Annual Report 2014

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Malformation Monitoring Centre Saxony-Anhalt

Medical Faculty

Otto-von-Guericke-University Magdeburg

SACHSEN-ANHALT
Ministerium für Arbeit und Soziales

Annual Report 2014
of the Federal State of Saxony-Anhalt
about the frequency of congenital malformations
and anomalies as well as chromosomal aberrations

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Introduction

Dear reader,

The early Romanticism poet Novalis who was born in Oberwiederstedt near Hettstett once said: "Children are hope." I totally agree with this sentence and would like to add: “So that they stay hope and so that the hope comes true, we as adults have to act responsibly. We have to protect our children, prevent them from harm and take care of them when they are ill.” Health care is a very important topic in this connection - and the Malformation Monitoring Centre Saxony-Anhalt forms an important part of this.

A congenital malformation does not only affect the child and its family. It also takes effects on the whole community, as the community has to bear the medical costs and has to create an adequate environment. Congenital malformations appear frequently. They often require an expensive medical treatment and therefore pose a challenge for the public health sector.

A malformation appears in one out of 33 children. Additionally, malformations are the most frequent reason of infant mortality. Infants which survive have, apart from the often severe impairment, an increased risk for a permanent development disorder.

Why do malformations appear during the development of a baby? This question does not only bother concerned parents. It also gives a lot of medical scientists from different medical fields a reason for their daily work. Determining the reason for a malformation makes it possible to find treatment options. The Monitoring of Congenital Malformations makes an important contribution on this.

In this year the current report of the Monitoring of Congenital Malformation deals with the main topic of distribution, reasons and consequences of congenital anomalies of the urinary tract, which are called hypospadias. Its prevalence, which means the relative frequency of cases that appear at a certain point of time, underlies according to current studies big geographical fluctuations.

Latest studies report increasing as well as decreasing temporary trends. The aim of the Monitoring of Congenital Malformations is to analyze prevalence and trends of hypospadias in Saxony-Anhalt and to evaluate the figure in the European comparison. A hypospadias develops during early pregnancy and in the most cases it is a genetically caused disease. When development disorders appear during the first trimester of pregnancy which is the time when the urinary tract is formed, a hypospadias may appear later. However, the exact mechanisms of malformation development are unknown until know. The Monitoring of Congenital Malformations included all cases of hypospadias which occurred from 1995 until 2014 in Saxony-Anhalt in its current analysis.

I would like to thank all participants and the team of authors under guidance of Dr. med Anke Rißmann, but also all our partners at the maternity clinics of the Federal State. The Monitoring of Congenital Malformations makes an important contribution to a healthy growing up of our children.

Your sincerely

Norbert Bischoff
Federal Minister of Labour and Social Affairs
Saxony-Anhalt

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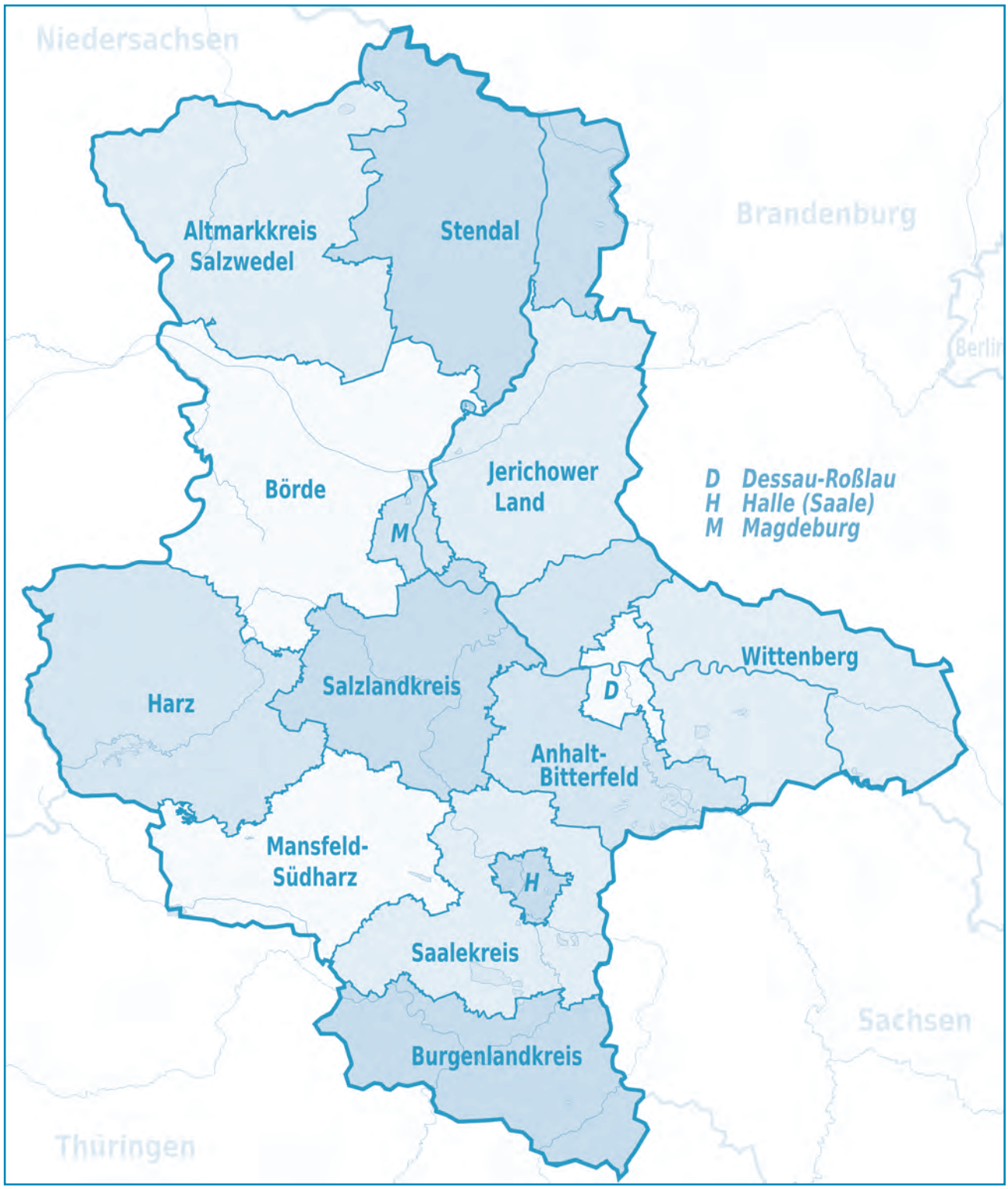
Abbreviations

AABR	automated auditory brainstem response (Hirnstammaudiometrie)
ASD	atrial septal defect
blt.	bilateral
BMI	Body-Mass-Index
BP	basis prevalence
CI	confidence interval
CNS	central nervous system
dB	dezibel
DD	differential diagnosis
DIV	double inlet ventricle
DORV	double outlet right ventricle
ENT	ears, nose, throat
EUROCAT	European Surveillance of Congenital Anomalies
FAS	Fetal alcohol syndrome
FASD	Fetal alcohol spectrum disorder
G-BA	Federal Joint Committee (Gemeinsamer Bundesausschuss
ICBDSR	International Clearinghouse for Birth Defects Surveillance and Research
ICSI	intracytoplasmatic sperm injection
LB	live births
MCA	multiple congenital anomalies
NHS	newborn hearing screening
n.o.s..	not otherwise specified
n.s.	not specified
NT	nuchal translucency
OR	Odds Ratio (Quotenverhältnis)
P	prevalence
PDA	persistent ductus arteriosus
PFO	persistent foramen ovale
SA	spontaneous abortion
SB	stillbirths
TEOAE	transistory evoked otoacoustic emissions
TOP	termination of pregnancy
VSD	ventricular septal defect
WOG	weeks of gestation

Figures

1 Saxony-Anhalt - Registration Area



2 Birth Rate 2014

	Live births*	Stillbirths*	Spontaneous Abortions (> 16 WOG)	Termination of Pregnancy for fetal anomaly following prenatal diagnosis	Total
Altmarkkreis Salzwedel	724	4	-	4	**732**
Anhalt-Bitterfeld	1,167	5	2	5	**1,179**
Börde	1,315	2	5	5	**1,327**
Burgenlandkreis	1,313	6	-	-	**1,319**
Dessau-Roßlau	558	2	-	1	**561**
Halle	2,179	8	3	11	**2,201**
Harz	1,555	7	-	6	**1,568**
Jerichower Land	666	4	1	3	**674**
Magdeburg	2,125	6	10	18	**2,159**
Mansfeld-Südharz	957	5	1	2	**965**
Saalekreis	1,373	5	-	9	**1,387**
Salzlandkreis	1,420	1	4	8	**1,433**
Stendal	848	9	3	4	**864**
Wittenberg	864	4	-	-	**868**
Unknown district	-	-	1	-	**1**
Major cities: Dessau-Roßlau, Halle, Magdeburg	4,862	16	13	30	**4,921**
Districts, in total	12,202	52	17	46	**12,317**
Saxony-Anhalt	**17,064**	**68**	**30**	**76**	**17,238**

* Federal Statistical Office Saxony-Anhalt 2015

3 Participating Institutions of the Region 2014

3.1 Maternity units / paediatric units / paediatric surgery / paedia tric cardiology (ordered by location)

- AMEOS Klinikum Aschersleben
- Gesundheitszentrum Bitterfeld/Wolfen
- HELIOS Klinik Jerichower Land Burg
- Städtisches Klinikum Dessau
- Altmark-Klinikum Krankenhaus Gardelegen
- AMEOS Klinikum Halberstadt
- AMEOS Klinikum Haldensleben
- Krankenhaus St. Elisabeth und St. Barbara Halle
- Universitätsklinikum Halle (Saale)
- HELIOS Klinik Köthen
- Krankenhaus St. Marienstift Magdeburg
- Klinikum Magdeburg
- Universitätsklinikum Magdeburg A.ö.R.
- Carl-von-Basedow-Klinikum Saalekreis Merseburg
- Harzklinikum Dorothea Christiane Erxleben Klinikum Quedlinburg
- Altmark-Klinikum Krankenhaus Salzwedel
- HELIOS Klinik Sangerhausen
- AMEOS Klinikum Schönebeck
- Johanniter-Krankenhaus Genthin-Stendal
- Asklepios Klinik Weißenfels
- Harzklinikum Dorothea Christiane Erxleben Klinikum Wernigerode
- Georgius-Agricola Klinikum Zeitz
- HELIOS Klinik Zerbst/Anhalt
- Herzzentrum Leipzig - Universitätsklinik, Klinik für Kinderkardiologie *(outside of Saxony-Anhalt)*

3.2 Institutions of pre- and postnatal diagnostics (ordered by location)

- Dipl.-Med. Heweker, Fachärztin für Frauenheilkunde und Geburtshilfe, Bernburg
- Dipl. Heilpädagogin Schlote, Glindenberg/Magdeburg
- AMEOS Klinikum Halberstadt, Pränatale Ultraschalldiagnostik: CA Dr. Schmidt
- Dr. Perlitz, Fachärztin für Frauenheilkunde und Geburtshilfe, Haldensleben
- PD Dr. Hahmann, Facharzt für Frauenheilkunde und Geburtshilfe, Halle
- Krankenhaus St. Elisabeth und St. Barbara Halle, Pränatale Ultraschalldiagnostik: CA Dr. Seeger / OÄ Dr. Radusch
- Universitätsklinikum Halle (Saale), Pränatale Ultraschalldiagnostik:
  CA Prof. Dr. Tchirikov / OÄ Dr. Scheler / OA Dr. Seliger / OA Dr. Thäle
- Dr. Altus, Fachärztin für Humangenetik, Magdeburg
- Dr. Karstedt, Facharzt für Kinder- und Jugendmedizin, Kinderkardiologie, Magdeburg
- Dr. Karsten, Facharzt für Frauenheilkunde und Geburtshilfe, Magdeburg
- Universitätsklinkum Magdeburg A.ö.R., Institut für Humangenetik
- Universitätsklinkum Magdeburg A.ö.R., Universitätsfrauenklinik, Pränatale Ultraschalldiagnostik: OÄ Dr. Gerloff
- Universitätsklinkum Magdeburg A.ö.R., Universitätskinderklinik, Screeninglabor
- Trackingstelle Neugeborenenhörscreening Sachsen-Anhalt, Magdeburg
- Dipl.-Med. Fiedler und Giesecke, Fachärzte für Orthopädie, Merseburg
- Altmark-Klinikum Krankenhaus Salzwedel, Pränatale Ultraschalldiagnostik: CA Dr. Müller
- Dr. Woltersdorf, Fachärztin für Frauenheilkunde und Geburtshilfe, Schönebeck
- Harzklinikum Dorothea Christiane Erxleben Klinikum Wernigerode, Pränatale Ultraschalldiagnostik: OÄ Dr. Schulze

3.3 Pathological-anatomical institutes (ordered by location)

- Institut für Pathologie Dr. Taege und Dr. Bilkenroth, Eisleben
- Universitätsklinikum Halle (Saale), Institut für Pathologie / Institut für Rechtsmedizin
- Klinikum Magdeburg, Institut für Pathologie
- Universitätsklinikum Magdeburg A.ö.R., Institut für Pathologie
- Praxis für Pathologie Dr. Schultz, Dr. Lüders, Dr. Gunia, Stendal

4 Malformation Registration in Saxony-Anhalt

4.1 General Information

We wish to place our thanks for the brilliant interdisciplinary collaboration of the different subdisciplines as well as our special thanks to our sender for the continuous malformation reportings in the current year just at the beginning of our report.
35 years after the start of the malformation registration in Magdeburg and the continuation of a population based analysis of congenital malformations for the whole Federal State of Saxony-Anhalt we collected valid data for already 15 years. The annual report 2014 outlines in the established form our data analysis about malformation epidemiology of our Federal State.
We wish to point out again that this would be not possible without the dedicated collaboration of all senders!

Our special topic in the current year deals with the most frequent malformation of the male genital, the hypospadias. We analysed its corresponding prevalence in the European comparison. Additionally, we focused on the primary prevention in form of modifiable risk factors. By an early vaccination against rubella for example, an infection of the pregnant women and thereby a later impairment of the unborn baby can be prevented.

This topic has an increasing importance again due to the expected migration movements in our Federal State. Another chance to inform the public about this topic and similar issues should be archived by the 2015 invented worldwide day of the congenital malformations (World Birth Defect Awareness Day) on March, 3rd. It was initiated by the ICBDSR (International Clearinghouse for Birth Defects Surveillance and Research) and is steadily accompanied by EUROCAT (European Surveillance of Congenital Anomalies).

What is EUROCAT? EUROCAT is the European Association of 38 malformation registration centres from 21 countries which monitor together 31% of the European population in regard to congenital malformations (more than 1.7 million births). Since 1992 the Monitoring of Congenital Malformations Saxony-Anhalt is a member of this network.
A new thing is that the central register of EUROCAT is located since 1st January 2015 at the JRC (Joint Research Center),which is the inhouse science service of the European Commission in Ispra, Italy. This relocation took its time and actual analysis of the European data for 2013 is not present yet. We therefore used as data of comparison in our current annual report the last available analysis (see in each case the analysis of the single malformation). Further information about EUROCAT is available at: www.eurocat-network.eu.

What is ICBDSR? The Monitoring of Congenital Malformations Saxony-Anhalt represents Germany with its collected data at the ICBDSR since 2001 (International Clearinghouse for Birth Defects Surveillance and Research), which is a WHO connected International Association of 42 malformation registers from 38 countries of the world. Further information about ICBDSR is available at: www.icbdsr.com.

Saxony-Anhalt is the only Federal State in Germany with a region wide population-based malformation registration. This steady and high quality work is only possible due to the consistent support of the Ministry of Employment and Social Affairs of the Federal State of Saxony-Anhalt. At this point we would like to thank especially our persons in charge in the Ministry Dr. Dr. R. Nehring and Dr. H. Willer and Mr. M. Schiener.

Additionally, we would like to thank our colleagues at the Medical Faculty of the Otto-von-Guericke University for their organisational support within the project of the Monitoring of Congenital Malformations and for the more than 20 years lasting collaboration. These persons are Mrs. Dipl.-Wirtsch. V. Rätzel, Dr. J. L. Hülsemann and Prof. Dr. med. H.-J. Rothkötter.

4.2 Registration and Analysis

The present report contains data about infants of the Federal State of Saxony-Anhalt with congenital malformations and chromosomal disorders in relation to the mother's place of residence during pregnancy, respectively at birth.

The total number of "births" includes
- live births,
- stillbirths,
- terminations of pregnancy after prenatal diagnostics (all weeks of gest.) sowie
- spontaneous abortions (>16 weeks of gest.)

and forms basis for the annual prevalence calculation.

The expected date of delivery is used as basis for analysing the termination of pregnancy, e.g. 2014 is considered the year of birth although some terminations of pregnancy after prenatal diagnostics took place at the end of 2013. This method is common on an international scale. In contrast, the time of delivery of spontaneous abortions is not corrected as the abortion is registered in the month when it actually took place.

The data of live births and stillbirths is provided annually by the Statistical Office of Halle. The outlined percentage indications and prevalences are rounded.

All data transmitted to the Monitoring of Congenital Malformations is medically controlled upon receipt and the diagnoses are encoded according to ICD-10 and according to another extension (Adaptation of the Royal College of Pediatrics and Child Health). Details about the intake of medication during pregnancy are registered by using the internationally recommended ATC codes.
The total number of infants with major malformations as well as the geographical distribution of appearance in the big cities and districts is outlined in chapter 7 and 8 (German version).

Infants with only minor malformations or rather norm variations are not evaluated separately since this data is only collected incompletely in the end. Chapter 11 outlines the most frequent single diagnoses of major malformations registered in 2014.

Similar to the previous years we analysed the reported pathological prenatal screening results separately in Chapter 10 (German version).

Chapter 12 contains again the analysis of the so-called indicator birth defects. As we have presented data in this way for a number of years, it is possible to evaluate the current prevalences of 2014 in comparison to the last 12 years (2002-2013). Here, a **total number of 207,962 births** forms basis for the **basis prevalence** calculation **2002 to 2013**.

The graphical presentation of the annual prevalences allows to identify frequent appearances and gives a good overview about rarely appearing indicator births defects.

The exact calculation of confidence levels is based on the binominal distribution with a confidence probability of 95%. To discover a certain trend the percentage change of an indicator malformation prevalence is illustrated as well during the publishing time of the Annual Report (Chapter 12.37).

Chapter 13 (German version) outlines data regarding genetically caused diseases, chromosomal disorders, sequences, associations, complexes and embryopathies. Chapter 14 (German version) contains an analysis of malformation caused terminations of pregnancy.

As usual, the Newborn hearing screening forms part of the Report of the Monitoring of Congenital Malformations Saxony-Anhalt and is outlined in chapter 18.
Chapter 19 presents the Annual Report of the department of newborn screening in Saxony-Anhalt with data regarding congenital metabolic disorders and endocrinopathies.

4.3 Data Quality and Completeness/Reporting Procedure

In **2014** the Monitoring of Congenital Malformations Saxony-Anhalt received data about **1,922 newborns and foetuses** which corresponds to a percentage of 11.2 % of all births in Saxony-Anhalt in 2014. Meanwhile the database contains information about newborns and fetuses of 35 years. Since the Annual Report 2013 was published the number of births and corresponding data records for 2013 increased from 1,940 to 2,013.

All data records from the maternity and paediatric units resp. from institutions of pre- and postnatal diagnostics which are mentioned in chapter 5.2 (German version) were stored in the database of the Monitoring of Congenital Malformations. They form the basis of the current annual report and will serve for future analysis.

We received 2,222 reportings for the year 2014. In 12.2 % of all cases we received information from two or more institutions. Receiving these double-reportings helps to reconfirm a diagnosis or to classify complex malformations exactly. Continuously high reporting rates in respect to the number of births per clinic are obtained for long years from the AMEOS Klinikum Schönebeck, HELIOS Klinik Köthen and the hospital St. Marienstift Magdeburg.

A correct and preferably detailed diagnosis description is therefore essential for a steady high data quality and consequently convincing statistics and complete indication of all items which are listed on the documentation sheets. They allow among others the classification of malformations risks.

The data quality remained also in 2014 on a high level thanks to the excellent work and dedication of all our senders. We received important information nearly in all cases: gender 99.1 %, maternal age 99.4 % and district 99.8 %. The births weight was not reported in 60 cases (3.16 %). 38 of these cases were terminations of pregnancy, whereby the birth weight indication was missing more often in case of the early terminations of pregnancy. The birth weight was missing 12 times in case of live births. The sender did not know the corresponding weight in these cases as we received the malformation reporting not from maternal clinic.

We kindly ask again all reporting institutions in Saxony-Anhalt to describe every diagnosed malformation as detailed as possible and to mention also additional malformations. In 2014 for example we were not able to include eight of 117 foetuses which showed prenatally an indicator malformation (chapter 10 (German version)) into our indicator malformation statistics (chapter 12), as without the postnatal reporting we cannot automatically assume that the diagnosis was confirmed. In four cases the prenatal diagnosis could not be matched to postnatal reporting.

The validity of our Annual Report mainly depends on complete and correct data records. We receive two thirds of malformation registrations and indications of control cases by means of the **"green documentation sheets"** , which we provide free of charge to the reporting institutions. Documentation sheets may be ordered at any time by phone **+49 391-6714174** or e-mail to **monz@med.ovgu.de**.

Additionally, it is also possible to report on so-called **"white documentation sheets"**. This form serves to register a minimum data set. The indication of the above mentioned information and possible risk factors like intake of medication or family histories and an exact description of the malformation and corresponding symptoms are important here.

Both documentation sheets are also available for download on our homepage **www.angeborene-fehlbildungen.com.** It is possible to complete them manually or to enter the data directly into the PDF file, print it out and send it back to us.

Mostly, we receive the reports by mail on our documentation form sheets. In many institutions fax reports have become the preferred method of transmission. Our fax number is: **+49 391-6714176**.

We will be at your disposal for answering any further questions about the reporting procedure and congenital malformations in general.

6 Sex Ratio

Sex ratio of all live births and stillbirths of Saxony-Anhalt according to the information of the Statistical Office Halle

male	8,852 live births and stillbirths
female	8,280 live births and stillbirths
total	17,132 live births and stillbirths

Sex ratio m : f = 1.07

The Statistical Office Halle registered in 2014 a total number of 17,132 births. These can be split up into 17,064 live births and 68 stillbirths. Compared to the previous year the total number of live births increased about 1.59 % (2013: 16,797). The number of stillbirths remained on a similar level (2013: 66). The sex ration shows in 2014 an androtropism. This androtropism appears more distinct in 2014 than in the previous years (2014: 1.07; 2013: 1.03; 2012: 1.04).

The sex ratio of the reported 589 births with major malformations also showed an androtropism in 2014. With 1.34 (330 male and 247 female births) the percentage remained similar to the previous years (2012: 1.33; 2011: 1.33). However, the value of 2013 did not show such a clear division (1.14).

Sex ratio of all births with major malformations (including abortions)

male	330	births
female	247	births
unknown	12	births
total	589	births

Sex ratio m : f = 1.34

Sex ratio pf all births with only minor malformations and anomalies

male	159	births
female	106	births
total	265	births

Sex ratio m : f = 1.50

11 Organ System Involvement in Infants and Foetuses with Major Malformations

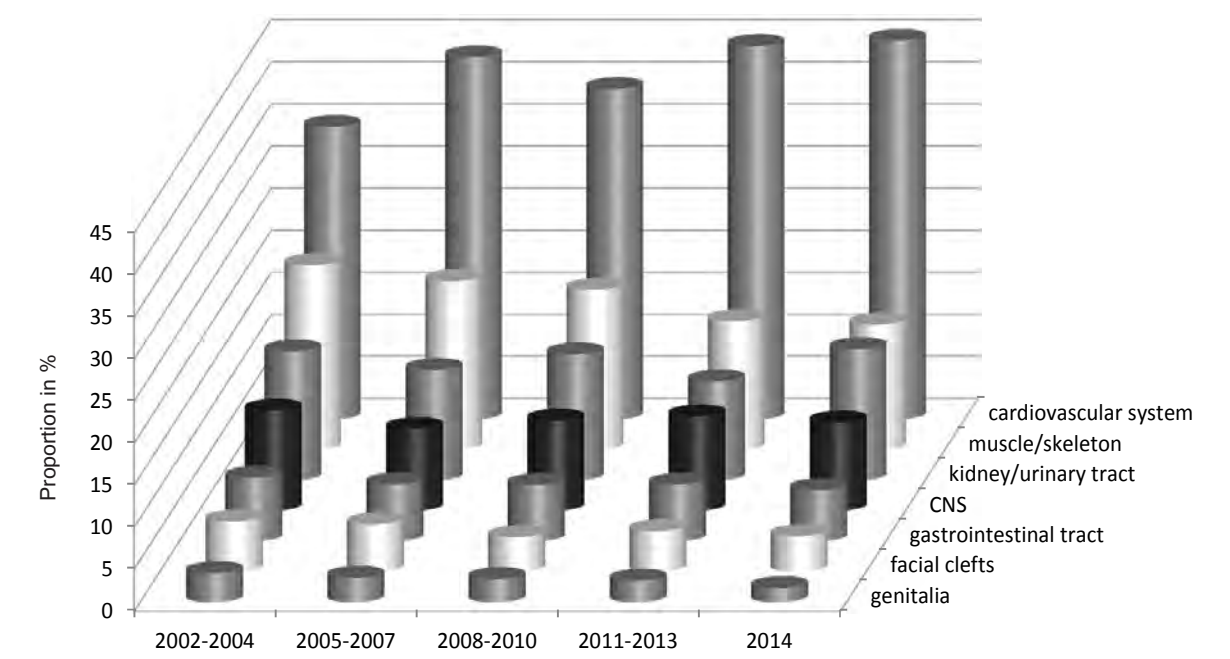


Fig. 5: Organ system involvement in major malformations (grouped)

We present the table above for the first time in this manner It shows the involvement of selected organ systems of the registered major malformations at infants and foetuses during the registration period. Only the most affected organ systems are categorized which makes the overview much more clearer (four groups of three years and one of the current year). Multiple malformations may appear at the same time at one birth, therefore multiple mentions are possible.

Similar to the last year, the cardiovascular system is the organ system which shows most frequently severe malformations (2014: 45.7 %). The total percentage of major malformations lies above the percentage of the years 2002-2013 (40.8%). We will continue to observe the future trend. Furthermore, the increasing number of reports we receive from the cardiac newborn centers in Saxony-Anhalt and the established postnatal pulse oximetry measurement gives the opportunity to detect additional cases.

Malformations of the kidney and urinary tract were registered second most frequently in 2014 (2014: 15.6 %). We observed here a value above the average value of the years 2002-2013 (13.9 %). The lowest percentage during the registration period was registered in 2013 (8.9 %) and the highest percentage was registered in 2010 (16.7 %)
.

The third place of ranking is occupied by malformations of the musculoskeletal system, they were registered in 2014 with a percentage of 14.9 %. This value was significantly lower than during the years 2002-2013: 19.2 % , but higher than in the previous year when we registered a low level of 11.5 %. The registered CNS malformations (2014: 10.5 %) and malformations of the gastrointestinal tract (2014: 6.1 %) lie within the expected level. We registered in 2014 a lower percentage of births with facial clefts (4.2 %) than we expected (2002-2013: 5.2 %). However, in 2009 we registered a value that was even lower in regard to all births with major malformations (3.2%). Furthermore, we observed a decreasing trend of malformations of the genitalia during the last years (2014: 1.7 %; 2002-2013: 2.9 %). We will continue to observe this trend further on.

	ICD-10	Diagnosis	Infants/Foetuses 2014		Infants/Foetuses 2002-2013 Prevalence /10.000
			Number	Prevalence /10.000	
1.	Q21.1	Atrial septal defect (inclusive persistent foramen ovale/PFO)	163	94.6	80.4
2.	Q21.0	Ventricular septal defect	72	41.8	46.6
3.	H90.	Conductive and sensorineural hearing loss	46	26.7	13.2 (19.9*)
4.	Q62.3	Other obstructive defects of renal pelvis and ureter (dilated uropathy grade II-IV)	39	22.6	19.8
5.	Q90.	Down syndrome (trisomy 21))	34	19.7	17.1
6.	Q25.0	Patent ductus arteriosus	26	15.1	8.6
7.	Q02.	Microcephaly	21	12.2	14.9
8.	Q65.3 Q65.4 Q65.5	Congenital subluxation of hip (unilateral/bilateral/laterality unspecified)	20	11.6	14.5
9.	Q66.0	Pes equinovarus congenitus (clubfoot)	19	11.0	16.6
10.	Q22.1	Pulmonary valve stenosis	16	9.3	6.2
	Q63.0	accessory kidney	16	9.3	6.5
	Q62.1	Stenosis and atresia of ureter	16	9.3	6.8
11.	Q62.2	Congenital megaureter	15	8.7	7.3
	Q25.1	Coactartion of aorta	15	8.7	5.0
12.	Q05.	Spina bifida	14	8.1	5.6
	Q61.4	Renal dysplasia	14	8.1	5.7
13.	Q37.	Cleft palate with cleft lip	12	7.0	10.7
	Q69.	Polydactyly (pre- and postaxial)	12	7.0	12.1
	Q71.3	Congenital absence of hand and finger	12	7.0	3.1
	Q21.3	Tetralogy of Fallot	12	7.0	3.3
14.	Q60.0	Renal agenesis, unilateral	11	6.4	6.7
15.	Q03.0 Q03.1 Q03.8 Q03.9	Congenital Hydrocephalus (without neural tube defect)	10	5.8	5.7
16.	Q79.3	Gastroschisis	9	5.2	4.1
	Q79.2	Omphalocele	9	5.2	3.2
	Q04.0	Hypoplasia/agenesis of corpus callosum	9	5.2	4.8

* 2007-2013 (since 2007 data is synchronised with the newborn hearing screening tracking centre)

The table presented on page 23 shows the most frequently registered single diagnosis in Saxony-Anhalt. 17,238 births form the basis of the prevalences of the year 2014 and the resulting ranking of frequencies. The right column presents the corresponding basis prevalences (2002-2013: 207,962 births).

40.8 % of all births with a major malformation suffered from cardiac malformation during the time period from 2002 to 2013. Annually, the malformations ASD (2002-2013: 80.4 per 10,000 births, CI 76.6 to 84.3) and VSD (2002-2013: 46.6 per 10,000 birth, CI 43.8 to 49.7) appeared most frequently. This trend also continued in 2014. Thereby, ADS was even more frequently registered (94.6 per 10,000 births) and the second most frequent malformation VSD (41.8 per 10,000 births), was registered less frequently.

The hearing loss occupies for the second time rank three of the list (2014: 26.7 per 10,000 births). Its prevalence is clearly higher than the prevalences we calculated during the years 2007-2013 (19.9 per 10,000 births, CI 17.5 to 22.5). Only since 2007 the Newborn Hearing Screening provides region wide (2007-2013: 121,198 births) secured data about this malformation. Therefore, the data of frequency can be used only from 2007 to analyse the current prevalence.

As we already did during the past years, we registered on rank four in 2014 the dilatative uropathy (from II. grade), (2014: 22.6 per 10,000 births; 2002-2013: 19.8 per 10,000 births, CI 18.0 to 21.8). This was however more often than the average value of the last years.

The Down Syndrome occupies again rank five on the current frequency list. We registered this malformation more often than expected (2014: 22.6 per 10,000 births; 2002-2013: 17.1 per 10,000 births, CI 15.4 to 19.0).

Since approximately five years we receive more detailed reportings of cardiac malformations. For this reason the single diagnoses of the cardiac malformations such as PDA (16.5 per 10,000 births, rank 6), stenosis of Arteria pulmonalis (9.3 per 10,000 births, rank 10), coarctation of aorta (8.7 per 10,000 births, rank 11) and Tetralogie of Fallot (7.0 per 10,000 births, rank 13) were registered more often in 2014 than during the whole registration period of 2002-2013. Although, the PDA belongs to the most frequent single diagnosis for many years it occupies for the entire time period of 2002-2013 only rank 11 (8.6 per 10,000 births). Also the other three cardiac malformations were registered less frequently until 2009.

The indicator malformations microcephaly (2014: 12.2 per 10,000 births, 2002-2013: 14.9 per 10,000 births, CI 13.3 to 16.6), subluxation of hip (2014: 11.6 per 10,000 births, 2002-2013: 14.5 per 10,000 births, CI 12.9 to 16.2) and clubfoot (2014: 11.6 per 10,000 births, 2002-2013: 16.6 per 10,000 births, CI 15.0 to 18.5) occupy rank seven to nine of the frequency list. All three were registered less frequently than expected in 2014. Additionally, the measurements of newborns enlarged during the last years, therefore Voigt et al. developed new percentile values (chapter 12.5).

In contrast to use of the old values the use of the new values reduces the number of as microcephalie seen head circumferences. Furthermore, we assume that the subluxation of hip is under reported, as the hip sonography is only optional in the materny clinic and not carried out in every hospital any more (mandatory at U3).

In 2014, more cases than usual (each 9.3 per 10,000 births) appeared of accessory kidney (2002-2013: 6.5 per 10,000 births, CI 5.5 to 7.7) and atresia and stenosis of ureter (2002-2013: 6.8 per 10,000 births, CI 5.8 to 8.0). Also the congenital megaureter which is a malformation of the urogenial system was registered more frequently than expected (2014: 8.7 per 10,000 births; 2002-2013: 7.3 per 10,000 births,
CI 6.2 to 8.5).

Spina bifida occupies rank 12 and was also registered more frequently than expected with 8.1 per 10,000 births (2013: 5.6 per 10,000 births, CI 4.7 to 6.7) as well as the renal dysplasia (2002-2013: 5.7 per 10,000 births, CI 4.7 to 6.8). During the whole registration period both values only exceeded one time the current years value: Spina bifida (2008: 8.9 per 10,000 births) and renal dysplasia (2010: 8.6 per 10,000 births).

We registered less frequently than in the past years the cleft lip and palate (main part of the indicator malformation cleft lip and cleft lip and palate) and the polydactyly which consists of the indicator malformation preaxial polydactyly and postaxial polydactyly (each 7.0 per 10,000 births). This was obvious in case of the preaxial and postaxial polydactyly (2002-2013: 12.1 per 10,000 births, CI 10.7 to 13.7) (chapter 12.28). However, the very low prevalence of the indicator malformation cleft lip and cleft lip with cleft palate originates in the current year from the low prevalence of the cleft lip with cleft palate as the prevalence of the cleft lip was with 2.3 per 10,000 birth within the confidence interval.

The missing of multiple or single phalanges, a malformation which does not belong to the most frequent ones, was registered in 2014 as often as never before. The current prevalence exceeds heavily (7.0 per 10,000 births) the prevalences of the years 2002-2013 (3.1 per10,000 births, CI 2.4 to 4.0).

Rank 16 is occupied by the both abdominal wall defects gastroschisis and omphalocele with each 5.2 per 10,000 births. These malformations appeared again more frequently than during the 2000s. Gastroschisis appeared only slightly more frequently than in the previous years (2002-2013: 4.1 per 10,000 births, CI 3.3 to 5.1). In contrast, omphalolece appeared clearly more frequently (2002-2013: 3.2 per 10,000 births, CI 2.4 to 4.1).

Within the average prevalence of the years 2002 to 2013 are the for 2014 calculated prevalences of unilateral renal agenesia (6.4 per 10,000 births), hydrocephalus (5.8 per 10,000 births) and hypoplasia/agenesia of Corpus callosum (5.2 per 10,000 births). They occupy rank 14 to16 in 2014
.

12 Indicator Defects of the International Clearinghouse for Birth Defects Surveillance and Research (ICBDSR)

12.0 Definitions

1. Neural tube defects: common congenital malformations that occur when the neural tube fails to achieve proper closure during early embryogenesis, resulting in defective development of the associated vertebral arches.
Synonyms: Spina bifida, anencephaly, NTD.

2. Anencephaly: a congenital malformation characterized by the total or partial absence of the cranial vault, the covering skin, and the brain missing or reduced to small mass. Inclusive craniorachischisis. Inclusive infants with iniencephaly and other neural tube defects as Encephalocele or open spina bifida, when associated with anencephaly. Exclusive acephaly, that is, absence of head observed in amorphous acardiac twins.

3. Spina bifida: a family of congenital malformation defects in the closure of the spinal column characterized by herniation or exposure of the spinal cord and/or meninges through an incompletely closed spine. Inclusive meningocele, meningomyelocele, myelocele, myelomeningocele, rachischisis. Spina bifida is not counted when present with anencephaly. Exclusive spina bifida occulta, sacrococcygeal teratoma without dysraphism.

4. Encephalocele: a congenital malformation characterized by herniation of the brain and/or meninges through a defect in the skull. Encephalocele is not counted when present with spina bifida.

5. Microcephaly: a congenitally small cranium, defined by an occipito frontal circumference (OFC) 3 standard deviation below the age and sex appropriate distribution curves (see growth charts Voigt et al. 2014, chapter 25).
Exclusive microcephaly associated with anencephaly or encephalocele.

6. Congenital Hydrocephaly: a congenital malformation characterized by dilatation of the cerebral ventricles, not associated with a primary brain atrophy, with or without enlargement of the head, and diagnosed at birth. Not counted when present with encephalocele or spina bifida. Exclusive macrocephaly without dilatation of ventricular system, skull of macerated fetus, hydranencephaly, holoprosencephaly, and postnatally acquired hydrocephalus.

7. Arhinencephaly/holoprosencephaly: a congenital malformation of the brain, characterized by various degrees of incomplete lobation of the brain hemispheres. Olfactory nerve tract may be absent. Holoprosencephaly includes cyclopia, ethmocephaly, cebocephaly, and premaxillary agenesis
.

8. Anophthalmos/microphthalmos: apparently absent or small eyes. Some normal adnexal elements and eyelids are usually present. In microphthalmia, the corneal diameter is usually less than 10 mm. and the antero posterior diameter of the globe is less than 20 mm.

9. Anotia/Microtia: a congenital malformation characterized by absent parts of the pinna (with or without atresia of the ear canal) commonly expressed in grades (I - IV) of which the extreme form (grade V) is anotia, absence of pinna. Exclusive small, normally shaped ears, imperforate auditory meatus with a normal pinna, dysplastic and low set ears.

10. Tetralogy of Fallot: a condition characterized by ventricular septal defect, overriding aorta, infundibular pulmonary stenosis, and often right ventricular hypertrophy.

11. Transposition of great vessels (TGV): a cardiac defect where the aorta exits from the right ventricle and the pulmonary artery from the left ventricle, with or without other cardiac defects. Inclusive double outlet ventricle so called corrected transposition.

12. Hypoplastic left heart syndrome: a cardiac defect with a hypoplastic left ventricle, associated with aortic and/or mitral valve atresia, with or without other cardiac defect.

13. Coarctation of the aorta: an obstruction in the descending aorta, almost invariably at the insertion of the ductus arteriosus.

14. Cleft lip with or without cleft palate: a congenital malformation characterized by partial or complete clefting of the upper lip, with or without clefting of the alveolar ridge or the hard palate. Exclusive midline cleft of upper or lower lip and oblique facial fissure (going towards the eye).

15. Cleft palate without cleft lip: a congenital malformation characterized by a closure defect of the hard and/or soft palate behind the foramen incisivum without cleft lip. Inclusive submucous cleft palate. Exclusive cleft palate with cleft lip, cleft uvula, functional short palate, and high narrow palate.

16. Choanal atresia, bilateral: congenital obstruction (membraneous or osseous) of the posterior choana or choanae. Exclusive choanal stenosis and congestion of nasal mucosa.

17. Oesophageal atresia/stenosisl: a congenital malformation characterized by absence of continuity or narrowing of the esophagus, with or without tracheal fistula. Inclusive Tracheoesophageal fistula with or without mention of atresia or stenosis of oesophagus.

18. Small intestine atresia/stenosis: complete or partial occlusion of the lumen of a segment of the small intestine. It can involve a single area or multiples areas of the jejunum or ileum. Exclusive duodenal atresia

.19. Anorectal atresia/stenosis: a congenital malformation characterized by absence of continuity of the anorectal canal or of communication between rectum and anus, or narrowing of anal canal, with or without fistula to neighbouring organs. Exclusive mild stenosis which does not need correction, and ectopic anus.

20. Undescended testis: bilateral undescended testes in at term newborn or at least unilateral undescended testis in males more than 1 year of age. Exclusive retractrile testis.

21. Hypospadias: a congenital malformation characterized by the opening of the urethra on the ventral side of the penis, distally to the sulcus. Incl. penile, scrotal, and perineal hypospadias. Exclusive glandular or first degree hypospadias and ambiguous genitalia (intersex or pseudohermaphroditism).

22. Epispadias: a congenital malformation characterized by the opening of the urethra on the dorsal surface of the penis. Not counted when part of exstrophy of the bladder.

23. Indeterminate sex: genital ambiguity at birth that does not readily allow for phenotypic sex determination. Incl. male or female true or pseudohermaphroditism.

24. Potter sequence: a congenital malformation characterized by complete absence of kidneys bilaterally or severely dysplastic kidneys.

25. Renal agenesis, unilateral: a congenital malformation characterized by complete absence of one kidney unilaterally. Exclusive unilateral dysplastic kidney.

26. Cystic kidney: a congenital malformation characterized by multiple cysts in the kidney. Inclusive infantile polycystic kidney, multicystic kidney, other forms of cystic kidney and unspecified cystic kidney. Exclusive single kidney cyst.

27. Bladder exstrophy: complex malformation characterized by a defect in the closure of the lower abdominal wall and bladder. Bladder opens in the ventral wall of the abdomen between the umbilicus and the symphysis pubis. It is often associated with epispadias and structural anomalies of the pubic bones.

28. Polydactyly, preaxial: extra digit(s) on the radial side of the upper limb or the tibial side of the lower limb. It can affect the hand, the foot, or both.

29. Limb reduction defects: a congenital malformation characterized by total or partial absence or severe hypoplasia of skeletal structures of the limbs. Inclusive femoral hypoplasia. Exclusive mild hypoplasia with normal shape of skeletal parts, brachydactyly, finger or toe reduction directly associated with syndactyly, general skeletal dysplasia and sirenomelia.

30. Diaphragmatic hernia: a congenital malformation characterized by herniation into the thorax of abdominal contents through a defect of the diaphragm. Inclusive total absence of the diaphragm. Exclusive hiatus hernia, eventration and phrenic palsy.

31. Omphalocele: a congenital malformation characterized by herniation of abdominal contents through the umbilical insertion and covered by a membrane which may or may not be intact. Exclusive gastroschisis (para umbilical hernia), a or hypoplasia of abdominal muscles, skin covere umbilical hernia.

32. Gastroschisis: a congenital malformation characterized by visceral herniation through a right side abdominal wall defect to an intact umbilical cord and not covered by a membrane. Exclusive hypoplasia of abdominal muscles, skin covered umbilical hernia, omphalocele.

33. Prune belly sequence: a complex congenital malformation characterized by deficient abdominal muscle and urinary obstruction/distension. It can be caused by urethral obstruction secondary to posterior urethral valves or urethral atresia. In the affected fetus the deficiency of the abdominal muscle may not be evident. It can be associated with undescended testes, clubfoot, and limb deficiencies.

34. Down syndrome (Trisomy 21): a congenital chromosomal malformation syndrome characterized by a well known pattern of minor and major anomalies and associated with excess chromosomal 21 material. Inclusive trisomy mosaicism and translocations of chromosome 21.

35. Patau syndrome (Trisomy 13): a congenital chromosomal malformation syndrome associated with extra chromosome 13 material. Inclusive translocation and mosaic trisomy 13.

36. Edwards syndrome (Trisomy 18): a congenital chromosomal malformation syndrome associated with extra chromosome 18 material. Inclusive translocation and mosaic trisomy 18.

Note:

The prevalences we calculated in the following chapters are population based. The value indicates the number of birth with malformations born in a certain population with reference to the total number of birth in this population. Since 2000 the prevalence calculations are only referring to children whose mothers have their residence in Saxony-Anhalt. Between 1996-1999 the registration area of the Monitoring of Congenital Malformations did not cover the entire area of Saxony-Anhalt (1996/1997: 14, 1998: 15, 1999: 16 of 21 districts). The calculation of the basis prevalences (2002-20113) is based on a total number of 207,962 births.

The analysis of the indicator malformations is made with regard to the diagnoses. It is possible that one child has more than one indicator malformation. Therefore the number of all indicator malformations might be higher than the total number of births with an indicator malformation.

12.1 Neural tube defects (Q00./Q01./Q05.)

	Number	Prevalence /10,000 births	Trend in comp. to basis prevalence
Major cities: 3 x Halle 7 x Magdeburg	10	20.3	↑
Districts: 1 x Anhalt-Bitterfeld 3 x Börde 1 x Harz 1 x Jerichower Land 2 x Saalekreis 3 x Salzlandkreis 2 x Stendal 1 x Wittenberg	14	11.4	↑
Saxony-Anhalt	**24**	**13.9**	↑

Neural tube defects (2002-2013)		
	Basis prevalence /10,000 births	**Confidence Interval (CI of 95%)/10,000 births**
Cities	9.53	7.12 - 12.50
Districts	8.80	7.47 - 10.35
Region	8.99	7.82 - 10.33
EUROCAT 2001-2012	9.69	9.50 - 9.89
		4.22 S Portugal* 18.56 Isle de la Reunion (France)**

*/** centres with lowest resp. highest prevalence/10,000 births

In 2014, we registered 24 cases of neural tube defects. These can be divided into 14 cases of spina bifida, seven cases of anencephalus and three cases of encephalocele.
In 20.8 % the affected infants were live births, these were all children with spina bifida. One child deceased one day after birth.

additional information:

pregnancy outcome	4 x live births 19 x termination of pregnancy 1 x live birth, deceased within 7 days
sex	12 x male 8 x female 4 x no indication
number of isolated malformations/MCA	11 x MCA 13 x isolated

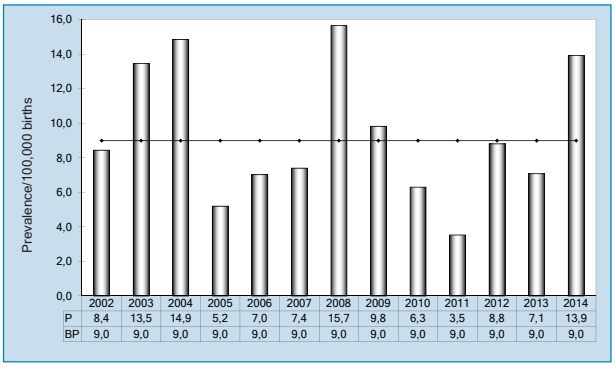


Fig. 6: Development of prevalence/10,000 births with neural tube defects in the registration area since 2002

The **prevalence of 13.9 per 10,000 births** is higher than the basis prevalence of the last 12 years. But the basis prevalence reflects with a value of 9.0 per 10,000 births the European trend.

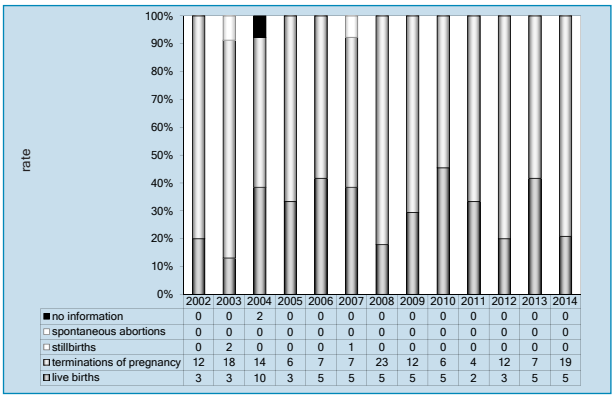


Fig. 7: Pregnancy outcomes of neural tube defects in the registration area since 2002

In 2014, one neural tube defect per 718 births was registered in Saxony-Anhalt.

Neural tube defects are probably the most investigated congenital malformation within scientific studies and a prevention measure exists for this malformation. In 1995, several German specialist societies published their recommendation regarding primary prevention of folic acid sensitive neural tube defects. A periconceptional intake of 0.4 mg folic acid was recommended to women at child-bearing age. A Cochrane Meta-analysis showed 2010 clearly the protective effect: OR 0.28 (CI 0.15-0.53). However, the expected decreasing trend fails to appear since 20 years in Germany. Our own data as well as results of a births cohort in Mainz (the so called Mainzer-Modell) as well as data from the European register EUROCAT prove this fact. Also for the time period of 1991 to 2011 no Europen wide decreasing trend of prevalences of all neural tube defects can be observed. Discussed reasons are:

- insufficient realisation of folic acid intake recommendation (unplanned pregnancy, first consultation of gynaecologist during fifths and seventh week of gestation)
- only 70 % of neural tube defects are "folic acid sensitive" at a known multifactorial origin
- only optional supplementation of folic acid at food
- folic acid supplementation at staple food as economic strategy does not exist in Europe

We are referring to the planned EUROCAT publication for further information.

Please note:

In case of a previous pregnancy with neural tube defect please consider recommendation regarding necessary folic acid prophylaxis with **5 mg folic acid equivalent per day** (please consider recommendation of specialist society) for a further wish to have a child.

12.2 Anencephaly (Q00.)

	Number	Prevalence /10,000 births	Trend in comp. to basis prevalence
Major cities: 1 x Halle 1 x Magdeburg	2	4.1	↑
Districts: 3 x Börde 1 x Salzlandkreis 1 x Stendal	5	4.1	↑
Saxony-Anhalz	**7**	**4.1**	↑

Anencephaly (2002-2013)		
	Basis prevalence /10,000 births	**Confidence Interval (CI of 95%)/10,000 births**
Cites	1.28	0.52 - 2.64
Districts	2.41	1.70 - 3.32
Region	2.12	1.54 - 2.84
EUROCAT 2001-2012	3.67	3.55 - 3.79
		1.38 Wielkopolska (Poland)* 7.23 Isle de la Reunion (France)**

*/** centres with lowest resp. highest prevalence/10,000 births

We registered seven births with anencephaly in 2014. The **prevalence of 4.1 per 10,000 births** is higher than the prevalence of the last four years (2009-2013) and it additionally exceeds with 2.1 per 10,000 births the calculated 12 years prevalence (BP).

All pregnancies with an affected foetus were terminated between 10 and 20 weeks of gestation.

additional information:

pregnancy outcome	7 x termination of pregnancy
sex	2 x male 2 x female 3 x no indication
number of isolated malformations/MCA	3 x MCA 4 x isolated

Malformation combinations (MCA) or superordinated syndromes detected:

- Body stalk anomaly with: amniotic band syndrome, amniotic band grooves at right hand and head
- omphalocele
- cardiac malformation

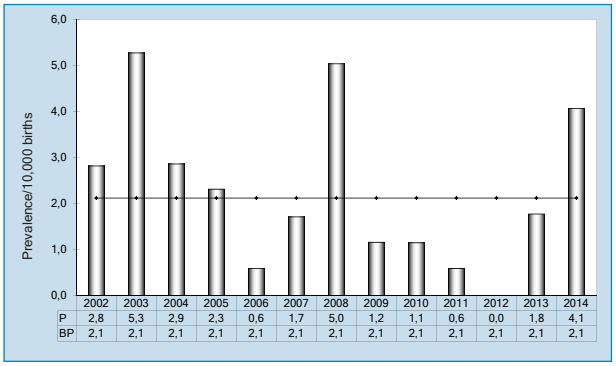


Fig. 8: Development of prevalence/10,000 births with anencephaly in the registration area since 2002

In 2014, one anencephaly per 2463 births was registered in Saxony-Anhalt.

12.3 Spina bifida (Q05.)

	Number	Prevalence /10,000 births	Trend in comp. to basis prevalence
Major cities: 2 x Halle 6 x Magdeburg	8	16.3	↑
Districts: 1 x Anhalt-Bitterfeld 1 x Jerichower Land 2 x Salzlandkreis 1 x Stendal 1 x Wittenberg	6	4.9	↔
Saxony-Anhalt	**14**	**8.1**	↑

Spina bifida (2002-2013)		
	Basis prevalence /10,000 births	**Confidence Interval (CI of 95%)/10,000 births**
Cities	6.05	4.17 - 8.50
Districts	5.41	4.31 - 6.71
Region	5.58	4.67 - 6.65
EUROCAT 2001-2012	4.91	4.77 - 5.05
		1.83 Zagreb (Croatia)* 9.34 Isle de la Reunion (France)**

*/** centres with lowest resp. highest prevalence/10,000 births

14 births with Spina bifida were registered in 2014. Five infants were live births, one of these deceased at the first day of life. The prevalence lies with 8.1 per 10,000 births above the basis prevalence of the last 12 years. Furthermore, the same value appeared for the last time in 2009.

A comparison with EUROCAT data shows that the prevalence is higher than the prevalence of the European bordering countries, however it does not reach the maximum values that were calculated in other registers.

additional information:

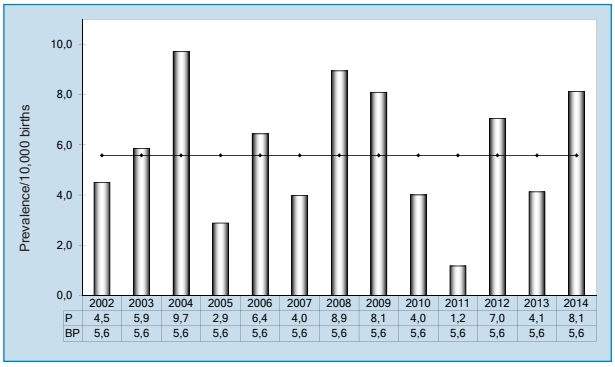
pregnancy outcome	4 x live births 1 x live birth, deceased within 7 days 9 x termination of pregnancy
sex	8 x male 5 x female 1 x no indication
number of isolated malformations/MCA	7 x MCA 7 x isolated

The terminations of pregnancy took place between 18 and 24 weeks of gestation. The defect was thoracic in two cases and an hydrocephalus resp. one Arnold-Chiari-II-malformation was suspected prenatally. The intake of vitamins resp. folic acid during pregnancy was only indicated in one case. But we do not have any information about beginning of intake and dose in this case.

In one case a lipomyelomeningocele was present.

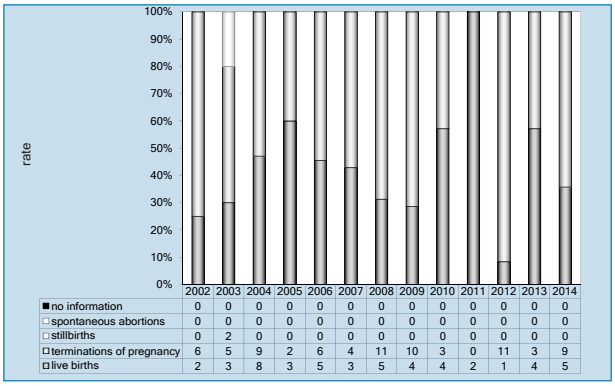
Malformation combinations (MCA) or superordinated syndromes detected:

- OEIS-complex with: Omphalocele, anal atresia with fistula, bladder exstrophy, unknown sex, cloacal persi tence, megaureter and DUP I. grade left, tethered cord syndrome, VSD, PFO
  and haemodynamic not effective PDA at preterm infant
- Fallot-Tetralogy, microcephaly
- Arnold Chiari syndrome with turricephaly, hemivertebra, hygroma colli cysticum right, clinodactyly of V. finger
- Arnold Chiari syndrome with macrocephaly
- 3 x Arnold Chiari syndrome



	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014
P	4,5	5,9	9,7	2,9	6,4	4,0	8,9	8,1	4,0	1,2	7,0	4,1	8,1
BP	5,6	5,6	5,6	5,6	5,6	5,6	5,6	5,6	5,6	5,6	5,6	5,6	5,6

Fig. 9: Development of prevalence/10,000 births with spina bifida in the registration area since 2002



	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014
no information	0	0	0	0	0	0	0	0	0	0	0	0	0
spontaneous abortions	0	0	0	0	0	0	0	0	0	0	0	0	0
stillbirths	0	2	0	0	0	0	0	0	0	0	0	0	0
terminations of pregnancy	6	5	9	2	6	4	11	10	3	0	11	3	9
live births	2	3	8	3	5	3	5	4	4	2	1	4	5

Fig. 10: Pregnancy outcomes of spina bifida in the registration area since 2002

In 2014, one spina bifida per 1231 births was registered in Saxony-Anhalt.

12.4 Encephalocele (Q01.)

	Number	Prevalence /10,000 births	Trend in comp. to basis prevalence
Major cities:	0	0.0	↓
Districts: 1 x Harz 2 x Saalekreis	3	2.4	↑
Saxony-Anhalt	**3**	**1.7**	↔

Encephalocele (2002-2013)		
	Basis prevalence /10,000 births	**Confidence Interval (CI of 95%)/10,000 births**
Cities	2.20	1.01 - 3.61
Districts	0.98	0.55 - 1.61
Region	1.30	0.86 - 1.89
EUROCAT 2001-2012	1.11	1.05 - 1.18
		0.19 S Portugal* 3.15 Mainz (Germany)**

*/** centres with lowest resp. highest prevalence/10,000 births

Three births with encephalocele were registered in 2014. The **prevalence of 1.7 per 10,000 births** is therefore slightly higher than the prevalence of the previous year. The value remains within the 12 years prevalence, this frequency also showed our data analysis for the years 2011 and 2012.

The prevalence of Saxony-Anhalt is in comparison with the EUROCAT data higher than the confidence interval, however we do not exceed the maximum value of the register of Mainz.

A termination of pregnancy during 14 and 21 weeks of gestation took place in all cases, as in all cases an occipital encephalocele was diagnosed.

additional information:

pregnancy outcome	3 x termination of pregnancy
sex	2 x male 1 x female
number of isolated malformations/MCA	1 x MCA 2 x isolated

Malformation combinations (MCA) or superordinated syndromes detected:

- unbalanced translocation (chromosome 13) with: blt shortened arms and legs, missing thumb, V. toes and metatarsalia, VSD, persistend truncus arteriosus, sectionally fusion of cervical vertebra and thoracic vertebra, hemivertebra, scoliosis, intestinal malrotation, blt unlobed lung, hypoplastic spleen, lateral ascending lid axis, short philtrum

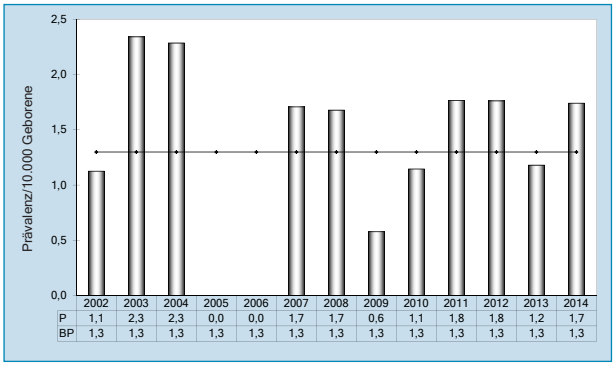


Fig. 11: Development of prevalence/10,000 births with encephalocele in the registration area since 2002

In 2014, one encephalocele per 5746 births was registered in Saxony-Anhalt.

12.5 Microcephaly (Q02.)

	Number	Prevalence /10,000 births	Trend in comp. to basis prevalence
Major cities: 1 x Dessau-Roßlau 2 x Halle 4 x Magdeburg	7	14.2	↓
Districts: 1 x Altmarkkreis Salzwedel 3 x Anhalt-Bitterfeld 1 x Burgenlandkreis 3 x Börde 1 x Harz 1 x Mansfeld-Südharz 4 x Salzlandkreis	14	11.4	↘
Saxony-Anhalt	**21**	**12.2**	↓

Microcephaly (2002-2013)		
	Basis prevalence /10,000 births	Confidence Interval (CI of 95%)/10,000 births
Cities	19.25	15.99 - 23.13
Districts	13.30	11.63 - 15.19
Region	14.86	13.32 - 16.56
EUROCAT 2001-2012	2.49	2.39 - 2.59
		0.47 Norway* 13.09 Saxony-Anhalt (Germany)**

*/** centres with lowest resp. highest prevalence/10,000 births

In 2014, a microcephalus was diagnosed at 21 births. The current head circumference was below the third percentile in relation to the body length and the gestational age (definition on page 25). The annual prevalence lies with **12.2 per 10,000 births** below the basis prevalence of the years 2002-2013.

Saxony-Anhalt shows the highest prevalence in comparison with the European data. Our data also remain on a level which is clearly higher than the confidence interval.

In the current year an adjustment to the 2014 published percentiles took places. These values were ascertained in a perinatal study during the time period of 2007-2011 with the involvement of all 16 Federal States (Voigt et al. 2014)

additional information:

pregnancy outcome	15 x live births 2 x spontaneous abortion 3 x termination of pregnancy 1 x stillbirth
sex	10 x male 11 x female
number of isolated malformations/MCA	13 x MCA 8 x isolated

The pregnancy outcome shows that 71.4 % of the affected infants/foetuses were live births.

In 13 cases the infants/foetuses showed additional malformations and only in eight cases the microcephalus occurred isolated.

Malformation combinations (MCA) or superordinated syndromes detected:

- Down's syndrome
- Zellweger syndrome with: polycystic kidney, malformation of the urinary tract, scaphocephaly, Corpus callosum hypoplasia, clubfoot, hepatic cyst, VSD, PFO and haemodynamical not effective PDA at full term infant, hypertelorism, epicanthus internus, wide nose bridge, blt. four finger groove, dilated cere bral ventricles and low set ears
- Potter-Sequence (bilateral renal agenesia) with: clubfoot, low set ears
- unilateral renal agenesia
- duplex right kidney
- lumbosacral spina bifida, Fallot-Tetralogy
- Dextro-transposition of aorta, persistent left vena cava superior, malformed backbone, hemivertebra, scoliosis PFO at full term infant, DUP I. grade left , hypertelorism, auricular tag right
- ASD II, haemodynamical not effective PDA and hernia inguinalis left at preterm infant
- ASD II, canalis atrioventricularis communis
- cleft lip with cleft palate, indifferent sex, cerebral reduction malformation, cardiac malformation, intesti nal malformation
- blt. choanal atresia
- hypospadias
- colonic atresia

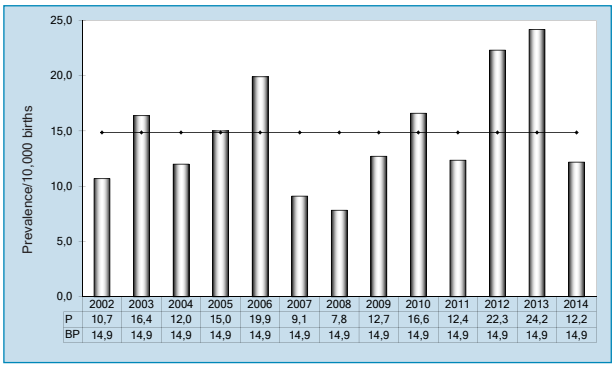


Fig. 12: Development of prevalence/10,000 births with microcephaly in the registration area since 2002

In 2014, one microcephaly per 821 births was registered in Saxony-Anhalt.

References:
Voigt M, Rochow N, Schneider KTM, et al.: Neue Perzentilwerte für die Körpermaße neugeborener Einlinge: Ergebnisse der deutschen Perinatalerhebung
der Jahre 2007-2011 unter Beteiligung aller 16 Bundesländer.
Z Geburtshilfe Neonatol 2014; 218: 210-7.

12.6 Congenital Hydrocephaly (Q03.)

	Number	Prevalence /10,000 births	Trend in comp. to basis prevalence
Major cities: 1 x Halle 1 x Magdeburg	2	4.1	↘
Districts:: 1 x Börde 2 x Jerichower Land 2 x Mansfeld-Südharz 1 x Saalekreis 2 x Salzlandkreis	8	6.5	↔
Saxony-Anhalt	**10**	**5.8**	↔

Congenital Hydrocephaly (2002-2013)		
	Basis prevalence /10,000 births	Confidence Interval (CI of 95%)/10,000 births
Cities	6.23	4.32 - 8.71
Districts	5.54	4.43 - 6.85
Region	5.72	4.80 - 6.80
EUROCAT 2001-2012	5.66	5.51 - 5.81
		1.34 S Portugal* 13.42 Paris (France)**

*/** centres with lowest resp. highest prevalence/10,000 births

A hydrocephalus in combination with a neural tube defect or the more frequently appearing hydrocephalus after a bleeding or infection is not classified heret.

10 births with congenital hydrocephalus were registered in 2014. The prevalence lies with 5.8 per 10,000 births within the range of the previous years. It also corresponds to the European comparison data.

The significant falling trend (-5.38 % per year) which was calculated in our last annual report for the years 2001-2013 resulted from high prevalences that were registered in 2001/2002 and low prevalences that were registered in 2008/2009. However, as the prevalences are within the range of the basis prevalence since 2010, this trend now relativizes taking into account the year 2014 (chapter 12.37). We will, of course continue to observe the future trend in this matter.

additional information:

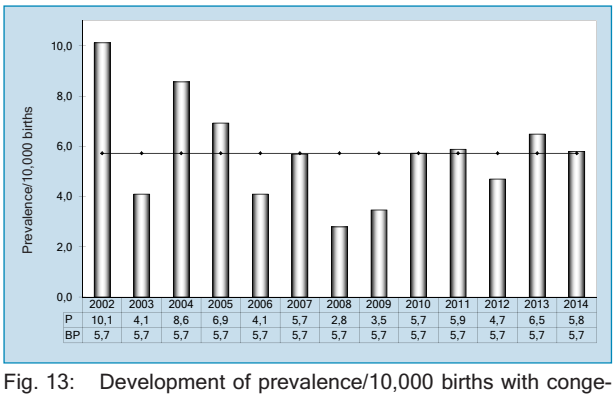
pregnancy outcome	6 x live births 1 x spontaneous abortion 3 x termination of pregnancy
sex	5 x male 5 x female
number of isolated malformations/MCA	8 x MCA 2 x isolated

In three cases a termination of pregnancy took place between 19 and 22 weeks of gestation at presence of other multiple malformations.

Only in two cases the hydrocephalus appeared isolated, in eight cases additional malformations were diagnosed.

Malformation combinations (MCA) or superordinated syndromes detected:

- Walker Warburg syndrome with: blt. renal dysplasia, submucosal cleft palate, aortic valve stenosis, cerebellum hypoplasia, ocular malformation, hypoplastic nasal bone, craniofacial dysmorphy
- caryotype 47,XYY with: club hands, corpus callosum agenesia, unilateral clubfoot
- unbalanced chromosomal translocation with: coarctation of aorta, right side located aorta ascendens, vascular ring through the abnormal right subclavicular artery, VSD, median cleft palate and cleft uvula, corpus callosum hypoplasia, intestinal malrotation, kyphosis, chicken breast, sacral dimple (1.2 cm deep), mandibular micrognathia, less marked philtrum, lateral ascending lid axis, epcanthus internus, wide cranial suture
- deletion of one chromosomal part with: Ebstein anomaly, ASD II
- agenesia of left kidney, corpus callosum hypoplasia, small hypophysis, partial agenesia of septum pellucidum, butterfly vertebra (BWK 11,12), sortened rib right at LWK 1, soliosis, abdominal muscle hypoplasia left
- cleft of soft palate, corpus callosum hypoplasia, DUP III. grade right and II. grade left, hypoplastic septum pellucidum
- Fallot tetralogy
- corpus callosum hypoplasia



	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014
P	10,1	4,1	8,6	6,9	4,1	5,7	2,8	3,5	5,7	5,9	4,7	6,5	5,8
BP	5,7	5,7	5,7	5,7	5,7	5,7	5,7	5,7	5,7	5,7	5,7	5,7	5,7

Fig. 13: Development of prevalence/10,000 births with congenital hydrocephalus in the registration area since 2002

In 2014, one congenital hydrocephalus per 1724 births was registered in Saxony-Anhalt.

12.7 Arhinencephaly/Holoprosencephaly (Q04.1/Q04.2)

	Number	Prevalence /10,000 births	Trend in comp. to basis prevalence
Major cities	0	0.0	↓
Districts	0	0.0	↓
Saxony-Anhalt	**0**	**0.0**	↓

Arhinencephaly/Holoprosencephaly (2002-2013)		
	Basis prevalence /10,000 births	Confidence Interval (CI of 95%)/10,000 births
Cities	2.75	1.54 - 4.54
Districts	1.30	0.80 - 2.01
Region	1.68	1.17 - 2.34
EUROCAT 2001-2012	1.31	1.24 - 1.39
		0.38 Wielkopolska (Poland)*
		2.77 Vaud (Switzerland)**

*/** centres with lowest resp. highest prevalence/10,000 births

No holoprosencephaly was registered in 2014. Recently, this was the case in 2008.
The basis prevalence for the years 2002-2013 amounts to 1.7 per 10,000 births.

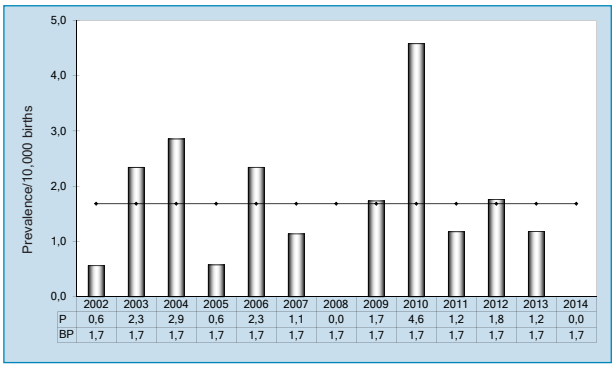


Fig. 14: Development of prevalence/10,000 births with arhinencephalie/holoprosencephalie in the registration area since 2002

In 2014, no case of arhinencephalie/holoprosencephalie was registered in Saxony-Anhalt.

12.8 Anophthalmos/Microphthalmos (Q11.0/Q11.1/Q11.2)

	Number	Prevalence /10,000 births	Trend in comp. to basis prevalence
Major cities: 1 x Halle	1	2.0	↔
Districts	0	0.0	↓
Saxony-Anhalt	**1**	**0.6**	↔

Anophthalmos/Microphthalmos (2002-2013)		
	Basis prevalence /10,000 births	**Confidence Interval (CI of 95%)/10,000 births**
Cities	1.10	0.40 - 2.39
Districts	0.72	0.36 - 1.28
Region	0.82	0.48 - 1.31
EUROCAT 2001-2012	0.99	0.93 - 1.05
		0.12 Zagreb (Croatia)* 3.22 Odense (Denmark)**

*/** centres with lowest resp. highest prevalence/10,000 births

One live birth with microphthalmos was registered in 2014.
The **prevalence** lies with **0.6 per 10,000 births** within the confidence interval of the previous years. The basis prevalence of 2002-2013 lies at 0.8 per 10,000 births.

additional information:

pregnancy outcome	1 x termination of pregnancy
sex	1 x no indication
number of isolated malformations/MCA	1 x MCA

The pregnancy was terminated after 27 weeks of gestation after a prenatal diagnosis of a complex malformation syndrome.

In total, this malformation appears rather infrequently. Data of other EUROCAT centres also approve this fact.

Malformation combinations (MCA) or superordinated syndromes detected:

- Cardiac malformation, renal dysplasia

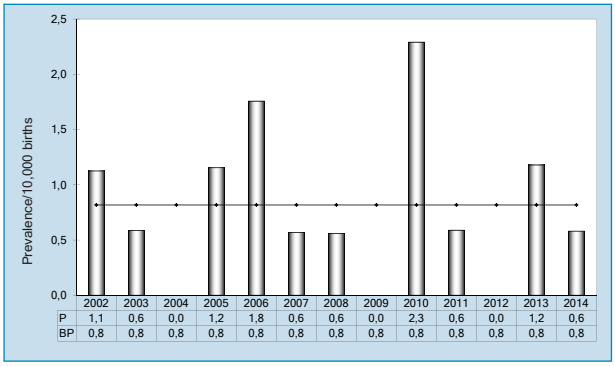


Fig. 15: Development of prevalence/10,000 births with anophthalmos/microphthalmos in the registration area since 2002

In 2014, one child/foetus with anophthalmos / microphthalmos per 17,238 births was registered in Saxony- Anhalt

12.9 Microtia/Anotia (Q16.0/Q17.2)

	Number	Prevalence /10,000 births	Trend in comp. to basis prevalence
Major cities	0	0.0	↓
Districts: 1 x Wittenberg	1	0.8	↔
Saxony-Anhalt	**1**	**0.6**	↓

Microtia/Anotia (2002-2013)		
	Basis prevalence /10,000 births	**Confidence Interval (CI of 95%)/10,000 births**
Cities	1.47	0.63 - 2.89
Districts	1.11	0.65 - 1.77
Region	1.20	0.78 - 1.77
EUROCAT	no information	no information

One birth with microtia was registered in 2014. The **prevalence of 0.6 per 10,000 births** lies under the confidence interval.

No EUROCAT data is present for comparison for this indicator malformation. EUROCAT indicates only for anotia a prevalence of 0,32 per 10,000 births (CI 0.29 - 0.36) for the years 2002-2013. The same data were registered in Saxony-Anhalt (2002-2013: 0.38 per 10,000 births, CI 0.17-0.76).

No additional hearing disorder was diagnosed at presence of a velocardiofacial syndrome.

additional information:

pregnancy outcome	1 x live birth
sex	1 x female
number of isolated malformations/MCA	1 x MCA

Malformation combinations (MCA) or superordinated syndromes detected:

- CATCH 22 with: Di George syndrome, truncus arterio sus communis, bicuspidal aortic valve, aortic vale insufficiency, VSD, ASD, right aortic arch, blt bony syndactyly of II. and III. toes, thymus hypoplasia

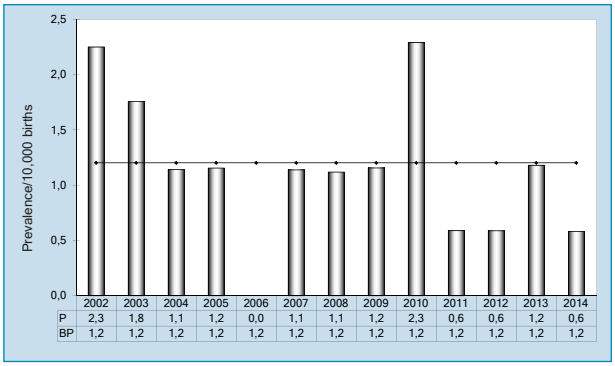


Fig. 16: Development of prevalence/10,000 births with micro tia/anotia in the registration area since 2002

In 2014, one child with microtia/anotia per 17,238 was registered in Saxony-Anhalt.

12.10 Tetralogy of Fallot (Q21.3)

	Number	Prevalence /10,000 births	Trend in comp. to basis prevalence
Major cities: 4 x Halle 2 x Magdeburg	6	12.2	↑
Districts: 1 x Börde 3 x Harz 2 x Salzlandkreis	6	4.9	↗
Saxony-Anhalt	**12**	**7.0**	↑

Tetralogy of Fallot (2002-2013)		
	Basis prevalence /10,000 births	**Confidence Interval (CI of 95%)/10,000 births**
Cities	3.30	1.96 - 5.22
Districts	3.32	2.48 - 4.37
Region	3.32	2.58 - 4.20
EUROCAT 2001-2012	3.20	3.09 - 3.32
		1.97 S Portugal* 5.16 Mainz (Germany)**

*/** centres with lowest resp. highest prevalence/10,000 births

12 registered births with Tetralogy of Fallot and a resulting **prevalence of 7.0 per 10,000 births** clearly exceeded our expectations for 2014 when regarding the number of cases we registered during the previous years.
As a result this issue was investigated for the first time in a cluster analysis in the present annual report. However, a common outer reason did thereby not turn out (see percentage of chromosomal reasons).

The 12-years basis prevalence lies with 3.3 per 10,000 births within the middle range of the EUROCAT register until 2012.

additional information:

pregnancy outcome	10 x live birth 1 x live birth, deceased at 7th day of life 1 x termination of pregnancy
sex	9 x male 3 x female
number of isolated malformations/MCA	11 x MCA 1 x isolated

In ten cases the diagnosis was already made prenatally. In one case the pregnancy was terminated after 21 weeks of gestation at presence of additional malformations. 11 infants were live births between 28 and 40 weeks of gestation. One infant was born after 37 weeks of gestation and deceased during the first month of life.

The cardiac malformation occurred in one case isolated. In two cases a microdeletion syndrome was already diagnosed prenatally.

Malformation combinations (MCA) or superordinated syndromes detected:

- CHARGE association with: cleft of hard palate with unilateral cleft lip, haemodynamical effective PDA at fullterm infant
- CATCH 22 with: Di George syndrome, multicystic dys plastic right kidney, small ears, thymus hypoplasia, missing septum pellucidum, craniofacial dysmorphy, PFO at preterm infant
- CATCH 22 with: Di George syndrome, blt not descended testis, PFO and haemodynamical effective PDA at fullterm infant, cerebellar hypoplasia, sound perception disorder (bilateral > 60 dB), DUP right
- CATCH 22 with: glandular hypospadias, blt hernia inguinalis at preterm infant
- lumbosacral spina bifida, microcephaly
- Omphalocele, glandular hypospadias
- Hydrocephalus internus
- Butterfly vertebrae, blt DUP II. grade, malformation of coronary vessels, tracheal stenosis, tracheomalacia, thrombosis of right Vena femoralis profunda, intestinal malformation, PFO at preterm infant
- Malformation of coronary vessels, haemodynamical not effective PDA at fullterm infant
- 2 x PFO at fullterm infant (1 x with blt retarded hip)

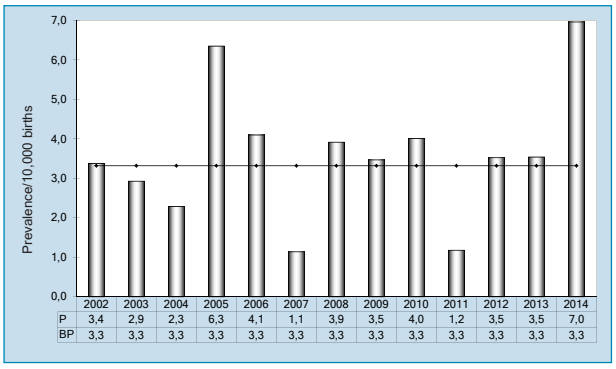


Fig. 17: Development of prevalence/10,000 births with tetralogy of fallot in the registration area since 2002

In 2014, one tetralogy of fallot per 1437 births was registered in Saxony-Anhalt.

12.11 Transposition of Great Vessels – TGV (Q20.1/Q20.3)

	Number	Prevalence /10,000 births	Trend in comp. to basis prevalence
Major cities: 4 x Halle 1 x Magdeburg	5	10.2	↑
Districts: 1 x Altmarkkreis Salzwedel 2 x Burgenlandkreis 1 x Börde 1 x Saalekreis	5	4.1	↔
Saxony-Anhalt	**10**	**5.8**	↗

Transposition of Great Vessels (2002-2013)		
	Basis prevalence /10,000 births	Confidence Interval (CI of 95%)/10,000 births
Cities	4.77	3.11 - 6.98
Districts	4.30	3.33 - 5.47
Region	4.42	3.57 - 5.42
EUROCAT 2001-2012 (Q20.3)	3.36	3.24 - 3.47
		1.34 S Portugal* 5.16 Styria (Austria)**

*/** centres with lowest resp. highest prevalence/10,000 births

A TGV was registered at 10 births in 2014.

The prevalence lies with 5.8 per 10,000 births at a rather high level and ranges slightly over the confidence interval of the previous years.

The basis prevalence of the years 2002 to 2013 lies with 4.4 per 10,000 births within the middle range of other EUROCAT register.

additional information:

pregnancy outcome	9 x live birth 1 x live birth, deceased until 7th day of life
sex	7 x male 3 x female
number of isolated malformations/MCA	8 x MCA 2 x isolated

All infants were live births between 29 and 39 weeks of gestation. In seven cases we received a prenatal finding about the TGV.

Malformation combinations (MCA) or superordinated syndromes detected:

- Edwards-Syndrome with: complete pulmonary vein misjunction, persistent left Vena cava superior, Corpus callosum agenesia, horseshoe kidney
- Microcephaly, persistent left Vena cava superior, malformed backbone, hemivertebrae, scoliosis, PFO at full term infant, DUP I. grade left, hypertelo rism, auricular tag right
- Stenosis and hypoplasia of pulmonary artery, ASD II, haemodynamical effective PDA at full term infant, malformation of urinary tract, malformed feet
- ASD, VSD, malformation of coronary vessels
- Pearson-syndrome with pancytopenia, PFO at full term infant, renal vein thrombosis
- 3 x PFO at full term infant (1 x with vein thrombosis)

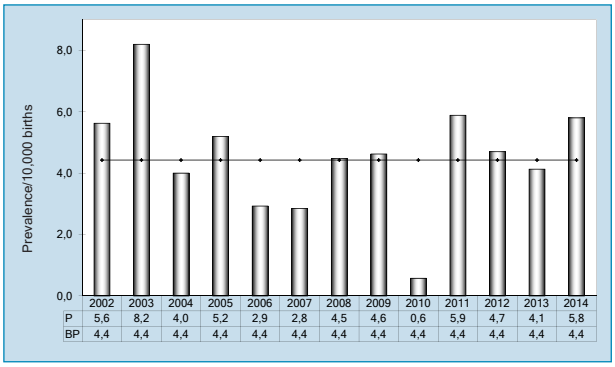


Fig. 18: Development of prevalence/10,000 births with transposition of great vessels in the registration area since 2002

In 2014, one transposition of great vessels per 1724 births was registered in Saxony-Anhalt.

12.12 Hypoplastic Left Heart Syndrome (Q23.4)

	Number	Prevalence /10,000 births	Trend in comp. to basis prevalence
Major cities	0	0.0	↓
Districts: 1 x Anhalt-Bitterfeld 1 x Börde 1 x Saalekreis 2 x Salzlandkreis	5	4.1	↑
Saxony-Anhalt	**5**	**2.9**	↔

Hypoplastic Left Heart Syndrome (2002-2013)		
	Basis prevalence /10,000 births	**Confidence Interval (CI of 95%)/10,000 births**
Cities	2.57	1.40 - 4.31
Districts	2.54	1.81 - 3.47
Region	2.55	1.91 - 3.33
EUROCAT 2001-2012	2.68	2.58 - 2.79
		0.86 Valencia Region (Spain)* 4.52 Malta**

*/** centres with lowest resp. highest prevalence/10,000 births

Five births with hypoplastic left heart syndrome were registered in 2014.
The prevalence of 2014 of 2.9 per 10,000 births lies within the range of the previous years and meets the values of 2012, 2009 and 2006. It also lies within the confidence interval.

Compared to other EUROCAT centres, the prevalence of Saxony-Anhalt lies within the middle range.

additional information:

pregnancy outcome	3 x live birth 2 x termination of pregnancy
sex	2 x male 3 x female
number of isolated malformations/MCA	5 x MCA

Two pregnancies were terminated at presence of a prenatal finding after 19 weeks of gestation. However, in all cases the prenatal diagnosis of hypoplastic left heart syndrome was made.

Malformation combinations (MCA) or superordinated syndromes detected:

- Gastroschisis, blt missing of thumbs and radius, blt hypoplastic ulna, clubhands, koilosternia, low set ears, mandibular micrognathy, hypertelorism, saddle nose
- Coarctation of aorta, corrected transposition of great vessels, laryngomalacia
- Stenosis of left and right pulmonary artery, splenic cyst
- Corpus callosum agenesia
- Fetopathia diabetica

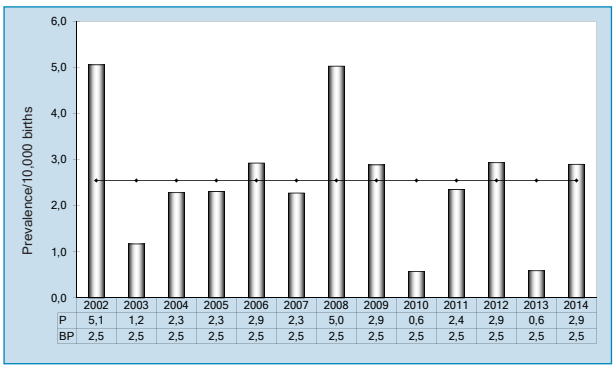


Fig. 19: Development of prevalence/10,000 births with hypoplastic left heart syndrome in the registration area since 2002

In 2014, one child with a hypolastic left heart syndrome per 3448 births was registered in Saxony-Anhalt.

12.13 Coarctation of Aorta (Q25.1)

	Number	Prevalence /10,000 births	Trend in comp. to basis prevalence
Major cities: 1 x Halle 2 x Magdeburg	3	6.1	↔
Districts: 2 x Anhalt-Bitterfeld 1 x Burgenlandkreis 1 x Börde 3 x Mansfeld-Südharz 1 x Saalekreis 2 x Salzlandkreis 1 x Stendal 1 x Wittenberg	12	9.7	↑
Saxony-Anhalt	**15**	**8.7**	↑

Coarctation of Aorta (2002-2013)		
	Basis prevalence /10,000 births	**Confidence Interval (CI of 95%)/10,000 births**
Cities	4.58	2.97 - 6.77
Districts	5.08	4.02 - 6.34
Region	4.95	4.10 - 5.96
EUROCAT 2001-2012	1.32	1.25 - 1.40
		0.24 S Portugal* 3.54 Vaud (Switzerland)**

*/** centres with lowest resp. highest prevalence/10,000 births

With 15 registered births with coarctation of aorta the number of cases slightly increased in 2014, however it remains under the peak value we registered in 2008.
The **prevalence** lies with **8.7 per 10,000 births** above the 12-years confidence interval.

A prenatal diagnosis of Vitium cordis was made in five cases. Two pregnancies were terminated at presence of complex additional malformations (16th and 19th WOG). Twelve infants were live births between 30 and 41 weeks of gestations.

additional information:

pregnancy outcome	12 x live births 1 x spontaneous abortion 2 x termination of pregnancy
sex	8 x male 7 x female
number of isolated malformations/MCA	14 x MCA 1 x isolated

Especially the coarctation of aorta is often not identified during prenatal diagnostics and it is also often not detected during the first two days after delivery in the materny clinic. However, the pulse oximetry screening has become a common examination method in Saxony-Anhalt and therefore the percentage of late diagnosed critical cardiac malformations is very low.

This aspect should be regarded when local data is compared to other EUROCAT register. The often late diagnosed cases therefore are not counted in some European registers and the European average prevalence of the years 2001-2012 is for this reason significantly lower than our value.

Only in two cases the coarctation of aorta occurred isolated. In one case it was classified in combination with a hypoplastic left heart syndrome, as an additional transposition was present.

Malformation combinations (MCA) or superordinated syndromes detected:

- Down syndrome with: Canalis atrioventricularis communis, bicuspidal aortic valve, subvalvular aortic stenosis, glandular hypospadias, nesidioblastosis, hepatic insufficiency
- Unbalanced chromosomal translocation with: hydrocephalus, right located aorta ascendens, vascular ring as a result of the abnormal right subclavicular artery, VSD, median cleft palate and uvula, corpus callosum hypoplasia, intestinal malrotation, kyphosis, chicken breast, sacral dimple (1,2 cm deep), mandibular micrognathia, less marked philtrum, lateral ascending lid axis, epicanthus internus, wide cranial sutures
- Turner syndrome with: hygroma colli cysticum, clubfoot right, flat chest, craniofacial dysmorphy
- Left heart hypoplasia syndrome, corrected transposition of great vessels, laryngomalacy
- Gastroschisis, VSD, lateral cervical cyst
- VSD, penoscrotal hypospadias
- Bicuspidal aortic valve, aortic valve insufficiency, sound perception disorder (right 50 dB, left 40 dB), high palate
- ASD II, bicuspidal aortic valve
- Persistent left vena cava superior, left ventricular myocardhypotrophy, blt hernia inguinalis at preterm infant
- VSD, haemodynamical effective PDA and PFO at preterm infant
- VSD, craniofacial dysmorphy
- 2 x VSD
- PFO at full term infant

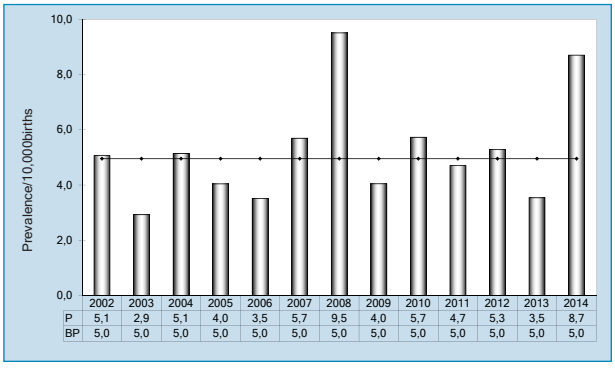


Fig. 20: Development of prevalence/10,000 births with coarctation of aorta in the registration area since 2002

In 2014, one coarctation of aorta per 1149 births was registered in Saxony-Anhalt.

12.14 Cleft Lip With or Without Cleft Palate (Q36./Q37.)

	Number	Prevalence /10,000 births	Trend in comp. to basis prevalence
Major cities: 1 x Dessau-Roßlau 2 x Halle 1 x Magdeburg	4	8.1	↓
Districts: 1 x Anhalt-Bitterfeld 1 x Burgenlandkreis 2 x Börde 1 x Harz 1 x Jerichower Land 2 x Mansfeld-Südharz 3 x Salzlandkreis 1 x Wittenberg	12	9.7	↓
Saxony-Anhalt	**16**	**9.3**	↓

Cleft Lip With or Without Cleft Palate (2002-2013)		
	Basis prevalence /10,000 births	**Confidence Interval (CI of 95%)/10,000 births**
Cities	14.49	11.47 - 18.05
Districts	13.23	11.57 - 15.12
Region	13.56	12.10 - 15.19
EUROCAT 2001-2012	8.79	8.60 - 8.98
		4.27 S Portugal* 14.31 Odense (Denmark)**

*/** centres with lowest resp. highest prevalence/10,000 births

In 2014, we registered 16 births with cleft lip with or without cleft palate.
Therefore, our **prevalence of 9.3 per 10,000 births** lies under the confidence interval of the previous years and meets the values we registered in 2008/2009.

Compared to EUROCAT data our prevalence lies within the middle range of other European malformation registration centres.

In ten cases a cleft lip with cleft jaw and palate was present, in four cases a cleft upper lip and in two cases a cleft lip and jaw. In 12 cases the cleft appeared unilateral, in two cases bilateral (no indication in two cases).

additional information:

pregnancy outcome	14 x live births 2 x termination of pregnancy
sex	15 x male 1 x female
number of isolated malformations/MCA	5 x MCA 11 x isolated

14 infants were live births between 36 and 40 weeks of gestation. In two cases the pregnancy was terminated after 16 weeks of gestation as prenatally additional complex cerebral malformations were diagnosed. One fetocide occurred after 33 weeks of gestation.

An isolated orofacial cleft formation appeared in 11 cases. In the remaining five cases a chromosomal aberration was the malformation reason or additional malformations were present. A combination with a hearing disorder (sound conduction disorder) was reported only in one case.

Malformation combinations (MCA) or superordinated syndromes detected:

- Triploidy with: VSD, right aortic arch, mandibular micrognathia, hypoplastic right kidney
- CHARGE association with: Fallot Tetralogy, haemodynamical effective PDA at full term infant
- indifferent sex, microcephaly, cerebral reduction malformation, cardiac malformation, intestinal malformation
- blt undescended testis
- sound conducting disorder right

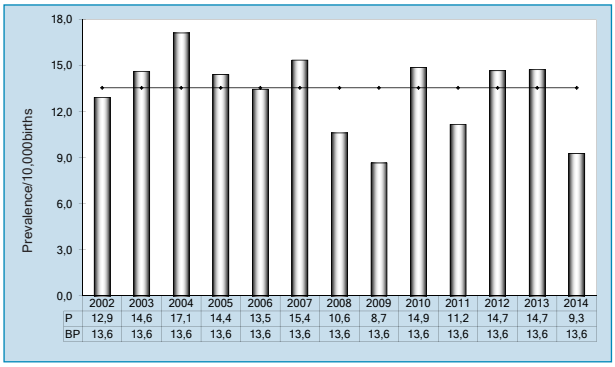


Fig. 21: Development of prevalence/10,000 births with cleft lip with or without cleft palate in the registration area since 2002

In 2014, one child with cleft lip with or without cleft palate per 1077 births was registered in Saxony-Anhalt.

12.15 Cleft Palate (Q35.1/Q35.3/Q35.5/Q35.9)

	Number	Prevalence /10,000 births	Trend in comp. to basis prevalence
Major citiese: 2 x Halle 2 x Magdeburg	4	8.1	↔
Districs: 1 x Börde 1 x Jerichower Land 2 x Mansfeld-Südharz 1 x Saalekreis 4 x Salzlandkreis	9	7.3	↔
Saxony-Anhalt	**13**	**7.5**	↔

Cleft Palate (2002-2013)		
	Basis prevalence /10,000 births	**Confidence Interval (CI of 95%)/10,000 births**
Cities	6.78	4.78 - 9.35
Districts	7.30	6.10 - 8.72
Region	7.16	6.13 - 8.37
EUROCAT 2001-2012	5.78	5.63 - 5.94
		2.99 Valencia Region (Spain)* 10.85 Malta**

*/** centres with lowest resp. highest prevalence/10,000 births

We registered 13 births with cleft palate in 2014, this corresponds to the number of cases we registered in 2013. The calculated **prevalence** lies with **7.5 per 10,000 births** within the middle range of the previous years.

A comparison with other EUROCAT centres shows that cleft palate has, similar to the cleft lip with cleft palate, a frequency of appearance within the upper third.

We analyzed how far the average prevalence (chapter 12.37) changed during the previous years. The result that was presented in our last two annual reports was a significant decreasing trend. These observations resulted from very high prevalences 2001/2002 and very low prevalences 2008-2011. However, when we include also the years before 2001 in our analysis the prevalence fluctuates very much. During the time period of 2002-2014 no significant decreasing prevalences can be observed any more.

Eleven infants were live births between 36 and 40 weeks of gestations. One full term infant was delivered with complex additional malformations and deceased after seven days. In two cases complex additional malformations were diagnosed prenatally and a termination of pregnancy took place in each case after 19 weeks of gestations.

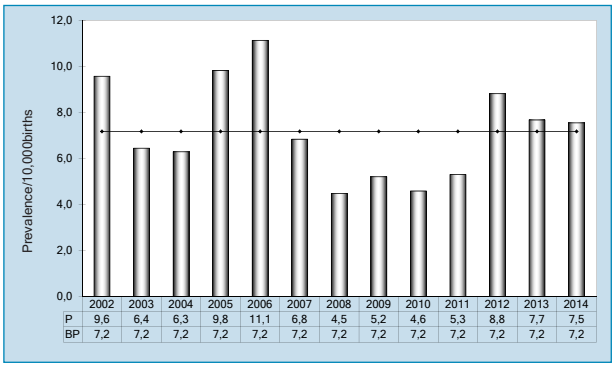
additional information:

pregnancy outcome	10 x live births 1 x live birth, deceased after 7 days 2 x termination of pregnancy
sex	9 x male 4 x female
number of isolated malformations/MCA	7 x MCA 6 x isolated

The cleft palate occurred in six cases isolated and in seven cases we registered additional malformations. The reported hearing disorder of a sound perception disorder was classified as an additional malformation and not as a result of the cleft palate. In three cases the cleft palate appeared in combination with a Pierre-Robin-Sequence.

Malformation combinations (MCA) or superordinated syndromes detected:

- Walker-Warburg-Syndrome with: blt renal dysplasia, hydrocephalus, cerebellar hypoplasia, aortic valve stenosis, ocular malformation, hypoplastic nasal bone, craniofacial dysmorphy
- Unbalanced chromosomal translocation with: coarctation of aorta, right located aorta ascendens, vascular ring through the abnormal right subclavicular artery, VSD, hydrocephalus, Corpus callosum hypoplasia, intestinal malrotation, khyphosis, chicken breast, sacral dimple (1,2 cm deep), mandibular micrognathia, not well marked philtrum, lateral ascending lid axis, epicanthus internus, wide cranial sutures
- Hydrocephalus, Corpus callosum hypoplasia, DUP III. Grade right and II. grade left, hypoplastic septum pellucidum
- VACTERL-association with: anal atresia (with fistula), blt hypoplasia of radius and thumb, canalis atrioventricularis communis, ASD II, mitral valve insufficiency, trikuspidal valve insufficiency, DUP II. Grade right, klinodactyly of V. finger, mandibular micrognathia, dysplastic ears
- combined sound conduction and perception disorder (blt 45 dB), undescended left testis at fullterm infant)
- sound perception disorder (right 30 dB, left 40 dB
- Sound conduction disorder (blt 45 dB), mandibular micrognathia, sacral dimple (ca. 6 mm)



	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014
P	9,6	6,4	6,3	9,8	11,1	6,8	4,5	5,2	4,6	5,3	8,8	7,7	7,5
BP	7,2	7,2	7,2	7,2	7,2	7,2	7,2	7,2	7,2	7,2	7,2	7,2	7,2

Fig. 22: Development of prevalence/10,000 births with cleft palate in the registration area since 2002

In 2014, one child with cleft palate per 1326 births was registered in Saxony-Anhalt.

12.16 Choanal Atresia (Q30.0)

	Number	Prevalence /10,000 births	Trend in comp. to basis prevalence
Major cities	0	0.0	↘
Districts: 1 x Anhalt-Bitterfeld 1 x Burgenlandkreis 2 x Harz 2 x Salzlandkreis 1 x Wittenberg	7	5.7	↑
Saxony-Anhalt	**7**	**4.1**	↑

Choanal Atresia (2002-2013)		
	Basis prevalence /10,000 births	**Confidence Interval (CI of 95%)/10,000 births**
Cities	0.37	0.04 - 1.32
Districts	0.46	0.18 - 0.94
Region	0.43	0.20 - 0.82
EUROCAT 2001-2012	0.89	0.83 - 0.95
		0.05 S Portugal* 2.04 Styria (Austria)**

*/** centres with lowest resp. highest prevalence/10,000 births

The rarely appearing malformation choanal atresia was registered more frequently than usual in 2014 in Saxony Anhalt and it was reported to our Monitoring Center in seven cases.
Therefore, the **prevalence of 4.1 per 10,000 births**, lies significantly above the confidence interval. Not more than three births with this malformation were registered in the last years.

Also the European comparison shows an average prevalence of under 1 of 10,000 births.

additional information:

pregnancy outcome	5 x live births 1 x live birth, deceased within 7 days of life 1 x live birth, deceased after 7 days
sex	4 x male 3 x female
number of isolated malformations/MCA	5 x MCA 2 x isolated

When analyzing the similarities of all seven live births, a geographical relation becomes obvious. Six infants are resident in a region between Halberstadt and Wörlitz. Additionally, the date of conception lies in all cases between May 2013 and January 2014.

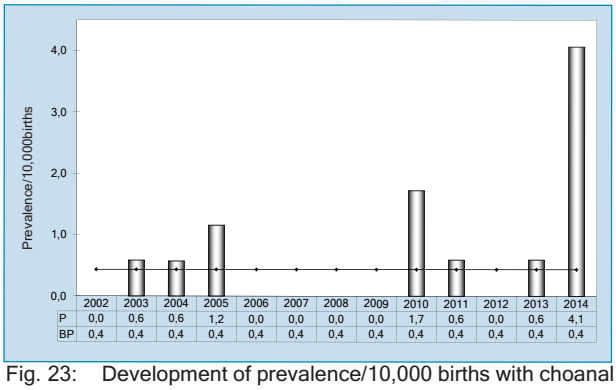
Another aspect is that a current case control study (Gnoth & Mallmann 2014) describes a significant connection between choanal atresia and hyperthyreosis of the child's mother. Two of the mothers suffered from this disease. We are not able to make a final conclusion in this issue as the permanent medication was not reported in all cases. However, further observations and case related cause studies are planned

.

In this connection we want to point out that thyreostatic drugs are diaplacental effective. However, thyroid diseases in need of a treatment can not remain without medical treatment during pregnancy. Especially, after "intake of Carbimazol/Thiamazol a rarely appearing malformation constellation is described", that corresponds to a VACTERL association (Source: www.embryotox.de).
A study by Yoshihara et al. 2012 investigates if a hyperthyreosis should be rather treated with Propylthiouracil (possible severe maternal liver toxicity) or with Carbimazol/Methimazol (possible fetal damage). This investigation comes to the conclusion that both options are possible as the mentioned consequences in both cases appear rather seldom.

Malformation combinations (MCA) or superordinated syndromes detected:

- VACTERL-association with: oesophageal atresia (with tracheoesophageal fistula), hemivertebra (T10 vertebra), right convex thoracic spine scoliosis, missing of 10th rib, mandibular retrognathia, low set ears, blt auricular tag, wide nose bridge
- Fallot-tetralogy, cleft of hard palate with unilateral cleft lip, haemodynamical effective PDA at fullterm infant
- CHARGE association with: renal agenesis left side, plasma protein metabolism disorder, Truncus arteriosus communis, ureteropelvic junction obstruction and DUP IV. grade right, auditory ossicle malformation left, low set dysplastic ears
- microcephalie
- truncus arteriosus communis, VSD, malformation of coronary vessels, laryngomalacia



	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014
P	0,0	0,6	0,6	1,2	0,0	0,0	0,0	0,0	1,7	0,6	0,0	0,6	4,1
BP	0,4	0,4	0,4	0,4	0,4	0,4	0,4	0,4	0,4	0,4	0,4	0,4	0,4

Fig. 23: Development of prevalence/10,000 births with choanal atresia in the registration area since 2002

In 2014, one child with a choanal atresia per 2463 births was registered in Saxony-Anhalt.

References:

- Gnoth C, Mallmann P: Perikonzeptionelle Frauenheilkunde: Fertilitätserhalt, Prävention und Management von Schwangerschaftsrisiken. Berlin Heidelberg: Springer Berlin Heidelberg 2014.
- Yoshihara A, Noh J, Yamaguchi T, et al.: Treatment of graves' disease with antithyroid drugs in the first trimester of pregnancy and the prevalence of congenital malformation. The Journal of clinical endocrinology and metabolism 2012; 97: 2396-403.

12.17 Oesophageal Atresia/-Stenosis/-Fistula (Q39.0-Q39.4)

	Number	Prevalence /10,000 births	Trend in comp. to basis prevalence
Major cities	0	0.0	↓
Districts: 1 x Harz	1	0.8	↓
Saxony-Anhalt	**1**	**0.6**	↓

Oesophageal Atresia/-Stenosis/-Fistula (2002-2013)		
	Basis prevalence /10,000 births	**Confidence Interval (CI of 95%)/10,000 births**
Cities	3.30	1.96 - 5.22
Districts	2.54	1.81 - 3.47
Region	2.74	2.08 - 3.55
EUROCAT 2001-2012 (Q39.0-Q39.1)	2.37	2.27 - 2.46
		0.46 SE Ireland*
		4.30 Mainz (Germany)**

*/** centres with lowest resp. highest prevalence/10,000 births

One birth with oesosophageal atresia was registered in 2014.
The **prevalence of 0.6 per 10,000 births** lies significantly under the 12-years prevalence of the time period 2002-2013 (2.7 per 10,000 births).

The European comparison for the years 2001 -2012 shows an average prevalence of the different registration centres of 2.4 per 10,000 births. The basis prevalence of Saxony Anhalt corresponds to the European prevalence.

additional information:

pregnancy outcome	1 x live birth, deceased within 7 days of life
sex	1 x male
number of isolated malformations/MCA	1 x MCA

The infant deceased at presence of compelex additional malformations within the first week of life.

Malformation combinations (MCA) or superordinated syndromes detected:

- VACTERL-association with: blt choanal atresia, hemivertebra (T10 vertebra), right convex thoracic spine scoliosis, missing of 10th rib, mandibular retrognathia, low set ears, blt auricular tag, wide nose bridge

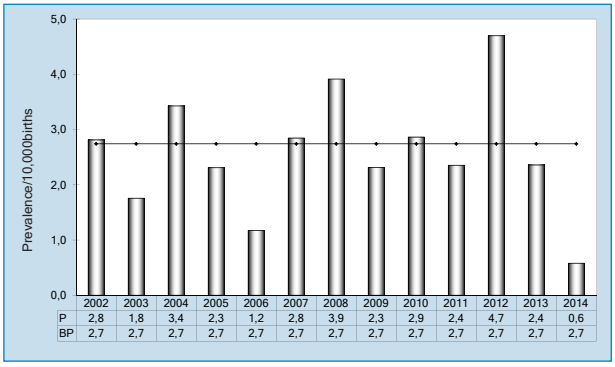


Fig. 24: Development of prevalence/10,000 births with oesophageal atresia/stenosis/fistula in the registration area since 2002

In 2014, one oesophageal atresia/fistula per 17238 births was registered in Saxony-Anhalt.

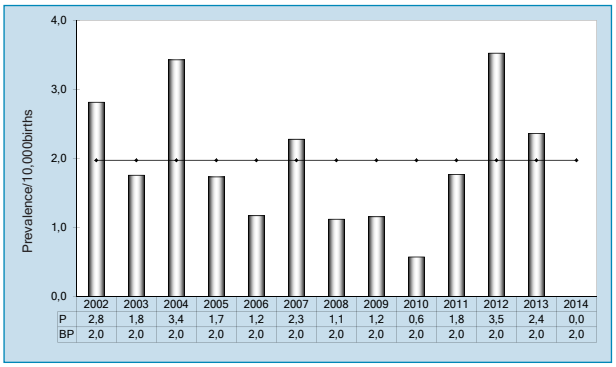
12.18 Small Intestinal Atresia/Stenosis(Q41.1/Q41.2/Q41.8/Q41.9)

	Number	Prevalence /10,000 births	Trend in comp. to basis prevalence
Major cities	0	0.0	↓
Districts	0	0.0	↓
Saxony-Anhalt	**0**	**0.0**	↓

Small Intestinal Atresia/Stenosis (2002-2013)		
	Basis prevalence /10,000 births	Confidence Interval (CI of 95%)/10,000 births
Cities	1.28	0.52 - 2.64
Districts	2.22	1.53 - 3.10
Region	1.97	1.41 - 2.67
EUROCAT 2001-2012 (Q41.1-Q41.8)	0.81	0.75 - 0.87
		0.27 Wielkopolska (Poland)*
		1.68 Isle de la Reunion (France)**

*/** centres with lowest resp. highest prevalence/10,000 births

In 2014, no births with small intestinal atresia were registered. The 12-years basis prevalence lies with 2,0 per 10,000 births above the maximum values of other EUROCAT register.



	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014
P	2,8	1,8	3,4	1,7	1,2	2,3	1,1	1,2	0,6	1,8	3,5	2,4	0,0
BP	2,0	2,0	2,0	2,0	2,0	2,0	2,0	2,0	2,0	2,0	2,0	2,0	2,0

Fig. 25: Development of prevalence/10.000 births with small intestinal atresia/stenosis in the registration area since 2002

In 2014, no small intestinal atresia/stenosis was registered in Saxony-Anhalt.

12.19 Anorectal Atresia/ Stenosis (Q42.0-Q42.3)

	Number	Prevalence /10,000 births	Trend in comp. to basis prevalence
Major cities: 1 x Halle	1	2.0	↓
Districts: 1 x Börde 1 x Stendal	2	1.6	↓
Saxony-Anhalt	**3**	**1.7**	↓

Anorectal Atresia/ Stenosis (2002-2013)		
	Basis prevalence /10,000 births	**Confidence Interval (CI of 95%)/10,000 births**
Cities	6.23	4.32 - 8.71
Districts	5.02	3.96 - 6.27
Region	5.34	4.45 - 6.38
EUROCAT 2001-2012	3.02	2.91 - 3.13
		1.34 S Portugal* 7.42 Styria (Austria)**

*/** centres with lowest resp. highest prevalence/10,000 births

We registered three births with anorectal atresia/stenosis in 2014.
The calculated **prevalence** of **1.7 per 10,000 births** is again regressive in contrast to the maximum value that was registered in 2008. It also lies below the confidence interval of the last 12 years.

In the European comparison our annual malformation prevalence for anorectal atresia/stenosis lies in the lower third.

additional information:

pregnancy outcome	2 x live births 1 x live birth, deceased after 7 days of life
sex	2 x male 1 x female
number of isolated malformations/MCA	3 x MCA

In all registered cases an anal atresia was present, one time it occurred without and two times with fistula.

In two cases additional malformations were already detected prenatally. However, a prenatal diagnosis of additional malformations was made in all cases. The infants were born between 35 and 38 weeks of gestations.

Malformation combinations (MCA) or superordinated syndromes detected:

- OEIS complex with: omphalocele, occult sacral meningocele, tethered cord syndrome, bladder extrophy, indifferent sex, cloacal persistence, megaureter and DUP I. grade left, VSD,
  PFO and haemodynamic not effective PDA at preterm infant
- VACTERL association with: cleft palate at Pierre-Robin-sequence, blt hypoplasia of radius and thumb, canalis atrioventricularis communis, ASD II, mitral valve insufficiency, tricuspidal valve insufficiency, DUP II. grade right, clinodactyly of V. finger, mandibular micrognathia, dysplastic ears
- VACTERL association with: aortic atresia, VSD, ASD, haemodynamic effective PDA at fullterm infant, vertebral body anomaly (T9,10 vertebra), scoliosis, duplex left kidney, low set ears, thymushypoplasia, sacral dimple, small haemangioma

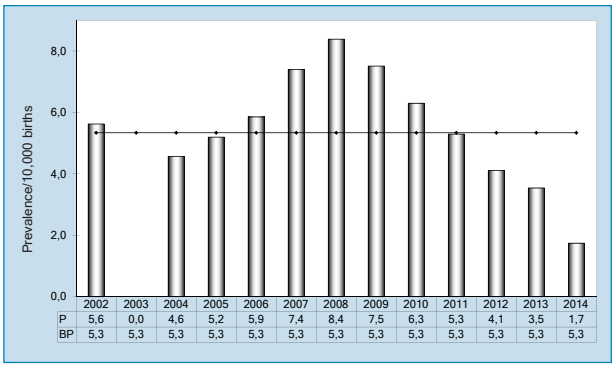


Fig. 26: Development of prevalence/10,000 births with anorectal atresia/-stenosis in the registration area since 2002

In 2014, one anorectal atresia/ stenosis per 5746 births was registered in Saxony-Anhalt.

12.20 Undescended Testis (Q53.1-Q53.9)

	Number	Prevalence /10,000 births	Trend in comp. to basis prevalence
Major cities: 6 x Magdeburg	6	12.2	↘
Districts: 1 x Altmarkkreis Salzwedel 3 x Anhalt-Bitterfeld 2 x Börde 1 x Harz 3 x Jerichower Land 1 x Saalekreis 5 x Salzlandkreis	16	13.0	↑
Saxony-Anhalt	**22**	**12.8**	↑

Undescended Testis (2002-2013)		
	Basis prevalence /10,000 births	Confidence Interval (CI of 95%)/10,000 births
Cities	15.77	12.62 - 19.47
Districts	5.34	4.25 - 6.63
Region	8.08	6.97 - 9.35
EUROCAT	no information	no information

We registered 22 male infants/foetuses with undescended testis in 2014t.
The prevalence of 12.8 per 10,000 births is higher than the prevalence we calculated in the last eight years.

At a missing clinical relevance of maldescensus testis until the sixth month of life, we have to assume that this malformation is underreported. Furthermore, the maldescensus testic can be considered as physiological state at a preterm infant. Therefore, a correct classification is urgently necessary and only fullterm infants are counted.

Both testicles were concerned in ten cases (four cases occurred isolated without any additional malformations), in seven cases the malformation occurred unilateral left and in another five cases unilateral right. No additional malformations appeared in 12 cases.

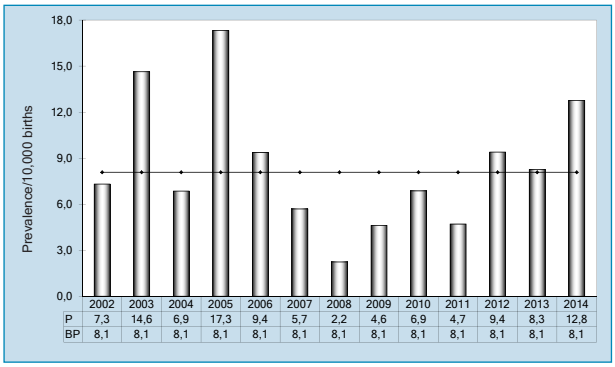
A routine registration via EUROCAT data does not take place as a correct classification cannot be assured in every case because of the physiological state. An under or over registration of this malformation is suggested by EUROCAT and for that reason no comparison data is present.

additional information:

pregnancy outcome	22 x live births
sex	22 x male
number of isolated malformations/MCA	10 x MCA 12 x isolated

Malformation combinations (MCA) or superordinated syndromes detected:

- Down syndrome with: haemodynamic not effective PDA at fullterm infant
- CATCH 22 with: Di George syndrome, Fallot Tetralogy, PFO and haemodynamic effective PDA at fullterm infant, cerebellar hypoplasia, sound perception disorder (blt > 60 dB), DUP right
- Megacystis-megaureter-syndrome with: blt megaureter and functionless right kidney, DUP III. grade right and II. grade left
- Blt duplex kidney and DUP I. grade, blt syndactyly of II. and III. toes
- Blt cleft palate, combined sound conduction and perception disorder (blt 45 dB)
- Blt cleft lip with cleft jaw and palate
- penoscrotal hypospadias
- 3 x ASD (1 x with PDA at fullterm infant)



	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014
P	7,3	14,6	6,9	17,3	9,4	5,7	2,2	4,6	6,9	4,7	9,4	8,3	12,8
BP	8,1	8,1	8,1	8,1	8,1	8,1	8,1	8,1	8,1	8,1	8,1	8,1	8,1

Fig. 27: Development of prevalence/10,000 births with undescended testis in the registration area since 2002

In 2014, one child with undescended testis per 784 births (405 boys) was registered in Saxony-Anhalt.

12.21 Hypospadias (Q54.0-Q54.3/Q54.8/Q54.9)

	Number	Prevalence /10,000 births	Trend in comp. to basis prevalence
Major cities: 5 x Halle 4 x Magdeburg	9	18.3	↔
Districts: 5 x Anhalt-Bitterfeld 2 x Burgenlandkreis 5 x Harz 2 x Jerichower Land 3 x Saalekreis 1 x Salzlandkreis 2 x Stendal 1 x Wittenberg	21	17.0	↔
Saxony-Anhalt	**30**	**17.4**	↔

Hypospadias (2002-2013)		
	Basis prevalence /10,000 births	Confidence Interval (CI of 95%)/10,000 births
Cities	21.27	17.82 - 25.33
Districts	17.92	15.97 - 20.11
Region	18.80	17.06 - 20.71
EUROCAT 2001-2012	17.42	17.16 - 17.69
		4.03 Northern England (UK)* 37.51 Malta**

*/** centres with lowest resp. highest prevalence/10,000 births

30 births with hypospadias were registered in 2014. The annual prevalence lies with a value of 17.4 per 10,000 births at the lower limit of the confidence interval of the previous years. At the same time it meets the values we registered in 2011 and 2012.

In the current year, a comparison with EUROCAT data takes place in chapter 16 (page 74) within the discussion of our special topic.

additional information:

pregnancy outcome	29 x live births 1 x live birth, deceased after 7 days of life
sex	30 x male
number of isolated malformations/MCA	11 x MCA 19 x isolated

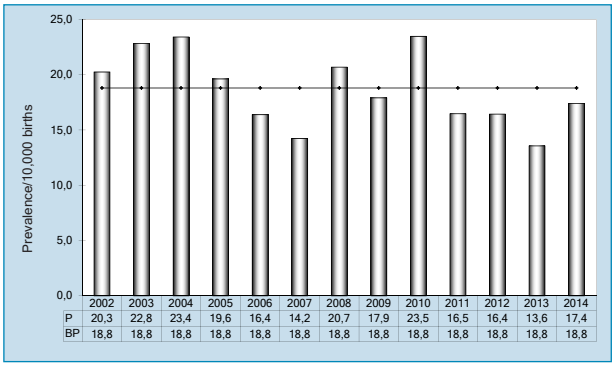
In 19 cases a hypospadias occured without any additional malformations. 21 boys suffered from a glandular hypospadias, one time a coronare hypospadias was present, another time a penile hypospadias was present and four infants suffered from a severe penoscrotale hypospadias. In three cases we received no indication about the severity of the malformation.

During the time period of 2011 to 2013 the annual prevalences of Saxony Anhalt remained clearly under the confidence interval of the basis prevalence.

In connection with annual prevalences above the confidence interval of the basis prevalence which we calculated during the time period of 2001 to 2005 a significant decreasing trend was presented in our last annual report (Chapter 12). The analysis of the years 2002-2014 shows that this trend is not significant any more. When including the values of the current year the result of the previous year is relativised.

Malformation combinations (MCA) or superordinated syndromes detected:

- Down syndrome with: coarctation of aorta, canalis atrioventricularis communis, bicuspidal aortic valve, subvalvular aortic stenosis, nesidioblastosis, hepatic insufficiency
- CATCH 22 with: Fallot tetralogy, blt hernia inguinalis at preterm infant
- Omphalocele, Fallot tetralogy
- Coarctation of aorta, VSD
- Microcephaly
- Blt undescended testis
- Silver-Russell-Syndrome with: blt sound perception disorder, nesidioblastosis, haemodynamic not effective PDA and PFO at preterm infant
- Arthrogryposis multiplex congenita, segmentation defects up to C3 vertebra, butterfly vertebra (C7 vertebra), Corpus callosum agenesia, dilated cerebral ventricle
- Truncus arteriosus communis, VSD, ASD II, vascular ring trough the abnormal right subclavicular artery, right aortic arch, urethral divertikel (at front), hypoplastic penis, ankyloglossia
- VSD, aortic anomaly, ASD II, persistence of the left vena cava superior
- Blt DUP III. grade, ASD, haemodynamic not effective PDA at fullterm infant, very big fontanelle



	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014
P	20,3	22,8	23,4	19,6	16,4	14,2	20,7	17,9	23,5	16,5	16,4	13,6	17,4
BP	18,8	18,8	18,8	18,8	18,8	18,8	18,8	18,8	18,8	18,8	18,8	18,8	18,8

Fig. 28: Development of prevalence/10,000 births with hypospadias in the registration area since 2002

In 2014, one hypospadias per 575 births (297 boys) was registered in Saxony-Anhalt.

12.22 Epispadias (Q64.0)

	Number	Prevalence /10,000 births	Trend in comp. to basis prevalence
Major cities	0	0.0	↔
Districts	0	0.0	↘
Saxony-Anhalt	**0**	**0.0**	↓

Epispadias (2002-2013)		
	Basis prevalence /10,000 births	Confidence Interval (CI of 95%)/10,000 births
Cities	0.18	0.00 - 1.02
Districts	0.33	0.11 - 0.76
Region	0.29	0.11 - 0.63
EUROCAT	no information	no information

No case of epispadias was registered in 2014. It is the fourth consecutive year without the appearence of epispadias.

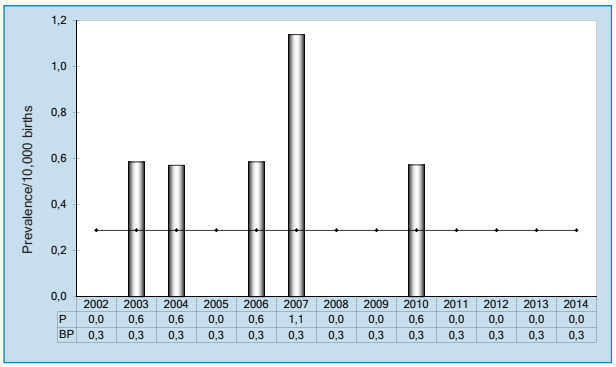


Fig. 29: Development of prevalence/10,000 births with epispadias in the registration area since 2002

In 2014, no birth with epispadias was registered in Saxony-Anhalt.

12.23 Indeterminate Sex (Q56.)

	Number	Prevalence /10,000 births	Trend in comp. to basis prevalence
Major cities: 1 x Halle	1	2.0	↑
Districts: 1 x Stendal	1	0.8	↔
Saxony-Anhalt	**2**	**1.2**	↗

Indeterminate sex (2002-2013)		
	Basis prevalence /10,000 births	**Confidence Interval (CI of 95%)/10,000 births**
Cities	0.18	0.00 - 1.02
Districts	0.65	0.31 - 1.20
Region	0.53	0.26 - 0.95
EUROCAT 2001-2012	0.66	0.61 - 0.72
		0.29 Mainz (Germany)* 1.60 Wessex (UK)**

*/** centres with lowest resp. highest prevalence/10,000 births

Two births with indeterminate sex were registered in 2014.
The calculated prevalence of 1.2 per 10,000 births lies slightly above the confidence interval of the last 12 years.

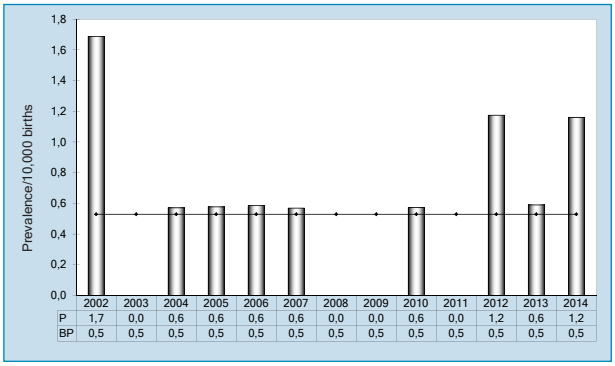
Compared to EUROCAT data, our calculated annual prevalence lies within the upper third of other registers' values for the years 2001-2012.

additional information:

pregnancy outcome	1 x live births 1 x termination of pregnancy
sex	2 x male
number of isolated malformations/MCA	2 x MCA

Malformation combinations (MCA) or superordinated syndromes detected:

- OEIS complex with: Omphalocele, occult sacral meningocele, tethered cord syndrome, bladde exstrophy, anal atresia with fistula, cloacal persistence, megaureter and DUP I. grade left, VSD, PFO and haemodynamic not effective PDA at preterm infant
- Cleft lip with cleft jaw and palate, microcephaly, cerebral reduction malformation, cardiac malformation, intestinal malformation



	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014
P	1,7	0,0	0,6	0,6	0,6	0,6	0,0	0,0	0,6	0,0	1,2	0,6	1,2
BP	0,5	0,5	0,5	0,5	0,5	0,5	0,5	0,5	0,5	0,5	0,5	0,5	0,5

Fig. 30: Development of prevalence/10,000 births with indeterminate sex in the registration area since 2002

In 2014, one birth with indeterminate sex per 8619 was registered in Saxony-Anhalt.

12.24 Potter Sequence (Q60.6)

	Number	Prevalence /10,000 births	Trend in comp. to basis prevalence
Major cities: 2 x Magdeburg	2	4.1	↗
Districts: 1 x Altmarkkreis Salzwedel 1 x Börde 1 x Harz 1 x Jerichower Land 1 x Saalekreis 1 x Stendal	6	4.9	↑
Saxony-Anhalt	**8**	**4.6**	↑

Potter sequence (2002-2013)		
	Basis prevalence /10,000 births	**Confidence Interval (CI of 95%)/10,000 births**
Cities	2.02	1.01 - 3.61
Districts	2.22	1.53 - 3.10
Region	2.16	1.58 - 2.90
EUROCAT 2001-2012	1.17	1.10 - 1.24
		0.53 S Portugal* 5.44 Mainz (Germany)**

*/** centres with lowest resp. highest prevalence/10,000 births

Eight births with Potter sequence (**prevalence: 4.6 per 10,000 births**) were registered in 2014. Therefore the prevalence exceeds again the already very high value of the previous year and lies clearly above the calculated confidence upper limit.

Our prevalence is also in comparison with other European registers very high and exceeds the corresponding confidence interval significantly.

additional information:

pregnancy outcome	6 x termination of pregnancy 2 x live births, deceased until 7th day of life
sex	6 x male 1 x female 1 x no indication
number of isolated malformations/MCA	2 x MCA 6 x isolated

The two deceased infants suffered in one case from a functionless hypoplastic kidney and another time from a bilateral agenesia. In case of the terminations of pregnancy a bilateral agenesia was diagnosed three times, functionless dysplastic kidneys two times and one time one missing and one functionless hypoplastic kidney left.

We received the information that two mothers suffered from a hypertonia. One of these women indicated a medical treatment with Dopegyt until 28 weeks of gestation. The second women indicated at an existing diabetes mellitus only the use of insulin. In six cases we have no information about any medication intake or maternal diseases. One sibling of a live birth already deceased in consequence of a Potter sequence.

Chapter 12.26 tells about an infant that after the maternal stop of the sartan therapy still suffered from damaged but not functionless kidneys.

Malformation combinations (MCA) or superordinated syndromes detected:

- Microcephaly, clubfoot, low set ears
- Horseshoe kidney, urethra stenosis, megacyst, low set ears, Potter face, wide philtrum, microstomia, hypertelorism, mandibular micrognathia

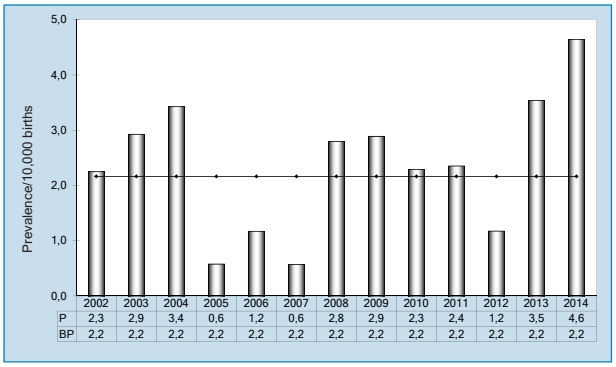


Fig. 31: Development of prevalence/10,000 births with Potter sequence in the registration area since 2002

In 2014, one Potter sequence per 2155 births was registered in Saxony-Anhalt.

Please note:

What are ACE inhibitors and what is Sartan fetopathie?

The group of pharmaceuticals "sartans" were developed from ACE inhibitors. Mainly used in the antihypertensive therapy, they have a teratogenic effect in case of maternal intake during second and third trimenon of pregnancy. The suspected pathomechanism of both substances results in a reduced perfusion of the foetal organs, in particular of the kidneys. That means both substances interrupt the renin-angiotensin system at different points. The result of such a foetal damage is an intrauterine oliguria. Since amniotic fluid production depends from the second trimenon on mainly from foetal urine production, an oligohydramnios can occur which might be diagnosed by prenatal ultrasound screening. This leads into **occurrence of a potter sequence** with lung and thorax hypoplasia, distorsion of limbs, characteristic face and further consequential problems. Affected infants often suffer postnatal from a renal failure which is in most cases not reversible. Additionally, a hypoplasia/dysplasia of the cranial bone can occur at insufficient cranial ossification (it is also possible that only gaping cranial sutures are present).
German speaking people can get further information about this topic by visiting the website of the pharmacovigilance and advisery centre for embryonic toxicology (www.embyotox.de).

12.25 Renal Agenesis, Unilateral (Q60.0/Q60.2)

	Number	Prevalence /10,000 births	Trend in comp. to basis prevalence
Major cities: 1 x Halle 2 x Magdeburg	3	6.1	↔
Districts: 1 x Anhalt-Bitterfeld 1 x Harz 3 x Jerichower Land 2 x Salzlandkreis 1 x Wittenberg	8	6.5	↔
Saxony-Anhalt	**11**	**6.4**	↔

Renal agenesis, unilateral (2002-2013)		
	Basis prevalence /10,000 births	Confidence Interval (CI of 95%)/10,000 births
Cities	7.52	5.40 - 10.2
Districts	6.45	5.25 - 7.85
Region	6.73	5.73 - 7.90
EUROCAT	no information	no information

We registered 11 births with renal agenesis in 2014.
The **prevalence of 6.4 per 10,000 births** lies within the confidence interval of the last 12 years.

No EUROCAT data is present here for comparison.

additional information:

pregnancy outcome	10 x live births 1 x live births, deceased after 7 days of life
sex	7 x male 4 x female
number of isolated malformations/MCA	6 x MCA 5 x isolated

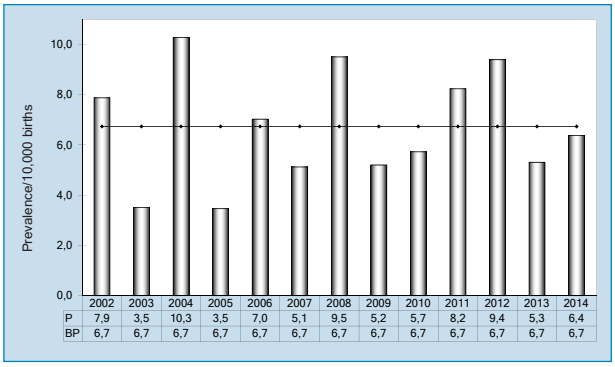
In six cases renal agenesis occurred at the left kidney and in four cases at the right kidney. In one case no laterality was indicated.

All infants were live births between 35 and 40 weeks of gestations.

In five cases no additional malformations were present.

Malformation combinations (MCA) or superordinated syndromes detected:

- CHARGE association with: blt choanal atresia, plasma protein metabolism disorder, Truncus arteriosus communis, ureteropelvic junction obstruction and DUP IV. grade right, auditory ossicle malformation left, low set dysplastic ears
- Bickers-Adams syndrome with: Corpus callosum hypoplasia, small hypophysis, partial agenesia of septum pellucidum, hemivertebrae (T11,12 vertebrae), incompletely developed rip right at L 1 vertebrae, scoliosis, abdominal muscle hypoplasia left
- Microcephaly
- Teleangiectasis in left striatum, asymmetric ventricle
- Duplex right kidney, DUP I. grade right
- Hip subluxation left



	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014
P	7,9	3,5	10,3	3,5	7,0	5,1	9,5	5,2	5,7	8,2	9,4	5,3	6,4
BP	6,7	6,7	6,7	6,7	6,7	6,7	6,7	6,7	6,7	6,7	6,7	6,7	6,7

Fig. 32: Development of prevalence/10,000 births with unilateral renal agenesis in the registration area since 2002

In 2014, one renal agenesis, unilateral per 1567 births was registered in Saxony-Anhalt.

12.26 Cystic Kidney (Q61.1-Q61.9)

	Number	Prevalence /10,000 births	Trend in comp. to basis prevalence
Major cities: 2 x Halle 6 x Magdeburg	8	16.3	↑
Districts: 1 x Altmarkkreis Salzwedel 2 x Harz 2 x Jerichower Land 1 x Saalekreis 1 x Salzlandkreis 1 x Wittenberg	8	6.5	↔
Saxony-Anhalt	**16**	**9.3**	↔

Cystic kidney (2002-2013)		
	Basis prevalence /10,000 births	Confidence Interval (CI of 95%)/10,000 births
Cities	9.90	7.44 - 12.92
Districts	7.43	6.21 - 8.86
Region	8.08	6.97 - 9.35
EUROCAT	no information	no information

We registered 16 births with cystic kidneys in 2014. In three cases the cystic kidneys occurred bilateral (in the sense of ADPKD (=autosomal recessive polycystic kidney disease) or ARPKD (= autosomal-recessive polycystic kidney disease). In 13 cases a multicystic dysplastic kidney unilateral was present (6 times left, 7 times right) and one time without indication of laterality.
The calculated **prevalence** returned with a value of **9.3 per 10,000 births** to the middle range of the last 12 years and lies within the confidence interval.

Cystic kidney is not classified consistently since 2006 and therefore EUROCAT does not publish any comparison data regarding this congenital malformation.

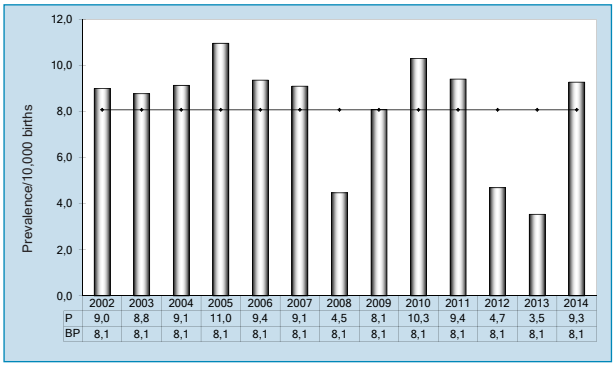
additional information:

pregnancy outcome	14 x live births 2 x termination of pregnancy
sex	10 x male 5 x female 1 x no indication
number of isolated malformations/MCA	7 x MCA 9 x isolated

14 infants were life births between 38 and 40 WOG. Two pregnancies were terminated at presence of additional cerebral malformations after 19 weeks of gestations and one fetocid took place after 27 weeks of gestations.

Malformation combinations (MCA) or superordinated syndromes detected:

- Walker-Warburg syndrome with: hydrocephalus, cerebellar hypoplasia, submucosal cleft palate, aortic valve stenosis, ocular malformation, hypoplastic nasal bone, craniofacial dysmorphy
- Zellweger syndrome with: microcephalus, malformation of urinary tract, scaphocephalus, corpus callosum hypoplasia, clubfoot, hepatic cyst, VSD, PFO and haemodynamic not effective PDA at full term infant, hypertelorism, epicanthus internus, wide nose, blt four finger groove, dilated cerebral ventricle and low set ears
- CATCH 22 with: Di George syndrome, Tetralogy of Fallot, small ears, thymus hypoplasia, missing septum pellucidum, craniofacial dysmorphy, PFO at preterm infant
- Megacystis megaureter syndrome with: blt megaureter, DUP III. grade right and II. grade left, undescended right testis
- Sartanembryopathy with: PFO at preterm infant
- Duplex left kidney, ASD II, trigonocephaly, anomalies of finger and toes, blt plexus cyst, craniofacial dysmorphy, sunken nose bridge, prominent forehead, low set ears
- Anopthalmus, cardiac malformations



	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014
P	9,0	8,8	9,1	11,0	9,4	9,1	4,5	8,1	10,3	9,4	4,7	3,5	9,3
BP	8,1	8,1	8,1	8,1	8,1	8,1	8,1	8,1	8,1	8,1	8,1	8,1	8,1

Fig. 33: Development of prevalence/10,000 births with cystic kidneys in the registration area since 2002

In 2014, one cystic kidney per 1077 births was registered in Saxony-Anhalt.

12.27 Bladder Exstrophy (Q64.1)

	Number	Prevalence /10,000 births	Trend in comp. to basis prevalence
Major cities	0	0.0	↔
Districts: 1 x Stendal	1	0.8	↗
Saxony-Anhalt	**1**	**0.6**	↗

Bladder exstrophy (2002-2013)		
	Basis prevalence /10,000 births	**Confidence Interval (CI of 95%)/10,000 births**
Cities	0.00	0.00 - 0.55
Districts	0.33	0.11 - 0.76
Region	0.24	0.08 - 0.56
EUROCAT	no information	no information

One birth with bladder exstrophy was registered in 2014t. The calculated **prevalence** lies at **0.6 per 10,000 births**.

No EUROCAT data is present for comparison for this rarely appearing malformation.

A prospective study of the European Society of paediatric urology was published in 2015. It analyses the reportings of 2010 that were made in regard to patients who needed a surgery in different European centres. The study regards only live births and shows lower prevalence values than the entire prevalence which includes terminations of pregnancy, stillbirths and spontaneous abortions. 31 cases of bladder exstrophy were published in this connection out of 677,900 live births in 2010 in Germany (calculated prevalence: 0.31 per 10,000 live births, CI: 0.19-0.47). This means that in the context of this study one infant per 32,200 life births was registered for a planned operative correction of a bladder extrophy (Cervellione et al. 2015).

additional information:

pregnancy outcome	1 x live birth
sex	1 x male
number of isolated malformations/MCA	1 x MCA

Malformation combinations (MCA) or superordinated syndromes detected:

- OEIS complex with: Omphalocele, covered sacral meningocele, tethered cord syndrome, indeterminate sex, anal atresia with fistula, cloacal persistence, megaureter and DUP I. grade left, VSD, PFO and haemodynamic not effective PDA at preterm infant

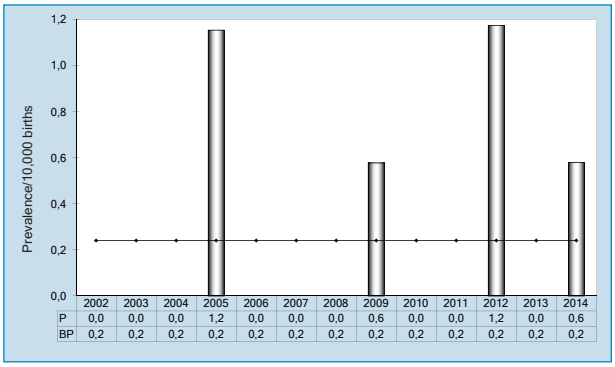


Fig. 34: Development of prevalence/10,000 births with bladder exstropy in the registration area since 2002

In 2014, one birth with a bladder exstrophy per 17238 births was registered in Saxony-Anhalt.

References:
Cervellione RM, Mantovani A, Gearhart J, et al.: Prospective study on the incidence of bladder/cloacal exstrophy and epispadias in Europe. Journal of Pediatric Urology 2015.

12.28 Preaxial Polydactyly (Q69.1/Q69.2)

	Number	Prevalence /10,000 births	Trend in comp. to basis prevalence
Major cities: 1 x Magdeburg	1	2.0	↘
Districts: 1 x Altmarkkreis Salzwedel 1 x Anhalt-Bitterfeld 1 x Salzlandkreis	3	2.4	↓
Saxony-Anhalt	**4**	**2.3**	↓

Preaxial polydactyly (2002-2013)		
	Basis prevalence /10,000 births	**Confidence Interval (CI of 95%)/10,000 births**
Cities	4.03	2.53 - 6.11
Districts	3.91	2.98 - 5.03
Region	3.94	3.14 - 4.89
EUROCAT	no information	no information

Four births with preaxial polydactyly were registered in 2014.
The **annual prevalence of 2.3 per 10,000 births** lies below the confidence interval of the last 12 years.

Comparative EUROCAT data for preaxial polydactyly is not available.

additional information:

pregnancy outcome	4 x live births
sex	2 x male 2 x female
number of isolated malformations/MCA	1 x MCA 3 x isolated

No additional malformations were present at three births.

Malformation combinations (MCA) or superordinated syndromes detected:

- Missing IV. finger right

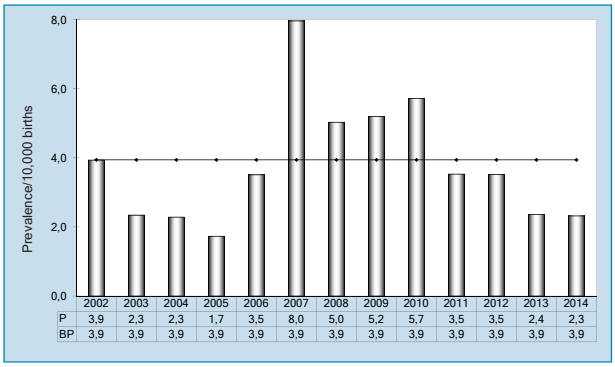


Fig. 35: Development of prevalence/10,000 births with preaxial polydactyly in the registration area since 2002

In 2014, one preaxial polydactyly per 4310 births was registered in Saxony-Anhalt.

12.29 Limb Reduction Defects of both Upper and Lower Limbs (Q71./Q72./Q73.)

	Number	Prevalence /10,000 births	Trend in comp. to basis prevalence
Major cities: 1 x Halle 1 x Magdeburg	2	4.1	↓
Districts: 2 x Anhalt-Bitterfeld 1 x Burgenlandkreis 3 x Börde 1 x Harz 1 x Mansfeld-Südharz 3 x Saalekreis 4 x Salzlandkreis	15	12.2	↑
Saxony-Anhalt	**17**	**9.9**	↑

Limb Reduction Defects of both Upper and Lower Limbs (2002-2013)		
	Basis prevalence /10,000 births	**Confidence Interval (CI of 95%)/10,000 births**
Cities	8.07	5.86 - 10.83
Districts	7.56	6.33 - 9.01
Region	7.69	6.61 - 8.94
EUROCAT 2001-2012	5.32	5.18 - 5.47
		1.80 Valencia Region (Spain)* 11.17 Mainz (Germany)**

*/** centres with lowest resp. highest prevalence/10,000 births

In 2014 we received information about 17 births with reductions defects of upper and lower limbs.

The **annual prevalence** lies with **9.9 per 10,000 births** slightly above the confidence interval of the registration period 2002-2013.

A comparison with EUROCAT data shows that the prevalence of Saxony-Anhalt is to find within the upper third.

additional information:

pregnancy outcome	9 x live births 1 x live birth, deceased after 7 days of life 7 x termination of pregnancy
sex	13 x male 3 x female 1 x no indication
number of isolated malformations/MCA	12 x MCA 5 x isolated

In six cases we received information about a suspicious prenatal finding. In further seven cases a termination of pregnancy took place at presence of complex additional malformations (14th to 23th WOG).

In five cases no other organ systems were concerned by any malformation.

Malformation combinations (MCA) or superordinated syndromes detected:

- Body stalk anomaly with: anencephalus, amniotic band at right hand and head
- Caryotype 47,XYY with: hydrocephalus, corpus callosum agenesia, unilateral clubfoot
- unbalanced translocation (chromosome 13) with: occipital encephalocele, VSD, persistent truncus arteriosus, partly fusion of cervical vertebrae and thoracic vertebrae, hemivertebrae, scoliosis, intestinal malrotation, blt unlobed lung, hypoplastic splenic, lateral ascending lid axis, short philtrum
- VACTERL association with: anal atresia (with fistula), cleft palate at Piere-Robin-Sequence, canalis atrioventricularis communis, ASD II, mitral valve insufficiency, tricuspidal valve insufficiency, DUP II. grade right, clinodactyly of V. finger, mandibular micrognathia, dysplastic ears
- Gastroschisis, left heart hypoplasia syndrome, coilosternia, low set ears, mandibular micrognathia, hypertelorism, saddle nose
- Omphalocele, cor triloculare biatriatum, persistent truncus arteriosus, agenesia of pulmonary artery, blt diaphragmatic hernia and renal hypoplasia, horseshoe kidney, pulmonary agenesia left, intestinal malrotation, turricephaly, triphalangeal left thumb, low set ears, hypertelorism
- Omphalocele, DUP I. grade
- Holt-Oram syndrome
- Clubfoot left, PFO at fullterm infant, syndactyly of right II. - V. finger at presence of amniotic bands
- PFO at fullterm infant
- Accessory right thumb
- Amniotic bands at right arm

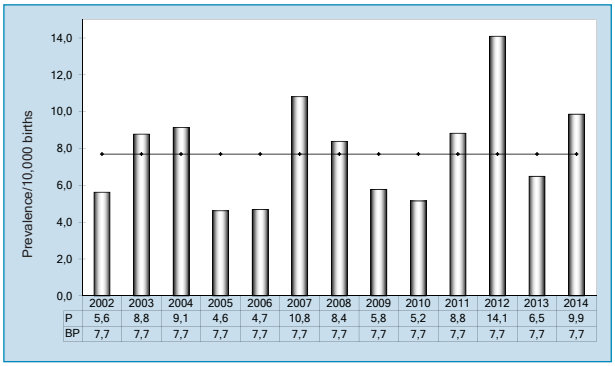


Fig. 36: Development of prevalence/10,000 births with limb reduction defects in the registration area since 2002

In 2014, one limb reduction defect per 1014 births was registered in Saxony-Anhalt.

12.30 Diaphragmatic Hernia (Q79.0/Q79.1)

	Number	Prevalence /10,000 births	Trend in comp. to basis prevalence
Major cities: 1 x Halle 1 x Magdeburg	2	4.1	↔
Districts: 1 x Harz	1	0.8	↓
Saxony-Anhalt	**3**	**1.7**	↓

Zwerchfellhernie (2002 bis 2013)		
	Basis prevalence /10,000 births	Confidence Interval (CI of 95%)/10,000 births
Cities	4.40	2.82 - 6.55
Districts	2.22	1.53 - 3.10
Region	2.79	2.12 - 3.61
EUROCAT 2001-2012 (Q79.0)	2.67	2.57 - 2.78
		1.01 S Portugal* 4.75 Malta**

*/** centres with lowest resp. highest prevalence/10,000 births

Three live births with diaphragmatic hernia were registered in 2014.
The annual prevalence of 1.7 per 10,000 births is nearly identically to the last three years. Accordingly, it lies within the confidence interval of the years 2002-2013.

Furthermore, the our annual prevalence clearly comes under the prevalence of EUROCAT comparison data.

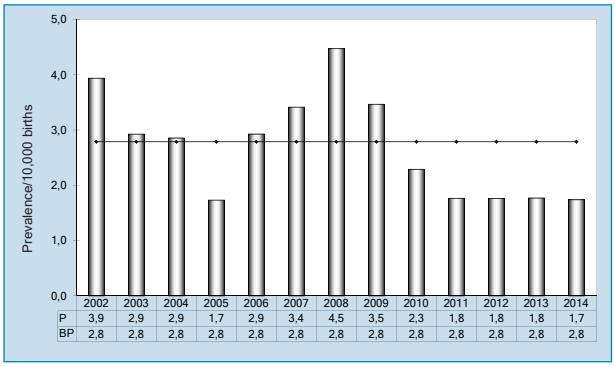
additional information:

pregnancy outcome	2 x live births 1 x termination of pregnancy
sex	2 x male 1 x female
number of isolated malformations/MCA	2 x MCA 1 x isolated

In one case the diaphragmatic hernia occurred isolated, additional malformations were present in two further cases. The diagnosis was confirmed prenatally in only one case.

Malformation combinations (MCA) or superordinated syndromes detected:

- Omphalocele, cor triloculare biatriatum, persistent truncus arteriosus, agenesia of pulmonary artery, pulmonary agenesia left, intestinal malrotation, turricephaly, left hypoplastic humerus, missing II. finger, triphalangeal thumb and brachydactyly of finger, horseshoe kidney, blt renal hypoplasia, low set ears, hypertelorismus
- Dextrocardia with situs inversus



	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014
P	3,9	2,9	2,9	1,7	2,9	3,4	4,5	3,5	2,3	1,8	1,8	1,8	1,7
BP	2,8	2,8	2,8	2,8	2,8	2,8	2,8	2,8	2,8	2,8	2,8	2,8	2,8

Fig. 37: Development of prevalence/10,000 births with diaphragmatic hernia in the registration area since 2002

In 2014, one diaphragmatic hernia per 5746 births was registered in Saxony-Anhalt.

12.31 Omphalocele (Q79.2)

	Number	Prevalence /10,000 births	Trend in comp. to basis prevalence
Major cities: 2 x Halle 3 x Magdeburg	5	10.2	↑
Districts: 1 x Anhalt-Bitterfeld 1 x Burgenlandkreis 1 x Börde 1 x Stendal	4	3.2	↔
Saxony-Anhalt	**9**	**5.2**	↑

Omphalocele (2002-2013)		
	Basis prevalence /10,000 births	Confidence Interval (CI of 95%)/10,000 births
Cities	2.93	1.68 - 4.76
Districts	3.26	2.42 - 4.30
Region	3.17	2.45 - 4.04
EUROCAT 2001-2012	2.96	2.85 - 3.07
		0.43 S Portugal* 5.88 Paris (France)**

*/** centres with lowest resp. highest prevalence/10,000 births

Nine births with omphalocele were registered in 2014. The calculated **annual prevalence** of **5.2 per 10,000 births** was on such a high level for the last time in 2005 and lies above the calculated confidence interval of the basis prevalence.

A comparison of our calculated basis prevalence with the average prevalence of EUROCAT shows similar values. In total, the annual prevalence lies within the upper third of other EUROCAT centres prevalences.

additional information:

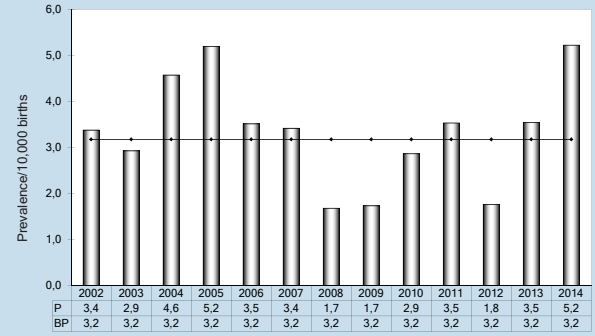
pregnancy outcome	3 x live births 1 x live birth, deceased after 7 days of life 5 x termination of pregnancy
sex	7 x male 2 x female
number of isolated malformations/MCA	6 x MCA 3 x isolated

One termination of pregnancy took place at presence of a omphalocele, similar to approximately one fourth of all cases with Edwards syndrome. In additional five cases, no chromosomal reason was documented. Furthermore, we did not receive any information about a chromosomal examination in three cases. However, in all cases the omphalocele was confirmed already during prenatal ultrasound screening.

The connection of maternal diabetes and appearance of infantile malformations is already known. Thereby, omphalocele belongs to the associated malformation spectrum, also when an embryopathy cannot be confirmed for sure. We were informed that four of the pregnant women suffered either from gestational diabetis, PCO syndrome, obesity or took metformin during pregnancy.

Malformation combinations (MCA) or superordinated syndromes detected:

- Edwards syndrome with: hypoplastic nasal bone
- OEIS complex with: anal atresia with fistula, cloacal persistence, bladder exstrophy, megaureter left, indifferent sex, covered sacral meningocele, tethered cord syndrome, VSD, DUP I. grade left, PFO and haemodynamic not effective PDA at preterm infant
- Cor triloculare biatriatum, persistent truncus arteriosus, agenesia of pulmonary artery, diaphragmatic hernia, pulmonary agenesia left, intestinal malrotation, turricephaly, hypoplastic humerus left, missing II. finger, triphalangeal thumb and brachydactyly of finger, horseshoe kidney, blt renal hypoplasia, low set ears, hypertelorism
- Anencephaly
- Tetralogy of Fallot, glandular hypospadias
- Missing tibia and fibula right, DUP I. grade



	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014
P	3,4	2,9	4,6	5,2	3,5	3,4	1,7	1,7	2,9	3,5	1,8	3,5	5,2
BP	3,2	3,2	3,2	3,2	3,2	3,2	3,2	3,2	3,2	3,2	3,2	3,2	3,2

Fig. 38: Development of prevalence/10,000 births with omphalocele in the registration area since 2002

In 2014, one omphalocele per 1915 births was registered in Saxony-Anhalt.

12.32 Gastroschisis (Q79.3)

	Number	Prevalence /10,000 births	Trend in comp. to basis prevalence
Major cities: 3 x Magdeburg	3	6.1	↔
Districts: 1 x Börde 1 x Jerichower Land 1 x Mansfeld-Südharz 1 x Salzlandkreis 2 x Wittenberg	6	4.9	↔
Saxony-Anhalt	**9**	**5.2**	↗

Gastrochisis (2002-2013)		
	Basis prevalence /10,000 births	**Confidence Interval (CI of 95%)/10,000 births**
Cities	4.40	2.82 - 6.55
Districts	3.98	3.04 - 5.11
Region	4.09	3.27 - 5.05
EUROCAT 2001-2012	2.61	2.50 - 2.71
		0.88 Tuscany (Italy)* 6.87 Mainz (Germany)**

*/** centres with lowest resp. highest prevalence/10,000 births

In 2014 we registered nine births with gastroschisist. The calculated **prevalence** lies at **5.2 per 10,000 births** and remained on a relative steady level during the last five years. In the current year it increased only a little and lies slightly above the confidence interval of the last 12 years.

Compared to other EUROCAT registers, the annual prevalence lies within the upper third. The highest prevalence was registered during the last years in the "Mainzer births cohort" (register Mainzer model) and also multiple studies confirmed a worldwide increasing trend of gastrochisis prevalence.

A recently published meta analysis confirmed again the good prenatal recognisability of gastrochisis (D'Antonio et al. 2015). Furthermore, a cochrane meta analysis of 2013 was not able find a conclusion in regard to the elective delivery after 34 weeks of gestations at presence of a gastrochisis (Grant et al. 2013).

References:

- D'Antonio F, Virgone C, Rizzo G, et al.: Prenatal Risk Factors and Outcomes in Gastroschisis: A Meta-Analysis. PEDIATRICS 2015; 136:e159-69.
- Grant NH, Dorling J, Thornton JG: Elective preterm birth for fetal gastroschisis. Cochrane Database Syst Rev 2013; 6: CD009394.

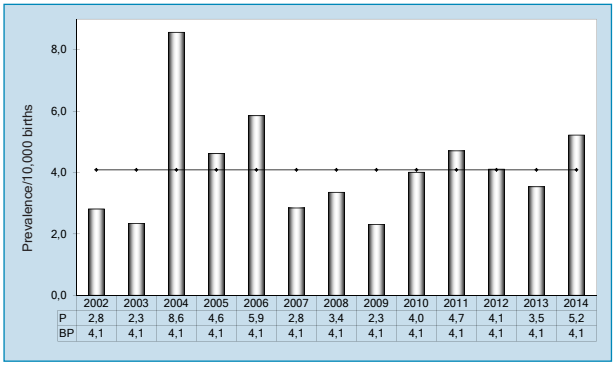
additional information:

pregnancy outcome	5 x live births 2 x spontaneous abortion 2 x termination of pregnancy
sex	2 x male 5 x female 2 x no indication
number of isolated malformations/MCA	4 x MCA 5 x isolatedt

In five cases the gastrochises occurred isolated. The planned delivery was carried out in four cases between 33 and 34 weeks of gestation, in one case the week of gestation is unknown. In two cases of termination of pregnancy (16 and 19 weeks of gestations) the already prenatally seen additional malformations were confirmed. No prenatal ultrasound screening took place in one case, in all other cases the diagnosis of gastrochisis was made prenatally between 13 and 20 weeks of gestations.

Malformation combinations (MCA) or superordinated syndromes detected:

- Hypoplastic left heart syndrome, blt missing thumbs and radius, blt hypoplastic ulna, clubhands, funnel chest, low set ears, mandibular micrognathia, hypertelorism, saddle nose
- Coarctation of aorta, VSD, lateral cervical cyst
- ASD II, microcolon
- Intestinal malrotation



	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014
P	2,8	2,3	8,6	4,6	5,9	2,8	3,4	2,3	4,0	4,7	4,1	3,5	5,2
BP	4,1	4,1	4,1	4,1	4,1	4,1	4,1	4,1	4,1	4,1	4,1	4,1	4,1

Fig. 39: Development of prevalence/10,000 births with gastroschisis in the registration area since 2002

In 2014, one gastroschisis per 1915 births was registered in Saxony-Anhalt.

12.33 Prune-belly-Sequence (Q79.4)

	Number	Prevalence /10,000 births	Trend in comp. to basis prevalence
Major cities: 2 x Halle	2	4.1	↑
Districts	0	0.0	↓
Saxony-Anhalt	**2**	**1.2**	↔

Prune-belly-Sequence (2002-2013)		
	Basis prevalence /10,000 births	**Confidence Interval (CI of 95%)/10,000 births**
Cities	1.28	0.52 - 2.64
Districts	0.78	0.40 - 1.37
Region	0.91	0.55 - 1.43
EUROCAT	no information	no information

In 2014 two births with Prune-belly-Sequence were registered.
The calculated **prevalence of 1.2 per 10,000 births** lies within the confidence interval of the last 12 years.

No EUROCAT data are present for comparison for this malformation.

After prenatal diagnosis one pregnancy was terminated after 13 weeks of gestations and one spontaneous abortion took place after 17 weeks of gestations.

additional information:

pregnancy outcome	1 x spontaneous abortiont 1 x termination of pregnancy
sex	1 x male 1 x no indication
number of isolated malformations/MCA	2 x isolated

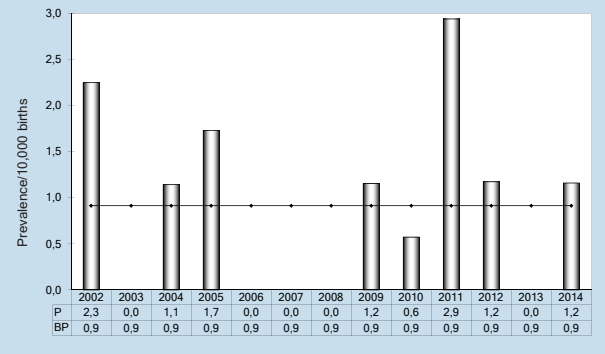


Abb. 40: Development of the prevalence/10,000 births with Prune-belly-Sequence in the registration area since 2002

In 2014, one Prune-belly-Sequence per 8619 births was registered in Saxony-Anhalt.

12.34 Down Syndrome - Trisomy 21 (Q90.)

	Number	Prevalence /10,000 births	Trend in comp. to basis prevalence
Major cities: 3 x Halle 9 x Magdeburg	12	24.4	↔
Districts: 3 x Altmarkkreis Salzwedel 1 x Anhalt-Bitterfeld 1 x Burgenlandkreis 5 x Börde 2 x Harz 2 x Mansfeld-Südharz 2 x Saalekreis 4 x Salzlandkreis 2 x Stendal	22	17.9	↗
Saxony-Anhalt	**34**	**19.7**	↗

Down's syndrome (2002-2013)		
	Basis prevalence /10,000 births	Confidence Interval (CI of 95%)/10,000 births
Cities	21.45	17.99 - 25.53
Districts	15.58	13.76 - 17.62
Region	17.12	15.46 - 18.95
EUROCAT 2001-2012	20.96	20.67 - 21.25
		7.10 S Portugal* 41.17 Paris (France)**

*/** centres with lowest resp. highest prevalence/10,000 births

We registered 34 births with Down's syndrome in 2014. The **prevalence** of **19.7 per 10,000 births** lies slightly above the confidence interval.

A comparison with other EUROCAT centres shows that the prevalence of Saxony-Anhalt, when considering the years of 2001-2012, continues to lie within the middle range of other European registers.

A free trisomy 21 was ascertained in 31 cases, in one case a translocation was present, in one case a mosaic was present and in one case we did not receive any further details. (Schade & Rissmann 2015).

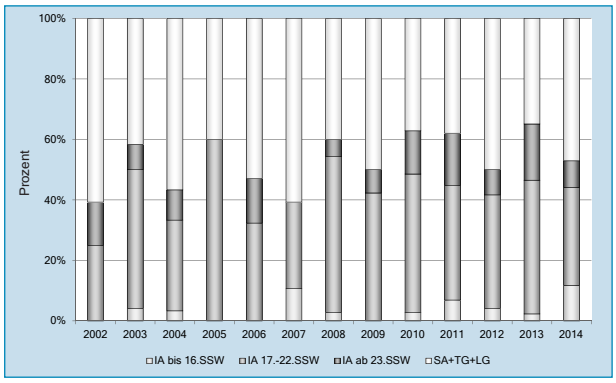


Fig. 41: Pregnancy outcome at Down syndrome 2002-2014, percentage of early terminations of pregnacy

References:

Schade K, Rissmann A: Führt der DNA-Test aus mütterlichem Blut zur stärkeren pränatalen Selektion des Down-Syndroms? Ärzteblatt Sachsen-Anhalt 2015; 26: 63-4.

additional information:

pregnancy outcome	14 x live births 1 x live birth, deceased after 7 days of life 1 x spontaneous abortion 18 x termination of pregnancy
sex	20 x male 14 x female
number of isolated malformations/MCA	17 x MCA 17 x isolated

Malformation combinations (MCA) or superordinated syndromes detected:

- Coarctation of aorta, canalis atrioventricularis communis, bicuspidal aortic valve, subvalvular aortic stenosis, glandular hypospadias, nesidioblastosis, hepatic insufficiency
- Microcephaly
- Stenosis of pulmonary artery, megaureter left, blt DUP I. grade, hepatomegaly, haemodynamic not effective PDA at fullterm infant
- Canalis atrioventricularis communis, pulmonary valve stenosis, mitral valve insufficiency, tricuspidal valve insufficiency
- Canalis atrioventricularis communis, vein thrombosis
- Canalis atrioventricularis communis, sound perception disorder (right 50 dB, left 60 dB)
- Cardiomegaly, PFO at fullterm infant, combined sound conduction and perception disorder (right 100 dB, left 30 dB), blt constricted acoustic meatus, short arms and legs
- 2 x VSD (1 x with aortic valve stenosis)
- VSD
- ASD II, sound conduction disorder (blt 90 dB)
- PFO at fullterm infant
- Cor triloculare biatriatum
- Blt undescended testis, haemodynamic not effective PDA at fullterm infant
- Duodenal atresia
- Hirschsprung's disease, macrocephaly
- Generalized lymphedema, liver haemanginoma, blt dilated cerebral ventricle, PFO at preterm infant
- Double lobed lung right

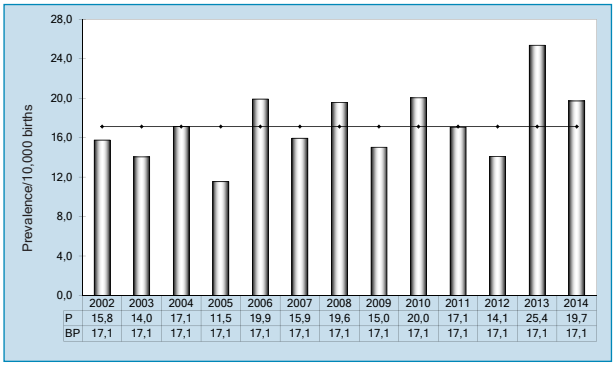


Fig. 42: Development of prevalence/10,000 births with Down syndrome in the registration area since 2002

In 2014, one Down syndrome (trisomy 21) per 507 births was registered in Saxony-Anhalt.

12.35 Patau Syndrome - Trisomy 13 (Q91.4-Q91.7)

	Number	Prevalence /10,000 births	Trend in comp. to basis prevalence
Major cities: 1 x Halle	1	2.0	↔
Districts	0	0.0	↓
Saxony-Anhalt	**1**	**0.6**	↘

Patau syndrome (2002-2013)		
	Basis prevalence /10,000 births	**Confidence Interval (CI of 95%)/10,000 births**
Cities	1.47	0.63 - 2.89
Districts	0.85	0.45 - 1.45
Region	1.01	0.63 - 1.54
EUROCAT 2001-2012	1.87	1.78 - 1.95
		0.38 S Portugal* 3.85 Paris (France)**

*/** centres with lowest resp. highest prevalence/10,000 births

In 2014 we registered one birth with trisomy 13.
The annual prevalence of 0.6 per 10,000 births lies slightly under the confidence interval of the last 12 years.

Furthermore, when comparing our data from Saxony-Anhalt with other EUROCAT centres, our prevalence lies within the lower third of the other registers.

additional information:

pregnancy outcome	1 x termination of pregnancy
sex	1 x no indication
number of isolated malformations/MCA	1 x isolated

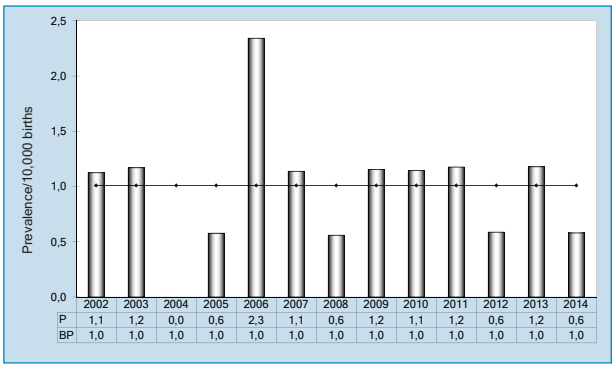


Fig. 43: Development of prevalence/10,000 births with a Patau syndrome in the registration area since 2002

In 2014, one Patau syndrome (trisomy 13) per 17238 births was registered in Saxony-Anhalt.

12.36 Edwards Syndrome - Trisomy 18 (Q91.0-Q91.3)

	Number	Prevalence /10,000 births	Trend in comp. to basis prevalence
Major cities: 2 x Halle 2 x Magdeburg	4	8.1	↑
Districts: 1 x Altmarkkreis Salzwedel 1 x Harz	2	1.6	↓
Saxony-Anhalt	**6**	**3.5**	↔

Edwards syndrome (2002-2013)		
	Basis prevalence /10,000 births	**Confidence Interval (CI of 95%)/10,000 births**
Cities	4.22	2.67 - 6.33
Districts	3.85	2.93 - 4.96
Region	3.94	3.14 - 4.89
EUROCAT 2001-2012	4.77	4.63 - 4.91
		0.91 S Portugal* 13.11 Paris (France)**

*/** centres with lowest resp. highest prevalence/10,000 births

We registered six births with Edwards syndrome in 2014. The prevalence of 3.5 per 10,000 births continues to lie within the confidence interval of the last 12 years.

Our calculated annual prevalence is within the lower third of other EUROCAT comparison data and at the same time it lies under the calculated confidence interval.

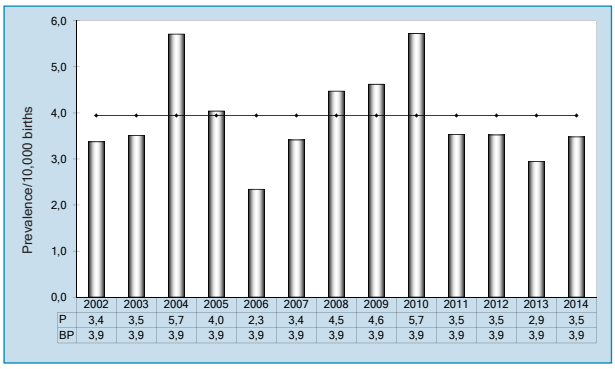
additional information:

pregnancy outcome	5 x termination of pregnancy 1 x live birth, deceased within 7 days of life
sex	6 x male
number of isolated malformations/MCA	3 x MCA 3 x isolated

In all five cases we registered a free trisomy 18, in one case we received no further details. Five pregnancies were terminated after prenatal diagnosis between 16 and 24 weeks of gestation.

Malformation combinations (MCA) or superordinated syndromes detected:

- Omphalocele, hypoplastic nasal bone
- DORV, complete misjunction of pulmonary vein, persistent left vena cava superior, Corpus callosum agenesia, horseshoe kidney
- Blt hypoplastic lung, adrenal gland and kidneys, urethra stenosis, dolichocephaly, thymus hypoplasia, talipes varus left



	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014
P	3,4	3,5	5,7	4,0	2,3	3,4	4,5	4,6	5,7	3,5	3,5	2,9	3,5
BP	3,9	3,9	3,9	3,9	3,9	3,9	3,9	3,9	3,9	3,9	3,9	3,9	3,9

Fig. 44: Development of prevalence/10,000 births with Edwards syndrome in the registration area since 2002

In 2014, one Edwards syndrome (trisomy 18) per 2873 births was registered in Saxony-Anhalt.

12.37 Indicator Malformations, In Total

The present Annual Report deals with 36 indicator malformations which are exactly defined (see definitions in chapter 12.0) by the ICBDSR (International Clearinghouse for Birth Defects) in chapters 12.1 to 12.36. Analysing only these clearly defined malformations bears the risk to overlook some developments of other malformations, however these fact is again revealed by the advantage of collecting globally temporal and spatial malformation rates.

Only 187 infants (72%) of 258 births with an indicator malformation were life births in the last year. This number of live births is clearly lower than expected in comparison with the percentage of the years 2002-2013 (76.7%). In contrast, the percentage of terminations of pregnancy (24.4%, 63 births) as well as the percentage of spontaneous abortions (2.7%, 7 births) is clearly higher in 2014 than during the time period of 2002-2013 (19.8% resp. 1.9%). Only one stillbirths (0.4%) with an indicator malformation was registered in 2014. However, the single percentages fluctuate in our reporting period between 0 and 3.4%.

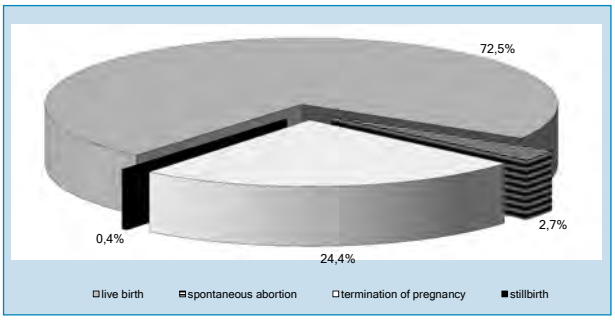


Fig. 45: Pregnancy outcomes of births with indicator malformations 2014

258 births with indicator malformations (1.50 per 10,000 births) showed in total 314 indicator malformations. The prevalence of all births with indicator malformations lies also in 2014 inconspicuously within the range of the basis values (2002-2013).

	Number	Prevalence in %	Trend in comp. to basis prevalence
Major cities	86	1.75	↔
Districts	172	1.40	↔
Saxony-Anhalt	258	1.50	↔

Indicator malformations, in total (2002-2013)		
	Basis prevalence in %	Confidence Interval (CI of 95%)
Cities	1.74	1.63 - 1.85
Districts	1.40	1.34 - 1.46
Region	1.49	1.44 - 1.54

Also when regarding the major cities and districts separately, the prevalences for 2014 lie within the confidence interval of the years 2002-2013. The current indicator malformation rate of the major cities is higher than the rate of the districts, similar to the previous years (except in 2006 and in 2008).

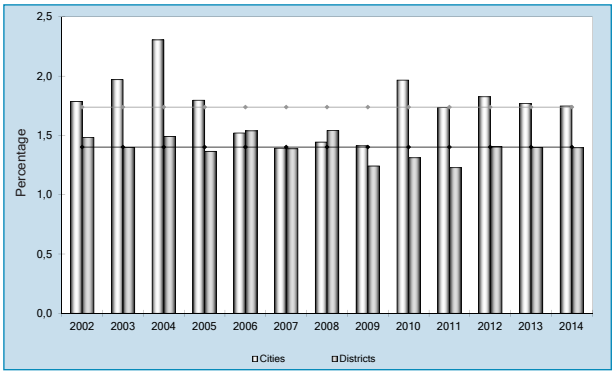


Fig. 46: Indicator malformations of ICBDSR in total (2002 to 2014), comparison of frequency (in %) in the major cities and districts

The aim of our trend analysis is to detect long term tendencies in the appearance of indicator malformations. Therefore, we analyse during the whole registration period (2002-2014) the intensity and orientation of prevalence changes.

The condition for the trend analysis is that we expect each malformation to appear at least five times or that we registered at least two cases of the corresponding malformation. Figure 47 on page 65 shows the average percentage changes of the annual prevalences of all indicator malformations that correspond to these conditions. They are rated by binary logistic regression analysis on the basis of the maximum-likelihood-estimation.

The regression coefficient represents the strength and direction of the percentage annual change. A significant increasing trend is indicated by a regression coefficient B, which is together with a confidence interval of 95% illustrated righthand of the axis of ordinates.
A descending trend can be identified by a regression coefficient that is presented lefthand of the axis (in the negative area). If the confidence interval overlaps the zero value the percentage change is not significant.

We tested the temporary change of the trend-coordinate and the non-linear coordinate for heterogeneity by use of the chi-squared test. We rate the trend as non-linear at a probability of $p > 0.05$ for the linear ratio and $p < 0.05$ for the non-linear ratio. In these cases we did not identify a **linear trend**. This applies for neural tube defects, spina bifida, anorectal atresia/ stenosis and undescended testis. A probability value for the linear percentage ($p= 0.046$) points to a significant trend for microcephaly but at the same time a strong non linear percentage exists ($p= 0.001$). The verification of values does not turn out a monotony so that also this trend can be rated as non linear. A probability value of $p < 0.05$ for the linear percentage and $p > 0.01$ for the non linear percentage means that the linear percentage dominates and the non linear percentage can be neglected. The observed trend is significant, corresponding to the regression coefficient B. A **significant ascending trend** was observed for Down syndrome (+2.67 %, CI 0,00% to 5.48%) during the registration period. A **significant decreasing trend** was not observed.

All below illustrated indicator malformations do not show a significant positive or negative trend. This is also the case for hypospadias where the linear percentage still lies within the coincidence range (p = 0.063) and the non linear percentage does hardly have any effect (p = 0.629).

The chi-squared test gives for the linear and non-linear component a probability of p > 0.05. For this reason, the non-linear ratio is not significant and also not decisive in regard to a disproportionate increase or decrease

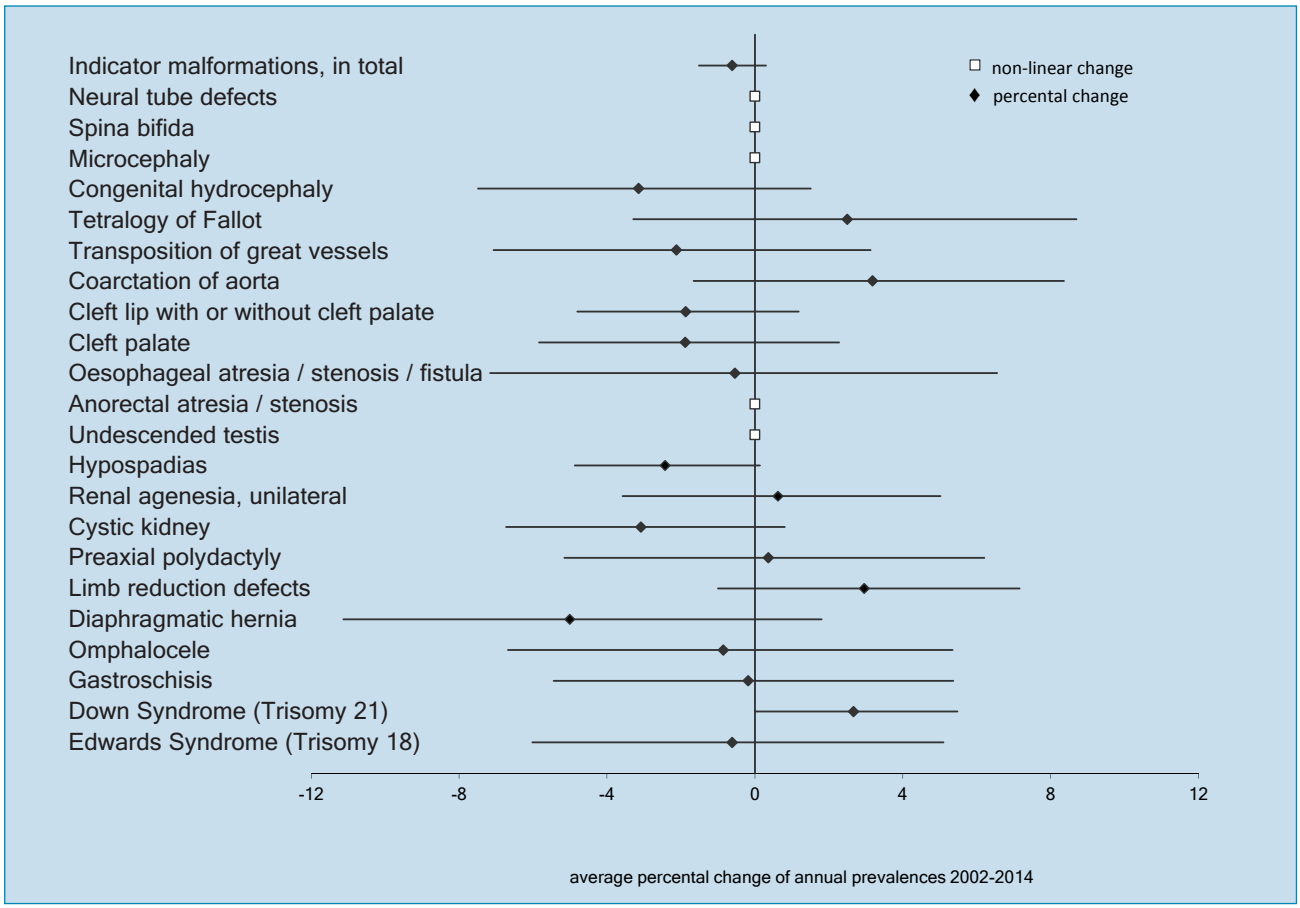


Fig. 47: Trend analysis 2002-2014 with average percental change of prevalence per year (95% confidence interval)

	regression coefficient B in %	confidence interval(CI of 95%)
Indicator malformations, in total	-0.61	-1.51% to 0.3%
Congenital hydrocephaly	-3.14	-7.49% to 1.51%
Tetralogy of Fallot	2.50	-3.28% to 8.7%
Transposition of great vessels	-2.12	-7.07% to 3.13%
Coarctation of aorta	3.18	-1.65% to 8.36%
Cleft lip with or without cleft palate	-1.87	-4.8% to 1.18%
Cleft palate	-1.88	-5.83% to 2.27%
Oesophageal atresia/stenosis/fistula	-0.54	-7.16% to 6.55%
Hypospadias	-2.43	-4.87% to 0.14%
Renal agenesia, unilateral	0.63	-3.58% to 5.02%
Cystic kidney	-3.08	-6.73% to 0.81%
preaxial polydactyly	0.37	-5.15% to 6.21%
Limb reduction defects	2.96	-0.99% to 7.16%
Diaphragmatic hernia	-5.01	-11.13% to 1.8%
Omphalocele	-0.85	-6.68% to 5.35%
Gastroschisis	-0.18	-5.44% to 5.37%
Down's-Syndrome (Trisomy 21)	2.67	0% to 5.48%
Edward's-Syndrome (Trisomy 18)	-0.62	-6.02% to 5.1%

15 Summary

The Annual Report 2014 about congenital malformations and anomalies as well as genetically caused diseases is based on registered data by the Monitoring of Congenital malformations Saxony-Anhalt. The statistical analysis of data is population-based by use of the nationwide malformation data and according to the official birth rate which is provided by the State Statistical Office in Halle. To better classify the calculated indicator malformation prevalences, we indicate, if available, European wide registered values (prevalence, confidence interval, minimum and maximum 2001-2012, see chapter 12), calculated by EUROCAT. Indications of current basis prevalences of Saxony-Anhalt for the same time period (2002-2013) are not yet provided by EUROCAT.

We register in Saxony-Anhalt a continuously decreasing birth rate, however the trend is not monotonous. The Statistical Office indicates for 2014 a slightly higher number of **live births (17,064) than** for 2013 (16,797).

The number of **68 stillbirths** which is provided by the Statistical Office corresponds in relation to the number of live births to the calculated expected value for 2002-2013 (69.4 stillbirths).

According to the Federal Statistical Office 714927 infants were live births in Germany in 2014. After 20 years of decreasing birth rates, we registered slightly more births in the last three years (2011: 662685 live births). The live births of Saxony-Anhalt represent approximately 2.5% of all births in Germany.

Data of **76 terminations of pregnancy** and **30 spontaneous abortions after 16 WOG** form also part of the current annual report beside the data of live and stillbirths of the year 2014. The indicated prevalences are therefore based on **a total number of 17.238 births** (see chapter 2).

589 births had at least **one major malformation** (3.42% of all births). In this way, the calculated malformation rate corresponds again to the rate of the previous 12 years (CI 3.40% to 3.55%) (see chapter 8).

85.9% of **infants with a major malformation** were live births in 2014, proportional only 1.9% of these births deceased (see chapter 7 and 8 (in German version)). At the beginning of the 1980s the percentage of deceased live births in regard to births with major malformations was only 20%. The percentage of terminations of pregnancies (2014: 12.2 %; 2002-2013: 10.2 %), as well as the spontaneous abortions (2014: 1.5 %; 2002-2013: 1.4 %) lies slightly above the registered percentage of the entire reporting period. Compared to the previous years, the number of stillbirths is currently very low (2014: 0.3 %; 2002-2013: 0.9 %).

The by far most frequent single diagnosis ASD and VSD appeared similar to the previous years also in 2014 most frequently again. We registered on rank three in the current year the hearing loss, as all cases of this malformation are now nearly completely detected. Next position is occupied by the dilated uropathy, which was registered more frequently than usual in 2014. Following are PDA and Down syndrome. We registered less frequently than expected microcephaly, subluxation of hip and clubfoot (see chapter 11).
1.49% of all births presented one strictly defined **indicator malformation** in 2014 (see chapter 12). **Higher prevalences** in comparison to the respective basis prevalences were registered in 2014 for anencephaly, spina bifida, tetralogy of Fallot, coartation of aorta, choanal atresia, undescended testis, Potter sequence, limb reduction malformations and omphalocele.In contrast, microcephaly, microtia/anotia, cleft lip with cleft upper jaw and palate, oesophageal atresia/-stenosis/-fistula, anorectal atresia, preaxial polydactyly and diaphragmatic hernia showed **lower prevalences**. The rarely appearing indicator malformations arhincephaly / holoprosencephaly, small instestinal atresia/-stenosis and epispadias were not registered in Saxony-Anhalt in 2014.

Furthermore, we received data about 75 terminations of pregnancy in 2014 (see chapter 14 (in German version)). These can be divided into: 32.0% CNS malformations, 40.0% chromosomal aberrations and 28.0% multiple anomalies and other malformations. Down syndrome, spina bifida, anencephaly and Potter sequence were the most decisive factors for a termination of pregnancy.

26 births suffered 2014 from a **genetically caused disease. Sequences, associations, resp. complexes** were diagnosed in 23 cases. Six births with **embryopathy or congenital infection** were registered. Again, one infant suffered from a Sartan embryofetopathie. The average maternal age of the above mentioned 65 births with **chromosomal aberration** was 33.2 years in 2014 (see chapter 13(in German version)).

Hypospadias, which is the most frequent congenital malformation of the male urogenital system is topic of chapter 16 of our present annual report. Beside giving information about classification and aetiology, we present prevalences of Saxony-Anhalt from the last 20 years as well as a topic related EUROCAT study and we discuss possible reasons such as regional influences and the maternal age.

In 2014 the Monitoring of Congenital Malformations received data about **589 births** from Saxony-Anhalt with at least one **major malformation** In 265 cases minor malformations or anomalies were registered (see chapter 6-8 (partly in German version)). In total, we received 2222 reportings about 1922 births.

The Monitoring of Congenital Malformations registers at the one hand data about infants and foetuses with congenital malformations and on the other hand data about infants without malformations as control cases. These control cases are necessary as the risk calculation in a scientifically founded analyses is only possible when both groups are compared.

Compilation of the present 2014 Annual Report was only possible due to ongoing voluntary reports about congenital malformations from our dedicated colleagues at various medical institutions of Saxony-Anhalt. By receiving these reports we created a solid data basis during the last years which serves to create our Report annually. **We would like to thank all "senders" and hope that this excellent cooperation will continue!**

16 Epidemiology of hypospadias in Saxony-Anhalt and in the European comparison

Classification and aetiology of hypospadias

Hypospadias belong to the most frequent congenital urogenital malformations.
It is to say that hypospadias is a development disorder of the male urethra where the urethral orifice is not located at the top of the penis (glans) but at the ventral side, that means at the underside of the penis. Different forms of appearance are the glandular, penile, scrotal and perineal hypospadias, depending on where the urethral meatus is located. Excluded is the indifferent sex (intersex or pseudohermaphroditism).

Hypospadias are classified in the clinical context into anterior hypospadias (the urethral orifice is slightly displaced, but is still located in the glandular or subcoronal region), central hypospadias (the urethral orifice is located at the ventral side of the penis) and posterior hypospadias (the orifice is located at the penoscrotal region, the scrotum or perineum). For the epidemiological research a classification into grade 1 to 3 is suitable (fig. 50).

Hypospadias can be accompanied by a curvature of the penis shaft (chorda), cleft preputium, constriction of the outer urethral orifice (meatal stenosis), undescended testis and other urogenital anomalies. An operative correction is not necessary in all cases of hypospadias.

The aetiology of hypospadias is widely unknown. In some cases hypospadias has a monogenetical cause, however the majority of cases seems to have a multifactorial origin, also influenced by genetical and environmental factors.

Different environmental pollution and maternal influencing factors were investigated, however only a low birth weight, maternal hypertension, preeclampsia and maternal intrauterine Diethylstilbestrol (DES)-burden (belongs to the group of synthetic, non-steroidal, selective estrogen-receptor- modulators = endocrine disruptors) could be associated with the appearance of hypospadias. An association of hypospadias with a high maternal age and a burden with endocrine disruptors remains controversial.

Big geographical differences are outlined in regard to the prevalence by current literature. The frequency of appearance lies at 2.0 up to 43.2 cases per 10,000 births. It is also not clear if the prevalence of hypospadias rises further on. Former studies showed increasing prevalences, while other studies informed about increasing, unchanged or regressive prevalences.

The different prevalences and trends may have their origin in genetical risk factors and environmental influences, which are more or less distinct in the different regions. Other explications for the varying prevalences are the different methods of investigation used by each study. The registration of the single cases of hypospadias is for example incompletely in some cases. This means that glandular hypospadias which do not need a surgical intervention in every case and hypospadias with known aetiology are excluded by some studies. This results into a low prevalence. Furthermore, data about the exact characteristic of the respective hypospadias is often not available.

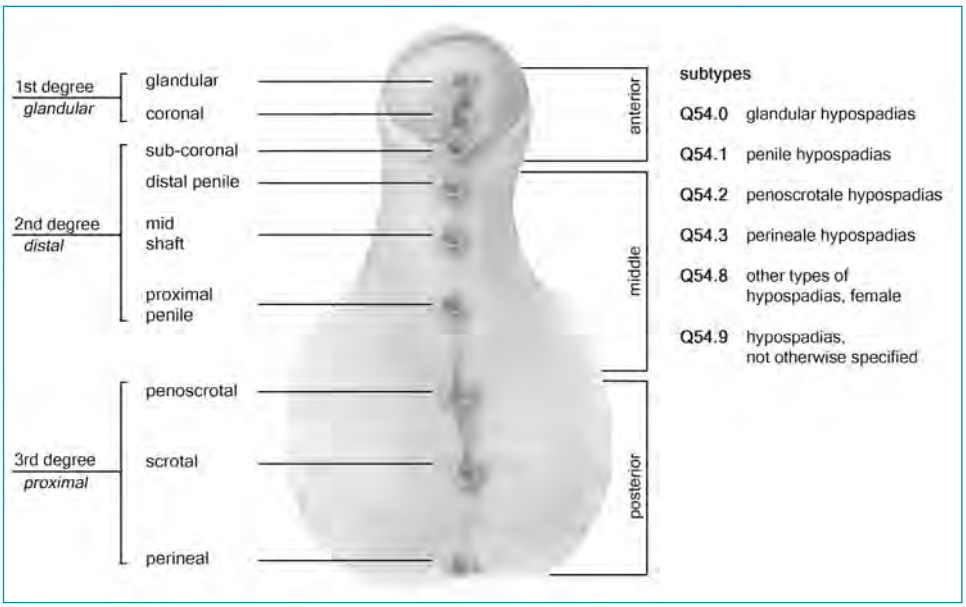
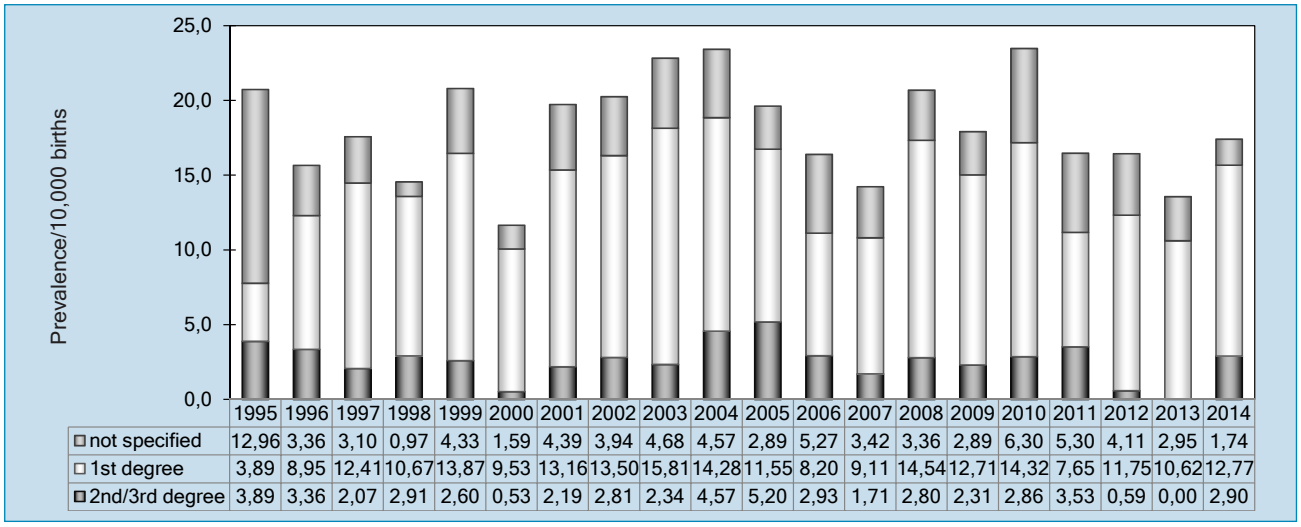


Fig. 50: Classification of hypospadias
(modified acc. to WHO, CDC, ICBDSR. Birth Defects Surveillance. A Manual for Programme Managers. 2014)

Prevalence of hypospadias in Saxony-Anhalt

Our data analysis for Saxony-Anhalt includes all hypospadias that were registered by the Monitoring of Congenital Malformations during the years 1995-2014 (registered hypospadias were differentiated into isolated hypospadias, hypospadias with multiple congenital malformations, hypospadias with known cause and hypospadias of different severity).
The number of live births amounts to 307,279 during the registration period.



	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014
not specified	12,96	3,36	3,10	0,97	4,33	1,59	4,39	3,94	4,68	4,57	2,89	5,27	3,42	3,36	2,89	6,30	5,30	4,11	2,95	1,74
1st degree	3,89	8,95	12,41	10,67	13,87	9,53	13,16	13,50	15,81	14,28	11,55	8,20	9,11	14,54	12,71	14,32	7,65	11,75	10,62	12,77
2nd/3rd degree	3,89	3,36	2,07	2,91	2,60	0,53	2,19	2,81	2,34	4,57	5,20	2,93	1,71	2,80	2,31	2,86	3,53	0,59	0,00	2,90

Fig. 51: Analysis of frequency of hypospadias in Saxony-Anhalt, classified acc. to severity

Prevalence of hypospadias in Europe

A EUROCAT study (Bergman et al. 2015) analysed prevalences and trends of hypospadias, isolated hypospadias, hypospadias with multiple congenital malformations, hypospadias with known cause and hypospadias of different subtypes from 23 EUROCAT registers for the time period of 2001-2010. Additionally, it was investigated if the maternal age is related to the prevalence of hypospadias. This study (data from Saxony-Anhalt is included) is the most comprehensive one of its kind until today in Europe.

Data from the central EUROCAT database was obtained in April 2013 to allow the study a calculation of prevalences for the years 2001-2012. A classification into hypospadias as isolated cases, MCA cases and cases with EUROCAT-MCA-algorithm took place. Isolated cases do not present another major structural malformation. MCA cases appear in combination with at least one further not related major malformation, which cannot be explained by an underlying syndrome or sequence. In cases of known reason, the registered hypospadias had a chromosomal, genetical or teratogen origin.

To analyse the maternal age the prevalences were classified into six groups (table 16.1). Hypospadias with unknown maternal age (1.5%) were excluded from this analysis.

Tab. 16.1: Total prevalence of hypospadias grouped acc. to maternal age in 20 EUROCAT-registers* 2001-2010 modified acc. to table 2 in Bergman et al.: Epidemiology of hypospadias in Europe: a registry-based study. World J Urol 2015

Maternal age, grouped	Number of hypospadias	Number of births	Total prevalence per 10,000 births (95% CI)	Unadjusted relative risk (95% CI)	Adjusted relative risk per register (95% CI))	Adjusted relative risk per register and maternal age (95% CI)
<20 years	385	194,807	19.8 (17.9-21.8)	1.13 (1.02-1.226)	1.12 (1.00-1.24)	**0.63 (0.20-1.99)**
20-24 years	1,333	710,660	18.8 (17.8-19.8)	1.08 (1.00-1.15)	1.06 (0.99-1.13)	**0.86 (0.56-1.30)**
25-29 years	2,161	1,239,528	17.4 (16.7-18.2)	1.00 (Referenz)	1.00 (Referenz)	**1.00 (Referenz)**
30-34 years	2,409	1,428,079	16.9 (16.2-17.6)	0.97 (0.91-1.03)	1.00 (0.94-1.06)	**1.08 (0.84-1.38)**
35-39 years	1,253	761,353	16.4 (15.6-17.4)	0.94 (0.88-1.01)	0.99 (0.92-1.06)	**1.03 (0.77-1.37)**
40+ years	269	156,496	17.2 (15.3-19.4)	0.99 (0.87-1.12)	1.04 (0.92-1.18)	**1.09 (0.71-1.68)**
total	7,810	4,490,923	17.4 (17.0-17.8)			

* Data from Isle de Reunion, Wessex (UK) and Hungary (n=3.002) were excluded from this analysis, as the maternal age was unknown in more than 20% of all cases. All other cases with unknown maternal age were also excluded from this analysis (n=117 from 20 registers).

Recent prevalence and development

10,929 cases of hypospadias were registered by 23 EUROCAT centres out of 5,871,855 births during the years 2001-2010. Therefore, a total prevalence of 18.61 per 10,000 births can be calculated. However, strong fluctuations between the single centres were registered, from 5.10 in South Portugal up to 36.83 per 10,000 births in Mainz. In total, the calculated prevalence remained stable during the time period of 2001-2010 (trend p = 0.136), but at the same time the data were heterogen (p = 0.013).

The majority of hypospadias occurred isolated (n = 9,667; 88.5%), 9.6% occurred as MCA (n = 1,053) and only 1.9% of all cases had a chromosomal (n = 112), genetical (n = 86) or teratogen origin (n = 11). In total, no significant trend of one group can be identified.

The subtypes of hypospadias were specified in 45.6 % of all cases (n = 4,980): 31.5 % belong to the group of anterior hypospadias (n = 3,443), 10.2% to the group of central hypospadias (n = 1,109) and 3.9% to the group of posterior hypospadias (n = 428). A significant regressive trend was registered for the not specified hypospadias (p < 0.001). Anterior and posterior hypospadias showed in contrast a significant increasing trend (p < 0.001 and p = 0.005). The central hypospadias showed heterogen data during the entire registration period (p = 0.001).

Maternal age and prevalence

In this study teenaged mothers had a higher prevalence of hypospadias in contrast to mothers aged from 25 to 29 years (adjusted relative risk 1.13, 95 % CI 1.02-1.26) (table 16.1). This association also remained when the analysis was repeated under exclusion of chromosomal anomalies.
However, after adjustment of register effects, the increased risk of young mothers to have a child which suffers from a hypospadias was not significant any more (adjusted relative risk 1.112, 95 % CI 1.00-1.24, p = 0.051) (table 16.1).

Discussion of the EUROCAT-study results

The registration of glandular hypospadias is decisive for the calculation of the total prevalence, as this form presents a huge part of the anterior hypospadias which belong to the most frequently appearing form of hypospadias. The registration of glandular hypospadias may be incompletely as it is sometimes not diagnosed until the end of the first year of life. This has a decisive effect on the calculation of the total prevalence and is rather hindering when evaluating certain trends. The registration depends on which information sources are available for each register (e.g. if only surgical data are available, milder forms might be missing), which form of data transmission is used (active or passive information), notification procedure (Data protection Directive), screening policy or possibility of receiving a treatment in the single countries (mild forms of appearance cannot be diagnosed, preputium anomalies are falsely diagnosed as hypospadias). However, we appreciate that no increasing trend of hypospadias prevalence was registered in all EUROCAT centres, even in the four EUROCAT centres with the highest prevalence and at the same time probably best form of registration.

Of course, environmental factors exist that influence the appearance of hypospadias, however their role in connection with the isolated or MCA hypospadias remains widely unknown. The present study shows no trends for isolated or MCA hypospadias during the observation period.

The registered hypospadias were classified according to severity into anterior, central and posterior hypospadias. Unfortunately, the degree of severity was unknown in more than half of the cases. In this connection a trend evaluation is difficult. Furthermore it is possible that the increasing trends of anterior and posterior subtypes which are shown here can be explained with the decreasing trend of not classified hypospadias.

Some studies hold the opinion that an increasing maternal age is associated with a higher risk for hypospadias, other studies do not support this theory. In the present study the prevalence does not vary significantly in the different age groups and after register data was adjusted. However, the highest prevalence of hypospadias was registered at teenage mothers and not at older mothers.

This EUROCAT study also shows which advantages and limits exist when data from different European malformation centres are pooled to determine prevalences and trends for hypospadias in Europe. Only the implementation and steady improvement of the EUROCAT coding guideline enables a European wide trend analysis. A combination of data from different malformation centres with certain studies makes it possible to register all cases more completely and classify them accordingly.

References:

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18 Newborn Hearing Screening 2014

Introduction

Every newborn is entitled to receive a general newborn hearing screening which belongs as from 01-01-2009 to the recommended early detection examinations after birth of a child.
The aim of the newborn hearing screening (NHS) is to detect **congenital hearing disorders at an early stage (up to the 3rd month of life)** and to **initiate the corresponding therapies (up to the 6th month of life)**.

The basis for this early detection examination is "Enclosure 6 - early detection examination of hearing disorders at newborns (newborn hearing screening)" of the **Children Directive issued by the Federal Joint Committee (G-BA)** on 19-06-2008.

The Children Directive determines the **process of the newborn hearing screening** in the following way:
- measurement of each ear by TEOAE or AABR up to the 3rd day of life (outside of hospital by no later than early detection examination 2 (U2))
- AABR examination is mandatory for children with increased risk for a hearing disorder
- examinations of premature infants by no later than calculated date of delivery and examinations of not healthy newborns by no later than 3rd month of life
- at suspicious first screening, repetition of examination on both ears by AABR preferably on the same day, but by no later than early detection examination 2 (U2)
- at suspicious finding of the follow-up AABR examination a comprehensive confirmation diagnostics is necessary up to the 12th week of life

According to the Children Directive **performance and results of the newborn hearing screening as well as a possible confirmation diagnostics** have to be **recorded** in the **"yellow book of examination" of every child**. The responsible paediatrist resp. ENT physician can evaluate by reading this information if the required diagnostics resp. the rapy in case of a hearing disorder was initiated.

The Monitoring of Congenital Malformations Saxony-Anhalt cooperates with the Centre for Newborn Hearing Screening Saxony-Anhalt since 2006 as **tracking centre for the newborn hearing screening** (Federal State dependent screening centre).

The Newborn Hearing Screening Directive stipulates that the hearing screening should be performed via AABR at **children with an increased risk for congenital hearing disorders.** The following overview outlines in extracts possible **indications for the performance of an AABR examination** due to an increased risk of hearing disorders (modified according to JCIH 2007*):
- positive family history regarding hearing disorders
- clinical suspicion of hearing disorder/ deafness
- premature birth, birth weight under 1500 g
- neonatal intensive care
- hyperbilirubinemia (exchange transfusion)
- pre-, peri- or postnatal hypoxia (pH < 7.20)
- peri- and postnatal cerebral hemorrhage, oedema
- intrauterine infections
- culture positive postnatal infections associated with increased risk of hearing loss
- craniofacial anomalies
- distinctive diseases with hearing loss
- neurodegenerative diseases or sensomotoric neuropathies
- outer characteristics, which point to a distinctive disease that appears in combination with a hearing disorder (e.g. white strand of hair)
- APGAR-values of 0-4 in the first minute and/or 0-6 after 5 minutes

** References:*
Joint Committee on Infant Hearing: Year 2007 position statement: Principles and guidelines for early hearing detection and intervention programs. PEDIATRICS 2007; 120: 898-921.

Participating institutions

25 maternity clinics existed in Saxony-Anhalt in 2014. All these clinics offer a newborn hearing screening already for several years by TEOAE or AABR. All 25 maternity clinics participated 2014 in the newborn hearing screening.
A screening-ID is assigned to each child - if there is no denial of this examination and /or data transmission by the parents/guardians - and the hearing screening results will be forwarded to the tracking centre of newborn hearing screening Saxony-Anhaltt.

The screening ID, which has to be assigned to each infant as condition to participate in the hearing screening trakking is also used by several midwifes. In this way also infants who are exclusively under care of a midwife (e.g. home births) can participate in the newborn hearing screening.

The following table on page 81 gives an overview about the single maternity clinics and number of births with a screening ID.

Maternity clinics in Saxony-Anhalt and participation in the Newborn Hearing Screening Tracking (ordered by location)

Maternity Clinic	Tracking period 2014	Lifebirths in this period*
Ameos Klinikum Aschersleben	01.01. - 31.12.2014	642
Gesundheitszentrum Bitterfeld/Wolfen	01.01. - 31.12.2014	451
Helios Klinik Jerichower Land	01.01. - 31.12.2014	360
Städtisches Klinikum Dessau	01.01. - 31.12.2014	809
Altmark-Klinikum Krankenhaus Gardelegen	01.01. - 31.12.2014	324
Ameos Klinikum Halberstadt	01.01. - 31.12.2014	620
Ameos Klinikum Haldensleben	01.01. - 31.12.2014	264
Krankenhaus St. Elisabeth und St. Barbara Halle	01.01. - 31.12.2014	1,981
Universitätsklinikum Halle (Saale)	01.01. - 31.12.2014	1,104
Helios Klinik Köthen	01.01. - 31.12.2014	450
Krankenhaus St. Marienstift Magdeburg	01.01. - 31.12.2014	863
Klinikum Magdeburg	01.01. - 31.12.2014	1,156
Universitätsklinikum Magdeburg A.ö.R.	01.01. - 31.12.2014	1,285
Carl-von-Basedow-Klinikum Saalekreis Merseburg	01.01. - 31.12.2014	657
Saale-Unstrut Klinikum Naumburg	01.01. - 31.12.2014	378
Harzklinikum Dorothea Christiane Erxleben, Klinikum Quedlinburg	01.01. - 31.12.2014	525
Altmark-Klinikum Krankenhaus Salzwedel	01.01. - 31.12.2014	437
Helios Klinik Sangerhausen	01.01. - 31.12.2014	758
Ameos Klinikum Schönebeck	01.01. - 31.12.2014	519
Johanniter-Krankenhaus Genthin-Stendal	01.01. - 31.12.2014	841
Asklepios Klinik Weißenfels	01.01. - 31.12.2014	467
Harzklinikum Dorothea Christiane Erxleben, Klinikum Wernigerode	01.01. - 31.12.2014	674
Evangelisches Krankenhaus Paul Gerhardt Stift Wittenberg	01.01. - 31.12.2014	590
Georgius-Agricola Klinikum Zeitz	01.01. - 31.12.2014	360
Helios Klinik Zerbst/Anhalt	01.01. - 31.12.2014	220
Total number of live births* in Saxony-Anhalt		**16,735**

Home births / Births in a birthing centre resp., infants not born in Saxony-Anhalt	01.01. - 31.12.2014	**165**

Tracked infants, in total	**16,900**

* births + multiple births, in case that no own birth register number was assigned, number of stillbirths is deducted

In total, **16,735 births** received a screening ID in their maternity clinic in Saxony-Anhalt in 2014. Therefore, these infants could participate in the hearing screening tracking.

Furthermore, **165 data records of infants** which were delivered at home or born in a birthing centre are included in our analyses. These infants received also a screening ID after birth, e.g. by their corresponding midwife.

Tracking Effort

Tracking of the newborn hearing screening requires an ample organising and personnel effort. It starts with recording the results of the hearing test in the maternity clinic and forwarding them by mail or fax to the Monitoring of Congenital Malformations. The results are entered here in a special tracking database. In total, we received results of 107 senders in 2014.

The following table shows how many newborns received a screening ID per month and and how many results were forwarded to the Monitoring of Congenital Malformations per month. Averagely, 1800-1900 results were registered per month, however in some cases we received multiple reportings for one child (e.g. from the maternity clinic, paediatric clinic, ENT clinic, ENT physician, paediatrist and from the parents).

Births with screening-ID and number of incoming result

2014	Infants with screening ID	Number of reportings
January	1,416	1,908
February	1,214	1.608
March	1,306	1,728
April	1,244	1,679
May	1,407	1,888
June	1,476	1,939
July	1,672	2,181
August	1,504	1,979
September	1,570	2,049
October	1,431	1,941
November	1,279	1,797
December	1,381	1,820
total	**16,900**	**22,517**

To carry out the tracking thoroughly, 2752 letters resp. faxes were forwarded in 2014 (one up to 11 letters per infant). With reference to all infants with screening ID this corresponds to an average of 0.16 letters per infant.

Additionally, the parents and attending physicians of the infants born in 2014 were contacted by telephone. In total 295 calls were made in connection with the hearing screening tracking (one up to four calls per infant).

Results (date September 2015)

All results, that were reported to the hearing screening tracking centre about infants that were born in 2014 are included in our analyses 2014 of the newborn hearing screening:

13,805 infants out of 16,900 infants with screening ID had an unsuspicious newborn hearing screening.
In 3,095 cases the first hearing test had to be followed-up, resp. no newborn hearing screening took place in the maternity clinic (these cases are regarded also as follow-up cases). There are numerous reasons why a hearing test did not take place, e.g. ambulant delivery, early discharge from maternity clinic, transfer of the child to another clinic or a defective hearing screening device.

The follow-up examination of the 3,095 infants showed in 2,416 cases an unsuspicious result. The remaining 679 infants had again a suspicious result.
265 of these 679 infants received a complete paediatric audiological confirmation diagnostics. According to our knowledge, 180 infants did not receive a confirmation diagnostics and therefore are considered as lost lost to follow-up.

214 infants did not participate in the screening (no reaction of parents to reminder letters or refusal of examination) and in eight cases the status is still pending, i.e. the examinations were not finished in September 2015 or the tracking process still requires more time.

In 12 cases the tracking was closed from our side without any result, because we could not get into contact with the parents.

In total, the follow up-examinations of 290 infants who were born in 2014 could be completed (confirmations diagnostics). Among 265 infants with a suspicious result, 25 infants had an unsuspicious first screening. Maybe these infants received a follow-up-examination due to present risk factors.
Within the follow-up examination, a hearing disorder could be excluded in 239 cases. In 51 cases a unilateral/bilateral hearing disorder was diagnosed and the corresponding therapy was initiated. For instance, 32 infants received a hearing aid (22 times hearing aid bilateral, 10 times hearing aid unilateral).

Evaluation of the Newborn hearing screening

The Federal Joint Committee (G-BA) already determined in 2008 when the newborn Hearing Screening was established, that this early detection examination should be evaluated regarding quality and goal attainment in an own study (§ 10 of Enclosure 6 - early detection examination of hearing disorders at newborns (newborn hearing screening) of the Children Directive about the early detection of diseases at children up to the 6th year of life).

In 2014, after a European wide public submission the Federal Joint Committee tasked a commission of experts to evaluate the newborn hearing screening for the birth cohorts 2011 and 2012. Members of the commission of experts were scientists of the Bavarian state office for health and food safety, of the University of Münster (Westfälische Wilhelms-Universität Münster) and of the University of Munich (Ludwig-Maximilians-Universität München).

The study should evaluate the quality of structure, process and aims of the early detection examination regarding congenital hearing disorders. Especially number of examinations,
number of suspicious first and control examinations, number of correct positive and false negative results should be analysed. Also the point of making a diagnosis and of the therapy initiation should be regarded.

As the newborn hearing screening is organised by each Federal State, the data registration is heterogeneous and therefore quality differences in the different Federal States may appear. The above mentioned evaluation should create consistent quality standards, respectively the standards should be unified and thereby the whole process of the newborn hearing screening can be optimised.

Data of the hearing screening centres of the different regions and Federal States is summarized and collected from the statistics of the hospitals within this evaluation. By standardised registration forms the data is also collected in pedaudiological facilities. This is done to get an overview about the whole process from first screening up to the diagnosis and initiating of a therapy. Routine data is also included into the analysis, e.g. from the Association of Statutory Health Insurance Physicians and Statistical Offices.

Furthermore, all tracing centres are consulted to gain information about structure of the tracing process.

At the moment, data collection and analysis take place. A summary will be published in 2016.

19 Annual Report 2014 of the Newborn Screening Centre Saxony-Anhalt

according to §14 Note 2 of the valid Children Directive

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Competence net newborn-screening

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Introduction

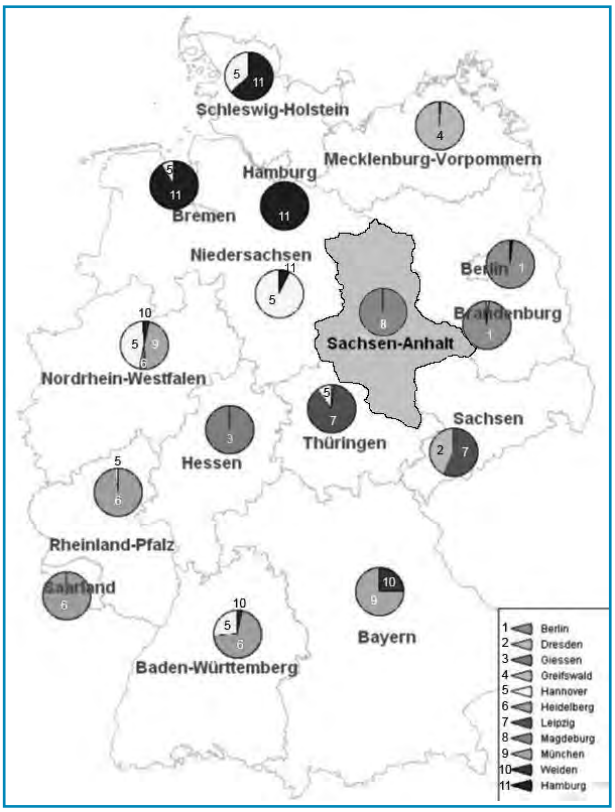
The newborn screening is a medical prevention measure which has the aim of a complete and early detection of endocrine and metabolic diseases and a high quality therapy for all infants with a treatable type of these diseases. The details of the newborn screening (NS) are stipulated in the enclosures 2-4 of the Directives about the early detection of diseases at children up to their 6th year of life ("Children's directive").

The German Society of newborn screening (DGNS) compiles annually a national screening report in cooperation with the German screening laboratories. The screening data is analysed on the basis of several quality criteria for realisation of NS in Germany which are defined by the Directive.The report only refers to congenital metabolicand endocrinologic diseases which are defined as "target" diseases by the Directive. Furthermore, it gives a complete statistical compilation of related screening figures, recall rates and confirmed diagnoses for the current year. Additionally, data about process quality for whole Germany is presented.

Screening samples from the single Federal States are divided to the laboratories as it is presented in figure 1. It shows that the screening laboratory Magdeburg completely handles all screening samples from Saxony-Anhalt.

Our laboratory works in due consideration of the diseases mentioned by the Directive. Table 1 shows the corresponding diseases with their frequency of appearance in Germany.

Fig. 1: Screening centres in Saxony-Anhalt



Tab. 1: Frequency of diseases in Germany, detected during screening

Disease	Prevalence
Hypothyroidism	1 : 3,275
Congenital adrenal hypoplasia (CAH)	1 : 17,383
Biotinidase deficiency (incl. partial defects)	1 : 24,212
Galactosemia (classical)	1 : 112,991
Phenylketonuria (PKU)/ hyperphenylalaninemia (HPA)// cofactor deficiency	1 : 5,022
Maple syrup urine disease (MSUD)	1 : 112,991
Medium-Chain-Acyl-CoA-Dehydrogenase deficiency (MCAD)	1 : 10,761
Long-Chain 3-OH-Acyl-CoA-dehydrogenase deficiency (LCHAD)	1 : 135,589
(Very-)Long-Chain-Acyl-CoA-dehydrogenase deficiency (VLCAD)	1 : 56,496
Carnitin-Palmitoyl-CoA-Transferase I deficiency (CPTI)	1 : 338,974
Carnitin-Palmitoyl-CoA-Transferase II deficiency (CPTII)	keine Angaben
Carnitin-Acylcarnitin-Translocase deficiency (CACT)	keine Angaben
Glutaric aciduria type I (GA I)	1 : 225,982
Isovaleric acidaemia (IVA)	1 : 56,496
Total	**1 : 1,309**

Screening data 2014 of Saxony-Anhalt is outlined in the following.

Process quality

The process quality describes the process itself and its evaluation on a basis of given indicators by expert committees.
Indicators for the newborn screening are:

- complete coverage of target population
  - coverage method and rate
  - blank card systems
- completeness of control (recall)- and follow up examinations
- registration of examination parameter and cut-offs
- according to disease, laboratory and age/gestational age stratified recall rates, positive
- predictive values, prevalences
- specificity and sensitivity of test methods
- process times (only in the preanalytic and laboratory field: age at time of blood taking, time between blood taking, arriving at laboratory and result transmission)
- individual screening results of newborns, which have to be examined further on
- confirmation diagnostics
  - diagnostics type
  - diagnostics period of time
- final diagnosis
- start of therapy

Registration Rates

To ensure that a screening is offered to every newborn, a tracking for completeness is necessary. This can be realised for children, which are delivered in obstetric clinics by control of the respective consecutive number in the birth register and by means of a so called blank card system. According to the Childrens Directive the obstetric clinics have to document on a blank test card the total refusal of screening, the refusal of an early blood taking within the screening, the transfer to specialised institutions or death of the newborn. This test card is send to the responsible laboratory; however it differs between the single Federal States how successful this method is.

We collected the following registration rates in Saxony-Anhalt in 2014:
According to the Federal Statistical Office 17,064 children were live births in Saxony-Anhalt
(according to the maternal residence)

.

Tab. 2: Registration rates of first tests

	Number	Difference/sum
First screening in Magdeburg	16,858	
Not resident in Saxony-Anhalt	687	16,171
Screening refused by parents resp. probably not shown up for U2, no response	12	16,183

The discrepancy between the number of live births and screened infants amounts to 881.

Data of the Federal Statistical Office are based on the data of the Statistical Office of Saxony-Anhalt. A corresponding basis is formed by the total number of births (sorted according to maternal residence) from the maternity clinics and which are reported to the register office.

However, the number of mothers with residence in Saxony-Anhalt but who delivered their infant in another Federal State can not be recorded in our screening statistics if the screening of the infant also took place in another Federal State.
We suppose that also newborns were screened in other Federal States, although they were born in Saxony-Anhalt and their mothers were resident in Saxony-Anhalt as well. We do not have further information about these cases.

Tab. 3: Registration rates by blank cards

Blank card	Number
Received in total	358
Infant deceased / stillbirth	59
Refusal of early taking	219
Transfer to another clinic	47

No blood sample arrived at our laboratory out of 40 blank cards (excluding deceased infants). One reason among others is that the screening was done in another Federal State.

Tab. 4: Completeness of control (recall) and follow up examinations

Reason for second screening	suspicious first screening	early taking < 36h	preterm births < 32 WOG
Requested	44	318	205
Received at own laboratory	44	297	195
Deceased before control examination	-	-	6
Received at other laboratory	-	11	4

WOG = weeks of gestation

Examination Numbers, Recall Rates and Assured Cases

Table 5 shows recall rates of the single parameter and assured cases.

In total, 107 control examinations had to be done in 2014.

Tab. 5: Samples, assured cases, recall-rate 2014, incidence 1992-2014

	First test	Second test**	Recall rate** 2014	Assured cases	Incidence in Saxony-Anhalt 1992-2014
TSH	16,858	492	0.03 %	3	1/3,977
PHE***	16,858	492	0.02 %	4	1/5,417
GALT	16,858	492	0.01 %	-	1/186,897
BIO	16,858	492	0.01 %	-	1/256,458
17OHP	16,858	492	0.16 %	2	1/16,325##
AC, AS (TMS)	16,858	492	0.02 %	4 x MCAD#	1/11,978–###

* Second transmissions, that were necessary due to an early blood taking at full-term infant <36 h or premature infant < 32 weeks of gestation, resp. positive first result (recall)
** Definition of recall: need for new blood sample due to suspicious first screening result, when the first test took place at an age of > 36 h at full-term infant or >32 weeks of gestation at premature infant
*** Phe = phenylalanine: parameter to identify a phenylketonuria and hyperphenylalaninemia
# MCAD: disorder in metabolising medium-chain fatty acids
Screening to detect congenital adrenal hyperplasia syndrome (since 1997 in Saxony-Anhalt)
Enlarged screening (TMS) since May 2001 in Saxony-Anhaltt

Process Times

Point of Taking Blood Samples

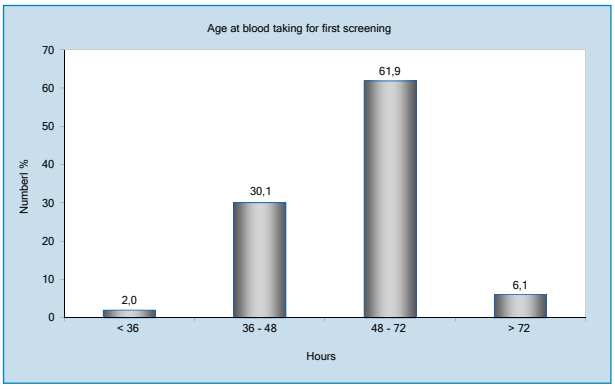


Fig. 2: Age at point of blood taking for first screening

The optimal point of taking blood samples for the newborn screening (36 –72 hours of life) took place within the required period of time at 92.0% of all cases (2013: 91.3%). At a total number of 8.1% the taking of blood samples took not place within the required period of time (2012: 8.6%). This trend remaines unchanged in comparison to the previous year.

Note: Data of newborn infants was only registered when all required information was given (date of birth and time as well as date of blood taking and time).

Transmission Time

Figure 3 shows that 43.1% of all transmittals reached the laboratory more than two days after the blood taking (2013: 38.1 %).

Problems with the transmission of blood samples also occurred in 2014.
The Children Directive requires a transmission of the pathological result by the laboratory back to the sender by no later than 72 hours after blood taking. The limiting factor is here
the time from blood taking up to the receipt of the blood sample (delivery time). In this connection we want to point out again that the Children Directive requires a transmission of each blood sample at the day of taking.

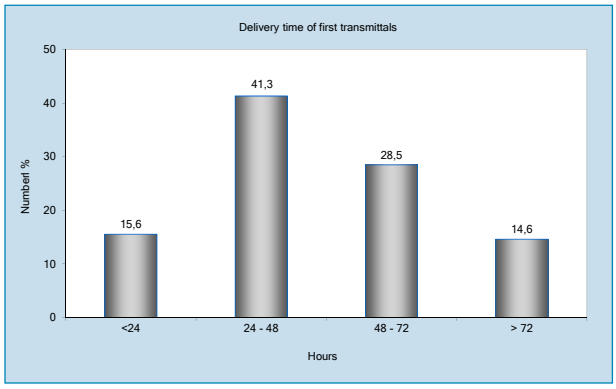


Fig. 3: Delivery time of transmittals

Transmission of Results

Figure 4 shows how much time a complete diagnostics of first examinations takes in the laboratory. Results which are finished after more than 36 hours are caused by internal repetitions. 4.2% of the results which were finished after more than 48 hours are the consequence of possible disturbances in the laboratory (maintenance of devices).

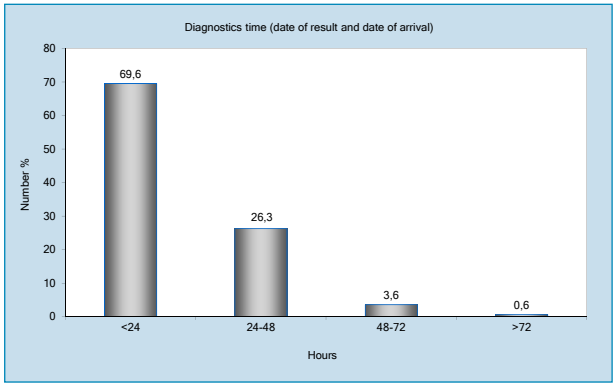


Fig. 4: Diagnostics time (date of result - date of arrival)

The result of first screenings which is shown by figure 4 reflects unfortunately also the diagnostics time of pathological results (in total 105) (figure 5).

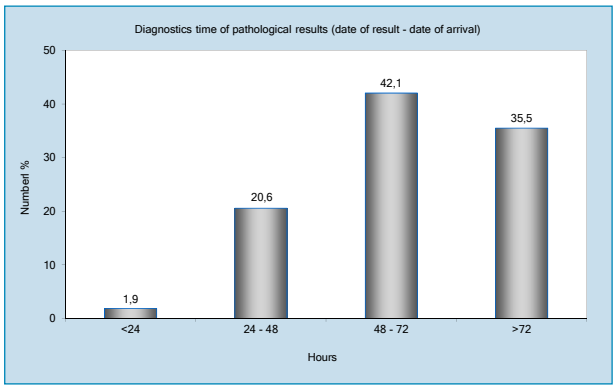


Fig. 5: Diagnostics time of pathological results

The following figure shows the time from oral transmission of 107 pathological results up to the arrival of a control sample. Generally, pathological results are transmitted orally and faxed as partial result after they were confirmed internally by the laboratory. All these activities are documented.
Four cases had a response time of more than 120 hours and concerned premature infants. In these cases, the taking of the sample to control was postponed to a gestational age of 32 weeks (timely second blood taking). As these infants are in custody of a hospital there is no risk when proceeding in this way and in case the first result was discussed with the responsible physician.

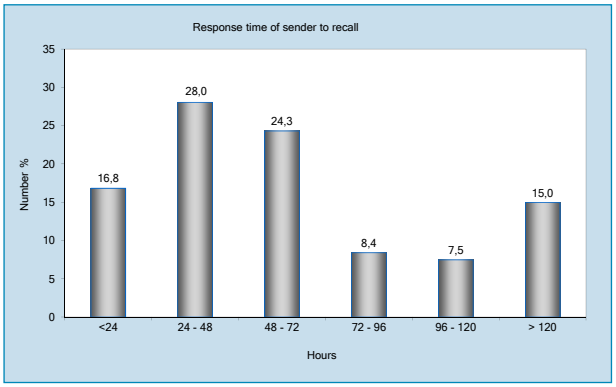


Fig. 6: Response time of sender to recall

13 suspicious screening cases were confirmed by confirmation diagnostics. These cases concerned three children with a hypothyreosis, four children with a phenylketonuria/ hyperphenylalaninemia (PKU/HPA), four infants with a disorder in metabolising
middle-chain fatty acids (MCAD) and four infants with congenital adrenal hyperplasia.

Therapy Starting at Patients with Positive Screening

10 patients needed a therapy:

Tab. 6: Diagnosis, confirmation diagnostics and therapy starting

Diagnosis	Confirmation diagnostics	Age at start of therapy
3 x Hypothyroidism	Serum-TSH, T4, sonography	5-6 days
1 x Phenylketonuria	Serum-Phe, BH4-test	11 days
2 x Congenital adrenal hypoplasia	analysis of multiple steriods in dried blood or serum	3-6 days
4 x MCAD deficiency	mutation analytics	7-10 days

Three infants with a HPA did not need a therapy.

Summary

Similar to the previous year, no changes took place in the specifications of the Federal Joint Committee of physicians and health insurances (G-BA) in 2014.
Thereby, the Gene Diagnostics Act still is and remains the superordinated act with its own paragraphs of penalty.

Again, the process quality was not improved in 2014 as our screening laboratory already has an optimal quality level in comparison to other German screening laboratories.

As usual, all patients with a positive first screening result were followed up and their diagnosis was assured resp. excluded.
Also the confirmation of a positive screening result (confirmation diagnostics) by the attending medical institution and the start of a therapy were documented in all cases.

We calculated an incidence of 1 : 1297 for all objective diseases of the newborn screening in Saxony-Anhalt in 2014.

For further information about the metabolic screening centre Magdeburg, we kindly invite you to visit our website:

www.stoffwechselzentrum-magdeburg.de

We would like to inform sender, parents and interested people here about the Newborn Screening and the Newborn Hearing Screening and provide downloads. We update our website on a regular basis.

The national screening report of the DGNS is available on their own website two years after the respective period of time.