# Annual Report 2018

## Malformation Monitoring Centre Saxony-Anhalt


OTTO VON GUERICKE UNIVERSITÄT MAGDEBURG

SACHSEN-ANHALT
Ministerium für Arbeit, Soziales und Integration

# Annual Report 2018
# of the Federal State of Saxony-Anhalt
# about the frequency of congenital malformations and anomalies as well as chromosomal aberrations


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# Introduction

**Dear readers,**

why does a prospective malformation registration make sense?

The majority of infants in Saxony-Anhalt are born healthy. However, scientific studies show that approximately 4 % of all infants suffer from a relevant structural malformation. In case a child is born with a major malformation or the malformation leads to a premature termination of pregnancy, this means a great stroke of fade. Every single case is tragic and poses special challenges for family members and relatives.

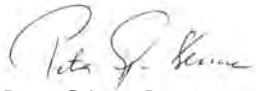
After media reports about congenital hand malformations in North Rhine-Westphalia were published in September of the current year, the prospective malformation registration ad hoc came into the fore. The population reacted partly uncertain. Was there an accidental accumulation of hand malformations in children? At the same time, some media speculated about possible reasons, up to mobile phone radiation. In this connection renowned physicians from the field of prenatal diagnostics and obstetrics warned not to jump to conclusions. We completely share this opinion. And in order to give the all clear signal an epidemiological analysis of registered data about 17,617 pregnancies for the birth cohort 2018 of Saxony-Anhalt was pre-published in September. It shows that in 2018, one reduction malformation of the upper and/or lower limbs was registered at one infant per 1,602 births in Saxony-Anhalt. In addition, a rather decreasing trend was observed in the registration area in comparison to the reference period since 2000.

Main purpose of a prospective malformation registration is the analysis of frequency of relevant malformations. In this process, it is necessary to include not only the live births into the analysis but also all pregnancy outcomes (stillbirths, spontaneous abortion, terminations of pregnancy after prenatal diagnosis) to identify temporal or regional trends. In regard to the temporal trends we focus on the one hand on short-term accumulations of malformations, on the other hand we observe also the long-term trend including well known statistical fluctuations during several years. Together with regional trends, we are in this way able to identify unexpected accumulations, the so-called cluster. Another task is the development of prevention measures and its effectiveness control (e.g. control of folic acid prophylaxis). Aim is the information and education of the population as part of health reporting.

In 2018, 17,410 infants were live births in Saxony-Anhalt and 787,523 infants were live births in Germany. For young parents the first time with their baby is mostly full of joy and a time of new challenges. However, this period of time may be totally different in case the infant is one of those 1000 which are statistically born with a congenital malformation. Professional support is helpful in these cases. Physicians, nurses and midwifes assist parents in such a situation and give advice to parents before and after birth of their child.

Saxony-Anhalt is the only Federal State with a comprehensive, population-based malformation registration in Germany. This is possible thanks to the last but not least excellent interdisciplinary cooperation and committed collaboration of all senders. I would like to thank all those who have supported cooperation within the framework of continuous malformation detection.

Your sincerely



Petra Grimm-Benne
Federal Minister of Labour, Social Affairs and Integration
Saxony-Anhalt

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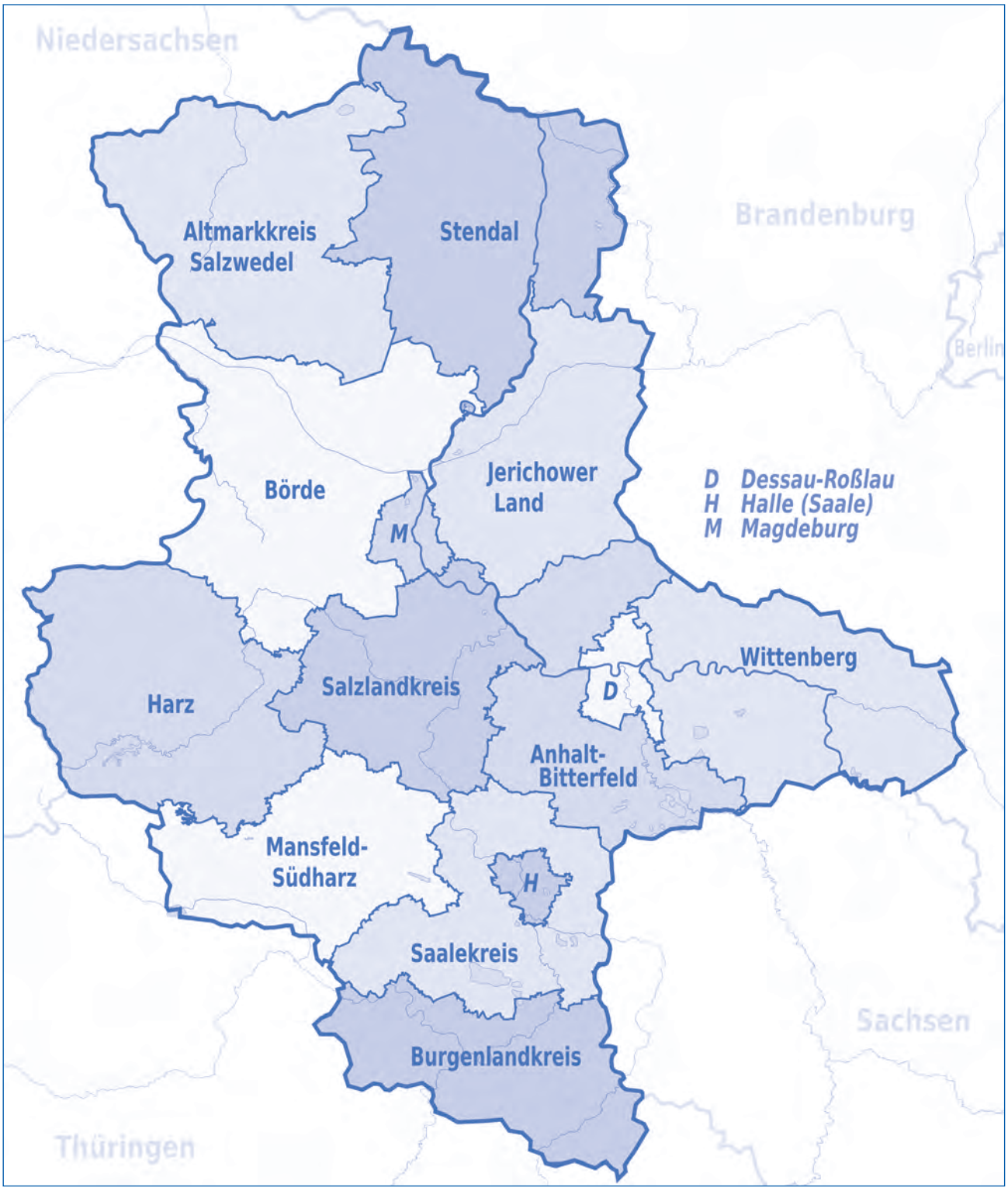
# Abbreviations

| | |
|---|---|
| AABR | automated auditory brainstem response |
| ASD | atrial septal defect |
| AVSD | atrioventricular septal defect |
| ATC | Anatomical-therapeutical-chemical classifikation |
| blt.. | bilateral |
| BMI | Body-Mass-Index |
| BP | basic prevalence |
| CI | confidence intervall |
| CNS | central nervous system |
| dB | decibel |
| DIV | Double Inlet Ventricle |
| DORV | Double Outlet Right Ventricle |
| DUP | dilated uropathy |
| EUROCAT | European Surveillance of Congenital Anomalies |
| ENT | ears, nose, throat |
| FASD | Fetal Alcohol Spectrum Disorder |
| G-BA | Federal Joint Comitee |
| ICBDSR | International Clearinghouse for Birth Defects Surveillance and Research |
| ICSI | Intracytoplasmatic sperm injection |
| IUGR | intrauterine growth restriction |
| LB | live births |
| MCA | multiple congenital anomalies |
| NHS | newborn hearing screening |
| NIPT | non-invasive prenatal test (cellfree DNA analysis) |
| NT | nuchal translucency |
| n. (o.) s. | not (otherwise) specified |
| OR | Odds Ratio |
| P | prevalence |
| PDA | persistent ductus arteriosus |
| PFO | persistent foramen ovale |
| SA | spontaneous abortion |
| SB | stillbirths |
| TEOAE | transitory evoked otoacoustic emissions |
| TOP | termination of pregnancy |
| UCS | urine conducting system |
| VSD | ventricular septual defect |
| WOG | week of gestation |

# 1 Saxony-Anhalt - Registration Area

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https://de.wikipedia.org/wiki/Datei:Saxony-Anhalt,_administrative_divisions_-_de_-_colored.svg#filelinks

# 2 Birth rate 2018

| Districts/major cities | Live births* | Stillbirths* | Spontaneous abortion (> 16 WOG) | Termination of pregnancy for fetal anomaly following pre-natal diagnosis | Total |
|---|---|---|---|---|---|
| Altmarkkreis Salzwedel | 636 | 3 | 2 | 1 | **642** |
| Anhalt-Bitterfeld | 1.105 | 6 | - | 4 | **1.115** |
| Börde | 1.272 | 7 | 2 | 10 | **1.291** |
| Burgenlandkreis | 1.416 | 11 | - | 3 | **1.430** |
| Dessau-Roßlau | 539 | 6 | - | 1 | **546** |
| Halle | 2.549 | 10 | 2 | 13 | **2.574** |
| Harz | 1.519 | 7 | 6 | 13 | **1.545** |
| Jerichower Land | 701 | 1 | - | 4 | **706** |
| Magdeburg | 2.347 | 10 | 6 | 15 | **2.378** |
| Mansfeld-Südharz | 869 | 5 | 3 | 2 | **879** |
| Saalekreis | 1.377 | 6 | 1 | 8 | **1.392** |
| Salzlandkreis | 1.348 | 8 | 1 | 12 | **1.369** |
| Stendal | 810 | 4 | 7 | 1 | **822** |
| Wittenberg | 922 | 3 | - | 2 | **927** |
| Unknown districts. | - | - | 1 | - | **1** |
| Major cities: Dessau-Roßlau, Halle, Magdeburg | 5.435 | 26 | 8 | 29 | **5.498** |
| Districts, in total | 11.975 | 61 | 23 | 60 | **12.118** |
| **Saxony-Anhalt** | **17.410** | **87** | **31** | **89** | **17.617** |

* Source: © Statistisches Landesamt Sachsen-Anhalt, Halle (Saale), 2019

# 3 Participating Institutions of the Region 2018

## 3.1 Maternity units / paedriatric units / paedriatric surgery / paedriatric cardiology (ordered by location)

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

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

- Dipl. Heilpädagogin Schlote, Glindenberg/Magdeburg
- Dr. Perlitz, Fachärztin für Frauenheilkunde und Geburtshilfe, Haldensleben
- AMEOS Klinikum Halberstadt, pränatale Ultraschalldiagnostik
- Krankenhaus St. Elisabeth und St. Barbara Halle, Pränatale Ultraschalldiagnostik: CA Dr. Seeger / OÄ Dr. Radusch
- Universitätsklinikum Halle (Saale), Universitätsklinik für Geburtshilfe und Pränatalmedizin, Pränatale Ultraschalldiagnostik
- Zentrum für Pränatale Medizin Halle: S. Rieße, PD Dr. Hahmann
- Dr. Altus, Fachärztin für Humangenetik, Magdeburg
- Dr. Jaekel, Fachärztin für Kinderchirurgie, Magdeburg
- Dr. Karstedt, Facharzt für Kinder- und Jugendmedizin, Kinderkardiologie, Magdeburg
- Dr. Karsten, Facharzt für Frauenheilkunde und Geburtshilfe, Magdeburg
- Klinikum Magdeburg, Pränatale Ultraschalldiagnostik: OÄ Dr. Schleef
- Universitätsklinkum Magdeburg A.ö.R., Institut für Humangenetik
- Universitätsklinkum Magdeburg A.ö.R., Universitätsfrauenklinik, Pränatale Ultraschalldiagnostik: OÄ Dr. Gerloff
- Universitätsklinkum Magdeburg A.ö.R., Institut für Klinische Chemie, Screeninglabor
- Trackingstelle Neugeborenenhörscreening Sachsen-Anhalt, Magdeburg
- Dr. Welger, Fachärztin für Frauenheilkunde und Geburtshilfe, Magdeburg
- Dipl.-Med. Fiedler und Giesecke, Fachärzte für Orthopädie, Merseburg
- Altmark-Klinikum Krankenhaus Salzwedel, Pränatale Ultraschalldiagnostik: CA Dr. Müller
- Dr. Achtzehn, Facharzt für Kinder- und Jugendmedizin, Dr. Blaschke, Wanzleben
- Harzklinikum Dorothea Christiane Erxleben Klinikum Wernigerode, Pränatale Ultraschalldiagnostik: OÄ Dr. Schulze

## 3.3 Pathological-anatomical institutes (ordered by location)

- Institut für Pathologie Dr. Taege, Dr. Bilkenroth und Dr. Irmscher, Eisleben
- Universitätsklinikum Halle (Saale), Institut für Pathologie
- 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 PD Dr. Schultz, Dr. Lüders, Dr. Hainz, Stendal

# 4 Malformation Registration in Saxony-Anhalt

## 4.1 General Information

Right at the beginning, we would thank you as sender for the excellent interdisciplinary cooperation within the framework of the continuous prospective malformation registration. The annual report 2018 (birth cohort 2018) presents now in proven quality and clearly arranged, data about malformation epidemiology for our Federal State. We wish to prepare you for the special topic in this year about “chromosomal aberrations “(chapter 16.1) with an x-ring chromosome of the here shown chromosome set on the cover photo.

Congenital malformations include all structural or functional anomalies with measurable effect for physical, mental and social well-being of the infant. Initially, the concerned parents and the whole family faces special challenges. But if not only the individual human being as a patient, but the population as a whole comes into the focus, the challenge and health policy significance in relation to congenital malformations becomes visible.

Malformations occur in about 1 of 33 births worldwide (EUROCAT, ICBDSR). This means for Germany (live births 787,523) 23,864 births, in the whole European Union (live births 4.9 Millionen) 150,000 births, which approximately suffer from a malformation. New infections, such as the Zika virus are detected as originator of malformations. Progress in the detection and characterisation of risk and influence factors of malformations can mainly be traced back to epidemiologic studies.

The Monitoring of Congenital Malformations Saxony-Anhalt represents Germany with its collected data at the ICBDSR since 1993 (International Clearinghouse for Birth Defects Surveillance and Research), which is a WHO connected International Association of 42 malformation registers from 38 countries of the world. Furthermore, we are working actively since 1992 in cooperation with the population-based malformation registration centre EUROCAT. The central register of EUROCAT is located since 2015 at the JRC (Joint Research Center), which is the inhouse science service of the European Commission in Ispra, Italy. Since 2018, Dr. med. A. Rißmann is working on both scientific board of directors.

We wish to point out again that this European and worldwide networking and epidemiological surveillance would not be possible without the dedicated collaboration of every single sender!

Saxony-Anhalt is the only Federal State with a regionwide population-based malformation registration in Germany. This state wide malformation registration is only possible thanks to the funding of the Ministry of Employment, Social Affairs and Integration of the Federal State of Saxony-Anhalt. After a personnel change in 2018, we are very pleased that our successful collaboration continues also with Mrs. K. Müller. Additionally, we wish to thank Dr. H. Willer und Mr. M. Schiener for the good collaboration within this interdisciplinary project.

Additionally, we would like to thank our colleagues at the Medical Faculty of the Otto-von-Guericke University for their support and productive collaboration in 2018 within the project of the Monitoring of Congenital Malformations. These persons are Prof. Dr. H.-J. Rothkötter, Dr. J. L. Hülsemann and the commercial director Mrs. Dr. K. Stachel. We are pleased that the support in organisational and administrative issues is continued also under the succession as Medical Director by Prof. Dr. med. H.-J. Heinze in 2019.

## 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. 2018 is considered the year of birth although some terminations of pregnancy after prenatal diagnostics took place at the end of 2017. 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 Statistical Office of Halle provides data of live births and stillbirths annually in the middle of the year and refers to the previous year.
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 a further extension (Adaptation of the Royal College of Paediatrics 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. Infants with only minor malformations or rather norm variations are not evaluated separately since this data is only collected incompletely in the end and not target of permanent observation.

Similar to the previous years we analysed the reported pathological prenatal screening results separately in Chapter 10.
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 2018 in comparison to the last 12 years (2006-2017). Here, a total number of 209,361 births forms basis for the basis prevalence calculation 2006 to 2017.

The graphical presentation of the annual prevalences allows to identify frequent appearances and gives a good overview about rarely appearing indicator births defects. The exact calculation of confidence levels is based on the binominal distribution with a confidence probability of 95%. To discover a certain trend the percentage change of an indicator malformation prevalence is illustrated as well during the publishing time of the Annual Report (Chapter 12.37).
Chapter 13 outlines data regarding genetically caused diseases, chromosomal disorders, sequences, associations, complexes and embryopathies. Chapter 14 contains an analysis of malformation caused terminations of pregnancy.

As usual, the Newborn hearing screening forms part of the Report of the Monitoring of Congenital Malformations Saxony-Anhalt and is outlined in chapter 18.
Chapter 19 presents the Annual Report of the department of newborn screening in Saxony-Anhalt with data regarding congenital metabolic disorders and endocrinopathies.
In Kapitel 19 liegt in gewohnter Weise der Jahresbericht des Zentrums für Neugeborenenscreening in Sachsen-Anhalt mit Daten zu angeborenen Stoffwechselstörungen und Endokrinopathien vor.

## 4.3 Data Quality and Completeness/Reporting Procedure

Meanwhile, the database of the Monitoring of congenital malformations contains data from nearly 40 years which form a valid basis for every annual report and which are used in scientific papers. The data basis is formed by information about data records about births and foetuses from the maternity and paediatric units resp. from institutions of pre- and postnatal diagnostics which are mentioned in chapter 5.2. They are analysed, encoded and stored in the database of the Monitoring of Congenital Malformations.
In 2018, the database grew by 1,767 records, which corresponds to a sample of about 10% of all births in Saxony-Anhalt. Since the last report, the number of data records has increased from 2,020 to 2,254 due to late registrations for the year of birth 2017.

We received 2044 reports for the year 2018, 482 of these from outpatient institutions. In 14.5% of all cases we received information from two or more institutions which improves data quality, especially in case of complex malformations.

For years the monitoring for congenital malformation receives, in relation to the births per hospital, the most reportings from the AMEOS Klinikum Schönebeck, followed by the University hospital Magdeburg and the hospital St. Marienstift Magdeburg. In 2018, the reporting rate of the five highest birth rate hospital was lower than in 2017. Very positive is the continuously high contribution of four outpatient institutions, the center for Prenatal Medicine (Halle), Dr. Altus (specialist for human genetics), Dr. Karstedt (specialist for paediatrics and adolescent medicine, paediatric cardiologist) und Dr. Karsten (specialist for gynaecology and obstetrics). We received more reporting than in the previous year from Dr. Welger (specialist for gynaecology and obstetrics) and Dr. Achtzehn (specialist for children and youth medicine).

Precondition for a high quality statistics is a consistently high data quality with complete indications on the registration sheets and a correct and preferably detailed diagnosis description. This is essential for the classification of malformations risks. Thanks to the esteemed assistance and due to the extraordinary support of all senders we received in 2018 a very good data quality. Decisive information was reported in 2018 nearly completely:
Gender 98,6 %, maternal age 99,3 % and district 99,8 %. The birth weight was not indicated in 63 cases (3.6 %), but only in case of six live births. In more than a quarter of those births (440 births, 27.9 %) the head circumference was missing, which is important in connection with the diagnosis of microcephaly.

We kindly ask again all reporting institutions in Saxony-Anhalt to report carefully and describe every diagnosed malformation as detailed as possible and to mention also additional malformations. Only in case of four foetuses the prenatal diagnosed indicator malformation could not be assigned to a postnatal reporting in 2018. However, when the diagnosis confirmation is missing, the prenatal results are not included into the statistics of the indicator malformations (Chapter 12).

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 in Saxony-Anhalt (according to the information of the Statistical Office Halle)

| | |
|---|---|
| male | 8,925 live births and stillbirths |
| female | 8,572 live births and stillbirths |
| total | 17,497 live births and stillbirths |

**Sex ratio m : f = 1.04**

The Statistical Office Saxony-Anhalt registered in 2018 a total number of 17,410 live births and 87 stillbirths. Compared to a peak value in 2016 (18,092), the number of live births decreased again. In contrast to the low number of stillbirths in 2016 (54), this number increased during the last years. The last time it was as high in 2003 as in 2018.

Similar to the previous years, the sex ratio of live and stillbirths shows an androtropism also in 2018. It lies during the years of the reference period (2006-2017: m : w = 1,06) between 1.03 and 1.09. In 2018, as in most years, the androtropism of stillbirths (2018: m : w = 1.56) is more distinctive than of live births (2018: m : w = 1.04).
The sex ratio of 661 births with major malformations which include life births, stillbirths, medical terminations of pregnancy and spontaneous abortions from the 16th WOG showed with a sex ratio (m : f) of 1.24 also an androtropism. This fact remains similar to the year 2017: m : f = 1.24 and to all previous years.

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

| | |
|---|---|
| male | 356 births |
| female | 288 births |
| unknown | 17 births |
| total | 661 births |

**Sex ratio m : f = 1.24**

### Sex ratio of all births with only minor malformations and anomalies

| | |
|---|---|
| male | 154 births |
| female | 124 births |
| total | 278 births |

**Sex ratio m : f = 1.24**

The percentage of boys with only minor malformations is also higher in comparison to the girls for a total of 278 infants. For 2018, a sex ratio of m : f = 1.24 was registered. The sex ratio for the exclusively small malformations is similar to the sex ratio of the major malformations. We observed an androtropism in 2018.

# 11 Organ System Involvement in Infants and Foetuses with Major Malformations

The monitoring of congenital malformations Saxony-Anhalt registered 661 births with major malformations, thereof 288 births with multiple congenital anomalies in 2018.

Figure 5 presents the proportionate appearance of malformations in seven important organ systems for births with major malformations. Multiple malformations may appear at the same time at one birth, therefore multiple mentions are possible. Data for 2018 is presented separately, those for previous years, starting with 2006, in 3-year groupings. The diagram does not present births with chromosomal aberrations and MCA without exact specification of the malformation. The proportions of concerned organ systems of all births with major malformations remain nearly unchanged in the same order since 2006.

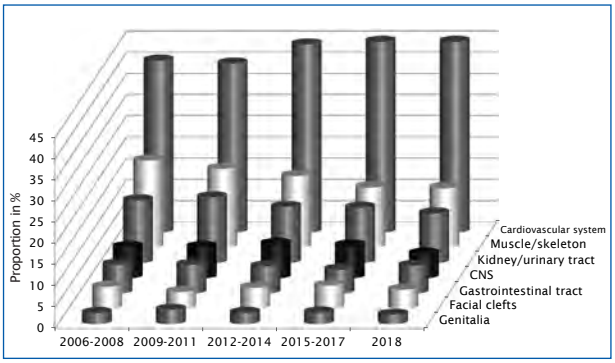



Abb. 5: Organ system involvement in major malformations (grouped)

Similar to the previous years, the organ system which was most frequently affected by a malformation in 2018, was the cardiovascular system. 324 cases were registered, this corresponds to a percentage of 49.02 % of all registered major malformations. Compared to the average of the years 2015-2017 (45.89 %), an increase can be recognised. The standardised good prenatal diagnostics enables a more precise recording of these malformations. This trend remains to be observed.

With 93 reports about malformations of the muscle/skeleton system the percentage decreased in comparison to the average of the years 2015–2017 (14.26 %) in 2018 with 14.07%. Muscular and skeletal malformations appeared proportionately second most frequently in 2018.

Malformations of the kidney/urinary tract were registered in 2017 second most frequently, but in 2018 we registered a value of 11.80 %. Thus, they occupy rank three now. We recognised after a peak value of 15.06 % during 2009-2011 in the present reporting period (2006-2017) a decrease of this value.

On rank four (6.66 %) we detected the malformations of the gastrointestinal tract. After a slightly lower percentage during the years 2015–2017 (5.76 %), the value adjusts in 2018 again to an equal value that was registered during the years 2012–2014 (6.46 %).

Malformations of the CNS appeared most frequently in births with major malformations during the time period of 2012–2014 (8.21 %) and decreased again between 2015–2017 with 7.82%. In 2018, the Monitoring of congenital malformations registered the so far lowest percentage of CNS malformations during the whole reporting period with only 5.90 %.

Since 2006, facial clefts were observed quite consistently around 5 %, as shown by the diagram. In 2018, this figure lies slightly lower (4.54 %).

In relation to all births with major malformations, we registered the malformations of the genitalia with a value of 2.27 % in 2018. During 2015 – 2017 (2.75 %) these malformations were observed with a slightly higher percentage. Compared to the whole registration period, a slight decreased can be recognised.

# The most frequent single diagnoses 2018 (only major malformations)

| | ICD-10 | Diagnosis | Infants/Foetuses 2018 | | Infants/ Foetuses 2006-2017 Prevalence /10,000** |
|---|---|---|---|---|---|
| | | | Number | Prevalence /10,000* | |
| 1. | Q21.1 | Atrial septal defect (inclusive persistent foramen ovale / PFO) | 214 | 121.5 | 90.1 |
| 2. | Q21.0 | Ventricular septal defect | 90 | 51.1 | 46.5 |
| 3. | H90. | Conductive and sensorineural hearing loss | 47 | 26.7 | 20.3 (21.8#) |
| 4. | Q90. | Down syndrome (trisomy 21) | 44 | 25.0 | 18.5 |
| 5. | Q62.3 | Other obstructive defects of renal pelvis and ureter (dilated uropathy grade II-IV/ureterocele) | 33 | 18.7 | 23.9 |
| 6. | Q66.0 | Pes equinovarus congenitus (clubfoot) | 26 | 14.8 | 14.9 |
| 7. | Q69. | Polydactyly (pre- and postaxial) | 18 | 10.2 | 12.2 |
| 8. | Q62.2 | Congenital megaureter | 17 | 9.6 | 8.6 |
| | Q62.1 | Stenosis and atresia | 17 | 9.6 | 8.5 |
| 9. | Q21.2 | Defects of the atrial and ventricular septum (AVSD/ASD I) | 15 | 8.5 | 4.9 |
| 10. | Q37. | Cleft palate with cleft lip | 14 | 7.9 | 10.6 |
| | Q61.4 | Renal dysplasia | 14 | 7.9 | 6.2 |
| 11. | Q63.0 | Accessory kidney/double kidney | 13 | 7.4 | 7.9 |
| | Q91.0 Q91.1 Q91.2 Q91.3 | Edwards syndrome (trisomy 18) | 13 | 7.4 | 3.9 |
| 12. | Q25.1 | Aortic coarctation | 12 | 6.8 | 5.6 |
| | Q03. | Congenital Hydrocephalus (without neural tube defect) | 12 | 6.8 | 5.3 |
| 13. | Q22.1 | Pulmonary valve stenosis | 11 | 6.2 | 7.1 |
| | Q25.4 | Right passing aortic arch | 11 | 6.2 | 2.7 |
| 14. | Q54.1 Q54.2 Q54.2 Q54.8 Q54.9 | Hypospadias (without glandular / coronar) | 10 | 5.7 | 6.7 |
| | Q60.0 | Renal agenesis, unilateral | 10 | 5.7 | 6.1 |
| | Q23.3 | Mitral valve insufficiency | 10 | 5.7 | 5.2 |
| | Q36. | Cleft lip | 10 | 5.7 | 2.5 |
| 15. | Q79.2 | Omphalocele | 9 | 5.1 | 3.4 |
| 16. | Q79.3 | Gastroschisis | 8 | 4.5 | 3.8 |
| 17. | Q65.3 Q65.4 Q65.5 | Subluxation of the hip joint (one sided/ both sided/without indication of side) | 7 | 4.0 | 10.7 |
| | Q23.0 | Aortic valve stenosis / atresia | 7 | 4.0 | 2.4 |

* in reference to 17,617 births

** in reference to 209,361 births

# 2007-2017 (since 2007 data is synchronised with the newborn hearing screening tracking centre)

The above presented table shows the actual prevalence, the basis prevalence and the most frequently registered single diagnoses in Saxony-Anhalt. 17,617 births form the basis of the prevalences of the year 2018 and 209,361 births of the basis prevalences (2006-2017).

Cardiac malformations always appear most frequently. They are reported more frequently and were described more in detailed during the last year. This results currently in higher prevalences than in the last years. The most frequent cardiac malformations ASD (2018: 121.5 pro 10,000 births, 2006-2017: 90.1 per 10,000 births; CI 86.1-94.3) and VSD (2018: 51.1 per 10,000 births, 2006-2017: 46.5 per 10,000 births; CI 43.6-49.5) always appear in the upper two lines. The current annual prevalence lies above the basis prevalence , as well as for defects of the atrium and ventricular septum (2018: 8.5 per 10,000 births, 2006-2017: 4.9 per 10,000 births; CI 4.1-5.9), aortic coarctation (chapter 12.13) (2018: 6.8 per 10,000 births, 2006-2017: 5.6 per 10,000 births; CI 4.7-6.7), right aortic arch (2018: 6.2 per 10,000 births, 2006-2017: 2.7 per 10,000 births; CI 2.0-3.5) and aortic valve stenosis/ atresia (2018: 4.0 per 10,000 births, 2006-2017: 2.4 per 10,000 births; CI 1.8-3.2).

The hearing loss (2.3 per 10,000 births) was registered very rarely in 2006. However, in 2007 Saxony-Anhalt started with the newborn hearing screening and tracking, this had a very positive influence on the detection and reporting rate. In 2018, the hearing loss lies with a prevalence of 26.7 per 10,000 births as third most frequent malformation as expected above the basis prevalence (2006-2017: 20.3 per 10,000 births: CI 18.4-22.3). The prevalence is very high in 2018, also in comparison with the prevalence since invention of the newborn hearing screening (2007-2017: 21.8 per 10,000 births; CI 19.9-24.0).

The Down`s syndrome appeared in 2018 again as fourth most frequent malformation with a value of 25.0 per 10,000 births over the basis prevalence (2006-2017: 18.5 per 10,000 births, CI 16.8-20.5). With a value of 25.4 per 10,000 births we only observed an even higher prevalence in 2013.

The dilated uropathy II.-IV. grade /ureterocele ranges in 2018 with unusually few cases on rank five of the frequency list (18.7 per 10,000 births; 2006-2017: 23.9 per 10,000 births; CI 21.9-26.1). It was observed even fewer during the reporting area only in 2013 with 16.5 per 10,000 births.

The clubfoot ranges on rank 6, within the basis prevalence (2018: 14.8 per 10,000 births;
2006-2017: 14.9 per 10,000 births; CI 13.3-16.6).

The polydactyly can be found as usual on rank seven, however its prevalence is slightly lower than normal (2018: 10.2 per 10,000 births; 2006-2017: 12.2 per 10,000 births; CI 10.8-13.8.). The polydactyly can be divided into the indicator malformation preaxial polydactyly (chapter 12.28) and the postaxial polydactyly. While the prevalence of the less frequent indicator malformation remains below the basis prevalence of both, the postaxial polydactyly does appear in the medium expected range.

Two malformations of the urogenital system, the megaureter and atresia/stenosis of ureter (2018: 9.6 per 10,000 births) can be found on rank eight and are each in the range of the basis prevalence (2006-2017: 8.6 per 10,000 births; CI 7.4-9.9 resp. 8.5 per 10,000 births, CI 7.4-9.8). Also, for the accessory kidney/duplex kidney and unilateral renal agenesis a prevalence (7.4 resp. 5.7 per 10,000 births) within the basis prevalence was calculated for 2018 (2006-2017: 7.9 per 10,000 births; CI 6.8-9.2 resp. 6.1 per 10,000 births; CI 5.1-7.2).

On rank ten, (2018: 7.9 per 10,000 births) the renal dysplasia appeared more frequently than expected (2006-2017: 6.2 per 10,000 births; CI 5.2-7.3). On the same rank, slightly under the basis prevalence (2006-2017:10.6 per 10,000 births; CI 9.3-12.0), the cleft lip with cleft palate can be found. It forms together with the cleft lip the indicator malformation cleft lip with cleft palate (chapter 12.14). The cleft lip which normally does not appear in the list of the most frequent single diagnosis, was registered in 2018 more than ever before during all years of the reporting period (5.7 per 10,000 births; 2006-2017: 2.5 per 10,000 births; CI 1.8-3.3).

The Edwards syndrome (chapter 12.36) ranges on rank eleven on the frequency list in the present year. It was diagnosed more frequently than usual (2018: 7.4 per 10,000 births; 2006-2017: 3.9 per 10,000 births; CI 3.1-4.8).

The indicator malformation hydrocephalus (chapter 12.6) can be found in 2018 with a prevalence of 6.8 per 10,000 births and more frequently than expected (2006-2017: 5.3 per 10,000 births; CI 4.4-6.4), on rank twelve of the malformation frequency list.

Two cardiac malformations appear within the unusual range of the basis prevalence: pulmonary valve stenosis with an actual annual prevalence of 6.2 per 10,000 births (2006-2017: 7.1 per 10,000 births) and mitral valve insufficiency (2018: 5.7 per 10,000 births, 2006-2017: 5.2 per 10,000 births).

With 5.7 per 10,000 births the hypospadias can be found on rank 14 within the most frequent malformations. The prevalence lies within the range of the basis prevalence (2006-2017: 6.7
per 10,000 births). When counting the major malformations glandular and coronary arteries are excluded as light forms, in contrast to the indicator malformation hypospadias (Chapter 12.21), for which the current annual prevalence lies slightly below the expected value.

Two further indicator malformations, omphalocele and gastroschisis (chapter 12.31 and 12.32), occupy the positions 15 and 16. Omphalocele appeared more frequently than normal (2018: 5.1 per 10,000 births; 2006-2017: 3.4 per 10,000 births; CI 2.6-4.3). The gastroschisis resulted in a value within the normal range (2018: 4.5 per 10,000 births).

Subluxation of hip joint is 2018 barely included in the table of the most frequent single malformations. With 4.0 per 10,000 births it appeared less frequently than expected (2006-2017: 10.7 per 10,000 births: CI 9.4-12.1). During the reporting period the minimum value lay at 3.3 (2016) and the maximum value at 18.8 per 10,000 births (2007).

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

## 12.0 Definition

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

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

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

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

**5. Microcephaly:** a congenitally small cranium, defined by an occipito frontal circumference (OFC) 3 standard deviation below the age and sex appropriate distribution curves. [If using a different definition or cut off point (e.g., 2 standard deviations), report but specify criteria]. Exclusive microcephaly associated with anencephaly or encephalocele

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

**36. Edwards yndrome (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 births with malformations born in a certain population with reference to the total number of births 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 (2006-2017) is based on a total number of 209.361 births.

The analysis of the indicator malformations is made with regard to the diagnosis. 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.

The in chapter 12 indicated comparison prevalences which correspond to the basis prevalences of Saxony-Anhalt are based on data of the years 2006-2017 of the Full-Member-Register of European Surveillance of Congenital Anomalies (EUROCAT) from 18 different European countries. Only registers are taken into account into the prevalence calculation of EUROCAT which presented data at EUROCAT for the last five years (2013-2017) or more and for at least five years during the time period of 2006-2017.

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

| | Number | Prevalence /10,000 births | Trend in comp. to basis prevalence |
|---|---|---|---|
| **Major cities:** 3 x Halle | 3 | 5.5 | ↓ |
| **Districts:** 1 x Altmarkkreis Salzwedel 1 x Anhalt-Bitterfeld 1 x Harz 1 x Mansfeld-Südharz 1 x Saalekreis | 5 | 4.1 | ↓ |
| **Saxony-Anhalt** | **8** | **4.5** | ↓ |

| Neural tube defects (2006-2017) | | |
|---|---|---|
| | **Basis prevalence /10,000 births** | **Confidence Interval (CI of 95%) /10,000 births** |
| **Cities** | 9.56 | 7.22 - 12.41 |
| **Districts** | 3.02 | 7.66 - 10.61 |
| **Region** | 9.17 | 7.99 - 10.52 |
| **EUROCAT** | 10.15 | 9.93 - 10.36 |
| | | 3.59 S Portugal* 20.13 Isle de la Reunion (France)** |

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

Neural tube defects include three severe CNS malformations: anencephaly, spina bifida and encephalocele. In 2018, three anencephalies, four spina bifida and one encephalocele were detected in Saxony-Anhalt. The prevalence of spina bifida, which usually represents about 60% of the neural tube defects, is far below the expected value for 2018. For anencephalies with normal frequency and only a small proportion of encephaloceles, this leads to a **prevalence** of **4.5 per 10,000 births** in 2018. This value remains far below the basis prevalence for neural tube defects of 9.17 per 10,000 births (2006- 2017).

Although the basis prevalence of Saxony-Anhalt corresponds to the European prevalence reported by EUROCAT (10.15 per 10,000 births), the current prevalence of Saxony- Anhalt is rather low in comparison with EUROCAT.

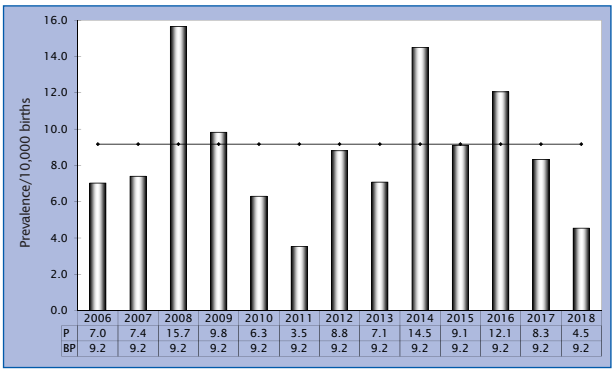



Fig. 6: Development of prevalence/10,000 births with neural tube defects in Saxony-Anhalt since 2006

Only two infants with neural tube defects were live births. The largest percentage is formed by the terminations of pregnancy (2018: 75 %, 2004-2015: 71 % of births with a neural tube defect).

### additional information:

| | |
|---|---|
| **Pregnancy outcome** | 2 x live births<br>6 x termination of pregnancy |
| **Sex** | 2 x male<br>3 x female<br>3 x no indication |
| **Number of isolated malformations/ MCA** | 5 x MCA<br>3 x isolated |

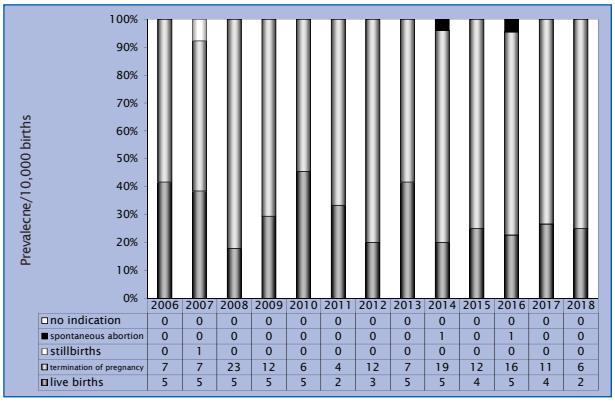



Fig. 7: Pregnancy outcomes of neural tube defects in Saxony-Anhalt since 2006

**In 2018, one neural tube defect per 2,202 births was registered in Saxony-Anhalt.**

Neural tube defects are probably the most investigated congenital malformation within scientific studies. Already in 1995, several German specialist societies published their recommendation regarding primary prevention of folic acid sensitive neural tube defects. A periconceptional intake of 0.4 mg folic acid was recommended to women at child-bearing age. On the other hand, insufficient realisation of this recommendation is urged by recent studies as in case of unplanned pregnancy (first consultation of gynaecologist not before 5 to 7 WOGs) and by risk groups with low socio-economic status or migrants. In a lot of countries outside from Europe it is therefore usual to decrease the neural tube defects rate by enriching basic food like flour with folic acid. New is a controversial discussed statement of September 2017 about the topic safety of folic acid enrichment on population level by the Federal Institute for Risk Assessment (BfR) [1]. This statement concludes that the majority of the German population is well nurtured with folic acid and a nationwide flour fortification is inadvisable at the moment due to possible health risks for older people. In contrast, but at the same point of time (July 2017), the English Scientific Advisory Committee on Nutrition comes to a completely different estimation of the topic. They recommend a mandatory folic acid enrichment [2]. However, which further scientific arguments support this folic acid enrichment and why also the working committee folic acid (Monitoring of Congenital malformations is also member) regards a re-evaluation also as necessary, is outlined in an article of the German magazine “Deutsches Ärzteblatt” [3]. Literature on page 29

# 12.2 Anencephaly (Q00.)

| | Number | Prevalence /10,000 births | Trend in comp. to basis prevalence |
|---|---|---|---|
| **Major cities:** 2 x Halle | 2 | 3.6 | ↗ |
| **Districts:** 1 x Harz | 1 | 0.8 | ↓ |
| **Saxony-Anhalt** | **3** | **1.7** | ↔ |

| Anencephaly (2006-2017) | | |
|---|---|---|
| | **Basis prevalence /10,000 births** | **Confidence Interval (CI of 95%) /10,000 births** |
| **Cities** | 1.71 | 0.82 - 3.14 |
| **Districts** | 2.45 | 1.73 - 3.38 |
| **Region** | 2.24 | 1.65 - 2.98 |
| **EUROCAT** | 3.93 | 3.80 4.07 |
| | | 0.54 Wielkopolska (Poland)* 7.56 Isle de la Reunion (France)** |

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

Three foetuses were affected by anencephaly in 2018 (prevalence of 1.7 per 10,000 births). The current year's prevalence is in the range of the basis prevalence (2006-2017: 2.24 per 10,000 births). Due to the small numbers, the annual prevalences fluctuate in the reporting years between 0.0 and 4.6 per 10,000 births.

Compared to the prevalence provided by EUROCAT (2006-2017), both the current year's value as well as the basis prevalence of Saxony-Anhalt lie far below the European average (3.93 per 10,000 births). However, in other regions of Europe even lower prevalences are indicated
.

The pregnancy was terminated prematurely in all three cases of anencephaly. The abruptions took place between the 11th and 16th week of gestation after diagnosis during prenatal ultrasound in the 11th to 15th week of gestation. Only one infant out of 47 foetuses with anencephaly was live birth between 2006 and 2017.

### additional information:

| | |
|---|---|
| **Pregnancy outcome** | 3 x termination of pregnancy |
| **Sex** | 3 x no indication |
| **Number of isolated malformations/ MCA** | 1 x MCA<br>2 x isolated |

### Malformation combinations (MCA) or superordinated syndromes detected:

- AVSD and other cardiac malformations

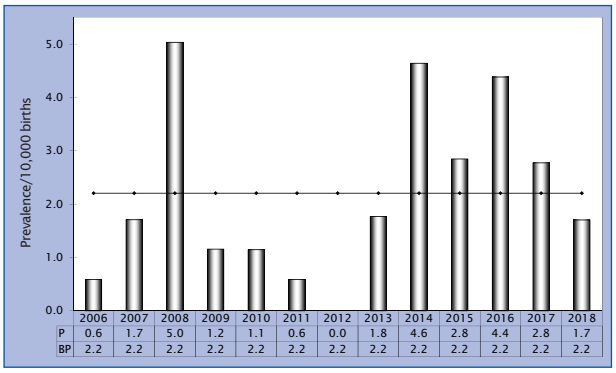



Fig. 8: Development of prevalence/10,000 births with anencephaly in Saxony-Anhalt since 2006

**In 2018, one anencephaly per 5,872 births was registered in Saxony-Anhalt.**

**NOTE**

After a pregnancy was affected by a neural tube defect, women with desire to have further children should be informed about an increased folic acid prophylaxis according to recommendation of the medical expert association (in Germany available preparation with 5 mg folic acid equivalent per day). Women with anti-epileptic medication and chronical malabsorption are recommended to take this higher dose, too.

Literature
1 Bundesinstitut für Risikobewertung (BfR). Nutzen-Risiko-Abwägung einer flächendeckenden Anreicherung von Mehl mit Folsäure. Stellungnahme Nr. 027/2017 des BfR vom 13. Sept. 2017., 2017. https://www.bfr.bund.de/de/bewertung_von_vitaminen_und_mineralstoffen_in_lebensmitteln-54416.html
2 Scientific Advisory Committee on Nutrition (SACN). Update on folic acid, 2017. https: //assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/637111/SACN_Update_on_folic_acid.pdf, 05.11.2018
3 Obeid R, Pietrzik K. Das Veto gegen Folsäure im Mehl sollte überdacht werden. Deutsches Ärzteblatt international 2018; 115(27-28): A1329-A1330 and A4

# 12.3 Spina bifida (Q05.)

| | Number | Prevalence /10,000 births | Trend in comp. to basis prevalence |
|---|---|---|---|
| **Major cities:**<br>1 x Halle | 1 | 1.8 | ↓ |
| **Districts:**<br>1 x Altmarkkreis Salzwedel<br>1 x Anhalt-Bitterfeld<br>1 x Mansfeld-Südharz | 3 | 2.5 | ↓ |
| **Saxony-Anhalt** | **4** | **2.3** | ↓ |

| Spina bifida (2006-2017) | | |
|---|---|---|
| | **Basis prevalence /10,000 births** | **Confidence Interval (CI of 95%) /10,000 births** |
| **Cities** | 5.81 | 4.02 - 8.11 |
| **Districts** | 5.44 | 4.33 - 6.75 |
| **Region** | 5.54 | 4.64 - 6.60 |
| **EUROCAT** | 4.99 | 4.84 - 5.14 |
| | | 1.91 S Portugal*<br>10.04 Isle de la Reunion (France)** |

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

IIn 2018, two infants with spina bifida were live births and two pregnancies of affected foetuses were terminated prematurely. The resulting specific **annual prevalence** of **2.3 per 10,000 births** lies clearly under the basis prevalence (2006-2017: 5.54 per 10,000 births; CI 4.64-5.14). Only in 2011 (1.2 per 10,000 births), even less births with spina bifida were registered. In contrast, a very high value was observed in 2014 (8.1 per 10,000 births).

While the basis prevalence lies slightly above the area of the indicated European prevalence by EUROCAT, the annual prevalence of Saxony-Anhalt is clearly lower in 2018.

### additional information:

| | |
|---|---|
| **Pregnancy outcome** | 2 x live births<br>2 x termination of pregnancy |
| **Sex** | 2 x male<br>2 x female |
| **Number of isolated malformations/ MCA** | 3 x MCA<br>1 x isolated |

The two live births with lumbar spina bifida and Arnold Chiari malformation with lumbosacral spina bifida and hydrocephaly received their diagnosis during prenatal ultrasound screening each in the 21st week of gestation. Two pregnancies were terminated: In case of one foetus the diagnosis of thoracic spina bifida and holoprosencephaly was made in the 20th week of gestation. Another foetus showed a spina bifida, which was diagnosed in the 22nd WOG.

### Malformation combinations (MCA) or superordinated syndromes detected:

- Holoprosencephaly Syndrome
- Arnold Chiari syndrome with syringomyelia, neurogenic bladder
- Corpus callosum agenesis

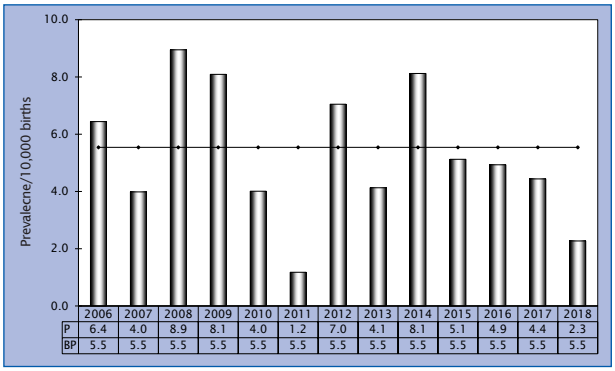



Fig. 9: Development of prevalence/10,000 births with spina bifida in Saxony-Anhalt since 2006

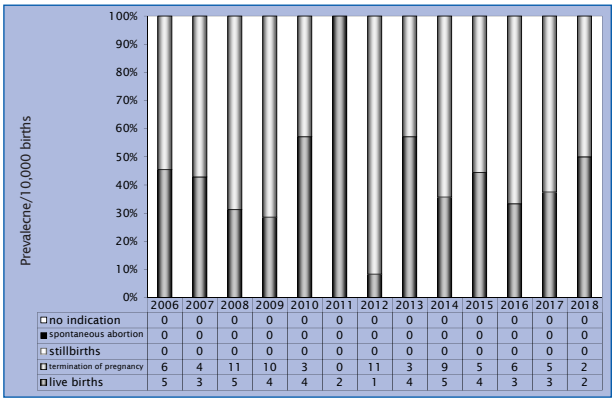



Fig. 10: Pregnancy outcomes of spina bifida in Saxony-Anhalt since 2006

**In 2018, one spina bifida per 4,404 births was registered in Saxony-Anhalt.**

# 12.4 Encephalocele (Q01.)

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

| Encephalocele (2006-2017) | | |
|---|---|---|
| | **Basis prevalence /10,000 births** | **Confidence Interval (CI of 95%) /10,000 births** |
| **Cities** | 2.05 | 1.06 - 3.58 |
| **Districts** | 1.13 | 0.66 - 1.80 |
| **Region** | 1.39 | 0.93 - 1.99 |
| **EUROCAT** | 1.22 | 1.15 - 1.30 |
| | | 0.18 S Portugal*<br>2.76 Mainz (Germany)** |

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

Only one infant with encephalocele was registered in 2018. The resulting **prevalence** of **0.6 per 10,000 births** lies clearly under the basis prevalence (2006-2017: 1.39 per 10,000 births; CI 0.93–1.99). Due to the small numbers this value is not unusual. The number of cases fluctuate between a minimum of zero (2006) and a maximum of five cases (2016) during the reporting period.

The basis prevalence of Saxony-Anhalt is in the European comparison similar to the confidence interval of the prevalence of EUROCAT registers. The current annual prevalence is significantly lower.

## additional information:

| | |
|---|---|
| **Pregnancy outcome** | 1 x termination of pregnancy |
| **Sex** | 1 x female |
| **Number pf islated malformations/ MCA** | 1 x MCA |

The parietal encephalocele was diagnosed together with other above-mentioned serious malformations during prenatal ultrasound in the 20th WOG. After that, a termination of pregnancy took place in the 21th week of gestation.

## Malformation combinations (MCA) or superordinated syndromes detected

- Gastroschisis, blt. cleft lip with cleft palate, midface hypoplasia, intestinal malrotation, missing nipple, thyroid anomaly, lateral ascending eyelid axis, prominent clitoris

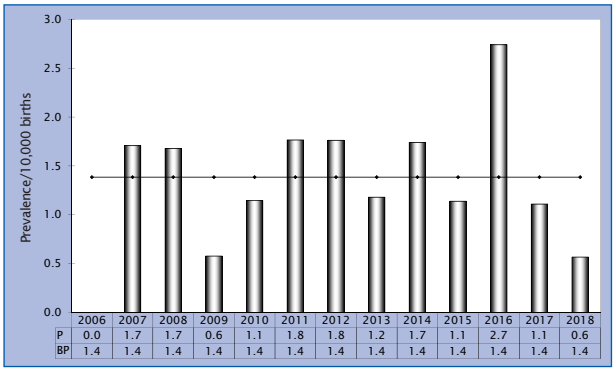



Fig. 11: Development of prevalence/10,000 births with encephalocele in Saxony-Anhalt since 2006

**In 2018, one encephalocele per 17,617 births was registered in Saxony-Anhalt.**

# 12.5 Microcephaly (Q02.)

| | Number | Prevalence /10,000 births | Trend in comp. to basis prevalence |
|---|---|---|---|
| **Major cities:** 1 x Halle | 1 | 1.8 | ↓ |
| **Districts:** 1 x Jerichower Land | 1 | 0.8 | ↓ |
| **Saxony-Anhalt** | **2** | **1.1** | ↓ |

| Microcephaly (2006-2017) | | |
|---|---|---|
| | **Basis prevalence /10,000 births** | **Confidence Interval (CI of 95%) /10,000 births** |
| **Cities** | 4.78 | 3.18 - 6.91 |
| **Districts** | 3.45 | 2.58 - 4.52 |
| **Region** | 3.82 | 3.03 - 4.76 |
| **EUROCAT** | 2.71 | 2.60 - 2.82 |
| | | 0.52 Zagreb (Croatia)* |
| | | 13.41 Auvergne (France)** |

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

In 2018, two infants with microcephaly were born in Saxony-Anhalt. The **prevalence** (2018: **1.1 per 10,000 births**) is in the current year clearly lower after it was registered for six years in the upper range or above the basis prevalence (3.82 per 10,000 births; CI 3.03–4.76). The years 2007 and 2008 showed similar low prevalences. But the ascending trend of the previous year does not continue in 2018.

A comparison with EUROCAT (2.71 per 10,000 births; CI 2.60–2.82) shows, that the value of Saxony-Anhalt is also low in regard to the European prevalences in 2018. However, the basis prevalence of Saxony-Anhalt can be found above the upper confidence limit.

### additional information:

| | |
|---|---|
| **Pregnancy outcome** | 2 x live births |
| **Sex** | 2 x male |
| **Number of isolated malformations/ MCA** | 2 x MCA |

The diagnosis microcephaly is made in newborns by evaluating the measured head circumference depending on the gestational age and maturity. Therefore, the monitoring of congenital malformations uses the international valid scales which were published in the INTERGROWTH-21st-project-study. Only during the first year of life, the diagnosis can be verified by observing an undeveloped brain and skull.

The occurrence of microcephaly is favoured by various factors. In case of one live birth a microcephaly developed after premature Valproic acid exposure. The second birth with microcephaly was a twin early birth.

### Malformation combinations (MCA) or superordinated syndromes detected:

- Embryo fetopathy caused by Valproat with: undescended right testis and not haemodynamically effective PDA at full-term infant, retarded hip left, craniofacial dysmorphia
- blt. DUP II. grade, not haemodynamically effective PDA and PFO at premature infant

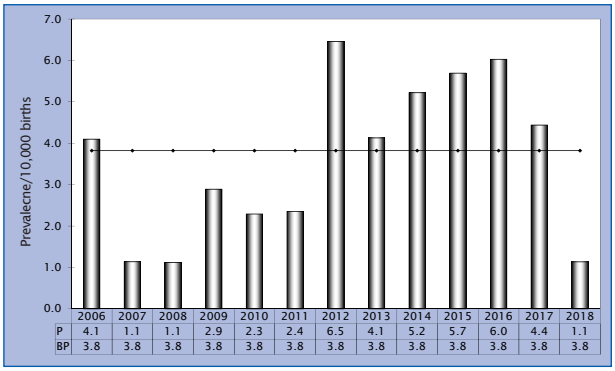



Fig. 12: Development of prevalence/10,000 births with microcephaly in Saxony-Anhalt since 2006

**In 2018, one microcephaly per 8,809 births was registered in Saxony-Anhalt.**

# 12.6 Congenital Hydrocephaly (Q03.)

| | Number | Prevalence /10,000 births | Trend in comp. to basis prevalence |
|---|---|---|---|
| **Major cities:**<br>1 x Halle<br>1 x Magdeburg | 2 | 3.6 | ↘ |
| **Districts:**<br>1 x Burgenlandkreis<br>2 x Börde<br>5 x Harz<br>1 x Salzlandkreis<br>1 x Stendal | 10 | 8.3 | ↑ |
| **Saxony-Anhalt** | **12** | **6.8** | ↗ |

| Congenital hydrocephaly (2006-2017) | | |
|---|---|---|
| | **Basis prevalence /10,000 births** | **Confidence Interval (CI of 95%) /10,000 births** |
| **Cities** | 5.46 | 3.74 - 7.71 |
| **Districts** | 5.24 | 4.15 - 6.53 |
| **Region** | 5.30 | 4.42 - 6.34 |
| **EUROCAT** | 5.62 | 5.47 - 5.79 |
| | | 1.86 S Portugal*<br>11.66 Paris (France)** |

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

12 cases of hydrocephaly were registered in Saxony-Anhalt in 2016. Excluded are such hydrocephalies which appear in connection with a neural tube defect, or occur after a bleeding or infection. After we registered a prevalence maximum value in 2017 (8.3 per 10,000 births), the **prevalence** for 2018 (**6.8 per 10,000 births**) exceeds only slightly the basis prevalence (2006-2017: 5.30 per 10,000 births).

In comparison with EUROCAT-data, we determine that the current years prevalence of Saxony-Anhalt lies above the indicated confidence interval of the years 2006-2017.

### additional information:

| | |
|---|---|
| **Pregnancy outcome** | 4 x live births<br>2 x live births, deceased up to the 7th days of life<br>1 x spontaneous abortion<br>4 x termination of pregnancy<br>1 x stillbirth |
| **Sex** | 6 x male<br>6 x female |
| **Number of isolated malformations/ MCA** | 8 x MCA<br>4 x isoliert |

Six infants with hydrocephalus were live births, two of them were preterm infants with additional severe malformations and died on their first day of life. In case of four terminations of pregnancy the foetuses showed the following additional severe malformations: Thanatophore dysplasia, skeleton and multiple malformations. The hydrocephalus was prenatally diagnosed in case of the spontaneous abortion and stillbirth.

### Malformation combinations (MCA) or superordinated syndromes detected:

- Edwards syndrome with: Omphalocele, clubfoot, macrocephaly
- Down syndrome with: ASD and PFO at preterm infant, septum pellucidum anomalies, blt. lateral ascending lid axis
- left hypoplastic radius, clubhand and hypoplastic ulna, underdeveloped nose, low set ears
- Klinefelter syndrome with: right aortic arch, ASD II, blt. DUP I. grade, ventricle asymmetry
- 2 x thanatophore dysplasia type I (1 x with plumpen, bent tubular bones of legs, bending contractures, clubfoot, short ribs, one missing rib right, thorax hypoplasia)
- VSD, malformed aorta, clubfoot, blt. cerebellar hypoplasia, renal hypoplasia
- Cytomegaly, corpus callosum agenesis, microgyria

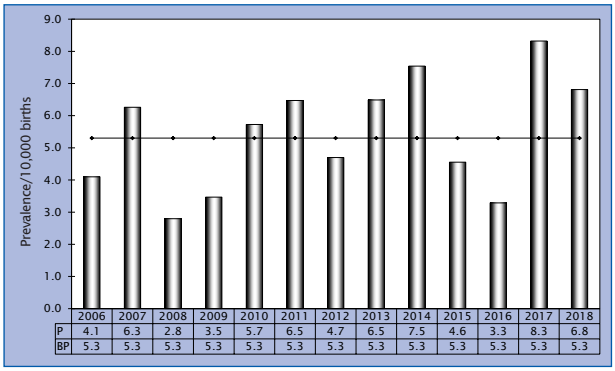



Fig. 13: Development of prevalence/10,000 births with congenital hydrocephalus in Saxony-Anhalt since 2006

**In 2018, one neural tube defect per 1,468 births was registered in Saxony-Anhalt.**

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

| | Number | Prevalence /10,000 births | Trend in comp. to basis prevalence |
|---|---|---|---|
| **Major cities:** 2 x Magdeburg | 2 | 3.6 | ↔ |
| **Districts:** 1 x Mansfeld-Südharz | 1 | 0.8 | ↔ |
| **Saxony-Anhalt** | **3** | **1.7** | ↔ |

| Arhinencephaly/Holoprosencephaly (2006-2017) | | |
|---|---|---|
| | **Basis prevalence /10,000 births** | **Confidence Interval (CI of 95%) /10,000 births** |
| **Cities** | 3.07 | 1.82 - 4.86 |
| **Districts** | 1.19 | 0.71 - 1.89 |
| **Region** | 1.72 | 1.20 - 2.38 |
| **EUROCAT** | 1.53 | 1.44 - 1.61 |
| | | 0.43 Malta*<br>3.17 Isle de la Reunion (France)** |

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

The indicator malformation arhinencephaly/holoprosencephaly appears very rarely with a basis prevalence of 1.72 per 10,000 births (2006-2017). In 2018, we registered three births with holoprosencephaly. For the last time, one case of arhincencephaly was observed in 2012, a cyclopia in 2010. The **prevalence** for 2018 (**1.7 per 10,000 births**) corresponds to the basis prevalence.

The European comparison with EUROCAT-data shows that the prevalence of Saxony-Anhalt lies slightly above the confidence interval of other European register in 2018.

**additional information:**

| | |
|---|---|
| **Pregnancy outcome** | 3 x termination of pregnancy |
| **Sex** | 1 x male<br>1 x female<br>1 x no indication |
| **Number of isolated malformations/ MCA** | 1 x MCA<br>2 x isolated |

In all three cases of holoprosencephaly the diagnosis was made during prenatal ultrasound screening. The pregnancies were terminated between 19 and 21 weeks of gestation.

**Malformation combinations (MCA) or superordinated syndromes detected:**

- thoracic Spina bifida

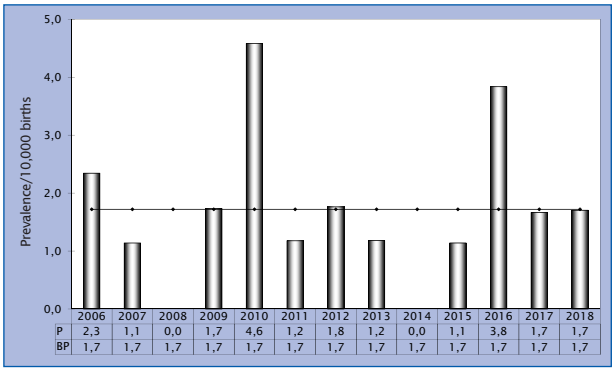



Fig. 14: Development of prevalence/10,000 births with arhinencephaly/holoprosencephaly in Saxony-Anhalt area since 2006

**In 2018, one arhinencephaly/holoprosencephaly per 5,872 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 basis prevalence |
|---|---|---|---|
| **Major cities:** 1 x Halle | 1 | 1.8 | ↔ |
| **Districts** | 0 | 0.0 | ↓ |
| **Saxony-Anhalt** | **1** | **0.6** | ↘ |

| Anophthalmos/Microphthalmos (2006-2017) | | |
|---|---|---|
| | **Basis prevalence /10,000 births** | **Confidence Interval (CI of 95%) /10,000 births** |
| **Cities** | 1.71 | 0.82 - 3.14 |
| **Districts** | 0.66 | 0.32 - 1.22 |
| **Region** | 0.96 | 0.58 - 1.48 |
| **EUROCAT** | 0.95 | 0.89 - 1.02 |
| | | 0.27 East Midlands & South Yorkshire (United Kingdom)* |
| | | 2.70 French West Indies (France)** |

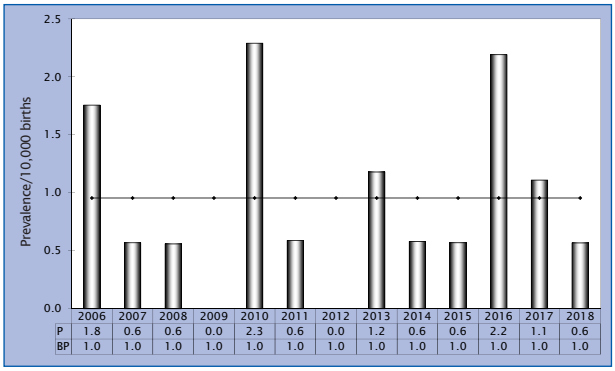
*/** centres with lowest resp. highest prevalence/10,000 births

Anophthalmia/microphthalmia is a very rarely occurring malformation. Only one case was registered in Saxony-Anhalt in 2018 and the **prevalence** therefore lies at **0.57 per 10,000 birth**. Since 2000 a maximum number of four births with anophthalmia/microphthalmia were registered per year. The current annual prevalence lies slightly under the lower limit of the calculated confidence interval of the basis prevalence (0.96 per 10,000 births; CI 0.58–1.48).

The indicated prevalence of EUROCAT for 2006-2017 lies slightly under the prevalence of Saxony-Anhalt. Therefore, the annual prevalence of Saxony-Anhalt can be rated also for 2018 as rather low.

### additional information:

| | |
|---|---|
| **Pregnancy outcome** | 1 x live birth |
| **Sex** | 1 x male |
| **Number of isolated malformations/ MCA** | 1 x isolated |




| | 2006 | 2007 | 2008 | 2009 | 2010 | 2011 | 2012 | 2013 | 2014 | 2015 | 2016 | 2017 | 2018 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| P | 1.8 | 0.6 | 0.6 | 0.0 | 2.3 | 0.6 | 0.0 | 1.2 | 0.6 | 0.6 | 2.2 | 1.1 | 0.6 |
| BP | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |

Fig. 15: Development of prevalence/10,000 births with anophthalmos/microphthalmos in Saxony-Anhalt since 2006

**In 2018, one anophthalmos/microphthalmos per 17,617 births was registered in Saxony-Anhalt.**

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

| | Number | Prevalence /10,000 births | Trend im Vergleich zur Basisprävalenz |
|---|---|---|---|
| **Major cities:** 1 x Halle | 1 | 1.8 | ↘ |
| **Districts:** 1 x Burgenlandkreis 1 x Mansfeld-Südharz 1 x Stendal | 3 | 2.5 | ↔ |
| **Saxony-Anhalt** | **4** | **2.3** | ↔ |

| Microtia/Anotia (2006-2017) | | |
|---|---|---|
| | **Basis prevalence /10,000 births** | **Confidence Interval (CI of 95%) /10,000 births** |
| **Cities** | 3.76 | 2.35 - 5.69 |
| **Districts** | 2.19 | 1.51 - 3.07 |
| **Region** | 2.63 | 1.98 - 3.42 |
| **EUROCAT** | no information | no information |

The indicator malformation microtia/anotia shows a basis prevalence of 2.63 per 10,000 births (2006-2017). The **annual prevalence** of **2.3 per 10,000 births** lies therefore within the normal range in 2018.

EUROCAT does not provide any data about the appearance of this indicator malformation. However, EUROCAT provides a prevalence of 0.26 per 10,000 births (2006-2017; CI 0.23–0.29) for the much rarer malformation anotia. The prevalence of anotia in Saxonia-Anhalt lies at 0.38 per 10,000 births for the time period of 2006-2017. In 2018, one case of anotia and a maximum of two cases of anotia were registered between 2006 and 2017.

### additional information:

| | |
|---|---|
| **Pregnancy outcome** | 2 x live births<br>1 x live birth, deceased after 7 days of life<br>1 x termination of pregnancy |
| **Sex** | 2 x male<br>2 x female |
| **Number of isolated malformations/ MCA** | 4 x MCA |

In all four cases, the microtia/anotia did not appear as isolated malformation. Three times the right ear was concerned, one time the left ear. Two infants suffered from a missing ear canal and a sound conduction disorder was diagnosed.

### Malformation combinations (MCA) or superordinated syndromes detected:

- VACTERL-association with: oesophagobronchial fistula (Vogt IV), laryngocele, tracheo-oesophageal cleft, VSD, atresia of the right osseous ear canal, butterfly vortex (3rd cervical vertebral body), scoliosis, missing 12th rip
- Goldenhar syndrome with: sound conduction disorder at atresia of right osseous ear canal (Altmann type III), preauricular tag right, face asymmetry, mandibular micrognathia
- Gastroschisis, hydranencephaly, dents in the skull, low set ears, prominent forehead, hypertelorism, varus deformity of the right foot
- sound conduction disorder at atresia of the right osseous ear canal type C (Weedra)

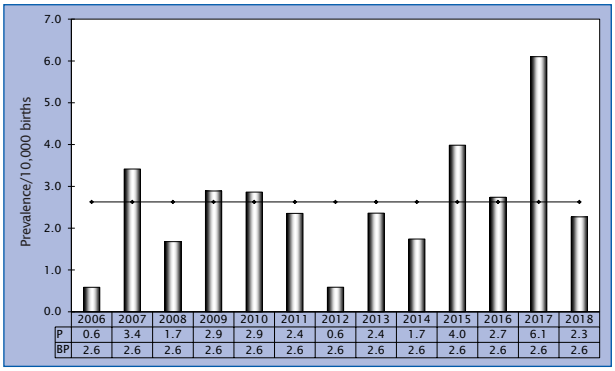



Fig. 16: Development of prevalence/10,000 births with microtia/anotia in Saxony-Anhalt since 2006

**In 2018, one microtia / anotia per 4,404 births was registered in Saxony-Anhalt.**

# 12.10 Tetralogy of Fallot (Q21.3)

| | Number | Prevalence /10,000 births | Trend in comp. to basis prevalence |
|---|---|---|---|
| **Major cities** | 0 | 0.0 | ↓ |
| **Districts:**<br>1 x Altmarkkreis Salzwedel<br>1 x Harz<br>1 x Salzlandkreis | 3 | 2.5 | ↘ |
| **Saxony-Anhalt** | **3** | **1.7** | ↓ |

| Tetralogy of Fallot (2006-2017) | | |
|---|---|---|
| | **Basis prevalence /10,000 births** | **Confidence Interval (CI of 95%) /10,000 births** |
| **Cities** | 3.76 | 2.35 - 5.69 |
| **Districts** | 3.38 | 2.52 - 4.45 |
| **Region** | 3.49 | 2.73 - 4.38 |
| **EUROCAT** | 3.44 | 3.32 - 3.57 |
| | | 1.92 Wielkopolska (Poland)*<br>5.62 Malta** |

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

Four cardiac malformations form the complex malformation Tetralogy of Fallot: Pulmonary stenosis, VSD, malformed aorta and right heart hypertrophy. The indicator malformation was registered in three cases in Saxony-Anhalt in 2018. The resulting **prevalence** lies at **1.7 per 10,000 births** in 2018. In relation to the basis prevalence of 3.49 per 10,000 births (2006-2017; CI 2.73-4.38) this is a very low value. We registered even lower prevalences only in 2007 and 2011.

The comparison of the annual prevalence with the European average prevalence shows for Saxony-Anhalt a value far below the confidence interval and even below the smallest average prevalence from the malformation register Wielkopolska (Poland). The confidence interval of the basis prevalence of Saxony-Anhalt however exceeds the interval of the average prevalence of the European register.

One live birth had another malformation of the skeletal system beside its cardiac malformation.

### additional information:

| | |
|---|---|
| **Pregnancy outcome** | 2 x live births<br>1 x termination of pregnancy |
| **Sex** | 1 x male<br>2 x female |
| **Anzahl isolierter Fehlbildungen/ MCA** | 2 x MCA<br>1 x isolated |

### Malformation combinations (MCA) or superordinated syndromes detected:

- CATCH 22 with: wedge vertebra formation
- PFO at full term infant

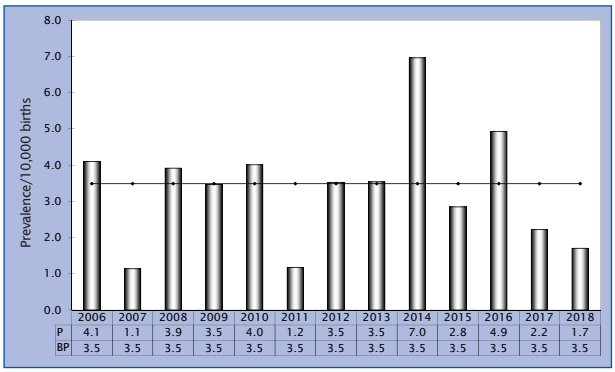



Fig. 17: Development of prevalence/10,000 births with Tetralogy of Fallot in Saxony-Anhalt since 2006

**In 2018, one Tetralogy of Fallot per 5,872 births was registered in Saxony-Anhalt.**

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

| | Number | Prevalence /10,000 births | Trend in comp. to basis prevalence |
|---|---|---|---|
| **Major cities:**<br>1 x Halle<br>2 x Magdeburg | 3 | 5.5 | ↔ |
| **Districts:**<br>1 x Anhalt-Bitterfeld<br>1 x Börde<br>1 x Mansfeld-Südharz<br>2 x Saalekreis | 5 | 4.1 | ↔ |
| **Saxony-Anhalt** | **8** | **4.5** | ↔ |

| Transposition of the great vessels (2006-2017) | | |
|---|---|---|
| | **Basis prevalence /10,000 births** | **Confidence Interval (CI of 95%) /10,000 births** |
| **Cities** | 4.95 | 3.32 - 7.11 |
| **Districts** | 4.11 | 3.15 - 5.27 |
| **Region** | 4.35 | 3.50 - 5.34 |
| **EUROCAT (Q20.3)** | 3.50 | 3.38 - 3.63 |
| | | 1.59 S Portugal*<br>5.04 Basque Country (Spain)** |

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

A transposition of great vessels (TGA) means that the from the heart outgoing vessels are switched. As indicator malformation it includes the rarely appearing double outlet ventricle (DORV).

The transposition of great vessels was observed in Saxony-Anhalt with a **prevalence** of **4.5 per 10,000 births** in 2018. The value can be found in the middle range for the time period of 2006-2017 of the calculated basis prevalence (4.35 per 10,000 births).

EUROCAT mentions a prevalence for TGA of 3.50 per 10,000 births. The prevalence of Saxony-Anhalt lies above the confidence interval for 2018. However, the calculated prevalences are only comparable with limitations as the prevalence of EUROCAT does not include the above mentioned malformation DORV.

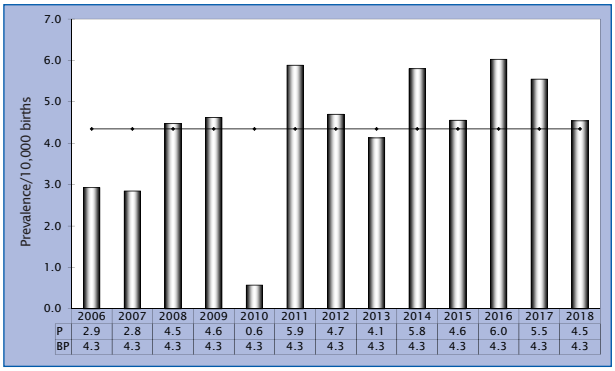
### additional information:

| | |
|---|---|
| **Pregnancy outcome** | 5 x live births<br>1 x live birth, deceased after 7 days of life<br>2 x termination of pregnancy |
| **Sex** | 6 x male<br>2 x female |
| **Number of isolated malformations/ MCA** | 8 x MCA |

All births were full term infants. One part was already transferred prematurely into a cardiac center. One infant deceased under one year. In case of two births, which received prenatally the diagnosis of DORV and other severe malformations, the pregnancies were terminated between 21 resp. 23 weeks of gestations.

### Malformation combinations (MCA) or superordinated syndromes detected:

- coarctation of aorta, VSD, PFO at full term infant, hydrocele left
- preductal aortic valve stenosis, VSD, ASD II, stenosis of arteria pulmonalis at full term infant
- oesophageal atresia, AVSD, pulmonary valve atresia, supracardiac pulmonary vein malformation
- tricuspid atresia, common ventricle, AVSD, partial misjunction of pulmonary veins, pulmonary valve atresia, dextrocardia, varus deformities of both feet
- Pulmonary valve stenosis, thymus agenesis
- VSD, pulmonary valve stenosis
- VSD, stenosis of arteria pulmonalis at full term infant
- VSD, PFO at full term infant




| | 2006 | 2007 | 2008 | 2009 | 2010 | 2011 | 2012 | 2013 | 2014 | 2015 | 2016 | 2017 | 2018 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| P | 2.9 | 2.8 | 4.5 | 4.6 | 0.6 | 5.9 | 4.7 | 4.1 | 5.8 | 4.6 | 6.0 | 5.5 | 4.5 |
| BP | 4.3 | 4.3 | 4.3 | 4.3 | 4.3 | 4.3 | 4.3 | 4.3 | 4.3 | 4.3 | 4.3 | 4.3 | 4.3 |

Fig. 18: Development of prevalence/10,000 births with transposition of the great vessels in Saxony-Anhalt since 2006

**In 2018, one transposition of great vessels per 2,202 births was registered in Saxony-Anhalt.**

# 12.12 Hypoplastic Left Heart Syndrome (Q23.4)

| | Number | Prevalence /10,000 births | Trend in comp. to basis prevalence |
|---|---|---|---|
| **Major cities** | 0 | 0.0 | ↓ |
| **Districts:**<br>1 x Jerichower Land<br>1 x Saalekreis<br>1 x Salzlandkreis | 3 | 2.5 | ↔ |
| **Saxony-Anhalt** | **3** | **1.7** | ↓ |

| Hypoplastic Left Heart Syndrome (2006-2017) | | |
|---|---|---|
| | Basis prevalence /10,000 births | Confidence Interval (CI of 95%) /10,000 births |
| **Cities** | 3.07 | 1.82 - 4.86 |
| **Districts** | 2.59 | 1.84 - 3.54 |
| **Region** | 2.72 | 2.06 - 3.53 |
| **EUROCAT** | 2.77 | 2.66 - 2.88 |
| | | 0.59 S Portugal*<br>4.09 Styria (Austria)** |

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

The **annual prevalence** of the left heart hypoplastic syndrome in Saxony-Anhalt (2018: **1.7 per 10,000 births**) lies clearly under the calculated basis prevalence for the time period of 2006-
2017 (2.72 per 10,000 births; CI 2.06–3.53). Seen as a whole, the values for hypoplastic left heart syndrome vary strongly over the years. The prevalence minimum was at 0.6 (201) and the maximum at 5.0 per 10,000 births (2008) during the reporting period.

A comparison with the European wide calculated prevalence shows that the prevalence of Saxony-Anhalt for 2018 lies also under the European basis prevalence. Both prevalences for the years 2006-2017 overlap each other, whereby a narrower range is given for the confidence interval of European prevalence due to the larger numbers.

### additional information:

| | |
|---|---|
| **Pregnancy outcome** | 1 x live birth, deceased before 7 days of life<br>2 x termination of pregnancy |
| **Sex** | 2 x male<br>1 x no indication |
| **Number of isolated malformations/ MCA** | 1 x MCA<br>2 x isolated |

The live birth was transferred already prenatally to a cardiac center and operated on the first day of life, however the infant deceased shortly after.

### Malformation combinations (MCA) or superordinated syndromes detected:

- total, supradiaphragmatic pulmonary vein misjunction, hydrothorax right

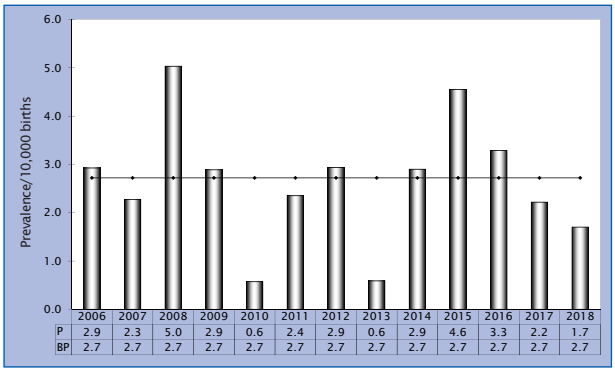



Fig. 19: Development of prevalence/10,000 births with hypoplastic left heart syndrome in Saxony-Anhalt since 2006

**In 2018, one child with a hypoplastic left heart syndrome per 5,872 births was registered in Saxony-Anhalt.**

# 12.13 Coarctation of Aorta (Q25.1)

| | Number | Prevalence /10,000 births | Trend in comp. to basis prevalence |
|---|---|---|---|
| **Major cities:**<br>1 x Halle<br>2 x Magdeburg | 3 | 5.5 | ↔ |
| **Districts:**<br>1 x Anhalt-Bitterfeld<br>1 x Burgenlandkreis<br>2 x Harz<br>2 x Jerichower Land<br>1 x Saalekreis<br>1 x Salzlandkreis<br>1 x Wittenberg | 9 | 7.4 | ↗ |
| **Saxony-Anhalt** | **12** | **6.8** | ↗ |

| Coarctation of aorta (2006-2017) | | |
|---|---|---|
| | **Basis prevalence /10,000 births** | **Confidence Interval (CI of 95%) /10,000 births** |
| **Cities** | 4.95 | 3.32 - 7.11 |
| **Districts** | 5.90 | 4.74 - 7.26 |
| **Region** | 5.64 | 4.73 - 6.70 |
| **EUROCAT** | 3.86 | 3.73 - 3.99 |
| | | 1.29 Zagreb (Croatia)*<br>6.46 Styria (Austria)** |

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

12 cases of haemodynamically relevant coarctation of aorta were registered in 2018. The **prevalencce** lies at **6.8 per 10,000 birth**, this value lies slightly over the confidence interval of the basis prevalence (2006-2017: 5.64 per 10,000 births; CI 4.73-6.70).

The current annual prevalence and the basis prevalence of Saxony-Anhalt lie above the upper confidence limit of the prevalence that is indicated by EUROCAT for the years 2006-2017 (3.86 per 10,000 births). Also, the maximum value of the European prevalences during this time period registered in Styria (Austria) is exceeded.

A coarctation of aorta is difficult to detect during prenatal ultrasound screening. However, in five cases it was already diagnosed prenatally. In case of another four infants, further complex or similar severe cardiac malformations were prenatally found. Nine infants were operated in a cardiac center, four were transferred to the cardiac center already prenatally. One birth with coarctation of aorta and TGA died under one year of live. All cases of coarctation of aorta appeared in connection with a syndrome or in combination with other cardiac malformations or other organs. None of the cases occurred isolated.

## additional information:

| | |
|---|---|
| **Pregnancy outcome** | 11 x live births<br>1 x live birth, deceased after 7 days of life |
| **Sex** | 6 x male<br>6 x female |
| **Number of isolated malformations/ MCA** | 12 x MCA |

## Malformation combinations (MCA) or superordinated syndromes detected:

- Down syndrome with: clubfoot, retarded hip
- DORV and dextro transposition of aorta, VSD, PFO at full tern infant, hydrocele left
- Dextro transposition of aorta, VSD, ASD II, stenosis of arteria pulmonalis at full term infant
- Hypoplastic right heart syndrome, VSD, ASD II
- Mitral valve stenosis, aortic valve stenosis, PFO at full term infant, vascular ring through the abnormal right subclavicular artery
- Hypoplastic aorta, bicuspid aortic valve, aortic valve stenosis, ASD II, mitral valve insufficiency, aortic valve insufficiency
- Hypoplastic aorta, bicuspid aortic valve, malposition of heart, VSD, PFO at full term infant, persistent left vena cava superior
- Hypoplastic aorta, bicuspid aortic valve, VSD, ASD II, left pelvic kidney
- Hypoplastic aorta, bicuspid aortic valve, VSD, PFO at full term infant
- VSD, ASD II, persistent left vena cava
- Mitral valve stenosis
- ASD II

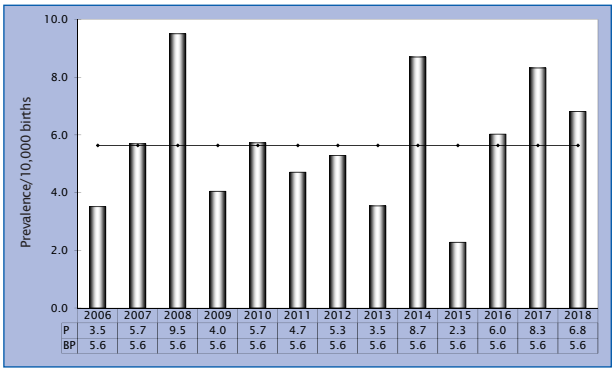



Fig. 20: Development of prevalence/10,000 births with coarctation of aorta in Saxony-Anhalt since 2006

**In 2018, one coarctation of aorta per 1,468 births was registered in Saxony-Anhalt.**

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

| | Number | Prevalence /10,000 births | Trend in comp. to basis prevalence |
|---|---|---|---|
| **Major cities:**<br>2 x Dessau-Roßlau<br>4 x Halle<br>1 x Magdeburg | 7 | 12.7 | ↔ |
| **Districts:**<br>2 x Altmarkkreis Salzwedel<br>1 x Burgenlandkreis<br>2 x Börde<br>3 x Harz<br>4 x Saalekreis<br>3 x Salzlandkreis<br>1 x Stendal<br>1 x Wittenberg | 17 | 14.0 | ↔ |
| **Saxony-Anhalt** | **24** | **13.6** | ↔ |

| Cleft Lip With or Without Cleft Palate (2006-2017) | | |
|---|---|---|
| | Basis prevalence /10,000 births | Confidence Interval (CI of 95%) /10,000 births |
| **Cities** | 13.15 | 10.38 - 16.43 |
| **Districts** | 13.00 | 11.34 - 14.89 |
| **Region** | 13.04 | 11.61 - 14.64 |
| **EUROCAT** | 8.76 | 8.57 - 8.97 |
| | | 3.32 S Portugal*<br>13.40 N Netherlands** |

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

Similar to the last two years, we observed also in 2018 a **prevalence** of **13.6 per 10,000 births** with 24 registered cases. This corresponds to an annual prevalence within the confidence area of the basis prevalence (13.4 per 10,000 births).

The prevalence of Saxony-Anhalt for 2018 as well as the basis prevalence (2006-2017) are rather high in comparison with the European values. The prevalence of Saxony-Anhalt can be found always within the upper third of the EUROCAT-registers. Our current value lies above the highest indicated prevalence (2006-2017) by the register in the North Netherlands.

### additional malformation:

| | |
|---|---|
| **Pregnancy outcome** | 20 x live births<br>4 x termination of pregnancy |
| **Sex** | 18 x male<br>6 x female |
| **Number of isolated malformations/ MCA** | 8 x MCA<br>16 x isolated |

In three termination of pregnancies, cleft lip with or without cleft palate were diagnosed as symptom of chromosomal aberration. One other foetus had a complex malformations syndrome with neural tube defects.

The indicator malformation cleft lip with or without cleft palate can be divided into four groups, depending on the characteristics: The cleft lip with cleft palate was registered in 12 cases in 2018, the upper lip cleft in 10 cases and the lips jaw cleft in two cases. A lip palate cleft was not observed in 2018.
As usual (2006-2017: 73.8 %), the cleft formation occurred mainly unilateral in 2018 (16 x, thereof: 12 x left, 4 x right). A bilateral cleft lip and cleft lip with cleft palate was registered in 2018 in 7 cases. In one case we received no information about the laterality. During the time period of 2006 to 2017 we registered more than twice as many cleft lips and cleft lips with cleft palate on the left side (114) than on the right side (50).
Mainly, the indicator malformation cleft lip and cleft lip with cleft palate (2018: 16 x) does not appear in combination with additional malformations. In three cases, the hearing ability was severely affected.

### Malformation combinations (MCA) or superordinated syndromes detected:

- Edwards syndrome with: Omphalocele, diaphragmatic hernia, cardiac malformation
- Edwards syndrome with: anal atresia, overlapping fingers, low set ears
- Triploidy with: low set ears, lateral descending lid axis
- CHARGE-association, VSD, blt. combined high grade sound conducting and perception disorder
- parietal encephalocele, gastroschisis, midface hypoplasia, intestinal malrotation, missing nipples, malformation of thyroid, lateral ascending lid axis, prominent clitoris
- glandular hypospadias, undescended left testis at full term infant, blt. preauricular tag, hydrocele
- sound conduction disorder left, retarded hip right, dysplastic and low set ears
- blt. sound conduction disorder

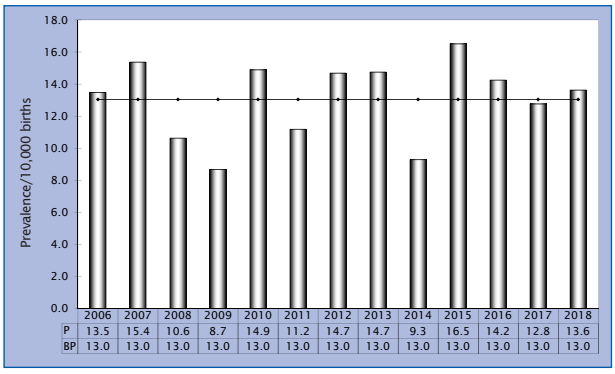



Fig. 21: Development of prevalence/10,000 births with cleft lip with or without cleft palate in Saxony-Anhalt since 2006

**In 2018, one child with cleft lip with or without cleft palate per 734 births was registered in Saxony-Anhalt.**

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

| | Number | Prevalence /10,000 births | Trend in comp. to basis prevalence |
|---|---|---|---|
| **Major cities:**<br>3 x Halle<br>2 x Magdeburg | 5 | 9.1 | ↔ |
| **Dictricts:**<br>1 x Burgenlandkreis<br>1 x Saalekreis<br>1 x Wittenberg | 3 | 2.5 | ↓ |
| **Saxony-Anhalt** | **8** | **4.5** | ↓ |

| Cleft palate (2006-2017) | | |
|---|---|---|
| | Basis prevalence /10,000 births | Confidence Interval (CI of 95%) /10,000 births |
| **Cities** | 7.00 | 5.02 - 9.50 |
| **Districts** | 7.49 | 6.26 - 8.95 |
| **Region** | 7.36 | 6.31 - 8.57 |
| **EUROCAT** | 5.96 | 5.76 - 6.12 |
| | | 3.28 French West Indies (France)*<br>12.53 Malta** |

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

Eight cases of cleft palate were registered in Saxony-Anhalt in 2018. The resulting **prevalence** of **4.5 per 10,000 births** is very low in comparison to the basis prevalence (2006-2017: 6.31-8.57 per 10,000 births). We expected five or six cases more. A similar low prevalence was only registered in 2008 (4.5 per 10,000 births).

A comparison of the confidence interval of the basis prevalence of Saxony-Anhalt with the confidence interval of the total prevalence of EUROCAT (2006-2017) shows for Saxony-Anhalt a noticeable higher range. The current year`s prevalence lies under the middle range of the European values.

One infant with cleft palate and velocardiofacial syndrome was stillbirth after 36 weeks of gestation. In most cases the indicator malformation cleft palate appeared in combination with other malformations in 2018.

### additional information:

| | |
|---|---|
| **Pregnancy outcome** | 7 x live births<br>1 x stillbirth |
| **Sex** | 3 x male<br>5 x female |
| **Number of isolated malformations/ MCA** | 7 x MCA<br>1 x isolated |

### Malformation combinations (MCA) or superordinated syndromes detected:

- velocardiofacial syndrome (CATCH 22) with: mandibular cleft, VSD, thymus agenesis
- 2 x Robin sequence with: mandibular micro- and retrognathia (1 x blt. hypoplastic humerus, radius and ulna, 1 x left plexus cyst and retarded hip)
- Robin sequence with: mandibular retrognathia
- pulmonary valve stenosis, VSD, oscillation failure of skull (sagittal suture, very prominent forehead), craniofacial dysmorphia, hypertelorism, sacral dimples, four finger grooves
- VSD, PFO at full term infant, retarded hip right
- hip luxation right, retarded hip left

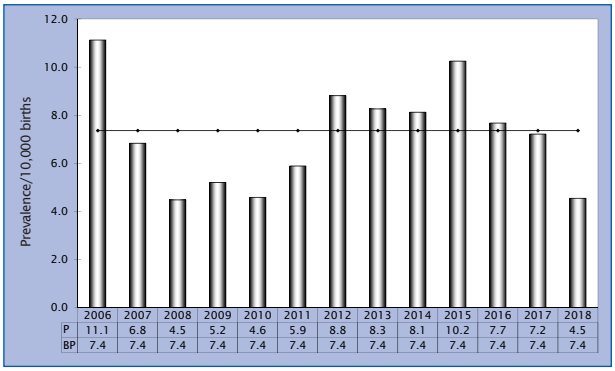



Fig. 22: Development of prevalence/10,000 births with cleft palate in Saxony-Anhalt since 2006

**In 2018, one child with cleft palate per 2,202 births was registered in Saxony-Anhalt.**

# 12.16 Choanal Atresia (Q30.0)

| | Number | Prevalence /10,000 births | Trend in comp. to basis prevalence |
|---|---|---|---|
| **Major cities:** 1 x Dessau-Roßlau | 1 | 1.8 | ↔ |
| **Districts** | 0 | 0.0 | ↓ |
| **Saxony-Anhalt** | **1** | **0.6** | ↘ |

| Choanal atresia (2006-2017) | | |
|---|---|---|
| | **Basis prevalence /10,000 births** | **Confidence Interval (CI of 95%) /10,000 births** |
| **Cities** | 0.85 | 0.28 - 1.99 |
| **Districts** | 0.99 | 0.56 - 1.64 |
| **Region** | 0.96 | 0.58 - 1.48 |
| **EUROCAT** | 0.89 | 0.83 - 0.96 |
| | | 0.05 S Portugal*<br>1.79 Isle de la Reunion (France)** |

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

A basis prevalence (2006-2017) of 0.96 per 10,000 births was calculated for the indicator malformation choanal atresia. The choanal atresia appears now and again and was not even registered in some years.
In 2018, it was only diagnosed in one case, this corresponds to a **prevalence** of **0.57 per 10,000 births**. The prevalence only slightly falls below the confidence interval of the basis prevalence. The small numbers of appearance cause significant fluctuations of the prevalence so that the current value is often not to find within the standard range. A maximum value with seven cases (4.1 per 10,000 births) was registered in 2014.

The European registers indicate a prevalence of 0.89 per 10,000 births. The confidence interval of Saxony-Anhalt corresponds to the confidence interval of EUROCAT. However, due to the smaller numbers it covers a much larger security range. The current value of Saxony-Anhalt lies slightly under the European total prevalence.

## additional information:

| | |
|---|---|
| **Pregnancy outcome** | 1 x live birth |
| **Sex** | 1 x female |
| **Number of isolated malformations/ MCA** | 1 x MCA |

## Malformation combinations (MCA) or superordinated syndromes detected:

- blt. cleft lip with cleft palate and combined profound sound conduction and perception disorder, VSD

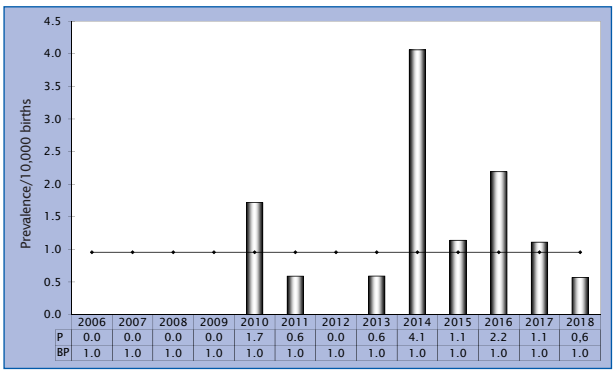



Fig. 23: Development of prevalence/10,000 births with choanal atresia in Saxony-Anhalt since 2006

**In 2018, one child with a choanal atresia per 17,617 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 basis prevalence |
|---|---|---|---|
| **Major cities:**<br>1 x Dessau-Roßlau<br>2 x Halle<br>2 x Magdeburg | 5 | 9.1 | ↑ |
| **Districts:**<br>1 x Börde<br>1 x Stendal | 2 | 1.7 | ↔ |
| **Saxony-Anhalt** | **7** | **4.0** | ↑ |

| Oesophageal atresia/stenosis/fistula (2006-2017) | | |
|---|---|---|
| | **Basis prevalence /10,000 births** | **Confidence Interval (CI of 95%) /10,000 births** |
| **Cities** | 3.42 | 2.09 - 5.27 |
| **Districts** | 2.32 | 1.62 - 3.23 |
| **Region** | 2.63 | 1.98 - 3.42 |
| **EUROCAT (Q39.0-Q39.1)** | 2.55 | 2.45 - 2.66 |
| | | 0.74 SE Ireland*<br>3.79 Mainz (Germany)** |

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

The indicator prevalence oesophageal atresia/stenosis/fistula occurred with a **prevalence** of **4.0 per 10,000 births** as frequently as in the previous year (3.9 per 10,000 births). The current prevalence lies clearly above the upper confidence limit of the basis prevalence (2006-2017: 2.63 per 10,000 births; CI 1.98-3.42). However, the maximum value of 2012 (4.7 per 10,000 births) was not reached again.

In comparison to the indicated prevalence by EUROCAT (2.55 per 10,000 births) we recognize that the annual prevalence lies also above the European middle value. Thereby, the confidence interval of the basis prevalence of Saxony-Anhalt overlaps the interval of the European total prevalence.

### additional information:

| | |
|---|---|
| **Pregnancy outcome** | 4 x live births<br>1 x live birth, deceased after 7 days of life<br>2 x termination of pregnancy |
| **Sex** | 4 x male<br>3 x female |
| **Number of isolated malformations/ MCA** | 6 x MCA<br>1 x isolated |

In four cases, an oesophageal atresia with fistula between trachea and the lower oesophagus pocket (Typ Vogt III b) was diagnosed and in one case an oesophagobronchial fistula (Vogt IV). Another foetus suffered from an oesophagotracheal fistula. Both terminations of pregnancy took place between 23 and 24 weeks of gestations.

### Malformation combinations (MCA) or superordinated syndromes detected:

- VACTERL association with: blt. missing radius, renal agenesis right, dextrocardia
- VACTERL association with: missing right ear cup, laryngocele, tracheal and oesophageal cleft, VSD, atresia of the right osseous ear canal, butterfly vertebra (cervical vertebral body 3), scoliosis, missing 12th rib
- DORV, AVSD, pulmonary valve atresia, supracardial pulmonary vein misjunction
- Feingold syndrome type 1 with: agenesis of the left kidney, duodenal atresia, presternal haemangioma (1,5 cm), septum pellucidum anomalies
- duodenal stenosis, pancreas anulare, ASD at preterm infant, blt. dysontogenic ovarian cysts, multiple small haemangioma
- PFO at full term infant, retarded hip right, DUP I. grade left, plexus cyst

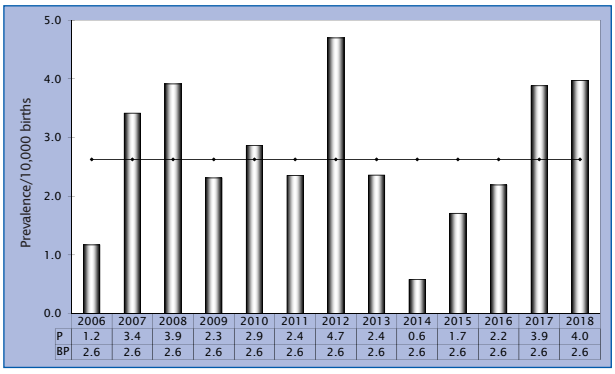



Fig. 24: Development of prevalence/10,000 births with oesophageal atresia/stenosis/fistula in Saxony-Anhalt since 2006

**In 2018, one child with a choanal atresia per 2,517 births was registered in Saxony-Anhalt.**

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

| | Number | Prevalence /10,000 births | Trend in comp. to basis prevalence |
|---|---|---|---|
| **Major cities:**<br>1 x Halle | 1 | 1.8 | ↔ |
| **Districts:**<br>1 x Altmarkkreis Salzwedel<br>1 x Stendal | 2 | 1.7 | ↔ |
| **Saxony-Anhalt** | **3** | **1.7** | ↔ |

| Small Intestinal atresia/stenosis (2006-2017) | | |
|---|---|---|
| | **Basis prevalence /10,000 births** | **Confidence Interval (CI of 95%) /10,000 births** |
| **Cities** | 0.85 | 0.28 - 1.99 |
| **Districts** | 2.12 | 1.45 - 3.00 |
| **Region** | 1.77 | 1.24 - 3.44 |
| **EUROCAT (Q41.1-Q41.8)** | 0.96 | 0.90 - 1.03 |
| | | 0.22 Wielkopolska (Poland)*<br>1.61 Styria (Austria)** |

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

With a basis prevalence of 1.77 per 10,000 births, the indicator malformation of small intestinal atresia/stenosis is one of the rarely appearing malformations. The numbers fluctuate in Saxony-Anhalt per year between zero (2014) and seven (2012). Three cases appeared in 2018, which leads to a current **prevalence** of **1.7 per 10,000 births**. This prevalence lies in the middle range of the confidence interval of the basis prevalence.

We observed the small intestinal atresia / stenosis European-wide with a prevalence (2006-2017) of 0.96 per 10,000 births. Basis prevalence as well as annual prevalence of Saxony-Anhalt can therefore be rated as rather high. The annual prevalence of 2018 exceeds also the maximum value of the register Styria (Austria).

### additional information:

| | |
|---|---|
| **Pregnancy outcome** | 3 x live births |
| **Sex** | 2 x male<br>1 x female |
| **Number of isolated malformations/ MCA** | 1 x MCA<br>2 x isolated |

All three infants were live births. The atresia affected in each case a part of the small intestine, once the jejunum and twice the ileum.

### Malformation combinations (MCA) or superordinated syndromes detected:

- Gastroschisis, microcolon

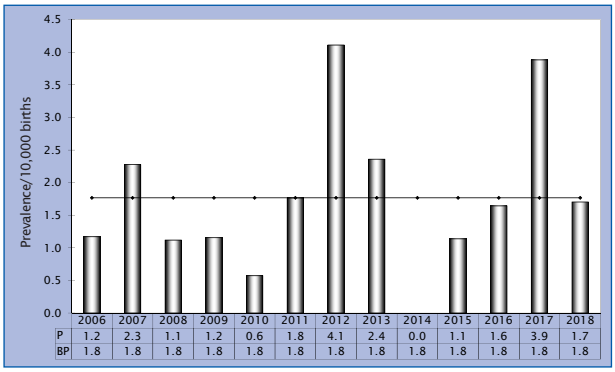



Fig. 25: Development of prevalence/10.000 births with small intestinal atresia/stenosis in Saxony-Anhalt since 2006

**In 2018, one child with cleft lip with or without cleft palate per 5,872 births was registered in Saxony-Anhalt.**

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

| | Number | Prevalence /10,000 births | Trends in comp. to basis prevalence |
|---|---|---|---|
| **Major cities:**<br>1 x Halle<br>1 x Magdeburg | 2 | 3.6 | ↔ |
| **Districts:**<br>1 x Anhalt-Bitterfeld | 1 | 0.8 | ↓ |
| **Saxony-Anhalt** | **3** | **1.7** | ↓ |

| Anorectal atresia/stenosis (2006-2017) | | |
|---|---|---|
| | **Basis prevalence /10,000 births** | **Confidence Interval (CI of 95%) /10,000 births** |
| **Cities** | 4.61 | 3.04 - 6.71 |
| **Districts** | 5.17 | 4.09 - 6.45 |
| **Region** | 5.02 | 4.16 - 6.03 |
| **EUROCAT** | 3.27 | 3.15 - 3.39 |
| | | 1.54 S Portugal*<br>6.35 Styria (Austria)** |

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

We calculated a **prevalence** of the indicator malformation anorectal atresia/ stenosis of **1.7 per 10,000 births** in 2018. It lies clearly under the calculated basis prevalence (2006-2017: 5.02 per 10,000 births; CI 4.16-6.03). During the time period of 2007 and 2010 we observed this malformation more frequently than ever before. Since 2011 and in the current year, the annual prevalences can be found within or under the range of the basis prevalence. All annual prevalences from 2006 to 2010 are in the upper range of the basis prevalence. Therefore, we recognize in total for the reporting period (2006-2018) a significant descending trend with a percentage change of -11.01 % (CI -15.03 % up to -5.58 %) (chapter 12.37). But this has its cause in the peak of 2007-2009 with a registered extreme value of 8.4 per 10,000 births (2008).

The current annual prevalence of Saxony-Anhalt lies clearly under the indicated prevalence of EUROCAT of 3.27 per 10,000 births. On the other hand, the confidence interval of the basis prevalence can be found far above the total prevalence of the European registers (2006-2017).

Malformations of anorectal atresia / stenosis are difficult to detect during prenatal ultrasound screening and are therefore often diagnosed not before birth. In all three cases, complex malformation syndromes and sequences were detected prenatally. Terminations of pregnancy took place after 17 resp. 18 weeks of gestations.
In two cases an anal atresia and in one case a rectal atresia without fistula was diagnosed.

### additional information:

| | |
|---|---|
| **Pregnancy outcome** | 3 x tremination of pregnancy |
| **Sex** | 2 x male<br>1 x female |
| **Number of isolated malformations/ MCA** | 3 x MCA |

### Malformation combinations (MCA) or superordinated syndromes detected:

- Sirenomelia with: persisted left vena cava superior, VSD, hypoplastic aorta, multicystic dysplastic kidneys, horseshoe kidney, agenesis of uterus, vagina and urethra, intestinal malrotation, pancreas anulare, turricephaly, blt. hypoplastic lung at incompletely lobed lung left, hypertelorism, epicanthus internus, low set ears
- Edwards syndrome with: cleft lip right, overlapping fingers, low set ears
- Potter sequence (functionless cystic dysplastic kidneys), blt. lateral ascending lid axis, low set ears

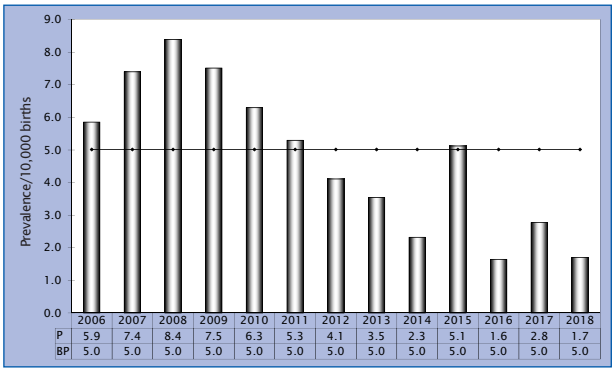



Fig. 26: Development of prevalence/10,000 births with anorectal atresia/stenosis in Saxony-Anhalt since 2006

**In 2018, one anorectal atresia/ stenosis per 5,872 births was registered in Saxony-Anhalt.**

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

| | Number | Prevalence /10,000 births | Trend in comp. to basis prevalence |
|---|---|---|---|
| **Major cities:**<br>7 x Halle<br>3 x Magdeburg | 10 | 18.2 | ↑ |
| **Districts:**<br>4 x Anhalt-Bitterfeld<br>1 x Burgenlandkreis<br>1 x Saalekreis | 6 | 5.0 | ↘ |
| **Sachsen-Anhalt** | **16** | **9.1** | ↗ |

| Undescended testis (2006-2017) | | |
|---|---|---|
| | Basis prevalence /10,000 births | Confidence Interval (CI of 95%) /10,000 births |
| **Cities** | 11.44 | 8.87 - 14.52 |
| **Districts** | 6.43 | 5.22 - 7.85 |
| **Region** | 7.83 | 6.75 - 9.08 |
| **EUROCAT** | no information | no information |

16 full term boys were affected by the malformation undescended testis in Saxony-Anhalt in 2018. With a **prevalence** of **9.1 per 10,000 births** (resp. 17.3 per 10,000 boys), the prevalence lies slightly above the basis prevalence (7.83 per 10,000 births; CI 6.75-9.08). In connection with the trend analysis it should be noted that (chapter 12.37) undescended testis is diagnosed mostly during the first year of life. Therefore, the central registration in inpatient facilities is incomplete.

Due to the registration problem the registered values are not comparable. Furthermore, EUROCAT does not provide any frequency information for the indicator malformation undescended testis.

## additional information:

| | |
|---|---|
| **Pregnancy outcome** | 15 x live births<br>1 x live birth, deceased after 7 days of life |
| **Sex** | 16 x male |
| **Number of isolated malformations/ MCA** | 8 x MCA<br>8 x isolated |

All 16 boys with undescended testis were live births. One infant with additional multiple malformations died after three months. In two cases with no additional malformations, both testicles had not moved into the scrotum. The malformation appeared 14 times unilateral, thereof one time left and 11 times right sided. In two cases the laterality was not indicated.

## Malformation combinations (MCA) or superordinated syndromes detected:

- Edwards syndrome with: VSD, ASD II, single cerebral cyst, blt. exophthalmia, sound perception disorder, DUP III. grade, hernia inguinalis and syndactyly type 1 (II./III. toes), malformed gall bladder, not hemodynamical effective PDA at full term infant, Varus deformity of both feet, hypertelorism, low set ears, mandibular micrognathia, large nipple separation, blt. overlapping fingers
- Down syndrome with: AVSD
- Embryo fetopathy caused by valproate with: microcephaly, not hemodynamical effective PDA at full term infant, retarded hip left, craniofacial dysmorphia
- blt. cleft lip with cleft palate, blt. preauricular tag, glandular hypospadias, hydrocele
- penile hypospadias
- DUP III. grade right, DUP II. grade left, blt. ureteral outlet stenosis
- Testicular torsion left, blt. hernia inguinalis at full term infant
- hypertrophic pylorus stenosis, haemangioma

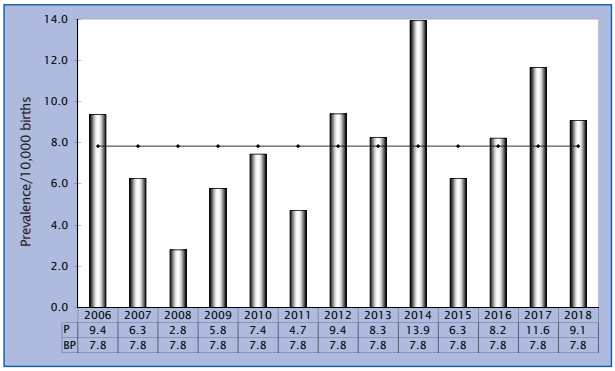



Fig. 27: Development of prevalence/10,000 births with undescended testis in Saxony-Anhalt since 2006

**In 2018, one child with undescended testis per 1,101 births (561 boys) was registered in Saxony-Anhalt.**

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

| | Number | Prevalence /10,000 births | Trend in comp. to basis prevalence |
|---|---|---|---|
| **Major cities:**<br>1 x Dessau-Roßlau<br>1 x Halle<br>9 x Magdeburg | 11 | 20.0 | ↘ |
| **Districts:**<br>3 x Altmarkkreis Salzwedel<br>4 x Anhalt-Bitterfeld<br>1 x Burgenlandkreis<br>2 x Börde<br>4 x Harz<br>2 x Mansfeld-Südharz<br>3 x Saalekreis<br>4 x Salzlandkreis<br>1 x Stendal | 24 | 19.8 | ↔ |
| **Saxony-Anhalt** | **35** | **19.9** | ↘ |

| Hypospadias (2006-2017) | | |
|---|---|---|
| | Basis prevalence /10,000 births | Confidence Interval (CI of 95%) /10,000 births |
| **Cities** | 24.93 | 21.29 - 29.15 |
| **Districts** | 21.35 | 19.19 - 23.75 |
| **Region** | 22.35 | 20.45 - 24.43 |
| **EUROCAT** | 17.71 | 17.43 - 17.99 |
| | | 7.13 S Portugal*<br>30.69 Mainz (Germany)** |

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

Hypospadias has a basis prevalence (2006-2017) of 22.35 per 10,000 births (43.54 per 10,000 boys). With this value it is the most frequently observed malformation of the 36 existing indicator malformations. In 2018, hypospadias was diagnosed in 35 cases. The resulting **prevalence** of **19.9 per 10,000 births** (39.0 per 10,000 boys) shows that hypospadias appeared less frequently than expected in the current year.
Glandular hypospadias is registered, similar to maldescensus testis, only during the first year of life. We therefore assume an under registration in the outpatient institutions. Severe forms of hypospadias were registered in Saxony-Anhalt for the years 2006-2017 with a frequency of 6.7 per 10,000 births (chapter 11).

The prevalence 2018 as well as the basis prevalence of Saxony-Anhalt can be found above the from EUROCAT determined European prevalence of 17.71 per 10,000 births. However, this prevlances do not reach the maximum value of the second German malformation register in Mainz, that indicated a value of 30.69 per 10,000 births.

34 of the affected boys were live births. In one case a penile hypospadias was diagnosed prenatally in combination with complex malformations and a chromosomal aberration. This pregnancy was terminated after 23 weeks of gestations.

## additional information:

| | |
|---|---|
| **Pregnancy outcome** | 34 x live births<br>1 x termination of pregnancy |
| **Sex** | 35 x male |
| **Number of isolated malformations/ MCA** | 8 x MCA<br>27 x isolated |

In 27 cases no further malformations were registered, of these three severe forms: two penile and one penoscrotal hypospadias. In total, 24 glandular hypospadias, one hypospadias coronaria, five penile, two penoscrotal and one perineal hypospadias were registered. The correct specification was not indicated in two cases.

## Malformation combinations (MCA) or superordinated syndromes detected:

- blt. cleft lip with cleft palate and preauricular tag, undescended left testis at full term infant, hydrocele
- deletion of the autosomes, malformation of pulmonary valve
- VSD, ASD II
- ASD and not haemodynamically effective PDA at full term infant
- ectopic and hypoplastic left kidney, scrotum bipartum
- undescended right testis at full term infant
- lateral penile curvature
- meatus stenosis

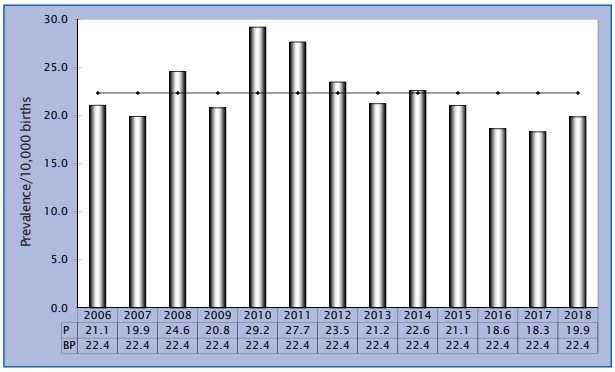



Fig. 28: Development of prevalence/10,000 births with hypospadias in Saxony-Anhalt since 2006

**In 2018, one hypospadias per 503 births (256 boys) was registered in Saxony-Anhalt.**

# 12.22 Epispadias (Q64.0)

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

| Epispadias (2006-2017) | | |
|---|---|---|
| | Basis prevalence /10,000 births | Confidence Interval (CI of 95%) /10,000 births |
| Cities | 0.51 | 0.11 - 1.50 |
| Districts | 0.27 | 0.07 - 0.68 |
| Region | 0.33 | 0.13 - 0.69 |
| EUROCAT | no information | no information |

Epispadias occurs very rarely. With a basis prevalence of 0.33 per 10,000 births it is only registered in a few cases. The basis prevalence of epispadias lies for boys at 0.65 per 10,000 boys. In eight out of 13 years of the reporting period, including the current year 2018, no cases have been recorded.

EUROCAT does not provide any European data for comparison of the prevalences of epispadias.

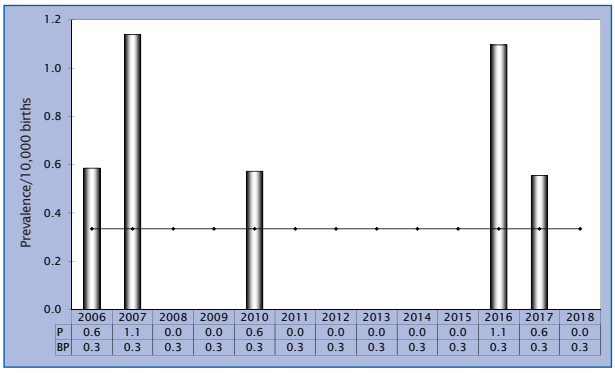



Fig. 29: Development of prevalence/10,000 births with epispadias in Saxony-Anhalt since 2006

**In 2018, no child with epispadias was registered in Saxony-Anhalt.**

# 12.23 Indeterminate Sex (Q56.)

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

| Indeterminate sex (2006-2017) | | |
|---|---|---|
| | Basis prevalence /10,000 births | Confidence Interval (CI of 95%) /10,000 births |
| Cities | 0.51 | 0.11 - 1.50 |
| Districts | 0.80 | 0.41 - 1.39 |
| Region | 0.72 | 0.40 - 1.18 |
| EUROCAT | 0.64 | 0.59 - 0.70 |
| | | 0.11 Styria (Austria)*<br>1.94 Malta** |

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

Indifferent sex belongs to the indicator malformations and we expect one or two cases to appear annually in Saxony-Anhalt at a maximum. The basis prevalence lies at 0.72 per 10,000 births. In 2018, no case of indifferent sex was registered.

EUROCAT indicated a total prevalence of 0.64 per 10,000 births for the time period of 2006-2017. Due to the low figures the fluctuations of the prevalence interval for Saxony-Anhalt are higher than for the total European malformation register. However, the prevalence level is nearly similar.

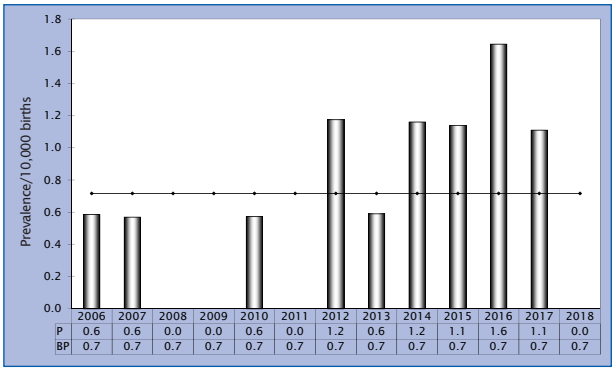



Abb. 30: Development of prevalence/10,000 births with indeterminate sex in Saxony-Anhalt since 2006

**In 2018, no birth with indeterminate sex was registered in Saxony-Anhalt.**

## Supplement to 12.24 Potter sequence (Q60.6)

NOTE

**What are ACE inhibitors and what is Sartan fetopathie?**

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

German speaking people can get further information about this topic by visiting the website of the pharmacovigilance and advisory centre for embryonic toxicology (www.embyotox.de).

# 12.24 Potter Sequence (Q60.6)

| | Number | Prevalence /10,000 births | Trend in comp. to basis prevalence |
|---|---|---|---|
| **Major cities** | 0 | 0.0 | ↓ |
| **Districts:**<br>1 x Altmarkkreis Salzwedel<br>1 x Anhalt-Bitterfeld<br>1 x Burgenlandkreis<br>1 x Harz<br>2 x Salzlandkreis | 6 | 5.0 | ↑ |
| **Saxony-Anhalt** | **6** | **3.4** | ↔ |

| Potter sequence (2006-2017) | | |
|---|---|---|
| | **Basis prevalence /10,000 births** | **Confidence Interval (CI of 95%) /10,000 births** |
| **Cities** | 1.71 | 0.82 - 3.14 |
| **Districts** | 2.98 | 2.18 - 3.99 |
| **Region** | 2.63 | 1.98 - 3.42 |
| **EUROCAT** | 1.25 | 1.18 - 1.33 |
| | | 0.22 Malta*<br>4.48 Mainz (Germany)** |

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

The **annual prevalence** for 2018 of **3.4 per 10,000 births** can be found in the middle range of the confidence interval of the basis prevalence (2.63 per 10,000 births) that was calculated for the years 2006-2017.
The range of prevalence for this indicator malformation is very large. A maximum value during the reporting period with a prevalence of 4.9 per 10,000 births was reached in 2016. Since 2013, the calculated prevalences were always within or above the confidence interval of the basis prevalence. In contrast, we observed in 2006, 2007 and 2012 with only one or two cases per year in Saxony-Anhalt a very low prevalence. According to this development, a trend analysis for Potter sequence over the entire reporting period (2006-2018) shows an increasing trend. The percentage change that was calculated for the linear portion amounts to +7.70 % (CI 0.84 % – 15.67 %), whereby the non-linear portion is not effective (chapter 12.37).

This year's prevalence can be found in the upper third of the basis prevalences of other European registers. The basis prevalence of Saxony-Anhalt lies above the total prevalence which is indicated by EUROCAT for the European registers.

NOTE

## additional information:

| | |
|---|---|
| **Pregnancy outcome** | 1 x live birth, deceased up to 7 days of life<br>5 x termination of pregnancy |
| **Sex** | 2 x male<br>3 x female<br>1 x no indication |
| **Number of isolated malformations/MCA** | 3 x MCA<br>3 x isolated |

A Potter sequence was caused by both sides functionless, 4 times cystic and one-time hypoplastic kidneys. One foetus suffered from a functionless solitary cystic kidney. Additional malformations such as clubfoot and hypoplasia of lung which are caused by the missing or malfunctioning kidneys are not part of the evaluations in the report (chapter 11).

After prenatal detection of severe malformations, the affected pregnancies were terminated in five cases between 19 and 26 weeks of gestations. One foetus was prenatally suspicious only in the 31st week of gestation. This infant was live birth in the 35th week of gestation and deceased during the first day of life. In one case of chronic illness of the mother and determination of pregnancy after 30 weeks of gestations a Sartan medication (pre-existing) must be assumed to be the cause of the malformation.

## Malformation combinations (MCA) or superordinated syndromes detected:

- Patau syndrome with: omphalocele, cerebellar hypoplasia, mandibular micro- and retrognathia, Potter- facies
- anal atresia, blt. ascending lid axis, low set ears
- complete Situs inversus, agenesis of lumbosacral spine, bending contractures of the lower legs, amyelia

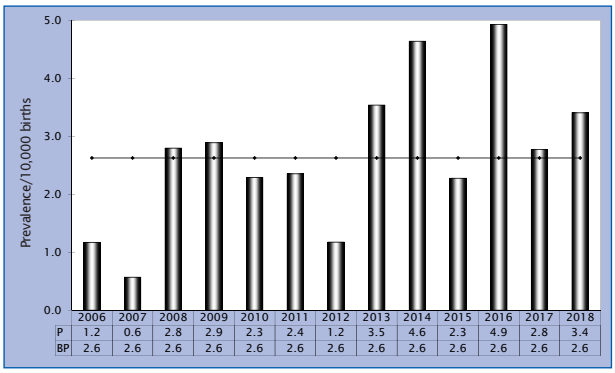



Fig. 31: Development of prevalence/10,000 births with Potter sequence in Saxony-Anhalt since 2006

**In 2018, one Potter sequence per 2,936 births was registered in Saxony-Anhalt.**

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

| | Number | Prevalence /10,000 births | Trend in comp. to basis prevalence |
|---|---|---|---|
| **Major cities:**<br>1 x Dessau-Roßlau<br>3 x Magdeburg | 4 | 7.3 | ↔ |
| **Districts:**<br>1 x Börde<br>1 x Harz<br>3 x Jerichower Land<br>1 x Stendal | 6 | 5.0 | ↔ |
| **Saxony-Anhalt** | **10** | **5.7** | ↔ |

| Renal agenesis, unilateral (2006-2017) | | |
|---|---|---|
| | Basis prevalence /10,000 births | Confidence Interval (CI of 95%) /10,000 births |
| **Cities** | 6.15 | 4.31 - 8.51 |
| **Districts** | 6.03 | 4.86 - 7.41 |
| **Region** | 6.07 | 5.12 - 7.17 |
| **EUROCAT** | no information | no information |

Unilateral renal agenesis was registered in 10 cases in Saxony-Anhalt in 2018. The indicator malformation has a **prevalence** of **5.7 per 10,000 births** and remains unsuspiciously within the normal range of the basis prevalence (2006-2017: 6.07 per 10,000 births). The frequency of unilateral renal agenesis fluctuates. It varied in the recent years between a minimum of 2.2 per 10,000 births (2016) and a maximum of 9.5 per 10,000 births (2008). However, during the last six years the prevalences were always within the range or below the basis prevalence.

EUROCAT does not provide any comparison data for unilateral renal agenesis.

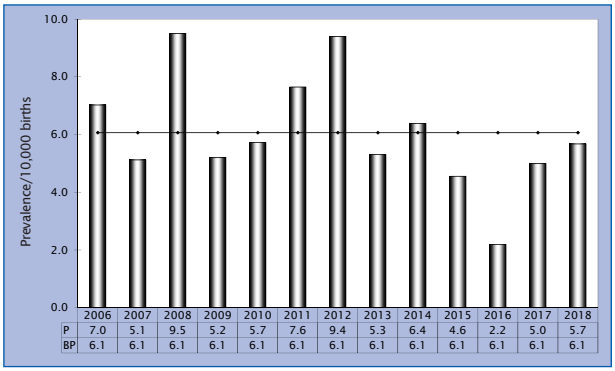
The left kidney was affected more frequently (6 x) than the right kidney (4 x), as known from literature. During the whole time period of 2006 to 2017 the left kidney was missing completely more often (56%) than the right one.

## additional information:

| | |
|---|---|
| **Pregnancy outcome** | 9 x live births<br>1 x termination of pregnancy |
| **Sex** | 9 x male<br>1 x female |
| **Number of isolated malformations/ MCA** | 4 x MCA<br>6 x isolated |

## Malformation combinations (MCA) or superordinated syndromes detected:

- VATCERL association with: oesophago tracheal fistula, blt. missing radius, dextrocardia
- Feingold syndrome type 1 with: oesophageal atresia with fistula between trachea and lower oesophagus pocket (Vogt IIIb), duodenal atresia, presternal haemangioma (1.5 cm), septum pellucidum anomalies
- tracheomalacia, corpus callosum hypoplasia, hyperplastic left kidney, PFO and not haemodynamically effective PDA at full term infant
- right DUP IV. grade and ureteral outlet stenosis, PFO at full term infant




| | 2006 | 2007 | 2008 | 2009 | 2010 | 2011 | 2012 | 2013 | 2014 | 2015 | 2016 | 2017 | 2018 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| P | 7.0 | 5.1 | 9.5 | 5.2 | 5.7 | 7.6 | 9.4 | 5.3 | 6.4 | 4.6 | 2.2 | 5.0 | 5.7 |
| BP | 6.1 | 6.1 | 6.1 | 6.1 | 6.1 | 6.1 | 6.1 | 6.1 | 6.1 | 6.1 | 6.1 | 6.1 | 6.1 |

Fig. 32: Development of prevalence/10,000 births with unilateral renal agenesis in Saxony-Anhalt since 2006

**In 2018, one renal agenesis, unilateral per 1,762 births was registered in Saxony-Anhalt.**

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

| | Number | Prevalence /10,000 births | Trend in comp. to basis prevalence |
|---|---|---|---|
| **Major cities:**<br>2 x Halle<br>2 x Magdeburg | 4 | 7,3 | ↘ |
| **Districts:**<br>2 x Altmarkkreis Salzwedel<br>1 x Anhalt-Bitterfeld<br>1 x Börde<br>2 x Harz<br>1 x Jerichower Land<br>2 x Mansfeld-Südharz<br>1 x Salzlandkreis | 10 | 8,3 | ↗ |
| **Saxony-Anhalt** | **14** | **7,9** | ↔ |

| Cystic kidney (2006-2017) | | |
|---|---|---|
| | Basis prevalence /10,000 births | Confidence Interval (CI of 95%) /10,000 births |
| **Cities** | 9.90 | 7.52 - 12.80 |
| **Districts** | 6.30 | 5.10 - 7.70 |
| **Region** | 7.31 | 6.26 - 8.52 |
| **EUROCAT** | no information | no information |

The indicator malformation cystic kidney comprises a heterogeneous group of renal malformations (chapter 12.0). The **prevalence** lies at **7.9 per 10,000 birth** in 2018. This means that after a period of three years with low occurrence a prevalence within the random range was registered. The basis prevalence (2006-2017) lies at 7.31 per 10,000 births. Between 2002 and 2011 we observed mainly higher prevalences, but could not identify a certain trend.

No EUROCAT data is available for comparison for the prevalence of cystic kidney.

### additional information:

| | |
|---|---|
| **Pregnancy outcome** | 11 x live births<br>3 x termination of pregnancy |
| **Sex** | 6 x male<br>8 x female |
| **Number of isolated malformations/ MCA** | 10 x MCA<br>4 x isolated |

In three cases other severe malformations were prenatally diagnosed and the pregnancies were terminated between 16 (Edwards syndrome) and 23 weeks of gestation.

Two births suffered from a bilateral cystic renal degeneration. In 12 cases the diagnosis was unilateral, four times left and eight times right sided.

### Malformation combinations (MCA) or superordinated syndromes detected:

- Edwards syndrome with: VSD, thymic hypoplasia, renal displacement left, dysplastic ears
- sirenomelia with: persistent left Vena cava superior, VSD, hypoplastic aorta, rectal agenesis, uterus, vagina and urethra, horseshoe kidney, intestinal malrotation, pancreas anulare, turricephaly, blt. hypoplastic lung at incompletely lobed lung left, hypertelorism, epicanthus internus, low set ears
- ASD, missing left thumb, blt. pulmonary hypoplasia at chest thorax, hypertelorism, mandibular retro- and micrognathia, low set ears, four finger groove, potter facies, sunken nose bridge
- vascular ring through the anomalous right sub clavicular artery
- multiple cerebral cysts
- ureter outlet stenosis and DUP IV. Grade right
- megaureter right
- ectopic kidney left
- hepatomegaly
- hernia inguinalis right at full term infant

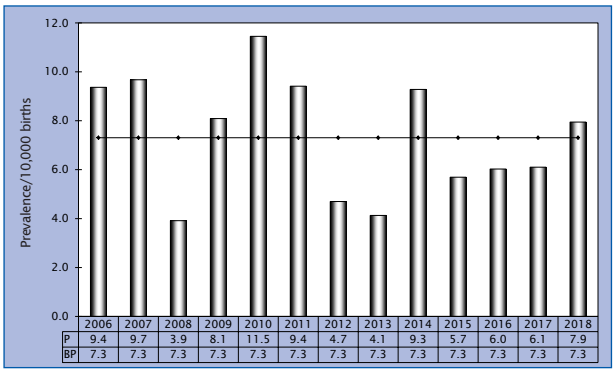



Fig. 33: Development of prevalence/10,000 births with cystic kidneys in Saxony-Anhalt since 2006

**In 2018, one child with cystic kidney per 1,258 births was registered in Saxony-Anhalt.**

# 12.27 Bladder Exstrophy (Q64.1)

| | Number | Prevalence /10,000 births | Trend in comp. to basis prevalence |
|---|---|---|---|
| **Major cities:** 1 x Halle | 1 | 1.8 | ↑ |
| **Districts** | 0 | 0.0 | ↓ |
| **Saxony-Anhalt** | **1** | **0.6** | ↔ |

| Bladder exstrophy (2006-2017) | | |
|---|---|---|
| | **Basis prevalence /10,000 births** | **Confidence Interval (CI of 95%) /10,000 births** |
| **Cities** | 0.00 | 0.00 - 0.51 |
| **Districts** | 0.40 | 0.15 - 0.87 |
| **Region** | 0.29 | 0.11 - 0.62 |
| **EUROCAT** | no information | no information |

Bladder exstrophy is the most rarely registered one of all indicator malformations. It was diagnosed during the years of the reporting period (2006-2017) only in six cases. In 2018, one infant with bladder exstrophy was live birth. This corresponds to a **prevalence** of **0.6 per 10,000 births**. The annual prevalence lies within the calculated confidence interval of the basis prevalence (0.29 per 10,000 births). With two cases per year instead of one, the normal range would already be exceeded with such a rare occurrence of the malformation.

EUROCAT does not provide data of comparison for bladder exstrophy.

## additional information:

| | |
|---|---|
| **Pregnancy outcome** | 1 x live birth |
| **Sex** | 1 x female |
| **Number of isolated malformations/ MCA** | 1 x MCA |

## Malformation combinations (MCA) or superordinated syndromes detected:

- subluxation of left hip, retarded hip right

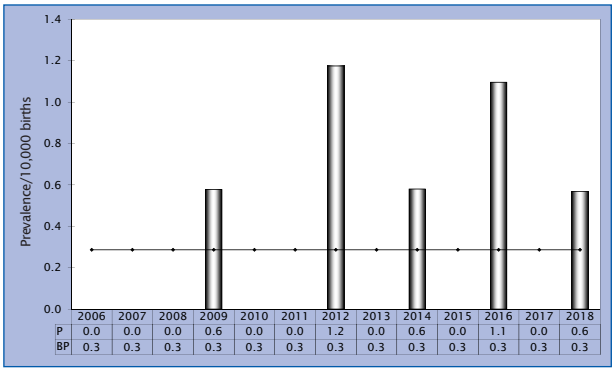



Fig. 34: Development of prevalence/10,000 births with bladder exstrophy in Saxony-Anhalt since 2006

**In 2018, one birth with a bladder exstrophy per 17,617 births was registered in Saxony-Anhalt.**

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

| | Number | Prevalence /10,000 births | Trend in comp. to basis prevalence |
|---|---|---|---|
| **Major cities:**<br>1 x Halle<br>1 x Magdeburg | 2 | 3.6 | ↔ |
| **Districts:**<br>1 x Anhalt-Bitterfeld | 1 | 0.8 | ↓ |
| **Saxony-Anhalt** | **3** | **1.7** | ↓ |

| Preaxial polydactyly (2006-2017) | | |
|---|---|---|
| | **Basis prevalence /10,000 births** | **Confidence Interval (CI of 95%) /10,000 births** |
| **Cities** | 3.93 | 2.49 - 5.89 |
| **Districts** | 3.85 | 2.92 - 4.97 |
| **Region** | 3.87 | 3.07 - 4.81 |
| **EUROCAT** | no information | no information |

Similar to the last five previous years, preaxial polydactyly was unusually rarely diagnosed in Saxony-Anhalt with three cases in 2018. The resulting **annual prevalence** of **1.7 per 10,000 births**, which is the second lowest in the reporting period, is considerably lower than the calculated basis prevalence (2006-2017: 3.87 per 10,000 births). Since we registered a maximum value in 2007 (8.0 per 10,000 births), the frequency decreases. The trend calculation for the whole reporting period of 2006-2018 (chapter 12.37) results for preaxial polydactyly in a significantly decreasing trend with a percentage change of -10.49 % (CI -15.16 % to -4.43 %).

Polydactyly was localized preaxial in about one third of cases and postaxial in about two thirds of cases during the reporting period. In contrast to preaxial polydactyly, no trend can be identified for postaxial polydactyly. In 2018, this malformation was diagnosed with an unusual high frequency (8.5 per 10,000 births).

Comparative EUROCAT data for preaxial polydactyly is not available.

### additional information:

| | |
|---|---|
| **Pregnancy outcome** | 3 x live births |
| **Sex** | 2 x male<br>1 x female |
| **Number of isolated malformations/ MCA** | 3 x isolated |

In all three cases the thumbs were affected, one time left, one time right and one time both thumbs. Apart from the additional thumbs, the infants had no further malformations.

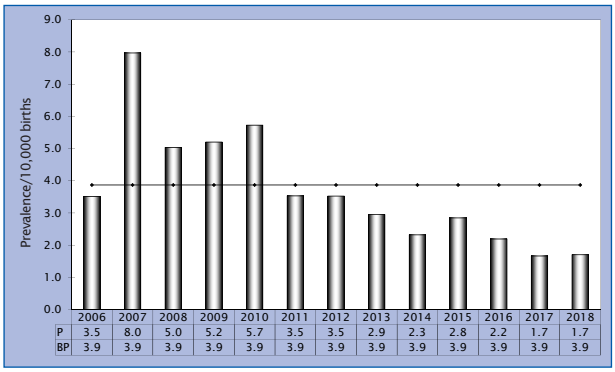



Fig. 35: Development of prevalence/10,000 births with preaxial polydactyly in Saxony-Anhalt since 2006

**In 2018, one preaxial polydactyly per 5,872 births was registered in Saxony-Anhalt.**

# 12.29 Limb Reduction Defects of both upper and lower limbs (Q71./Q72./Q73.)

| | Number | Prevalence /10,000 births | Trend in comp. to basis prevalence |
|---|---|---|---|
| **Major cities:**<br>3 x Halle | 3 | 5.5 | ↓ |
| **Districts:**<br>1 x Altmarkkreis Salzwedel<br>1 x Anhalt-Bitterfeld<br>3 x Börde<br>2 x Harz<br>1 x Jerichower Land | 8 | 6.6 | ↘ |
| **Saxony-Anhalt** | **11** | **6.2** | ↓ |

| Limb reduction Defects of both upper and lower limbs (2006-2017) | | |
|---|---|---|
| | Basis prevalence /10,000 births | Confidence Interval (CI of 95%) /10,000 births |
| **Cities** | 9.39 | 7.08 - 12.22 |
| **Districts** | 8.29 | 6.99 - 9.81 |
| **Region** | 8.60 | 7.46 - 9.90 |
| **EUROCAT** | 5.47 | 5.31 - 5.62 |
| | | 2.63 S Portugal*<br>9.55 Auvergne (France)** |

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

The **prevalence** of limb reduction malformations lies with a value of **6.2 per 10,000 births** well below the lower confidence limit of the basis prevalence (2006-2017: 8.60 per 10,000 births; CI 7.46-9.90) in 29018. During the last twelve years, the frequency fluctuated between a minimum of 5.7 per 10,000 births (2010) and a maximum of 14.1 per 10,000 births (2012).
The limb reduction defects include very different malformations with very different causes, whereby so far only a part of the aetiology is known. The variety of possible causes means also a large fluctuation margin of the values. An analysis and representation for a longer period of time provides more information (chapter 16.2). The media attention in September 2019 caused an early publication of the current prevalence (see article: No increased number of hand malformations in Saxony-Anhalt. Ärzteblatt Sachsen-Anhalt 2019; 30(11): 18-19)
The trend analysis (2006-2018) results in only a slight negative regression coefficient, the confidence interval of prevalence change covers thereby the value zero and no trend can be described consequently (Chapter 12.37).

The fluctuation range of the total prevalence of the European malformation registers (2006-2017) is lower than that one of the basis prevalence of Saxony-Anhalt.

Reduction malformations occurred mostly (8x) only on the upper extremities, twice only on the lower extremities and once on the lower legs and hands. 4 times both sides were affected, two times right only and 5 times left only.

### additional information:

| | |
|---|---|
| **Pregnancy outcome** | 5 x live births<br>6 x termination of pregnancy |
| **Sex** | 6 x male<br>4 x female<br>1 x no indication |
| **Number of isolated malformations/ MCA** | 6 x MCA<br>5 x isolated |

Two micromyelia were detected during prenatal ultrasound screening and the pregnancies were terminated already at the end of the first trimenon. In case of four further infants with malformations, the termination of pregnancy took place between 18 and 24 weeks of gestations.

### Malformation combinations (MCA) or superordinated syndromes detected:

- VATCERL-association with: oesophago tracheal fistula, renal agenesis right, dextrocardia
- ASD, multicystic dysplastic kidney right, blt. pulmonary hypoplasia at chest thorax, hypertelorism, mandibular retro- and micrognathia, low set ears, four finger grooves, potter facies, sunken nose bridge
- hydrocephalus internus, underdeveloped nose, low set ears
- thanatophoric dysplasia type I, thorax hypoplasia, short ribs
- Robin sequence with: median cleft palate, mandibular micro- and retrognathia
- osseous syndactyly of finger II./III. right

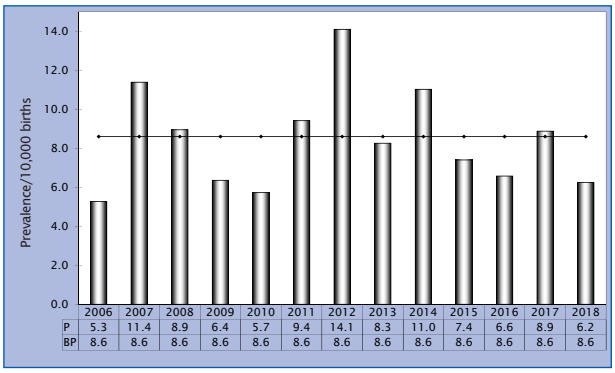



Abb. 36: Development of prevalence/10,000 births with limb reduction defects in Saxony-Anhalt since 2006

**In 2018, one limb reduction defect per 1,602 births was registered in Saxony-Anhalt.**

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

| | Number | Prevalence /10,000 births | Trend in comp. to basis prevalence |
|---|---|---|---|
| **Major cities:**<br>1 x Halle<br>2 x Magdeburg | 3 | 5.5 | ↔ |
| **Districts:**<br>1 x Börde<br>3 x Harz<br>1 x Salzlandkreis | 5 | 4.1 | ↑ |
| **Saxony-Anhalt** | **8** | **4.5** | ↑ |

| Diaphragmatic hernia (2006-2017) | | |
|---|---|---|
| | **Basis prevalence /10,000 births** | **Confidence Interval (CI of 95%) /10,000 births** |
| **Cities** | 3.93 | 2.49 - 5.89 |
| **Districts** | 1.92 | 1.29 - 2.76 |
| **Region** | 2.48 | 1.86 - 3.26 |
| **EUROCAT (Q79.0)** | 2.87 | 2.76 - 2.99 |
| | | 1.29 Zagreb (Croatia)*<br>6.05 Malta** |

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

8 cases of diaphragmatic hernia were registered in 2018. The **prevalence** of **4.5 per 10,000 births** is again very high after a period of low prevalences during the last ten years. The annual prevalence clearly exceeds the confidence interval of the basis prevalence (2006-2017: 2,.8 per 10,000 births; CI 1.86-3.26). In 2016, only one case of diaphragmatic hernia was registered in Saxony-Anhalt.

The total prevalence of the European registers is similar to the basis prevalence of Saxony-Anhalt. However, due to the dimensions of the respective population the fluctuation margin is much smaller. This prevalence is significantly exceeded in 2018.

Diaphragmatic hernia occurred mainly on the left side (5x). Only in one case it occurred on the right side. An additional Edwards syndrome was diagnosed prenatally in case of two terminations of pregnancy.

## additional information:

| | |
|---|---|
| **Pregnancy outcome** | 3 x live births<br>1 x live birth, deceased after 7 days of life<br>4 x termination of pregnancy |
| **Sex** | 4 x male<br>4 x female |
| **Number of isolated malformations/ MCA** | 6 x MCA<br>2 x isolated |

## Malformation combinations (MCA) or superordinated syndromes detected:

- 2 x Edwards syndrome (1 x with: omphalocele, cleft lip with cleft palate, cardiac malformation)
- Gastroschisis, intestinal malrotation, thyroid abnormality
- Duodenal atresia, VSD, low set ears
- ASD II
- PFO at full term infant

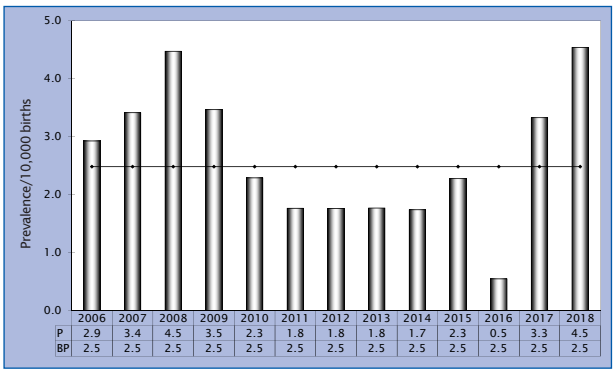



Fig. 37: Development of prevalence/10,000 births with diaphragmatic hernia in Saxony-Anhalt since 2006

**In 2018, one diaphragmatic hernia per 2,202 births was registered in Saxony-Anhalt.**

# 12.31 Omphalocele (Q79.2)

| | Number | Prevalence /10,000 births | Trend in comp. to basis prevalence |
|---|---|---|---|
| **Major cities:**<br>1 x Magdeburg | 1 | 1.8 | ↘ |
| **Districts:**<br>1 x Anhalt-Bitterfeld<br>2 x Börde<br>3 x Harz<br>1 x Saalekreis<br>1 x Salzlandkreis | 8 | 6.6 | ↑ |
| **Saxony-Anhalt** | **9** | **5.1** | ↑ |

| Omphalocele (2006-2017) | | |
|---|---|---|
| | Basis prevalence /10,000 births | Confidence Interval (CI of 95%) /10,000 births |
| **Cities** | 3.59 | 2.22 - 5.48 |
| **Districts** | 3.32 | 2.46 - 4.37 |
| **Region** | 3.39 | 2.65 - 4.28 |
| **EUROCAT** | 3.37 | 3.24 - 3.49 |
| | | 0.77 S Portugal*<br>6.85 Vaud (Switzerland)** |

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

The prevalence of the indicator malformation omphalocele was in 2018 and in five out of seven years before above the upper confidence limit of the basis prevalence of Saxony-Anhalt. The current years **prevalence** lies with nine cases (**5.1 per 10,000 births**) clearly above the basis prevalence (2006-2017: 3.39 per 10,000 births; CI 2.65-4.28). The trend analysis (chapter 12.37) identifies a significantly ascending trend for omphalocele during the whole reporting period (2006-2018). The percentage increase that was calculated for the linear share is +6.78 % (CI 0.83 % to 13.58 %). The non-linear component is ineffective in this case.
This is directly related to the increasing number of numerical chromosomal aberrations (see chapter 16.1).

The basis prevalence of Saxony-Anhalt remains on the same level in comparison to the total European prevalence, but with a larger random range. The annual prevalence of Saxony-Anhalt lies in the upper third of the average prevalences of the single European malformation registers.

The malformation omphalocele develops when up to 10 weeks of gestation the umbilical hernia is not regressing physiologically. In four cases it was detected during 12 and 14 weeks of gestation. In one case it was detected after 23 weeks of gestations during prenatal ultrasound screening.

The diagnosis of omphalocele was made in case of one foetus only after 28 weeks of gestations. The infant died intrauterine shortly after. One live birth with Edwards syndrome died at the first day of life. The two other infants were born after 38 weeks of gestation and operated shortly after birth.

### additional information:

| | |
|---|---|
| **Pregnancy outcome** | 2 x live births<br>1 x live birth, deceased up to 7 days of life<br>5 x termination of pregnancy<br>1 x stillbirth |
| **Sex** | 5 x male<br>2 x female<br>2 x no indication |
| **Number of isolated malformations/ MCA** | 7 x MCA<br>2 x isolated |

### Malformation combinations (MCA) or superordinated syndromes detected:

- Edwards syndrome with: hydrocephalus, clubfoot, macrocephaly
- Edwards syndrome with: diaphragmatic hernia, cleft lip with cleft palate, cardiac malfomation
- 2 x Patau syndrome (1 x with: Potter sequence, cerebellar hypoplasia, mandibular micro- and retrognathia, Potter facies)
- blt. lung hypoplasia
- ASD II, persistent yolk stalk
- VSD

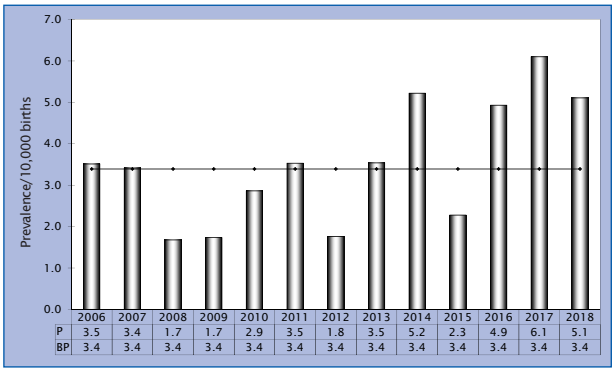



Fig. 38: Development of prevalence/10,000 births with omphalocele in Saxony-Anhalt since 2006

**In 2018, one omphalocele per 1,957 births was registered in Saxony-Anhalt.**

# 12.32 Gastroschisis (Q79.3)

| | Number | Prevalence /10,000 births | Trend in comp. to basis prevalence |
|---|---|---|---|
| **Major cities:**<br>2 x Halle<br>2 x Magdeburg | 4 | 7.3 | ↑ |
| **Districts:**<br>1 x Altmarkkreis Salzwedel<br>1 x Harz<br>1 x Mansfeld-Südharz<br>1 x Saalekreis | 4 | 3.3 | ↔ |
| **Saxony-Anhalt** | **8** | **4.5** | ↔ |

| Gastroschisis (2006-2017) | | |
|---|---|---|
| | Basis prevalence /10,000 births | Confidence Interval (CI of 95%) /10,000 births |
| **Cities** | 3.76 | 2.35 - 5.69 |
| **Districts** | 3.78 | 2.86 - 4.90 |
| **Region** | 3.77 | 2.99 - 4.70 |
| **EUROCAT** | 2.84 | 2.73 - 2.96 |
| | | 0.99 Emilia Romagna (Italy)*<br>5.51 Northern England (UK)** |

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

Eight cases of gastroschisis were registered in Saxony-Anhalt in 2018. Therefore, the current years **prevalence** (**4.5 per 10,000 births**) lies inconspicuously within the normal range of the basis prevalence (2006- 2017: 3.77 per 10,000 births) after two years of rather low prevalences.

In comparison with the European total prevalence the annual prevalence of Saxony-Anhalt is higher because the confidence interval of the prevalence of the European malformation registers is lower.
The values of Saxony-Anhalt can be found in the upper third of the comparison values of the EUROCAT centres.

The gastroschisis was detected prenatally between 14 and 25 weeks of gestations in case of seven out of eight infants. All three live births were delivered via cesarean section between 32 and 36 weeks of gestations.

## additional information:

| | |
|---|---|
| **Pregnancy outcome** | 3 x live births<br>4 x termination of pregnancy<br>1 x stillbirth |
| **Sex** | 6 x male<br>1 x female<br>1 x no indication |
| **Number of islated malformations/ MCA** | 6 x MCA<br>2 x isolated |

## Malformation combinations (MCA) or superordinated syndromes detected:

- parietal encephalocele, blt. cleft lip with cleft palate, midface hypoplasia, intestinal malrotation, missing nipples, thyroid abnormality, lateral ascending lid axis, prominent clitoris
- microtia left, hydranencephaly, dents in the skull, low set ears, prominent forehead, hypertelorism, varus deformities of the right foot
- diaphragmatic hernia left, intestinal malrotation, thyroid abnormality
- jejunum atresia with missing fixation at posterior abdominal wall (Apple-peel), microcolon
- duplex kidney left, DUP I. grade left, PFO at preterm infant
- Kinking of the lumbar and thoracic spine

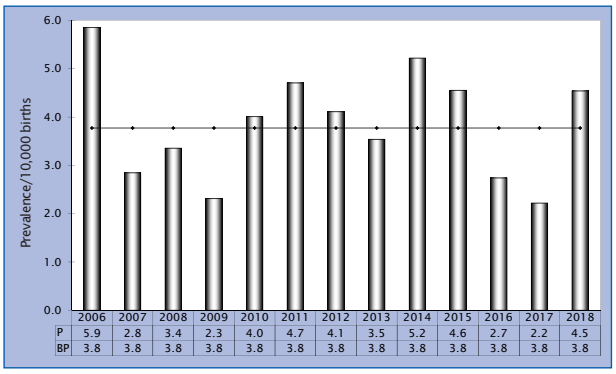



Fig. 39: Development of prevalence/10,000 births with gastroschisis in Saxony-Anhalt since 2006

**In 2018, one gastroschisis per 2,202 births was registered in Saxony-Anhalt.**

# 12.33 Prune belly Syndrome (Q79.4)

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

| Prune belly syndrome (2006-2017) | | |
|---|---|---|
| | **Basis prevalence /10,000 births** | **Confidence Interval (CI of 95%) /10,000 births** |
| **Cities** | 1.54 | 0.70 - 2.92 |
| **Districts** | 0.46 | 0.19 - 0.96 |
| **Region** | 0.76 | 0.44 - 1.24 |
| **EUROCAT** | no information | no information |

Prune belly sequence belongs to the rare appearing malformations, which are not seen every year in Saxony-Anhalt. With an exception in 2011 (5 x), it never occurred more than twice a year during the reporting period. 2018 it was registered in one case. Therefore, the **annual prevalence** of **0.6 per 10,000 births** lies within the random range of the basis prevalence (2006-2017: 0.76 per 10,000 births).

A European total prevalence is not present for comparison.

The foetus with prune belly sequence suffered beside a malformation of the urinary transport system from a lung hypoplasia. The malformations were detected via ultrasound screening in the 12th week of gestation.

## additional information:

| | |
|---|---|
| **Pregnancy outcome** | 1 x termination of pregnancy |
| **Sex** | 1 x no indication |
| **Number of isolated malformations/ MCA** | 1 x MCA |

## Malformation combinations (MCA) or superordinated syndromes detected:

- urethral atresia, blt. DUP and hypoplasia of lung, megacystis

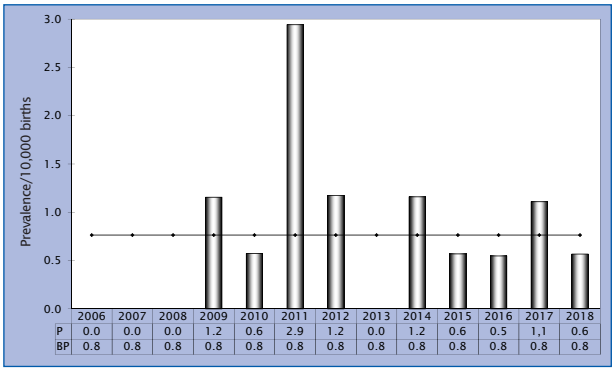



Fig. 40: Development of the prevalence/10,000 births with Prune belly syndrome in Saxony-Anhalt since 2006

**In 2018, one Prune-Belly-syndrome per 17,617 births was registered in Saxony-Anhalt.**

# 12.34 Down Syndrome - Trisomy 21 (Q90.)

| | Number | Prevalence /10,000 births | Trend in comp. to basis prevalence |
|---|---|---|---|
| **Major cities:**<br>5 x Halle<br>11 x Magdeburg | 16 | 29.1 | ↑ |
| **Districts:**<br>2 x Anhalt-Bitterfeld<br>7 x Börde<br>5 x Harz<br>2 x Jerichower Land<br>4 x Saalekreis<br>4 x Salzlandkreis<br>3 x Stendal<br>1 x Wittenberg | 28 | 23.1 | ↑ |
| **Saxony-Anhalt** | **44** | **25.0** | ↑ |

| Down syndrome (2006-2017) | | |
|---|---|---|
| | Basis prevalence /10,000 births | Confidence Interval (CI of 95%) /10,000 births |
| **Cities** | 21.52 | 18.15 - 25.45 |
| **Districts** | 17.37 | 15.43 - 19.55 |
| **Region** | 18.53 | 16.81 - 20.42 |
| **EUROCAT** | 23.47 | 23.15 - 23.80 |
| | | 10.22 S Portugal*<br>41.80 Paris (France)** |

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

Every 540th pregnancy between 2006 and 2017 in Saxony-Anhalt was affected by a Down`s syndrome. Therefore, Down`s syndrome is the second most common indicator malformation and by far the most common chromosomal aberration. With 44 cases and a calculated **prevalence** of **25.0 per 10,000 births** we saw a prevalence which was considerably above the confidence interval of the basis prevalence in 2018 (2006-2017: 18.53 per 10,000 births).

The risk of Down's syndrome grows with increasing maternal age. The comparison of the prevalence of Saxony-Anhalt with the total European prevalence (23.47 per 10,000 births) reflects the fact that the average maternal age in Saxony-Anhalt is lower than in the European average (2017: 28.7 years vs. 29.1 years*). This year's prevalence is above the average of other European malformation registries. Chapter 16.1 discusses changes in the frequency of occurrence in a European comparison.

### additional information:

| | |
|---|---|
| **Pregnancy outcome** | 20 x live births<br>1 x spontaneos abortion<br>23 x termination of pregnancy |
| **Sex** | 22 x male<br>20 x female<br>2 x no indication |
| **Number of isolated malformations/ MCA** | 24 x MCA<br>20 x isoliert |

In case of 23 foetuses the termination of pregnancy resp. the spontaneous abortion took place after averagely 16.3 weeks of gestation (median 17th WOG), at the earliest in the 12th WOG and at the latest in the 26th WOG.

### Malformation combinations (MCA) or superordinated syndromes detected:

- hydrocephalus internus, ASD and PFO at preterm infant, septum pellucidum anomalies
- preductal aortic coarctation, clubfoot, retarded hip
- univacuolar heart, lateral throat cyst
- VSD, sound perception disorder right
- VSD, PFO at preterm infant, haemangioma
- VSD, not haemodynamically effective PDA at full term infant
- AVSD, undescended right testis at full term infant
- AVSD, VSD, mitral valve insufficiency, tricuspid insufficiency 1st grade, umbilical hernia
- AVSD, uvula cleft, sound perception disorder (left 40 dB), blt. narrow auditory canal
- AVSD, blt. retarded hip
- AVSD, micropenis
- 2 x AVSD
- ASD II, AVSD, short philtrum, prominent clitoris, blt. brachydactyly of fingers
- ASD II, retarded hip right
- 2 x ASD II
- mitral valve insufficiency
- haemodynamically effective PDA at preterm infant
- 2 x PFO at full term infant (1 x umbilical hernia)
- clubfoot, ASD at preterm infant
- clubfoot right
- hydrothorax, plexus cyst

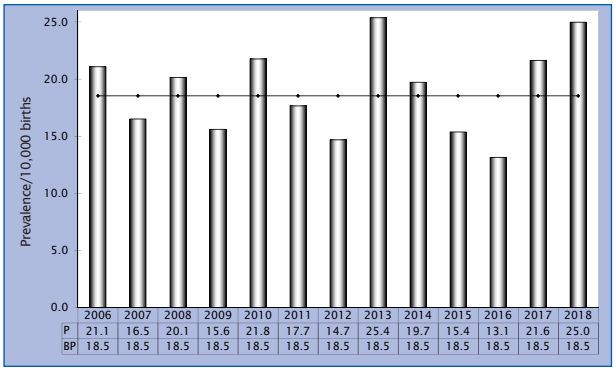



Fig. 41: Development of prevalence/10,000 births with Down syndrome in Saxony-Anhalt since 2006

**In 2018, one Down syndrome (trisomy 21) per 400 births was registered in Saxony-Anhalt.**

* Source: https://de.statista.com/infografik/17418/durchschnittsalter-von-muettern-in-europa/

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

| | Number | Prevalence /10,000 births | Trend in comp. to basis prevalence |
|---|---|---|---|
| **Major cities** | 0 | 0.0 | ↓ |
| **Districts:**<br>1 x Saalekreis<br>2 x Salzlandkreis | 3 | 2.5 | ↑ |
| **Saxony-Anhalt** | **3** | **1.7** | ↔ |

| Patau syndrome (2006-2017) | | |
|---|---|---|
| | **Basis prevalence /10,000 births** | **Confidence Interval (CI of 95%) /10,000 births** |
| **Cities** | 1.20 | 0.48 - 2.46 |
| **Districts** | 1.19 | 0.71 - 1.89 |
| **Region** | 1.19 | 0.77 - 1.76 |
| **EUROCAT** | 2.20 | 2.10 - 2.30 |
| | | 0.68 S Portugal*<br>4.63 Paris (France)** |

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

The Patau syndrome was prenatally genetically determined in Saxony-Anhalt in case of three foetuses in 2018. This means that a **prevalence** of **1.7 per 10,000 births** was calculated, which lies in the normal range of the basis prevalence (2006-2017: 1.19 per 10,000 births). Since 2000, we observe a maximum of four cases per year in Saxony-Anhalt. The median ist two. Due to the small numbers, Chapter 16.1 presents among other things a trend analysis in two-year groups for Patau's syndrome and discusses possible causes for prevalence changes.

EUROCAT indicates a prevalence of 2.20 per 10,000 births for Patau syndrome. The basis prevalence of Saxony-Anhalt as well as the prevalence of 2018 can be found below the confidence interval of the total European prevalence and in comparison, in the lower third of other malformation registers.

## additional information:

| | |
|---|---|
| **Pregnancy outcome** | 3 x termination of pregnancy |
| **Sex** | 2 x male<br>1 x female |
| **Number of isolated malformations/ MCA** | 2 x MCA<br>1 x isolated |

## Malformation combinations (MCA) or superordinated syndromes detected:

- Potter sequence, omphalocele, cerebellum hypoplasia, mandibular micro- and retrognathia, Potter facies
- omphalocele

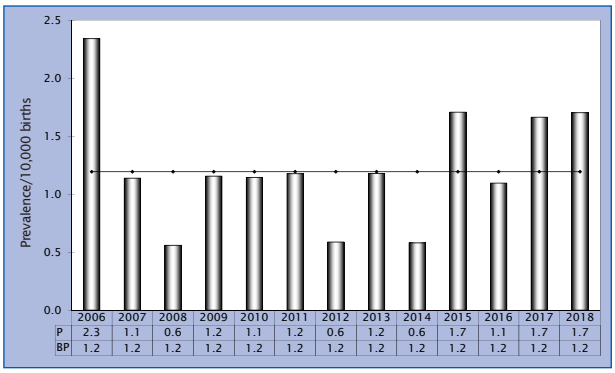



Fig. 42: Development of prevalence/10,000 births with a Patau syndrome in Saxony-Anhalt since 2006

**In 2018, one Patau syndrome (trisomy 13) per 5,872 births was registered in Saxony-Anhalt.**

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

| | Number | Prevalence /10,000 births | Trend in comp. to basis prevalence |
|---|---|---|---|
| **Major cities:**<br>2 x Halle<br>2 x Magdeburg | 4 | 7.3 | ↗ |
| **Districts:**<br>2 x Burgenlandkreis<br>2 x Börde<br>2 x Harz<br>1 x Mansfeld-Südharz<br>1 x Saalekreis<br>1 x Salzlandkreis | 9 | 7.4 | ↑ |
| **Saxony-Anhalt** | **13** | **7.4** | ↑ |

| Edwards syndrome (2006-2017) | | |
|---|---|---|
| | **Basis prevalence /10,000 births** | **Confidence Interval (CI of 95%) /10,000 births** |
| **Cities** | 4.78 | 3.18 - 6.91 |
| **Districts** | 3.51 | 2.63 - 4.60 |
| **Region** | 3.87 | 3.07 - 4.81 |
| **EUROCAT** | 5.70 | 5.54 - 5.86 |
| | | 1.06 Wielkopolska (Poland)*<br>13.35 Paris (France)** |

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

The second most common trisomy is the Edwards syndrome. In 2018, it was detected by amniocentesis in 13 cases. The **annual prevalence** of **7.4 per 10,000 births** lies clearly above the upper limit of the confidence interval of the basis prevalence (2006-2017: 3.87 per 10,000 births). Chapter 16.1 goes into detail in regard to the reasons of the prevalence development during the last years.

In the European comparison, we can find the basis prevalence of Saxony- Anhalt below the total prevalence. It can be located in the lower third of the average prevalence of the EUROCAT centres which show for Edwards Syndrome a wide range. This year's annual prevalence in Saxony-Anhalt is rather high in the European comparison.

## additional information:

| | |
|---|---|
| **Pregnancy outcome** | 1 x live birth, deceased up to 7 days of life<br>1 x live birth, deceased after 7 days of life<br>10 x termination of pregnancy<br>1 x stillbirth |
| **Sex** | 6 x male<br>6 x female<br>1 x no indication |
| **Number of isolated malformations/ MCA** | 10 x MCA<br>3 x isolated |

In all 13 cases a chromosomal finding was made by amniocentesis. The reason for this were usual abnormalities or malformations that were observed during prenatal ultrasound screening. In seven cases the reason was the maternal age and in two cases a NIPT with pathological finding was made.
In case of the terminations of pregnancies, the first indications were found three times during ultrasound screening already at the end of the 1st trimenon, 5 times at the beginning of the 2nd trimenon, once in the 22nd and once in the 29th week of gestation. Both live births died, one on the first day of life and one after three months.

## Malformation combinations (MCA) or superordinated syndromes detected:

- hydrocephaly, omphalocele, clubfoot, macrocephaly
- omphalocele, diaphragmatic hernia, cleft lip with cleft palate, cardiac malformation
- anal atresia, cleft lip right, overlapping finger
- VSD, ASD II, single cerebral cyst, blt. exophthalmia, sound perception disorder, DUP III. Grade, hernia inguinalis and syndactyly type 1 (II./III. toes), malformed gall bladder, undescended right testis and not haemodynamically effective PDA at full term infant, varus deformities of both feet, mandibular micrognathia, wide nipple space, blt. overlapping finger
- VSD, thymus hypoplasia, renal dysplasia and -displacement left
- diaphragmatic hernia
- VSD
- cardiac malformation
- clubfoot, missing nose tip, macroglossia
- pterygium colli, mandibular retrognathia

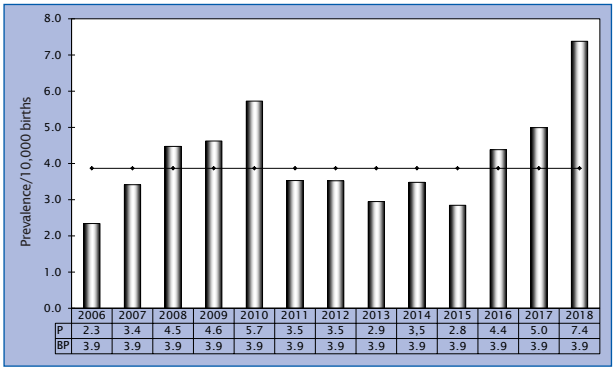



Fig. 43: Development of prevalence/10,000 births with Edwards syndrome in Saxony-Anhalt since 2006

**In 2018, one Edwards syndrome per 1,355 births was registered in Saxony-Anhalt.**

# 12.37 Indicator Malformations, In Total

The malformation monitoring offers the precondition for an assessment of the frequency of malformations with temporal and spatial reference and enables the identification of trends and clusters. Chapters 12.1 to 12.36 describe the occurrence of 36 from the ICBDSR (International Clearinghouse for Birth) Defects Surveillance and Research) worldwide unequivocal defined indicator malformations (Chapter 12.0).

245 births were concerned by an indicator malformation in 2018. Only 166 (67.8 %) of these were live births. The percentage of live births was always higher during the years of 2006-2017 (minimal 2017: 72,0 %, maximal 2007: 81,3 %), however with falling tendency. Indicator malformations were registered in 2018 at five stillbirths and two spontaneous abortions after 16 WOG`s. Their total share is 2.9 %, this lies slightly above the reporting period (2006-20017: 2.4 %). The percentage of terminations of pregnancy lies within the middle range (2006-2017) at 21.2 % and reached a new maximum value in 2018 (29.4 %).

284 indicator malformations were registered at 245 births which were concerned by an indicator malformation. Almost half of them (119 births) suffered from an isolated indicator malformation. 126 births were affected by multiple malformations. One termination of pregnancy showed two indicator malformations and 13 additional major malformations. 31 births had between two and four indicator malformations.

| | Number | Prevalence /10,000 births | Trend in comp. to basic prevalence |
|---|---|---|---|
| Major cities | 87 | 1.58 | ↔ |
| Districts | 158 | 1.30 | ↘ |
| Saxony-Anhalt | 245 | 1.39 | ↔ |

| Indicator malformations, in total (2006-2017) | | |
|---|---|---|
| | Basic prevalence in % | Confidence interval (CI of 95%) |
| Cities | 1.61 | 1.51 - 1.71 |
| Districts | 1.38 | 1.32 - 1.44 |
| Region | 1.44 | 1.39 - 1.49 |

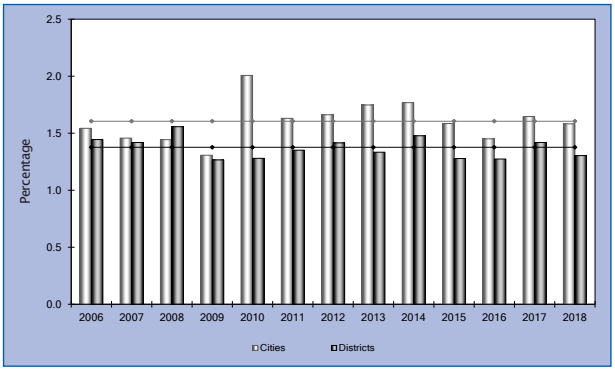



Fig. 44: Indicator malformations in total (2006 to 2017), comparison of frequency (in %) in the major cities and districts

1.39% of all births suffered from indicator malformations in 2018. The value lies at the lower confidence limit of the calculated basis prevalence for the years 2006-2017 (1.44 %,
CI 1.39 to 1.49).

A comparison of the observed prevalences shows also in 2018 lower values in the districts than in the independent towns (2018: 1.36 % vs. 1.44 %). The current prevalence of the independent towns lies within the confidence interval (2006-2017: 1.61 %, CI 1.51 to 1.71) and in the districts slightly under the basis prevalence (2006-2017: 1.38 %, CI 1.32 to 1.44).

Aim of our trend analysis is to detect long term tendencies in the appearance of indicator malformations. Therefore, we are analysing intensity and orientation of indicator prevalence changes during the whole registration period (2006-2017).

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 45 on page 65 shows the average percentage changes of the annual prevalences of all indicator malformations that correspond to these initial conditions. They are rated by binary logistic regression analysis on the basis of the maximum-likelihood-estimation.

The regression coefficient B 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 left hand of the axis (in the negative area). The recorded trend is significant if the confidence interval does not cover the zero value.

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 identify a non-linear trend. This applies for neural tube defects.

A probability value of $p < 0.05$ for the linear percentage and $p > 0.01$ for the non-linear percentage means that the linear percentage dominates and the non-linear percentage can be neglected. The observed trend is significant, corresponding to the regression coefficient B. A significant ascending trend was observed during the registration period for non-descended testis (+4.57 %; CI 0.64-8.87), Potter sequence (+7.70 %; CI 0.84-15.67) and omphalocele
(+6.78 %; CI 0.83-13.58). A significant decreasing trend, according to a negative regression coefficient B and a not effective non-linear percentage can be observed for rectum- and anal atresia/-stenosis and preaxial polydactyly.

All other 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, no decision regarding a more frequently increase or decrease can be made even though the non-linear percentage is not decisive for the trend evaluation.

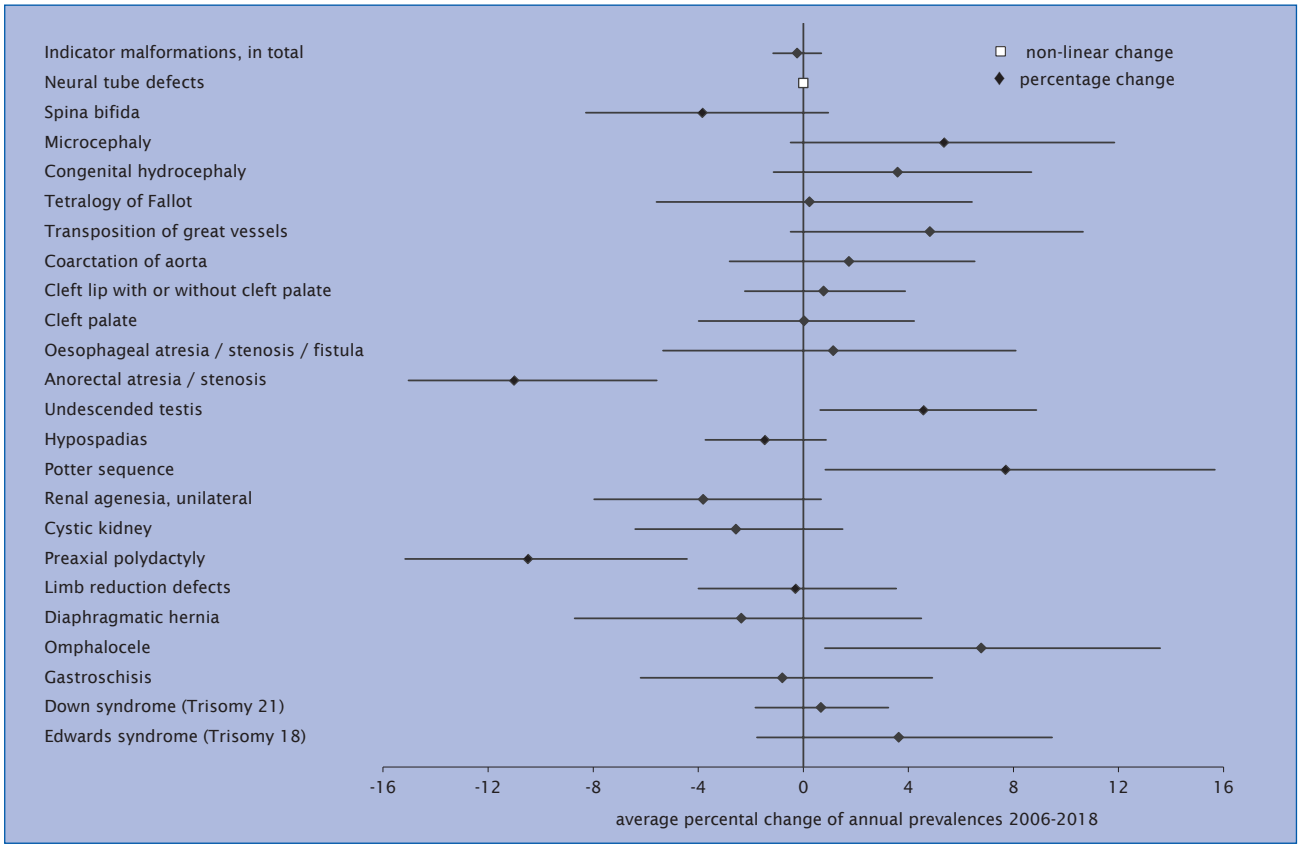



Fig. 45: Trend analysis 2006 - 2018 with average percental change of prevalence per year (95% confidence interval)

| | Regression coefficient B in % | confidence interval (CI of 95 %) |
|---|---|---|
| Indicator malformations, in total | -0.23 | -1.15 bis 0.69 |
| Spina bifida | -3.84 | -8.27 bis 0.95 |
| Microcephaly | 5.35 | -0.48 bis 11.84 |
| Congenital hydrocephaly | 3.59 | -1.14 bis 8.68 |
| Tetralogy of Fallot | 0.24 | -5.58 bis 6.42 |
| Transposition of the great vessels | 4.82 | -0.48 bis 10.65 |
| Coarctation of aorta | 1.74 | -2.81 bis 6.53 |
| Cleft lip with or without cleft palate | 0.78 | -2.23 bis 3.88 |
| Cleft palate | 0.04 | -3.98 bis 4.22 |
| Oesophageal atresia/stenosis/fistula | 1.15 | -5.34 bis 8.09 |
| Anorectal atresia/stenosis | -11.01 | -15.03 bis -5.58 |
| Undescended testis | 4.57 | 0.64 bis 8.87 |
| Hypospadias | -1.47 | -3.73 bis 0.86 |
| Potter sequence | 7.70 | 0.84 bis 15.67 |
| Renal agenesis, unilateral | -3.81 | -7.96 bis 0.67 |
| Cystic kidney | -2.57 | -6.40 bis 1.49 |
| Preaxial polydactyly | -10.49 | -15.16 bis -4.43 |
| Limb reduction defects | -0.30 | -4.00 bis 3.54 |
| Diaphragmatic hernia | -2.36 | -8.70 bis 4.49 |
| Omphalocele | 6.78 | 0.83 bis 13.58 |
| Gastroschisis | -0.80 | -6.19 bis 4.91 |
| Down syndrome (Trisomy 21) | 0.68 | -1.82 bis 3.24 |
| Edwards syndrome (Trisomy 18) | 3.63 | -1.77 bis 9.47 |

# 15 Summary

The present annual report about frequency of congenital malformations and anomalies as well as genetically caused diseases is the 20th of its kind that is based on malformation reports from the entire Federal State of Saxony-Anhalt. The nationwide malformation data received by the malformation monitoring is evaluated, sorted and under application of the number of births population-based, statistically analysed by the Statistical Office Saxony-Anhalt. The values indicated by EUROCAT for whole Europe are compared with the calculated prevalences of the indicator malformations. There is no comparative data from other Federal States.

For the year 2018, the Land Statistical Office indicates **17,410 live births**. Since we registered a peak in 2016 (18,092) the number is declining again, but in 2018 it lies still above the average of the years 2006-2017 (17.282).

The Land Statistical Office registered **87 stillbirths** in 2018. Based on the number of live- and stillbirths from 2006-2017, only 69 stillbirths would have been expected in relation to the number of live births.

According to the Federal Statistical Office 787,523 children were born in 2018, slightly more than in 2017 (784,901), but less than 2016 (792.141). About 2.2 % of all newborns in Germany are from the Federal state of Saxony-Anhalt.

In addition to data from live and stillbirths, the prevalences that are presented in the annual report 2018 are based on data of **89 terminations of pregnancy** and **31 spontaneous abortions after 16 WOG`s**. The statistical calculation of the report is therefore based on a **total number of 17,617 births** in 2018 (chapter 2).

**661 births** (3.75 % of all births) showed a **major malformation** in 2018. For the fourth year in a row, the malformation rate is above the basis prevalence (2006-2017: 3.58 %, CI 3.50 to 3.66 %) (Chapter 8). 563 (85.2%) of infants/foetuses with major malformations were live births in 2018. 17 of these infants (2.6 %) died during their first year of life. The percentage of terminations of pregnancy reached a maximum value with 13 % in 2018 (chapter 7,8).

As every year, the **most frequent single diagnoses** are VSD and ASD. In 2018, both cardiac malformations were registered more often than usual with values of 1.21% and 0.51%. Hearing loss, the third most common malformation in 2018, appeared also more frequently as usual with a value of 0.27%. 0.25% of all children/foetuses were affected by Down syndrome in 2018, significantly more than expected (Chapter 11).

1.39 % of all births were affected by one of the 36 exact defined indicator malformation (chapter 12) in 2018.

Compared to the respective basis prevalences, **higher prevalences** were calculated for oesophageal atresia/-stenosis/-fistula, diaphragmatic hernia, omphalocele, Down syndrome and Edwards syndrome. In contrast, **lower prevalences** were calculated for neural tube defects, spina bifida, encephalocele, microcephaly, Tetralogy of Fallot, left heart hypoplasia, cleft palate, rectal and anal atresia/-stenose, epispadias, preaxial polydactyly and limb reduction malformations.

In 2018, the monitoring of congenital malformations received information about **86 malformation caused terminations of pregnancy**. The analysis shows different points of termination depending on the malformation. Malformations of the CNS (14.0 %) are discovered at the latest and pregnancies are terminated at an average of 19.8 weeks of gestations. In contrast to that, foetuses with chromosomal aberrations (51.2 %) and multiple anomalies and other malformations (34.9 %) are aborted with 18.1 resp. 13.3 WOG`s.

**A genetically caused/correlated disease or microdeletion** was detected at 38 births in 2018. A **sequence, association or complex** was detected at 17 births. Five infants showed a **foetopathy**, two births suffered from the results of a **congenital infection**. Also in this year, at more than half of the77 births with a chromosomal aberration, a Down syndrome (44x) was diagnosed (chapter 13).

Chapter 16.1 of the current Annual Report discusses the occurrence of the five most frequent numerical chromosomal aberrations in Saxony-Anhalt since 2000. The annual prevalences are shown in general and for live births in particular as well as the trend over the years. In addition, in view of the current media interest, Chapter 16.2 deals with limb reduction malformations in Saxony-Anhalt.

The monitoring of congenital malformations received in 2018 **2,044 reportings** about 1,767 births. These include data from children and foetuses with at least one major malformation (661) and data from children/ foetuses with minor malformations or anomalies (278) and control data from children without malformations or anomalies. Control data from infants without malformations is necessary, as risk evaluation can only be made in scientific founded analyses when both groups are compared.

A solid data base was created by the help of our engaged colleagues from different medical institutions which are reporting voluntary and selfless congenital malformations to the monitoring of congenital malformations for many years. By receiving these reports, we created a solid data basis which serves to create our report annually, also in 2018. **We would like to thank all „senders“ and hope that this excellent cooperation will continue!**

# 16. Focus Theme

## 16.1 Chromosomal aberrations - Epidemiological aspects

Chromosomal aberrations are disorders of the number of chromosomes (diploid chromosome number 46, 23 chromosome pairs, thereof 22 autosomes and two sex chromosomes) or of the structure of a chromosome (balanced and unbalanced rearrangements). One, two or more chromosomes can be concerned or just a part of the chromosome. Congenital malformations, growth disorders and mental disabilities are the most common findings at humans with chromosomal aberrations. Apart from that, also cytogenetic aberrations are existing, which have only little or no clinical impact. Progress in human cytogenetics increasingly permit to demonstrate a causal relation between different chromosomal anomalies and different phenotypic manifestations at the patients. Furthermore, specific chromosomal aetiologies of a large number of syndromes are known.

Structural chromosomal anomalies, which are also called chromosomal mutations include changes that are resulting from one or more chromosomal breaks. These can lead to a shift of chromosome regions. These shifts or rearrangements take place without the loss of genetic material or duplication of material (balanced rearrangements). Or they can lead to an increase or loss of chromosomal material (unbalanced rearrangements). Balanced rearrangements are frequently inherited and are often not connected with phenotypic abnormalities. But there are two exceptions: if a breakpoint is involved that directly interferes with a gene/gene function as well as the relocation of chromosomal material from an X chromosome to an autosome or reverse. Unbalanced rearrangements lead to a partial trisomy or monosomy and are well known as cause for congenital anomalies or development delays.

At the submicroscopic level, gene mutations such as substitutions, insertions, deletions, duplications, nucleotide repeat expansions and inversions of single base pairs are usually too small. They cannot be identified by standard karyotyping and require a DNA analysis as evidence. These submicroscopic mutations can be as small as a change in a single base pair or as large as megabase DNA sequence segments in very large genes.

In the following, the focus lies on numerical chromosomal aberrations, since they are the most common.

### Prevalence and live births prevalence of trisomy 21

Trisomy 21 (Down syndrome) is still the most common chromosomal anomaly at neworns. The prevalence and live births prevalence of trisomy 21 and other trisomies depends on demographic particularities (maternal age) and differences in prenatal diagnostic procedures. Figure 48 (page 76) shows a comparison of prevalence and live births prevalence of trisomy 21.

It has been known for a long time that the maternal age-specific rate of trisomy 21 and other chromosomal abnormalities at diagnosis in the early second trimester through prenatal diagnosis (amniocentesis) is about 30% higher than in the case of postnatal diagnosis. These differences can be partly explained by a spontaneous foetal loss (after the early second trimester) at foetuses with chromosomal abnormalities [1–4].

A EUROCAT study of 2013 showed, with the inclusion of our data and another 20 population-related registers, an increase of the overall prevalence of trisomy 21 over time to 22 per 10,000 births. From 1990 to 2009, this comprised 6.1 million births (95 % CI 21.7-22.4) (1 of 455 births) [5].

This change is also caused by an increase of the maternal delivery age of 35 years and older from 13% in 1990 to 19% in 2009. At the same time, the prevalence of trisomy 13, 18 and 21 remained stable at live births (1 of 20,830 at trisomy 13, 1 of 9,614 at trisomy 18 and 1 of 890 at trisomy 21).
The rise of maternal age has resulted in Europe to an increase of the number of pregnancies with trisomy 21. The stable prevalence of live births compared to the increase of the total prevalence results most likely from an improved prenatal screening and increased foetal loss rate (spontaneous abortions, abortions) [5].

### Prevalence and live births prevalence of trisomy 18 and 13

Trisomy 18 and trisomy 13 are after trisomy 21 the second and third most common autosomal trisomies. The prevalence indications of trisomy 13 range from 1.9 to 2.8 and for trisomy 18 from 4.8 to 7 per 10,000 births resulting from studies in Great Britain and Europe during the last twenty years [5–8].

The reported live births prevalence of trisomy 13 lies at 0.43-0.54 and of trisomy 18 at 0.96-1.12 per 10,000 births [5]. The prevalence of these trisomies is also increasing, which is largely due to the increasing maternal age and improved prenatal ultrasound technique [5, 9, 10].

Both trisomy 13 and trisomy 18, also known as Patau and Edwards Syndrome, are associated with a large number of congenital malformations. These include cardiac malformations, orofacial clefts, abdominal wall defects (omphalocele), tracheo-oesophageal stenosis or atresia, urogenital malformations, limb or CNS malformations [6, 11]. These associated malformations allow a suspected diagnosis to be made in many cases by prenatal ultrasound screening. The diagnosis can then be confirmed by cytogenetic analysis. In risk pregnancies, trisomy 21, 18 and 13 can be detected in prenatal screening since 2012 by cell-free DNA analysis from maternal blood.

Trisomy 13 and trisomy 18 are associated with a bad prognosis and most live births die within the first days or weeks of their life [5–8, 12, 13]. The median survival rate for live births with trisomy13/trisomy18 is reported in the literature to be 10 to 14 days, the 1-year survival rate is about 8-10% [13, 14].

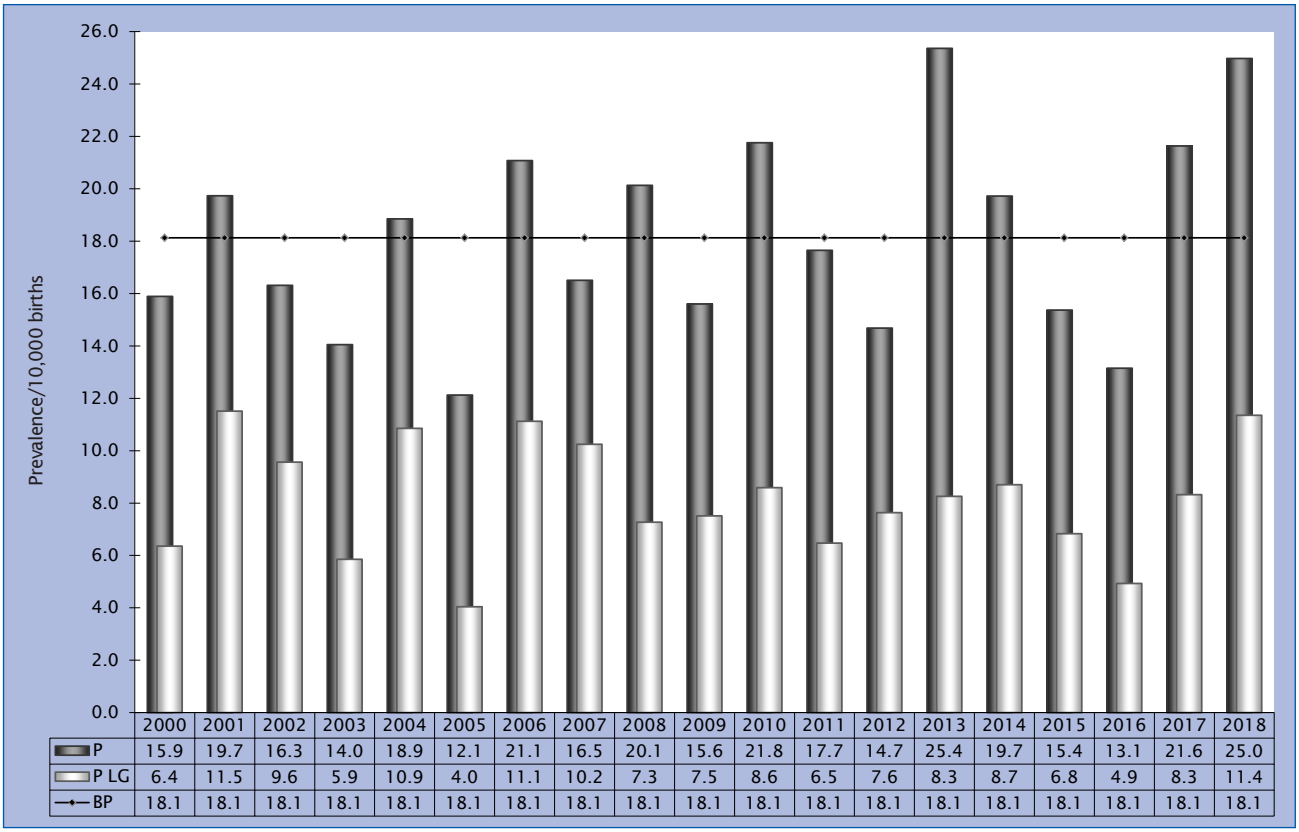
In 2019, the WHO associated network ICBDSR was able to publish a study about the mortality of trisomy 13 and 18, including data from Saxony-Anhalt and further 23 population-based registers from a total number of 18 countries (North and South America, Asia, Europe) [15].

The study population comprised in the period from 1974 to 2014 about 27.1 million births. The prevalence of trisomy 13 was 1.68 (95% CI 1.3-2.06) and the prevalence of trisomy 18 4.08 (95% CI 3.01-5.15) per 10,000 births.

The average live births prevalence in this study was 0.55 (95 % CI 0.38- 0.72) for trisomy 13 and for trisomy 18 1.07 (95 % CI 0.77-1.38) per 10,000 births. The median mortality in the first week of life was 48 % for trisomy 13 and 42 % for trisomy 18 in all registers. Half of these live births died on the first day of life. In 16 registers with complete 1-year follow-up monitoring the mortality was during the first year at 87 % for trisomy 13 and at 88% for trisomy 18. About half of the live births died during the first week of life. However, it could also be shown that about 10% survived the first year of life [16].

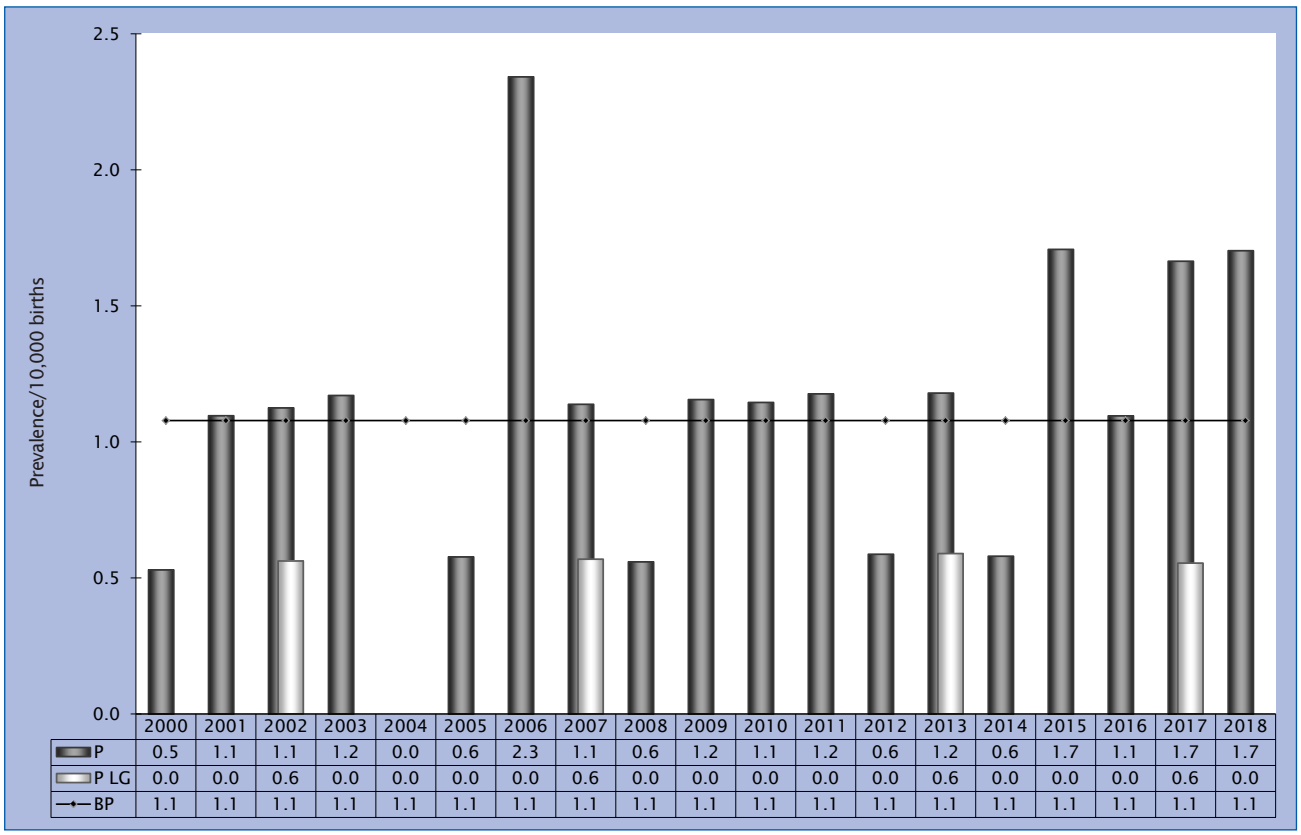
## Numeric chromosomal aberrations – data from Saxony-Anhalt

Data of 333,783 pregnancies (concerns 330,600 live births) for the three most frequent autosomal aneuploidies (trisomy 21, 18, 13) and the two most frequent sex chromosomal aneuploidies with 45, X0 (Turner syndrome) and 47, XXY (Klinefelter syndrome) was analysed for the time period of 2000 to 2018. This was done with regard to prevalence and live birth prevalence.
Chapter 13.1 (page 66) of the present annual report gives a detailed analysis of the maternal age at chromosomal aberrations.



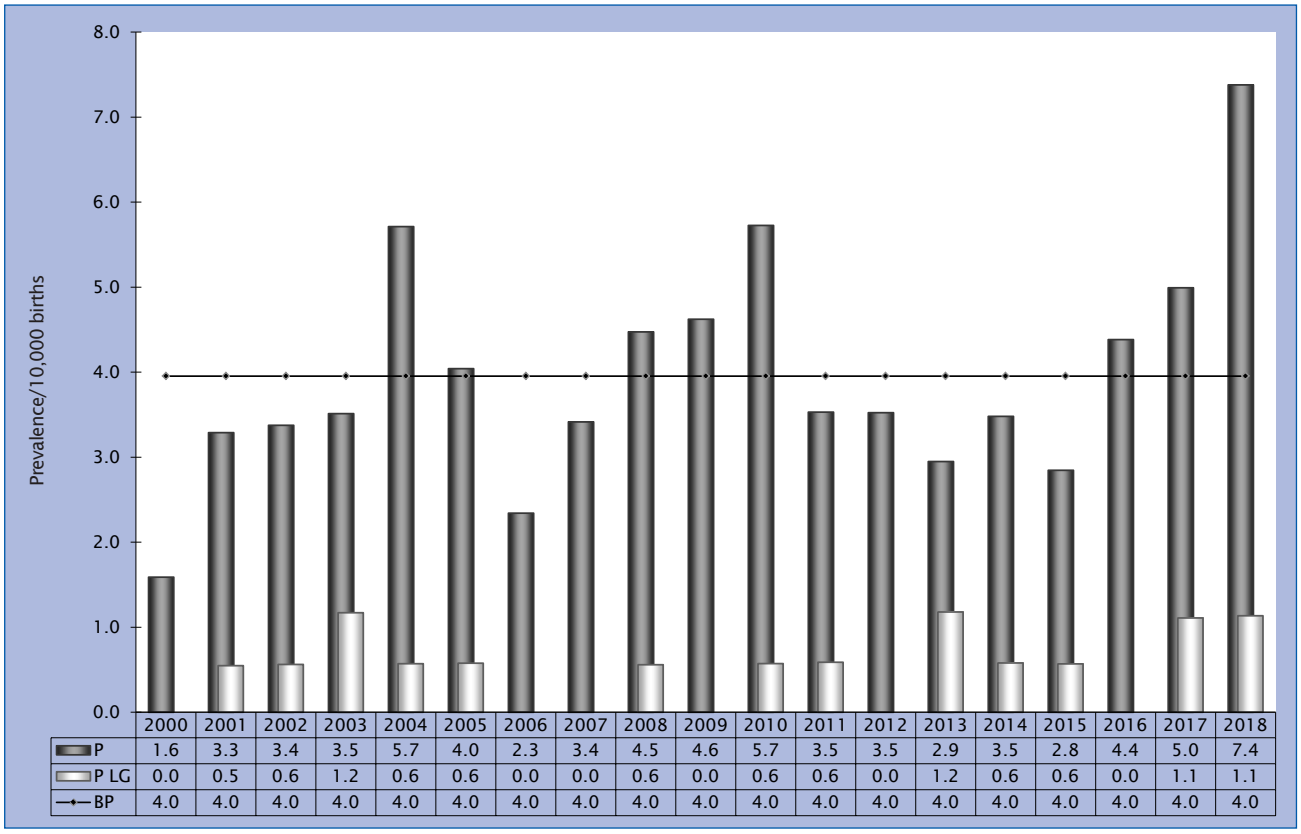

| | 2000 | 2001 | 2002 | 2003 | 2004 | 2005 | 2006 | 2007 | 2008 | 2009 | 2010 | 2011 | 2012 | 2013 | 2014 | 2015 | 2016 | 2017 | 2018 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| P | 15.9 | 19.7 | 16.3 | 14.0 | 18.9 | 12.1 | 21.1 | 16.5 | 20.1 | 15.6 | 21.8 | 17.7 | 14.7 | 25.4 | 19.7 | 15.4 | 13.1 | 21.6 | 25.0 |
| P LG | 6.4 | 11.5 | 9.6 | 5.9 | 10.9 | 4.0 | 11.1 | 10.2 | 7.3 | 7.5 | 8.6 | 6.5 | 7.6 | 8.3 | 8.7 | 6.8 | 4.9 | 8.3 | 11.4 |
| BP | 18.1 | 18.1 | 18.1 | 18.1 | 18.1 | 18.1 | 18.1 | 18.1 | 18.1 | 18.1 | 18.1 | 18.1 | 18.1 | 18.1 | 18.1 | 18.1 | 18.1 | 18.1 | 18.1 |

Fig. 48: Development of prevalence and live births prevalence per 10,000 births at Down syndrome (trisomy 21) since 2000



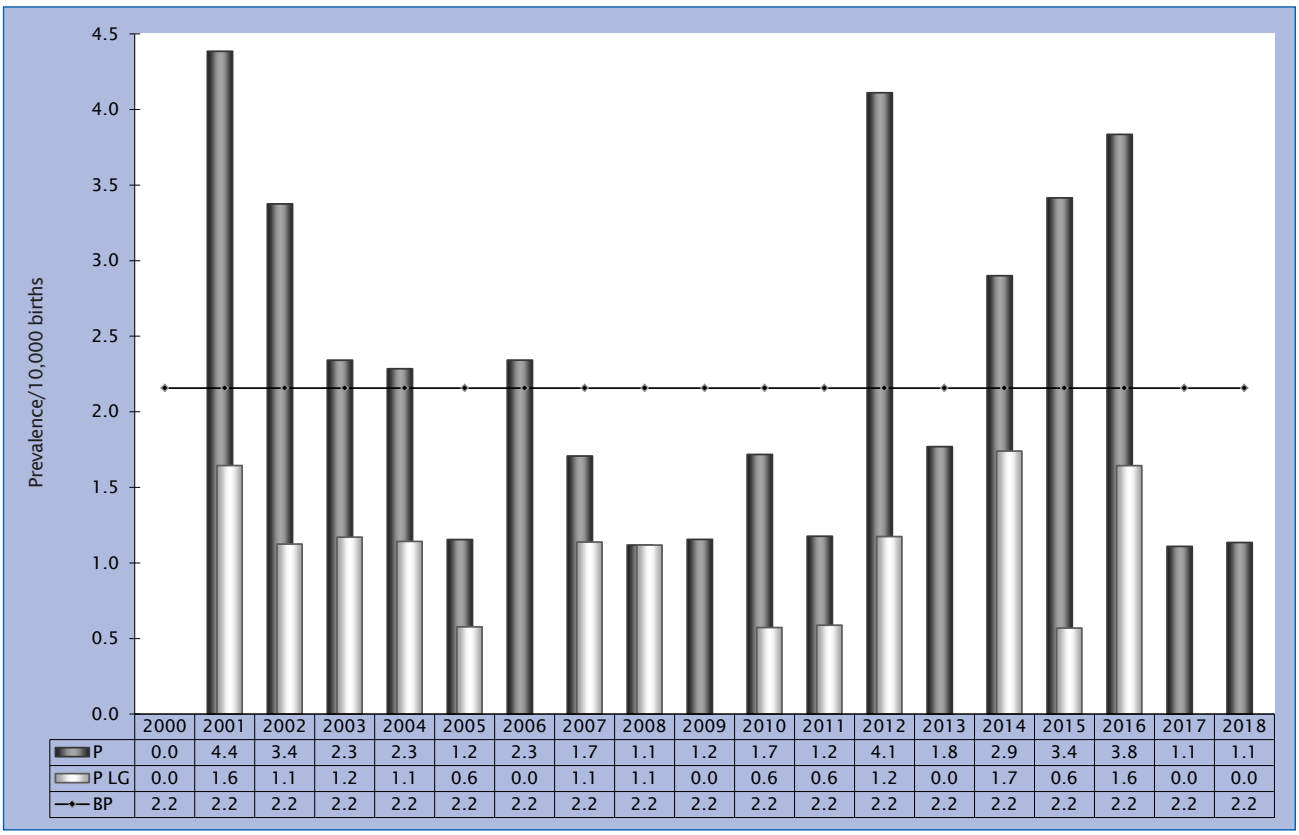

| | 2000 | 2001 | 2002 | 2003 | 2004 | 2005 | 2006 | 2007 | 2008 | 2009 | 2010 | 2011 | 2012 | 2013 | 2014 | 2015 | 2016 | 2017 | 2018 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| P | 0.5 | 1.1 | 1.1 | 1.2 | 0.0 | 0.6 | 2.3 | 1.1 | 0.6 | 1.2 | 1.1 | 1.2 | 0.6 | 1.2 | 0.6 | 1.7 | 1.1 | 1.7 | 1.7 |
| P LG | 0.0 | 0.0 | 0.6 | 0.0 | 0.0 | 0.0 | 0.0 | 0.6 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.6 | 0.0 | 0.0 | 0.0 | 0.6 | 0.0 |
| BP | 1.1 | 1.1 | 1.1 | 1.1 | 1.1 | 1.1 | 1.1 | 1.1 | 1.1 | 1.1 | 1.1 | 1.1 | 1.1 | 1.1 | 1.1 | 1.1 | 1.1 | 1.1 | 1.1 |

Fig. 49: Development of prevalence and live births prevalence per 10,000 births at Patau syndrome (trisomy 13) since 2000



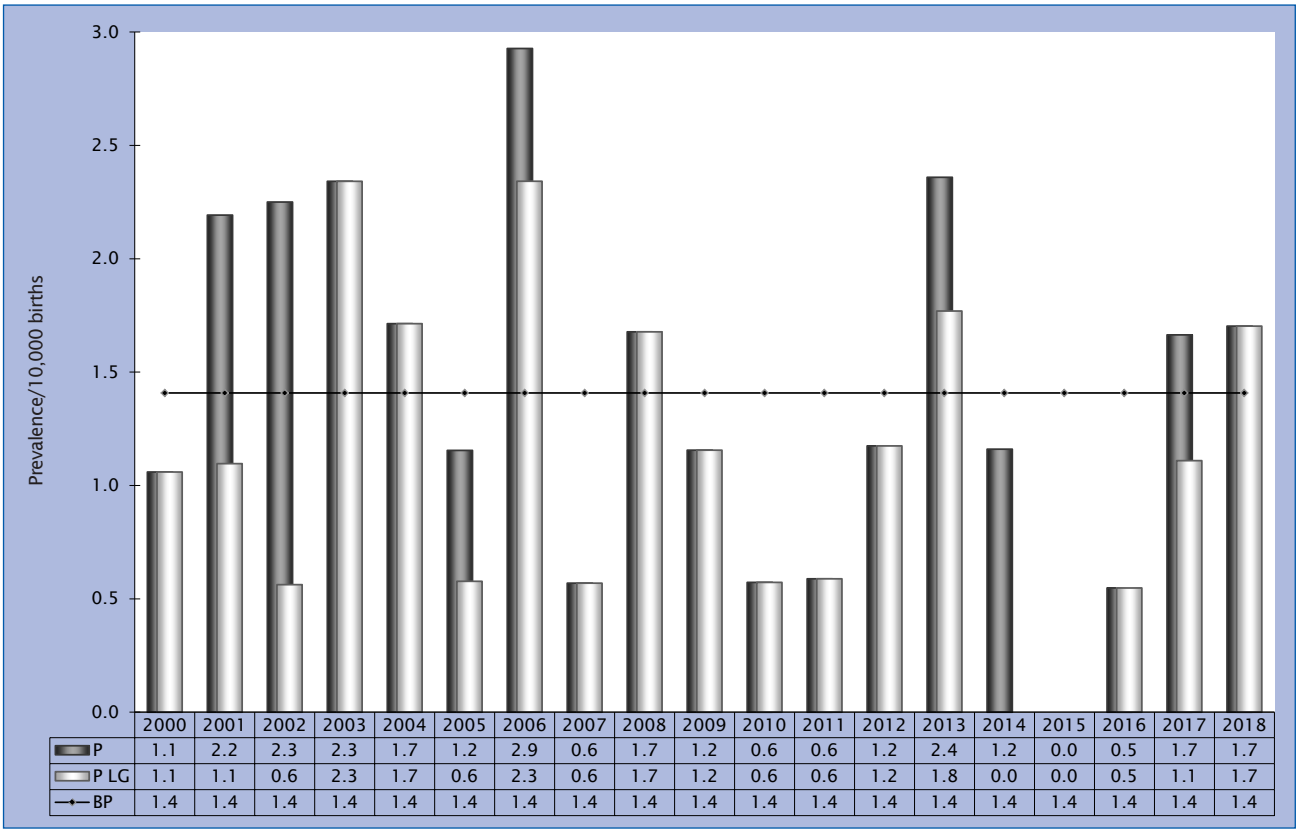

| | 2000 | 2001 | 2002 | 2003 | 2004 | 2005 | 2006 | 2007 | 2008 | 2009 | 2010 | 2011 | 2012 | 2013 | 2014 | 2015 | 2016 | 2017 | 2018 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| P | 1.6 | 3.3 | 3.4 | 3.5 | 5.7 | 4.0 | 2.3 | 3.4 | 4.5 | 4.6 | 5.7 | 3.5 | 3.5 | 2.9 | 3.5 | 2.8 | 4.4 | 5.0 | 7.4 |
| P LG | 0.0 | 0.5 | 0.6 | 1.2 | 0.6 | 0.6 | 0.0 | 0.0 | 0.6 | 0.0 | 0.6 | 0.6 | 0.0 | 1.2 | 0.6 | 0.6 | 0.0 | 1.1 | 1.1 |
| BP | 4.0 | 4.0 | 4.0 | 4.0 | 4.0 | 4.0 | 4.0 | 4.0 | 4.0 | 4.0 | 4.0 | 4.0 | 4.0 | 4.0 | 4.0 | 4.0 | 4.0 | 4.0 | 4.0 |

Fig. 50: Development of prevalence and live births prevalence per 10,000 births at Edwards syndrome (trisomy 18) since 2000




| | 2000 | 2001 | 2002 | 2003 | 2004 | 2005 | 2006 | 2007 | 2008 | 2009 | 2010 | 2011 | 2012 | 2013 | 2014 | 2015 | 2016 | 2017 | 2018 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| P | 0.0 | 4.4 | 3.4 | 2.3 | 2.3 | 1.2 | 2.3 | 1.7 | 1.1 | 1.2 | 1.7 | 1.2 | 4.1 | 1.8 | 2.9 | 3.4 | 3.8 | 1.1 | 1.1 |
| P LG | 0.0 | 1.6 | 1.1 | 1.2 | 1.1 | 0.6 | 0.0 | 1.1 | 1.1 | 0.0 | 0.6 | 0.6 | 1.2 | 0.0 | 1.7 | 0.6 | 1.6 | 0.0 | 0.0 |
| BP | 2.2 | 2.2 | 2.2 | 2.2 | 2.2 | 2.2 | 2.2 | 2.2 | 2.2 | 2.2 | 2.2 | 2.2 | 2.2 | 2.2 | 2.2 | 2.2 | 2.2 | 2.2 | 2.2 |

Fig. 51: Development of prevalence and live births prevalence per 10,000 births at Turner syndrome since 2000




| | 2000 | 2001 | 2002 | 2003 | 2004 | 2005 | 2006 | 2007 | 2008 | 2009 | 2010 | 2011 | 2012 | 2013 | 2014 | 2015 | 2016 | 2017 | 2018 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| P | 1.1 | 2.2 | 2.3 | 2.3 | 1.7 | 1.2 | 2.9 | 0.6 | 1.7 | 1.2 | 0.6 | 0.6 | 1.2 | 2.4 | 1.2 | 0.0 | 0.5 | 1.7 | 1.7 |
| P LG | 1.1 | 1.1 | 0.6 | 2.3 | 1.7 | 0.6 | 2.3 | 0.6 | 1.7 | 1.2 | 0.6 | 0.6 | 1.2 | 1.8 | 0.0 | 0.0 | 0.5 | 1.1 | 1.7 |
| BP | 1.4 | 1.4 | 1.4 | 1.4 | 1.4 | 1.4 | 1.4 | 1.4 | 1.4 | 1.4 | 1.4 | 1.4 | 1.4 | 1.4 | 1.4 | 1.4 | 1.4 | 1.4 | 1.4 |

Fig. 52: Development of prevalence and live births prevalence per 10,000 births at Klinefelter syndrome since 2000

A corresponding trend analysis with two-year grouping shows no significant increase of one the five selected aneuploidies for the period of 2001 to 2018 (figure 53).

Binary logistic regression based on the maximum likelihood method was used for the analysis. Details of the description of the mathematical model can be found in chapter 12.37 on page 64.

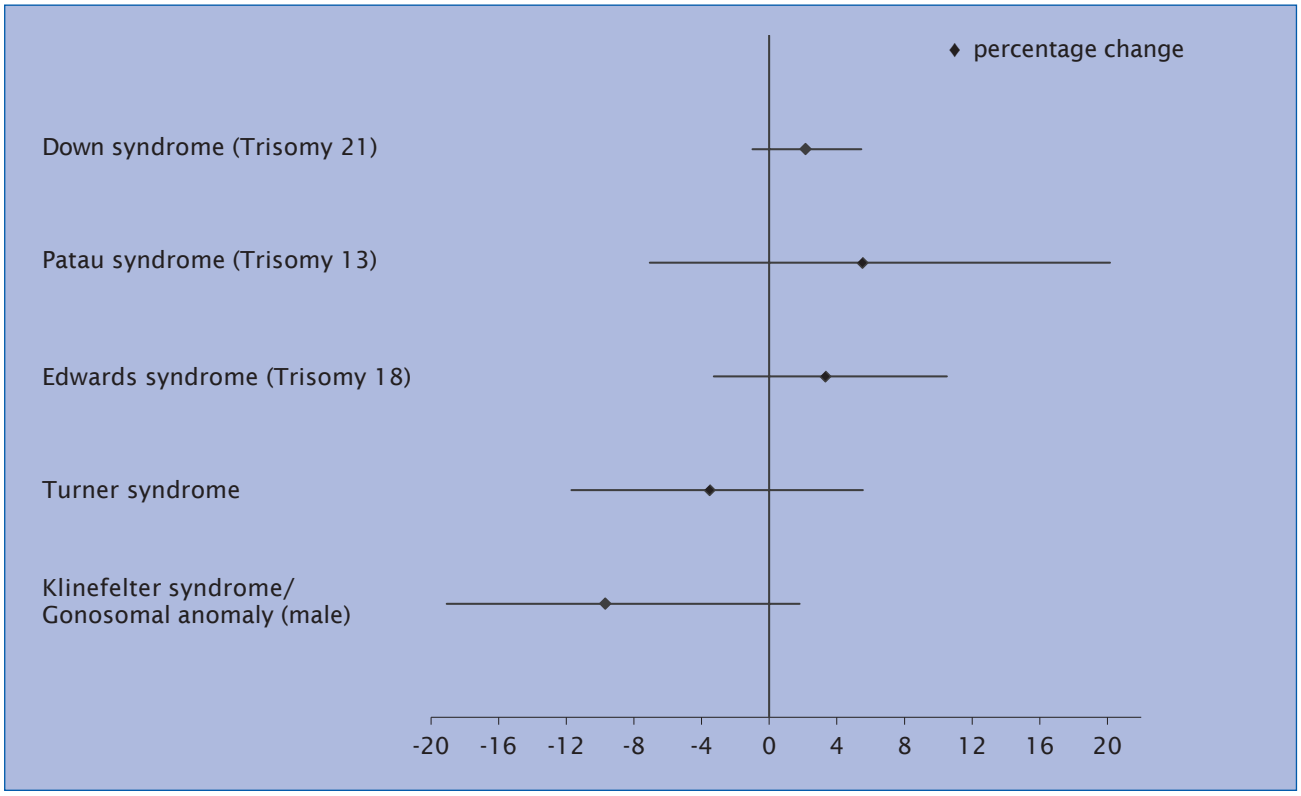



Fig. 53: Trend analysis of selected chromosomal aberrations 2001 to 2018 with average percentage change of the two-years prevalence (95 % CI)

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# 16.2 Limb malformations in Saxony-Anhalt

Malformations of the hand at newborns were in the focus of media attention in September 2019. This is the basis for the following presentation of data about reduction malformations of the extremities (malformations of hand, arm, leg and/or foot).

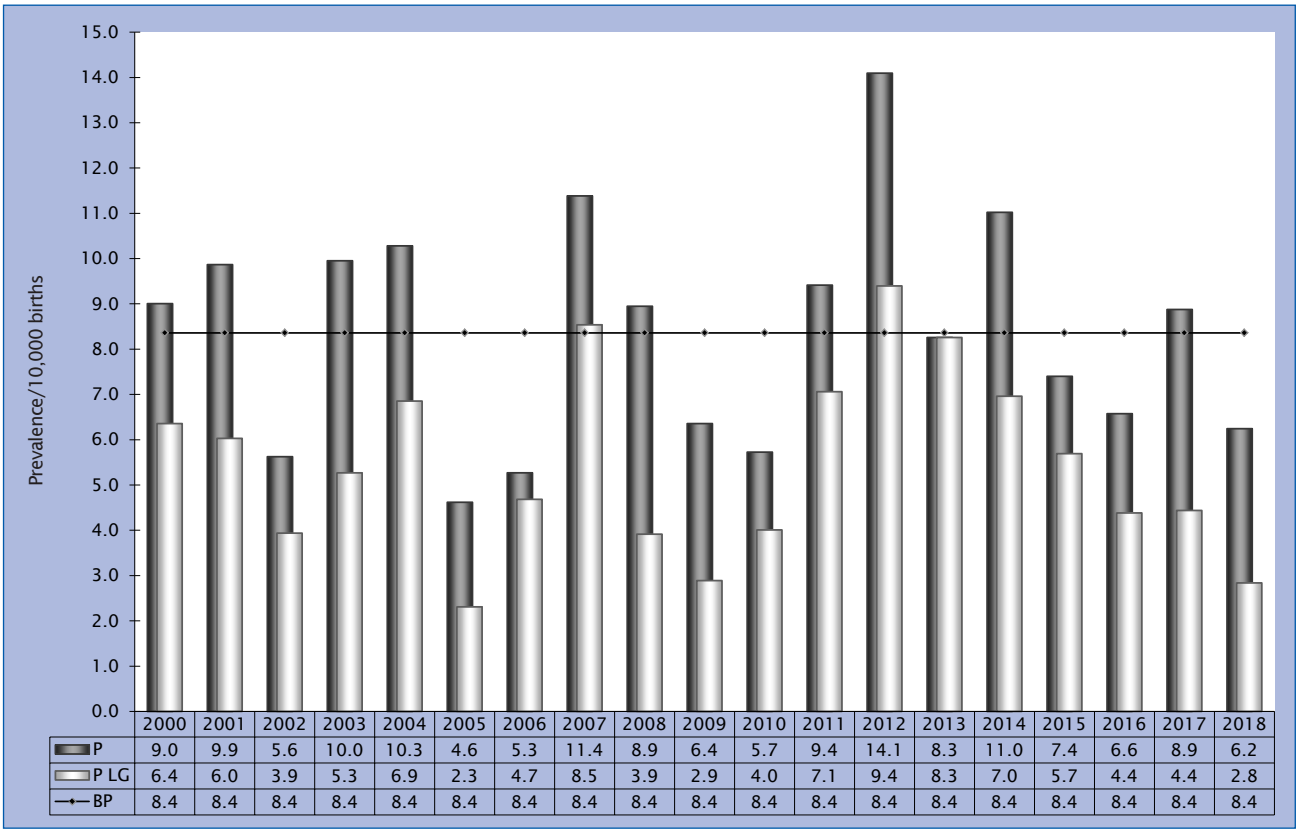
The epidemiological data analysis includes 17,617 pregnancies in 2018 in the Federal State of Saxony-Anhalt. In total, information about 333,783 pregnancies was analysed during the time period of 2000 to 2018. In this analysis, 661 pregnancies (1 of 27 pregnancies) were affected by major malformations in 2018.

Congenital malformations, in particular malformations of the hands, arms, feet and/or legs, occur regularly with varying frequency (see figures with presentation of different prevalence per year).
In 2018, one limb reduction defect per 1,602 births was registered in Saxony-Anhalt. In comparison to the reporting period since 2000, a regressing trend can be identified in the region. Figure 54 and 55 show the natural fluctuations of frequencies in the single years and the resulting average value for the reduction malformations in total (Figure 54) and the reduction malformations of the upper limbs (Figure 55). The analysis of current data gives no reason for a locally or temporally conspicuous unusual accumulation of limb malformations in Saxony-Anhalt.

The experiences in the epidemiology of malformations are continuously documented for you as interested reader in form of this annual report. Anomalies of individual medicine, such as hand malformations of infants, which recently have been the subject of much publicity and excitement underline the importance of a prospective malformation detection and analysis in the population-based epidemiology. This is the only way to make valid statements about current phenomena of accumulations and their classification in the temporal trend. With help of mathematical models, they can be calculated on the basis of basic data. For further analyses, it is advisable to have a competent examination of the individual cases with regard to external factors and genetic evaluation.

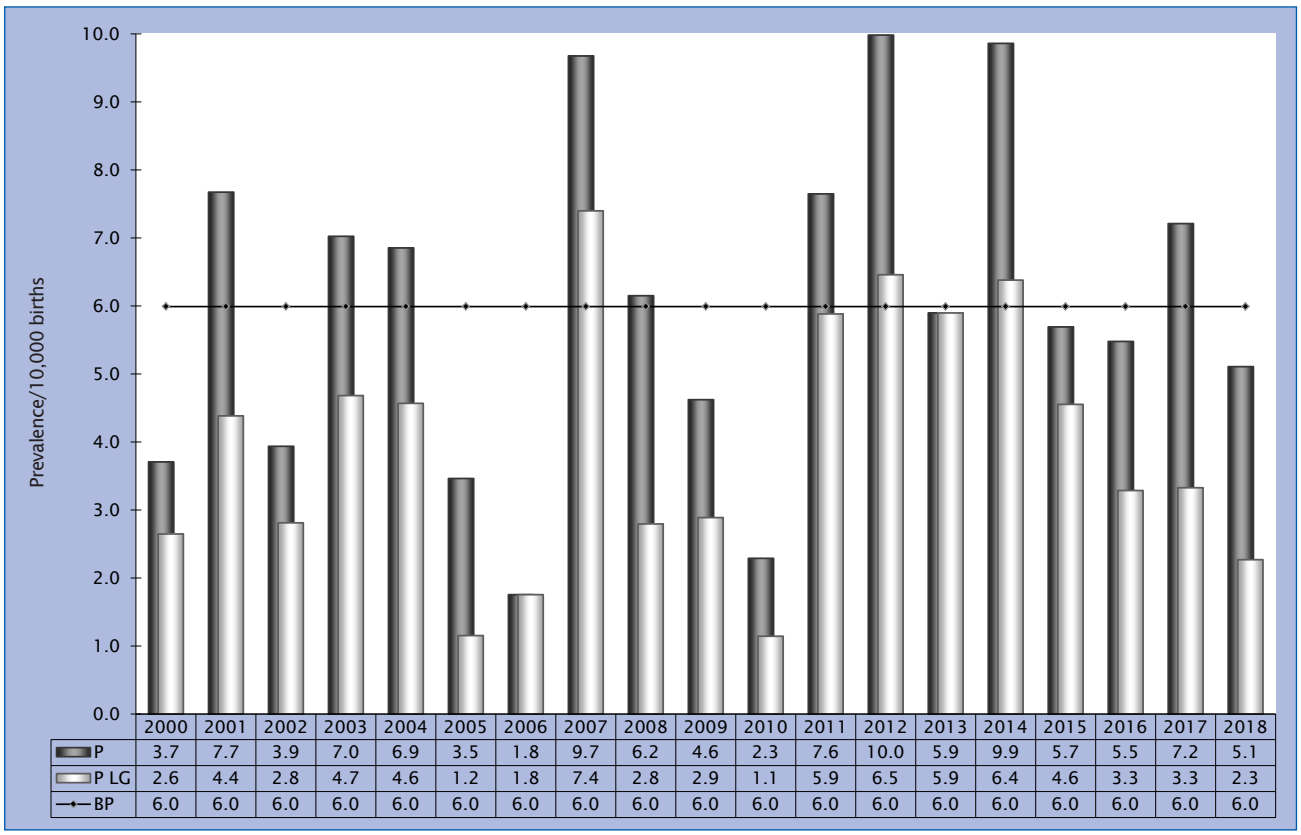
Causes for congenital malformations are multifactorial. Possible causes are not only genetic defects, infections, drugs, chemical noxae, mechanical effects and/or developmental physiological deficits. In 50% of cases the cause still remains unexplained despite all methods of modern medicine.

Accumulations of malformations in Saxony-Anhalt could be determined in connection with improved prenatal diagnostics (e.g. at cardiac malformations) and the increased maternal age (e.g. chromosomal aberrations see Chapter 16.1) in the previous years. These are risk factors that cannot be influenced.




| | 2000 | 2001 | 2002 | 2003 | 2004 | 2005 | 2006 | 2007 | 2008 | 2009 | 2010 | 2011 | 2012 | 2013 | 2014 | 2015 | 2016 | 2017 | 2018 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| P | 9.0 | 9.9 | 5.6 | 10.0 | 10.3 | 4.6 | 5.3 | 11.4 | 8.9 | 6.4 | 5.7 | 9.4 | 14.1 | 8.3 | 11.0 | 7.4 | 6.6 | 8.9 | 6.2 |
| P LG | 6.4 | 6.0 | 3.9 | 5.3 | 6.9 | 2.3 | 4.7 | 8.5 | 3.9 | 2.9 | 4.0 | 7.1 | 9.4 | 8.3 | 7.0 | 5.7 | 4.4 | 4.4 | 2.8 |
| BP | 8.4 | 8.4 | 8.4 | 8.4 | 8.4 | 8.4 | 8.4 | 8.4 | 8.4 | 8.4 | 8.4 | 8.4 | 8.4 | 8.4 | 8.4 | 8.4 | 8.4 | 8.4 | 8.4 |

Fig. 54: Development of prevalence and live birth prevalence per 10,000 births with reduction malformations of upper and/or lower limbs since 2000




| | 2000 | 2001 | 2002 | 2003 | 2004 | 2005 | 2006 | 2007 | 2008 | 2009 | 2010 | 2011 | 2012 | 2013 | 2014 | 2015 | 2016 | 2017 | 2018 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| P | 3.7 | 7.7 | 3.9 | 7.0 | 6.9 | 3.5 | 1.8 | 9.7 | 6.2 | 4.6 | 2.3 | 7.6 | 10.0 | 5.9 | 9.9 | 5.7 | 5.5 | 7.2 | 5.1 |
| P LG | 2.6 | 4.4 | 2.8 | 4.7 | 4.6 | 1.2 | 1.8 | 7.4 | 2.8 | 2.9 | 1.1 | 5.9 | 6.5 | 5.9 | 6.4 | 4.6 | 3.3 | 3.3 | 2.3 |
| BP | 6.0 | 6.0 | 6.0 | 6.0 | 6.0 | 6.0 | 6.0 | 6.0 | 6.0 | 6.0 | 6.0 | 6.0 | 6.0 | 6.0 | 6.0 | 6.0 | 6.0 | 6.0 | 6.0 |

Fig. 55: Development of the prevalence and live birth prevalence per 10,000 births of reduction malformations of the upper limbs since 2000

In general, however, it is necessary to minimize known influenceable risk factors. For example, alcohol, drugs and/or nicotine during pregnancy should be avoided. The timely intake of folic acid (already from the desire to have children) is also an established prevention measure.

Region-specific risk factors, average maternal age and socio-economic characteristics mean that data from Saxony-Anhalt cannot be transferred unconditionally to other Federal States. However, there is currently no nationwide registration of malformations in Germany. Experiences from Saxony-Anhalt show that an extension of monitoring to the Central German region (plus Saxony and Thuringia) appears to be quite possible. A corresponding interest from medical colleagues in management responsibility from these Federal States was expressed.

# 18 Newborn Hearing Screening 2018

## 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 Guidline** issued by the **Federal Joint Committee (G-BA)** on 19-06-2008.

The Children Guidline 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 births 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 Guidline **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 specific screening centre).

The Newborn Hearing Screening Guidline stipulates that the hearing screening should be performed via **AABR** at **children with an increased risk for congenital hearing disorder**.
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 (> 2 days)
- hyperbilirubinemia (exchange transfusion)
- pre-, peri- or postnatal hypoxia (pH < 7.20)
- peri- and postnatal cerebral haemorrhage, 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 0-6 after 5 minutes

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

## Participating institutions

**23 maternity clinics** existed in Saxony-Anhalt in 2018. All these clinics offer a newborn hearing screening already for several years by TEOAE or AABR. These maternity clinics all participated 2018 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 are 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 tracking is also used by several midwifes. In this way also infants who are exclusively under care of a midwife (e.g. home births) can participate in the newborn hearing screening.

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

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

| Maternity clinics | Tracking period 2018 | Live births with Screening-ID in this period |
|---|---|---|
| AMEOS Klinikum Aschersleben | 01.01.-31.12.2018 | 485 |
| Gesundheitszentrum Bitterfeld/Wolfen | 01.01.-31.12.2018 | 456 |
| HELIOS Klinik Jerichower Land Burg | 01.01.-31.12.2018 | 376 |
| Städtisches Klinikum Dessau | 01.01.-31.12.2018 | 800 |
| Altmark-Klinikum Krankenhaus Gardelegen | 01.01.-31.12.2018 | 342 |
| AMEOS Klinikum Halberstadt | 01.01.-31.12.2018 | 523 |
| Krankenhaus St. Elisabeth und St. Barbara Halle | 01.01.-31.12.2018 | 2,220 |
| Universitätsklinikum Halle (Saale) | 01.01.-31.12.2018 | 1,306 |
| HELIOS Klinik Köthen | 01.01.-31.12.2018 | 431 |
| Krankenhaus St. Marienstift Magdeburg | 01.01.-31.12.2018 | 986 |
| Klinikum Magdeburg | 01.01.-31.12.2018 | 1,444 |
| Universitätsklinikum Magdeburg | 01.01.-31.12.2018 | 1,223 |
| Carl-von-Basedow-Klinikum Saalekreis Merseburg | 01.01.-31.12.2018 | 973 |
| Saale-Unstrut Klinikum Naumburg | 01.01.-31.12.2018 | 499 |
| Harzklinikum Dorothea Christiane Erxleben, Klinikum Quedlinburg | 01.01.-31.12.2018 | 535 |
| Altmark-Klinikum Krankenhaus Salzwedel | 01.01.-31.12.2018 | 402 |
| HELIOS Klinik Sangerhausen | 01.01.-31.12.2018 | 647 |
| AMEOS Klinikum Schönebeck | 01.01.-31.12.2018 | 503 |
| Johanniter-Krankenhaus Genthin-Stendal | 01.01.-31.12.2018 | 742 |
| Harzklinikum Dorothea Christiane Erxleben, Klinikum Wernigerode | 01.01.-31.12.2018 | 717 |
| Evangelisches Krankenhaus Paul Gerhardt Stift Wittenberg | 01.01.-31.12.2018 | 775 |
| Georgius-Agricola Klinikum Zeitz | 01.01.-31.12.2018 | 440 |
| HELIOS Klinik Zerbst/Anhalt | 01.01.-30.06.2018 | 95 |
| **Total number of live births with Screening-ID in Saxony-Anhalt** | | **16,920** |

| | | |
|---|---|---|
| Further live births with Screening-ID: e.g. home births / births in a birthing centre resp., infants not born in Saxony-Anhalt | 01.01.-31.12.2018 | 128 |

| | |
|---|---|
| **Tracked infants, in total** | **17,048** |

In total, **16,920 births** received a screening ID in their maternity clinic in Saxony-Anhalt in 2018. In this way, these infants could participate in the hearing screening tracking.

Furthermore, **128 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 **99 senders** in 2018.

Births with screening-ID and number of incoming result

| 2018 | Infants with screening ID | Number of reportings |
|---|---|---|
| January | 1,490 | 1,936 |
| February | 1,330 | 1,668 |
| March | 1,388 | 1,801 |
| April | 1,288 | 1,617 |
| May | 1,468 | 1,843 |
| June | 1,500 | 2,031 |
| July | 1,609 | 2,004 |
| August | 1,500 | 1,872 |
| September | 1,565 | 1,983 |
| October | 1,375 | 1,762 |
| November | 1,284 | 1,714 |
| December | 1,251 | 1,603 |
| **Total** | **17,048** | **21,834** |

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.
It becomes apparent that currently per month an average of approx. 1,820 reports can be expected, 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).

To carry out the tracking thoroughly, **2770 letters resp. faxes** (were forwarded in 2018 (one up to eight letters per infant). With reference to all infants with screening ID this corresponds to an average of 0.16 letters per infant. Additionally, the parents and attending physicians of the infants born in 2018 were contacted by telephone. In total, **222 calls** were made in connection with the hearing screening tracking (one up to four calls per infant).

## Results (date September 2019)

All results, that were reported to the hearing screening tracking centre about infants that were born in 2018 are included in our analyses 2018 of the newborn hearing screening:

**14,610 infants** out of **17,048 infants** with screening ID had an **unsuspicious newborn hearing screening result**.
In **2,438 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 2,438 infants showed in **1,571 cases** an **unsuspicious result**. The remaining **867 infants** had again a **suspicious result**.
**394** of these 867 infants received a **complete paediatric audiological confirmation diagnostic**. According to our knowledge, **224 infants** did **not receive a confirmation diagnostic** and therefore are considered as **lost to follow-up**.

**222 infants** did **not participate in the screening** (no reaction of parents to reminder letters or refusal of examination) and in **6 cases** the **status** ist still **pending**, i.e. the examinations were not finished in September 2019 or the tracking process still requires more time. In **21 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 421 infants** who were born in 2018 could be **completed (confirmations diagnostics)**. Among 394 infants with a suspicious result, 27 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 375 cases**. In **46 cases** a **hearing disorder was diagnosed** (32 x bilateral and 14 x unilateral hearing disorder) and the corresponding therapy was initiated. For instance, **32 infants** received a **hearing aid** (23 times hearing aid bilateral, 9 times hearing aid unilateral).

# 19 Annual Report 2018 of the Newborn Screening Centre Saxony-Anhalt

according to §13 to § 42 inclusive attachments of the valid Children Directive of the Federal Joint Committee about early detection of diseases at infants up t the end of their 6th year of life

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Kompetenznetz Neugeborenen-Screening
Berlin • Greifswald • Magdeburg • Weiden

## 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 initiation of a high-quality therapy for all infants with a treatable type of these diseases.
The Guidline of the Joint Federal Committee about the early detection of childhood diseases (Children's Guidline) stipulates the details of the newborn screening (NGS) and screening for cystic fibrosis (CF) in paragraphs 13 to 42.
The German Society of newborn screening (DGNS) compiles annually a national screening report in cooperation with the German screening laboratories (http://screening-dgns.de/reports.php). The screening data is analysed on the basis of distinctive realisation and quality criteria of the newborn screening in Germany which are defined by the Guidline.

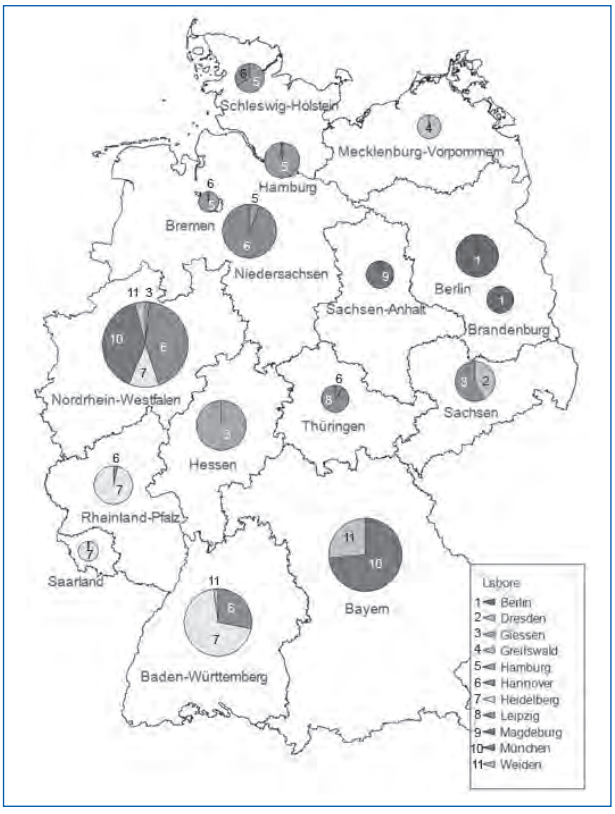


Fig. 1: Sample distribution of the screening centers in Germany[1]

The report only refers to congenital metabolic and endocrinologic diseases which are defined as „target" diseases by the Directive. Furthermore, it gives a complete statistical compilation of related screening figures, recall rates and confirmed diagnoses for the current year. Additionally, data about process quality for whole Germany is presented.
Screening samples from the single Federal States are divided to the laboratories as it is presented in figure 1[1]. The screening laboratory in Magdeburg handles the dry blood samples of all infants born in Saxony-Anhalt.
Table 1 shows the frequencies of the screening target diseases in Germany[1] for a total number of 784,900 screened births in 2017.

Tab. 1: Frequency of diseases detected in screening in Germany 2017[1] (including mild forms)

| Disease | Confrimed cases | Prevalence |
|---|---|---|
| Congenital hypothyroidism (CH) | 279 | 1 : 2,813 |
| Congenital adrenal hypoplasia (CAH) | 48 | 1 : 16,352 |
| Biotinidase deficiency (incl. partial defects) | 20 | 1 : 39,245 |
| Galactosemia (classical) | 6 | 1 : 130,817 |
| Phenylketonuria (PKU) / hyperphenylalaninemia (HPA) / cofactor deficiency | 157 | 1 : 4,999 |
| Maple syrup urine disease (MSUD) | 6 | 1 : 130,817 |
| Medium-Chain-Acyl-CoA-Dehydrogenase deficiency (MCAD) | 77 | 1 : 10,194 |
| Long-Chain 3-OH-Acyl-CoA-dehydrogenase deficiency (LCHAD) | 11 | 1 : 71,355 |
| (Very-)Long-Chain-Acyl-CoA-dehydrogenase deficiency (VLCAD) | 11 | 1 : 71,355 |
| Carnitin-Palmitoyl-CoA-Transferase I deficiency (CPTI) | - | |
| Carnitin-Palmitoyl-CoA-Transferase II deficiency (CPTII) | 1 | 1 : 784,900 |
| Carnitin-Acylcarnitin-Translocase deficiency (CACT) | - | |
| Glutaric aciduria type I (GA I) | 5 | 1 : 156,980 |
| Isovaleric acidaemia (IVA) | 5 | 1 : 156,980 |
| Cystic Fibrosis (CF) / CFSPID | 160 | 1 : 4,906 |
| **Total** | **786** | **1 : 999** |

Screening data 2018 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 standard values / 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 (here 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

Since according to §15 and §31 of the Children's Guidline each newborn has a right of participation in the extended newborn screening and cystic fibrosis screening, a tracking for completeness is necessary. This can be realised for children which are delivered in obstetric clinics by control of the respective consecutive number in the birth register and by means of a so-called blank card system in the screening laboratory. According to the Children's Guidline the obstetric clinics have to document on a blank test card the total refusal of screening, the refusal of an early blood taking within the screening, the transfer to specialised institutions or death of the newborn. This test card is sent to the responsible laboratory; however, it differs between the single Federal States how successful this method is.

We collected the following registration rates in Saxony-Anhalt in 2018:
According to the Federal Statistical Office 17,410 children were live births in Saxony-Anhalt (according to the maternal residence).

Tab. 2: Initial examinations according to the mother's place of residence

| | Number |
|---|---|
| First screening in Magdeburg, in total | 16,987 |
| Non-resident in Saxony-Anhalt | 810 |
| **Screening of children living in Saxony-Anhalt** | **16,177** |

The discrepancy between the number of live births and screened infants with residence in Saxony-Anhalt amounts to 1293. This number increased significantly in contrast to the previous year (2017: 869). Main reason might be the closure of two maternity clinics in Weißenfels and Zerbst.

Basis for the data of the State Statistical Office are the births that are reported by the birth centres to the registry offices and which are sorted according to the place of maternal residence. However, the number of mothers with residence in Saxony-Anhalt but who delivered their infant in another Federal State can not be recorded in our screening statistics if the screening of the infant also took place in another Federal State.

Tab. 3: Registration rates by blank cards

| | |
|---|---|
| **Blank cards in total** | **301** |
| Blank card: infant deceased/ stillbirth | 59 |
| Blank card: refusal of early sampling | 194 |
| Blank card: transfer to another hospital | 27 |
| Blank card: screening refused by parents | 16 |
| Screening took place | 222 |

The follow-up (telephone calls, letters to parents) meant that only 1.3 % of the blank cards sent in were without result. All other live births participated later successfully in the newborn screening and the CF screening in our or in a neighbouring screening laboratory.
Furthermore, the tracking of missing screening examinations is performed successfully according to the reasons mentioned in table 4.

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

| Reason for second screening | suspicious first screening | First screening < 36h or < 32 WOG |
|---|---|---|
| Requested | 67 | 465 |
| Received at own laboratory | 67 | 428 |
| Deceased before control examination | - | 12 |
| Received at another laboratory | - | 20 |

WOG = weeks of gestation

# Examination Numbers, Recall Rates and Assured Cases

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

A total of 110 control examinations had to be carried out in 2018.

Tab. 5: Recall-rate 2017 and diagnosed patients with a metabolic disease in reference to 16,7987 screening examinations (includes also early withdrawal < 36h and preterm births < 32 WOG), prevalence 1992-2018

| Target disease incl. all forms of disease | Number of recalls 2018* | Assured cases 2018 | Prevalence in Saxony-Anhalt 1992-2018 |
|---|---|---|---|
| Hypothyroidism (CH) | 47 | 5 | 1 : 3,808 |
| Phenylketonuria (PKU/ HPA) | 6 | 5 | 1 : 5,078 |
| Galactosemia (classical) | 4 | 1 | 1 : 106,629 |
| Biotinidase deficiency | 6 | 1 | 1 : 101,423 |
| Congenital adrenal hypoplasia (CAH) | 46 | - | 1 : 17,281# |
| Medium-Chain-Acyl-CoA-Dehydrogenase deficiency (MCAD) | 2 | 2 | 1 : 9,815## |
| Long-Chain 3-OH-Acyl-CoA-dehydrogenase deficiency (LCHAD) | - | - | 1 : 76,068 |
| (Very-)Long-Chain-Acyl-CoA-dehydrogenase deficiency (VLCAD) | 4 | 1 | 1 : 152,135 |
| Maple syrup urine disease (MSUD) | - | - | |
| Carnitin-Palmitoyl-CoA-Transferase I and II deficiency (CPTI) | - | - | |
| Carnitin-Acylcarnitin-Translocase deficiency (CACT) | - | - | |
| Glutaric aciduria type I (GA I) | - | - | 1 : 304,270 |
| Isovaleric acidaemia (IVA) | 7 | - | |
| Mucoviscidosis | 8 | 2 | 1 : 6,942### |
| Tyrosinemia type I | 1 | 1 | |
| Other | 9 | - | |

* Recall: Request of a new blood sample at suspicious screening result at first examination.
Here illustrated the number inclusive early blood withdrawal (<36 h) or premature infant (< 32 weeks of gestation).
\# Screening to detect congenital adrenal hyperplasia syndrome (since 1997 in Saxony-Anhalt)
## Enlarged screening (TMS) since 05/2001 in Saxony-Anhalt
### Screening for mucoviscidosis since 09/2016
#### Screening for tyrosinemia since 04/2017

# Process Times

## *Point of Taking Blood Samples*

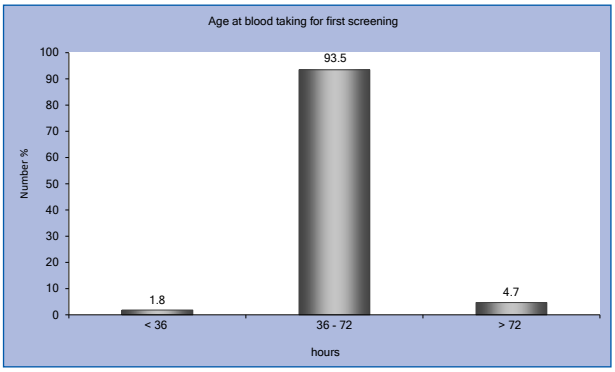


Fig. 2: Age at point of blood taking for first screening

The optimal point of taking blood samples for the newborn screening (36 –72 hours of life, §20 Children`s Directive) took place within the required period of time at 93.5% of all cases (2017: 92.3%). At a total number of 6.5% the taking of blood samples took not place within the required period of time (2017: 7.6%). We regard this trend as slightly positive in comparison to the previous years.

Note: Data of a 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*

According to §21 of the Children‘s Directive, the date of dispatch of the blood sample shall be equal to the date of blood collection. The aim is to ensure that the postal route does not exceed 72 hours. Figure 3 shows that 18.0% (2017: 18.5%) of all transmittals reached the laboratory more than three days after the blood taking. On average, samples from the 22 clinics reach the laboratory in the required time window, although in some cases there are major differences in the shipping time (table 6).

Similar to previous years, there were also delays of the postal shipment in 2018. Some dry blood cards that reached the laboratory after more than 10 days. Three of 22 clinics have too high shipping times (< 72 h). Compared to 2015, the delivery time of three hospitals has become considerably worse. Since any delayed blood collection or any extended postal route means a potential (life) risk for the affected children, the laboratory tries to improve the duration of shipment by means of trainings (an-

nual training event). The main reason for this is surely the dispatch via private mail deliverers. We recommend urgently to ship the samples therefore with the Deutsche Post directly to the screening mailbox. The following information must also be observed:

- send blood samples on the day of collection, i.e. do not collect over several days, the letter should leave the hospital mailroom as soon as possible
- not send to the hearing screening tracking center

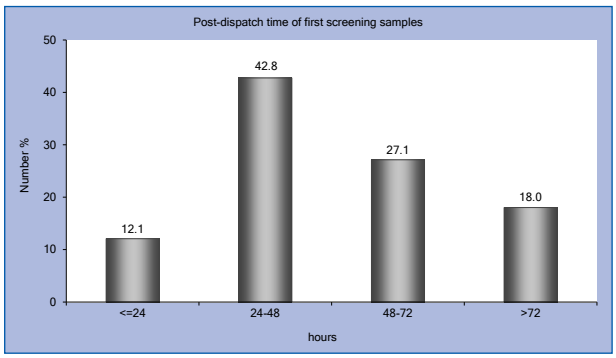


Fig. 3: Post-dispatch time of the dry blood cards (first screening) Time from blood collection to arrival at the laboratory

Tab. 6: Post-dispatch time of dry blood cards per sending hospital (average value of all wards of a hospital), Comparison between 2018 and 2015

| Maternity clinics | Average shipping time (hours) | |
|---|---|---|
| | 2018 | 2015 |
| Magdeburg St. Marienstift* | 22,1 | 12,1 |
| Magdeburg Universitätsklinikum* | 30,5 | 28,9 |
| Magdeburg Klinikum* | 30,9 | 25,4 |
| Quedlinburg | 40,5 | 44,1 |
| Gardelegen | 40,7 | 41,5 |
| Naumburg | 42,1 | 40,9 |
| Halle St. Elisabeth und St. Barbara | 44,0 | 50,1 |
| Zeitz | 45,3 | 49,2 |
| Schönebeck | 45,7 | 40,8 |
| Salzwedel | 48,6 | 45,1 |
| Bitterfeld-Wolfen | 49,8 | 55,5 |
| Wernigerode | 50,6 | 49,8 |
| Köthen | 50,7 | 48,8 |
| Aschersleben | 53,0 | 49,7 |
| Merseburg | 53,9 | 50,5 |
| Halle Universitätsklinikum | 55,8 | 53,4 |
| Sangerhausen | 56,1 | 49,6 |
| Lutherstadt Wittenberg | 57,2 | 56,0 |
| Stendal | 57,4 | 46,0 |
| Dessau-Roßlau | 73,0 | 44,0 |
| Burg | 86,0 | 44,2 |
| Halberstadt | 94,1 | 62,1 |

* Clinic with a courier service

## *Transmission of Results*

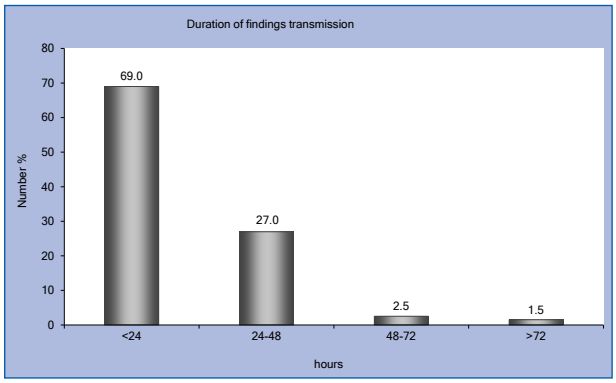


Fig. 4: Duration of findings transmission

Figure 4 shows the duration of laboratory analysis of all first screening tests. Results which are finished after more than 36 hours are caused by internal repetitions. The 4 % (2017: 11.1 %) of all findings, which leave the laboratory after more than 48 hours essentially reflect the extended finding duration due to cystic fibrosis screening (3-step screening) and possible disturbances in the laboratory process (equipment maintenance, repairs, etc.).

In case of a highly suspicious finding, the information is immediately transmitted by telephone to the attending physician as partial finding. Due to the urgency, we do not wait for the completion of all laboratory analyses in such cases.

# Cystic fibrosis screening

Tab. 7: CF-Screening, participation and confirmed cases

| | 2018 | 2017 |
|---|---|---|
| Screenin, in total | 16.987 | 17.722 |
| there of with CF-Screening | 99,7 % | 99,3 % |
| CF-Screening positive | 8 | 16 |
| sweat test performed | 7 | 15 |
| CF confirmed | 2 | 3 |

The screening for cystic fibrosis (CF) is offered since 09/2016 for all children throughout Germany. During the course of the 3-step laboratory analysis no control card is requested in case of a suspicious finding, but the children have to be come to a CF outpatient clinic in order to exclude CF by means of a sweat test.

There is an increasing participation in the CF screening and a good acceptance of the program. In the year 2018 no parent or guardian rejected the participation in the CF screening. 0.3 % of CF analyses were not carried out due to the special fact that midwives are not allowed to take blood samples for this screening without permission from a doctor. Usually the cooperation between midwifes and paediatricians works well. Not all children received a sweat test after positive CF screening. Among these was

one child with trisomy 18 (2017) and in a second case (2018) the parents did not show up for the examination even after repeated requests by the certified CF outpatient clinic.

## Confirmation diagnostics and therapy of screening-positive patients

20 suspected screening cases could be confirmed by confirmation diagnostics, 16 of these patients needed a therapy:

Tab. 8: Diagnosis, confirmation diagnostics and therapy starting

| Diagnosis | Confirmation diagnostics | Age at start of therapy |
|---|---|---|
| 1 x Galaktosemia<br>1 x Duarte-variant | Complete galactose, mutation analysis | 4 days<br>No treatment required |
| 5 x Hypothyroidism | Serum-TSH, fT3, fT4, sonography,<br>1 infant with a complex malformation | 4-9 days |
| 1 x Phenylketonuria<br>4 x Hyperphenylalanemia | Serum-Phe, BH4-Test | 10 days<br>No treatment required |
| 2 x classical MCAD deficiency | Organic acids in urine,<br>partly mutation analysis,<br>partly enzyme activity | 5-6 days |
| 1 x VLCAD deficiency | Enzyme activity in lymphocytes,<br>mutation analysis | asymptomatic, no treatment required<br>(at the time of the report) |
| 1 x classical Biotinidase deficiency | Enzyme activity, multisteroid analysis | 2 days |
| 1 x Tyrosinemia type I | Amino acids in serum, organic acids in urine,<br>mutation analysis | 2 days |
| 2 x Mucoviscidosis<br>(1 x classical homocygotic CF) | Sweat test<br>Mutation analysis | 16-20 days |

## Summary

On September 01, 2016 and March 15, 2017, a new version of the Children`s Directive became effective. The screening for cystic fibrosis and tyrosinemia type 1 were included.
As a result, new declarations of consent have been developed and the layout of the dry blood cards has been adapted. Parents have the option to accept or deny the participation in the screening for cystic fibrosis independent from the participation in the extended neonatal screening (checkbox on the dry blood card). This is possible until the 4th week of life of the newborn. Both screening programs can be performed from one blood collection if there was enough blood taken.
The Gene Diagnostics Act also applies to cystic fibrosis screening and is the overarching law with penalty paragraphs. Midwives are only allowed to take blood from newborns for the cystic fibrosis screening after permission by a paediatrician. Forms can be found on our homepage (www.stwz.ovug.de).

The Newborn Screening and Metabolism Laboratory belongs to the Institute of Clinical Chemistry and Pathobiochemistry since October 2015 (central laboratory of the University Hospital Magdeburg A.ö.R.). Nevertheless, an intensive cooperation with specialists in paediatrics continues and is strongly encouraged.

In 2017, a new LC tandem mass spectrometer was purchased for the newborn screening. This device is also capable to meet new requirements and can be applied for the detection of new target diseases.

The process quality of the newborn screening of Saxony-Anhalt remains very good, similar to the previous years and lies in the middle of the national average of all German screening laboratories (national screening report of the German society of newborn screening).

As usual, all patients with a positive first screening result were followed up and their diagnosis was assured resp. excluded. We thank all medical centres and ambulances for the good and smooth collaboration.

We calculated an incidence of 1: 1,655 for all objective diseases of the newborn screening in Saxony-Anhalt in 2018.

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

**www.stwz.ovgu.de**

We would like to inform sender, parents and interested people here about the Newborn Screening and about special metabolic diagnostics and provide downloads/ forms.

The national screening report of the DGNS[1] is available on their own website (http://screening-dgns.de) two years after the respective period of time.

[1] Source: Deutsche Gesellschaft für Neugeborenenscreening e.V. (DGNS): Nationaler Screeningreport Deutschland 2017 http://www.screening-dgns.de/Pdf/Screeningreports/DGNS-Screeningreport-d_2017.pdf