 37.0°C but there was variation in the upper and lower range limits. The reported cut-offs for hypo- and hyperthermia were independent of gestational age and birthweight with a tendency for higher temperature targets in smaller infants. All participating units preferred the incubator to the heat radiator as heat therapy device. 68% of the NICUs preferred air temperature control to skin servo-control in routine practice. There was significant variation between incubator air temperature and humidity values at admission. 42% of the units based their thermal management on clinical bedside assessment only, 46% reported the use of standard operating procedures. Body temperature targets and incubator settings were related to staff position, center experience and the use of standard operating procedures.

#### CONCLUSIONS

Our assessment revealed significant variations in temperature goals, initial incubator settings and humidity management across different NICUs. Almost half of the centers do not base their thermal management decisions on standard operating procedures. There is a need for the establishment of evidence-based guidelines to guide and standardize clinical practice.

#### ABS 12

### REGIONAL ELECTRONIC RESEARCH SYSTEM E-WCZEŚNIAK (E-PREEMIE) IN MAZOVIA, POLAND

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#### INTRODUCTION

Poland is divided into 16 geographic voivodeships regions among which Mazovia is the biggest and the one of the most dynamically developing regions in Poland. Mazovia is located in the centre of the country, contains the capital city and occupies 11% of the country's territory. It is the biggest local

community, which numbers over 5 million people and approximately 55,000 deliveries annually in 52 perinatal departments. Until 2014 we did not have any neonatal systemic data collection. Electronic network system E-wcześniak (E-Preemie) in Mazovia was entering to each level II and level III departments of the region in January 2014.

#### PATIENTS AND METHODS

The main goal of this network is to analyse all clinical data regarding newborns  $\leq 32$  weeks of gestational age born from 1.01.2014 till 31.12.2014. The electronic research system E-wcześniak was introduced in 21 research facilities in the Mazovian region. All data collected by doctors during the research was available in the analytics panel, which enabled creating up-to-date analysis, reports and monitoring provided data. We have received data of 645 newborns  $\leq 32$  gestational age (GA) and analyse the data in four groups regarding the gestational age ( $< 24$  GA [7%]; 25-27 GA [18%]; 28-30 GA [38%]; 31-32 GA [38%]).

#### RESULTS

Among 645 newborns we had 55.3% male and 44.7% female. Cesarean section was performed in 75.5% newborns. Incidence of antenatal steroids was in 62.3%. One hundred fifty two newborns (23.6%) were born from multiple pregnancies. Surfactant was given to 269 newborns (41.7%) and in 12%, 32%, 45% and 13% consequently in each of 4 groups. Sixty nine babies died. Mortality rate was 60% in newborns  $\leq 24$  GA, 22.6% in newborns in 25-27 GA, 4.2% of the newborns in 28-30 GA and 2.4% in newborns 31-32 GA. Hemodynamic PDA was diagnosed on ECHO in 97 (15% newborns) among them 9 (1.8%) needed surgical ligation. Severe BPD had 11% babies while moderate 21.9% and mild 67.1%. ROP was recognized in 13.8% newborns  $\leq 32$  GA among which only 1.5% needed laser treatment.

#### CONCLUSIONS

1. The data received from 645 newborns  $\leq 32$  GA from the capital city, which is the most populated Polish town, can be representative for whole country.
2. The electronic research system E-wcześniak (E-Preemie) in Mazovia is dedicated to health care professional. It is a very useful vehicle for the exchange of information regarding evidence of neonatal clinical practice.

#### ABS 13

### MORTALITY AND EARLY MORBIDITY IN VERY LOW BIRTH WEIGHT NEWBORNS DURING THE TWELVE YEAR PERIOD IN SLOVAK REPUBLIC

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## INTRODUCTION

Improvements in perinatal and neonatal care have increased the survival of very low birth weight infants (VLBWI). These newborns still represent the largest share of neonatal mortality in the Slovak Republic, exceeding 50% of newborn deaths. They are a priority in care in Slovak neonatology. The main perinatal medicine's focus is the quality of life not just the survival. The goal of the study was to evaluate and compare the mortality and early morbidity in VLBWI during the twelve year period in the Slovak republic.

## PATIENTS AND METHODS

The data were collected from 14 perinatal centers and neonatal intensive care units in Slovakia retrospectively, annually, using standard definitions by electronic schedule. The goal of the study is to provide data about the rate of mortality and early morbidity of VLBWI born during the period from January 2003 to December 2014. The studied population consists of 2,458 newborns with birth weight less than 1,001 g (average 27.0 weeks GA and 819 g) and 4,884 newborns with birth weight between 1,001 and 1,500 g (average 30.7 weeks GA and 1,301 g).

## RESULTS

Comparing periods 2003-2008 and 2009-2014, the specific neonatal mortality rate was 166 and 139 per thousand live births, respectively. The incidence of severe brain diseases decreased in PIVH grade III and IV (10.9% to 8.2%); in PVL (6.7% to 5.2%). Though the incidence of respiratory distress slightly increased (75.1% to 79.4%), the BPD at 28 day remained almost the same (19.0% vs. 18.5%) and the BPD at 36 weeks decreased (6.3% to 4.7%). The study revealed high incidence with no improvement in NEC stage II or III (5.5% vs. 5.2%); EOS (9.9% vs. 9.5%) and LOS (18.6% vs. 18.7%). The study distinguishes infants by the number of serious illnesses they have undergone. Results show that 15.01% vs. 15.51% newborns did not overcome any disease; 21.54% vs. 33.72% overcame one disease; 11.96% vs. 18.21% two diseases; 7.54% vs. 8.67% three diseases and 7.51% vs. 8.47% four or more diseases between the two periods.

## CONCLUSIONS

One of the most important factors influencing the quality of life is the number of serious illnesses

that very low birth weight infants have undergone during hospital stay. These illnesses also include infections and their occurrence is not decreasing. This led to the introduction of the Uniform Infections Surveillance system at all NICUs and Perinatal Centers in Slovakia.

## ABS 14

### VLBW INFANTS OUTCOMES: A 12 YEARS REPORT IN A SOUTH AMERICAN NEONATAL NETWORK (NEOCOSUR)

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## INTRODUCTION

Neocosur is a South American collaborative neonatal network created in 1997 to survey VLBW infants's outcomes. The participant Centers are University-affiliated. Neonatal Intensive Care Units (NICUs) in each country vary in size, population served and resources.

## OBJECTIVE

To describe main outcomes of VLBW infants admitted in 14 centers level III NICUs from 4 South American countries (Argentina-Chile-Paraguay-Peru) members of Neocosur Network during at least 10 years.

## PATIENTS AND METHODS

A cohort observational population based study. Between 01/01/2001 until 31/12/2012 all live inborn infants with birth weight (BW) 500 to 1,500 g in the participating Centers were included. Bio-demographic data and multiple outcome measures were prospectively collected. Data registration was made online with predefined diagnostic criteria and analyzed by a central database unit. Statistical significance of  $X^2$  p-value and Cochran Armitage trend test significance at  $< 0.05$ .

Mortality was adjusted by the Neocosur mortality risk score (J Perinatol. 2005;25:577).

## RESULTS

10,728 VLBW infants were enrolled (50.8% males): mean BW 1,077 g ( $\pm$  284), 34.1% under BW 1,000 g, mean GA 28.8 weeks ( $\pm$  3).

Global mortality was 27.6%. 5% died in the delivery room and 22.6% died after admission. Pregnancy control (82.7 to 90.8%), antenatal steroids use (71 to 80.9%), multiple gestations (17.4 to 22.6%), major congenital malformations (5.2 to 7.6%), Apgar < 3 at 5' (7.1 to 9.6%), CPAP (37.9 to 57.6%), prophylactic CPAP (2.4 to 15.8%) and PDA (29.9 to 42.3%) showed a significant increase. Vaginal delivery (34.0 to 26.1%), early onset sepsis (7.1 to 2.3%), late-onset sepsis (26.6 to 20.4) and ROP (30.1 to 22.4%) showed a significant decrease. Death at delivery room (5.0%), O<sub>2</sub> 36 weeks (17.6%), IVH G III-IV (11.2%) and NEC (11.1%) remained with non-significant changes.

Furthermore, adjusted by risk there was a 5% decrease in mortality over the last 6 years period.

## CONCLUSIONS

Through this 12 year period, raw mortality and the incidence of many major morbidities have remained unchanged in our Network despite improvements in both obstetrical and neonatal practice. However an improvement in mortality was found when adjusting for perinatal risk factors. This fact, together with the significant increases in multiple gestation, congenital malformations and low Apgar scores point towards a shift in the population served.

## ABS 15

### IMPACT OF VARICELLA VACCINATION IN CHILDREN UNDER 1 YEAR OF AGE IN ITALY (2006-2011)

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## INTRODUCTION

Varicella represents the most widespread vaccine preventable childhood infectious disease in Italy. In children under 1 year of age, it tends to be more severe with a higher rate of complications like pneumonia, hepatitis and encephalitis, and is associated with higher mortality. In Italy, between

2003 and 2010, 8/21 Regions have progressively introduced Universal Varicella Vaccination (UVV) in their immunization programs, with different schedules in children aged 13-15 months and 5-6 years. Objective of this study was to analyze hospitalization rates (HR) in children under 1 year of age, by the different vaccination policies in Italy in 2006-2011.

## PATIENTS AND METHODS

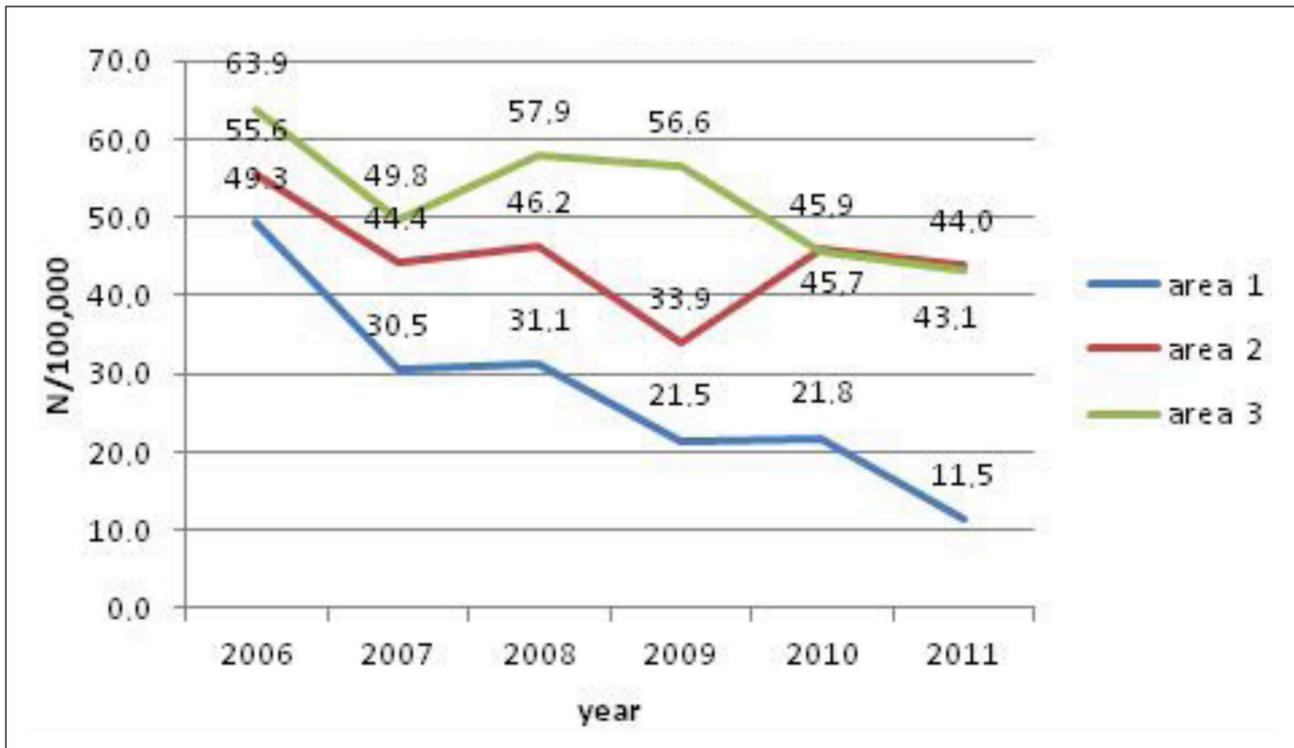
We performed a retrospective review of hospitalization data from Italian hospital discharge forms, provided by the Ministry of Health. We considered the codes 052.0-052.9 by ICD9-CM system (primary or secondary diagnosis). HR of varicella in children under 1 year of age were calculated by different vaccination policies (referring to the year 2008) in 3 different areas: area 1, with a UVV policy (Veneto, Sicilia, Puglia, Toscana), area 2, with policy of vaccinating susceptible adolescents and at-risk population (Piedmont, Friuli Venetia Giulia, Liguria, Lazio, Campania, Basilicata, Calabria, Sardinia) and area 3 with vaccination of only at-risk population (the remaining regions). The denominator for HR was calculated using resident population aged less than 1 year numbers according to ISTAT.

## RESULTS

10,483 hospitalizations for varicella were identified in patients of any age. The peak in varicella hospitalizations was observed in the first year of life. In this age group varicella was responsible of 13.7% of hospitalizations. 71.5% of cases in primary diagnosis (PD) were varicella without mention of complications, followed by the varicella with other specified complication (9.6%). 32 diagnosis reported post-varicella encephalitis and 15 hemorrhagic pneumonia. When varicella diagnosis was reported as secondary (SD), the most frequent PD were pneumonia or respiratory failure (25.7%). Annual HR globally declined in this age group from 56.4 to 34.2/100,000 children. The greatest HR were in area 3 and they declined from 63.9 to 44/100,000. In area 2 HR declined from 55.6 to 43.1/100,000, and in area 1 HR significantly decreased from 49.3 to 11.5/100,000 (test for trend,  $p < 0.001$ ) (Fig. 1).

## CONCLUSIONS

This study demonstrated that varicella continues to represent a relevant health problem in Italy, especially in the pediatric age. Data obtained by the Italian Regions that first introduced universal vaccination demonstrated that it allows to reduce the incidence of varicella and hospitalization rates.



**Figure 1 (ABS 15).** Hospitalization rates (x 100,000) in children under 1 year of age in Italy in 2006-2011 by vaccination policies.

## ABS 16

### GENERAL HEALTH PERCEPTION OF YOUNG ADULTS BORN PRETERM OR WITH A VERY LOW BIRTH WEIGHT IN THE NETHERLANDS VERSUS PEERS

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#### INTRODUCTION

Studies have shown adverse outcomes for those born very preterm or with a very low birth weight, even until adulthood. The aim of the current study is to gain insight in the general health perception of young adults in the Dutch nationwide POPS (Project On Preterm and Small for gestational age infants) cohort study, who were born very preterm (< 32 weeks of gestation) and/or with a very low birth weight (< 1,500 grams) in 1983, at two different ages in young adulthood.

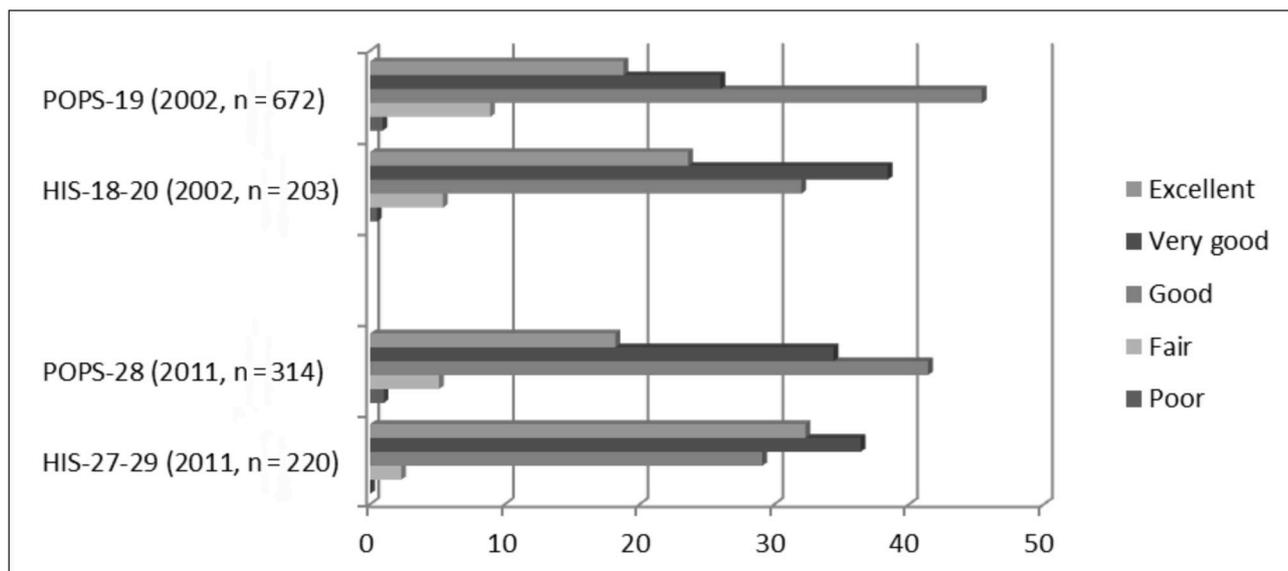
#### PATIENTS AND METHODS

At 19 years of age, the participants of the POPS cohort were asked to complete questionnaires

at home before their visit for a full physical examination (n = 672). At 28 years of age, they completed various online questionnaires (n = 314). At both ages a general health question used in the CBS (Statistics Netherlands) Health Interview Survey (HIS) was asked, originating from the SF-36 questionnaire: "In general, would you say that your health is: excellent, very good, good, fair, or poor?". The HIS data from the same year that the POPS cohort completed the questionnaires was used as control data. In the HIS data bases, 18-20 year olds were selected from the data file of the year 2002 (n = 203) and 27-29 year olds (n = 220) of 2011.

#### RESULTS

**Fig. 1** shows significant differences between the POPS participants and their peers within the HIS at both 19 (p = .001) and 28 (p < .001) years of age. At 19 years of age, 44.8% of the POPS participants reported 'excellent' or 'very good' health, versus 62% of their peers within the HIS. At 28 years of age, 52.6% of the POPS participants reported 'excellent' or 'very good' health, versus 68.7% of their peers. Gender also affected general perceived health; women perceived their health as poorer, compared to men. In a multivariate analysis, including both gender and groups, the differences



**Figure 1 (ABS 16).** Differences between the POPS participants and their peers within the Health Interview Survey (HIS).

between the preterm born young adults and their peers remained highly significant.

#### CONCLUSIONS

Despite the selective non-response of the POPS cohort of those most handicapped at 19 and 28 years, this study shows that adults born very preterm and/or with a very low birth weight perceive their health as less optimal, compared to their peers from the general population. This difference does not seem to decrease as they grow older.

#### ABS 17

#### INTRAUTERINE GROWTH RESTRICTION, HEAD SIZE AT BIRTH AND OUTCOME IN VERY PRETERM INFANTS

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#### INTRODUCTION

To determine whether small head circumference (HC) or birth weight (BW) or both are associated with neonatal and long-term neurological outcome in very preterm infants.

#### PATIENTS AND METHODS

Data came from the 1997 Epipage study: all 2,442 live births between 26 and 32 weeks of gestational age in 9 regions of France were included. 1,395 were tested at age 5 years for cognitive performance and 1,315 with school performance reports at age 8. Symmetric growth restriction (SGR) was defined in our population by HC and BW < 20<sup>th</sup> percentile and in the same percentile range, and asymmetric growth restriction (AGR) by at least one of HC and BW 20<sup>th</sup> percentile.

#### RESULTS

Compared to AGA, SGR was significantly associated with neonatal mortality (adjusted odds ratio [aOR] 2.99 [95% confidence interval (95%CI) 1.78-5.03]), moderate and severe cognitive deficiency (respectively aOR 1.65 [95%CI 1.01-2.71] and aOR 2.61 [95%CI 1.46-4.68]), and poorer school performance (aOR 1.79 [95%CI 1.13-2.83]). HGR

was significantly associated with severe cognitive deficiency (aOR 2.07 [95%CI 1.15-3.74]). WGR was not significantly associated with cognitive or school performance despite higher rates of neonatal morbidity.

#### CONCLUSIONS

SGR in preterm infants was associated with neonatal mortality and impaired cognitive and school performance. The outcome of AGR differed according to HC: HGR was associated with impaired cognitive function, WGR was not.

#### ABS 18

### PREMEDICATION FOR NON-EMERGENCY NEONATAL INTUBATIONS: SURVEY OF PRACTICE ACROSS UNITED KINGDOM

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#### INTRODUCTION

Endotracheal intubation is a common procedure in neonatal units and is a stressful procedure associated with pain and adverse physiological responses. The American Academy of Pediatrics recommends that premedications should be used for all neonatal intubations except for emergencies. Previous reports from United Kingdom (UK) inform us that there is no consensus on the need, choice or dose of premedications. We aim to identify the current practice of premedication use prior to intubation in the neonatal units across UK.

#### PATIENTS AND METHODS

A web-based questionnaire was distributed to all the neonatal units in UK. The proforma was designed to include information about neonatal unit and local network, availability of local guidelines, premedications used, use of pre-filled syringes and the average time from decision to intubate to administration of medication. Order in which drugs were given and dosage were also noted. The study had approval from the local audit and research committee.

#### RESULTS

Of the 52 units that participated, 51 units (98%) routinely used premedications and 49 (94%) had written guidelines. Morphine and fentanyl were the most popular sedatives, used in 26 and 25 units respectively. Most units (88%) used suxamethonium as the muscle relaxant, with

atracurium, pancuronium and vecuronium being the alternatives. Atropine was used routinely in 40% of the units while 60% would use if there was bradycardia. Only 15% used pre-filled syringes for premedications. The responders were unable to answer the question pertaining to average time between administration of premedications and intubation. Encouraging local audits within neonatal networks would provide further information on this.

#### CONCLUSIONS

In comparison with the previous 2007 UK survey, most of the neonatal units have a written policy for premedication use and an increased number routinely use premedications for elective intubations. There was consistency in suxamethonium use. However, there was variation in choice and dosage of analgesics and vagolytics. Developing unifying guidelines may reduce prescription error and uncertainty.

#### ABS 19

### HEALTH-RELATED QUALITY OF LIFE IN VERY PRETERM CHILDREN ASSESSED AT SCHOOL AGE: COMPARISON BETWEEN THE CHILDREN'S AND PARENTS' REPORTS

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#### INTRODUCTION

Improved survival of very preterm (VP) infants is leading to increased attention towards their subsequent development and health-related quality of life (QOL). While subjective reporting is considered the standard for QOL assessments, in case of children parent-reported evaluations are often used. Studies comparing the children's and parents' assessments have produced inconsistent results.

#### PATIENTS AND METHODS

We used the Pediatric Quality of Life Inventory Generic Core Scales (PedsQL™), vers. 4.0, to explore health-related QOL in an area-based cohort

of VP children assessed at school age. PedsQL™ includes 23 items in four subscales: physical, emotional, social and school. The last 3 subscales produce an overall psychosocial score. 439 children born in 2003-2004 in the Italian regions of Friuli-Venezia Giulia and Lazio participated (response rate 67%). For this analysis, 26 children with severe disability (cerebral palsy, blindness or deafness) were excluded. Thus, 413 cases were analyzed. Comparisons between the children's and parents' assessments were carried out using non-parametric Spearman's correlation coefficient and Wilcoxon signed-rank test for paired data.

## RESULTS

228 children were males (55.2%) and 93 (22.5%) were born with gestational age < 28 weeks. Mean age at assessment was 9 years (standard deviation 0.7 years). Overall, the PedsQL™ showed satisfactory internal consistency (Cronbach alpha 0.82 and 0.90 for children and parents respectively). Mean values of the total QOL score were 78.5 for children's and 84.6 for parents' reports ( $p < 0.001$ ), with higher scores indicating better QOL. For Physical Health, results were 78.7 and 86.7 respectively ( $p < 0.001$ ), and for Psychosocial Health 78.3 and 83.5 ( $p < 0.001$ ). The correlation coefficients between the children's and parents' responses were all quite low ( $< 0.35$ ), although statistically significant.

## CONCLUSIONS

In this study the reported quality of life in school age very preterm children without severe neuromotor and sensorial disabilities was good. However, assessments by children were systematically lower than those obtained by their parents, and the differences were statistically significant. Further analyses will focus on identifying the factors responsible for these discrepancies.

## ABS 20

### THE EPIDEMIOLOGY OF LISTERIOSIS DURING PREGNANCY IN NORTHERN ITALY

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## INTRODUCTION

Invasive listeriosis usually affects pregnant women, newborns, the elderly, and immunocompromised individuals. Listeriosis can develop at any time during pregnancy and it is one of the most common causes of neonatal sepsis and meningitis. While maternal

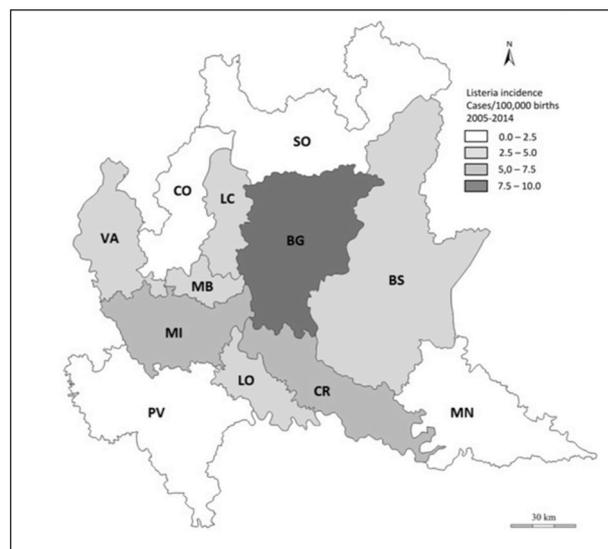
illness is generally mild, neonatal illness is often fatal. In western countries clinical cases are reported with a proportion of pregnancy-related listeriosis averaging about 20% in Spain, United States and France. The aim of this study was to analyze all pregnancy-related listeriosis cases observed in Lombardy (Italy), during the ten-year period 2005-2014.

## PATIENTS AND METHODS

The case definition of invasive *Listeria spp.* infection was based on the Commission Decision 2002/253/CE. A case is considered maternal/neonatal when diagnosed in a pregnant woman, foetus or a newborn below one month of age. Demographical, clinical and microbiological data about pregnancy-related cases were collected from the regional notification database (MAINF) and the Regional Reference Laboratory (RRL) database. Statistical analysis was performed using Epi-Info 6.04 software (Centers for Disease Control and Prevention, USA). Associations between categorical variables were assessed using the chi-square test or Fisher exact test as appropriate. Differences were considered statistically significant when  $p$  was  $< 0.05$ . The study was approved by the Ethics Committee of the University of Milan.

## RESULTS

Overall, 6.6% ( $n = 40$ ) of the total *L. monocytogenes* infections were pregnancy-related during the ten-year period under study (2005-2014). Interestingly, the incidence of listeriosis was seven-fold higher in pregnant women (4.3 cases per 100,000 births) than in general population (0.6 cases per 100,000 inhabitants). Cases were distributed in eight out of the twelve provinces in Lombardy (**Fig. 1**). Clinical



**Figure 1 (ABS 20).** Distribution of pregnancy-related listeriosis in Lombardy (2005-2014).

presentation and characteristics are shown in **Tab. 1**. Regarding fetus outcome, all cases reported in the second trimester ( $n = 5$ ) resulted fatal, while those reported in third trimester ( $n = 32$ ) showed an increased survival. The percentage of pregnancy-related listeriosis among foreign population (30%) including people from Peru, Ecuador, Albania, Ukraine, Romania, Hungary, Marocco, Saudi Arabia, was significantly higher compared to general population (3.5%) ( $p < 0.01$ ).

#### CONCLUSIONS

Listeriosis is an infection with a greater incidence during pregnancy. Neonatal infection can be a devastating disease associated with high mortality and morbidity unless promptly diagnosed and treated. Prevention and control are difficult, the most effective strategy is to avoid the source of

infection. Thus, pregnant women should refrain from consuming raw or partially cooked food of animal origin, soft unpasteurized cheeses and raw vegetables.

## Host responses and early diagnosis of infection

#### ABS 21

#### HEARING IMPAIRMENT IN PREMATURE NEWBORNS – ANALYSIS BASED ON THE NATIONAL HEARING SCREENING DATABASE

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#### INTRODUCTION

The incidence of sensorineural hearing loss is between 1 and 3 per 1,000 in healthy neonates and 2-4 per 100 in high-risk children. The national universal neonatal hearing screening carried out in Poland since 2002 enables to select children with the negative result of screening and those with risk factors of hearing loss for regular follow-up and appropriate treatment. The aim of this study was to assess the risk for hearing impairment in preterm babies ( $\leq 33$  weeks) and to analyze the risk factors of hearing loss in this population.

#### PATIENTS AND METHODS

The analysis of the data of 11,438 neonates born before 33 weeks, between 2010 and 2013. The study group was divided into two subgroups:  $\leq 28$  weeks (2,884 children) and 29-32 weeks (8,554 neonates). The control group consisted of 1,487,730 newborns born  $\geq 33$  weeks. In all children hearing screening by transient evoked otoacoustic emissions (TEOAEs) was performed and the risk factors of hearing loss recorded. Children who failed the screening test or had risk factors of hearing impairment were referred to the audiology clinic for evaluation by means of auditory brainstem response. All children in the study group were treated as children with risk factor. Only about 55% of referred children turned up to

**Table 1 (ABS 20).** Clinical presentation and characteristics of pregnancy-related listeriosis.

Variable	Number (%)
Total number of cases	610
Pregnancy-related cases	40 (6.6)
Mother age (min-max)	34 (17-45)
<b>Ethnicity</b>	
Italian	28 (70)
Other	12 (30)
<b>Maternal symptoms</b>	
Present	20 (50)
Absent	7 (17.5)
Unknown	13 (32.5)
<b>Clinical presentation</b>	
Septicemia	19 (47.5)
Meningitis	4 (10)
Other infections	8 (20)
Pregnancy complications	10 (25)
Unknown	4 (10)
<b>Trimester</b>	
First	-
Second	5 (12.5)
Third	32 (80)
Unknown	3 (7.5)
<b>Outcome of pregnancy</b>	
Live birth	26 (65)
Stillbirth	3 (7.5)
Miscarriage	8 (20)
Unknown	3 (7.5)
Fatality rate ( $n = 37$ )	11 (29.7)
<b>Reported pregnancy-related cases</b>	
MAINF system	11 (27.5)
RRL network	6 (15)
MAINF and RRL	23 (57.5)

be assessed during the observation period. Some analyses based on the reduced number of patients.

## RESULTS

Hearing deficit (HD) was diagnosed in 11% of neonates  $\leq$  25 weeks, in 5% 26-27<sup>th</sup> weeks, 3.46% 28<sup>th</sup> weeks and 2-3% 29<sup>th</sup> and 32<sup>nd</sup> weeks. In the control group the incidence of HD was 0.2% (2.87% in children with risk factors). The most frequent risk factors in the study group were: VLBW, ototoxic drugs and intensive care with mechanical ventilation; in the control group: ototoxic drugs, TORCH infections and family history. The most significant risk factors were congenital malformations of the head (OR 3.4, CI 1.04-11.23), low Apgar score (OR 1.9 CI 1.2-3.0) and mechanical ventilation (OR 2.8 CI 1.6-4.8). The hearing screening was positive in 22.42% newborns  $\leq$  28<sup>th</sup> weeks and in 10% of those born in 29<sup>th</sup>-32<sup>nd</sup> weeks and in the control group. Hearing impairment was then diagnosed in 15.8% newborns  $\leq$  28<sup>th</sup> weeks, in 10% born in 29<sup>th</sup>-32<sup>nd</sup> weeks and in the control group with negative result of hearing screening.

## CONCLUSIONS

Hearing impairment is an important and severe consequence of prematurity and its prevalence is inversely related to the maturity of the baby. The concomitant risk factors such as low Apgar score, intensive care treatment with mechanical ventilation and congenital defects enable to select the children most at risk for hearing impairment who should be strictly followed-up and receive appropriate treatment.

## ABS 22

### IS ROUTINE USE OF ANTIBIOTICS IN PRETERM INFANTS BORN BY ELECTIVE CAESAREAN SECTION (COLD SECTION) WITH RESPIRATORY DISTRESS SYNDROME JUSTIFIABLE?

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## INTRODUCTION

Congenital pneumonia may mimic respiratory distress syndrome (RDS) and the commonest organism are GBS, *E. Coli* and others. For this reason it has been considered good practice to screen all babies with RDS and initiating antibiotic therapy whilst awaiting results. This routine antibiotic therapy approach is debatable as there is no evidence to support it.

It is routine policy in our NICU to start antibiotics for a preterm infant with respiratory distress. Infants born by elective caesarean section (cold section) with no risk factors of infection are unlikely to have infection. Many will have RDS due to surfactant deficiency.

## PATIENTS AND METHODS

Retrospective study of all the preterm infants (26 weeks to 37 weeks) born by elective caesarean section during 5 year study period (Jan 2010 to Dec 2014).

Infants less than 26 weeks were excluded as they were usually not delivered by elective caesarean section and also the need for umbilical lines in this group increases the risk of infection. Infants with risk factors for infection at birth (e.g., GBS carrier in mum, PROM, chorioamnionitis, maternal pyrexia) were excluded.

## RESULTS

We included 126 elective caesarean section with no infection risk factors. 56 infants met the inclusion criteria. All were commenced on first line antibiotics at birth because of prematurity and RDS.

Infants in our study had a median GA of 34<sup>+2</sup> weeks (range 27<sup>+5</sup> to 36<sup>+9</sup>); median BW was 1.99 kg (range 0.54-3.98 kg). There was no significant difference in gender, comorbidities. 12% of infants received mechanical ventilation, 75% had non-invasive ventilation (CPAP), 9% did not require any oxygen support. Four patients had raised inflammatory marker (CRP) and subsequently required a prolonged course of antibiotics. Blood cultures were reported negative in all infants.

## CONCLUSIONS

All infants who were born by elective caesarean section and were started on antibiotics at birth had blood culture negative at 36 hrs, regardless of the gestation age and birth weight. 93% of babies had antibiotics discontinued at 48 hrs.

Starting prophylactic antibiotics for preterm infants born by elective caesarean section with no risk factor for infection is not a valuable use of antibiotics.

## Nosocomial infection and colonization

## ABS 23

### CLEARING SERIOUS INFECTION: A QUALITY IMPROVEMENT INITIATIVE TO REDUCE NOSOCOMIAL INFECTION

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## INTRODUCTION

A quality improvement program was introduced at the Belfast neonatal unit in response to benchmarking data revealing a high rate of late onset infection caused by *coagulase negative staphylococcus* (CoNS) in very low birthweight (VLBW) infants, against other units in the Vermont Oxford Network. In 2009 the rate of CoNS late onset sepsis was noted to be significantly higher than network counterparts. A multidisciplinary group was set up, comprised of neonatal medical, nursing and microbiology staff, practice development staff and infection control nurses, to co-ordinate the delivery of a quality improvement program with the aim of reducing the frequency and impact of nosocomial infection.

## PATIENTS AND METHODS

A staff education program was undertaken to explain the problem and interventions planned. This communication was sustained through notice board and email updates and presentations for all incoming medical and nursing staff.

The organisms causing nosocomial and central line infections were identified by microbiology. The structured quality improvement program targeted handwashing, aseptic technique and central line care. Specific interventions included:

- nurse led engagement with parents;
- simulation and multimedia teaching to all staff on aseptic no touch technique;
- audits of skin breakages leading to the introduction of alternative arterial line fluids to reduce peripheral blood glucose monitoring;
- revision of enteral feeding protocols reducing the length of time required to reach full feeds.

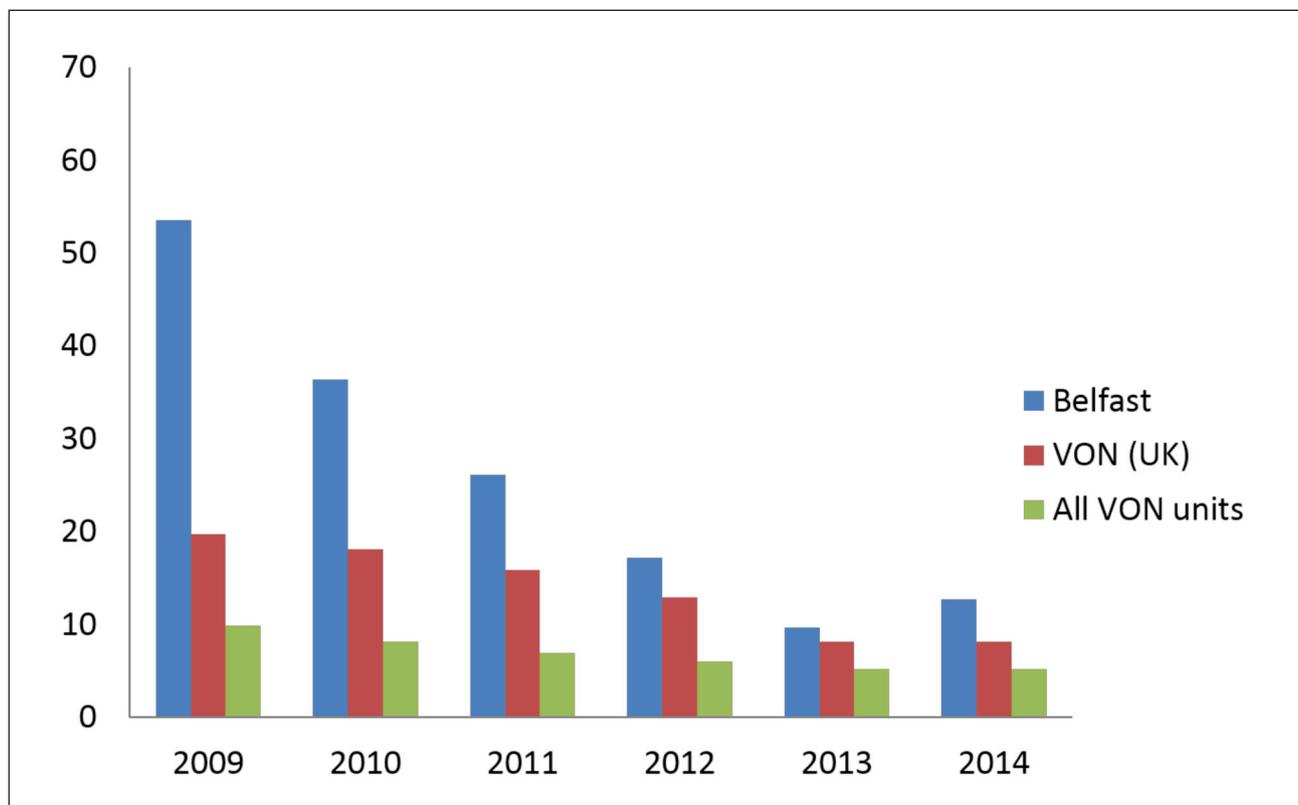
## RESULTS

Between 2010 and 2014, there was a decrease in the rates of CoNS infections from 53.6% of all VLBW infants admitted to our unit to 12.7%.

The total number of bacteraemias has fallen each year since 2011.

The central line associated blood infection (CLABSI) rate per 1,000 catheter days has dropped from 225.4 to 101.7 in that same time.

Benchmarking shows that our unit's rates of CoNS sepsis are now in line with the rest of the United Kingdom.



**Figure 1 (ABS 23).** Percentage of VLBW babies with CoNS infection in Belfast since 2009 compared to other UK units in VON and all VON units.

VLBW: very low birth weight, < 1,500 g; VON: Vermont Oxford Network; CoNS: *coagulase negative staphylococcus*.

**CONCLUSIONS**

There has been sustained reduction in neonatal nosocomial infections over the past five years. The effects of the changes brought about through the coordinated quality improvement program have led to a marked change in culture where infection is no longer seen as inevitable in VLBW infants.

Attitudes and behaviours of healthcare staff can be improved through provision of education, ongoing monitoring and support and introduction of new practices.

**ABS 24**

**VAGINAL UREAPLASMA PARVUM BUT NOT UREALYTICUM COLONIZATION AT 12 TO 14 WEEKS OF GESTATION IS SIGNIFICANTLY ASSOCIATED WITH PRETERM DELIVERY**

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**INTRODUCTION**

*Ureaplasma (U.) spp.* are the most prevalent pathogens within the genital tract in asymptomatic sexually active women. *U. spp.* infection of the upper genital tract during pregnancy is associated with adverse pregnancy outcome and neonatal short and long-term morbidity. Proof of a causal relation between vaginal isolation of *U. spp.* – which can easily be screened for – and both preterm delivery and morbidity of the preterm infants is lacking. The aim of the present study was to screen women during early pregnancy for vaginal *U. spp.* colonization and correlate biovar results with pregnancy outcomes in order to identify women at increased risk for preterm delivery.

**PATIENTS AND METHODS**

Between May 2009 and December 2012 4,330 pregnant women attending routine nuchal translucency screening between 12 and 14 weeks of gestation were enrolled in this prospective observational multicenter study. In study patients,

a vaginal swab was taken and tested for presence of *U. spp.* biovars by PCR. Primary outcome variable was the rate of spontaneous abortion or spontaneous preterm birth (SPB) at less than 37 weeks of gestation. Multiple pregnancies, medically-induced preterm deliveries and induced abortions were excluded, and 127 were lost to follow-up, leaving 3,643 pregnancies for statistical analyses.

**RESULTS**

1,347 women (36.9%) were positive for *U. parvum*, 214 (5.9%) for *U. urealyticum*, and 113 (3.1%) for both. Vaginal colonization with *U. parvum* was significantly associated with an increased risk of SPB (OR 1.7, CI 1.3-2.2) as opposed to colonization with *U. urealyticum* or both biovars. The significant association between vaginal *U. parvum* in early pregnancy and preterm delivery was true for all investigated subgroups of prematurity as well as for very-low and extremely-low birthweight infants. The rate of colonization with *U. parvum* was particularly elevated in cases of extreme prematurity (70.6% at 21-23 weeks; 62.5% at 24-26 weeks of gestation). In a multivariable logistic-regression model, history of previous SPB was the strongest independent risk factor for SPB (OR 1.9, CI 1.5-2.4), followed by colonization with *U. parvum* (OR 1.6, CI 1.2-2.1) and diagnosis of bacterial vaginosis (OR 1.6, CI 1.1-2.4).

**CONCLUSIONS**

Results of our study proof a statistically significant association between first trimester isolation of vaginal *U. parvum* and subsequent preterm delivery at all gestational age groups, particularly at extremely low gestational ages. The lower the gestational age at delivery, the higher the percentage of *U. parvum* colonization in the first trimester of pregnancy.

## ORAL COMMUNICATIONS

**ABS 25**

**RESPIRATORY OUTCOMES IN LATE AND MODERATELY PRETERM INFANTS: RESULTS FROM A POPULATION-BASED STUDY**

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## INTRODUCTION

Infants born very preterm (< 32 weeks of gestation) are at the highest risk of respiratory disease relating to lung immaturity. However, recent studies have shown that those born late preterm (34<sup>+0</sup>-36<sup>+6</sup> weeks) and moderately preterm (32<sup>+0</sup>-33<sup>+6</sup> weeks) are also at increased risk of adverse outcomes when compared with term-born infants. Within the setting of a UK prospective, population-based study, the Late And Moderately preterm Birth Study (LAMBS), we sought to compare respiratory outcomes in the neonatal period and at 2 years corrected age between infants born late and moderately preterm (LMPT) and those born at ≥ 37 weeks of gestation.

## PATIENTS AND METHODS

LAMBS was conducted in the East Midlands region of the United Kingdom between September 2009 and December 2010. All mothers delivering LMPT were invited to participate, together with a randomly selected sample of term infants (≥ 37 weeks of gestation). This analysis relates to singletons without major congenital anomalies. Neonatal data were obtained from neonatal medical records and data at 2 years corrected age were collected by parent questionnaire. Outcomes compared between LMPT and term-born infants were neonatal unit (NNU) admission for respiratory distress, investigation with chest x-ray (CXR), and at 2 years corrected age, wheeze and treatment for wheeze during the previous 6 months.

## RESULTS

907 LMPT and 972 term-born infants were studied. Infants born LMPT were more likely to be admitted to a NNU for respiratory disease (20.8% vs. 2.0%;  $p < 0.001$ ) and to have a CXR performed (175/905 [19.3%] vs. 23/971 [2.4%];  $p = 0.001$ ) and to have used an inhaler in the previous 6 months (114/531 [21.5%] vs. 91/614 [14.8%];  $p = 0.003$ ). On multivariate analysis, a significant association between LMPT birth and wheeze at 2 years corrected age remained after adjustment for NNU admission for respiratory distress and administration of antenatal corticosteroids (OR 1.37 [1.07 to 1.77];  $p = 0.01$ ).

## CONCLUSIONS

Compared with term-born infants, infants born at LMPT gestations are more likely to require admission to a neonatal unit for investigation and management of respiratory disease. There is an increased risk of wheeze in children born LMPT in early childhood, and this association remains significant even after adjustment for neonatal unit admission for respiratory distress and administration of antenatal corticosteroids.

## ABS 26

### PERFLUOROALKYL ACID EXPOSURE AND INFANTILE COLIC: A STUDY IN THE DANISH NATIONAL BIRTH COHORT

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## INTRODUCTION

Perfluoroalkyl acids (PFAAs) are environmentally persistent chemicals that are measurable in blood samples from populations worldwide and known to cross the placenta. Infantile colic is a common condition of unknown etiology characterized by excessive crying during the first months of life. Our objective was to investigate the association between maternal levels of the two most common PFAAs, perfluorooctanoate (PFOA) and perfluorooctane sulfonate (PFOS), and infantile colic in the offspring.

## PATIENTS AND METHODS

We studied 1,728 live-born singletons from the Danish National Birth Cohort (1996-2002). Women gave blood samples in early pregnancy and participated in computer assisted telephone interviews assessing infant crying symptoms at 6 months post partum. Infantile colic was defined according to the modified Wessel's criteria (crying or fussing for > 3 hours per day, > 3 days per week), starting before the age of 3 months. We investigated the association between quartiles of PFOA or PFOS and infantile colic (binary) by multivariate logistic regression. Covariates chosen with guidance from a directed acyclic graph included cohort sample, socio-economic status, maternal pre-pregnancy body mass index, age, and parity.

## RESULTS

There was no obvious association between PFAA exposure and infantile colic (adjusted odds ratios [95% confidence intervals] for the highest PFOA

and PFOS quartiles compared to the lowest were 1.04 [0.59-1.82] and 0.70 [0.40-1.22], respectively).

#### CONCLUSIONS

In the first study to investigate the association between PFAA exposure and infantile colic we found no association. Larger studies, preferably with higher exposure contrasts, are needed.

#### ABS 27

### NORMAL REFERENCE VALUES FOR UMBILICAL CORD ARTERIAL PH IN PRETERM AND TERM INFANTS

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#### INTRODUCTION

Infants born with fetal acidemia, suggesting intra-uterine compromise, face increased risks of adverse outcomes. Despite known developmental changes of acid-base values within the term age range, stationary cut-off values for defining fetal acidemia are commonly used for all gestational ages. We aimed to determine the normal reference values of umbilical arterial pH in a large cohort of vigorous infants born at 28-43 gestational weeks, and explore how different definitions of low pH discriminate for low Apgar scores.

#### PATIENTS AND METHODS

We performed a population-based cohort study of all deliveries in the Stockholm-Gotland region from 2008-2014. In total 105,799 singletons with a gestational age (GA) of 28-43 weeks had complete data on umbilical pH and Apgar scores (AS). Of these, 66,234 (63%) were defined as a reference population (AS of  $\geq 9$  at 1 and 5 minutes, normal non-instrumental vaginal delivery, and birth weight for GA  $\geq 3^{\text{rd}}$  and  $\leq 97^{\text{th}}$  percentile).

In addition to descriptive statistics of pH variations related to GA, linear regression was used to investigate the associations between GA and arterial pH. Acidosis defined as  $< -2$  standard deviations (SD) below the GA-specific mean, was compared to a fixed definition of pH  $< 7.10$ , with regard to AS of 0-6 at one and five minutes.

#### RESULTS

Within the reference population (n = 66,234), umbilical arterial pH increased with decreasing GA.

The mean pH values (SD) were 7.32 (0.07), 7.28 (0.07), 7.26 (0.07) and 7.24 (0.07) among infants born very preterm, moderately preterm, term and post-term, respectively.

Within the whole cohort (n = 105,799), the GA-adjusted definition of acidosis (pH  $< -2$  SD) defined a greater proportion of infants with AS 0-6, especially at one minute, as compared to the fixed definition of acidosis (pH  $< 7.10$ ). For example, according to the GA-adjusted definition, acidosis was seen in 15% of very preterm infants with AS 0-6 at the first minute, compared to 5% using the fixed pH  $< 7.10$  cut-off. Corresponding figures for moderately preterm and term infants were 19% versus 12%, and 28% versus 22% (all p  $< 0.05$  according to Chi-squared test).

#### CONCLUSIONS

Umbilical artery pH varies according to GA in vigorous infants. A GA-adjusted definition of fetal acidemia discriminates a greater proportion of infants with reduced AS, compared to a fixed definition of pH  $< 7.10$ . The presented pH reference curve enables a more accurate definition of acidemia at birth, also in preterm infants where robust reference values have been lacking. The significance for long-term clinical outcomes remains to be determined.

#### ABS 28

### PREDICTORS OF HOSPITAL DISCHARGE IN A SWISS NATIONAL COHORT OF VERY PRETERM INFANTS

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#### INTRODUCTION

As very preterm infant survival rates have increased, concerns regarding resource use have intensified. Length of stay in the hospital (LOS) has been identified as the most cost-driving factor in the care of very preterm infants. However, very preterm infants must remain in the hospital as long as they need highly specialized care, which is until they are of sufficient size and maturity to allow safe discharge home. Understanding the effect of clinical factors, mortality, and hospital policy on LOS could help in resource planning, family counselling, and stimulate quality-improvement initiatives.

## PATIENTS AND METHODS

A retrospective analysis was conducted of all live born infants with < 32 weeks gestational age (GA) or < 1,500 g birth weight (BW) who were born between 2006 and 2012 in Switzerland. Two approaches were used to select and validate models for predicting LOS: 1) Survivors only, LOS was modelled as continuous variable and multivariable linear regression analysis was applied. 2) Survivors and non-survivors together, LOS was estimated using Kaplan-Meier probability estimates. Deaths and patients who remained in hospital after the median age at discharge home of the whole study population were censored. Multivariable analysis was conducted using Cox proportional hazards regression modelling to investigate the simultaneous effect of centre and other factors that influence neonatal outcome.

## RESULTS

Data from 5,622 infants were included. Median age at discharge home was 37.9 weeks postmenstrual age. LOS was extended independently by 24 days from moderate or severe bronchopulmonary dysplasia (BPD,  $n = 487$ , 8.7%), 12 days from heart surgery ( $n = 184$ , 3.3%), 12 days from abdominal surgery ( $n = 245$ , 4.4%), 7 days from necrotizing enterocolitis  $\geq$  stage 2 ( $n = 190$ , 3.4%), 5 days from intraventricular haemorrhage > grade 3 or cystic periventricular leukomalacia ( $n = 590$ , 10.5%), 4 days from blood stream proven late onset sepsis ( $n = 464$ , 8.3%), and 3 days from transfer to a secondary hospital ( $n = 1,886$ , 33.5%). Irrespective of mortality rate, one out of nine centres had a shorter LOS (6 days), whereas three had an extended LOS (2 to 4 days). These data match remarkably well with the specific discharge home policy of the indicated centres, as revealed by an expert survey.

## CONCLUSIONS

The Cox proportional hazards model is superior as it considers mortality and, therefore, allows a better centre-to-centre comparison. Centres with extended LOS may implement distinct policy elements of early discharging centres. Measures should specifically address infants with extended LOS, e.g. supply of home oxygen for BPD. To improve future benchmarking, rehospitalisation data after final discharge home should be recorded systematically.

## ABS 29

### HYPOTHERMIA AND RESPIRATORY DISTRESS SYNDROME IN PREMATURE INFANTS

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## INTRODUCTION

Hypothermia is considered by many to be a risk factor for developing respiratory distress syndrome (RDS), but the underlying pathology for this is not completely understood. However, in term infants hypothermia is used therapeutically in the treatment of hypoxic ischemic encephalopathy caused by severe asphyxia. Furthermore, animal studies suggest that hypothermia may protect against lung injury. The mechanism behind this may be a decrease in the metabolic rate and therefore oxygen consumption, and furthermore an inhibition of the inflammatory processes involved in lung injury. We aim to investigate the association between hypothermia and severe RDS in premature infants.

## PATIENTS AND METHODS

The study population consisted of all infants born before 32 weeks of gestation and admitted to the neonatal intensive care unit (NICU), Aalborg University Hospital, Denmark, from April 1997 to December 2011. Rectal temperature was measured at admission. Severe RDS was defined as the need for surfactant treatment or death within the first 3 days of life in premature infants born before 32 weeks of gestation. Data was provided by national registries and a local neonatal database. We used multivariable logistic regression stratified according to the presence of early-onset infection, adjusted for gestational age, asphyxia, infant sex, and small for gestational age.

## RESULTS

We included 676 infants with complete data on hypothermia, RDS or death, and covariates. Among these infants 64% ( $n = 433$ ) had hypothermia ( $< 36.5^\circ\text{C}$ ), 34% ( $n = 228$ ) had a temperature within the normal range ( $36.5\text{--}37.5^\circ\text{C}$ ) and 2% ( $n = 15$ ) had hyperthermia ( $> 37.5^\circ\text{C}$ ). In infants without infection, 40% ( $n = 122$ ) had RDS or death, and the adjusted odds ratio for RDS or death was 2.06 (95% CI 1.13–3.73). In infants with infection 45% ( $n = 169$ ) had RDS or death, and the corresponding estimate was 0.99 (0.54–1.83).

**CONCLUSIONS**

In very preterm neonates we found differing results according to the presence of infection when investigating the association between hypothermia and RDS or death. Our results suggest that there is only an association between hypothermia and RDS or death in infants without infection.

**ABS 30**

**INCIDENCE OF ACUTE KIDNEY INJURY IN PREMATURE INFANTS ACCORDING TO ACUTE KIDNEY INJURY NETWORK (AKIN) CRITERIA**

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**INTRODUCTION**

Acute kidney injury (AKI) affects around 6% to 24% of newborns in NICUs and is associated with higher morbidity and mortality in affected patients. Causes for AKI may be multifactorial. Studies so far have been difficult to interpret as criteria varied extensively between studies.

The Acute Kidney Injury Network (AKIN) has proposed new criteria to unify standards for diagnosing and classifying AKI. We attempted to apply these new criteria to our patient population to assess the incidence of AKI in our premature infants.

Identifying the population at risk should help in enabling prevention or offering treatment options in the future.

**PATIENTS AND METHODS**

We included our cohort of premature infants below 35 weeks gestation treated at the NICUs of the Vienna General Hospital, Austria, from 2007 to 2010. Data were extracted from the computerized patient documentation system (CareVue®, Philips, NL) as well as from discharge letters and lab results.

We applied AKIN criteria for diagnosing AKI which have been published previously and use a combination of serum creatinine levels and urine output to classify severity of injury (stages 1-3). Applying exclusion criteria (complex malformations, died or transferred within 48 hours after admission) left 1,060 patients for analysis.

The statistical analyses were performed using STATA/IC™ 13.0 (StataCorp LP, Texas, USA). The study was approved by the local ethics board.

**RESULTS**

214 newborns (20.2%) of our population had any stage of AKI. We identified 98 patients (9.3%) with stage 1 AKI, 44 patients (4.2%) with stage 2 severity and 72 patients (6.8%) with stage 3 AKI. Risk factors associated with any AKI assessed in unadjusted analysis were female sex (odds ratio [OR] 0.78, 95% CI 0.57 to 1.06), 5-minute APGAR < 7 (OR 2.72) and any therapy for open ductus arteriosus (OR 5.16). Each additional week of gestational age decreased the incidence of AKI by 20% (OR 0.80, 95% CI 0.76 to 0.84). Prenatal factors such as birth mode, antenatal steroids, pre-eclampsia had no impact on incidence.

In adjusted analysis gestational age (aOR 0.89, 95% CI 0.83 to 0.94), and PDA therapy (aOR 3.40, 95% CI 2.28 to 5.07) became a less prominent factor, but female sex (aOR 0.69, 95% CI 0.50 to 0.96) became a more significant factor.

**CONCLUSIONS**

We present the largest data set to date to describe the incidence of AKI in premature infants by using recommended AKIN criteria. The incidence was comparable to previous studies. Gestational age was inversely linearly associated with the development of AKI, interestingly antenatal factors did not play a role.

Further studies will help to investigate the independent role of AKI for morbidity and mortality in these patients.

## Early origins of adult disease

**ABS 31**

**EARLY LIFE EXPOSURE TO ENDOCRINE DISRUPTORS AND TSH LEVELS IN NEWBORNS – ANALYSIS OF THREE EUROPEAN COHORTS**

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**OBJECTIVE**

Chemicals present in the environment may disrupt thyroid hormones, which in early life are essential for brain development. Observational studies regarding this topic are currently still limited, however as the presence of chemicals in the environment is ubiquitous, further research is warranted. The objective of the current study was to assess the association between exposure markers of various chemicals determined in cord blood and/or breast milk in three European cohorts and thyroid stimulating hormone (TSH) levels determined in heel prick blood spots.

**PATIENTS AND METHODS**

Methods: Mother-child pairs of three cohorts, FLEHS (Belgium, n = 1,105), HUMIS (Norway, n = 230), and Michalovce (Slovakia, n = 449) were included. Exposure to polychlorinated biphenyls (PCB), dichlorodiphenyldichloroethylene (DDE), hexachlorobenzene (HCB), brominated flame retardants (PBDEs), and perfluorinated alkyl acids was determined in cord plasma or breast milk, and information on TSH was obtained through country specific neonatal screening programmes. All cohorts were pooled for analysis. Linear regression models were composed to determine associations between the compounds in quartiles and TSH, which were adjusted for a priori defined covariates. Effect modification by gender was considered.

**RESULTS**

TSH levels were comparable for FLEHS and HUMIS, while median TSH in the Michalovce cohort was considerably higher (median TSH respectively 1.00, 1.10, and 2.76 mU/mL). For PCB-153 an overall significant effect on TSH was observed in the crude models ( $p = 0.018$ ). This effect remained significant after adjustment ( $p = 0.015$ ). Also for BDE-47 overall significant effects on TSH were observed after adjustment ( $p = 0.015$ ). For these two compounds, effects were most evident for the third quartiles, in which a consistent lower TSH was observed compared to the first quartiles. No effects were observed for the other compounds, as well as for the effect modification by gender.

**CONCLUSIONS**

Overall significant effects on TSH were observed for exposure to PCB-153, and BDE-47. These effects were most evident in the third quartiles, in which lower TSH levels were observed. Whether these lower TSH levels posed the infants at increased risk for disturbed thyroid function remains to be determined.

**ABS 32****RELATIVE SIZE AT BIRTH AND PARENTAL CARDIOVASCULAR MORBIDITY, A NATIONAL REGISTER STUDY**

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**INTRODUCTION**

Small relative size at birth is associated with a higher incidence of hypertension, altered glucose metabolism and cardiovascular disease (CVD) in adulthood. This may be due to circumstances during fetal and early postnatal life, or confounders such as genetic effects or unhealthy lifestyle of childhood home.

We hypothesized that small relative size at birth predicts cardiovascular disease in both parents.

**PATIENTS AND METHODS**

Pregnancy data came from Finnish Medical Birth Register that covers all births in Finland. During Jan 1, 1987 to Sep 30, 1990, we included as index children the first singleton birth for each of the 196,427 mothers (27 with incomplete ID, 0.01%). National Population Register Centre tracked the fathers with 3,048 (1.55% remaining missing).

We obtained Hospital Discharge Register data on in-patient care and specialized outpatient care from index child birth until Dec 31, 2012. ICD-9 and ICD-10 codes for coronary heart disease, stroke, or closely related conditions indicated CVD.

We applied Cox regression for proportional hazards to analyze the effect of BW SDS group on first CVD for mothers and fathers separately. Smoking during pregnancy and parental age were included as covariates.

**RESULTS**

Low offspring BW SDS ( $< -2$ ), as compared to that between  $-1$  and  $1$ , was associated with higher CVD hazard among their mothers (hazard ratio, HR, 1.5; 95% CI, 1.1 to 1.9). Among fathers, respective HR was 1.5 (1.1 to 2.0). Higher CVD rates were seen as well among mothers and fathers whose offspring BW SDS were  $> +2$ . Adjustments left the results unchanged.

## CONCLUSIONS

Both small and large relative size predicted CVD in both parents. Therefore, parental disease history needs to be accounted for when trying to assess possible effects of intrauterine conditions on later cardiovascular disease.

## Genetically defined risk

## ABS 33

### GILBERT GENOTYPES AND RESPIRATORY DISEASE IN VERY PRETERM INFANTS, A COHORT STUDY

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## INTRODUCTION

Respiratory disease in the very preterm infant is frequent and often severe. Bilirubin is both a potent neurotoxin and antioxidant, and may thus have clinical impact on preterm respiratory disease. The

Gilbert genotype, the *UGT1A1*\*28 allele, is the major known genetic cause of variation in bilirubin. We aimed to study the effect of bilirubin on respiratory disease in the very preterm infant using the *UGT1A1*\*28 allele as a measure of bilirubin.

## PATIENTS AND METHODS

Cohort study of 1,354 very preterm infants (gestational age < 32 weeks) born in Jutland, Denmark, 1996-2011. Genotypes were obtained from the Danish Neonatal Screening Biobank and clinical information from the databases of two tertiary neonatal intensive care units. Predefined outcomes were the need for surfactant therapy, any need for and duration of supplementary oxygen and bronchopulmonary dysplasia (BPD).

## RESULTS

Per *UGT1A1*\*28 allele the odds ratio for any need of supplementary oxygen was 1.26 (1.05 to 1.50), for need of surfactant 1.08 (0.91 to 1.28) and for BPD 1.71 (1.23 to 2.39), and hazard rate for discontinuation of supplementary oxygen was 0.84 (0.76 to 0.93) and per allele the number of excess days in oxygen were 6.38 (1.87 to 10.89) (**Tab. 1**). Hardy Weinberg equilibrium was unlikely for the cohort ( $p < 0.012$ ) seemingly associated with death prior to genotype sampling. In several tests of robustness this did not seem to invalidate primary results.

## CONCLUSIONS

Compared to the common genotype *UGT1A1*\*28 genotypes were associated with an increased need of oxygen supplementation and risk of BPD in very preterm newborns.

**Table 1 (ABS 33).** The association between *UGT1A1*\*28 genotypes and respiratory morbidity for 1,354 very preterm infants.

	Surfactant treatment OR <sup>a</sup>	Any need of oxygen OR <sup>a</sup>	Cessation of supplementary oxygen HR <sup>a</sup>	Duration of oxygen treatment Difference days	BPD <sup>b</sup> OR <sup>a</sup>
Common genotype	Ref	Ref	Ref	Ref	Ref
<i>UGT1A1</i> *28 heterozygous	1.08 (0.91-1.28)	1.25 (1.05-1.50)	0.84 (0.76-0.93)	6.38 (1.87-10.89)	1.71 (1.23-2.39)
<i>UGT1A1</i> *28 homozygous	1.17 (0.83-1.64)	1.57 (1.10-2.24)	0.71 (0.58-0.87)	12.75 (3.73-21.78)	2.93 (1.51-5.70)

Odds Ratios (OR) are estimated by conditional logistic regression, Hazard Rates (HR) by Cox regression and numeric difference in days with oxygen by generalized linear methods with pseudo values. 95 % confidence intervals (CI).

<sup>a</sup>Adjusted for sex, birth year and African race; <sup>b</sup>bronchopulmonary dysplasia defined as need of supplemental oxygen at 36 weeks post menstrual age.