Annual Report 2013

Malformation Monitoring Centre Saxony-Anhalt

Medical Faculty

Otto-von-Guericke-University Magdeburg

SACHSEN-ANHALT
Ministerium für Arbeit und Soziales

Annual Report 2013
of the Federal State of Saxony-Anhalt
about the frequency of congenital malformations
and anomalies as well as genetically caused diseases

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Introduction

Dear reader,

It should be part of the general knowledge that intake of alcohol during pregnancy is a strict no-go for the expectant mother. Every single glass of wine, beer or spirit or even mixed alcohol drinks which are often regarded as harmless can have a negative impact on the foetus. A reason is that contrary to the widespread assumption, not only the first three months are responsible for the main development of the foetus. Damages by alcohol may also occur later, for example during cerebral development. Therefore experts recommend a strict abandonment of alcohol as this cytotoxin can reach the foetus via maternal placenta.

A professional examination about the dimensions of alcohol damage on babys is provided by the annual malformation monitoring in Saxony-Anhalt. Our register, situated at the Medical Faculty of the Otto-von-Guericke-University Magdeburg, collects data about FAS (fetal alcohol syndrom) cases since 1980. An extreme case can be that the affected infant is not viable.

During 1980 to 1996, 23 FAS cases out of 234,359 births were registered in the region of Magdeburg. Stillbirths are included in this number. According to this figures experts calculated a prevalence of 0.098 FAS per 1,000 births. When only taking the life births as reference, a prevalence of 0.099 FAS per 1,000 births or one case out of 10,117 appears. Also during the time period until 2010 these figures remained unchanged. However, there is no systematic registration of frequency like this for the whole Federal Republic of Germany. There can be only guessed a frequency of 0.5 to 2.0 FAS per 1,000 births, this would mean that 350 to 1,400 new FAS cases would appear annually.

But also when the infants are unsuspicious at delivery, maternal intake of alcohol during pregnancy may have caused permanent cerebral damage of the foetus. This can become obvious at a later point during life. Development disorder and intellectual disturbance are consequences. However, there are also children with normally developed intelligence, but which suffer from concentration problems, who cannot evaluate the consequences of their actions or who cannot independently resolve tasks. In these cases the fetal alcohol spectrum disorder is present. These children are often outsiders and not accepted by their social environment. Without an expert diagnosis, no specific support can be supplied to these children.

According to experts opinion, one percent of all children in Germany suffer from FASD at birth every year. This means that FASD would appear more frequently than the Downs syndrome.

I consider intake of alcohol during pregnancy as abuse. It should be a matter of interest of the whole society to condemn intake of alcohol during pregnancy. Therefore further educational work has to be done. One possibility might be a warning notice printed on every bottle that contains alcohol which informs about risk factors for the baby. These warning notices already exist in some countries.

My wish is that the Monitoring of Congenital Malformations reaches a wide public platform as this register offers an excellent basis for preventive health care and active child protection. Therefore I would like to thank all participants and the team of authors, Dr. med Anke Rißmann, but also all our partners at the materny clinics of the Federal State.

Yours sincerely

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

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Abbreviations

AABR	automated auditory brainstem response
ASD	atrial septal defect
bil	bilateral
BMI	Body-Mass-Index
BP	basis prevalence
CI	confidence interval
CNS	central nervous system
dB	decibel
DD	differential diagnosis
DIV	double inlet ventricle
DORV	double outlet right ventricle
EUROCAT	European Surveillance of Congenital Anomalies
ENT	ears, nose, throat
FAS	Fetal alcohol syndrome
FASD	Foetal 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
P	prevalence
PDA	persistent ductus arteriosus
PFO	persistent foramen ovale
SA	spontaneous abortion
SB	stillbirths
s.o.	suspicion of
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 2013

	Life births*	Stillbirths*	Spontaneous Abortions (> 16 WOG)	Terminations of Pregnancy	Total
Altmarkkreis Salzwedel	646	1	-	2	**649**
Anhalt-Bitterfeld	1,143	6	-	5	**1,154**
Börde	1,342	3	-	5	**1,350**
Burgenlandkreis	1,317	4	2	2	**1,325**
Dessau-Roßlau	566	3	-	-	**569**
Halle	2,064	8	2	9	**2,083**
Harz	1,526	7	1	6	**1,540**
Jerichower Land	687	2	1	3	**693**
Magdeburg	2,124	9	8	12	**2,153**
Mansfeld-Südharz	954	4	2	4	**964**
Saalekreis	1,344	6	-	7	**1,357**
Salzlandkreis	1,425	5	4	5	**1,439**
Stendal	828	5	4	3	**840**
Wittenberg	831	3	-	-	**834**

Major cities: Dessau-Roßlau, Halle, Magdeburg	4,754	20	10	21	4,805
Districts, in total	12,043	46	14	42	12,145
Saxony-Anhalt	**16,797**	**66**	**24**	**63**	**16,950**

* Federal Statistical Office Saxony-Anhalt 2014

3 Participating Institutions of the Region 2013

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

- AMEOS Klinikum Aschersleben
- AMEOS Klinikum Bernburg
- 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 Grimm, Glindenberg/Magdeburg
- AMEOS Klinikum Halberstadt, Pränatale Ultraschalldiagnostik: CA Dr. Schmidt
- PD Dr. Hahmann, Facharzt für Frauenheilkunde und Geburtshilfe, Halle
- Krankenhaus St. Elisabeth und St. Barbara Halle, Pränatale Ultraschalldiagnostik: CA Dr. Seeger / OA Dr. Seliger
- Universitätsklinikum Halle (Saale), Pränatale Ultraschalldiagnostik:
  CA Prof. Dr. Tchirikov / OA Dr. Thäle / OÄ Dr. Scheler
- 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
- Harzklinikum Dorothea Christiane Erxleben Klinikum Wernigerode, Pränatale Ultraschalldiagnostik: OÄ Dr. Schulze

3.3 Pathological-anatomical institutes (ordered by location)

- Universitätsklinikum Halle (Saale), Institut für Rechtsmedizin
- Klinikum Magdeburg, Institut für Pathologie
- Universitätsklinikum Magdeburg A.ö.R., Institut für Pathologie
- Harzklinikum Dorothea Christiane Erxleben Klinikum Quedlinburg, Institut für Pathologie
- Praxis für Pathologie Dr. Schultz, Dr. Lüders, Dr. Gunia, Stendal

4 Malformation Registration in Saxony-Anhalt

4.1 General Information

The present Annual Report 2013 outlines in the established form the epidemiological data which we collected during the last year regarding congenital malformations in Saxony-Anhalt. Without the thorough and dedicated work of our senders who provided this information, the data collection of the monitoring of congenital malformations Saxony-Anhalt would not be possible. Therefore we want to thank all associated institutions for the brilliant collaboration just at the beginning of this Report!

The primary prevention of avoidable malformations and improving the health condition of the German population is the main goal of malformation epidemiology. A new chance to inform and attract the attention of the public about congenital malformations is created by the invention of the World Birth Defect Awareness day in March 2015. Created by the ICBDSR (International Clearinghouse for Birth Defects Surveillance and Research) and supported by EUROCAT, both organisations applied for recognition by the WHO and UN. We also take part.

What is EUROCAT? Since 1992 the Monitoring of Congenital Malformations Saxony-Anhalt is a member of EUROCAT (European Surveillance of Congenital Anomalies). 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). All these registration centres consider themselves also as epidemiological monitoring stations. Observed topics are drug safety, eating, lifestyle and environmental pollution.
Furthermore, the European initiative about rarely appearing diseases is an important topic. 69 of the malformation groups definded by EUROCAT comply with the European criterion of rare diseases (not more than 5 out of 10,000 persons are affected).

Especially in this connection we benefit from the European network, as in this way we are able to collect a sufficient number of cases of rare diseases for a scientific evaluation and further on to improve the health condition of the affected persons (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 the International Association of 42 malformation registers from 38 countries of the world (www.icbdsr.com).

The special topic in chapter 16 deals in the current year with fetal alcohol exposition. Is the public aware of which long term impacts on the fetal development are caused by alcohol consumption? The zero alcohol limit applies, otherwise physical and mental damage of the foetus may appear. Thereby, the fetal alcohol syndrome (FAS) represents only the complete disorder syndrome. In comparison, the fetal alcohol spectrum disorders (FASD) describe a connection between behavioural problems and adolescent capability and the prenatal alcohol exposition. But FASD is not only a particular problem in families with addiction problems, it concerns all social classes.

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, Prof. Dr. Dr. R. Nehring, Dr. H. Willer and Mr. M. Schiener.
Additionally, we would like to thank our colleagues at the Medical Faculty for their organisational support, these persons are Mrs. Dipl.-Wirtsch. V. Rätzel, Dr. J. L. Hülsemann and 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.)
- 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. 2013 is considered the year of birth although some terminations of pregnancy after prenatal diagnostics took place at the end of 2012. 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 (Adaption 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 2013.
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 2013 in comparison to the last 12 years (2001-2012). Here, a **total number of 209,249 births** forms basis for the **basic prevalence** calculation **2001 to 2012**.
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 13 outlines data regarding genetically caused diseases, chromosomal disorders, sequences, associations, complexes and embryopathies (German version).
Chapter 14 contains an analysis of malformations that caused terminations of pregnancy (German version).

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

The database of the Monitoring of Congenital Malformations Saxony-Anhalt includes data about newborns and foetuses with congenital malformations as well as births without any malformation, which form a control group.
In **2013** we received information about **1,940 births** (11.4% of all births in Saxony-Anhalt). During the whole registration period (2001-2012) the absolute number as well as the number of births for which we have data available decreased since the middle of 2000.

We received for the reporting year 2013 a total number of 2,197 data records from the materny and paediatric units resp. from institutions of pre- and postnatal diagnostics which are mentioned in chapter 5.2 (german version). In 10.7% 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. A correct and preferably detailed diagnosis description is therefore essential for a steady high data quality and consequently convincing statistics.

Since the Annual Report 2012 was published the number of births and corresponding data records for 2012 increased from 2,059 to 2,152 as we received so called "late reportings". The later registered births are now included into the analyses of the current report and taken into account in any future analyses.

Carefully completed data records are very important to evaluate risks and identify possible characteristics. The data quality remained also in 2013 on a high level thanks to the excellent work and dedication of all our senders. Important data was reported in nearly 100% of the cases: Birth weight (97.5%), gender (99.2%), maternal age (99.5%), pregnancy outcome and administrative district (99.9%). The gestational age was reported as completely as never before (99.8%). Only in case of two live births and one termination of pregnancy it was missing.

We kindly ask again all reporting institutions in Saxony-Anhalt to describe every diagnosed malformation as detailed as possible when completing the documentation sheet, a coding is not necessary. Unfortunately, we did not receive postnatally any information or no detailed information in 13 of the 80 cases where an indicator malformation was diagnosed during prenatal ultrasound screening. As we cannot assume that these diagnoses were confirmed after birth it is not possible to include them into our statistics.

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	8,574	live births and stillbirths
female	8,289	live births and stillbirths
total	16,863	live births and stillbirths

Sex ratio m : f = 1.03

The Statistical Office Halle registered in 2013 a total number of 16,863 births. These can be split up into 16,797 live births and 66 stillbirths. Compared to the previous year (2012: 16,951) the number of life births and stillbirths slightly decreased. The sex ratio shows also in 2013 a slight androtropism with a value of 1.03. However, the previous years showed a clearly stronger androtropism (2012: 1.04; 2011: 1.06).

608 births with only major malformations showed a sex ratio of 1.15 (320 male and 279 female births). This corresponds again to an androtropism, which we already registered in the previous years (2012: 1.32; 2011: 1.34).

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

male	320	births
female	279	births
unknown	9	births
total	608	births

Sex ratio m : f = 1.15

Sex ratio of all births with only minor malformations and anomalies

male	112	births
female	91	births
total	203	births

Sex ratio m : f = 1.23

11 Organ System Involvement in Infants and Foetuses with Major Malformations

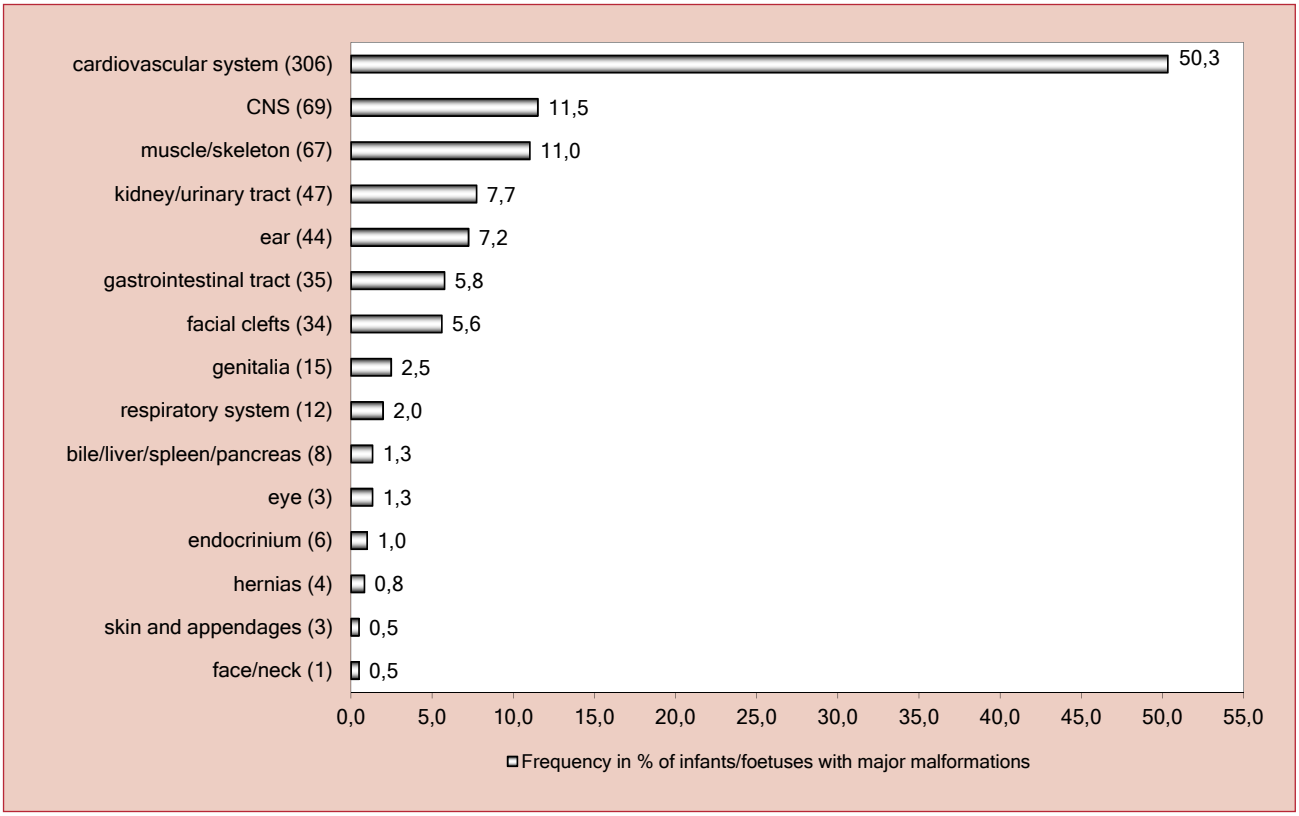


Fig. 5: Organ system involvement in major malformations (absolute figures and percentages of reported malformations)

Chapter 11 gives an overview of the frequency of major malformations, classified according to organ systems. For the analysis of 2013, 608 births are regarded. Infants/foetuses with malformations of different organ systems are mentioned multiply within the above shown diagram. Births with multiple malformations which cannot be assigned to one organ system like chromosomal disorders, infections and metabolic diseases are not included in the figure.

Similar to the previous year, malformations of the cardiovascular system form the biggest part among births with major malformations. Additionally, the frequency even increased compared to 2012 (2013: 50.33%; 2012: 41.07%).

By regarding the confidence interval of the years 2001-2012 an increase is shown very clearly. A reason for the increase might be the intensified collaboration since 2012 with the nearby located cardiac centres which report births from Saxony-Anhalt who suffer from malformations of the cardiovascular system to us. We will observe in the future if this frequency will remain on a constant level.

CNS malformations were registered second most frequently. Compared to the previous years the frequency slightly decreased (2013: 11.51%; 2012: 12.50%), but still lies above the basis prevalence (2001-2012: 10.67%).
The third place of the ranking is occupied by malformations of the musculoskeletal system. However, as the number of registered cases remained nearly unchanged, we never registered such a low frequency of these cases as in the present year (2013: 11.02%; 2001-2012: 20.07%).

Furthermore, we registered a clearly decreasing frequency of malformations of the kidney and urinary tract (2013: 7.73%; 2012: 12.66%; 2011: 13.48%). This is the lowest value for the first time and requires further analysis.

After we documented a very high rate of malformations of the ear the last year (2012: 8.28%) also in 2013 the registered frequency (2013: 7.24%) lies above the average value of the years 2007-2012 (5.59%).
Malformations of the genitalia were registered less frequently (2.47%) in 2013 than in the previous years (2001-2012: 3.52%). A similar low value was registered for the last time in 2009 (2.01%).

The most frequent single diagnoses 2013 (only major malformations)

	ICD-10	Diagnosis	Infants/Foetuses 2013		Infants/Foetuses 2000-2012 Prevalence /10,000
			Number	Prevalence /10,000	
1.	Q21.1	Atrial septal defect (inclusive persistent foramen ovale/PFO)	186	109.7	74.7
2.	Q21.0	Ventricular septal defect	97	57.2	45.1
3.	Q90.	Down`s syndrome (trisomy 21)	44	26.0	16.6
4.	H90.	Conductive and sensorineural hearing loss	43	25.4	9.9 (18.3*)
5.	Q02.	Microcephaly	36	21.2	13.1
6.	Q25.0	Patent ductus arteriosus	28	16.5	8.1
7.	Q62.3	other obstructive defects of renal pelvis and ureter (dilated uropathy grade II-IV/ureterocele)	20	11.8	19.8
8.	Q37.	Cleft hard and soft palate with unilateral/bilateral cleft lip	19	11.2	10.9
9.	Q69.	Polydactyly (pre- and postaxial)	17	10.0	12.6
10.	Q25.6	Stenosis of pulmonary artery	12	7.1	2.3
	Q25.4	Right aortic arch, persistent / dextroposition of aortic arch / overriding aorta	12	7.1	1.5
11.	Q66.0	Talipes equinovarus (clubfoot)	11	6.5	17.5
	Q65.3 Q65.4 Q65.5	Congenital subluxation of hip (unilateral/bilateral/laterality unspecified)	11	6.5	15.4
	Q03.0 Q03.1 Q03.8 Q03.9	Congenital hydrocephalus (without neural tube defect)	11	6.5	6.0
12.	Q21.2	Atrial and ventrical septal defect	10	5.9	4.5
13.	Q60.0	Renal agenesia (unilateral)	9	5.3	6.9
	Q22.1	Pulmonary valve stenosis	9	5.3	6.3
14.	Q62.2	Congenital megaureter	8	4.7	7.3
15.	Q63.0	Accessory kidney	7	4.1	6.5
	Q05.	Spina bifida	7	4.1	5.8
	Q35.1 Q35.5 Q35.9	Cleft palate	7	4.1	4.6
	Q23.3	Congenital mitral valve stenosis	7	4.1	4.2
	Q71.3	Missing of several or single phalanges	7	4.1	3.1
	Q36.	Cheiloschisis (cleft lip)	7	4.1	2.9

* 2007-2012 (since 2007 data is synchronised with the newborn hearing screening tracking centre)

The overleaf shown table presents the most frequently registered single diagnosis, ordered by frequency of appearance in 2013 (16,950 births). The right column shows for comparison the basis prevalences of these diagnoses as they appeared during the time period of 2001 to 2012 (209,249 births).

The atrial septal defect (2013: 109.7 per 10,000 births) and the ventricular septal defect (2013: 57.2 per 10,000 births) are always the most frequently appearing malformations during the registration period. In 2013, the prevalences of both cardiac malformations are higher than every annual prevalence we registered during the period of 2001-2012. Therefore, also the corresponding basis prevalence is exceeded significantly (ASD 2001-2012: 74.7 per 10,000 births, CI 71.1 to 78.6; VSD 2001-2012: 45.1 per 10,000 births, CI 42.3 to 48.1). Nearly two out of five births with major malformations suffered in 2013 from one of these two cardiac malformations.

Also the Downs Syndrome, which occupies rank three in the present year, was registered more often than ever before (2013: 26.0 per 10,000 births) during the registration period 2001-2012 (chapter 12.34). The current prevalence lies significantly above the prevalences we calculated during 2001-2012 (16.6 per 10,000 births, CI 15.0 to 18.5).

On the fourth place we registered in 2013 the hearing loss. This is also a higher frequency than the average frequency of the years before. Only since 2007 the Newborn Hearing Screening provides region wide secured data about this malformation. Therefore, the data of frequency can be used only from 2007 to analyse the current prevalence. The prevalence of 2013 is with a value of 25.4 per 10,000 births clearly higher than the values we registered in the years 2007-2012 (18.3 per 10,000 births, CI 15.9 to 21.0).

The indicator malformation microcephaly (2013: 21.2 per 10,000 births, 2001-2012: 13.1 per 10,000 births, CI 11.6 to 14.7) occupies rank five of the table. Similar to the previous year (2012: 21.1 per 10,000 births), microcephaly shows also in 2013 a very high prevalence (chapter 12.5). Extremely low values of some recent years (minimal value 2001: 5.5 per 10,000 births) may indicate an underregistration during these years.

Approximately since 2010 we receive more detailed reportings about cardiac malformations of births from Saxony-Anhalt. As a result, cardiac malformations such as PDA (16.5 per 10,000 births, place 6), stenosis of arteria pulmonalis, right aortic arch (7.1 per 10,000 births, place 10) and atrial and ventrical septal defect (5.9 per 10,000 births, rank 12) were registered more frequently in 2013 than in the average during 2001-2012. Only PDA was one of the most frequent single malformations also in the previous years (2001-2012: 8.1 per 10,000 births). The other three cardiac malformations were registered less frequently.

In 2013 we registered less frequently than expected (11.8 per 10,000 births, rank 7) the dilatative uropathy (from II. grade), which is one of the most frequent malformations. This malformation occupied during 2001-2012 rank three of the entire list (19.8 per 10,000 births, CI 18.0 to 21.8).

The indicator malformation cleft lip with cleft upper jaw and palate includes the cleft lip with cleft upper jaw and palate (2013: 11.2 per 10,000 births, rank 8) and cleft lip (2013: 4.1 per 10,000 births, rank 15). While the prevalence of the cleft lip with cleft upper jaw and palate remains on a constant level in the current year (2001-2012: 10.9 per 10,000 births, CI 9.6 to 12.4), the prevalence of the cleft lip is significantly higher than in the previous years (2001-2012: 2.9 per 10,000 births, CI 2.2 to 3.8). Normally, cleft lip is not to find among the most frequent major malformations.

Polydactyly (2013: 10.0 per 10,000 births) occupies in 2013 rank 9 of the major malformation list. This rank was occupied in the previous year by cleft upper lip with cleft upper jaw and palate. Polydactyly was registered pre- and postnatally less frequently than during the years 2001-2012 (12.6 per 10,000 births, CI 11.2 to 14.2). Therefore, the assumed increasing trend of postaxial polydactyly as observed during the last years, does not continue.

On rank 11 and with a clearly lower prevalence than we documented during the whole registration period (2013: 6.5 per 10,000 births) we can find the clubfoot (2001-2012: 17.5 per 10,000 births, CI 15.8 to 19.4) and subluxation of hip (2001-2012: 15.4 per 10,000 births, CI 13.8 to 17.2). Both malformations even occupied three times rank 3 of the major malformations between 2001 and 2012. An ultrasound screening of the hip forms part of the early detection examination U3. Therefore, many hospitals do not carry out the ultrasound screening within the early detection examination U2. This can be a reason for a less frequent reporting of hip malformations to our malformation registration centre.
Furthermore, the hydrocephaly was observed with a value of 6.5 per 10,000 births. This value lies within the average prevalence of the registration period.

The pulmonary valve stenosis was registered less frequently in 2013 and is therefore to find on rank 13 (2013: 5.3 per 10,000 births, 2001-2012: 6.3 per 10,000 births, CI 5.3 to 7.5).
Rank 13 -15 are occupied in 2013 by three renal malformations: Unilateral renal agenesia (5.3 per 10,000 births), megaureter (4.7 per 10,000 births) and duplex kidney (4.1 per 10,000 births). In contrast to the previous year, the values of 2013 are lower than the average value of 2001-2012 (6.9 per 10,000 births, CI 5.9 to 8.1; 7.3 per 10,000 births, CI 6.2 to 8.5 resp. 6.5 per 10,000 births, CI 5.5 to 7.7).

Spina bifida was registered less frequently than expected (2013: 4.1 per 10,000 births, 2001-2012: 5.8 per 10,000 births, CI 4.9 to 6.9).
With a similar prevalence and also on rank 15, we can find in 2013 the missing of single or multiple phalanges. The average prevalence of this malformation which is normally not to find among the most frequent malformations lies within the registration period of 2001-2012 at 3.1 per 10,000 births (CI 2.4 to 4.0).
The prevalences of cleft palate and mitral valve insufficiency, which are also to find on rank 15 in 2013 lie within the average prevalence we calculated for the years 2001-2012.

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.
Composed of: 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 and 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) two standard deviations below the age and sex appropriate distribution curves. 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.

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 defects.

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/stenosis: a congenital malformation characterized by absence of continuity or narrowing of the oesophagus, 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 multiple 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 neighboring organs. Exclusive mild stenosis which does not need correction and ectopic anus.

20. Undescended testis: bilateral undescended testis in at term newborn or at least unilateral undescended testis in males more than one 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) and hypoplasia of abdominal muscles (skin covered 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 foetus the deficiency of the abdominal muscle may not be evident. It can be associated with undescended testis, 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 (2001-2012) is based on a total number of 209,249 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 basic prevalence
Major cities: 3 x Halle	3	6.2	↓
Districts: 2 x Börde 1 x Harz 2 x Jerichower Land 2 x Mansfeld-Südharz 2 x Stendal	9	7.4	↘
Saxony-Anhalt	**12**	**7.1**	↓

Neural tube defects (2001-2012)		
	Basic prevalence /10,000 births	Confidence Interval (CI of 95%) /10,000 births
Cities	10.02	7.53 - 13.07
Districts	9.01	7.67 - 10.57
Regions	9.27	8.08 - 10.63
EUROCAT	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 2013 we registered 12 cases of neural tube defects. These can be divided into seven cases of spina bifida, three cases of anencephalus and two cases of encephalocele. In 41.7% the affected infants were live births, these were four children with spina bifida and one child with encephalocele.

The prevalence of 7.1 per 10,000 births is lower than the basis prevalence of the last twelve years. The basis prevalence is with a value of 9.3 per 10,000 births similar to the European trend.

additional information:

Pregnancy outcome	5 x live birth 7 x termination of pregnancy
Sex	7 x male 4 x female 1 x no indication
Number of isolated malformations/MCA	8 x MCA 4 x isolated

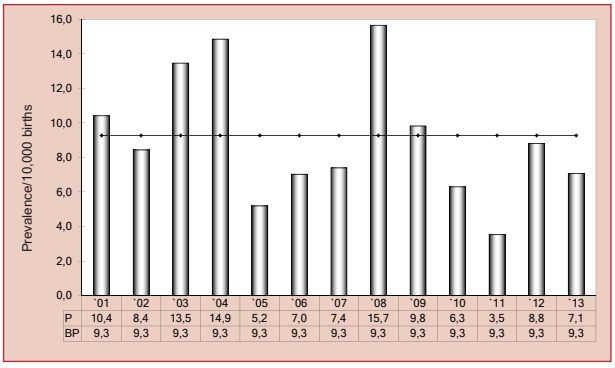


Fig. 6: Development of prevalence/10,000 births with neural tube defects in the registration area since 2001

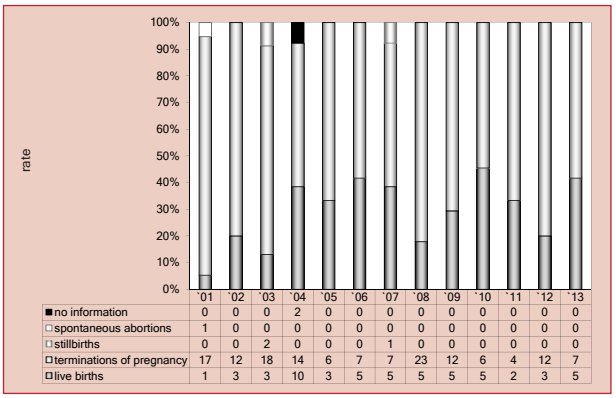


Fig. 7: Pregnancy outcomes of neural tube defects in the registration area since 2001

In 2013 one neural tube defect per 1,413 births was registered in Saxony-Anhalt.

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 during a time period of four weeks before conception up to the end of the first trimester of pregnancy. Women who already had a pregnancy where a neural tube defect was detected should intake a daily dose of 4 mg of folic acid (in Germany compounds with 5 mg / dose avaliable). (Addition: also women with antiepileptic therapy are recommended an intake of this higher dose).

However, twenty years later current scientific publications indicate that the neural tube prevalence has Europe-wide not decreased as much as expected. Continuously, 4,800 infants/foetuses in Germany suffer from this malformation every year. In 2005, there were also studies for Germany existing which showed that only 10% of the pregnant women followed the folic acid intake recommendation. Our own data indicates that not even 30% of pregnant women took a sufficient dose of folic acid before knowing of their pregnancy.
Now there are controverse discussions if recent information campaigns provided sufficient information and if women had the chance to decide for folic acid intake in case of the wish to have a child. Another option would be the continuing demand for voluntary or involuntary intake of food that is enriched with folic acid (in 70 European countries flour already contains folic acid).

Please note:
In case of a previous pregnancy where a neural tube defect was diagnosed and a termination of pregnancy or spontaneous abortion took place please consider recommendation regarding necessary folic acid prophylaxis with 5 mg folic acid equivalent per day (please consider recommendations of specialist societies) for a further wish to have a child.

12.2 Anencephaly (Q00.)

	Number	Prevalence /10,000 births	Trend in comp. to basic prevalence
Major cities: 1 x Halle	1	2.1	↔
Districts: 1 x Harz 1 x Stendal	2	1.6	↘
Saxony-Anhalt	**3**	**1.8**	↔

Anencephaly (2001-2012)		
	Basic prevalence /10,000 births	**Confidence Interval (CI of 95%) /10,000 births**
Cities	1.11	0.41 - 2.42
Districts	2.45	1.73 - 3.36
Region	2.10	1.53 - 2.82
EUROCAT	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

Three infants/foetuses with anencephaly were registered in 2013.The **prevalence** of **1.8 per 10,000 births** is higher than the prevalence of the previous years. However it is at the same time lower than the 12 years prevalence. For this prevalence a value of 2.1 per 10,000 births was calculated.

additional information:

Pregnancy outcome	3 x termination of pregnancy
Sex	1 x male 1 x female 1 x no indication
Number of isolated malformations/MCA	3 x isolated

The affected pregnancies were terminated after 11 and 17 weeks of gestation. In one case a prenatal encephalocele was suspected, later the cranial defect was detected.

The anencephalus occured isolated in all cases.

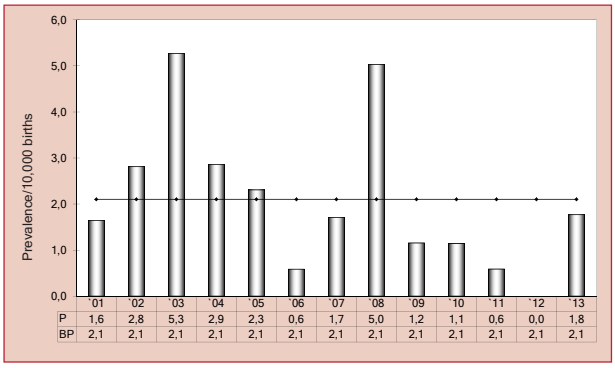


Fig. 8: Development of prevalence/10,000 births with anencephaly in the registration area since 2001

In 2013 one anencephaly per 5,650 births was registered in Saxony-Anhalt.

12.3 Spina bifida (Q05.)

	Number	Prevalence /10,000 births	Trend in comp. to basic prevalence
Major cities: 1 x Halle	1	2.1	↓
Districts: 1 x Börde 2 x Jerichower Land 2 x Mansfeld-Südharz 1 x Stendal	6	4.9	↔
Saxony-Anhalt	**7**	**4.1**	↓

Spina bifida (2001-2012)		
	Basic prevalence /10,000 births	Confidence Interval (CI of 95%) /10,000 births
Cities	6.68	4.68 - 9.24
Districts	5.54	4.43 - 6.84
Region	5.83	4.91 - 6.92
EUROCAT	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

Seven births with spina bifida were registered in Saxony-Anhalt in 2013.
The prevalence of 4.1 per 10,000 births lies slightly under the basis prevalence of the last 12 years. Compared to European data records the prevalence of 2013 is in the average not higher than the prevalence of other European countries.

additional information:

Pregnancy outcome	4 x live birth 3 x termination of pregnancy
Sex	4 x male 3 x female
Number of isolated malformations/MCA	6 x MCA 1 x isolated

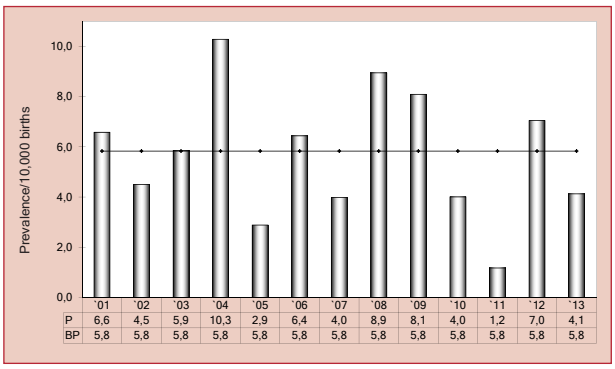
In four cases the infants were live births. In two of these cases a lumbosacral myelomeningocele (LS5-S1) was present. One infant suffered from the defect in combination with an Arnold-Chiari-II-malformation and a hydrocephalus. In case of one live birth a lipomyelomeningocele and in an additional case a lipomeningocele was diagnosed postnatally.
The terminations of pregnancy took place after 18 and 20 weeks of gestation. In two cases the defect was thoracic and the diagnosis of hydrocephalus and Arnold-Chiari-II-malformation was already confirmed prenatally. One foetus suffered from a lubosacral defect with hydrocephalus.

Three of the affected mothers indicated a folic acid intake and intake of vitamines, however the beginning of intake and dose is unknown.

A combination with Arnold-Chiari-II-malformation (smaller posterior cranial fossa and dislocation of cerebellar vermis) was present in four cases and a combination with intraspinal lipom such as a lipo(myelo)meningocele was present in two cases.

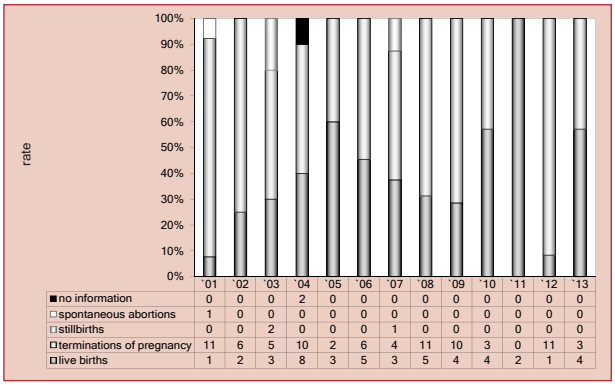
Malformation combinations (MCA) or superordinated syndromes detected:

- Arnold-Chairi-syndrome with: renal agenesis left side, dysplastic right kidney, kyphoscoliosis
- Arnold-Chairi-syndrome with: microcephalie, PFO at full term infant, neurogenic bladder, DUP I. grade blt.
- Arnold-Chiari-syndrome with: diastematomyelie, low set ears
- Arnold-Chiari-syndrome
- intraspinale lipom, neurogenic bladder, DUP I. grade left
- intraspinale lipom, sacral dimple (approx. 1 cm)



	'01	'02	'03	'04	'05	'06	'07	'08	'09	'10	'11	'12	'13
P	6,6	4,5	5,9	10,3	2,9	6,4	4,0	8,9	8,1	4,0	1,2	7,0	4,1
BP	5,8	5,8	5,8	5,8	5,8	5,8	5,8	5,8	5,8	5,8	5,8	5,8	5,8

Fig. 9: Development of prevalence/10,000 births with spina bifida in the registration area since 2001



	'01	'02	'03	'04	'05	'06	'07	'08	'09	'10	'11	'12	'13
no information	0	0	0	2	0	0	0	0	0	0	0	0	0
spontaneous abortions	1	0	0	0	0	0	0	0	0	0	0	0	0
stillbirths	0	0	2	0	0	0	1	0	0	0	0	0	0
terminations of pregnancy	11	6	5	10	2	6	4	11	10	3	0	11	3
live births	1	2	3	8	3	5	3	5	4	4	2	1	4

Fig. 10: Pregnancy outcomes of spina bifida in the registration area since 2001

In 2013 one spina bifida per 2,421 births was registered in Saxony-Anhalt.

12.4 Encephalocele (Q01.)

	Number	Prevalence /10,000 births	Trend in comp. to basic prevalence
Major cities: 1 x Halle	1	2.1	↔
Districts: 1 x Börde	1	0.8	↔
Saxony-Anhalt	**2**	**1.2**	↔

Encephalocele (2001-2012)		
	Basic prevalence /10,000 births	Confidence Interval (CI of 95%) /10,000 births
Cities	2.23	1.15 - 3.89
District	1.03	0.59 - 1.67
Region	1.34	0.89 - 1.93
EUROCAT	1.11	1.05 - 1.18
		0.19 S Portugal* 3.15 Mainz (Germany)**

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

Two infants/foetuses with encephalocele were registered in 2013. Therefore the **prevalence** we calculated in 2013 is **1.2 per 10,000 births**. This corresponds to the trend of the previous years.

In comparison to EUROCAT our result lies within the confidence interval.

additional information:

Pregnancy outcome	1 x live birth 1 x termination of pregnancy
Sex	2 x male
Number of isolated malformations/MCA	2 x MCA

After prenatal diagnosis of one occipital encephalocele, the pregnancy was terminated after 16 weeks of gestation. In this case also a hypoplastic heart and adrenal gland was diagnosed histologically. At one preterm infant which was delivered after 29 weeks of gestation a cherry stone sized bulging was detected postnatally.

Malformation combinations (MCA) or superordinated syndromes detected:

- hypospadias n.o.s.
- hypoplastic heart, hypoplastic adrenal gland

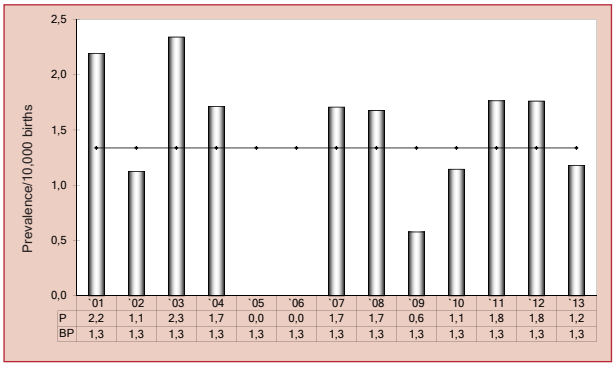


Fig.11: Development of prevalence/10,000 births with encephalocele in the registration area since 2001

In 2013 one encephalocele per 8,475 births was registered in Saxony-Anhalt.

12.5 Microcephaly (Q02.)

	Number	Prevalence /10,000 births	Trend in comp. to basic prevalence
Major cities: 1 x Dessau-Roßlau 2 x Halle 10 x Magdeburg	13	27.1	↑
Districts: 4 x Anhalt-Bitterfeld 3 x Börde 2 x Jerichower Land 4 x Saalekreis 8 x Salzlandkreis 1 x Stendal 1 x Wittenberg	23	18.9	↑
Saxony-Anhalt	**36**	**21.2**	↑

Microcephaly (2001-2012)		
	Basic prevalence /10,000 births	Confidence Interval (CI of 95%) /10,000 births
Cities	17.25	13.93 - 21.13
Districts	11.65	10.11 - 13.42
Region	13.09	11.66 - 14.69
EUROCAT	2.49	2.39 - 2.59
		0.47 Norway* 13.09 Saxony-Anhalt (Germany)**

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

In 2013, 36 births with microcephaly were registered. These births had a head circumference below the 3rd percentile in regard to the body length and to the reported gestational age. The annual **prevalence** of **21.2 per 10,000 births** is similar to the previous year higher than the basis prevalence of the years 2001-2012.

In comparison with other European registration centres Saxony-Anhalt has the highest prevalence which lies clearly above the confidence interval.

additional information:

Pregnancy outcome	32 x live birth 1 x live birth, deceased after 7 days 1 x spontaneous abortion 2 x stillbirth
Sex	16 x male 20 x female
Number of isolated malformations/MCA	15 x MCA 21 x isolated

The pregnancy outcome shows that 92% of the affected infants/foetuses were live births. In 21 cases the microcephalus occured isolated. A rare combination of microcephalus appeared together with a VP shunt requiring hydrocephalus and microcephalus. In total, 15 births showed additional malformations.

Malformation combinations (MCA) or superordinated syndromes detected:

- Down syndrome with: VSD, PFO at full term infant
- Trisomy 22 mosaic with: membranuous cardiac septum, PFO at full term infant
- Arnold-Chiari-syndrome with: sacrale spina bifida with hydrocephalus, PFO at full term infant, neurogenic bladder, DUP I. grade blt.
- Pierre-Robin-sequence, median cleft palate, horseshoe kidney and DUP II. grade blt., mandibular micrognathy, glossoptosis
- Fallot-tetralogy, PFO at full term infant
- Potter-sequence (bilateral renal agenesis)
- Omphalocele
- Undescended right testis
- Missing phalanx of finger (at II.-V. finger right, II.-III. finger left)
- Stenosis of arteria pulmonalis, PFO at full term infant, blt. testicular torsion
- ASD, PDA, PFO at full term infant
- ASD, PDA at full term infant
- Subluxation of right hip, talipes varus
- DUP II. grade left
- postaxial accessory finger left

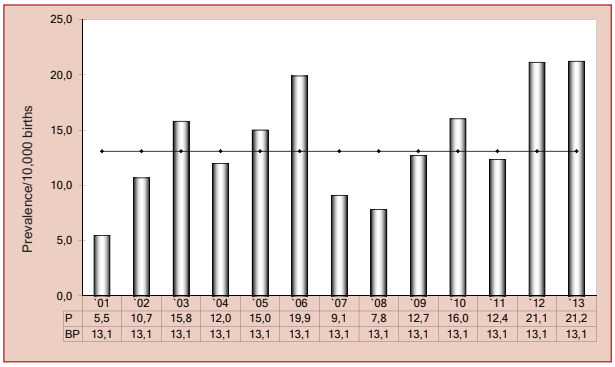


Fig. 12: Development of prevalence/10,000 births with microcephaly in the registration area since 2001

In 2013 one microcephaly per 471 births was registered in Saxony-Anhalt.

12.6 Congenital Hydrocephaly (Q03.)

	Number	Prevalence /10,000 births	Trend in comp. to basic prevalence
Major cities: 1 x Dessau-Roßlau 1 x Halle 3 x Magdeburg	5	10.4	↗
Districts: 3 x Anhalt-Bitterfeld 1 x Burgenlandkreis 1 x Harz 1 x Salzlandkreis	6	4.9	↔
Saxony-Anhalt	**11**	**6.5**	↔

Congenital Hydrocephaly (2001-2012)		
	Basic prevalence /10,000 births	Confidence Interval (CI of 95%) /10,000 births
Cities	6.49	4.52 - 9.03
Districts	5.86	4.72 - 7.19
Region	6.02	5.08 - 7.12
EUROCAT	5.66	5.51 - 5.81
		1.34 S Portugal* 13.42 Paris (France)**

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

11 births with congenital hydrocephalus were registered in 2013. Hydrocephalus in combination with a neural tube defect or the more frequently appearing hydrocephalus after a bleeding or infection are not classified here.

The **prevalence** lies with **6.5 per 10,000 births** unchanged slightly above the confidence interval of the European comparison data.

In regard to the prevalence we calculated in Saxony-Anhalt our value lies within the basis prevalence. In 2001, 2002, 2004 and 2005 we observed high prevalences and in the following years low prevalences in Saxony-Anhalt. The descending trend of hydrocephaly can also be identified when regarding figure 46 on page 65. An average change of prevalence of -5.38% per year can be calculated for the years 2001-2013 (chapter 12.37). However, when also including further previous years into this calculation the descending trend is balanced again as the values of the previous years lie within the average prevalence. Therefore, the future trend has to be observed.

additional information:

Pregnancy outcome	3 x live birth 1 x live birth, deceased after 7 days 7 x termination of pregnancy
Sex	7 x male 4 x female
Number of isolated malformations/MCA	7 x MCA 4 x isolated

Seven pregnancies were terminated. The earliest termination of pregnancy took place after 18 weeks of gestation, two after 23 weeks of gestation. Mainly, additional cerebral anomalies were present.

Only in four cases the hydrocephalus appeared isolated, in seven cases additional malformations were diagnosed.

Malformation combinations (MCA) or superordinated syndromes detected:

- Down syndrome with: plexus cyst
- Edwards syndrome with: dysplasia of cerebellum, agenesia of cereballar vermis, missing osseous acoustic meatus, choanal stenosis, VSD, horseshoe kidney, cholestasis, hepatomegaly, blt. hydrocele, umbilical hernia, hernia inguinalis right at preterm infant
- Triple X-syndrome
- autosomal duplicature with blt. dysplastic kidney, VSD, missing vermis cerebelli
- cleft of the soft palate, septooptic dysplasia, hypoplastic septum pellucidum, DUP I. grade left, torticollis muscularis, shortened lingual frenulum, craniofacial dysmorphy with high forehead
- Corpus callosum agenesia, midline defect of cranial bone, saddle nose, hypertelorismus
- cerebellar hypoplasia

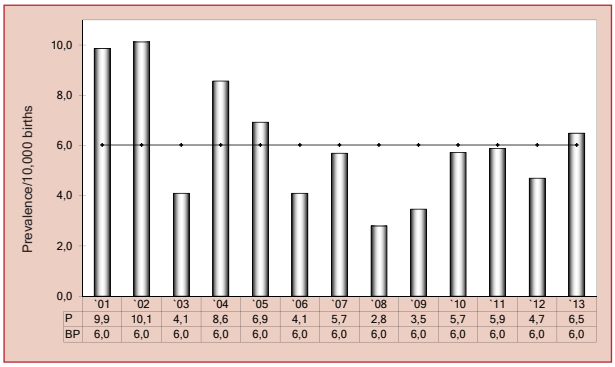


Fig 13: Development of prevalence/10,000 births with congenital hydrocephalus in the registration area since 2001

In 2013 one congenital hydrocephalus per 1,541 births was registered in Saxony-Anhalt.

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

	Number	Prevalence /10,000 births	Trend in comp. to basic prevalence
Major cities: 1 x Dessau-Roßlau 1 x Magdeburg	2	4.2	↗
Districts	0	0.0	↓
Saxony-Anhalt	**2**	**1.2**	↘

Arhinencephaly/Holoprosencephaly (2001-2012)		
	Basic prevalence /10,000 births	**Confidence Interval (CI of 95%) /10,000 births**
Cities	2.41	1.28 - 4.12
Districts	1.48	0.94 - 4.22
Region	1.72	1.21 - 2.38
EUROCAT	1.31	1.24 - 1.39
		0.38 Wielkopolska (Poland)* 2.77 Vaud (Switzerland)**

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

In 2013 two births with holoprosencephaly were registered.
The **prevalence** of **1.2 per 10,000 births** is similar to the prevalence of the previous years and is at the same time slightly lower than the basis prevalence of the years 2001-2012 (1.7 per 10,000 births).

Compared to EUROCAT, the Saxony-Anhalt prevalence lies within the confidence interval.

additional information:

Pregnancy outcome	1 x live birth 1 x termination of pregnancy
Sex	1 x male 1 x female
Number of isolated malformations/MCA	2 x MCA

One pregnancy was terminated after 22 weeks of gestation and after prenatally confirmed diagnosis. In the other case we have no indication about possible pregnancy complications or prenatal diagnosis.

Malformation combinations (MCA) or superordinated syndromes detected:

- Klinefelter-syndrome
- Corpus callosum hypoplasia, accessory mamilla left, sacral dimple

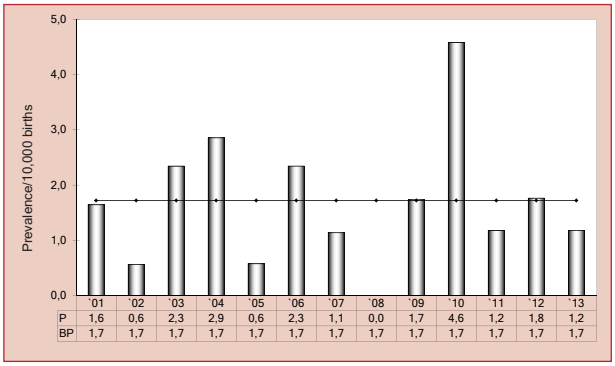


Fig. 14: Development of prevalence/10,000 births with arhinencephaly/holoprosencephaly in the registration area since 2001

In 2013 one case of arhinencephalie/holoprosencephalie per 8,475 births was registered in Saxony-Anhalt.

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

	Number	Prevalence /10,000 births	Trend in comp. to basic prevalence
Major cities	0	0.0	↓
Districts: 1 x Anhalt-Bitterfeld 1 x Harz	2	1.6	↑
Saxony-Anhalt	**2**	**1.2**	↔

Anophthalmos/Microphthalmos (2001-2012)		
	Basic prevalence /10,000 births	**Confidence Interval (CI of 95%) /10,000 births**
Cities	1.30	0.52 - 2.68
Districts	0.58	0.26 - 1.10
Region	0.76	0.44 - 1.24
EUROCAT	0.99	0.93 - 1.05
		0.12 Zagreb (Croatia)* 3.22 Odense (Denmark)**

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

Two live births with microphthalmos were registered in 2013. The **prevalence** lies with **1.2 per 10,000 births** within the confidence interval of the previous years. The basis prevalence of 2001-2012 lies at 0.76 per 10,000 births.

additional information:

Pregnancy outcome	1 x live birth 1 x live birth, deceased within 7 days
Sex	2 x female
Number of isolated malformations/MCA	2 x MCA

In both cases additional malformations were present. In one case a chromosomal aberration was the reason for the malformation appearence.

Malformation combinations (MCA) or superordinated syndromes detected:

- Patau syndrome with: Corpus callosum agenesia, blt. cleft lip with cleft palate and postaxial hexadactyly, dextrocardia, scalp defects
- cleft lip with cleft palate right, blt. blindness

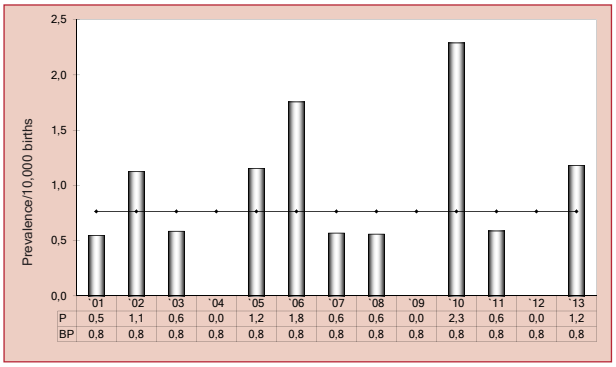


Fig. 15: Development of prevalence/10,000 births with anophthalmos/microphthalmos in the registration area since 2001

In 2013 one child/foetus with anophthalmos / microphthalmos per 8,475 births was registered in Saxony- Anhalt.

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

	Number	Prevalence /10,000 births	Trend in comp. to basic prevalence
Major cities: 1 x Halle	1	2.1	↔
Districts: 1 x Börde 1 x Salzlandkreis	2	1.6	↔
Saxony-Anhalt	**3**	**1.8**	↔

Microtia/Anotia (2001-2012)		
	Basic prevalence /10,000 births	Confidence Interval (CI of 95%) /10,000 births
Cities	1.67	0.76 - 3.17
Districts	1.16	0.69 - 1.83
Region	1.29	0.85 - 1.88
EUROCAT	no information	no information

One birth with anotia (acoustic meatus atresia) and two births with microtia and external ear dysplasia type III were registered in 2013.
The **prevalence** of **1.8 per 10,000 births** lies within the confidence interval.

No EUROCAT data is present for comparison for this malformation.

additional information:

Pregnancy outcome	3 x live birth
Sex	2 x male 1 x female
Number of isolated malformations/MCA	3 x MCA

In all three cases additional hearing disorders were registered.

Malformation combinations (MCA) or superordinated syndromes detected:

- sound conduction disorder (right sound conduction block) at missing right osseous acoustic meatus
- sound conduction disorder (right 30 dB, left 70 dB) at missing left osseous acoustic meatus
- hearing disorder and auricular tag left

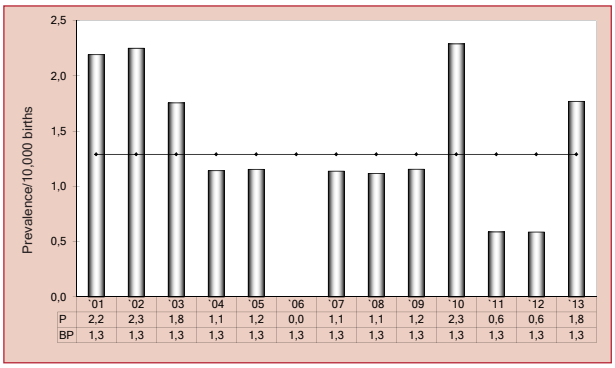


Fig. 16: Development of prevalence/10,000 births with microtia/anotia in the registration area since 2001

In 2013 one child with microtia/anotia per 5,650 was registered in Saxony-Anhalt.

12.10 Tetralogy of Fallot (Q21.3)

	Number	Prevalence /10,000 births	Trend in comp. to basic prevalence
Major cities: 1 x Halle 2 x Magdeburg	3	6.2	↑
Districts: 1 x Altmarkkreis Salzwedel 1 x Börde 1 x Saalekreis	3	2.5	↔
Saxony-Anhalt	**6**	**3.5**	↔

Tetralogy of Fallot (2001-2012)		
	Basic prevalence /10,000 births	Confidence Interval (CI of 95%) /10,000 births
Cities	3.15	1.84 - 5.05
Districts	3.28	2.44 - 4.32
Region	3.25	2.52 - 4.12
EUROCAT	3.20	3.09 - 3.32
		1.97 S Portugal* 5.16 Mainz (Germany)**

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

With six registered cases of tetralogy of fallot the prevalence of 3.5 per 10,000 births lies exactly within the expected range of the previous years.

The comparison with EUROCAT data also shows that the average prevalence lies exactly within the range of other European malformation registers.

additional information:

Pregnancy outcome	6 x live birth
Sex	4 x male 2 x female
Number of isolated malformations/MCA	5 x MCA 1 x isolated

An androtropism is present.

In all cases the infants were live births between 34 and 40 weeks of gestation. Three foetuses were prenatally suspicious, in two cases no prenatal diagnoses was made and we have no information about any prenatal finding in one case. Five times the diagnosis was corrected postnatally, however in one case we have no indication about such a correction.

The cardiac malformation occured isolated in one case. In another case a chromosomal aberration was the reason for the malformation appearence and in four cases further additional malformations were present.

Malformation combinations (MCA) or superordinated syndromes detected:

- Down syndrome with: accessory right thumb, canalis atrioventricularis communis, ASD II, haemodynamically effective PDA at full term infant
- Choanal stenosis, close pharynx with functional laryngxobstruction, tracheal bronchus right, PFO at full term infant, persistence of left vena cava superior, hypoplastic right thumb, cataract blt., sunken nose bridge
- microcephaly, PFO at full term infant
- ASD, haemodynamically effective PDA at full term infant, malformation of coronary circulation
- postaxial accessory finger left

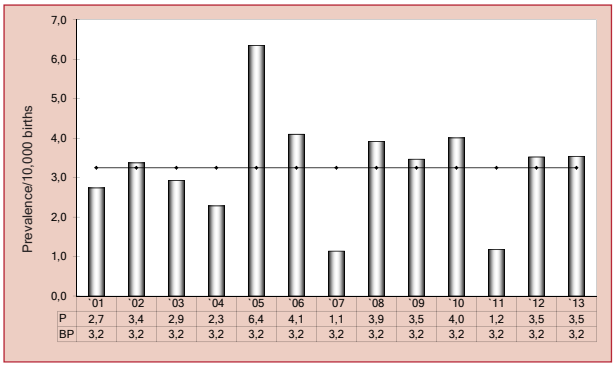


Fig. 17: Development of prevalence/10,000 births with tetralogy of fallot in the registration area since 2001

In 2013 one tetralogy of fallot per 2,825 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 basic prevalence
Major cities: 1 x Halle	1	2.1	↓
Districts: 2 x Anhalt-Bitterfeld 1 x Burgenlandkreis 1 x Saalekreis 1 x Stendal 1 x Wittenberg	6	4.9	↔
Saxony-Anhalt	**7**	**4.1**	↔

Transposition of Great Vessels (2001-2012)		
	Basic prevalence /10,000 births	Confidence Interval (CI of 95%) /10,000 births
Cities	4.82	3.15 - 7.07
Districts	4.12	3.17 - 5.26
Region	4.30	3.46 - 5.29
EUROCAT (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

We registered seven births with TGV in Saxony-Anhalt in 2013.
The prevalence of 4.1 per 10,000 births lies within the prevalence range of the previous years.

additional information:

Pregnancy outcome	7 x live birth
Sex	4 x male 3 x female
Number of isolated malformations/MCA	4 x MCA 3 x isolated

All infants with TGV were live births between 36 and 41 weeks of gestation. In none of the cases a prenatal diagnosis was reported.

Additionally, an androtropism is present.

Malformation combinations (MCA) or superordinated syndromes detected:

- right aortic arch, malfomation of the right coronary artery, PFO at full term infant
- VSD, PFO at full term infant
- PFO at full term infant, talipes valgus left
- PFO at full term infant

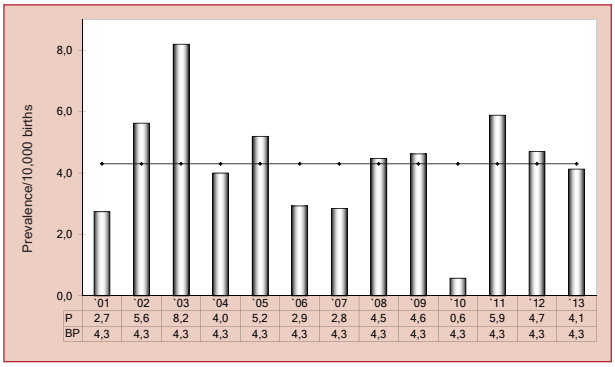


Fig. 18: Development of prevalence/10,000 births with transposition of great vessels in the registration area since 2001

In 2013 one transposition of great vessels per 2,421 births was registered in Saxony-Anhalt.

12.12 Hypoplastic Left Heart Syndrome (Q23.4)

	Number	Prevalence /10,000 births	Trend in comp. to basic prevalence
Major cities: 1 x Halle	1	2.1	↔
Districts	0	0.0	↓
Saxony-Anhalt	**1**	**0.6**	↓

Hypoplastic Left Heart Syndrome (2001-2012)		
	Basic prevalence /10,000 births	**Confidence Interval (CI of 95%) /10,000 births**
Cities	2.41	1.28 - 4.12
Districts	2.83	2.06 - 3.80
Region	2.72	2.06 - 3.53
EUROCAT	2.68	2.58 - 2.79
		0.86 Valencia Region (Spain)* 4.52 Malta**

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

One foetus with hypoplastic left heart syndrome was registered in 2013.
Therefore, we calculated a **prevalence** of **0.6 per 10,000 births**. This prevalence is, compared to the values of the previous years, lower than expected.

Compared to EUROCAT centres, the prevalence of Saxony-Anhalt lies also clearly under the confidence interval.

additional information:

Pregnancy outcome	1 x termination of pregnancy
Sex	1 x male
Number of isolated malformations/MCA	1 x MCA

The pregnancy was terminated after 20 weeks of gestation. The diagnosis of aortic atresia was confirmed histologically afterwards.

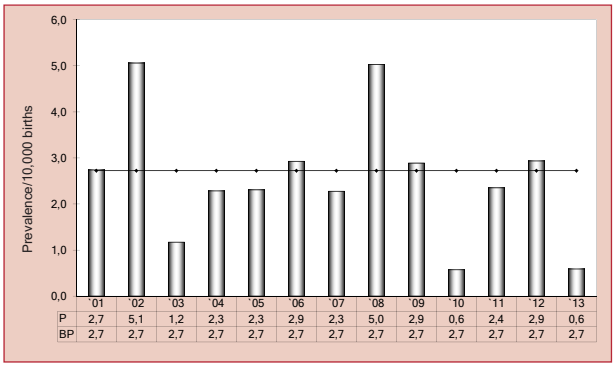


Fig. 19: Development of prevalence/10,000 births with hypoplastic left heart syndrome in the registration area since 2001

In 2013 one child with a hypolastic left heart syndrome per 16,950 births was registered in Saxony-Anhalt.

12.13 Coarctation of Aorta (Q25.1)

	Number	Prevalence /10,000 births	Trend in comp. to basic prevalence
Major cities: 1 x Magdeburg	1	2.1	↓
Districts: 1 x Burgenlandkreis 2 x Börde 1 x Jerichower Land 1 x Stendal	5	4.1	↔
Saxony-Anhalt	**6**	**3.5**	↘

Coarctation of Aorta (2001-2012)		
	Basic prevalence /10,000 births	**Confidence Interval (CI of 95%) /10,000 births**
Cities	4.45	2.85 - 6.62
Districts	4.89	3.85 - 6.12
Region	4.78	3.89 - 5.77
EUROCAT	1.32	1.25 - 1.40
		0.24 S Portugal* 3.54 Vaud (Switzerland)**

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

We registered six births with coarctation of aorta in 2013. The number of cases is therefore lower than in the previous years. Also the **prevalence** of **3.5 per 10,000 births** lies slightly under the confidence interval of the last 12 years.

A comparison with EUROCAT data shows that the coarctation of aorta can often not be identified during prenatal diagnostics and is also often not detected after delivery in the materny clinics. Partly, the malformation is identified after the mother has left the hospital and a physiological duct closure already took place. However, as a result, it is not always registered by our European centres. As conclusion, the average European prevalence of 2001-2012 lies clearly under our documented prevalence. Additionally, the pulse oximetry screening has become a common examination method in Saxony-Anhalt's materny clinics and therefore the percentage of late diagnosed critical cardiac malformations is very low.

additional information:

Pregnancy outcome	5 x live birth 1 x live birth, deceased within 7 days
Sex	4 x male 2 x female
Number of isolated malformations/MCA	5 x MCA 1 x isolated

The sex ratio shows an androtropism.

All six infants were live births. In one case a coarctation of aorta was suspicious during prenatal screening and postnatally confirmed as a Shone complex with involved and affected left ventricular outlet tract. In five cases additional malformations were detected, only in one case the coarctation of aorta occured isolated.

Malformation combinations (MCA) or superordinated syndromes detected:

- Potter sequence, choanal stenosis blt., tricuspid insufficiency, mitral valve insufficiency, lung hypoplasia, low set, dysplastic ears
- Plagiocephaly, bicuspid aortic valve, mitral valve insufficiency III. grade, endocardial fibroelastosis, PFO at full term infant, left ventricular myocardial hypertrophy
- Hypoplasia of aorta, bicuspid aortic valve, left ventricular myocardial hypertrophy, PFO at preterm infant
- Pulmonary valve stenosis, retarded hip blt.
- PFO, retarded hip left, DUP I. grade blt.

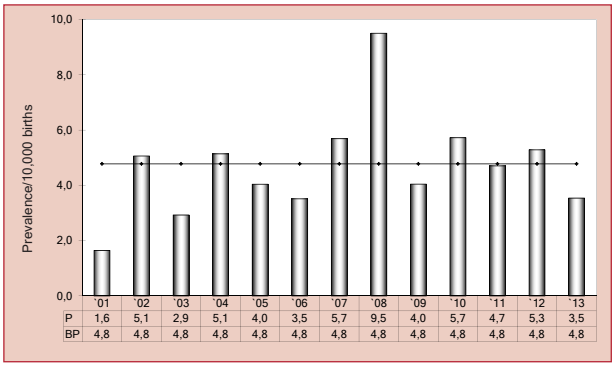


Fig. 20: Development of prevalence/10,000 births with coarctation of aorta in the registration area since 2001

In 2013 one coarctation of aorta per 2,825 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 basic prevalence
Major cities: 2 x Dessau-Roßlau 3 x Halle 3 x Magdeburg	8	16.6	↔
Districts: 4 x Anhalt-Bitterfeld 1 x Burgenlandkreis 2 x Börde 2 x Harz 1 x Jerichower Land 1 x Mansfeld-Südharz 1 x Saalekreis 4 x Salzlandkreis 2 x Stendal	18	14.8	↔
Saxony-Anhalt	**26**	**15.3**	↔

Cleft Lip With or Without Cleft Palate (2001-2012)		
	Basic prevalence /10,000 births	Confidence Interval (CI of 95%) /10,000 births
Cities	14.47	11.44 - 18.05
Districts	13.58	11.91 - 15.48
Region	13.81	12.34 - 15.45
EUROCAT	8.79	8.60 - 8.98
		4.27 S Portugal* 14.31 Odense (Denmark)**

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

In 2013, we registered 26 births with cleft lip with or without cleft palate.
Our calculated **prevalence** of **15.3 per 10,000 births** still lies within the confidence interval of the previous years.

Compared to EUROCAT data our prevalence lies within the upper third of the values calculated by other European malformation centres.

Mainly, isolated oriofacial clefts were registered in 18 cases. In eight cases a chromosomal aberration was the reason for the malformation appearence and additional malformations were present. Also a combination with a relevant hearing disorder was reported in four cases. 16 births suffered from a cleft lip with cleft jaw and palate, seven births from a cleft upper lip, two births suffered from cleft lip with cleft jaw and one birth from a cleft lip with cleft palate. In 13 cases the cleft appeared unilateral, in six cases bilateral (no indication in seven cases).

The infants were live births between 32 and 41 weeks of gestation. One pregnancy was terminated after 18 weeks of gestation as additional complex cerebral malformations were diagnosed.

additional information:

Pregnancy outcome	24 x live birth 1 x live birth, deceased within 7 days 1 x termination of pregnancy
Sex	17 x male 8 x female 1 x no indication
Number of isolated malformations/MCA	8 x MCA 18 x isolated

Malformation combinations (MCA) or superordinated syndromes detected:

- Edwards syndrome with: cerebellar hypoplasia, VSD, ASD II, misjunction of pulmonary vein, PDA at full term infant, flatfoot, prominent clitoris, DUP I. grade blt. retarded hip right, finger malposition, auricular tag blt., craniofacial dysmorphy with low set, dysplastic ears and epicanthus internus
- Patau syndrome with: microphthalmy, corpus callosum agenesia, blt. postaxial hexadactyly, dextrocardia, scalp defects
- Orbital cysts and blindness blt. at agenesia of left eye and microphthalmus right
- Hydranencephaly
- Combined sound conduction and perception disorder (right 40 dB, left 30 dB)
- Sound conduction disorder (blt. 45 dB)
- Sound conduction disorder (blt. 30 dB)
- Sound conduction disorder blt.

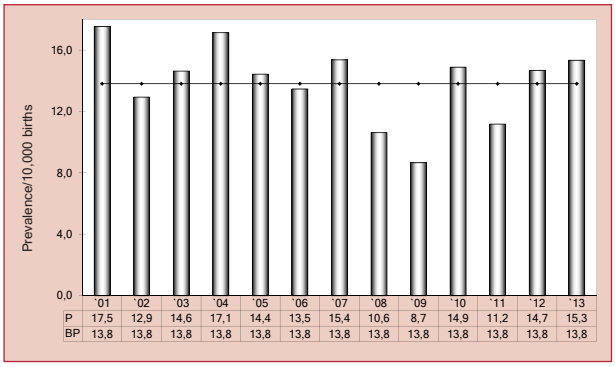


Fig. 21: Development of prevalence/10,000 births with cleft lip with or without cleft palate in the registration area since 2001

In 2013 one child with cleft lip with or without cleft palate per 652 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 basic prevalence
Major cities: 1 x Halle 2 x Magdeburg	3	6.2	↔
Districts: 2 x Anhalt-Bitterfeld 1 x Harz 1 x Jerichower Land 2 x Saalekreis 2 x Salzlandkreis 2 x Stendal	10	8.2	↔
Saxony-Anhalt	**13**	**7.7**	↔

Cleft Palate (2001-2012)		
	Basic prevalence /10,000 births	Confidence Interval (CI of 95%) /10,000 births
Cities	7.05	4.99 - 9.67
Districts	7.92	6.67 - 9.39
Region	7.69	6.62 - 8.93
EUROCAT	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 2013.
The calculated **prevalence** of **7.7 per 10,000 births** corresponds exactly to the average value of the previous years.

Therefore, the comparison with other EUROCAT centres shows for cleft palate, similar to the cleft lip with cleft jaw and palate, a frequency within the upper third.

We registered in 2001, 2002, 2005 and 2006 high prevalences for cleft palate and for the following years we registered low prevalences. Figure 46 on page 65 illustrates apparently a decreasing trend for cleft palate for the time period of 2001-2013. But if the registration period is extended, strong fluctuations can also be observed during the years before 2001. The prevalence of 1996 was lower than in 2008 for example. However, in the last two years our prevalences remained unsuspicious within the confidence interval of the basis prevalence. Therefore, we have to observe if any trend changes will take place in the future.

additional information:

Pregnancy outcome	11 x live birth 1 x termination of pregnacy 1 x stillbirth
Sex	6 x male 7 x female
Number of isolated malformations/MCA	7 x MCA 6 x isolated

The celft palate occured in six cases isolated, in seven cases additional malformations were present.

11 infants were live births between 36 and 40 weeks of gestation. One full term infant with additional cerebral malformation was stillbirth after 40 weeks of gestation. One pregnancy was termianted after 22 weeks of gestation after prenatally diagnosed presence of complex malformations.

Malformation combinations (MCA) or superordinated syndromes detected:

- Smith-Lemli-Opitz-syndrome with: canalis atrioventricularis communis, Haortic hypoplasia, blt. uncompletely lobed lung, hexadactyly of both feet, blt. postaxial accessory finger and clinodactyly of 5th finger, cleft uvula, mandibular micrognathia, epicanthus internus, low set ears, cleft scrotum
- Microcephaly, horseshoe kidney and DUP II. grade blt., mandibular micrognathia, glossoptosis
- Hydrocephalus internus, septooptic dysplasia, hypoplastic septum pellucidum, DUP I. grade left, torticollis muscularis, shortened lingual frenulum , craniofacial dysmorphiy with high forehead
- Foetal alcohol syndrome
- Acrocephaly, mandibular micrognathia
- Subluxation of left hip, mandibular micrognathia, teeth at birth
- postaxial accessory finger blt.

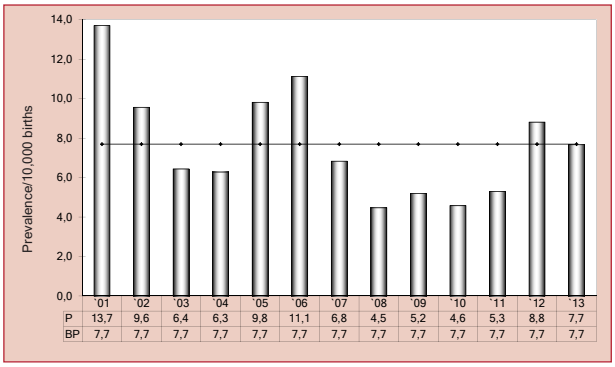


Fig. 22: Development of prevalence/10,000 births with cleft palate in the registration area since 2001

In 2013 one child with cleft palate per 1,304 births was registered in Saxony-Anhalt.

12.16 Choanal Atresia (Q30.0)

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

Choanal Atresia (2001-2012)		
	Basic prevalence /10,000 births	**Confidence Interval (CI of 95%) /10,000 births**
Cities	0.37	0.04 - 1.34
Districts	0.39	0.14 - 0.84
Region	0.38	0.17 - 0.75
EUROCAT	0.89	0.83 - 0.95
		0.05 S Portugal* 2.04 Styria (Austria)**

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

One infant with the rarely appearing malformation choanal atresia (isolated) was reported in 2013.
The **prevalence** of **0.6 per 10,000 births** lies within the confidence interval of the last 12 years.

additional information:

Termination of pregnancy	1 x live birth
Sex	1 x male
Number of isolated malformations/MCA	1 x isolated

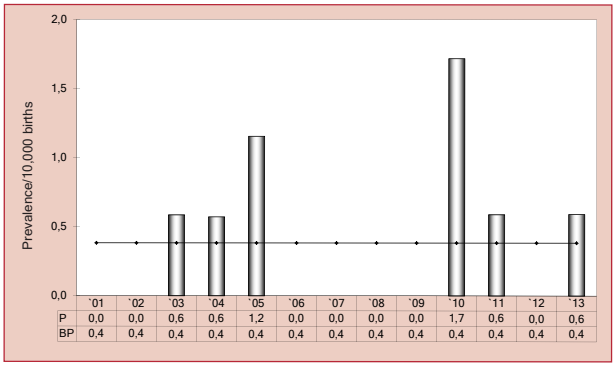


Fig. 23: Development of prevalence/10,000 births with choanal atresia in the registration area since 2001

In 2013 one child with a choanal atresia per 16,950 births was registered in Saxony-Anhalt.

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

	Number	Prevalence /10,000 births	Trend in comp. to basic prevalence
Major cities: 1 x Halle	1	2.1	↘
Districts: 1 x Burgenlandkreis 1 x Börde 1 x Mansfeld-Südharz	3	2.5	↔
Saxony-Anhalt	**4**	**2.4**	↔

Oesophageal Atresia/Stenosis/Fistula (2001-2012)		
	Basic prevalence /10,000 births	**Confidence Interval (CI of 95%) /10,000 births**
Cities	3.90	2.41 - 5.95
Districts	2.51	1.79 - 3.43
Region	2.87	2.19 - 3.69
EUROCAT (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

Four births with oesophageal atresia were registered in 2013. The prevalence of 2.4 per 10,000 births lies within the confidence interval of the 12-years prevalence from 2001-2012 (2.9 per 10,000 births).

EUROCAT calculated for the different registration centres and the time period of 2001-2012 an average prevalence of 2.4 per 10,000 births.

additional information:

Pregnancy outcome	4 x live birth
Sex	1 x male 3 x female
Number of isolated malformations/MCA	4 x isolated

All infants were live births between 37 and 40 weeks of gestation. Only in one case a suspicious diagnosis was prenatally confirmed. No additional malformations were reported. In one case a polyhydramnion gave the hint.

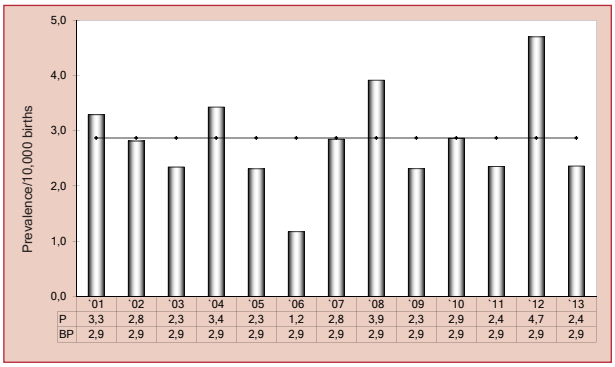


Fig. 24: Development of prevalence/10,000 births with oesophageal atresia/stenosis/fistula in the registration area since 2001

In 2013 one oesophageal atresia/stenosis/fistula per 4,238 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 basic prevalence
Major cities	0	0.0	↓
Districts: 1 x Saalekreis 1 x Salzlandkreis	2	1.6	↔
Saxony-Anhalt	**2**	**1.2**	↘

Small Intestinal Atresia/Stenosis (2001-2012)		
	Basic prevalence /10,000 births	**Confidence Interval (CI of 95%) /10,000 births**
Cities	1.30	0.52 - 2.68
Districts	2.12	1.46 - 2.98
Region	1.91	1.37 - 2.60
EUROCAT (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 2013, only two births with small intestinal atresia were registered. The prevalence of 1.2 per 10,000 births lies therefore minimally under the confidence interval of the last 12 years.

additional information:

Pregnancy outcome	2 x live birth
Sex	2 x male
Number of isolated malformations/MCA	1 x MCA 1 x isolated

The small intestinal atresia occurred in one case isolated, in the other case additional malformations were present.

Malformation combinations (MCA) or superordinated syndromes detected:

- Porencephaly, blt. processus vaginalis peritonei and retarded hip

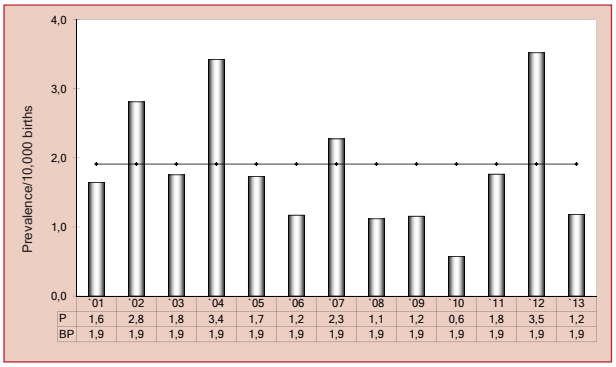


Fig. 25: Development of prevalence/10.000 births with small intestinal atresia/stenosis in the registration area since 2001

In 2013 one small intestinal atresia/stenosis per 8,475 births was registered in Saxony-Anhalt.

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

	Number	Prevalence /10,000 births	Trend in comp. to basic prevalence
Major cities: 1 x Halle 1 x Magdeburg	2	4.2	↔
Districts: 1 x Harz 1 x Mansfeld-Südharz 1 x Saalekreis 1 x Salzlandkreis	4	3.3	↓
Saxony-Anhalt	**6**	**3.5**	↓

Anorectal Atresia/Stenosis (2001-2012)		
	Basic prevalence /10,000 births	**Confidence Interval (CI of 95%) /10,000 births**
Cities	5.94	4.06 - 8.38
Districts	5.02	3.97 - 6.27
Region	5.26	4.38 - 6.29
EUROCAT	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 six births with anorectal atresia/stenosis in 2013. The calculated **prevalence** of **3.5 per 10,000 births** is again regressive in contrast to the maximum value that was registered in 2008. It also lies under the confidence interval of the last 12 years.

In the European comparison our annual malformation prevalence for anorectal atresia/stenosis lies within the average, but is at the same time still higher than the confidence interval of the last 12 years.

additional information:

Pregnancy outcome	3 x live birth 1 x live birth, deceased within 7 days 1 x spontaneous abortion 1 x termination of pregnancy
Sex	3 x male 3 x female
Number of isolated malformations/MCA	4 x MCA 2 x isolated

In all registered cases an anal atresia was present, four times it occured without and two times with fistula. In two cases additional malformations were already detected prenatally. The anal atresia occured in two cases isolated and there were no abnormalities detected prenatally. One pregnancy was terminated after 18 weeks of gestation.

Malformation combinations (MCA) or superordinated syndromes detected:

- Klinefelter-syndrome with: Potter-Sequence (bilateral renal agenesis), hypospadias, undescended testis, turricephaly, ASD, haemodynamically not effective PDA at full term infant, craniofacial dysmorphy with low set ears
- VSD
- Cytomegaly
- Subluxation of right hip, retarded hip left

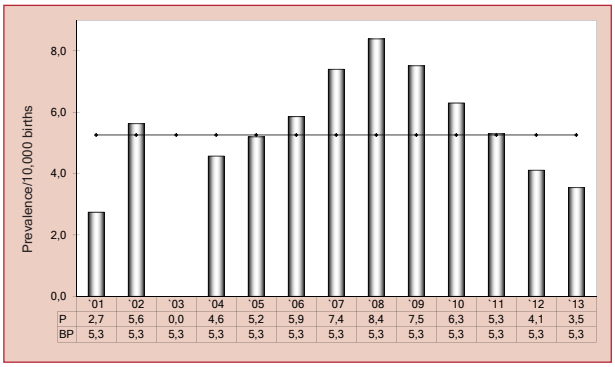


Fig. 26: Development of prevalence/10,000 births with anorectal atresia/-stenosis in the registration area since 2001

In 2013 one anorectal atresia / stenosis per 2,825 births was registered in Saxony-Anhalt.

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

	Number	Prevalence /10,000 births	Trend in comp. to basic prevalence
Major cities: 1 x Dessau-Roßlau 3 x Halle 2 x Magdeburg	6	12.5	↔
Districts: 1 x Altmarkkreis Salzwedel 1 x Börde 2 x Harz 1 x Mansfeld-Südharz 2 x Saalekreis 1 x Salzlandkreis	8	6.6	↗
Saxony-Anhalt	**14**	**8.3**	↔

Undescended Testis (2001-2012)		
	Basic prevalence /10,000 births	Confidence Interval (CI of 95%) /10,000 births
Cities	15.40	12.27 - 19.08
Districts	4.89	3.85 - 6.12
Region	7.60	6.53 - 8.83
EUROCAT	no information	no information

We registered 14 male infants/foetuses with undescended testis in 2013. Therefore, the prevalence of 8.3 per 10,000 births remains unchanged in comparison to the previous year.

The maldescensus testis can be considered as physiological state at preterm infants. Therefore, a correct classification is important here and only fullterm infants are counted.

In eleven cases, no additional malformations were registered. Three boys suffered from a bilateral maldescensus, in three cases the malformation occured unilateral left and in another three cases unilateral right. In case of one unilateral maldescensus testis we have no infomation if it appeared on the left or right side.

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 overregistration of this malformation is suggested by EUROCAT and for that reason no comparison data is present.

additional information:

Pregnancy outcome	13 x live birth 1 x live birth, deceased within 7 days
Sex	14 x male
Number of isolated malformations/MCA	3 x MCA 11 x isolated

Malformation combinations (MCA) or superordinated syndromes detected:

- Klinefelter-syndrome with: Potter-sequence (bilateral renal agenesis), anal atresia, hypospadias, turricephaly, ASD, haemodynamical not effective PDA at full term infant, craniofacial dysmorphy with low set ears
- Microcephaly
- Hernia inguinalis right at full term infant, abdominal separation,craniofacial dysmorphy with low set ears and flat nose

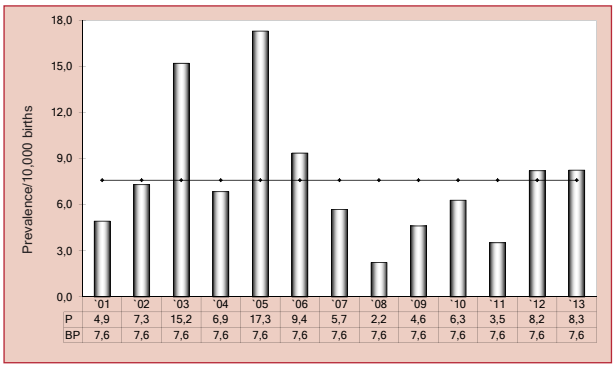


Fig. 27: Development of prevalence/10,000 births with undescended testis in the registration area since 2001

In 2013 one child with undescended testis per 1,211 births (615 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 basic prevalence
Major cities: 1 x Dessau-Roßlau 3 x Halle 3 x Magdeburg	7	14.6	↓
Districts: 2 x Anhalt-Bitterfeld 2 x Burgenlandkreis 4 x Harz 1 x Jerichower Land 2 x Mansfeld-Südharz 2 x Saalekreis 2 x Salzlandkreis	15	12.4	↓
Saxony-Anhalt	**22**	**13.0**	↓

Hypospadias (2001-2012)		
	Basic prevalence /10,000 births	Confidence Interval (CI of 95%) /10,000 births
Cities	20.78	17.35 - 24.82
Districts	18.54	16.56 - 20.75
Region	19.12	17.36 - 21.04
EUROCAT	17.42	17.16 - 17.69
		4.03 Northern England (UK)* 37.51 Malta**

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

A hypospadias was registered in 22 cases in 2013. The annual **prevalence** lies with a value of **13.0 per 10,000 births** under the confidence interval of the previous years and is at the same time the lowest value we registered during the last 12 years. Therefore, a descending trend can be observed in Saxony-Anhalt (see chapter 12.37).

A comparison with EUROCAT data shows an annual prevalence below the average European frequency of the years 2001-2012. Furthermore, a new EUROCAT study also outlines the same result for the years 2001-2010, however no descending trend was observed here (so far unpublished EUROCAT data).

additional information:

Pregnancy Outcome	21 x live birth 1 x live birth, deceased within 7 days
Sex	22 x male
Number of isolated malformations/MCA	6 x MCA 16 x isolated

In 16 cases hypospadias occured without any additional malformations. 17 boys suffered from a glandular hypospadias and in five cases we received no indication about the severeness of the malformation.

Malformation combinations (MCA) or superordinated syndromes detected:

- Klinefelter-syndrome with: Potter-sequence (bilateral renal agenesis), anal atresia, undescended testis, turricephaly, ASD, haemodynamically not effective PDA at full term infant, craniofacial dysmorphy with low set ears
- Cerebral meningolele
- Stenosis of right arteria pulmonalis, ASD II, DUP I. grade right, macrocephaly
- Arachnoidal cyst, persistence of left vena cava superior
- Cytomegaly, PFO at preterm infant
- Clubfoot

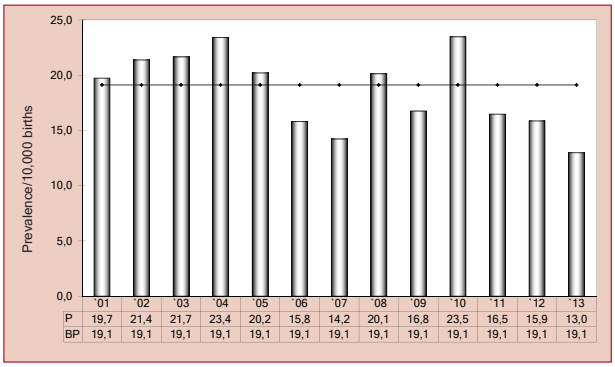


Fig. 28: Development of prevalence/10,000 births with hypospadias in the registration area since 2001

In 2013 one hypospadias per 770 births (392 boys) was registered in Saxony-Anhalt.

12.22 Epispadias (Q64.0)

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

Epispadias (2001-2012)		
	Basic prevalence /10,000 births	Confidence Interval (CI of 95%) /10,000 births
Cities	0.19	0.00 - 1.03
Districts	0.32	0.10 - 0.75
Region	0.29	0.11 - 0.62
EUROCAT	no information	no information

Similar to the previous two years, we registered no case of epispadias in 2013.

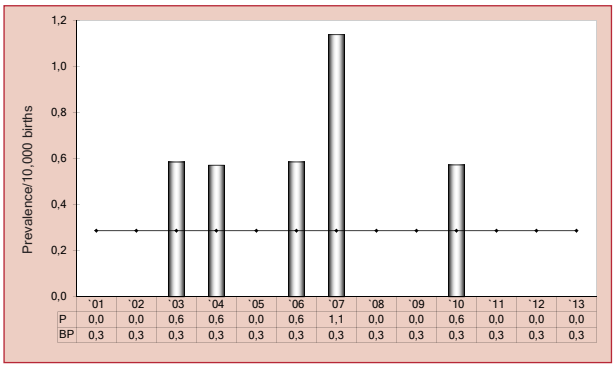


Fig. 29: Development of prevalence/10,000 births with epispadias in the registration area since 2001

In 2013 no birth with epispadias was registered in Saxony-Anhalt.

12.23 Indeterminate Sex (Q56.)

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

Indeterminate Sex (2001-2012)		
	Basic prevalence /10,000 births	Confidence Interval (CI of 95%) /10,000 births
Cities	0.19	0.00 - 1.03
Districts	0.58	0.26 - 1.10
Region	0.48	0.23 - 0.88
EUROCAT	0.66	0.61 - 0.72
		0.29 Mainz (Germany)* 1.60 Wessex (UK)**

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

One birth with indeterminate sex was registered in 2013. The calculated **prevalence** of **0.6 per 10,000 births** corresponds to the average value of the basis prevalence which was calculated for the years 2001-2012.

Compared to EUROCAT data, our annual prevalence lies slightly under the prevalences of 2001-2012 of other European registers.

additonal information:

Pregnancy outcome	1 x termination of pregnancy
Sex	1 x male
Number of isolated malformations/MCA	1 x MCA

Malformation combinations (MCA) or superordinated syndromes detected:

- Mitral valve insufficiency, haemodynamically effective PDA at preterm infant, hernia inguinalis bilateral, umbilical hernia, hydrocele right, cleft scrotum, micropenis

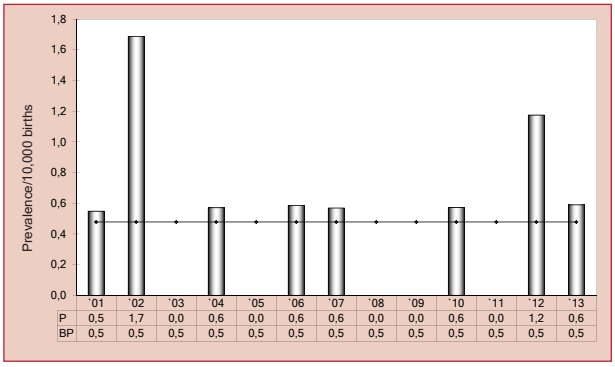


Fig. 30: Development of prevalence/10,000 births with indeterminate sex in the registration area since 2001

In 2013 one birth with indeterminate sex per 16,950 was registered in Saxony-Anhalt.

12.24 Potter Sequence (Q60.6)

	Number	Prevalence /10,000 births	Trend in comp. to basic prevalence
Major cities: 1 x Halle	1	2.1	↔
Districts: 1 x Börde 1 x Harz 1 x Jerichower Land 1 x Mansfeld-Südharz 1 x Saalekreis	5	4.1	↑
Saxony-Anhalt	**6**	**3.5**	↑

Potter Sequence (2001-2012)		
	Basic prevalence /10,000 births	Confidence Interval (CI of 95%) /10,000 births
Cities	1.86	0.89 - 3.41
Districts	2.00	1.36 - 2.83
Region	1.96	1.41 - 2.66
EUROCAT	1.17	1.10 - 1.24
		0.53 S Portugal* 5.44 Mainz (Germany)**

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

We registered six births with Potter sequence in 2013. The annual prevalence of 3.5 per 10,000 births is the highest prevalence we registered during the whole time period of 2001-2012. At the same time the value lies above the confidence interval.

In comparison to other EUROCAT registers the current annual prevalence is within the upper third. The prevalence of 2013 clearly exceeds the corresponding confidence interval.

additional information:

Pregnancy outcome	1 x live birth 4 x live birth, deceased within 7 days 1 x termination of pregnancy
Sex	3 x male 3 x female
Number of isolated malformations/MCA	5 x MCA 1 x isolated

In four cases a bilateral rena agenesis was present, in two cases bilateral functionless multicystic dysplastic kidneys were reported.

In one case the pregnancy was unknown and therefore a Valsartan intake by the mother until 25 weeks of gestation took place. After ascertainment of pregnancy an anhydramnion was detected prenatally. Due to a chronical renal insufficiency the infant needed postnatally a peritoneal dialysis. In additional four cases a bilateral renal agenesis was detected prenatally. One pregnancy was terminated after 20 weeks of gestation.

Malformation combinations (MCA) or superordinated syndromes detected:

- Klinefelter-syndrome with: anal atresia, hypospadias, undescended testis, turricephaly, ASD, haemodynamically not effective PDA at full term infant, craniofacial dysmorphy with low set ears
- Choanal stenosis blt., tricuspidal insufficiency, mitral valve issufficiency, coarctation of aorta, dysplastic ears, mandibular micrognathia
- Microcephaly
- Embryofetopathy caused by Valsartan, wide gaping cranial sature
- Clubfoot, potter-facies with dysplastic, low set ears, epicanthus internus, mandibular retrognathia and flat nose

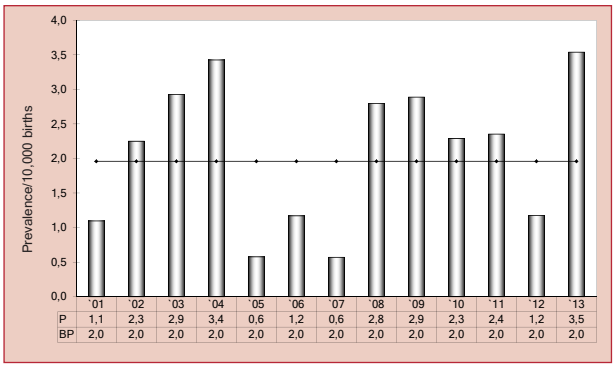


Fig. 31: Development of prevalence/10,000 births with Potter sequence in the registration area since 2001

In 2013 one Potter sequence per 2,825 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 on 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 basic prevalence
Major cities: 1 x Halle	1	2.1	↓
Districts: 1 x Altmarkkreis Salzwedel 1 x Anhalt-Bitterfeld 1 x Burgenlandkreis 1 x Harz 3 x Mansfeld-Südharz 1 x Salzlandkreis	8	6.6	↔
Saxony-Anhalt	**9**	**5.3**	↓

Renal Agenesis, Unilateral (2001-2012)		
	Basic prevalence /10,000 births	Confidence Interval (CI of 95%) /10,000 births
Cities	7.98	5.77 - 10.74
Districts	6.57	5.44 - 7.91
Region	6.93	5.91 - 8.11
EUROCAT	no information	no information

We registered nine births with unilateral renal agenesis in 2013.
The prevalence of 5.3 per 10,000 births lies under the confidence interval of the last 12 years.

No EUROCAT data is present here for comparison.

additional information:

Pregnancy outcome	8 x live birth 1 x termination of pregnancy
Sex	6 x male 3 x female
Number of isolated malformations/MCA	3 x MCA 6 x isolated

In six cases renal agenesis occurred at the left kidney and in three cases at the right kidney. In six cases no additional malformations were present.

Prenatal abnormalities were diagnosed in six cases. In further three cases we have no indication about any prenatal findings.

One pregnancy was terminated after 18 weeks of gestation after the diagnosis of complex additional malformations and a dysplastic solitary kidney.

Malformation combinations (MCA) or superordinated syndromes detected:

- Arnold-Chiari-syndrome with: double dorsal spina bifida, dysplastic right kidney, kyphoscoliosis
- Melded right kidney
- Duplex left kidney

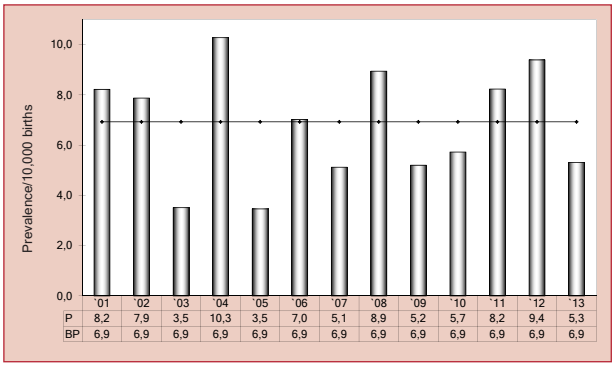


Fig. 32: Development of prevalence/10,000 births with unilateral renal agenesis in the registration area since 2001

In 2013 one renal agenesis, unilateral per 1,883 births was registered in Saxony-Anhalt.

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

	Number	Prevalence /10,000 births	Trend in comp. to basic prevalence
Major cities: 1 x Halle 1 x Magdeburg	2	4.2	↓
Districts: 1 x Harz 1 x Mansfeld-Südharz 1 x Saalekreis	3	2.5	↓
Saxony-Anhalt	**5**	**2.9**	↓

Cystic Kidney (2001-2012)		
	Basic prevalence /10,000 births	Confidence Interval (CI of 95%) /10,000 births
Cities	9.65	7.21 - 12.65
Districts	7.72	6.49 - 9.18
Region	8.22	7.10 - 9.50
EUROCAT	no information	no information

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

In 2013 we registered five births with cystic kidneys. The calculated **prevalence** of **2.9 per 10,000 births** is one of the lowest values we registered during the last 12 years and it lies clearly under 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	3 x live birth 2 x termination of pregnancy
Sex	2 x male 3 x female
Number of isolated malformations/MCA	3 x MCA 2 x isolated

Mainly female infants were affected.

In one case cystic kidneys were present bilateral, in the remaining cases a multicystic-dysplastic kidney was present one time left side and three times right side.

One pregnancy was terminated after 18 weeks of gestation and one after 19 weeks of gestation after prenatal diagnosis of combined CNS malformations.

Malformation combinations (MCA) or superordinated syndromes detected:

- Arnold-Chiari-syndrome with: double dorsal spina bifida, renal agenesis left side, kyphoscoliosis
- Autosomale duplication with: VSD, Dandy-Walker-syndrome, missing Vermis cerebelli
- VSD, haemodynamically effective PDA and PFO at preterm infant, umbilical hernia

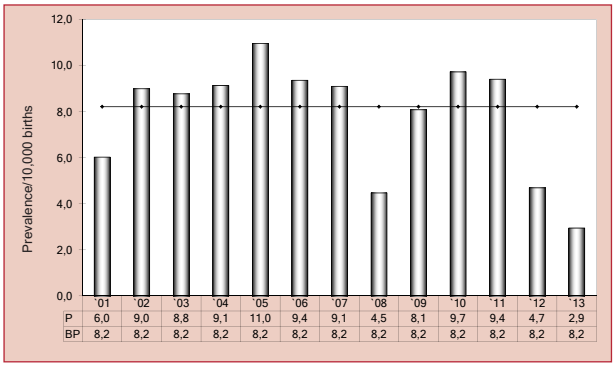


Fig. 33: Development of prevalence/10,000 births with cystic kidneys in the registration area since 2001

In 2013 one cystic kidney per 3,390 births was registered in Saxony-Anhalt.

12.27 Bladder Exstrophy (Q64.1)

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

Bladder Exstrophy (2001-2012)		
	Basic prevalence /10,000 births	Confidence Interval (CI of 95%) /10,000 births
Cities	0.00	0.00 - 0.56
Districts	0.32	0.10 - 0.75
Region	0.24	0.08 - 0.56
EUROCAT	no information	no information

No birth with bladder exstrophy was registered in 2013.

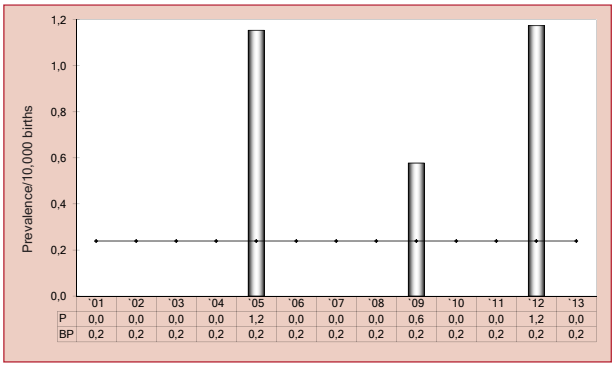


Fig. 34: Development of prevalence/10,000 births with bladder exstrophy in the registration area since 2001

In 2013 no birth with a bladder exstrophy was registered in Saxony-Anhalt.

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

	Number	Prevalence /10,000 births	Trend in comp. to basic prevalence
Major cities: 1 x Halle 1 x Magdeburg	2	4.2	↔
Districts: 1 x Anhalt-Bitterfeld 1 x Börde	2	1.6	↓
Saxony-Anhalt	**4**	**2.4**	↓

Preaxial Polydactyly (2001-2012)		
	Basic prevalence /10,000 births	Confidence Interval (CI of 95%) /10,000 births
Cities	4.45	2.85 - 6.62
Districts	4.38	3.40 - 5.55
Region	4.40	3.54 - 5.39
EUROCAT	no information	no information

Four births with preaxial polydactyly were registered in 2013.
The annual **prevalence** of **2.4 per 10,000 births** lies under the confidence interval of the last 12 years.

Comparative EUROCAT data for preaxial polydactyly is not available.

additional information:

Pregnancy outcome	4 x life birth
Sex	3 x male 1 x female
Number of isolated malformations/MCA	2 x MCA 2 x isolated

Two infants did not present any additional malformations. In three cases the right hand was concerned and in one case the left hand.

Malformation combinations (MCA) or superordinated syndromes detected:

- Down syndrome with: Tetralogy of Fallot, canalis atrioventricularis communis, ASD II, haemodynamically effective PDA at full term infant
- Plagiocephaly, VSD, pulmonary valve stenosis, PFO at full term infant, ectasia of sinus coronarius and left lower pulmonary vein, phlebectasia, anemia

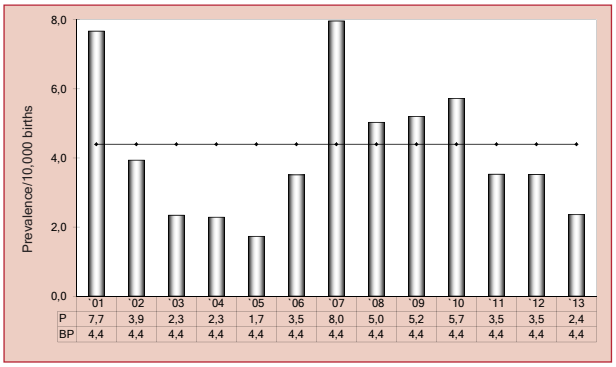


Fig. 35: Development of prevalence/10,000 births with preaxial polydactyly in the registration area since 2001

In 2013 one preaxial polydactyly per 4,238 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 basic prevalence
Major cities: 1 x Halle 4 x Magdeburg	5	10.4	↗
Districts: 2 x Anhalt-Bitterfeld 1 x Burgenlandkreis 2 x Saalekreis 1 x Salzlandkreis	6	4.9	↓
Saxony-Anhalt	**11**	**6.5**	↘

Limb Reduction Defects of both Upper and Lower Limbs (2001-2012)		
	Basic prevalence /10,000 births	Confidence Interval (CI of 95%) /10,000 births
Cities	7.61	5.46 10.32
Districts	8.05	6.78 - 9.53
Region	7.93	6.84 - 9.19
EUROCAT	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 2013 we received reportings about 11 births with reduction defects of upper and lower limbs.
The annual prevalence of 6.5 per 10,000 births lies slightly under the confidence interval of the registration period 2001-2012.

A comparison with EUROCAT data shows that the Saxony-Anhalt prevalence is to find within the upper third. The prevalence we calculated in 2013 as well as the basis prevalence of Saxony-Anhalt clearly exceed the prevalences of other European centres (5.32 per 10,000 births, CI 5.18 - 5.47).

additional information:

Pregnancy outcome	10 x life birth 1 x life birth, deceased within 7 days
Sex	2 x male 9 x female
Number of isolated malformations/MCA	4 x MCA 7 x isolated

In seven cases no furhter organ systems were affected by this malformation. Only in three cases we received information about a suspicious prenatal finding.
One infant was delivered after premature rupture of membranes after 31 weeks of gestation and all other infants were born between 38 and 41 weeks of gestation.

Malformation combinations (MCA) or superordinated syndromes detected:

- Tetralogy of Fallot, PFO at full term infant, persistence of left vena cava superior, choanal stenosis, close pharynx with functional larynx obstruction, tracheal bronchus right, cataract blt., sunken nose bridge
- Microcephaly
- Achondroplasia
- Right DUP III. grade and ureteropelvic junction obstruction

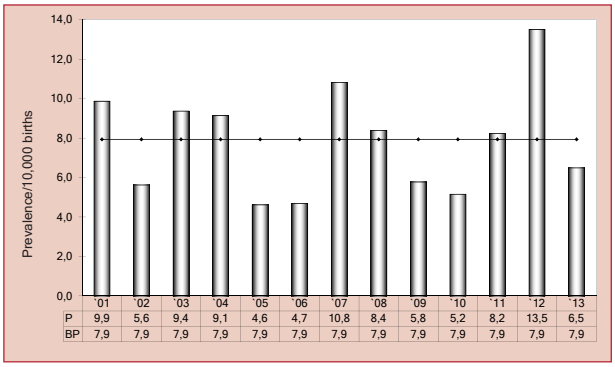


Fig. 36: Development of prevalence/10,000 births with limb reduction defects in the registration area since 2001

In 2013 one limb reduction defect per 1,541 births was registered in Saxony-Anhalt.

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

	Number	Prevalence /10,000 births	Trend in comp. to basic prevalence
Major cities: 2 x Magdeburg	2	4.2	↔
Districts: 1 x Saalekreis	1	0.8	↓
Saxony-Anhalt	**3**	**1.8**	↓

Diaphragmatic Hernia (2001-2012)		
	Basic prevalence /10,000 births	Confidence Interval (CI of 95%) /10,000 births
Cities	4.08	2.56 - 6.18
Districts	2.32	1.62 - 3.21
Region	2.77	2.10 - 3.58
EUROCAT (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 2013.
The annual prevalence of 1.8 per 10,000 births is identically to the last three years. However, it lies clearly under the confidence interval of the years 2001-2012.

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

additional information:

Pregnancy outcome	2 x live birth 1 x live birth, deceased within 7 days
Sex	2 x male 1 x female
Number of isolated malformations/MCA	1 x MCA 2 x isolated

In two cases no other organ systems were affected by this malformation.

One birth deceased after 24 hours, liver and intestine entered into the thorax. In all three cases the diagnosis was confirmed prenatally.

Malformation combinations (MCA) or superordinated syndromes detected:

- VSD, not haemodynamically effective PDA at preterm infant, polycystic ovaries, small thoracic skin tag, macrocephaly

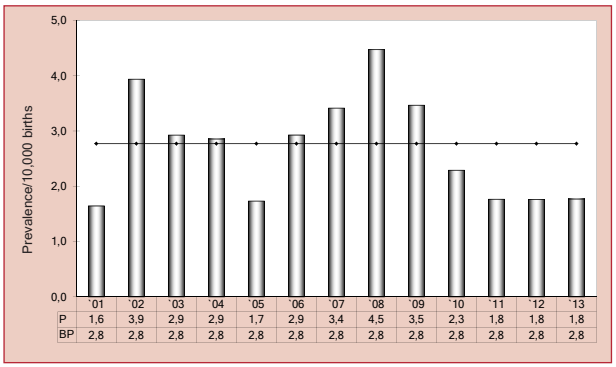


Fig. 37: Development of prevalence/10,000 births with diaphragmatic hernia in the registration area since 2001

In 2013 one diaphragmatic hernia per 5,650 births was registered in Saxony-Anhalt.

12.31 Omphalocele (Q79.2)

	Number	Prevalence /10,000 births	Trend in comp. to basic prevalence
Major cities: 1 x Halle	1	2.1	↔
Districts: 1 x Burgenlandkreis 1 x Börde 1 x Jerichower Land 1 x Saalekreis 1 x Salzlandkreis	5	4.1	↔
Saxony-Anhalt	**6**	**3.5**	↔

Omphalocele (2001-2012)		
	Basic prevalence /10,000 births	Confidence Interval (CI of 95%) /10,000 births
Cities	2.78	1.56 - 4.59
Districts	3.15	2.33 - 4.17
Region	3.06	2.36 - 3.91
EUROCAT	2.96	2.85 - 3.07
		0.43 S Portugal* 5.88 Paris (France)**

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

Six births with omphalocele were registered in 2013. The calculated annual prevalence of 3.5 per 10,000 births is nearly similar to the basis prevalence of the last 12 years.

In comparison with EUROCAT data the average prevalence of Saxony-Anhalt lies within the upper European middle range.

additional information:

Pregnancy outcome	2 x live birth 3 x termination of pregnancy 1 x stillbirth
Sex	4 x male 1 x female 1 x no indication
Number of isolated malformations/MCA	4 x MCA 2 x isolated

In four cases addtitional malformations were present.

The diagnosis of omphalocele was confirmed pre- and postnatally in five cases. One intrauterine fetal death occured after 32 weeks of gestation. One pregnancy was terminated after 11 weeks of gestation and two further pregnancies after 15 weeks of gestation, as additional combinations with malformations and chromosomal aberrations were diagnosed in these cases.

Malformation combinations (MCA) or superordinated syndromes detected:

- Edwards syndrome with: Canalis atrioventricularis communis
- Microcephaly
- VSD, Meckel`s diverticulum, bilateral hernia inguinalis, processus vaginalis peritonei, liver cyst
- blt. hypoplastic lung

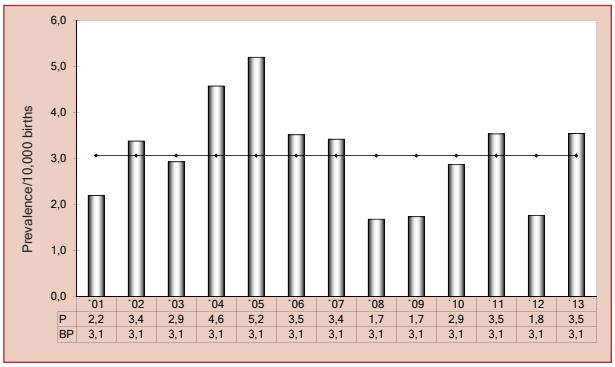


Fig. 38: Development of prevalence/10,000 births with omphalocele in the registration area since 2001

In 2013 one omphalocele per 2,825 births was registered in Saxony-Anhalt.

12.32 Gastroschisis (Q79.3)

	Number	Prevalence /10,000 births	Trend in comp. to basic prevalence
Major cities	0	0.0	↓
Districts: 2 x Burgenlandkreis 1 x Harz 1 x Jerichower Land 2 x Salzlandkreis	6	4.9	↔
Saxony-Anhalt	**6**	**3.5**	↔

Gastroschisis (2001-2012)		
	Basic prevalence /10,000 births	**Confidence Interval (CI of 95%) /10,000 births**
Cities	4.64	3.00 - 6.85
Districts	3.86	2.95 - 4.97
Region	4.06	3.24 - 5.02
EUROCAT	2.61	2.50 - 2.71
		0.88 Tuscany (Italy)* 6.87 Mainz (Germany)**

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

In 2013 we registered six births with gastroschisis.
We calculated an annual **prevalence** of **3.5 per 10,000 births**. During the last four years our prevalence remained on a constant level. However, it decreases minimally in the current year but still lies within the confidence interval of the last 12 years.

Compared to other EUROCAT registers, the annual prevalence lies within the middle/upper range and even above the confidence interval. The higest prevalence is registered by the malformation register in Mainz since five years. Also single studies confirmed a worldwide increasing trend of gastroschisis (ICBDSR 2002 and 2011). A maternal age under 20, a low BMI and the exposition of vasoactive substances (medicine, drugs) were declared as risk factors. In our our case-control-study we confirmed also the risk factors of low BMI and staying on a diet before pregnancy (published in 2011).

additional information:

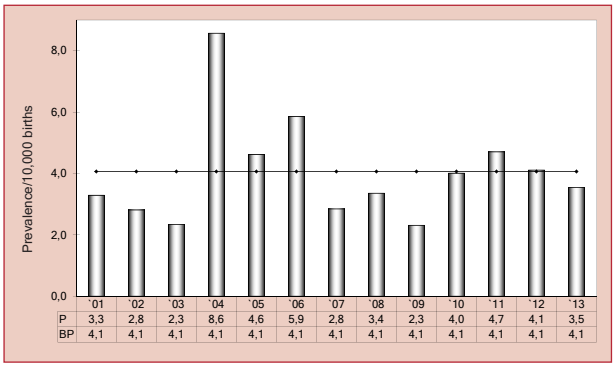
Pregnancy outcome	5 x live birth 1 x termination of pregnancy
Sex	3 x male 3 x female
Number of isolated malformations/MCA	1 x MCA 5 x isolated

In five cases the gastroschisis occured isolated.

The planned delivery was carried out in all cases between 32 and 34 weeks of gestation. One pregnancy was terminated after 18 weeks of gestation and the prenatally diagnosed additional malformations were confirmed postnatally. One pregnancy was unknown and no prenatal ultrasound screening took place until 34 weeks of gestation. All other diagnoses were prenatally confirmed between 13 and 15 weeks of gestation.

Malformation combinations (MCA) or superordinated syndromes detected:

- VSD, hydronephrosis



	`01	`02	`03	`04	`05	`06	`07	`08	`09	`10	`11	`12	`13
P	3,3	2,8	2,3	8,6	4,6	5,9	2,8	3,4	2,3	4,0	4,7	4,1	3,5
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 2001

In 2013 one gastroschisis per 2,825 births was registered in Saxony-Anhalt.

12.33 Prune-Belly-Sequence (Q79.4)

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

Prune-Belly-Sequence (2001-2012)		
	Basic Prevalence /10,000 births	Confidence Interval (CI of 95%) /10,000 births
Cities	1.30	0.52 - 2.68
Districts	0.77	0.40 - 1.35
Region	0.91	0.55 - 1.42
EUROCAT	no information	no information

In 2013 one prenatal suspicion of Prune-Belly-Sequence (abdominal muscle deficiency) was reported. The following invasive diagnostics confirmed a chromosomal aberration and the pregnancy was terminated. Unfortunately, an evaluation of this Prune-Belly-Sequence is not possible and it cannot be counted as confirmed malformation in our present annual report.

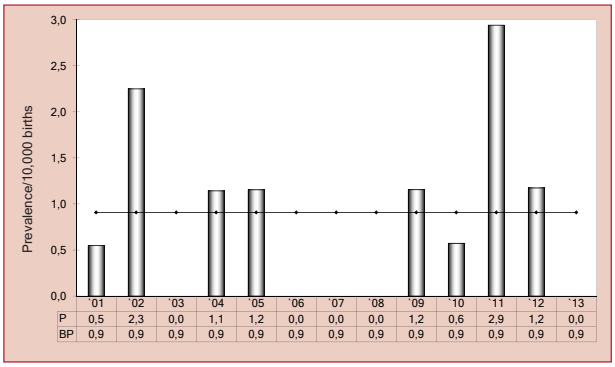


Fig. 40: Development of the prevalence/10,000 births with Prune-Belly-Sequence in the registration area since 2001

In 2013 no birth with Prune-Belly-Sequence was registered in Saxony-Anhalt.

12.34 Down Syndrome - Trisomy 21 (Q90.)

	Number	Prevalence /10,000 births	Trend in comp. to basic prevalence
Major cities: 1 x Dessau-Roßlau 6 x Halle 11 x Magdeburg	18	37.5	↑
Districts: 1 x Altmarkkreis Salzwedel 3 x Anhalt-Bitterfeld 1 x Burgenlandkreis 4 x Börde 3 x Harz 1 x Mansfeld-Südharz 9 x Saalekreis 2 x Salzlandkreis 1 x Stendal	25	20.6	↑
Saxony-Anhalt	**43**	**25.4**	↑

Down syndrome (2001-2012)		
	Basic prevalence /10,000 births	Confidence Interval (CI of 95%) /10,000 births
Cities	20.59	17.18 - 24.62
Districts	15.19	13.41 - 17.20
Region	16.58	14.96 - 18.38
EUROCAT	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 43 births with Down syndrome in 2013. The **prevalence** of **25.4 per 10,000 births** lies clearly above the confidence interval and is the highest calculated prevalence since the beginning of malformation registration by our register in Saxony-Anhalt.

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/ upper range but is still above the confidence interval.

additional information:

Pregnancy outcome	13 x live birth 1 x live birth, deceased within 7 days 28 x termination of pregnancy 1 x stillbirth
Sex	24 x male 16 x female 3 x no indication
Number of isolated malformations/MCA	15 x MCA 28 x isolated

The trisomy 21 occured in 40 cases as free trisomy 21, in the remaining three cases we did not receive further information about this. Ten times an additional cardiac malformation and two times a duodenal stenosis was diagnosed.
An amniocentesis confirmed the trisomy 21, this was carried out in 21 cases due to prenatal ultrasound findings and a suspicious first trimester screening and in 14 cases due to the maternal age.

In six cases the prenatal ultrasound screening was unsuspicious and in two cases no further invasive prenatal diagnostics was requested although the ultrasound screening was suspisious. 13 infants were live births. 29 pregnancies were terminated between 11 and 29 weeks of gestation. In one case an intrauterine fetal death occurred after 37 weeks of gestation.

The development of maternal age (continuous increasing maternal age) during the last years shows as expected an increasing prevalence of Down syndrome, that is however not saltatory. We have to discuss additionally the influence of a very early dignosis during the first trimester screening.
For further information about this topic we recommend to our German speaking colleagues an article in the medical journal „Ärzteblatt Sachsen-Anhalt“ which is called „Führt der DNA-Test aus mütterlichem Blut zur stärkeren pränatalen Selektion des Down Syndroms?“

Malformation combinations (MCA) or superordinated syndromes detected:

- Trisomy 17 (mosaic)
- Tetralogy of Fallot, canalis atrioventricularis communis, ASD II, haemodynamically effective PDA at full tem infant, acessory right thumb
- Microcephaly, VSD, PFO at full term infant
- Hydrocephalus externus and internus, plexus cyst
- Double ASD II, blt. sound perception disorder (right side slightly unti fairly serious, left side fairly serious), blt. buphthalmus, micropapilla and strabismus, hypothyreosis
- Canalis atrioventricularis communis, duodenal stenosis
- 2 x canalis atrioventricularis communis
- Aortic arch anomaly, duodenal stenosis
- VSD, pulmonary valve stenosis, ASD II, bilateral hernia inguinalis at full term infant
- VSD, ASD
- VSD, PFO at full term infant
- ASD
- uncompletely separated additional lobe of lung right side
- omphalomesenteric cyst

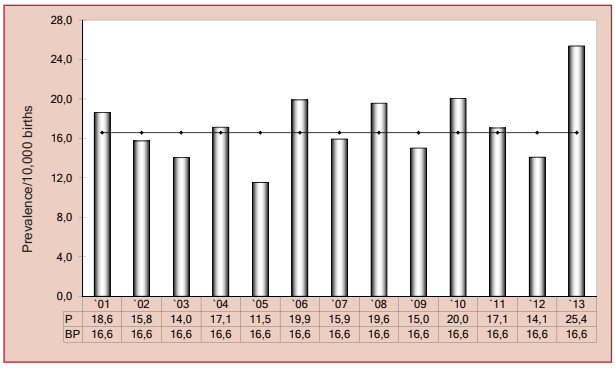


Fig. 41: Development of prevalence/10,000 births with Down syndrome in the registration area since 2001

In 2013 one Down syndrome (trisomy 21) per 394 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 basic prevalence
Major cities	0	0.0	↓
Districts: 1 x Harz 1 x Mansfeld-Südharz	2	1.6	↗
Saxony-Anhalt	**2**	**1.2**	↔

Patau syndrome (2001-2012)		
	Basic prevalence /10,000 births	**Confidence Interval (CI of 95%) /10,000 births**
Cities	1.48	0.64 - 2.92
Districts	0.84	0.45 - 1.43
Region	1.00	0.62 - 1.53
EUROCAT	1.87	1.78 - 1.95
		0.38 S Portugal* 3.85 Paris (France)**

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

In 2013 we registered two births with trisomy 13.
The annual prevalence of 1.2 per 10,000 births lies within the confidence interval of the last 12 years.

However, when comparing our data from Saxony-Anhalt with other EUROCAT centres, our prevalence lies under the confidence interval of the years 2001-2012.

additional information:

Pregnancy outcome	1 x live birth, deceased within 7 days 1 x termination of pregnancy
Sex	1 x female 1 x no indication
Number of isolated malformations/MCA	1 x MCA 1 x isolated

In both cases the trisomy 13 appeared as free trisomy 13. The suspicious diagnosis was made in both cases during ultrasound screening. One pregnancy was terminated after 13 weeks of gestation.

Malformation combinations (MCA) or superordinated syndromes detected:

- Microphthalmy, Corpus callosum agenesia, blt. cleft lip wuth cleft palate and postaxial hexadactyly, dextrokardia, Scalp defects

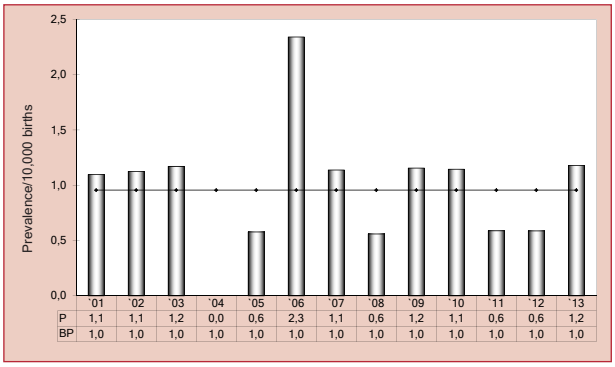


Fig. 42: Development of prevalence/10,000 births with a Patau syndrome in the registration area since 2001

In 2013 one Patau syndrome (trisomy 13) per 8,475 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 basic prevalence
Major cities: 1 x Magdeburg	1	2.1	↓
Districts: 3 x Jerichower Land 1 x Salzlandkreis	4	3.3	↔
Saxony-Anhalt	**5**	**2.9**	↘

Edwards syndrome (2001-2012)		
	Basic prevalence /10,000 births	Confidence Interval (CI of 95%) /10,000 births
Cities	4.45	2.85 - 6.62
Districts	3.80	2.89 - 4.90
Region	3.97	3.16 - 4.92
EUROCAT	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 five births with Edwards syndrome in 2013. The **prevalence** of **2.9 per 10,000 births** continues to decrease since 2010 and lies at the same time slightly under the confidence interval of the last twelve years.

Our calculated annual prevalence is lower than the EUROCAT comparison data and lies under the consequentially calculated confidence interval.

additional information:

Pregnancy outcome	1 x live birth 1 x live birth, deceased after 7 days 3 x termination of pregnancy
Sex	2 x male 3 x female
Number of isolated malformations/MCA	3 x MCA 2 x isolated

In all five cases we registered a free trisomy 18. Three pregnancies were terminated after prenatal diagnosis between 15 and 21 weeks of gestation. Two infants were live births.

Malformation combinations (MCA) or superordinated syndromes detected:

- Cerebellar hypoplasia, VSD, ASD II, misjunction of pulmonary veins, PDA at full term infant, median cleft upper lip, pes planus congenitus, prominent clitoris, retarded hip right, blt. DUP I. grade, malposition of finger and auricular tag, craniofacial dysmorphy with low set dysplastic ears and epicanthus internus
- Hydrocephalus, cerebellar dysplasia, agenesia of cerebellar vermis, missing osseous acoustic meatus, choanal stenosis, VSD, horseshoe kidney, cholestasis, hepatomegaly, hydrocelen blt., umbilical hernia, hernia inguinalis right at preterm infant
- Omphalocele, canalis atrioventricularis communis

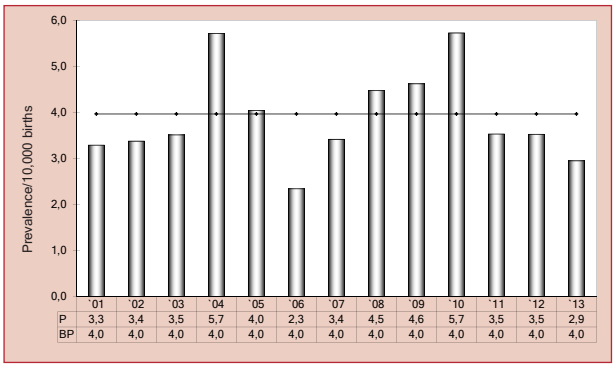


Fig. 43: Development of prevalence/10,000 births with Edwards syndrome in the registration area since 2001

In 2013 one Edwards syndrome (trisomy 18) per 3,390 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. By analysing each of these indicator malformations separately a temporal and regional comparison of malformation rates is possible.

In 2013 we registered 248 births with an indicator malformation in Saxony-Anhalt. 188 (75.8%) of these 252 were live births. This corresponds to the average value of 76.5% that we registered during the years 2001 to 2012. The percentage of terminations of pregnancies is with a value of 21.8% higher than in the previous years (2012: 16.8%; 2011: 17.8%), but only slightly higher than the total average percentage (2001-2012: 19.9%). In 2013 the percentage of spontaneous abortions (0.8%, 2 births) and stillbirths (1.6%, 4 births) added up to a value of 2.4%. The maximum percentage during 2001 to 2012 was a value of 6.8% (2009) and the minimum percentage 1.9% (2006).

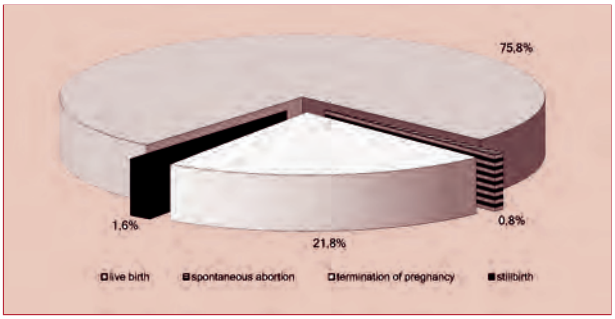


Fig. 44: Pregnancy outcomes of births with indicator malformations 2013

248 births with indicator malformations in 2013 (1.46 per 10,000 births) showed in total 275 indicator malformations. To detect conspicuous accumulations of malformations the current prevalence of each indicator malformation is compared to the basis prevalence of the years 2001-2012. In 2013 the prevalence does not differ from the basis value in none of the cases with an indicator malformation.

	Number	Prevalence in	Trend in comp. to basic prevalence
Major cities	83	1.73	↔
Districts	165	1.36	↔
Saxony-Anhalt	**248**	**1.46**	↔

Indicator malformations, in total (2001-2012)		
	Basic prevalence	Confidence Interval (CI of 95%)
Cities	1.70	1.60 - 1.82
Districts	1.40	1.34 - 1.46
Region	1.48	1.43 - 1.53

In 2013 each prevalence of the major cities, districts and overall Saxony-Anhalt lies inconspicuously within the confidence interval of 2001 to 2012. While we observed prevalences above the confidence interval during 2002 to 2004, the values for 2007, 2009 and 2011 are to find below. Similar to the previous years we calculated also in 2013 an indicator malformation rate which is higher in the major cities than in the districts.

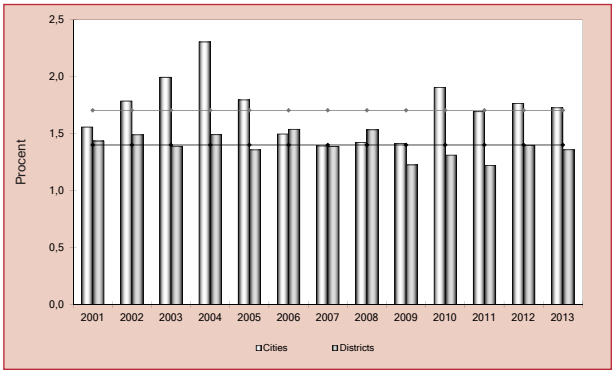


Fig. 45: Indicator malformations of ICBDSR in total (2000 to 2013), comparison of frequency (in %) in the major cities and districts

The analysis of the indicator malformation prevalence during the registration period allows to forecast the future development. As in our previous Annual Report we analysed again the trend of indicator malformation prevalences by considering the whole registration period (12 years). 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 46 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 spina bifida, undescended testis and preaxial polydactyly.
A probability value of $p > 0.05$ for the linear ratio points to the influence of a linear component. However, if the probability value for the non-linear ratio is $p < 0.01$ at the same time, the sequence of values has to be checked. If the sequence of values is not monotone, as it is in case of neural tube defects and microcephaly, we rate the trend also as non linear. The observed trend can be classified as significant at a probability of $p < 0.05$ for the linear ratio and $p > 0.01$ for the non-linear ratio. A significant decreasing trend, corresponding to a negative regression coefficient, can be observed for congenital hydrocephalus, ceft palate and hypospadias.

None of the indicator malformations showed a significant increasing trend in this year. Furthermore, all below illustrated indicator malformations do not show a significant positive or negative trend. 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.

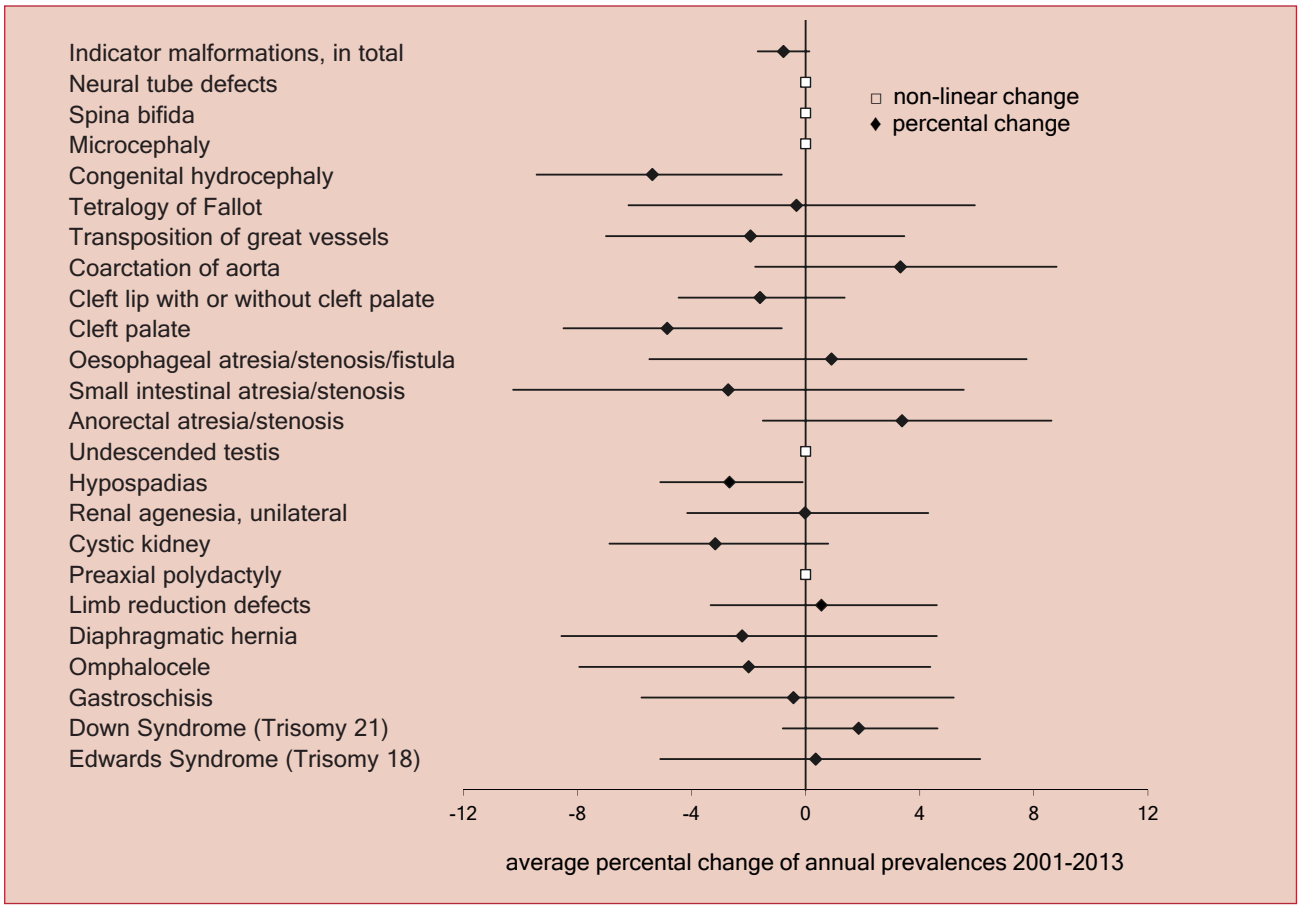


Fig. 46: Trend analysis 2001 - 2013 with average percental change of prevalence per year (95% confidence interval)

	Regression Coefficient B in %	Confidence Interval (CI of 95%)
Indicator malformations, in total	-0.78	-1.68 to 0.13
Congenital hydrocephaly	-5.38	-9.43 to -0.84
Tetralogy of Fallot	-0.32	-6.21 to 5.94
Transposition of great vessels	-1.93	-7.00 to 3.45
Coarctation of aorta	3.33	-1.77 to 8.80
Cleft lip with or without cleft palate	-1.60	-4.45 to 1.37
Cleft palate	-4.85	-8.48 to -0.84
Oesophageal atresia/stenosis/fistula	0.91	-5.48 to 7.74
Small intestinal atresia/stenosis	-2.71	-10.26 to 5.54
Anorectal atresia/stenosis	3.38	-1.49 to 8.61
Hypospadias	-2.67	-5.09 to -0.11
Renal agenesia, unilateral	-0.02	-4.15 to 4.29
Cystic kidney	-3.17	-6.87 to 0.79
Limb reduction defects	0.56	-3.33 to 4.59
Diaphragmatic hernia	-2.22	-8.56 to 4.60
Omphalocele	-1.99	-7.93 to 4.37
Gastroschisis	-0.43	-5.75 to 5.19
Down Syndrome (Trisomy 21)	1.86	-0.80 to 4.62
Edwards Syndrome (Trisomy 18)	0.35	-5.09 to 6.12

15 Summary

The Annual Report 2013 of the Monitoring of Congenital Malformations outlines registered data from Saxony-Anhalt about congenital malformations and anomalies as well as genetically caused diseases. We analysed the registered data statistically and present it now again in the approved manner. In this way our analysed data can be compared to each other. At the same time the analysis of data is population-based according to the official birth rate provided by the State Statistical Office in Halle. To better classify the calculated indicator malformation prevalences for Saxony-Anhalt, we indicate, if available, European wide registered values, calculated by EUROCAT.

We register in Saxony-Anhalt a continuously decreasing birth rate, which will decline further according to the forecast of the Statistical Office. In 2013 **16,797 live births** were registered in Saxony-Anhalt. This is a slightly lower number than in the previous year (2012: 16,888). The biggest decrease of live births from 2012 to 2013 was registered in the district Wittenberg with a value of -3.8% and the biggest increase could be observed in the district Jerichower Land with +6.0%.
The Statistical Office indicates a number of **66 stillbirths** for 2013. This number is rather low in the absolute comparison to the whole registration period (2001-2012: 70.5 per year). However this figure corresponds to the values we registered during the last five years (2006-2012: 66.0 per year).
According to the Federal Statistical Office 682,100 infants were live births in Germany in 2013. These are slightly more births than in the previous year (2012: 673,544). The live births of Saxony-Anhalt represent 2.5% of all births in Germany.

The Monitoring of Congenital Malformations registered among data of live and stillbirths **63 terminations of pregnancy** and **24 spontaneous abortions after 16 weeks of gestation**. The prevalence calculations of the current report are therefore based on a total number of **16,950 births** (see chapter 2).

608 births had at least one **major malformation** (3.59% of all births). Therefore, the calculated malformation rate lies slightly above the rate of the previous twelve years (CI 3.40% to 3.56%) (see chapter 8, German version).
88.32% of **infants with a major malformation** were live births in 2013 (1980-2012: 87.35%). The number of terminations of pregnancies remained on a constant level during the last four years (2008-2011: 10.46%). In contrast, the percentage of spontaneous abortions is very low in comparison to the previous year (2013: 0.66%; 2012: 1.46%). The number of stillbirths remained nearly unchanged (2012: 0.65%; 2013: 0.66%) (see chapter 7 and 8, German version).

Atrial Septal Defect (ASD) and ventricular septal defect (VSD) are the **most frequent diagnoses** in 2013 again. It is surprising that on rank three we registered in the current year the Down's syndrome. Rank four is occupied by the hearing loss, which was already registered very often in the last year. Microcephaly and PDA were diagnosed more frequently than ever and are therefore to find on rank five and six. Dilatative uropathy, polydactyly, clubfoot and hip subluxation appeared less frequently than expected (see chapter 11).

Approximately 1.46% of all births presented an **indicator malformation** in 2013 (see chapter 12). Furthermore, we calculated for the following three indicator malformations **higher rates** in regard to their corresponding basis prevalence: Microcephaly, Potter sequence and Down syndrome. We calculated **lower rates** in comparison to the basis prevalence in 2013 for: Spina bifida, arhin/holoprosencephalie, hypoplastic left heart syndrome, coarctation of aorta, small intestinal atresia/stenosis, anorectal atresia/stenosis, hypospadias, renal agenesia unilateral, cystic kidney, preaxial polydactyly, limb reductions, diaphragmatic hernia and Edwards syndrome. The rarely appearing indicator malformations epispadias, bladder exstrophy and Prune-Belly-sequence were not registered in Saxony-Anhalt in 2013.
Furthermore, we received data about **63 terminations of pregnancies** in 2013 (see chapter 14, German version). Most frequently, the pregnancies were terminated at presence of a chromosomal aberration (68.3%). In nearly two thirds of the cases the most frequent numeric chromosomal aberration Down syndrome was diagnosed. Furthermore, a malformation of the central nervous system was the decisive factor for a termination of pregnancy in one fifth of the cases (19.0%). An increasing number of terminations of pregnancies took place before 18 weeks of gestation (2013: 45.2%; 2012: 37.7%; 2011: 35.2%).
19 births suffered in 2013 from a **genetically caused disease**. **Sequences, associations, resp. complexes** were diagnosed in nine cases. 10 births with **embryopathy or congenital infection** were registered. Again, one infant suffered from a Sartan embryofetopathie. The average maternal age of the above mentioned 68 births with **chromosomal aberration** was 33.2 years in 2013 (see chapter 13, German version).
Prenatal alcohol exposition is the leading avoidable reason for congenital malformations. Therefore, chapter 16 of our Annual Report deals with the topic **"effects of alcohol during pregnancy"**. After the fetal alcohol syndrome was confirmed as medical diagnosis during the 1970s, the Majewski score became a milestone in diagnosis finding. Since December 2012 the European S3-guideline applies for diagnosing fetal alcohol spectrum disorders (FASD). In this connection, chapter 16 presents the latest figures regarding prenatal alcohol exposition.

In 2013 the Monitoring of Congenital Malformations received data about 1,940 births from Saxony-Anhalt. At least one **major malformation** was present at **608 infants/foetuses** (chapter 6-8). In **203 cases minor malformations or anomalies** were registered.
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 2013 Annual Report was only possible due to ongoing voluntary reports about congenital malformations from 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 Effects of alcohol intake during pregnancy

Epidemiological data from Saxony-Anhalt

Definition

Prenatal alcohol exposition is the leading avoidable reason for congenital malformations. **Foetal alcohol spectrum disorder (FASD)** describes multiple effects when a child was exposed to alcohol as foetus and has to live his whole life with the consequences.

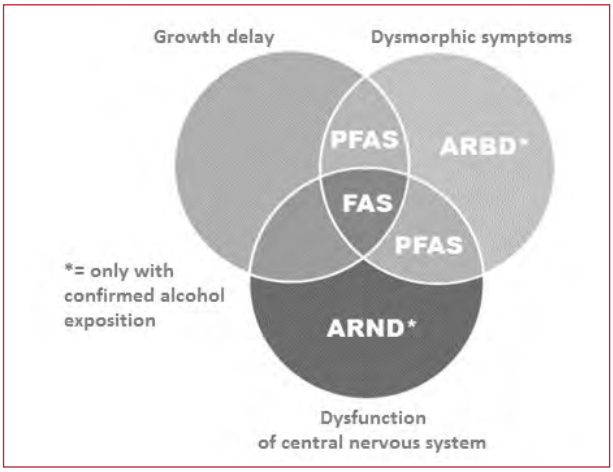


Fig. 49: Complexity of foetal alcohol spectrum disorders (FASD) modified according to Susan J. Astley

Alcohol is a known teratogenic noxe. Formerly known as alcohol embryopathy, the foetal alcohol syndrome represents all symptoms which arise from alcohol impact on the foetus. However, the so far common classification within the alcohol embryopathy (Q86.0) does not represent the complex clinical picture adequately. Especially, as a diagnosis can be confirmed in nearly all cases only after several years and when the newborn time of affected patients has already passed.

Even if infants were affected intrauterine by alcohol intake, this impairment often does not become obvious before the growing up time and can then be considered especially by cognitive deficits (mainly disorder of executive functions). A missing evaluation of later abnormalities in development as symptom of FASD often has serious consequences for the affected children. They suffer from multiple comorbidities (ADD, adaption difficulties) and secondary diseases (addictive disorder) which exist during their whole lives.

Majewski-Score

The definition as independent clinical picture was published by Jones and Smith (US Americans) in Lancet 1973. Majewski was the leading scientist on the field of standard diagnostics in Germany after invention of the so-called Majewski Score in 1978. His publications deal with alcohol embryopathy and alcohol effects.

For a long time the theory deduced from Majewskies work existed that a "slight" impairment of the child as consequence of prenatal alcohol influence would disappear in time and the affected persons could live a normal life. Therefore, the indication of alcohol intake by the physical mother was essential to diagnose possible alcohol effects or an alcohol embryopathy which comes along with central nervous modifications and behaviour disorders.

As indications about the physical mother and pregnancy of the affected children were often not possible (did not grow up in their original family) it was very difficult to make a diagnosis and it was hopeless to initiate a specific therapy or provide assistance.

Four columns of diagnosis have established successfully in clinical practice:

(1) Growth abnormalities,
(2) Facial abnormalities,
(3) CNS-abnormalities and
(4) Maternal alcohol intake during pregnancy.

The 4-Digit Diagnostic Code which is a standardised diagnostics instrument was invented in America. It is based on the four diagnostics columns and was used also in Germany from 2004 on. However, the 4-Digit-Code is very complex and was only used by some experts in this field.

Therefore, the term foetal alcohol spectrum disorder (FASD) is used today more commonly to describe the numerous possibilities of foetal damage by alcohol which exist apart from the clinical picture of the foetal alcohol syndrome.

Current chance: S3-guideline for diagnostics

The S3-guideline for diagnosis of the foetal alcohol syndrome was published in December 2012 and provides significant help to diagnose FAS and pFAS, also in cases where there is no information available about maternal alcohol intake.

The diagnostics of FASD includes:
- Facial dysmorphic signs (short lid fissure, less marked philtrum, slim upper lip)
- Growth retardation (before and after delivery in size and weight)
- CNS-abnormality (microcephalus, dysfunction of central nervous system with global diminution of intelligence or development retardation, epilepsy, partly disturbed performance, e.g. in the field of speech, fine motor skills, visuo-spatial perception, spatial-constructive skills, executive functions, calculating skills, learning ability and retentiveness, attentiveness, social skills and behaviour)

Classification

Fetal Alcohol Spectrum Disorder (FASD):

Fetal alcohol syndrome (FAS)
= Complete syndrome with abnormalities in all three fields
(growth, facial dysmorphic signs, microcephaly or CNS dysfunction)

Partial Fetal Alcohol Syndrome (pFAS)
- Diagnosed at presence of abnormalities in two fields
- Dysmorphic signs and additional growth diminution or CNS dysfunction

Alcohol Related Neurodevelopmental Disorder (ARND)
- Diagnosed only with confirmed alcohol exposition
- Dysfunction of CNS and/or microcephalus, affected patients do not present any physical signs (growth diminuation, typical facial signs)

Alcohol Related Birth Defects (ARBD)
- Diagnosed only with confirmed alcohol exposition
- Symptoms: dysmorphic signs and additional malformations of skeleton and organ systems (cardiac malformations, cleft lip with cleft palate, kidney or urinary tract)
- Patients with prenatal alcohol exposition as reason for a malformation appearance always show facial abnormalities and can be classified in some cases as ARND cases

In view of the complexity of symptoms a diagnosis should always be made by an interdisciplinary team. In this connection a careful differential diagnostics consideration of numerous genetically caused diseases is also necessary.

Need of an early diagnosis?

The early diagnosis was identified in several studies as important protective factor in development of humans with FASD. To know the reason for the abnormalities means that the symptoms can be classified as cerebral damage and not as personality trait or education failure. Concerned people are often limited in such a way in their daily life competences that they might be classified as disabled person. A prenatal toxic cerebral damage of a child by alcohol is irreversible, however an early diagnosis can moderate the effects of possible handicaps by providing helping measures.

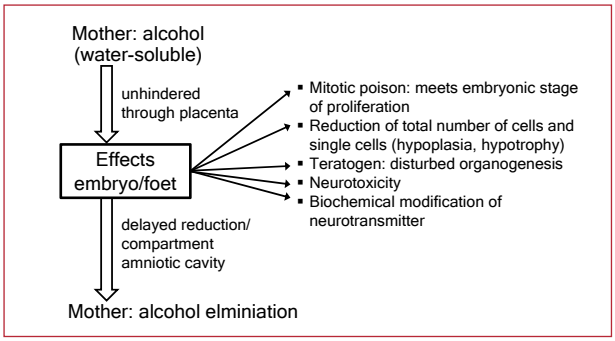


Fig. 50: Mechanism of alcohol damage

Considerations about threshold dose

The EUROMAC-study (European Maternal Alcohol Consumption), which was published in 1992 only considers the weight at births as criterion of a possible damage. Results of this study - the daily intake of a standard alcoholic drink (10g pure alcohol) seems to have no harmful influence to the foetal growth - were wrongly quoted for a long time. In this relation the threshold value only refers to postnatal measurable consequential damage and not to the "neurotoxicity". However, as precisely the brain reacts tenderestly to an alcohol exposition it is to assume that the threshold value is much lower.

Information about the real dose of alcohol intake can only be provided by the mother and this source is often unreliable. Population based studies do not have an objective parameter (alcohol reduction products in meconium) for alcohol intake. As no linear relation between consumed alcohol quantity and clinical severity of damage of the children was illustrated by recent studies (neither in animal experiments), no "assured threshold value" can be determined. Experts therefore recommend: Sobriety during the whole pregnancy.

Figures about prenatal alcohol exposition

First epidemiological examinations (prospective and retrospective), which were published by Olegard et al. in 1979, state a figure of 1 : 300 of births who suffer from alcohol associated abnormalities (whereof only half of the children presented the full clinical picture of FAS). No systematically registered prevalences do exist for Germany. However, according to a recent KiGGS-study (Children and youth health survey) realised by the Robert-Koch-institute, the alcohol intake during pregnancy from 2000 to 2008 was at 14.4% - 16.2% (in total 108,000 sampled population). However, the number of women who consume alcohol during pregnancy is significantly higher than the diagnosed FAS cases.

Frequency in Europe

A systematic literature research about the frequency of prenatal alcohol exposition in Europe generates that Landgraf et al. assume in their preparation about the S3-guideline that 14.4% - 30.0% of pregnancies are threatened by relevant alcohol intake (exception: alcohol intake before knowing about the pregnancy is not quoted). Comparable European studies indicate prevalences for FAS at life births with a value of 0.2 to 8.2 per 10,000 births. In contrast, the most common congenital malformation originating from a chromosomal aberration which is the Down syndrome is indicated by EUROCAT from 1990 to 2009 with a total prevalence value of 2.2 per 10,000 births (for comparison please see indicator malformations, chapter 12.34 Down syndrome). It appears less frequently than FAS but it is diagnosed significantly more often in the clinical routine.

Frequency of alcohol exposition in Saxony-Anhalt

A prospective registration of alcohol intake (Fig. 51) by voluntary information shows a regressive trend when analysing the corresponding data from the Monitoring of Congenital Malformations Saxony-Anhalt for the years 2000 to 2012. However, it is not sure if information campaigns can help that less women consume alcohol during pregnancy or if just the voluntary indication of alcohol intake is still as reliable as before. Nevertheless, in both cases we assume that the public is aware that **alcohol is a noxe for the unborn baby**.

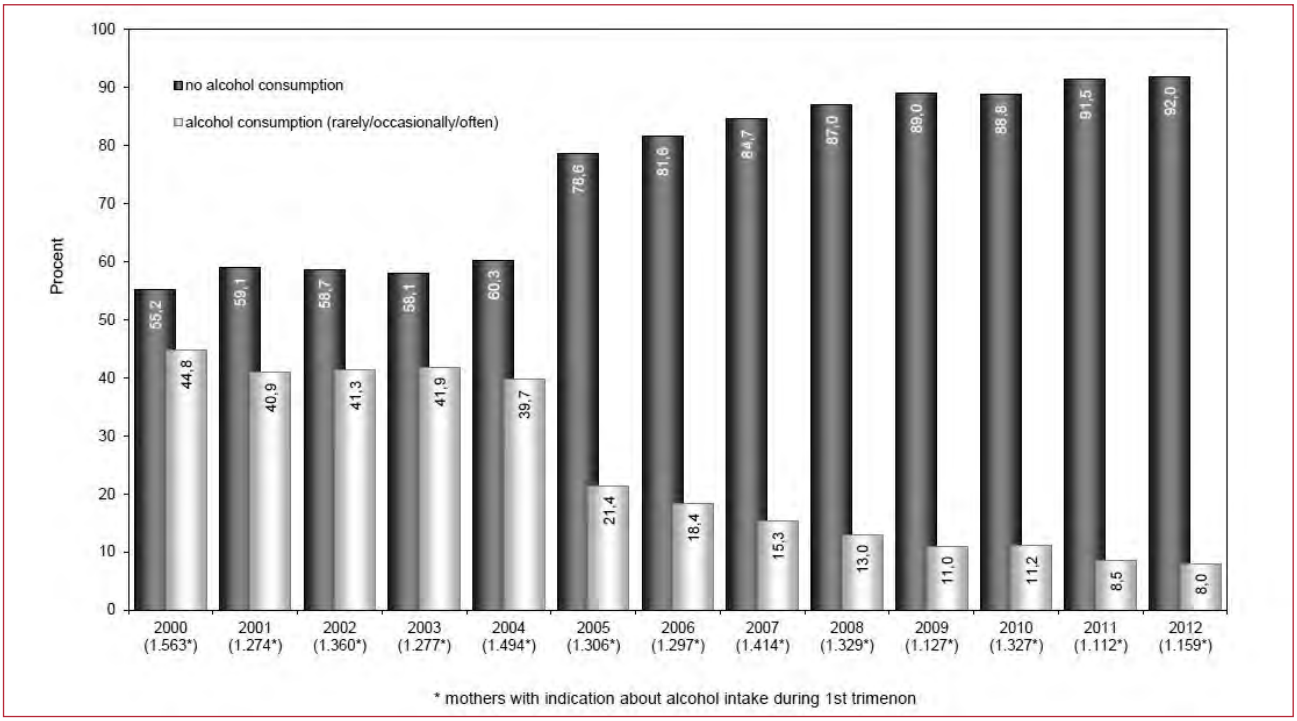


Fig. 51: Alcohol intake during pregnancy (%-share) in Saxony-Anhalt

Alcohol intake during delivery

An analysis of voluntary data and reports about alcoholised delivering women from 2000 to 2012 showed a suspicious/abusive alcohol consumption in 87 cases during delivery. That means that the delivering women was under influence of alcohol when arriving at the hospital. No abnormalities were reported postnatal in 42 of these 87 cases (48.28%). It is to assume that the estimated number of unknown cases is much higher than the confirmed cases of children which present the full clinical picture of FAS and which are described in already existing studies. Therefore, the indicated number of 1 : 2,597 can be only the tip of the iceberg.

FAS-frequency in Saxony-Anhalt

When analysing the data of 2000 to 2009 regarding typical symptoms (without counting voluntary indications) we registered 1,520 cases with microcephaly, pre- and postnatal growth retardation and facial dysmorphy (out of 174,960 births). This would mean that 0.87% of children/foetuses were affected by FAS according to our projection. Approximately 100 affected people per year in Saxony-Anhalt would result in approximately 4,000 affected people per year in Germany (2012: Germany 673,544 life births).

Literature in possession of the authors

18 Newborn Hearing Screening 2013

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. **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)**.

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. therapy 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

* Joint Committee on Infant Hearing (JCIH): Year 2007 Position Statement: Principles and Guidelines for Early Hearing Detection and Intervention Programs. Pediatrics. 120. 898-921 (2007) DOI: 10.1542/peds.2007-2333

Participating Institutions

In 2013, **26 maternity clinics** existed in Saxony-Anhalt. In all these clinics a newborn hearing screening is offered already for several years by TEOAE or AABR. All 26 maternity clinics participated 2013 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-Anhalt.

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 the number of births with a screening ID.

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

Maternity units	Tracking period 2013	Live births in this period*
Ameos Klinikum Aschersleben	01-01 to 31-12-2013	612
Ameos Klinikum Bernburg	01-01 to 15-08-2013	150
Gesundheitszentrum Bitterfeld/Wolfen gGmbH	01-01 to 31-12-2013	449
Krankenhaus Jerichower Land GmbH Burg	01-01 to 31-12-2013	407
Städtisches Klinikum Dessau	01-01 to 31-12-2013	818
Altmark-Klinikum gGmbH Krankenhaus Gardelegen	01-01 to 31-12-2013	316
Ameos Klinikum St. Salvator Halberstadt	01-01 to 31-12-2013	648
Sana Ohre-Klinikum GmbH Haldensleben	01-01 to 31-12-2013	244
Krankenhaus St. Elisabeth und St. Barbara Halle	01-01 to 31-12-2013	1,851
Universitätsklinikum Halle (Saale)	01-01 to 31-12-2013	1,061
Krankenhaus Köthen GmbH	01-01 to 31-12-2013	389
Klinik St. Marienstift Magdeburg	01-01 to 31-12-2013	844
Klinikum Magdeburg gGmbH	01-01 to 31-12-2013	1,204
Universitätsklinikum Magdeburg A.ö.R.	01-01 to 31-12-2013	1,273
Carl-von-Basedow-Klinikum Saalekreis GmbH Merseburg	01-01 to 31-12-2013	631
Saale-Unstrut Klinikum Naumburg	01-01 to 31-12-2013	381
Harzklinikum Dorothea Christiane Erxleben GmbH Quedlinburg	01-01 to 31-12-2013	517
Altmark-Klinikum gGmbH Krankenhaus Salzwedel	01-01 to 31-12-2013	393
Helios Klinik Sangerhausen	01-01 to 31-12-2013	754
Ameos Klinikum Schönebeck	01-01 to 31-12-2013	509
Johanniter-Krankenhaus Genthin-Stendal gGmbH	01-01 to 31-12-2013	826
Asklepios Klinik Weißenfels	01-01 to 31-12-2013	476
Harz-Klinikum Wernigerode-Blankenburg GmbH	01-01 to 31-12-2013	654
Evangelisches Krankenhaus Paul Gerhardt Stift Wittenberg	01-01 to 31-12-2013	522
Georgius-Agricola Klinikum Zeitz	01-01 to 31-12-2013	360
Krankenhaus Zerbst GmbH	01-01 to 31-12-2013	203
Total number of births* in Saxony-Anhalt		**16,492**

Home births / Births in a birthing centre resp. infants not born in Saxony-Anhalt	01-01 to 31-12-2013	**119**

Tracked infants, in total	**16,611**

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

In total, **16,492 births** received a screening ID in their maternity clinic in Saxony-Anhalt in 2013. Therefore, these infants could participate in the hearing screening tracking.

Furthermore, **119 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 **110 senders** in 2013.

The following table shows how many newborns received a screening ID per month and how many results were forwarded to the Monitoring of Congenital Malformations per month. Averagely, 1,800 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 results

2013	Infants with screening ID	Number of reportings
January	1,386	1,836
February	1,258	1,737
March	1,293	1,681
April	1,341	1,759
May	1,338	1,750
June	1,393	1,789
July	1,583	2,075
August	1,500	1,909
September	1,535	2,011
October	1,367	1,823
November	1,332	1,724
December	1,285	1,609
total	**16,611**	**21,703**

To carry out the tracking thoroughly, **2,376 letters resp. faxes** were forwarded in 2013 (one up to nine letters per infant). With reference to all infants with screening ID this corresponds to an average of 0.14 letters per infant.

Additionally, the parents and attending physicians of the infants born in 2013 were contacted by telephone. In total **223 calls** were made in connection with the hearing screening tracking (one up to four calls per infant).

Results (date August 2014)

All results that were reported to the hearing screening tracking centre about infants that were born in 2013 are included in the analyses 2013 of the newborn hearing screening:

13,805 infants out of **16,611 infants** with screening ID had an **unsuspicious newborn hearing screening**.
In **2,806 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 2,806 infants showed in **2,249 cases** an **unsuspicious result**. The remaining **557 infants** had again a **suspicious result**.
164 of these 557 infants received a **complete paediatric audiological confirmation diagnostics**.
According to our knowledge, **153 infants did not receive a confirmation diagnostics** and therefore are considered as **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 **nine cases** the **status** is **still pending**, i.e. the examinations were not finished in August 2014 or the tracking process still requires more time.

In **17 cases** the **tracking** was closed from our side **without any result**, because we could not get into connection with the parents.

In total, the **follow up-examinations** of **189 infants** who were born in 2013 could be completed **(confirmations diagnostics)**. Among 164 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 **146 cases**. In **43 cases** a unilateral/bilateral **hearing disorder** was diagnosed and the corresponding therapy was initiated. For instance, **17 infants** received a **hearing aid** (seven times hearing aid bilateral, 10 times hearing aid unilateral).

Parents satisfaction survey about the newborn hearing screening (NHS) in Saxony-Anhalt

The following article deals with a parents satisfaction survey (n = 394) about the newborn hearing screening (NHS) in Saxony-Anhalt that was conducted by a student as part of her bachelor thesis during the time period of November 2013 until April 2014.

Similar to other scientific studies, parents received also in this case initial information about the topic NHS in their maternity clinic. In most cases (31.3%) relevant information was given by a nurse or medical assistant. 69.3% of the parents were satisfied with the amount and content of information given about the NHS. Approximately one sixth (15.7%) were not satisfied with the given information, 13.2% did not remember the information and 1.0% had the impression that the informing was too extensive. 0.8% of the parents did not respond to this question. When analysing the questionnaires it became apparent that only 66.2% of the parents read the NHS related handout of the Federal Joint Committee (G-BA). 19.0% of the persons who did not read the handout indicated in three thirds (76.0%) of the cases that they did not receive this information brochure. Furthermore, 17.7% were not satisfied with the professionalism, 23.9% were dissatisfied with the empathy of the examining personnel and 12.7% found the given information to be incomprehensible. Despite these facts, 97.7% of the parents support the general offer of a NHS and 83.0% have a positive attitude towards NHS in Saxony-Anhalt. In contrast, 12.2% take up a neutral position and 4.3% have a rather negative attitude towards the NHS. Only 11.9% of the parents made improvement suggestions. Nearly half (48.9%) of these suggestions refer to a better NHS informing. Especially more information about screening procedure and test results are required. Another 21.3% of the suggestions refer to the wish for better integration of the parents during hearing screening and 10.6% claim a better qualification of the medical personnel and a separate examination room (4.3%). Overall, the NHS is accepted as a good possibility to test the hearing ability of the child in a simple and painless way. We wish to point to the positive aspect that 21.8% of the parents indicated explicitly that they do not have any improvement suggestions or that an improvement is not necessary.

Further on we analysed how far the parents graduation, the screening result and the age of the infant influenced the answer to the following questions:

- What was your impression about the information you received about the NHS?
- Were you satisfied with the professional competence of examining doctors and nurses?
- Did you have the feeling that the medical personnel responded to your fears and worries in regard to the NHS adequately?
- Were all information you received by the medical personnel about the NHS comprehensible?
- Do you have a positive or negative attitude towards the NHS?

Our analysis did not show a significant relation between the parents satisfaction and their graduation. However, we registered the trend that the dissatisfaction increased with higher school education. There was also no significant difference in regard to the age of the infant.
We did also not register the trend that the higher the age of the infant the higher the satisfaction with comprehensibility and amount of given information. Only the screening result was a decisive factor regarding the evaluation of professional competence of the medical personnel (Fig. 52) and regarding the general attitude towards NHS (Fig. 53).

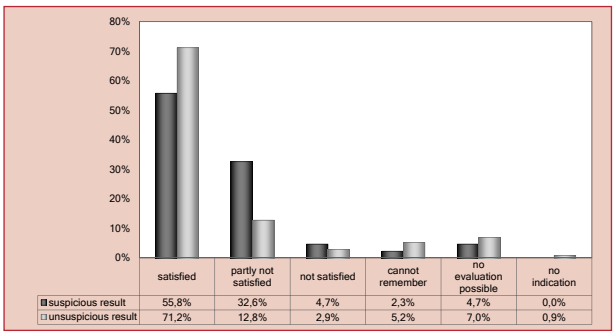


Fig. 52: Satisfaction with professional competence of medical personal - answer in relation to screening result

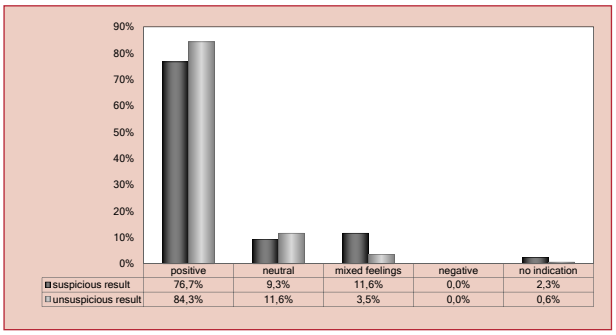


Fig. 53: Attitude towards NHS - answer in relation to screening result

Currently, the ideal point of time for informing about NHS has not been determined. However our study shows that an early point of information is appropriate. It would be therefore desirable to involve medical personal like gynecologists and midwifes more already during pregnancy in the information process about NHS. Future trainings of the screening personal should include theoretical and technical knowledge as well as trainings for a better contact with the parents. Fears and worries could be reduced by improved information policy as well as presence and integration of parents during the screening process. This analysis offers the possibility to improve information giving in Saxony-Anhalt and overall increases parents satisfaction.

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19 Annual Report 2013 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 the realisation of NS in Germany which are defined by the Directive. The report only refers to congenital metabolic and endocrinologic diseases which are defined as "target" diseases by the Directive.

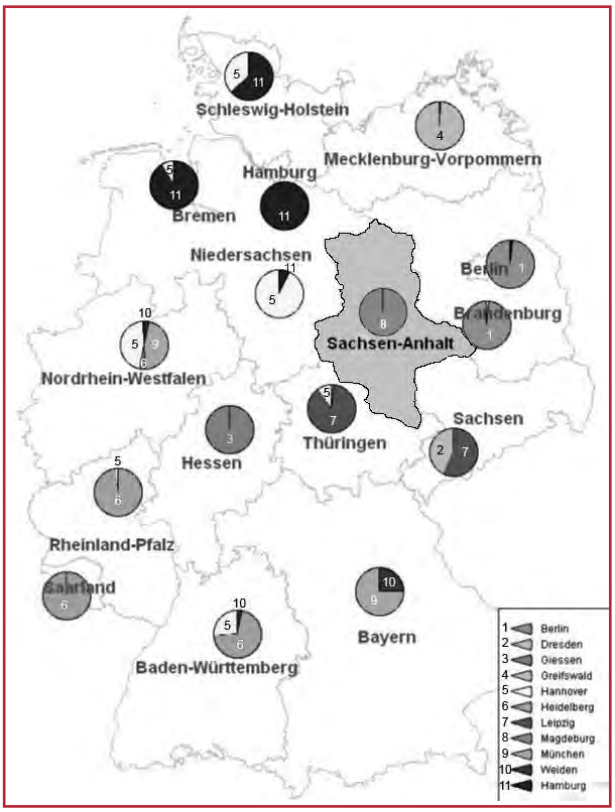

Fig. 1: Screening centres in Saxony-Anhalt

Furthermore, it gives a complete statistical compilation of related screening figures, recall rates and confirmed diagnoses for the current year. Additionally, data about the 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.

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)	no information
Carnitin-Acylcarnitin-Translocase deficiency (CACT)	no information
Glutaric aciduria type I (GA I)	1 : 225,982
Isovaleric acidaemia (IVA)	1 : 56,496
total	**1 : 1,309**

Screening data 2013 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 assure that a screening is offered to every newborn, a tracking for completeness is necessary. This is done for children which are delivered in obstetric clinics by control of the consecutively numbers in the births 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. The test card has to be send to the laboratory, however it differs between the single Federal States how successful this medhod is.

We collected the following registration rates in Saxony-Anhalt in 2013:
According to the Federal Statistical Office 16,797 children were live births in Saxony-Anhalt (according to the residence of the mother).

Tab. 2: Registration rates of first tests

	Number	Difference/Sum
first screening in Magdeburg	16,601	
not resident in Saxony-Anhalt	724	15,877
Screening refused by parents resp. probably not shown up for U2, no response	3	15,890

The discrepancy between the number of live births and screened infants amounts to 907.

Data of the Federal Statistical Office are based on the data of the Statistical Office of Saxony-Anhalt. A corresponding basis form all births (sorted according to maternal residence) from the maternity clinics which are reported to the register offices.

However, the number of mothers with residence in Saxony-Anhalt who delivered their infants in another Federal State is not recorded in our screening statistics when the screening of the infant also took place in another Federal State.
We assume that 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 cards	Number
Received in total	389
Infant deceased / stillbirth	29 / 41
Refusal of early taking	277
Transfer to another clinic	39

No blood sample arrived at our laboratory from 26 kids that were reported on blank cards (without 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

Second screening due to	suspicious first screening	early taking < 36h	preterm births < 32 WOG
requested	37	352	155
arrived at our own laboratory	37	338	146
deceased before control examination	-	3	6
arrived at other laboratory	-	10	3

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, 104 control examinations had to be done in 2013.

Tab. 5: Samples, assured cases, recall-rate 2013, incidence 1992-2013

	First test	Second test*	Recall rate** 2013	Assured cases	Incidence in Saxony-Anhalt 1992-2013
TSH	16,601	521	0.02 %	2	1/3,838
PHE***	16,601	521	0.02 %	3	1/5,491
GALT	16,601	521	0.02 %	-	1/178,468
BIO	16,601	521	0.01 %	-	1/239,601
17OHP	16,601	521	0.10 %	2	1/17,263##
AC, AS (TMS)	16,601	521	0.02 %	2 x MCAD#	1/13,805###

* 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-Anhalt

Process Times

Point of Taking Blood Samples

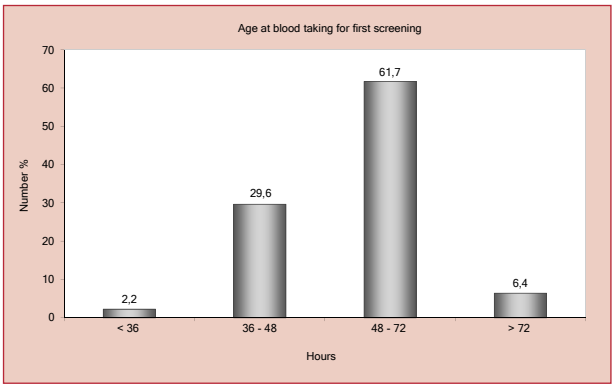

Fig. 2: Age at point of blood taking for first screening

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 91.3% of all cases (2012: 90.7%). At a total number of 8.7% the taking of blood samples took not place within the required period of time (2012: 9.3%). 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 38.1% of all transmittals reached the laboratory more than two days after the blood taking (2012: 39.4%).

Problems with the transmission of blood samples also occurred in 2013.
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.

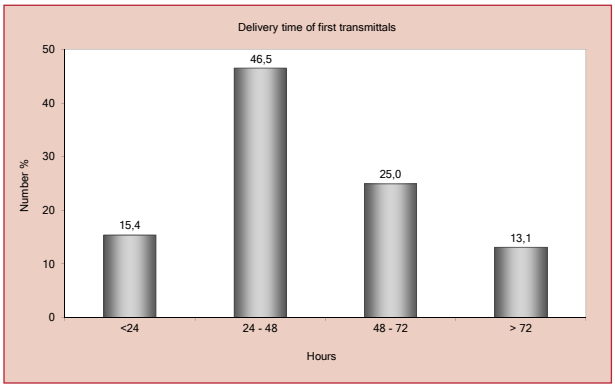

Fig. 3: Delivery time of transmittals

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. 2.5% of the results which were finished after more than 48 hours are the consequence of possible disturbances in the laboratory (maintenance of devices).

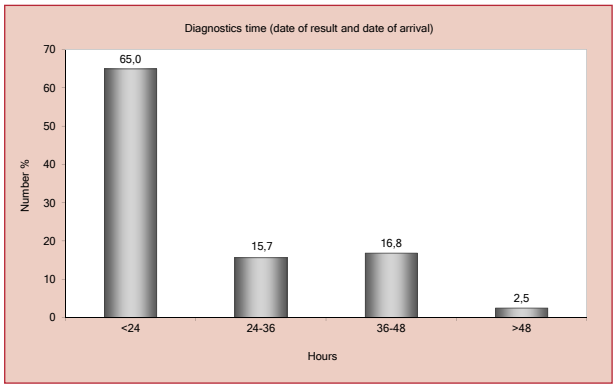

Fig. 4: Diagnostics time (date of result - date of arrival)

The result of first screenings which is shown by figure 4 reflects unfortunately also the diagnostics time of pathological results (in total 104) (figure 5).

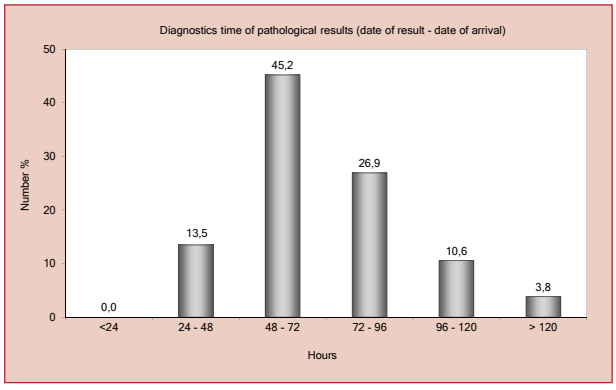

Fig. 5: Diagnostics time of pathological results

The following figure shows the time from oral transmission of 104 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.
Eight 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.

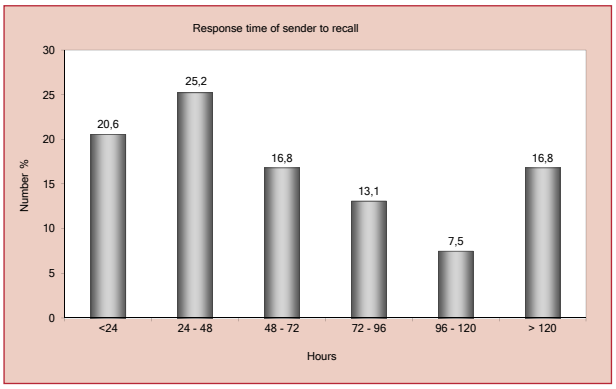

Fig. 6: Response time of sender to recall

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

Therapy Starting at Patients with Positive Screening

Seven patients needed a therapy:

Tab. 6: Diagnosis, confirmation diagnostics and therapy starting

Diagnosis	Confirmation diagnostics	Age at start of therapy
2 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
2 x MCAD deficiency	mutation analytics	7-10 days

Two 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 2013.
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 2013 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 was documented in all cases.

We calculated an incidence of 1 : 1,509 for all objective diseases of the newborn screening in Saxony-Anhalt in 2013.

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 senders, parents and interested people here about the Newborn 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 concerned period of time.