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EuroHOPE Very Low Birth Weight (VLBW) & Very Low Gestational Age (VLGA) Infants: Material, Methods and Indicators

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Table of Contents

Introduction and objectives

The main aim of the EuroHOPE very low birth weight (VLBW) and very low gestational age (VLGA) infants project is to compare performance in the care of very low birth weight and very preterm infants between countries from birth through one year of follow-up in cohorts ranging over three years of study. This comparison is made for various purposes. We will implement European-wide benchmarking of outcomes and quality. This will enable decision-makers and health professionals to learn from the best practices. We will investigate the relationship between outcomes/quality and costs/resources between European countries and selected providers (based on numerosity of cases), applying a multilevel approach. Finally, we will explore reasons behind the differences in outcomes and use of resources.

This paper defines specific protocols for international comparisons that are based on the data of medical birth registrers (MBR), hospital discharge registers (HDR), mortality registers, and other available registers (use of outpatient services in specialist care or medical emergency registers etc.). The protocol has been used in preparing both **national VLBW and VLGA infant databases for each country and for a limited international comparative VLBW and VLGA infant database** which was produced from the national VLBW and VLGA infant databases from several countries and was used for risk analysis. The comparative databases has been used for basic reporting on care of VLBW and VLGA infants, and for research on reasons behind differences in performance.

This protocol defines how we have produced indicators at national levels. The basic report includes basic information on patients (number of very preterm and very low weight infants born, gestational age and weigth distribution, co-morbidity), indicators on content of care (use of services and procedures, costs, treatment practices, process indicators), and indicators of outcomes. The current discussion paper belongs to the VLBW and VLGA infants subproject of the EuroHOPE project. The following institutions in the seven countries participate in the VLBW and VLGA infants subproject: National Institute for Health and Welfare (Helsinki, Finland); Centre for Research on Health and Social Care Management, Università Commerciale Luigi Bocconi (Milan, Italy); Semmelweis University, Health Services Management Training Centre (Budapest, Hungary); National Institute of Public Health and the Environment (Bilthoven, the Netherlands); Ragnar Frisch Centre for Economic Research (Oslo, Norway); University of Edinburgh (Scotland, UK); Medical Management Centre, LIME, Karolinska Institutet (Stockholm, Sweden) ; Department of Health Management and Health Economics, Institute of Health and Society, University of Oslo(Oslo, Norway).

This paper is a joint work established (in alphabetical order) by Helen Banks, Giovanni Fattore, Eilidh Fletcher, Unto Häkkinen, Amber van der Heijden, Richard Heijink, Tor Iversen, Søren Toksvig Klitkou, Péter Mihalicza, Dino Numerato, Mikko Peltola, Timo T. Seppälä, Sofia Sveréus, Fabrizio Tediosi, and Rinaldo Zanini

Definition of VLBW and VLGA infants

Infants born with a weight under or equal to 1500 g or below 32 weeks of gestational age (GA), as specified in the respective national MBR.

National Databases

Each country in the EuroHOPE project has established a national VLBW and VLGA infant database. From medical birth registers (MBR) very low birth weight and very preterm live-born infants weighing 1500 g or below and at less than 32 weeks GA were included.

At present each database includes very low birth weight and very preterm infants born during the years 2006, 2007 and 2008 for Finland, Hungary, Italy,Scotland and Sweden; during the years 2005, 2006 and 2007 for the Netherlands; and during the years 2008 and 2009 for Norway. The databases were constructed by combining patient level data from each country's national registers.

Using personal identification numbers, patient information from the following registers was linked:

- Medical birth registers (MBR)
- Registers of congenital malformations (when the information is not included in the MBR)
- Hospital discharge registers (HDR)
- Outpatient services in specialist care / hospitals
- Emergency services registers
- National mortality registers

International database used for calculating indicators

Data restrictions

Infants born weighing less than or equal to 1500 g and/or below 32 weeks GA between 2006 and 2008 were included. In the Netherlands and Norway the data for these cohorts were not available, and the following cohorts were therefore used: 2005-2007 in the Netherlands and 2008-2009 in Norway.

Infants with at least one of the following conditions were excluded:

- major disparity between birth weight and GA (LGA or SGA) or missing data on either one of these variables (please see Appendix 1 for the definition of the disparities)
- missing data on the initial hospitalisation period or with incomplete MBR data, which would prevent a comparative analysis (see exceptions for Hungary, Norway and Sweden below)
- an incomplete personal identification number (this can also be an incomplete social security number) or other information, which would prevent data linkage
- lethal congenital malformations as defined in Appendix 1
- less than 22 weeks GA or more than 39 weeks GA
- in each country, the infants with a length of stay (LoS) of the continuous hospital treatment longer than the 99th percentile in that country
- stillborn infants

The main analysis was carried out by using the data collected from medical birth registers and national discharge registers. The specific information regarding registers in each country is provided in Appendix 2. Appendix 3 describes the definitions that have been used in preparing and analysing the data.

Definition of a hospital

A hospital is a health care institution providing treatment by specialized staff and equipment for a number of medical conditions. In EuroHOPE, we speak of hospitals meaning institutions providing somatic (non-psychiatric) inpatient care for patients staying overnight (for at least one night, "inpatients"), and very often also health care services (for diagnosis, treatment, or therapy) for patients without staying overnight ("outpatients"). A hospital may be a single building or a number of buildings on a campus. Also, in some countries a hospital can consist on many buildings in a certain geographical area. For example, in Finland after reorganization of the Helsinki University Hospitalin 2006, it refers to several buildings in the municipalities of the capital area.

Definition of the first hospital episode

The total episode of care was defined as the entire treatment pathway from the day of birth to the end of treatment throughout any hospital admissions, other health service provisions or purchased medication in order to treat the health problem at hand in a specified time frame of 365 days (Figure 1).

First hospital episode: hospital inpatient treatment beginning on the day of birth, also including possible discharges to another hospital, and terminating on the first discharge to home, one year of continuous inpatient care, or death (Figure 1). If the patient is transferred to an inpatient rehabilitation center this is included in the first hospital episode (Häkkinen and Peltola 2013).

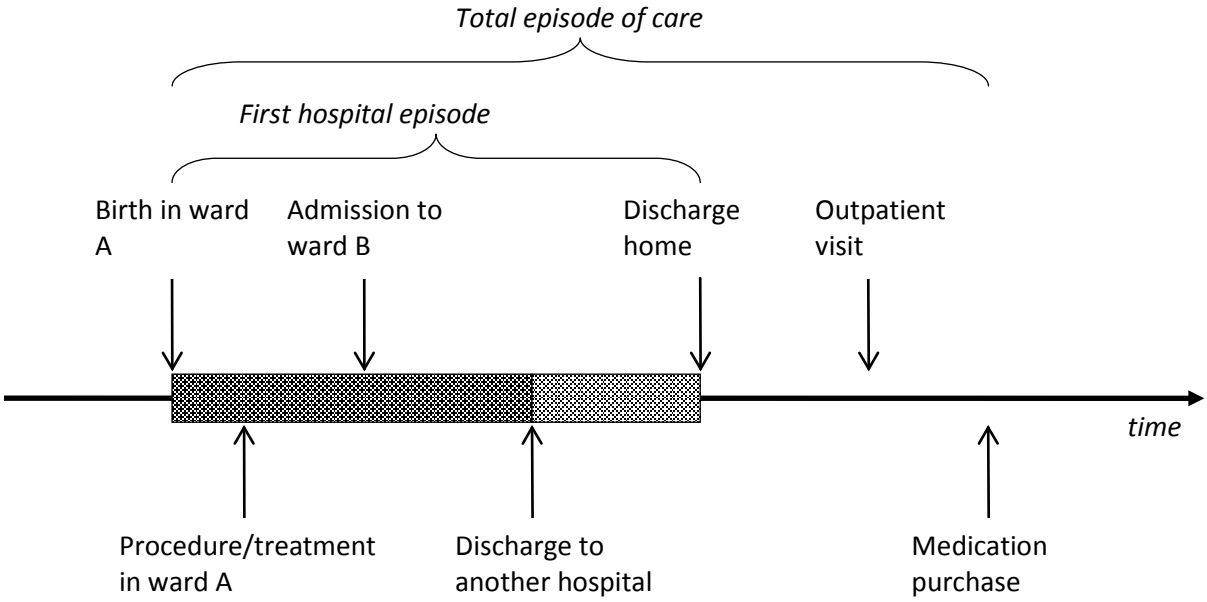

Figure 1. A schematic presentation of the follow-up of patients throughout the treatment pathway demonstrating the definitions of first hospital episode and the total episode of care.

Description of indicators

Baseline indicators of infants:

- gestational age
- weight
- gender
- apgar (measures used in different countries vary: either apgar at 5 or apgar at 10 minutes is used)

Process indicators:

- LoS of the first hospital admission, days per infant at three different levels of care as defined by the American Academy of Pediatrics (2012)
  - Level III NICU
  - Level II Specialty Care Nurseries
  - Level I Units
- LoS of first hospital episode, days per infant
- Transfers and back-transfers during the first hospital admission[1]
- Total inpatient days per patient over the first year after birth
- Number and share of patients with a LoS of the first hospital episode of 90 days or more
- Number and share of patients that received catheterization during the first hospital episode

[1] Transfers are defined as transfers from level I or level II hospitals to level III hospitals; back-transfers are defined as transfers from Level III hospital to level I or level II hospitals

- Number and share of patients that received ventilation during the first hospital episode
- Number and share of patients that received continuous positive airway pressure during the first hospital episode

Outcome indicators:

- Mortality at 1, 7, 30 and 365 days from the day of birth
- Morbidities at birth or during the first hospital episode:
    - Respiratory distress syndrome
    - Neonatal jaundice
    - Anemia of prematurity
    - Persisting ductus arteriosus
    - Other respiratory problems after birth
    - Bronchopulmonary dysplasia
    - Intraventricular hemorrhage
    - Retinopathy of prematurity
    - Necrotizing enterocolitis

Risk adjustment

One of the challenges when comparing health outcomes between countries is to adjust for differences among infants. This is further complicated by the fact that detailed information on the infants may not be available, or that variables can be very differently defined across countries. In order to define comparable performance indicators, the indicators have to be adjusted for confounding factors. EuroHOPE aims to solve this problem by using register data available for everyone with a specified health problem, which contains detailed information on variables with an effect on health outcomes.

Standardization of variables

The first question was how to determine appropriate gestational age and related small and large for gestational age variables. Although there are apparent differences in fetal growth across countries (e.g. Bertino, 2010), its potential to confound the results decreases with increasing rates of infants born to parents who are not nationals of the countries where the infants are born. To deal with the issue of international differences in fetal growth charts, the international standardized average fetal growth tables were considered to calculate appropriateness for gestational age (Fenton et al, 2013). Considering a lack of information on length and/or head circumference in some of the EuroHOPE countries (Hungary, the Netherlands), only infants' weight was used for comparative purporses to calculate the appropriateness for gestational age. Fenton's calculator is available online[2] separately for boys and girls.

In addition, hospitals were classified in each country according to the levels of neonatal care provided, as defined by the American Academy of Pediatrics (AAP), The AAP classifies levels of neonatal care as follows: level III hospitals are equipped with a neonatal intensive care unit, with personnel and equipment sufficient to provide continuous care and life support for as long as needed for infants <32 weeks GA and <1500 g at birth and/or with critical illness; a level II hospital posssesses a specialty care nursery and can provide care to infants

[2] http://www.ucalgary.ca/fenton/2013chart

who are moderately ill with problems that are expected to resolve rapidly, for infants >=32 weeks GA and >=1500 g; level I hospitals have well newborn nurseries and can provide basic levels of newborn care (AAP, 2012). A fourth level was introduced with the 2012 guidelines to denote hospitals in possession of pediatric surgical subspecialties, but was not used in this study.

The ability to compare between countries necessitated a trade-off in terms of limited risk adjustment methods. In particular, the availability of important factors (e.g. information on maternal smoking) to be included in the risk adjustment model varied across countries.

For each outcome, three different risk adjusted outputs are produced: 1. adjusted for sex and age only, 2. adjusted for sex, age, disease specific co-morbidities based on primary and secondary diagnosis, and 3. identical to 2 except co-morbidities are based on both primary and secondary diagnosis and medication purchase. **For detailed descriptions, see Appendix 4.**

Based on the experiences in the PERFECT project (Peltola *et al.*, 2011), the observed/expected approach described in Ash *et al.* (2003) was used, which roughly corresponds to indirect standardization. Specifically, the method uses regression modelling for the risk adjustment. For mortality outcomes up to one year, logistic regression was used, while for the LOS outcomes negative binomial regression was used. The method is described in more detail in Moger and Peltola, 2014.

Case-mix standardisation was used when comparing countries, hospitals and eventually regions. Variables which are considered potential prognostic factors (and thus confounders) were used for adjustment. These were derived from medical birth registers. The following were used:

- gestational age (in weeks)
- gender
- SGA/LGA (small or large for gestational age): calculated on the basis of internationally standardized average fetal growths (e.g. Fenton et al. 2013)
- mode of delivery
- type of delivery
- presence of malformations (narrow and broad definitions were used in two different risk adjustment models)

Levels of analysis

Indicators were produced at the national and - within some selected countries also - at the regional level. Regional information was based on patients' place of residence. The definitions for regions were determined in each country according to classifications from the Organisation for Economic Co-Operation and Development (OECD) and national statistical institutions . The per-capita GDP, unemployment rates, population and population density figures were determined for each of the defined regions and for each nation as a whole.

Remarks on interpretation of indicators

The most important caveats related to differences in coding practices, availability of data and differences in classifications are discussed below. In particular three main issues were addressed.

First, the issue of linkage between medical birth registers and other hospital discharge registers affected the EuroHOPE project similarly to previous studies (e.g. Pezzotti et al. 2009). The problem appeared to be due to underdeveloped systems of identification number (ID) attribution. Whereas the majority of countries were able to employ deterministic linkage based on a unique ID for each infant; however, Hungary, had to use stochastic linkage methodologies to combine the medical birth register and the hospital discharge register for the infant, as well as a hospital discharge register related to mothers where there was no clear, unique ID for the infant. The experiences from different countries demonstrate that deterministic linkage can have particular limits in case of multiple births, especially in the Netherlands, but also in Italy. A duplication of the collected information in medical birth registers and hospital discharge registers might have further affected the analysis. VLBW and VLGA infants in the Hungary dataset were identified by means of the Tauffer statistics that include 96-100% of all newborn infants.

The possibility to link the HDR with MBR was substantially limited in Sweden and Norway. As a consequence, for some infants it was not possible to follow their treatment during the first year (linkage rates for follow-up care for Sweden and Norway were 58% and 65%, respectively). A more detailed analysis suggested that the problems with linkage in the analysed sample of infants led to a comparatively healthier cohort in comparison to general VLBW and VLGA infant population. Therefore the decision was made to include the entire population of infants from the MBR and the mortality registers for the mortality analysis and the more limited, linkable database gleaned from the MBRs and HDRs for the LoS analyses.

Second, different coding systems limited the comparative potential of the EuroHOPE study: for example, coding practices differed across countries in terms of how procedures and diagnoses were defined and under what system, as well as the number of diagnoses and procedures reported in MBRs and/or HDRs.

Third, the absence of a classification system (using, or similar to, the AAP definitions) for the level of neonatal care provided by the hospitals resulted in only an approximate definition of these levels in several countries.

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Appendix 1: List of Lethal Congenital Malformations as Criterion of Exclusion

Malformation	ICD-9-CM	ICD-10
Anencephaly/Acrania	740.0	Q00.0
Transposition of great vessels	745.15	Q20.1
Hypoplastic left heart syndrome:	746.7	Q23.4
Renal agenesis and dysgenesis	753.0	Q60.2
Anomalies of diaphragm: Absence of diaphragm, Congenital hernia: diaphragmatic, foramen of Morgagni, Eventration of diaphragm	756.6	Q79.0, Q79.1,
Patau's syndrome	758.1	Q91.7
Edward's syndrome	758.2	Q91.3

Exclusion Criteria for Large Disparities between Birth Weight and Gestational Age

In reference to the exclusion criteria described in the data section above, the following definitions were applied to exclude those records exhibiting large disparities between gestational age and birth weight. This was done to correct for likely errors in the data from the hospital registers. The exclusions were applied as follows (based on the definition employed in a number of studies conducted by the Performance, Effectiveness, and Cost of Treatment Episodes (PERFECT) Preterm Infant Study Group in Finland (Korvenranta et al. 2009, Lehtonen et al. 2011)):

birth weight greater than **3600** grams
or (birth weight greater than **900** and gestational age **22** weeks)
or (birth weight greater than **1000** and gestational age **23** weeks)
or (birth weight greater than **1150** and gestational age **24** weeks)
or (birth weight greater than **1200** and gestational age **25** weeks)
or (birth weight greater than **1500** and gestational age **26** weeks)
or (birth weight greater than **1800** and gestational age **27** weeks)
or (birth weight greater than **2300** and gestational age **28** weeks)
or (birth weight greater than **2700** and gestational age **29** weeks)
or (birth weight greater than **2800** and gestational age **30** weeks)
or (birth weight greater than **3000** and gestational age **31** weeks)
or (birth weight greater than **3500** and gestational age **32** weeks)
or (birth weight less than **500** and gestational age **35** weeks)
or (birth weight less than **700** and gestational age **36** weeks)
or (birth weight less than **800** and gestational age **37** weeks)
or (birth weight less than **900** and gestational age **38** weeks)
or (birth weight less than **1000** and gestational age **39** weeks)
or (ga greater than **39** weeks**)**
or (ga less than **22** weeks and ga ne **.**)
or (both gestational age and birth weight missing

Appendix 2. Particular characteristics of national registers and databases

Medical birth register

Finland	from 1987
Hungary	from 2000
Italy, province of Rome	from 2001
the Netherlands	NPR (combination of three registers), linkable 2004-2007
Scotland	from 1974
Sweden	from 1973
Norway	from 1967

Register of congenital malformations

Finland	1963
Hungary	included in the MBR
Italy, province of Rome	included in the MBR
the Netherlands	NPR (combination of three registers), since 2001
Scotland	from the 1980s
Sweden	included in the MBR
Norway	included in the MBR

Hospital discharge register for inpatient care

Finland	1967
Hungary	1997
Italy, province of Rome	since 1997
the Netherlands	linkable since 1995
Scotland	from 1975
Sweden	from 1987/private from 2001
Norway	linkable since January 2008

Outpatient care register

Finland	2000, data on diagnosis is not complete
Hungary	2004-
Italy, province of Rome	since 2000
the Netherlands	not available
Scotland	from 1997
Sweden	from 2001
Norway	linkable since January 2008

Cause of death register

Finland	2000-
Hungary	1997
1Italy, province of Rome	from 1987
the Netherlands	from 1995, linking is questionable
Scotland	from 1974
Sweden	from 1961
Norway	from 1951

Appendix 3. Variable definitions

Variable(s)	Type	Definition	Classes/Coding
GENERAL INFORMATION			
ID	Char	Newborn ID	
C	Char	Country ID	FIN=Finland, SWE=Sweden, SCO=Scotland, HUN=Hungary, ITA=Italy, NOR=Norway, NL=Netherlands
MALE	Num	Male	1/0; missing, if unknown
DIST	Char	Area (e.g. hospital district) of the patient	*See sheet DIST* (missing, if unknown)
MUNI	Char	Municipality/Postal area of the patient	*See sheet DIST* (missing, if unknown)
GESTAGE_M	Num	Gestational Age	In weeks
GESTAGE_D	Num	Gestational Age in days specifying the number of weeks if available	In days 0-6 if available, missing if unknown
WEIGHT	Num	Birth Weight	in grams
LENGTH	Num	Length	in cm
CIRC	Num	Skull circumference	in cm
INFORMATION OF THE BIRTH, INDEX EVENT/BIRTH ("FST") / FIRST HOSPITAL EPISODE ("HEP")			
YEAR	Num	Year of birth	Yyyy
DBIRTH	Char	Day of birth	dd/mm/yyyy
FSTDIAG	Char	Main Diagnosis at birth	ICD-9/ICD-10 coding, w/o special marks (e.g. dots), missing if not indicated
SECDIAG1	Char	Secondary Diagnosis at birth – 1	ICD-9/ICD-10 coding, w/o special marks (e.g. dots), missing if not indicated
SECDIAG2	Char	Secondary Diagnosis at birth – 2	ICD-9/ICD-10 coding, w/o special marks (e.g. dots), missing if not indicated
SECDIAG3	Char	Secondary Diagnosis at birth – 3	ICD-9/ICD-10 coding, w/o special marks (e.g. dots), missing if not indicated
SECDIAG4	Char	Secondary Diagnosis at birth – 4	ICD-9/ICD-10 coding, w/o special marks (e.g. dots), missing if not indicated
SECDIAG5	Char	Secondary Diagnosis at birth – 5	ICD-9/ICD-10 coding, w/o special marks (e.g. dots), missing if not indicated
SECDIAG6	Char	Secondary Diagnosis at birth – 6	ICD-9/ICD-10 coding, w/o special marks (e.g. dots), missing if not indicated
SECDIAG7	Char	Secondary Diagnosis at birth – 7	ICD-9/ICD-10 coding, w/o special marks (e.g. dots), missing if not indicated
SECDIAG8	Char	Secondary Diagnosis at birth – 8	ICD-9/ICD-10 coding, w/o special marks (e.g. dots), missing if not indicated
SECDIAG9	Char	Secondary Diagnosis at birth – 9	ICD-9/ICD-10 coding, w/o special marks (e.g. dots), missing if not indicated
SECDIAG10	Char	Secondary Diagnosis at birth – 10	ICD-9/ICD-10 coding, w/o special marks (e.g. dots), missing if not indicated
MALFRM1	Char	Congenital Malformations at birth (ICD-9: 740–759; ICD-10: Q00–Q89, may be included in specific malformation registers)	ICD-9/ICD-10 coding, w/o special marks (e.g. dots), missing if not indicated
MALFRM2	Char	Congenital Malformations at birth (ICD-9: 740–759; ICD-10: Q00–Q89, may be included in specific malformation registers)	ICD-9/ICD-10 coding, w/o special marks (e.g. dots), missing if not indicated
MALFRM3	Char	Congenital Malformations at birth (ICD-9: 740–759; ICD-10: Q00–Q89, may be included in specific malformation registers)	ICD-9/ICD-10 coding, w/o special marks (e.g. dots), missing if not indicated
FSTLOS	Num	Length of the index admission By definition: (discharge day of index admission - day of birth) + 1	in days
FSTHOSP	Char	ID of the index admission hospital	
HEPLOS	Num	Length of the first hospital episode By definition: (discharge day of first hospital episode - day of birth) + 1 Note: An admission starting the same or the next day the previous admission ended is considered to belong to the same hospital episode	in days
HEPADM	Num	Sum of hospital admissions within the first hospital episode (excluding the index admission)	
HEPHOSP	Char	ID of the hospital in charge during the first hospital episode	
HEPFUTR	Char	Follow-up treatment: where did the patient go to when the first hospital episode ended.	**0:** Home **1:** Institution (other than hospital), for example outpatient visit. **2:** Dead Missing, if unknown

Variable(s)	Type	Definition	Classes/Coding
INFORMATION ON DELIVERY			
APGAR5	Num	Apgar at 5 minutes after birth	missing if uknown
APGAR10	Num	Apgar at 10 minutes after birth	missing if uknown
RESUSC	Num	Resuscitation	1/0; missing, if unknown
TYPEDEL	Num	Number of born infants	missing, if unknown
HOURDEL	Num	Hour of delivery	HH (from 00-23)
FRSTORDR	Num	Order in case of multiple births	missing, if unknown
SPNTDEL	Num	Spontaneous delivery	1/0; missing, if unknown
ELECTCES	Num	Elective Caesarean section	1/0; missing, if unknown
EMGCES	Num	Emergency Caesarean section	1/0; missing, if unknown
INFORMATION ON MOTHER			
MDBIRTH	Char	Day of birth	dd/mm/yyyy
MNATION	Num	Mother's nationality	**1**: Country's nationality (e.g. Italian for Italian data), **2**: Foreign Nationality
PRECONC	Num	Number of previous conceptions	missing, if unknown
PREALIVE	Num	Previous born alive	missing, if unknown
PRECES	Num	Previous cesarean section	1/0; missing, if unknown
FSTDEL	Num	Mother's first delivery	1/0; missing, if unknown
MORTALITY			*All variables get a missing value, if patient alive in the end of follow-up*
DTIME	Num	Time to death Define: (date of death - date of birth) + 1	in days
DCAUSE1	Char	Cause of death	ICD-9/ICD-10 coding
DCAUSE2	Char	Cause of death	ICD-9/ICD-10 coding
DCAUSE3	Char	Cause of death	ICD-9/ICD-10 coding
DCAUSE4	Char	Cause of death	ICD-9/ICD-10 coding
DCAUSE5	Char	Cause of death	ICD-9/ICD-10 coding
DCAUSE6	Char	Cause of death	ICD-9/ICD-10 coding
TREATMENT			
STATE1-STATE365	Char	infant's state during first, second, etc. day of the first year of follow-up –	**0:** Home
		In case of overlapping admissions, the STATE variable is marked with the hospital	**1*:** Hospital/outpatient visit (see sheet Hospital hierarchy)
		being in the highest step of *hospital hierarchy* (defined by each country). The variable	**2:** Dead
		will be composed of 5 digits. The first digit 0, 1, 2 (home, hospital/outpatient, dead) is	**2***: Died in hospital
		defined in this sheet , further four digits in the *hospital hierachy* sheet	

	Variable(s)	Type	Definition	Classes/Coding
PROCEDURES				
	T***OPE***	Num	Time between day of birth and 'OPE' operation/procedure - Define: day of operation/procedure - day of birth - If operation/procedure day is missing, define: admission day of the operation admission - day of birth - See classes of 'OPE' below	In days; missing, if no operation has been done
	N***OPE***	Num	Operation date NOT registered	1/0 (1, if operation date NOT registered); missing, if no operation done
	OPE			
	ACT		Time between day of birth and Arterial Catheterization	
	UVC		Time between day of birth and Umbilical Vein Catheterization	
	VCT		Time between day of birth and Venous Catheterization	
	UHN		Time between day of birth and Diagnostic Ultrasound Of Head And Neck	
	UHR		Time between day of birth and Diagnostic Ultrasound Of Heart	
	CPA		Time between day of birth and Continuous Positive Airway Pressure	
	ETT		Time between day of birth and Insertion Of Endotracheal Tube	
	IVU		Time between day of birth and Continuous Invasive Mechanical Ventilation Of Unspecified Duration	
	IVS		Time between day of birth and Continuous Invasive Mechanical Ventilation For Less Than 96 Consecutive Hours	
	IVL		Time between day of birth and Continuous Invasive Mechanical Ventilation For 96 Consecutive Hours Or More	
	NVS		Time between day of birth and Non-Invasive Mechanical Ventilation For Less Than 96 Consecutive Hours	
	PIN		Time between day of birth and Parenteral Infusion Of Concentrated Nutritional Substances	
	RIH		Time between day of birth and Other And Open Repair Of Indirect Inguinal Hernia	
	BRH		Time between day of birth and Open And Other Bilateral Repair Of Indirect Inguinal Hernia	
	CPR		Time between day of birth and Cardiopulmonary Resuscitation	
	TAC		Time between day of birth and Computerized Axial Tomography Of Bead	
	RMN		Time between day of birth and Magnetic resonance imaging of brain and brain stem	
MEDICATION				
	TCSTDRG	Num	Total cost of drug consumption in 365 days after the birth	In Euros, missing, if no previous medication purchases

Variable(s)	Type	Definition	Classes/Coding
DIAGNOSIS			
T*DIAG*	Num	Time of the first 'DIAG' diagnosis Define: first 'DIAG' diagnosis - day of birth - see classes of 'DIAG' below - include both the main and secondary diagnoses - follow-up at least 365 days after the day of birth	In days; missing, if such 'DIAG' diagnose is not included
DIAG			
RDS		Time between day of birth and Respiratory distress syndrome	
NJD		Time between day of birth and Neonatal jaundice	
ANP		Time between day of birth and Anemia of prematurity	
PDA		Time between day of birth and Persisting ductus arteriosus	
ORS		Time between day of birth and Other respiratory problems after birth	
BPD		Time between day of birth and Bronchopulmonary dysplasia	
IVH		Time between day of birth and Intraventricular hemorrhage	
ROP		Time between day of birth and Retinopathy of prematurity	
NEC		Time between day of birth and Necrotizing enterocolitis	
TREATMENT COSTS			
FSTCOST		Total costs (according to information available) of the first length of stay	€, missing if uknown
HEPCOST		Total costs (according to information available) of the first hospital episode	€, missing if uknown
TCST365		Total costs (according to information available) during the first year after the day of birth	€, missing if uknown

Hospital hierarchy used when defining the highest level hospital the patienthas been treated in during the first hospital episode

Hospital hierarchy used in STATE-variables

Ward Speciality/Level (2nd digit)

	Long name	***AAP definition applied available at: http://pediatrics.aappublications.org/content/114/5/1341.full***
X1XX	Level III NICU	continuously available personnel and equipment to provide life support for as long as needed
X2XX	Level II Specialty Care Nurseries	provide care to infants who are moderately ill with problems that are expected to resolve rapidly
X3XX	Level I Units	well-newborn nurseries, basic level of newborn care
X9XX	Outpatient visit	

Hospital Level (3nd digit)	**Hospital/institution hierarchy**
XX1X	Pediatric hospital
XX2X	University hospital
XX3X	Central or regional hospital
XX4X	General or local hospital
XX9X	Outpatient visit

If applicable a distinction between public and private hospital should be made (4th digit)

XXX1	Public hospital
XXX2	Private hospital
XXX9	Outpatient visit

If applicable neuropsychiatry and rehabilitation ward should be specified (5th digit)

XXXX1	*neuropsychiatry ward*
XXXX2	*rehabilitation ward*
XXXX8	*Other ward*
XXXX9	*Outpatient visit*

Variable(s)	Definition	Classes/Coding	
OPE	**Procedure**	**Source**	**Codes (ICD-9-CM)**
ACT	Arterial Catheterization	MBR-HDR-EMERG-EMERG	38.91
UVC	Umbilical Vein Catheterization	MBR-HDR-EMERG-EMERG	38.92
VCT	Venous Catheterization	MBR-HDR-EMERG-EMERG	38.93
UHN	Diagnostic Ultrasound Of Head And Neck	MBR-HDR-EMERG-EMERG	88.71
UHR	Diagnostic Ultrasound Of Heart	MBR-HDR-EMERG-EMERG	88.72
CPA	Continuous Positive Airway Pressure	MBR-HDR-EMERG-EMERG	93.90
ETT	Insertion Of Endotracheal Tube	MBR-HDR-EMERG-EMERG	96.04
IVU	Continuous Invasive Mechanical Ventilation Of Unspecified Duration	MBR-HDR-EMERG-EMERG	96.70
IVS	Continuous Invasive Mechanical Ventilation For Less Than 96 Consecutive Hours	MBR-HDR-EMERG-EMERG	96.71
IVL	Continuous Invasive Mechanical Ventilation For 96 Consecutive Hours Or More	MBR-HDR-EMERG-EMERG	96.72
NVS	Non-Invasive Mechanical Ventilation For Less Than 96 Consecutive Hours	MBR-HDR-EMERG-EMERG	96.81
PIN	Parenteral Infusion Of Concentrated Nutritional Substances	MBR-HDR-EMERG-EMERG	99.15
RIH	Other And Open Repair Of Indirect Inguinal Hernia	MBR-HDR-EMERG-EMERG	53.02
BRH	Open And Other Bilateral Repair Of Indirect Inguinal Hernia	MBR-HDR-EMERG-EMERG	53.12
CPR	Cardiopulmonary Resuscitation	MBR-HDR-EMERG-EMERG	99.60
TAC	Computerized Axial Tomography Of Bead	MBR-HDR-EMERG-EMERG	87.03
RMN	Magnetic resonance imaging of brain and brain stem	MBR-HDR-EMERG-EMERG	88.91
DIA	**DIAGNOSIS**	**Codes (ICD-9-CM)**	**Codes (ICD-10)**
RDS	Respiratory distress syndrome	769.X	P22
NJD	Neonatal jaundice	774.X	P59
ANP	Anemia of prematurità	776.6	P61.2
PDA	Persisting ductus arteriosus	747.0	Q25.0
ORS	Other respiratory problems after birth	770.8	P22.8, P22.9, P28.2-P28.5, P28.8
BPD	Bronchopulmonary dysplasia	770.7	P27
IVH	Intraventricular hemorrhage	772.1	P52
ROP	Retinopathy of prematurity	362.2	H35.1
NEC	Necrotizing enterocolitis	777.5	P77

Appendix 4. Instructions for adjustment for confounding factors (which apply for between and within country comparisons).

The point estimates and confidence intervals for incidence, process variables and treatment outcomes are produced as follows:

1. **Unadjusted data**
    - Gestational Age
    - Gender
    - Weight
    - Proportions treated at different levels of hospitals according to AAP definition
    - transfers and backtransfers

2. **Data adjusted for gestational age and gender**

    a. Length of stay at hospital: first admission, hospital episode, total length of stay during one year after birth
    b. All cause mortality at 7, 30, 90 and 365 days after birth

3. **Adjusted for gestational age (classified, gestational age of 30 as the reference gestational age), gender, apgar5 score, multiple births, and first delivery**

    a. Length of stay at hospital: first admission, hospital episode, total length of stay during one year after birth
    b. All cause mortality at 7, 30, 90 and 365 days after birth

4. **Adjusted for gestational age, gender, apgar5 score, small for gestational age, maternal age (classified, 20-24 as the reference group)**

    a. Length of stay at hospital: first admission, hospital episode, total length of stay during one year after birth
    b. All cause mortality at 7, 30, 90 and 365 days after birth

5. **Adjusted for gestational age (gestational age of 30 as the reference gestational age), gender, sga, apgar5, multiple births, and fstdel**

    a. Length of stay at hospital: first admission, hospital episode, total length of stay during one year after birth
    b. All cause mortality at 7, 30, 90 and 365 days after birth