Annual Report 2019

Malformation Monitoring Centre Saxony-Anhalt

OTTO VON GUERICKE UNIVERSITÄT MAGDEBURG

SACHSEN-ANHALT
Ministerium für Arbeit, Soziales und Integration

Annual Report 2019
of the Federal State of Saxony-Anhalt
about the frequency of congenital malformations and anomalies as well as genetically cause diseases

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Introduction

Dear readers,

There are numerous reasons for the development of malformations. In addition to genetic and chromosomal disorders, there are also exogenous causes such as prenatal infections, e.g. rubella during pregnancy or prenatal intoxications, excessive use of alcohol or nicotine, or the use of medicines, such as thalidomide in the 1960s.
Seen from this angle, we are paying particular attention to the global course of the Corona pandemic. According to initial scientific reports from China, there is a possible risk of fetal growth restriction or prematurity if the pregnant woman became seriously ill with COVID-19 infection. There is currently no evidence for the occurrence of specific malformations.
However, it is too early to give the all-clear on the basis of valid data. Because even in Italy not all the children are born who were exposed to the Corona virus infection in the first trimester in 2019. Particularly in the European network (EUROCAT network of European malformation registries) we will evaluate these data separately.

A malformation register is the most important epidemiological basis for recording and preventing malformations. In medicine, a malformation (malformation or deformity) is defined as a malformation of one or more organs that has already developed or been created before birth. These can be changes in the shape and size of organs up to the absence or also a restricted function of organ systems, e.g. gastrointestinal tract in the case of a congenital intestinal obstruction.

Many congenital malformations can already be detected during prenatal ultrasound examination. That is why it is necessary to include all pregnancy outcomes in a prospective registration of malformations. Thus, with this report we are able to publish an epidemiological analysis of the collected data with regard to congenital malformations for the birth cohort 2019 (16,717 births in Saxony-Anhalt with 16,618 live births and 99 stillbirths).

In Saxony-Anhalt, 16,618 children were born in 2019. In 581 cases, the pregnancy was affected by at least one major malformation, which corresponds to a proportion of 3.5 %. If minor malformations are also included, 5.1 % of all children and foetuses in Saxony-Anhalt were affected by a malformation. This is a minimal decrease compared to the previous year.
With a malformation rate of five per cent, the total number of births with malformations for the entire Federal Republic of Germany in 2019 amounts to approximately 38,900. A total of 778,090 children were born in Germany in 2019.

We have a special responsibility, as Saxony-Anhalt is the only federal state in Germany which records population-related malformations nationwide. Our thanks therefore go to all of those who are committed to actively shaping this interdisciplinary cooperation within the framework of the prospective recording of malformations.

My thanks go to all those who enable the reporting with their active cooperation. I would also like to thank the organisers of the senders‘ meeting and wish the event a good success and a lively discussion.

Yours sincerely

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

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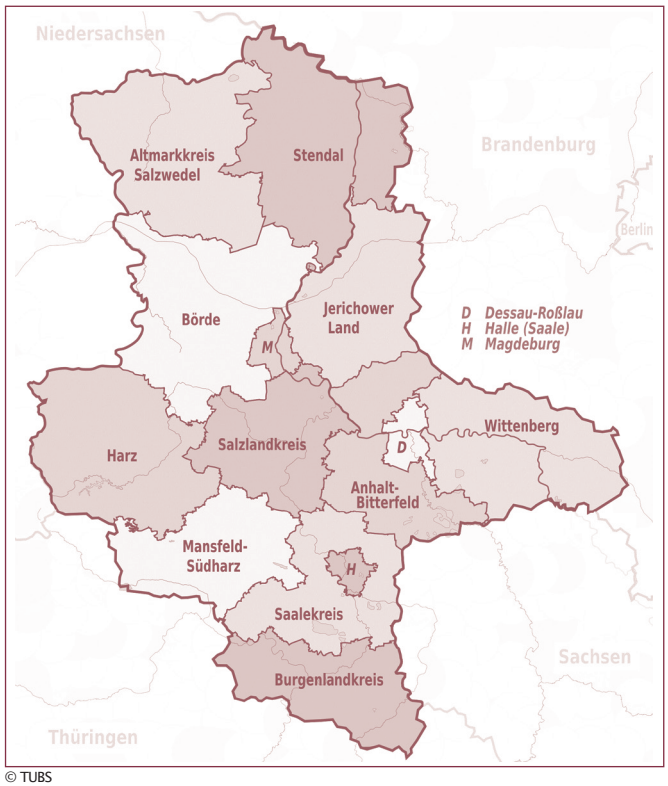
Abkürzungen

AABR	automated auditory brainstem response
ASD	atrial septal defect
AVSD	atrioventricular septal defect
ATC	anatomical-Therapeutic-Chemical classification
blt.	bilateral
BMI	Body-Mass-Index
BP	basis prevalence
CI	confidence interval
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
FAS	fetal alcohol syndrome
FASD	fetal alcohol spectrum disorder
G-BA	Federal Joint Committee
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 (cell-free 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	transitorisch evozierte otoakustische Emissionen
TOP	termination of pregnancy
UTS	urinary tract system
VSD	ventricular septal defect
WOG	weeks of gestation

1 Births and fetuses 2019 in the registration region

Districts / major cities	Live births*	Stillbirths*	Live births and stillbirths in total*	*Spontaneous abortions (> 16 WOG)#*	*Terminations of pregnancy#*
Altmarkkreis Salzwedel	662	3	665	-	*1*
Anhalt-Bitterfeld	1.077	9	1.086	-	*2*
Börde	1.277	13	1.290	*2*	*8*
Burgenlandkreis	1.252	5	1.257	-	-
Dessau-Roßlau	551	3	554	-	*1*
Halle	2.291	10	2.301	-	*6*
Harz	1.472	4	1.476	*1*	*7*
Jerichower Land	649	5	654	*1*	*1*
Magdeburg	2.242	11	2.253	*2*	*9*
Mansfeld-Südharz	848	10	858	-	*6*
Saalekreis	1.320	8	1.328	-	*4*
Salzlandkreis	1.275	11	1.286	*3*	*8*
Stendal	863	3	866	*3*	*6*
Wittenberg	839	4	843	-	*2*
Landkreis in Sachsen-Anhalt o.n.A.	-	-	-	*4*	*2*
Saxony-Anhalt	**16.618**	**99**	**16.717**	*16*	*63*

* Source: © Statistical office Saxony-Anhalt, Halle (Saale), 2020
 # Data of the Monitoring of malformation registration Saxony-Anhalt



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

2 Participating institutions of the region 2019

2.1 Maternity units / paediatric units / paediatric surgery / paediatric 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 Saalekreis 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
- Evangelisches Krankenhaus Paul Gerhardt Stift Wittenberg
- Georgius-Agricola Klinikum Zeitz

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

- Dipl. Heilpädagogin Schlote, Glindenberg/Magdeburg
- Dr. Perlitz, Fachärztin für Frauenheilkunde und Geburtshilfe, Haldensleben
- Krankenhaus St. Elisabeth und St. Barbara Halle, Pränatale Ultraschalldiagnostik: CA Dr. Seeger / OÄ Dr. Radusch
- Universitätsklinikum Halle (Saale), Institut für Humangenetik und Medizinische Biologie
- Zentrum für Pränatale Medizin Halle: S. Rieße, N. Manthey, PD Dr. Hahmann
- Dr. Altus, Dr. Ababei, Fachärztinnen 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, Dr. Adams, Dr. Blaschke, Fachärzte für Kinder- und Jugendmedizin, Wanzleben
- Harzklinikum Dorothea Christiane Erxleben Klinikum Wernigerode, Pränatale Ultraschalldiagnostik: OÄ Dr. Schulze

2.3 Pathological-anatomical institutes (ordered by location)

- Universitätsklinikum Halle (Saale), Institut für Pathologie
- Klinikum Magdeburg, Institut für Pathologie
- Universitätsklinikum Magdeburg A.ö.R., Institut für Pathologie
- Praxis für Pathologie PD Dr. Schultz, Dr. Lüders, Dr. Hainz, Stendal

3 Malformation registration in Saxony-Anhalt

3.1 General information

Our **thanks** for the continued interdisciplinary cooperation **to you as sender** should be placed at the beginning of the current annual report (data evaluation birth cohort 2019). Saxony-Anhalt is the only federal state in Germany with a population-based registration of malformations. The beginnings can be traced back 40 years. This state-wide registration of malformations would not be possible without the continuous support of the Ministry of Labour, Social Affairs and Integration of Saxony-Anhalt. We are pleased that the successful cooperation under Ms Karen Müller has continued. Furthermore, we would like to personally thank Dr. H. Willer and Mr. M. Schiener for the good cooperation.

This year we had planned to outline prenatal diagnostics and CNS malformations as a special topic. The health policy significance of congenital malformations can be illustrated by these examples in particular (see chapter 14.1). However, a new type of viral infection (coronavirus Sars-CoV-2) developed into a global challenge within a few months and is not leaving the epidemiology of malformations unscathed.
COVID-19 disease was shown to have reached Germany as of 27 January 2020. On 30 January 2020, the coronavirus pandemic was declared a „public health emergency of international concern" by the World Health Organisation (WHO). From 10 March 2020, the first cases were registered in Saxony-Anhalt. Until now, there were sufficient staff and resources available to offer all prenatal care procedures in a timely manner. However, with the first lockdown in Germany from 22 March 2020 and the current partial lockdown from 22 November 2020, the question of possible changes in obstetric management and fetal therapy for congenital anomalies in SARS-CoV2-negative and SARS-CoV2-positive patients arises again. So far, there are only a few published cases that indicate vertical transmission (transmission to the foetus). The risk of such transmission during some fetal interventions may theoretically be increased. You can learn more about this in chapter 14.2. It is still too early to be sure that fetuses, if infected during the vulnerable first trimester, will not be harmed. The children who were conceived early in the pandemic in Europe will not be born until October. The European network EUROCAT and the WHO-associated network ICBDSR are focusing on prevalence progression during the pandemic.
With the data from Saxony-Anhalt, the malformation monitoring has represented Germany since 1993 at the International Clearinghouse for Birth Defects Surveillance and Research (ICBDSR), a WHO-associated institution of 42 malformation registries from 38 countries around the world (www.icbdsr.com).
Furthermore, we have been a member since 1992 of the population-based malformation register EUROCAT (https://eu-rd-platform.jrc.ec.europa.eu/eurocat).

We would also like to thank the Medical Faculty of Otto von Guericke University Magdeburg for its constant cooperation and involvement in the Saxony-Anhalt malformation monitoring project. We are pleased that this support has continued quite productively under Prof. Dr. med. H.-J. Heinze, Medical Director, and Dr. K. Stachel, Commercial Director, in 2019. We would like to express our special thanks to Prof. Dr. med. H.-J. Rothkötter on the occasion of his retirement as Dean. We are looking forward to continue our work with the Dean, Prof. Dr. rer. nat. D. C. Dieterich.

3.2 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 forms basis of the annual prevalence calculations, i.e. live births and stillbirths in Saxony-Anhalt. Those affected by congenital malformations and anomalies as well as genetically caused diseases include live births, stillbirths, terminations of pregnancy (of all gestational weeks) as well as spontaneous abortions from the 16th week of gestation. The percentages and prevalences shown are rounded values.

The expected date of delivery is used as basis for analysing the termination of pregnancy, e.g. 2019 is considered the year of birth although some terminations of pregnancy after prenatal diagnostics took place at the end of 2018. 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. Data on live births and stillbirths is provided annually in mid-year by the Land Statistical Office in Halle for the previous year. The amendment to §31 PStV of 01.11.2018 regarding the definition of stillbirth becomes relevant for the birth year 2019, resulting in an increase of the stillbirth rate.

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 6 and 7. 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.

Chapter 9 outlines the most frequent single diagnoses of major malformations registered in 2019.
Similar to the previous years we analysed the reported pathological prenatal screening results separately in Chapter 8.
Chapter 10 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 2019 in comparison to the last 12 years (2007-2018). Here, a **total number of 208,701 births** forms basis for the **basis prevalence calculation 2007 to 2018.**

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 12.38).

Data regarding genetically caused diseases, chromosomal disorders, sequences, associations, complexes and embryopathies is outlined in chapter 11. Chapter 12 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 16.

Chapter 17 presents the Annual Report of the department of newborn screening in Saxony-Anhalt with data regarding congenital metabolic disorders and endocrinopathies.

3.3 Data quality and completeness/reporting procedure

The beginnings of the observation of malformations in Magdeburg date back 40 years. For 20 years, the malformation monitoring has been collecting information on newborns and fetuses from the federal state of Saxony-Anhalt, receiving reports from maternity and paediatric clinics and from prenatal and postnatal diagnostic facilities (Chapter 4.2).

The database of the malformation monitoring forms the valid basis for the annual reports and for scientific work on and around the topic of malformations. It was expanded by **1,738 data records for the 2019 birth cohort**. This corresponds to about 10 % of all children/fetuses in Saxony-Anhalt. Since the last report, the number of data sets has grown from 1,767 to 1,807 due to subsequent registrations for 2018.

For the reporting year 2019, the malformation monitoring received 1,898 reports, 470 of them from outpatient facilities. For 10.2 % of the children/fetuses, the data came from multiple facilities. The redundancy ensures confirmation or exclusion of a suspected malformation and improves the evaluation of complex malformations.

Our special thanks goes to the AMEOS Klinikum Schönebeck. In terms of births per clinic, this clinic continuously sends the most reporting forms. The large contribution of outpatient facilities such as the Centre for Prenatal Medicine (Halle), Dr. Karstedt's practice (specialist in paediatrics and adolescent medicine, paediatric cardiologist) and Dr. Achtzehn's practice (specialist in paediatrics and adolescent medicine) has a very positive effect on the recording of malformations.

High data quality is achieved through complete information on the reporting sheets and detailed descriptions of diagnoses. They are a precondition for the correct entry of information into the database and have an impact on the quality of the statistics. Thanks to the excellent cooperation of the respondents, the data quality was again very good in 2019. Important information was submitted almost in full in 2019: Gender at 98.7 %, age of mother at 99.4 % and district at 99.4 %. Birth weight was not reported 62 times (3.6%), but of these only eight were born alive. The head circumference, which is relevant for the assessment of a microcephaly, was not given for 28.5 % of the children.

We ask all senders to continue to report all malformations, to indicate all accompanying malformations and to describe them as completely as possible. For eight of 136 prenatally detected indicator malformations, no postnatal report was found for the year of birth 2019. In 6 cases, the postnatal description of the finding was incomplete. If there is no confirmation of the findings, the prenatal findings do not count as indicator malformations (Chapter 10).

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.

5 Sex Ratio

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

male	8,578 live births and stillbirths
female	8,139 live births and stillbirths
total	16,717 live births and stillbirths

Sex ratio m : f = 1.05

DThe State Statistical Office of Saxony-Anhalt reports 16,618 live births and 99 stillbirths for 2019. The number of children born alive has been decreasing since the maximum value in 2016 (18,092). In contrast, stillbirths showed a peak in 2019. Such a high value has not been recorded in terms of the number of live births since the end of the 1990s.
The sex ratio of children born alive and stillborn is always boy-gendered, and this is also the case in 2019. During the reporting period (2007-2018: m : f = 1.05), the range for the sex ratio of m : f was between 1.03 and 1.07. In 2019, as in four other years of the reporting period, gynaecotropy is evident for stillbirths (2010: m : f = 0.98).

In the 581 children/fetuses with major malformations, which include live births and stillbirths, terminations of pregnancy and spontaneous abortions from the 16th week of gestation, the sex ratio of m : f = 1.10 showed an androtropy. In previous years, the ratio of m : f could be located between 1.10 and 1.38.

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

male	298 births
female	272 births
unknown	11 births
total	581 births

Sex ratio m : f = 1.10

Sex ratio of all births with only minor malformations and anomalies

male	155 births
female	113 births
total	268 births

Sex ratio m : f = 1.37

Among the reported 268 children/fetuses with exclusively small malformations, there are also more boys than girls. The sex ratio for 2018 is m : f = 1.37. As with the major malformations, the sex ratio for exclusively minor malformations is almost always boyish, including in 2019.

9 Organ system involvement and most frequent single diagnoses in infants and foetuses with major malformations

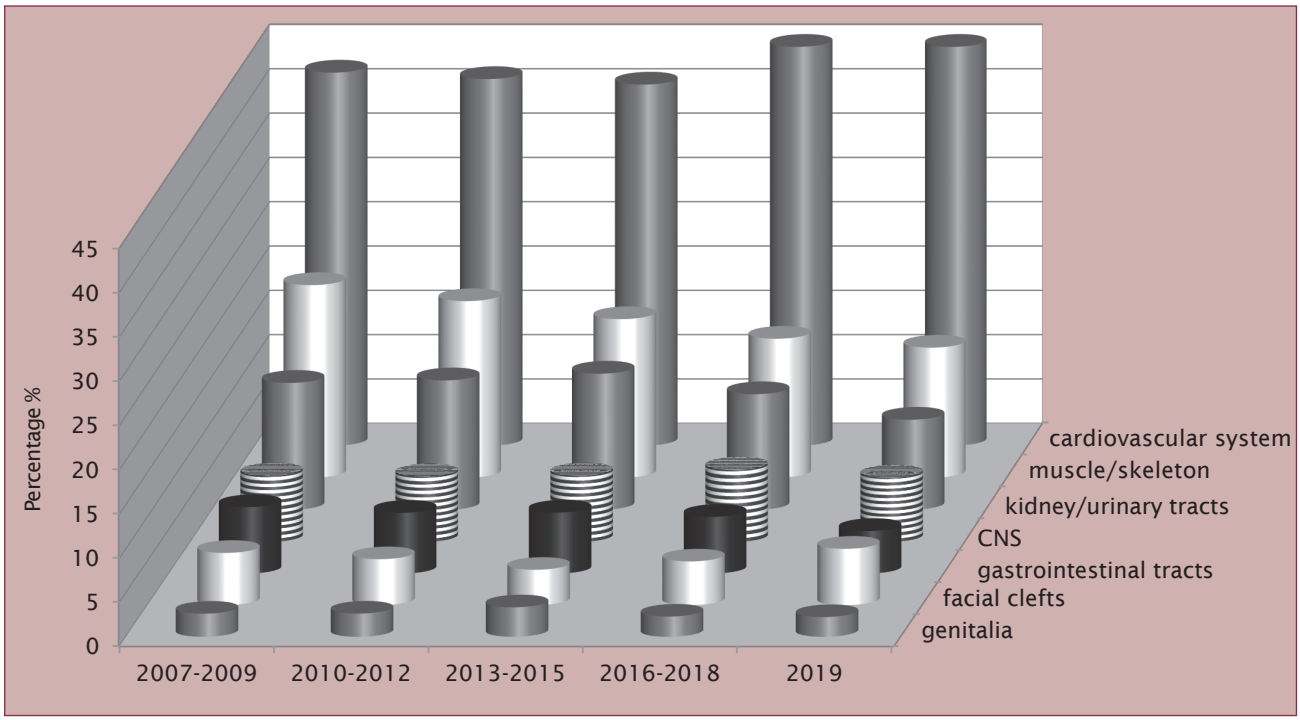


Fig. 5: Organ system involvement in major malformations (grouped)

In 2019, 581 children/fetuses were reported to have major malformations in Saxony-Anhalt. The diagram above (Fig. 5) shows for seven selected organ systems the proportion of children/fetuses that are affected by a malformation in these organ systems. Since slightly more than one third of the children/fetuses with major malformations (223) have multiple malformations, i.e. several organ systems can be affected in one child/fetus, multiple reportings are possible. In order to be able to show changes, the reporting period in Figure 5 is divided into four time periods of three years each and the current year is shown in addition.

Malformations from the cardiovascular system group always occur most frequently. On average, 43.2 % (2007-2018) of all children/fetuses who have a major malformation have a cardiac malformation. There is an increasing trend during the reporting period (2019: 49.7%). This development matches the evaluation of the most frequent individual malformations (table page 22).

For the musculoskeletal system, the organ system with the second highest incidence of malformations (2007-2018: 17.5%), the proportion has decreased over the years and currently lies at 13.4% (2109).

In 2019, the proportion of children/fetuses with malformations of the kidneys and urinary tract (13.8%) out of all children/fetuses with major malformations is similar to that for the musculoskeletal system. Over the years (2007-2018), a stable proportion can be seen, with an average of 13.8 %.

For CNS malformations, the proportion (2019: 6.4%) of all children/fetuses with major malformations is slightly below the usual range (2007-2018: 7.7%). NRD and congenital hydrocephaly each account for about one third of CNS malformations, which could be found overall in the baseline prevalence range in 2019 (Chapters 10.1, 10.6).

The proportion of children/fetuses with malformations of the digestive tract (4.6 %) in relation to all children/fetuses with major malformations is also low in 2019. During the years of the reporting period, it was always higher (2007- 2019: 6.5 %).

The proportion of children/fetuses with facial clefts is high in 2019 (5.7%). Facial clefts include cleft palate in about one third and cleft lip and cleft lip and palate in about two thirds, the latter being observed slightly more than normal in the current year (Chapter 10.14).
In addition to epispadias, ectopia testis and female genital malformations, the genital malformations mainly include severe hypospadias. As hypospadias occurred very rarely in 2019 (Chapter 10.20), the proportion of children/fetuses with malformations of the genital system in relation to all malformed children/fetuses in 2019 is very low.

Most frequent single diagnosis 2019 (only major malformations)

	ICD-10	Diagnosis	Children/foetuses 2019		Children/foetuses 2007-2018**	
			Number	Prevalence /10,000*	Prevalence /10,000	Confidence interval (CI 95%)
1.	Q21.1	Atrial septal defect (without PFO)	190	113.7	93.1	89.0 - 97.3
2.	Q21.0	Ventricular septal defect	68	40.7	46.7	43.8 - 49.7
3.	Q62.3	Dilated uropathy grade II-IV/ ureterocele	42	25.1	23.5	21.4 - 25.7
4.	H90.	Conductive and sensorineural hearing loss	36	21.5	22.6	20.6 - 24.7
5.	Q66.0	Pes equinovarus congenitus (clubfoot)	28	16.7	15.0	13.4 - 16.8
6.	Q90.	Down syndrome (trisomy 21)	27	16.2	19.2	17.4 - 21.2
7.	Q22.1	Pulmonary valve stenosis	21	12.6	10.3	8.9 - 11.7
8.	Q63.0	Accessory kidney/duplex kidney	18	10.8	8.0	6.9 - 9.4
	Q69.	Polydactyly (pre- and postaxial)	18	10.8	12.4	10.9 - 14.0
9.	Q65.3-5	Subluxation of the hip joint (one sided/both sided/ without indication of side)	11	6.6	7.0	5.9 - 8.2
	Q60.0	Unilateral renal agenesis	11	6.6	6.0	5.0 - 7.1
	Q21.2	Defects of the atrial and ventricular septum (AVSD/ASD I)	11	6.6	5.1	4.2 - 6.2
10.	Q25.0	Open ductus botalli (PDA), haemo-dynamically effective	10	6.0	10.1	8.7 - 11.5
11.	Q37.	Cleft palate with cleft lip	9	5.4	10.3	8.9 - 11.7
	Q62.2	Congenital megaureter	9	5.4	8.5	7.3 - 9.9
	Q23.3	Mitral valve insufficiency	9	5.4	5.0	4.1 - 6.1
	Q23.4	Hypoplastic left heart syndrome	9	5.4	2.6	2.0 - 3.4
12.	Q62.1	Stenosis and atresia of ureter	8	4.8	8.8	7.6 - 10.2
	Q03.	Congenital Hydrocephalus (without neural tube defect)	8	4.8	5.6	4.6 - 6.7
	Q91.0-3	Edwards syndrome (trisomy 18)	8	4.8	4.3	3.5 - 5.3
	Q05.	Spina bifida	8	4.8	5.2	4.3 - 6.3
13.	Q25.1	Aortic coarctation	7	4.2	6.0	5.0 - 7.1
	Q61.4	Renal dysplasia	7	4.2	6.4	5.3 - 7.6
	Q35.1 Q35.5 Q35.9	Cleft palate	7	4.2	4.1	3.3 - 5.0
14.	Q04.0	Hypoplasia/agenesis of the corpus callosum	6	3.6	5.1	4.2 - 6.1
	Q21.3	Tetralogy of fallot	6	3.6	3.3	2.6 - 4.2

* in reference to 16,717 births
** in reference to 208,701 births

The table on the opposite page presents the most frequently observed major individual malformations in Saxony-Anhalt, ordered by the frequency of occurrence in the 2019 birth cohort. The prevalence for 2019 is based on a population of 16,717 births and the basis prevalence (2007- 2018) is based on 208,701 births.

The heart is the organ system that is always most affected by malformations. The two leading individual malformations are therefore regularly atrial septal defect (2019: 113.7 per 10,000 births) and ventricular septal defect (2019: 40.7 per 10,000 births). Since malformations of the heart were reported more frequently and in greater detail, especially in the second half of the reporting period, four of the five most frequent individual malformations for which the current prevalence value is above the respective base prevalence are cardiac malformations: The most common malformation, atrial septal defect (2007-2018: 93.1 per 10,000 births), pulmonary valve stenosis (2019: 12.6 per 10,000 births, 2007-2018: 10.3 per 10. 000 births), atrial and ventricular septal defects (2019: 6.6 per 10,000 births, 2007-2018: 5.1 per 10,000 births) and hypoplastic left heart syndrome (2019: 5.4 per 10,000 births, 2007-2018: 2.6 per 10,000 births).

In the list of individual malformations ordered by frequency, the atrial septal defect and the ventricular septal defect are followed at some distance by four very different malformations, but in varying order over the years: Dilated uropathy grade II-IV/ureterocele (2019: 25.1 per 10,000 births), hearing loss (2019: 21.5 per 10,000 births) and clubfoot (2019: 16.7 per 10,000 births) were recorded with an expected frequency last year. Down syndrome (2019: 16.2 per 10,000 births, 2007-2018: 19.2 per 10,000 births) was recorded slightly less frequently than usual.

From 2007, the newborn hearing screening with tracking of congenital hearing disorders took place in Saxony-Anhalt. Before the introduction of this newborn screening, the recorded prevalence of hearing loss was at a maximum of 9.4 per 10,000 births (2003). For the first time, the baseline prevalence reported in this year‘s report (2007-2018: 20.5 per 10,000 births) only includes the years in which newborn hearing screening was already active. Before 2007, hearing disorders that are often only detected after the newborn age can be assumed to be significantly under-reported.

The eighth position of the ranking, at 10.8 per 10,000 births, is occupied by renal duplication and polydactyly in 2019. Renal duplication was more common than expected in 2019. During the reporting period, it was only found more often in 2007 (11.4 per 10,000 births) and in 2017 (12.3 per 10,000 births). Polydactyly was seen slightly less frequently than expected in 2019 (2007-2018: 12.4 per 10,000 births). Polydactyly includes the indicator malformation preaxial polydactyly (Chapter 12.28) and postaxial polydactyly. While in 2019 the prevalence of the rarer indicator malformation is below the baseline prevalence (1.8 per 10,000 births; 2007-2018: 3.7 per 10,000 births, CI 3.0-4.7), the value for postaxial polydactyly lies within the expected range (2019: 9.0 per 10,000 births; 2007-2018: 8.7 per 10,000 births, CI 7.5-10.0).

With only eight cases in 2019 (4.8 per 10,000 births), atresia and stenosis of the ureter occurred unusually rarely (2007-2018: 8.8 per 10,000). However, it was recorded even less frequently during the reporting period in 2012 (4.7 per 10,000 births) and 2007 with a minimum value (2.9 per 10,000 births). Also with a lower prevalence than normal, the top 14 places in the frequency ranking of individual malformations in 2019 include the malformations PDA, cleft lip and palate, megaureter, aortic coarctation, renal dysplasia and hypoplasia/genesis of the corpus callosum.

For a large proportion of the most common individual malformations on the list, the prevalence calculated for 2019 was within the confidence interval of the basis prevalence. Beside the already mentioned malformations dilated uropathy II.-IV. grade/ureterocele, hearing loss and clubfoot, there were further malformations at the same level as in previous years: subluxation of the hip joint, unilateral renal agenesis, mitral valve insufficiency, hydrocephaly, Edwards syndrome, spina bifida, cleft palate and tetralogy of Fallot.

10 Indicator Defects modified according to the International Clearinghouse for Birth Defects Surveillance and Research (ICBDSR)

10.0 Definitions

1. Neural tube defects:
common congenital malformations that occur when the neural tube fails to achieve proper closure during early embryogenesis, resulting in defective development of the associated vertebral arches. Anencephaly, Spina bifida, and Encephalocele fall under the definition.

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 pulmonaryartery from the left ventricle, with or without other cardiac defects. Inclusive double outlet ventricle so called corrected transposition.

12. Hypoplastic left heart syndrome:
a cardiac defect with a hypoplastic left ventricle, associated with aortic and/or mitral valve atresia, with or without 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:
a congenital malformation characterized by absence of continuity or narrowing of the esophagus, with or without

tracheal fistula. Inclusive Tracheoesophageal fistula with or without mention of atresia or stenosis of oesophagus.

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

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

20. 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).

21. 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.

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

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

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

25. 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.

26. 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.

27. 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.

28. 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.

29. 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.

30. 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.

31. 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.

32. 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.

33. 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.

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

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

36. Turner syndrome:
Turner syndrome, also Ullrich-Turner syndrome or monosomy X, is characterised by the partial or complete absence of one of the two X chromosomes in a girl (gonosomal monosomy). A mosaic of the one gonosomal abnormality is possible.

37. Klinefelter syndrome/male gonosome anomalies:
Klinefelter syndrome is caused by two or more X chromosomes in a male phenotype (Karoy type 47,XXY). Anomalies of the gonosomes in a male phenotype also include structural anomalies of the gonosomes or a gonosome mosaic.

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 the birth cohort 2000, the coverage area of the malformation monitoring includes the entire Federal State of Saxony-Anhalt. The prevalence calculations starting with the birth cohort 2000 are based on live and stillbirths of mothers who have their place of residence in Saxony-Anhalt during pregnancy and at the time of birth. Between 1980 and 1993, the coverage area grew to include the former district of Magdeburg. After the district reform in 1993, it comprised 13 (1994/1995), 14 (1996/1997), 15 (1998) and 16 (1999) of 21 districts in Saxony-Anhalt. The calculation of the basic prevalences (2007 to 2018) is based on a total number of 208,701 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 10 indicated comparison prevalences which correspond to the basis prevalences of Saxony-Anhalt are based on data of the years 2007-2018 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 (2014-2018) or more and for at least five years during the time period of 2007-2018.

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

	Year 2019		
Saxony-Anhalt	Number	Prevalence /10,000 births	Comp. to basis prevalence
	15	8.97	↔
	Reporting period 2007-2018		
	Basis prevalence /10,000 births	Confidence interval (CI 95%)	
	9.01	7.77 - 10.39	
EUROCAT (Full members)	Period 2007-2018		
	Basis prevalence /10,000 births	Confidence interval (CI 95%)	
	10.20	9.99 - 10.42	

Anencephaly, spina bifida and encephalocele form the group of neural tube defects. More than half of the children/fetuses with these severe CNS malformations are also affected by spina bifida in the year 2019. In Saxony-Anhalt, five anencephalies, eight spina bifida and two encephaloceles were reported. All three entities were observed at usual frequencies in 2019. The current **prevalence** of neural tube defects of **9.0 per 10,000 births** corresponds to the basis prevalence (2007-2018: 9.0 per 10,000 births).

The basis prevalence of Saxony-Anhalt corresponds, with a slightly wider interval, to the prevalence given by EUROCAT for Europe (10.2 per 10,000 births). The annual prevalence of Saxony-Anhalt is slightly lower compared to the EUROCAT prevalence.

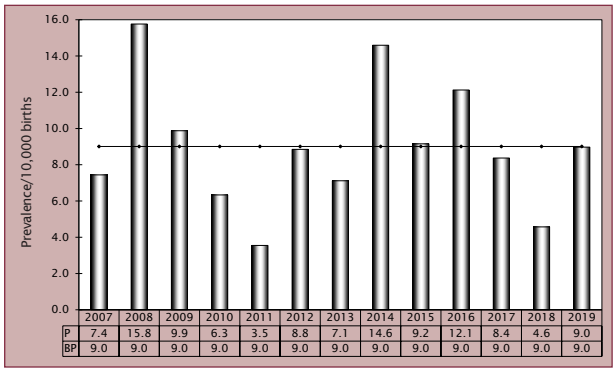


Fig. 6: Development of prevalence/10,000 births with neural tube defects in Saxony-Anhalt since 2007

NOTE

After a pregnancy affected by a neural tube defect, increased folic acid prophylaxis according to the recommendations of the medical societies (preparation available in Germany with 5 mg folic acid equivalent per day) should be explained to those who wish to have children. This higher dose is also recommended today for women with antiepileptic medication and chronic absorption disorders.

additional information:

Pregnancy outcome	1 x live birth 3 x live births, deceased up to 7th day 1 x live birth, deceased after 7th day 10 x termination of pregnancy
Sex	5 x male 4 x female 6 x no indication
Number of isolated malformation/MCA	4 x MCA 11 x isolated

With five children, one third of those affected by a neural tube defect were live births. Four of the children died in the first year of life. As in previous years, terminations of pregnancy account for the largest proportion (2019: 66.7%, 2007-2018: 71.8% of children/fetuses with a neural tube defect).

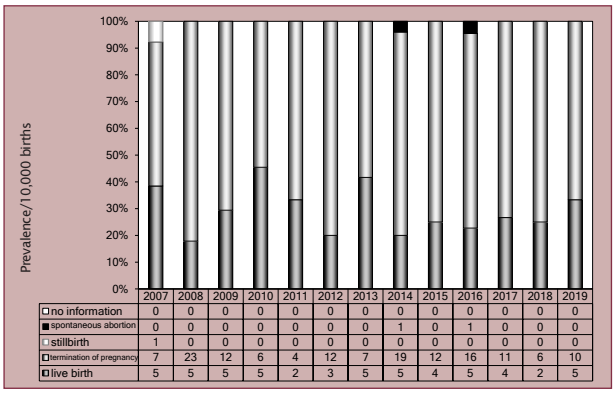


Fig. 7: Pregnancy outcomes of neural tube defects in Saxony-Anhalt since 2007

In 2019, one neural tube defect per 1,114 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. An own sample confirmed this insufficient implementation [1].

Literature

1 Wegner C, Kancherla V, Lux A, Köhn A, Bretschneider D, Freese K, Heiduk M, Redlich A, Schleef D, Jorch G, Rissmann A. Periconceptional folic acid supplement use among women of reproductive age and its determinants in central rural Germany: Results from a cross sectional study. Birth defects research 2020; 112(14): 1057-1066

10.2 Anencephaly (Q00.)

	Year 2019		
Saxony-Anhalt	Number	Prevalence /10,000 births	Comp. to basis prevalence
	5	2.99	↔
	Reporting period 2007-2018		
	Basis prevalence /10,000 births	Confidence interval (CI 95%)	
	2.35	1.74 - 3.10	
EUROCAT (Full members)	Period 2007-2018		
	Basis prevalence /10,000 births	Confidence interval (CI 95%)	
	3.98	3.85 - 4.12	

Anencephaly occurred 5 times in Saxony-Anhalt within the birth cohort 2019 (**prevalence** of **3.0 per 10,000 births**). The current year's prevalence is within the range of Saxony-Anhalt's basis prevalence (2007-2018: 2.3 per 10,000 births).

The comparison with the prevalence provided by EUROCAT for 2007-2018 (4.0 per 10,000 births) indicates a prevalence value for Saxony-Anhalt, for 2019 as well as for the reporting period, far below the European average. Prevalences of more than 6.0 per 10,000 births were reported from six of 37 registries.

The pregnancy was terminated in three cases of anencephaly. The abortions took place between the 14th and 20th week of gestation, in each case one week after the diagnosis was made during prenatal ultrasound. This year, two children with prenatally known anencephaly were born alive and died on the first day of life.

additional information:

Pregnancy outcome	2 x live births, deceased up to 7th day 3 x termination of pregnancy
Sex	3 x female 2 x no indication
Number of isolated malformation/MCA	5 x isolated

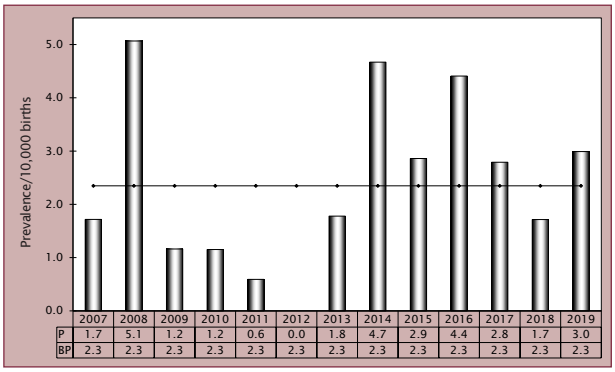


Fig. 8: Development of prevalence/10,000 births with anencephaly in Saxony-Anhalt since 2007

In 2019, one anencephaly per 3,343 births was registered in Saxony-Anhalt.

10.3 Spina bifida (Q05.)

	Year 2019		
Saxony-Anhalt	Number	Prevalence /10,000 births	Comp. to basis prevalence
	8	4.79	↔
	Reporting period 2007-2018		
	Basis prevalence /10,000 births	Confidence interval (CI 95%)	
	5.22	4.29 - 6.30	
EUROCAT (Full members)	Period 2007-2018		
	Basis prevalence /10,000 births	Confidence interval (CI 95%)	
	5.00	4.85 - 5.15	

The **prevalence** of **4.8 per 10,000 births** recorded for 2019 is back within the range of the baseline prevalence (2007-2018: 5.2 per 10,000 births) after a very low value in the previous year (2018: 2.3 per 10,000 births). Three children with spina bifida were born alive, only one child with isolated spina bifida survived the first year of life. In 2019, five pregnancies of fetuses with spina bifida were terminated prematurely between the 17th and 21st WOG.

Although this year's prevalence in Saxony-Anhalt is slightly lower than the European prevalence provided by EUROCAT (2007-2018: 5.0 per 10,000 births), both confidence intervals link the same level. At the same time, the confidence interval of Saxony-Anhalt's basis prevalence has a much wider range of variation than the confidence interval of the European prevalence due to the smaller population included.

additional information:

Pregnancy outcome	1 x live birth 1 x live birth, deceased up to 7th day 1 x live birth, deceased after 7th day 5 x termination of pregnancy
Sex	5 x male 1 x female 2 x no indication
Number of isolated malformation/MCA	4 x MCA 4 x isolated

Five pregnancies were terminated prematurely: One cervical and one lumbar spina bifida were each seen during prenatal ultrasound at 16 weeks of gestation, one thoracolumbar and one lumbosacral spina bifida, each with Arnold-Chiari syndrome, were diagnosed at 19 weeks of gestation and one thoracic spina bifida was discovered at 20 weeks gestation. Two of the live births died. They were affected by spina bifida with hydrocephaly and had multiple malformations.

Malformation combinations (MCA) or superordinated syndromes detected:

- Caudal regression syndrome with: Tetralogy of Fallot, unilateral multicystic dysplastic kidney and agenesis of the other kidney
- 2 x Arnold-Chiari syndrome (1 x with renal agenesis on the right and duplex kidney on the left)
- PRUNE1 syndrome with: PFO and non-haemodynamically effective PDA at full term infant, mandibular retrognathia, neurogenic bladder, talus verticalis

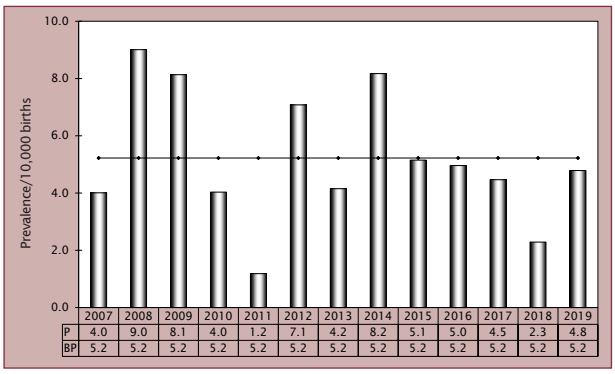


Fig. 9: Development of prevalence/10,000 births with spina bifida in Saxony-Anhalt since 2007

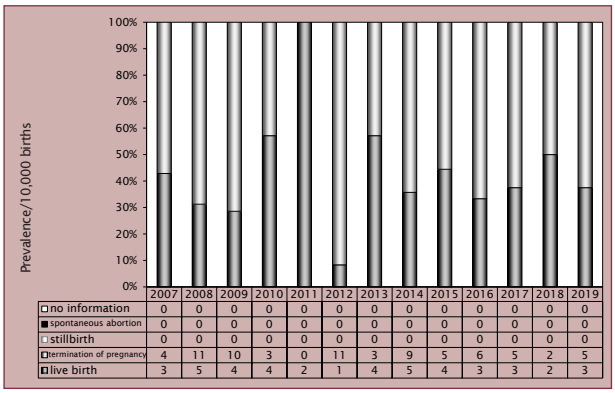


Fig. 10: Pregnancy outcomes of spina bifida in Saxony-Anhalt since 2007

In 2019, one spina bifida per 2,090 births was registered in Saxony-Anhalt.

10.4 Encephalocele (Q01.)

	Year 2019		
Saxony-Anhalt	Number	Prevalence /10,000 births	Comp. to basis prevalence
	2	1.20	↔
	Reporting period 2007-2018		
	Basis prevalence /10,000 births	Confidence interval (CI 95%)	
	1.44	0.97 - 2.05	
EUROCAT (Full members)	Period 2007-2018		
	Basis prevalence /10,000 births	Confidence interval (CI 95%)	
	1.22	1.15 - 1.29	

Two fetuses with encephalocele were registered in 2019. This year's **prevalence** of **1.2 per 10,000 births** is within the range of the basis prevalence in Saxony-Anhalt (2007-2018: 1.4 per 10,000 births) and also corresponds to the European basis prevalence (2007-2018: 1.2 per 10,000 births).
In 2018, the annual prevalence reached the minimum value of the reporting period of 0.6 per 10,000 births and in 2016 a maximum value of 2.8 per 10,000 births was achieved. The small numbers are responsible for this range of variation.

additional information:

Pregnancy outcome	2 x termination of pregnancy
Sex	2 x no indication
Number of isolated malformation/MCA	2 x isolated

In each of both cases, the encephalocele was discovered in the 9th and 12th week of gestation during the first prenatal ultrasound examination and the pregnancies were terminated one week later.

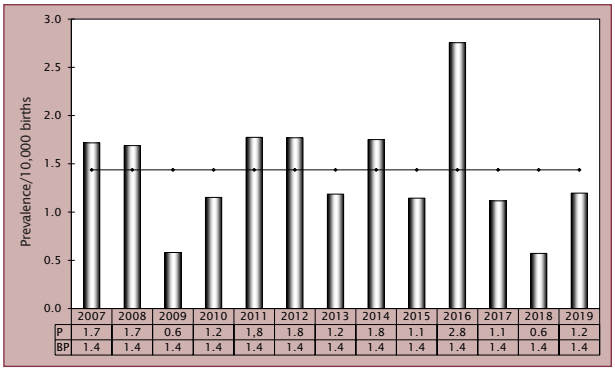


Fig. 11: Development of prevalence/10,000 births with encephalocele in Saxony-Anhalt since 2007

In 2019, one encephalocele per 8,359 births was registered in Saxony-Anhalt.

10.5 Microcephaly (Q02.)

	Year 2019		
Saxony-Anhalt	Number	Prevalence /10,000 births	Comp. to basis prevalence
	3	1.79	↓
	Reporting period 2007-2018		
	Basis prevalence /10,000 births	Confidence interval (CI 95%)	
	3.64	2.87 - 4.56	
EUROCAT (Full members)	Period 2007-2018		
	Basis prevalence /10,000 births	Confidence interval (CI 95%)	
	2.68	2.57 - 2.79	

Three children who were affected by microcephaly were born alive in Saxony-Anhalt in 2019. With a **prevalence** of **1.8 per 10,000 births**, the prevalence in 2019, for the second year in a row, is below the basis prevalence (2007-2018: 3.6 per 10,000 births). In previous years, an increasing trend was noticed, but this has not continued since 2018. The change in prevalence over the reporting period is therefore categorised as non-linear (Chapter 10.38)

The basis prevalence of microcephaly for Saxony-Anhalt is rather high compared to the prevalence reported by EUROCAT. The lower confidence limit of the basis prevalence in Saxony-Anhalt is still above the European confidence interval. This year's prevalence value for Saxony-Anhalt is also lower than the European comparative values.

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.

additional information:

Pregnancy outcome	2 x livebirths 1 x live birth, deceased after 7th day
Sex	1 x male 2 x female
Number of isolated malformation/MCA	2 x MCA 1 x isolated

One child with microcephaly, in whom the microcephaly manifested itself postnatally and which occurred in combination with other disorders, did not complete the first year of life.

Malformation combinations (MCA) or superordinated syndromes detected:

- Deficiency of pyruvate dehydrogenase, epilepsy, bilateral dysplastic ears

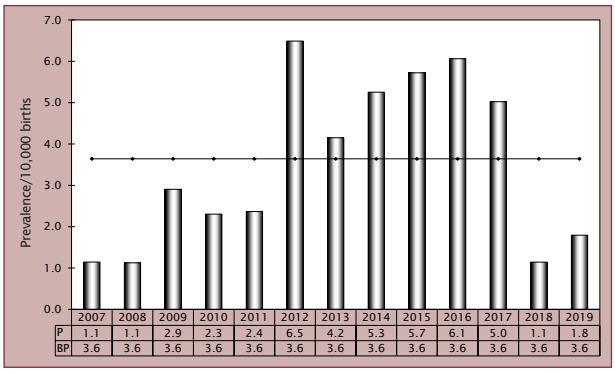


Fig. 12: Development of prevalence/10,000 births with microcephaly in Saxony-Anhalt in 2007

In 2019, one microcephaly per 5,572 births was registered in Saxony-Anhalt.

10.6 Congenital Hydrocephaly (Q03.)

	Year 2019		
Saxony-Anhalt	Number	Prevalence /10,000 births	Comp. to basis prevalence
	8	4.79	↔
	Reporting period 2007-2018		
	Basis prevalence /10,000 births	Confidence interval (CI 95%)	
	5.61	4.64 - 6.72	
EUROCAT (Full members)	Period 2007-2018		
	Basis prevalence /10,000 births	Confidence interval (CI 95%)	
	5.50	5.34 - 5.65	

Hydrocephaly was observed 8 times in Saxony-Anhalt in 2019. Only hydrocephalies that do not occur as a result of a neural tube defect and that do not develop after a haemorrhage or infection are included. The **prevalence** of **4.8 per 10,000 births** determined for Saxony-Anhalt in 2019 lies in the lower range of the calculated basis prevalence (2007-2018: 5.6 per 10,000 births).

In comparison with EUROCAT-data, we determine that the current year's prevalence of Saxony-Anhalt lies within the normal range of the years 2007-2018 (5.5 per 10,000 births).

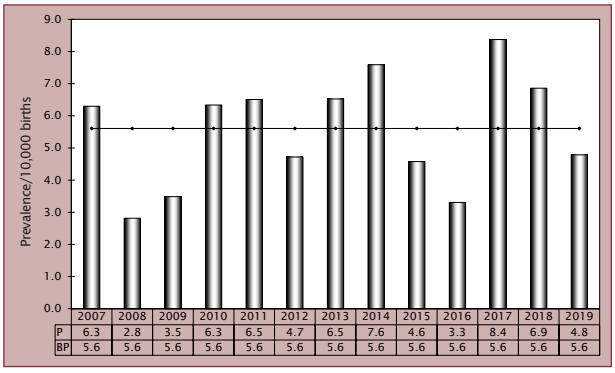
additional information:

Pregnancy outcome	3 x live births 1 x stillbirth 4 x termination of pregnancy
Sex	4 x male 4 x female
Number of isolated malformation/MCA	6 x MCA 2 x isolated

Four pregnancies with fetuses affected by hydrocephalus were terminated between the 19th and 23rd week of gestation. The amniocentesis revealed molecular genetic abnormalities in two of the four cases. One child, who was diagnosed with hydrocephalus and other severe malformations in the 20th week of gestation, was stillborn.

Malformation combinations (MCA) or superordinated syndromes detected:

- Patau syndrome with: cleft lip and palate, brachycephaly
- Bilateral microphthalmia with associated malformations: unilateral cleft lip and palate, cerebellum hypoplasia
- unbalanced translocations and insertions, cerebellar agenesis
- ASD II, stenosis of the pulmonary artery in preterm birth
- Cardiac malformation, accessory kidney, hypertelorism
- Hernia inguinalis in premature infant on left side



	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019
P	6.3	2.8	3.5	6.3	6.5	4.7	6.5	7.6	4.6	3.3	8.4	6.9	4.8
BP	5.6	5.6	5.6	5.6	5.6	5.6	5.6	5.6	5.6	5.6	5.6	5.6	5.6

Fig. 13: Development of prevalence/10,000 births with congenital hydrocephalus in Saxony-Anhalt since 2007

In 2019, one neural tube defect per 2,090 births was registered in Saxony-Anhalt.

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

	Year 2019		
Saxony-Anhalt	Number	Prevalence /10,000 births	Comp. to basis prevalence
	1	0.60	↓
	Reporting period 2007-2018		
	Basis prevalence /10,000 births	Confidence interval (CI 95%)	
	1.68	1.17 - 2.33	
EUROCAT (Full members)	Period 2007-2018		
	Basis prevalence /10,000 births	Confidence interval (CI 95%)	
	1.57	1.48 - 1.65	

Arhinencephaly/holoprosencephaly is a rarely occurring indicator malformation. With a **prevalence** of **0.6 per 10,000 births**, it was only seen once in Saxony-Anhalt in 2019. With a prevalence of otherwise 1.7 per 10,000 births (2007-2018), this year's prevalence is to be considered low. However, a shortfall of the confidence interval of the basis prevalence is not unusual due to the small numbers and the resulting wide range of variation. In 2008 and 2014, the malformation was not observed at all in Saxony-Anhalt, in 2010 it occurred 8 times.

In a Europe-wide comparison, the prevalence in Saxony-Anhalt for 2019 is also far below the confidence interval of the overall prevalence of the European malformation centres (1.6 per 10,000 births). The basis prevalence of Saxony-Anhalt and the prevalence determined by EUROCAT have the same level.

additional information:

Pregnancy outcome	1 x termination of pregnancy
Sex	1 x female
Number of isolated malformation/MCA	1 x MCA

The pregnancy of the fetus affected by holoprosencephaly in connection with a present Patau syndrome ended spontaneously in the 20th week of gestation. The malformations had been diagnosed one week earlier.

Malformation combinations (MCA) or superordinated syndromes detected:

- Patau syndrome with: Omphalocele, bilateral. cleft lip and palate, cardiac malformation

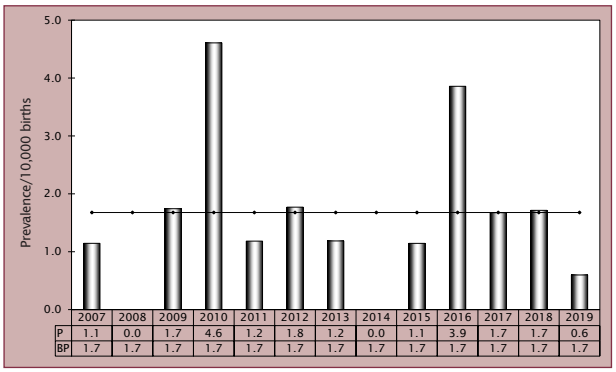


Fig. 14: Development of prevalence/10,000 births with arhinencephalie/holoprosencephalie in Saxony-Anhalt since 2007

In 2019, one arhinencephaly/holoprosencephaly per 16,717 births was registered in Saxony-Anhalt.

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

	Year 2019		
Saxony-Anhalt	Number	Prevalence /10,000 births	Comp. to basis prevalence
	2	1.20	↔
	Reporting period 2007-2018		
	Basis prevalence /10,000 births	Confidence interval (CI 95%)	
	0.86	0.51 - 1.36	
EUROCAT (Full members)	Period 2007-2018		
	Basis prevalence /10,000 births	Confidence interval (CI 95%)	
	0.94	0.88 - 1.01	

The indicator malformation anophthalmia/microphthalmia is a very rarely observed malformation with a basis prevalence of 0.9 per 10,000 births (2007-2018). Two fetuses were affected in 2019. The calculated **prevalence** of **1.2 per 10,000 births** corresponds to the basis prevalence. Even three cases would exceed the upper confidence limit. In the reporting period, a maximum of four children/fetuses per year were seen in Saxony-Anhalt (2010, 2016).

The basis prevalence of Saxony-Anhalt is similar to the prevalence of the years 2007-2018 which was reported by EUROCAT, with a slightly larger range. The annual prevalence of Saxony-Anhalt lies indeed within the normal range of Saxony-Anhalt but due to the smaller European confidence interval it is slightly above this range.

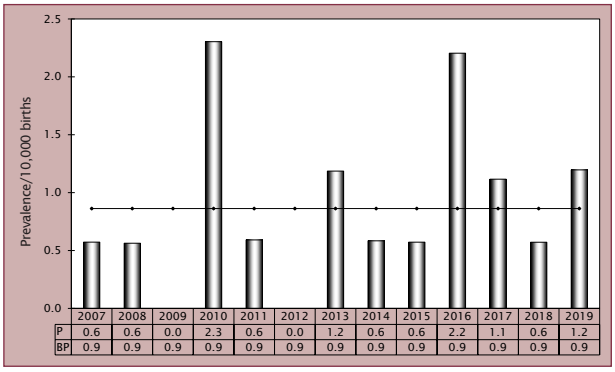
additional information:

Pregnancy outcome	2 x termination of pregnancy
Sex	2 x male
Number of isolated malformation/MCA	2 x MCA

Among other severe malformations, one fet was affected by a bilateral anophthalmia and one by a bilateral microphthalmia. The malformations were diagnosed by ultrasound screening in the 18th and 19th week of pregnancy.

Detected malformation combinations (MCA) or superordinate syndromes:

- Hydrocephalus internus, unilateral cleft lip and palate, cerebellar hypoplasia
- Cardiac malformation, hypoplasia of the diaphragm, bilateral lung hypoplasia, synechiae of the eyelids



	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019
P	0.6	0.6	0.0	2.3	0.6	0.0	1.2	0.6	0.6	2.2	1.1	0.6	1.2
BP	0.9	0.9	0.9	0.9	0.9	0.9	0.9	0.9	0.9	0.9	0.9	0.9	0.9

Fig. 15: Development of prevalence/10,000 births with anophthalmos/microphthalmos in Saxony-Anhalt since 2007

In 2019, one anophthalmos/microphthalmos per 8,359 births was registered in Saxony-Anhalt.

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

	Year 2019		
Saxony-Anhalt	Number	Prevalence /10,000 births	Comp. to basis prevalence
	9	5.38	↑
	Reporting period 2007-2018		
	Basis prevalence /10,000 births	Confidence interval (CI 95%)	
	2.78	2.11 - 3.59	
EUROCAT (Full members)	Period 2007-2018		
	Basis prevalence /10,000 births	Confidence interval (CI 95%)	
	no information	no information	

In 2019, nine children with the indicator malformation microtia/anotia were reported to the malformation monitoring. This results in an annual **prevalence** of **5.4 per 10,000 births**, which is significantly above the basis prevalence of 2.8 per 10,000 births (2007-2018). The basis prevalence was also significantly exceeded in 2015 and 2017, whereas in 2008, 2012 and 2014 the annual prevalence was located significantly below the confidence interval of the basis prevalence. For the indicator malformation microtia/anotia, a significant increasing trend with a percentage change of 12.86 % (CI 0.72 % to 28.40 %) can be observed for the period 2006-2019 (Chapter 10.38).

EUROCAT does not provide any data for the indicator malformation microtia/anotia. For the significantly rarer malformation anotia, EUROCAT reports a prevalence of 0.26 per 10,000 births (2007-2018), similar to that of Saxony-Anhalt (2007-2018: 0.29 per 10,000 births).

additional information:

Pregnancy outcome	8 x live births 1 x live birth, deceased after 7th day
Sex	2 x male 7 x female
Number of isolated malformation/MCA	8 x MCA 1 x isolated

In 2019, the malformation occurred unilaterally in six cases, three times on the right and three times on the left side. Three times both ears were affected. Anotia was found three times, microtia 6 times.

Detected malformation combinations (MCA) or superordinate syndromes:

- CHARGE association with: immunodeficiency, cleft lip and palate on the right side, vascular ring through the anomalous right subclavicular artery, ASD II, bilateral coloboma of the papilla, bilateral sensorineural defect, tracheomalacia, athyreosis, non-haemodynamically effective PDA at full term infant, laterally rising lid axes, plexus cyst
- common ventricle, pterygium colli, low-set ears
- 2 x bilateral conductive disorder (1 x with narrowing and 1 x with atresia of the osseous auditory canal)
- 4 x unilateral conductive disorder (2 x with atresia of the osseous auditory canal, 1 x with atresia of the auditory canal entrance and 1 x with hypoplasia and narrowing of the auditory canal and preauricular appendage)

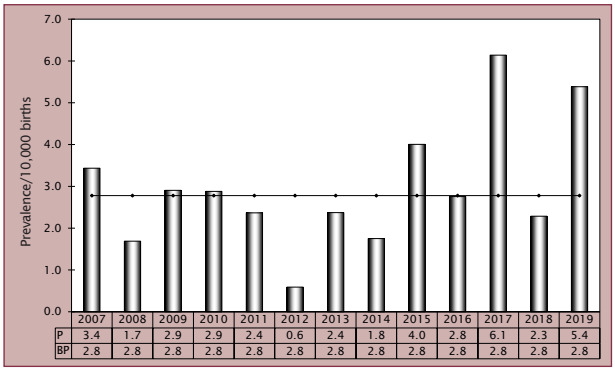


Fig. 16: Development of prevalence/10,000 births with microtia/ anotia in Saxony-Anhalt since 2007

In 2019, one microtia/anotia per 1,857 births was registered in Saxony-Anhalt.

10.10 Tetralogy of Fallot (Q21.3)

	Year 2019		
Saxony-Anhalt	Number	Prevalence /10,000 births	Comp. to basis prevalence
	6	3.59	↔
	Reporting period 2007-2018		
	Basis prevalence /10,000 births	Confidence interval (CI 95%)	
	3.31	2.57 - 4.18	
EUROCAT (Full members)	Period 2007-2018		
	Basis prevalence /10,000 births	Confidence interval (CI 95%)	
	3.60	3.48 - 3.73	

The complex cardiac malformation tetralogy of Fallot consists of a combination of four cardiac malformations: Pulmonary stenosis, VSD, malformed aorta and right heart hypertrophy. The malformation was diagnosed in six cases in Saxony-Anhalt in 2019. This results in a **prevalence** of **3.6 per 10,000 births** for 2019. The current year's prevalence is inconspicuously within the range of Saxony-Anhalt's basis prevalence (2007- 2018: 3.3 per 10,000 births).

The annual prevalence of Saxony-Anhalt is also within the normal range compared to the prevalence reported by EUROCAT for the years 2007-2018 (3.6 per 10,000 births). However, due to smaller numbers, the confidence interval of Saxony-Anhalt's basis prevalence spans a larger safety range than the interval of the average prevalence of the European registers.

additional information:

Pregnancy outcome	3 x live births 1 x live birth, deceased up to 7th day 2 x termination of pregnancy
Sex	2 x male 4 x female
Number of isolated malformation/MCA	5 x MCA 1 x isolated

One child was affected by multiple malformations of other organ systems in addition to the cardiac malformations and died on the first day of life. Three other live births had no malformations other than a malformed heart.

Malformation combinations (MCA) or superordinated syndromes detected:

- Edwards syndrome with: cleft lip, plexus cyst
- caudal regression syndrome with: hydrocephaly with spina bifida, unilateral multicystic dysplastic kidney and agenesis of the other kidney
- persistent left superior vena cava, thymic hypoplasia
- ASD II
- haemodynamically effective PDA and right inguinal hernia at preterm birth, craniofacial dysmorphia

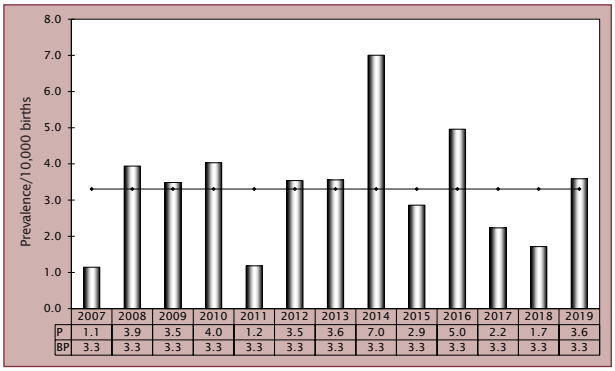


Fig. 17: Development of prevalence/10,000 births with Tetralogy of Fallot (Q21.3) in Saxony-Anhalt since 2007

In 2019, one Tetralogy of Fallot per 2,786 births was registered in Saxony-Anhalt.

10.11 Transposition of great vessels – TGV (Q20.1/Q20.3)

	Year 2019		
Saxony-Anhalt	Number	Prevalence /10,000 births	Comp. to basis prevalence
	7	4.19	↔
	Reporting period 2007-2018		
	Basis prevalence /10,000 births	Confidence interval (CI 95%)	
	4.50	3.64 - 5.51	
EUROCAT (Full members)	Period 2007-2018		
	Basis prevalence /10,000 births	Confidence interval (CI 95%)	
	3.58	3.45 - 3.71	

A characteristic feature of transposition of the great vessels (TGA) is that the vessels leading from the heart are reversed. Additionally, this malformation includes the rare malformation of the double outlet right ventricle (DORV).

In 2019, seven children were born with a transposition of the great vessels in Saxony-Anhalt. This results in a **prevalence** of **4.2 per 10,000 births**, which is in line with the basis prevalence calculated for 2007-2018 (4.5 per 10,000 births).

EUROCAT gives a prevalence of 3.6 per 10,000 births for TGV. The 2019 annual prevalence of Saxony-Anhalt lies above the confidence interval. However, the stated prevalences are only comparable to a limited extent, as the prevalence of EUROCAT does not include DORV.

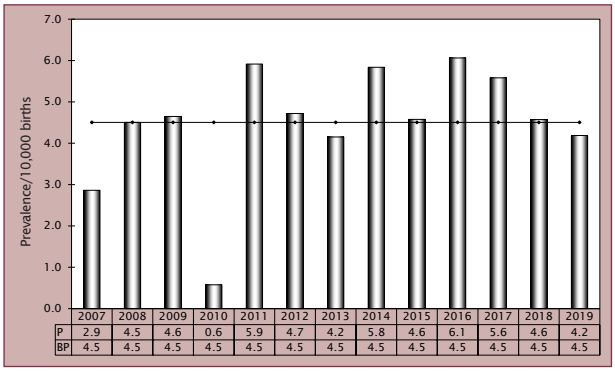
additional information:

Pregnancy outcome	4 x live births 1 x live birth, deceased after 7th day 2 x stillbirths
Sex	6 x male 1 x female
Number of isolated malformation/MCA	7 x MCA

One stillbirth and one live birth were affected by DORV. All children suffered from other cardiac malformations in addition to the TGV. One child died two weeks after an operation when it was about two months old.

Malformation combinations (MCA) or superordinated syndromes detected:

- VSD, ASD II, persistent left superior vena cava, stenosis of the pulmonary artery in a full term infant
- VSD, ASD II, vascular ring of the great arteries, right aortic arch, hypoplasia of the aorta, plexus cyst
- VSD, ASD II, vascular ring of the great arteries
- VSD, ASD II
- Dextrocardia with situs inversus
- 2 x pulmonary valve stenosis (1 x dextrocardia, right ventricular myocardial hypertrophy)



	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019
P	2.9	4.5	4.6	0.6	5.9	4.7	4.2	5.8	4.6	6.1	5.6	4.6	4.2
BP	4.5	4.5	4.5	4.5	4.5	4.5	4.5	4.5	4.5	4.5	4.5	4.5	4.5

Fig. 18: Development of prevalence/10,000 births with transposition of great vessels in Saxony-Anhalt since 2007

In 2019, one transposition of great vessels per 2,388 births was registered in Saxony-Anhalt.

10.12 Hypoplastic Left Heart Syndrome (Q23.4)

	Year 2019		
Saxony-Anhalt	Number	Prevalence /10,000 births	Comp. to basis prevalence
	9	5.38	↑
	Reporting period 2007-2018		
	Basis prevalence /10,000 births	Confidence interval (CI 95%)	
	2.64	1.99 - 3.43	
EUROCAT (Full members)	Period 2007-2018		
	Basis prevalence /10,000 births	Confidence interval (CI 95%)	
	2.75	2.64 - 2.86	

After a very low prevalence value of hypoplastic left heart syndrome in 2018 we registered nine children/fetuses from Saxony-Anhalt in 2019 with this cardiac malformation. This resulted in a **prevalence** of **5.4 per 10,000 births**, which is the maximum value in the reporting period. For the last time the annual prevalence exceeded this value in the year 2000 (5.9 per 10,000). The prevalence value of 2019 is significantly higher than the basis prevalence of 2.6 per 10,000 births calculated for the years 2007-2018.

The 2019 annual prevalence of Saxony-Anhalt also exceeds the European prevalence provided by EUROCAT (2007-2018: 2.7 per 10,000 births). However, there is an overlapping of the confidence intervals of the basis prevalence for the years 2007-2018, whereby the confidence interval of the Saxony-Anhalt prevalence being wider than the one of the European prevalence due to smaller numbers.

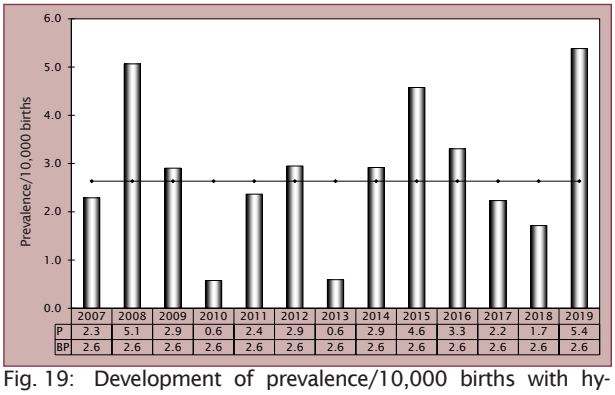
additional information:

Pregnancy outcome	3 x live births 2 x live births, deceased after 7th day 4 x termination of pregnancy
Sex	8 x male 1 x female
Number of isolated malformation/MCA	6 x MCA 3 x isolated

In one case the hypoplastic left heart syndrome was not recognised prenatally. This infant was immediately transferred to another hospital for surgical correction on the second day of life. All births were full term infants. Two children died at about six months of age. Four pregnancies were terminated prematurely after the diagnosis of hypoplastic left heart syndrome was made in two cases in the 15th and in two cases in the 21st week of gestation.

Malformation combinations (MCA) or superordinated syndromes detected:

- Anal atresia with fistula, horseshoe kidney
- Stenosis of the jejunum, stenosis of the pulmonary artery at full term infant
- ASD II, tricuspid insufficiency
- ASD II
- Malformation of a large vein
- VSD



	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019
P	2.3	5.1	2.9	0.6	2.4	2.9	0.6	2.9	4.6	3.3	2.2	1.7	5.4
BP	2.6	2.6	2.6	2.6	2.6	2.6	2.6	2.6	2.6	2.6	2.6	2.6	2.6

Fig. 19: Development of prevalence/10,000 births with hypoplastic left heart syndrome in Saxony-Anhalt since 2007

In 2019, one child with a hypoplastic left heart syndrome per 1,857 births was registered in Saxony-Anhalt.

10.13 Coarctation of aorta (Q25.1)

	Year 2019		
Sachsen-Anhalt	Number	Prevalence /10,000 births	Comp. to basis prevalence
	7	4.19	↓
	Reporting period 2007-2018		
	Basis prevalence /10,000 births	Confidence interval (CI 95%)	
	5.99	4.99 - 7.14	
EUROCAT (Full members)	Period 2007-2018		
	Basis prevalence /10,000 births	Confidence interval (CI 95%)	
	3.93	3.80 - 4.07	

Seven births with a haemodynamically relevant coarctation of aorta were registered in 2019. The resulting annual **prevalence** of **4.2 per 10,000 births** is clearly below the confidence interval of the basis prevalence in Saxony-Anhalt (2007-2018: 6.0 per 10,000 births). A minimum was recorded in the reporting period in 2015 with 2.3 per 10,000 births.

The tolerance range of the 2007-2018 prevalence (3.9 per 10,000 births) determined by EUROCAT across Europe is far below the confidence interval of the basis prevalence from Saxony-Anhalt. This year's annual prevalence of Saxony-Anhalt is in between and lies at the same time above the upper confidence limit of the European prevalence.

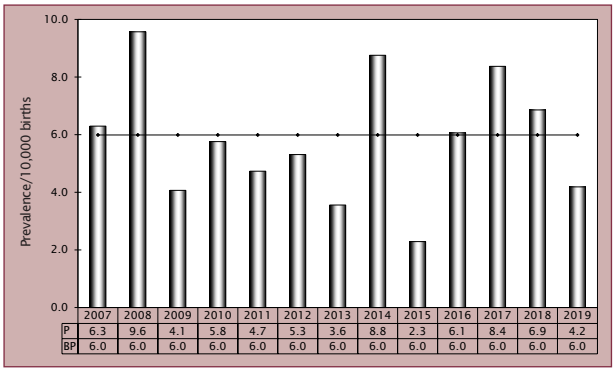
additional information:

Pregnancy outcome	7 x live births
Sex	2 x male 5 x female
Number of isolated malformation/MCA	6 x MCA 1 x isolated

A coarctation of aorta is difficult to detect during prenatal ultrasound screening. Nevertheless, it was known prenatally in four children. Only one child had an isolated coarctation of aorta. In 5 cases, the coarctation of aorta was associated with other cardiac malformations and once in combination with multiple malformations of the heart and other organ systems.

Malformation combinations (MCA) or superordinated syndromes detected:

- VSD, ASD II, mitral valve insufficiency, bicuspid aortic valve, aortic valve stenosis, hypoplasia of aorta, haemangioma of the liver, splenic malformation, capillary haemangioma, 1st degree tricuspid insufficiency, macroglossia
- 2 x VSD, ASD II
- Aortic valve stenosis, VSD
- Hypoplasia of aorta, PFO at fullterm infant
- Stenosis of the pulmonary artery, retarded right hip maturity



	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019
P	6.3	9.6	4.1	5.8	4.7	5.3	3.6	8.8	2.3	6.1	8.4	6.9	4.2
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

Fig. 20: Development of prevalence/10,000 births with coarctation of aorta in Saxony-Anhalt since 2007

In 2019, one coarctation of aorta per 2,388 births was registered in Saxony-Anhalt.

10.14 Cleft lip with or without cleft palate (Q36./Q37.)

Saxony-Anhalt	Year 2019		
	Number	Prevalence /10,000 births	Comp. to basis prevalence
	25	14.95	↗
	Reporting period 2007-2018		
	Basis prevalence /10,000 births	Confidence interval (CI 95%)	
	13.13	11.62 - 14.78	
EUROCAT (Full members)	Period 2007-2018		
	Basis prevalence /10,000 births	Confidence interval (CI 95%)	
	8.75	8.56 - 8.95	

The indicator malformation cleft lip and cleft lip and palate occurs in various forms. Four variants are described: The most common, cleft lip, jaw and palate, was seen 19 times in 2019, cleft upper lip 4 times and cleft lip and jaw twice. Cleft lip and palate was not observed in 2019.

In 2019, a total of 25 children/fetuses with cleft lip and cleft lip, jaw and palate were reported to the monitoring of congenital malformations. This results in a **prevalence** of **15.0 per 10,000 births** for Saxony-Anhalt, which is slightly above the upper confidence limit of the basis prevalence (2007-2018: 13.1 per 10,000 births).

Compared to the prevalence of the EUROCAT registers (2007-2018: 8.7 per 10,000 births), the basis prevalence of Saxony-Anhalt is to be considered very high, similar to the previous years, as well as in comparison to the current annual prevalence (2019). The basis prevalence of Saxony-Anhalt is regularly found in the upper third of the prevalence values of the European registers. This year's value is even higher than the maximum value of the European prevalences (2007-2018: 13.9 per 10,000 births) from the register Pleven (Bulgaria).

additional information:

Pregnancy outcome	18 x live births 1 x live birth, deceased after 7th day 1 x spontaneous abortion 5 x termination of pregnancy
Sex	12 x male 13 x female
Number of isolated malformation/MCA	10 x MCA 15 x isolated

In three cases of termination of pregnancy, the cleft lip, jaw and palate occurred in connection with a trisomy. The other two pregnancies which were terminated prematurely were also affected by other severe malformations of other organ systems in addition to the cleft lip, jaw and palate.

As expected, the cleft formation was again registered predominantly unilateral in 2019 (16 x, of which: 8 x left, 6 x right, 2 x unilateral n.o.s.). Typically, left-sided cleft lip, jaw and palate occurs much more frequently than right-sided unilateral cleft lip and palate. In the period from 2007 to 2018 more than twice as many left-sided (114) than right-sided (47) cases were observed. Bilateral cleft lip and cleft lip, jaw and palate were present in five cases in 2019. Four times, no information about the laterality was provided.

Malformation combinations (MCA) or superordinated syndromes detected:

- Patau syndrome with: holoprosencephaly, omphalocele, cardiac malformation
- Patau syndrome with: hydrocephalus internus in Dandy-Walker syndrome, brachycephaly
- Patau syndrome with: cardiac malformation
- Edwards syndrome with: Tetralogy of Fallot, plexus cyst
- Potter sequence, broad nasal root, low-set ears, Potter facies
- CHARGE association with: immunodeficiency, bilateral anotia, vascular ring through the anomalous right subclavicular artery, ASD II, bilateral coloboma of the papilla, bilateral sensorineural defect, tracheomalacia, athyreosis, non-haemodynamically effective PDA at full term infant, laterally rising eyelid axes, plexus cyst
- Bilateral microphthalmia with associated malformations: hydrocephalus internus, cerebellar hypoplasia
- ASD II, DUP grade I right
- Mitral valve insufficiency
- PFO and non haemodynamically effective PDA at full term infant, bilateral retarded hip

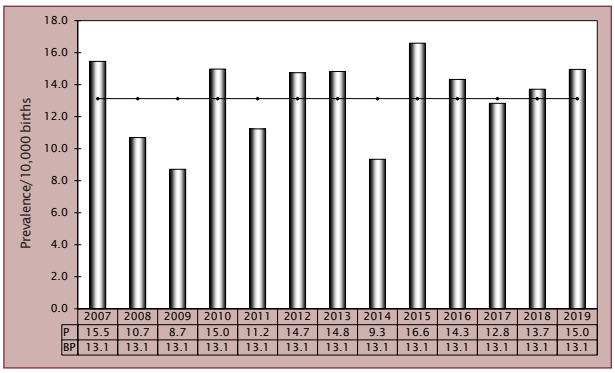


Fig. 21: Development of prevalence/10,000 births with cleft lip with or without cleft palate in Saxony-Anhalt since 2007

In 2019, one child with cleft lip with or without cleft palate per 669 births was registered in Saxony-Anhalt.

10.15 Cleft palate (Q35.1/Q35.3/Q35.5/Q35.9)

	Year 2019		
Saxony-Anhalt	Number	Prevalence /10,000 births	Comp. to basis prevalence
	10	5.98	↔
	Reporting period 2007-2018		
	Basis prevalence /10,000 births	Confidence interval (CI 95%)	
	7.00	5.91 - 8.23	
EUROCAT (Full members)	Period 2007-2018		
	Basis prevalence /10,000 births	Confidence interval (CI 95%)	
	5.88	5.72 - 6.04	

In the birth year 2019, a cleft palate was diagnosed 10 times in Saxony-Anhalt. The **prevalence** determined from this number (2019: **6.0 per 10,000 births**) is in the lower normal range of the basis prevalence of Saxony-Anhalt (2007-2018: 7.0 per 10,000 births).

Compared to the average prevalence of EUROCAT (2007-2018: 5.9 per 10,000 births), the annual prevalence of 2019 is in the upper normal range of the European-wide values. The value of the basis prevalence of Saxony-Anhalt is higher than the prevalence value given by EUROCAT. The confidence intervals overlap each other slightly.

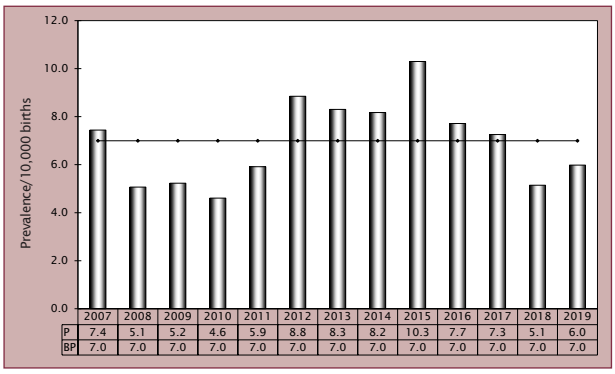
additional information:

Pregnancy outcome	9 x live births 1 x spontaneous abortion
Sex	5 x male 5 x female
Number of isolated malformation/MCA	6 x MCA 4 x isolated

The cleft palate occurred as a symptom of chromosomal aberration in one pregnancy that ended spontaneously in the 16th week of gestation. Three children with cleft palate had a severely impaired hearing disorder. Two other children with the indicator malformation cleft palate were also affected by malformations of other organ systems.

Malformation combinations (MCA) or superordinated syndromes detected:

- Triploidy with: bilateral lung hypoplasia, low-set ears, mandibular retrognathia
- Dysplasia spondyloepiphysaria with: low-set ears, hypertelorism, four-finger furrows, sandal gaps, craniofacial dysmorphia, sunken nasal root
- single cerebral cyst on the left, PFO at full term infant, mandibular retro- and micrognathia
- 2 x bilateral sound perception disorder (1 x uvula cleft)
- Sound conduction disorder left



	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019
P	7.4	5.1	5.2	4.6	5.9	8.8	8.3	8.2	10.3	7.7	7.3	5.1	6.0
BP	7.0	7.0	7.0	7.0	7.0	7.0	7.0	7.0	7.0	7.0	7.0	7.0	7.0

Fig. 22: Development of prevalence/10,000 births with cleft palate in Saxony-Anhalt since 2007

In 2019, one child with cleft palate per 1,672 births was registered in Saxony-Anhalt.

10.16 Choanal atresia (Q30.0)

	Year 2019		
Saxony-Anhalt	Number	Prevalence /10,000 births	Comp. to basis prevalence
	2	1.20	↔
	Reporting period 2007-2018		
	Basis prevalence /10,000 births	Confidence interval (CI 95%)	
	1.01	0.62 - 1.54	
	Period 2007-2018		
EUROCAT (Full members)	Basis prevalence /10,000 births	Confidence interval (CI 95%)	
	0.91	0.85 - 0.97	

The indicator malformation choanal atresia belongs to the very rarely occurring malformations. In the years 2007-2018, a total of 21 cases were registered in Saxony-Anhalt. This results in a basis prevalence of 1.0 per 10,000 births (2007-2018). In 2019, choanal atresia was observed twice, in some years it does not occur at all. This year's **prevalence** of **1.2 per 10,000 births** is within the confidence interval of the basis prevalence of Saxony-Anhalt. The low numbers lead to strong fluctuations of the annual prevalence values.

The confidence interval of the basis prevalence of Saxony-Anhalt corresponds to the interval limits given by EUROCAT. However, it is wider due to smaller numbers and covers the interval of the total prevalence of the European registers. The prevalence value of Saxony-Anhalt of 2019 lies only slightly above the European overall prevalence.

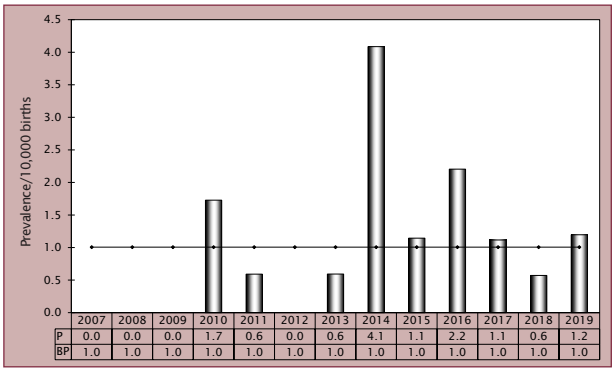
additional information:

Pregnancy outcome	1 x live birth 1 x live birth, deceased after 7th day
Sex	2 x female
Number of isolated malformation/MCA	1 x MCA 1 x isolated

One child with choanal atresia as part of a CHARGE association died in the second year of life.

Malformation combinations (MCA) or superordinated syndromes detected:

- Immunodeficiency, bilateral anotia, cleft lip and palate on the right side, vascular ring through the anomalous right subclavian artery, ASD II, bilateral coloboma of the papilla, bilateral sensorineural defect, tracheomalacia, athyreosis, non-haemodynamically effective PDA at full term infant, laterally rising eyelid axes, plexus cyst



	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019
P	0.0	0.0	0.0	1.7	0.6	0.0	0.6	4.1	1.1	2.2	1.1	0.6	1.2
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. 23: Development of prevalence/10,000 births with choanal atresia in Saxony-Anhalt since 2007

In 2019, one child with a choanal atresia per 8,359 births was registered in Saxony-Anhalt.

10.17 Oesophageal atresia/stenosis/fistula (Q39.0-Q39.4)

	Year 2019		
Saxony-Anhalt	Number	Prevalence /10,000 births	Comp. to basis prevalence
	3	1.79	↓
	Reporting period 2007-2018		
	Basis prevalence /10,000 births	Confidence interval (CI 95%)	
	2.92	2.24 - 3.75	
EUROCAT (Full members)	Period 2007-2018		
	Basis prevalence /10,000 births	Confidence interval (CI 95%)	
	2.63	2.52 - 2.74	

With three children and a resulting **prevalence** of **1.8 per 10,000 births**, the indicator malformation oesophageal atresia/stenosis/fistula was seen less frequently in 2019, after it appeared two years above the expected prevalence value. This year's prevalence is substantially below the lower confidence limit of the basis prevalence (2007-2018: 2.9 per 10,000 births). During the reporting period, a minimum was observed in 2014 (0.6 per 10,000 births), which was not undercut in 2019.

The basis prevalence of Saxony-Anhalt corresponds to the prevalence of the EUROCAT registers (2007-2018: 2.6 per 10,000 births). The confidence interval of the basis prevalence of Saxony-Anhalt is wider than the interval of the total European prevalence because of the smaller numbers. The annual prevalence of Saxony-Anhalt of 2019 is also lower than the European average.

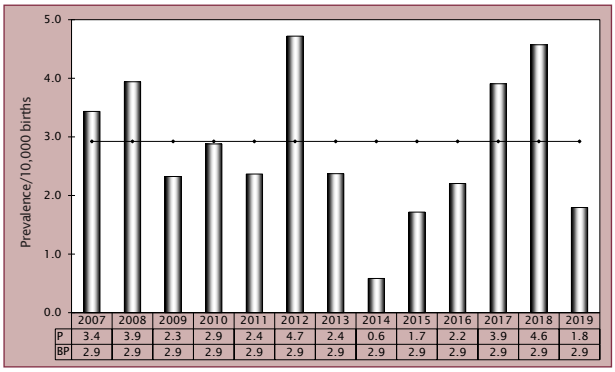
additional information:

Pregnancy outcome	3 x live births
Sex	3 x male
Number of isolated malformation/MCA	1 x MCA 2 x isolated

Two children were affected by an atresia of the oesophagus with fistula between trachea and the lower oesophageal pouch (type Vogt III b). One child was affected by oesophageal atresia without fistula (type Vogt I). In all three children, a polyhydramnios was conspicuous during pregnancy. One oesophageal atresia was diagnosed prenatally. It was revealed postnatally as part of a VACTERL association.

Malformation combinations (MCA) or superordinated syndromes detected:

- VACTERL association with: total supradiaphragmatic misjunction of the pulmonary veins, split vertebra with scoliosis



	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019
P	3.4	3.9	2.3	2.9	2.4	4.7	2.4	0.6	1.7	2.2	3.9	4.6	1.8
BP	2.9	2.9	2.9	2.9	2.9	2.9	2.9	2.9	2.9	2.9	2.9	2.9	2.9

Fig. 24: Development of prevalence/10,000 births with oesophageal atresia/stenosis/fistula in Saxony-Anhalt since 2007

In 2019, one child with oesophageal atresia/-stenosis/-fistula per 5,572 births was registered in Saxony-Anhalt.

10.18 Small intestinal atresia/stenosis (Q41.1/Q41.2/Q41.8/Q41.9)

	Year 2019		
Saxony-Anhalt	Number	Prevalence /10,000 births	Comp. to basis prevalence
	3	1.79	↔
	Reporting period 2007-2018		
	Basis prevalence /10,000 births	Confidence interval (CI 95%)	
	1.82	1.29 - 2.50	
EUROCAT (Full members)	Period 2007-2018		
	Basis prevalence /10,000 births	Confidence interval (CI 95%)	
	0.96	0.89 - 1.02	

With a basis **prevalence** of **1.8 per 10,000 births**, the indicator malformation small intestinal atresia/stenosis is one of the rarer malformations, with numbers ranging from a minimum of zero (2014) to a maximum of seven (2012) in Saxony-Anhalt during the reporting period. In 2019, the current prevalence lies at 1.8 per 10,000 births and is similar to the basis prevalence.

Compared to the European prevalence determined by EUROCAT (2007-2018: 1.0 per 10,000 births), both the basis prevalence and the annual prevalence of Saxony-Anhalt can be rated as high. However, the maximum value of the European register of Pleven (Bulgaria) of 2.0 per 10,000 births is not reached.

additional information:

Pregnancy outcome	2 x live births 1 x stillbirth
Sex	2 x male 1 x female
Number of isolated malformation/MCA	1 x MCA 2 x isolated

The three children were each diagnosed with stenosis of a part of the small intestine, once of the jejunum and once of the ileum, in one case the exact location was not given.

Malformation combinations (MCA) or superordinated syndromes detected:

- Left heart hypoplasia, stenosis of arteria pulmonalis at full term infant

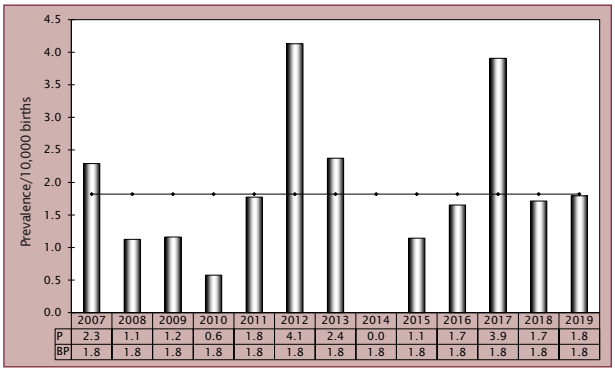


Fig. 25: Development of prevalence/10.000 births with small intestinal atresia/stenosis in Saxony-Anhalt since 2007

In 2019, one child with small intestinal atresia/stenosis per 5,572 births was registered in Saxony-Anhalt.

10.19 Anorectal atresia/stenosis (Q42.0-Q42.3)

	Year 2019		
Saxony-Anhalt	Number	Prevalence /10,000 births	Comp. to basis prevalence
	5	2.99	↓
	Reporting period 2007-2018		
	Basis prevalence /10,000 births	Confidence interval (CI 95%)	
	4.70	3.81 - 5.72	
	Period 2007-2018		
EUROCAT (Full members)	Basis prevalence /10,000 births	Confidence interval (CI 95%)	
	3.35	3.23 - 3.48	

In 2019, the annual **prevalence** of the indicator malformation rectal and anal atresia/stenosis (2019: **3.0 per 10,000 births**) lies significantly below the basis prevalence determined for Saxony-Anhalt (2007-2018: 4.7 per 10,000 births). In the period 2007 to 2010 alone, the malformation was seen much more frequently than in all years since the beginning of malformation recording in 1980. As the annual prevalence has been at or below the confidence interval of the basis prevalence since 2011, a significant downward trend is emerging for rectal and anal atresia/stenosis, with a percentage change of -21.24 % (CI -26.63 % to -10.89 %) (Chapter 10.38). The reason for this is the peak of 2007-2009 with an extreme value of 8.4 per 10,000 births which was registered in 2008.

The current annual prevalence value for Saxony-Anhalt is also lower than the overall prevalence of the European registries documented by EUROCAT (2007-2018: 3.4 per 10,000 births); in contrast, the confidence interval of the basis prevalence is well above the overall prevalence of the European registries (2007-2018).

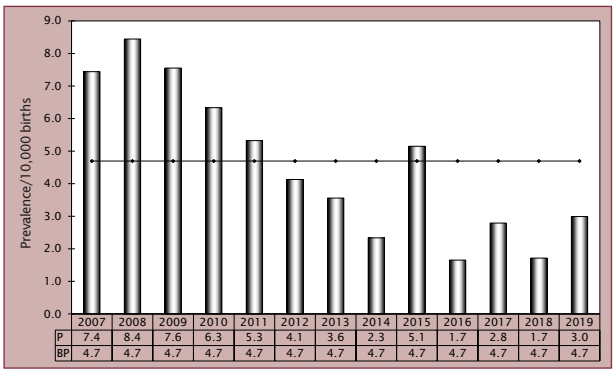
additional information:

Pregnancy outcome	3 x live births 1 x live birth, deceased after 7th day 1 x termination of pregnancy
Sex	3 x male 2 x female
Number of isolated malformation/MCA	3 x MCA 2 x isolated

Rectal and anal atresia/stenosis are often diagnosed postnatally because they are difficult to identify during prenatal sonographic examinations. One pregnancy was terminated due to cardiac and CNS malformations.
In 2019, anal atresia with fistula was diagnosed twice, without fistula once and rectal atresia with fistula twice postnatally.

Malformation combinations (MCA) or superordinated syndromes detected:

- Edwards syndrome with: AVSD, skeletal malformation, bilateral hearing loss, plexus cyst
- Caudal regression syndrome with: malformed os sacrum, hemivertebra, DUP grade II right
- Left heart hypoplasia, horseshoe kidney



	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019
P	7.4	8.4	7.6	6.3	5.3	4.1	3.6	2.3	5.1	1.7	2.8	1.7	3.0
BP	4.7	4.7	4.7	4.7	4.7	4.7	4.7	4.7	4.7	4.7	4.7	4.7	4.7

Fig. 26: Development of prevalence/10,000 births with anorectal atresia/-stenosis in Saxony-Anhalt since 2007

In 2019, one anorectal atresia/ stenosis per 3,343 births was registered in Saxony-Anhalt.

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

Saxony-Anhalt	Year 2019		
	Number	Prevalence /10,000 births	Comp. to basis prevalence
	26	15,55	↓
	Reporting period 2007-2018		
	Basis prevalence /10,000 births	Confidence interval (CI 95%)	
	22,81	20,81 - 24,95	
EUROCAT (Full members)	Period 2007-2018		
	Basis prevalence /10,000 births	Confidence interval (CI 95%)	
	17,68	17,40 - 17,96	

Hypospadias is usually the most frequently observed of the known 37 indicator malformations. In 2019, however, it was seen in only 26 boys. The **prevalence** of **15.6 per 10,000 births** (30.3 per 10,000 boys) which was calculated from this value lies strongly below the basis prevalence (2007-2018: 22.8 per 10,000 births, 44.5 per 10,000 boys). Hypospadias has been registered in Saxony-Anhalt during the period of 2007-2018 with a frequency of 7.0 per 10,000 births. The variants hypospadia glandis and hypospadia coronaria are partly only detected in the course of the first year of life.

The basis prevalence of Saxony-Anhalt lies well above the European prevalence of 17.7 per 10,000 births determined by EUROCAT, but falls far short of the maximum value of the EUROCAT registers of Zagreb (Croatia) with a value of 30.5 per 10,000 births. The current prevalence of 2019 lies still below the normal range of the overall prevalence of the European registers.

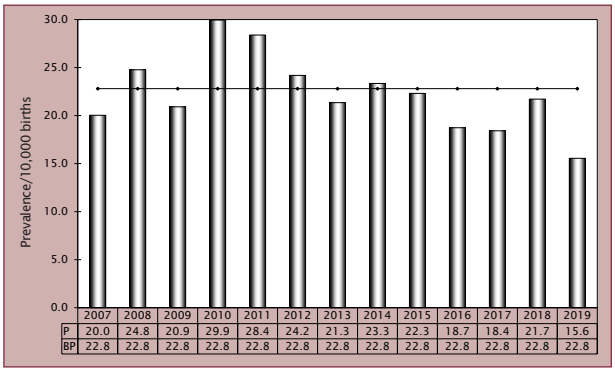
additional information:

Pregnancy outcome	26 x live births
Sex	26 x male
Number of isolated malformation/ MCA	1 x MCA 25 x isolated

All affected boys were born alive in 2019. Only one child had other malformations in several organ systems in addition to the hypospadias, 25 times the hypospadias occurred in isolation.
In 2019, 21 glandular hypospadias, one hypospadia coronaria, three penile and one perineal hypospadias were reported.

Malformation combinations (MCA) or superordinated syndromes detected:

- Corpus callosum hypoplasia, solitary renal cyst on the right, ASD II, strabismus



	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019
P	20.0	24.8	20.9	29.9	28.4	24.2	21.3	23.3	22.3	18.7	18.4	21.7	15.6
BP	22.8	22.8	22.8	22.8	22.8	22.8	22.8	22.8	22.8	22.8	22.8	22.8	22.8

Fig. 27: Development of prevalence/10,000 births with hypospadias in Saxony-Anhalt since 2007

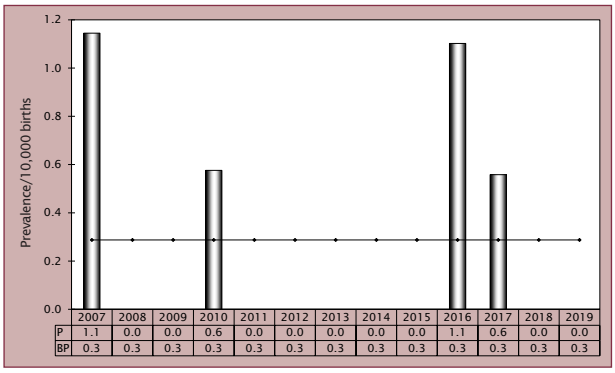
In 2019, one hypospadias per 643 births (330 boys) was registered in Saxony-Anhalt.

10.21 Epispadias (Q64.0)

Saxony-Anhalt	Year 2019		
	Number	Prevalence /10,000 births	Comp. to basis prevalence
	0	0,0	↓
	Reporting period 2007-2018		
	Basis prevalence /10,000 births	Confidence interval (CI 95%)	
	0,29	0,10 - 0,63	
EUROCAT (Full members)	Period 2007-2018		
	Basis prevalence /10,000 births	Confidence interval (CI 95%)	
	keine Angaben	keine Angaben	

Epispadias is a rarely seen indicator malformation. With a basis prevalence of 0.3 per 10,000 births, it occurs only once or at most twice in some years in Saxony-Anhalt. In nine of the 13 years of the reporting period, including 2019, no cases were registered. When taking into account only the live born and stillborn boys, the basis prevalence for epispadias lies at 0.60 per 10,000 boys.

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



	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019
P	1.1	0.0	0.0	0.6	0.0	0.0	0.0	0.0	0.0	1.1	0.6	0.0	0.0
BP	0.3	0.3	0.3	0.3	0.3	0.3	0.3	0.3	0.3	0.3	0.3	0.3	0.3

Fig. 28: Development of prevalence/10,000 births with epispadias in Saxony-Anhalt since 2007

In 2019, no child with epispadias was registered in Saxony-Anhalt.

10.22 Indeterminate sex (Q56.)

Saxony-Anhalt	Year 2019		
	Number	Prevalence /10,000 births	Comp. to basis prevalence
	0	0.0	↓
	Reporting period 2007-2018		
	Basis prevalence /10,000 births	Confidence interval (CI 95%)	
	0.67	0.37 - 1.13	
EUROCAT (Full members)	Period 2007-2018		
	Basis prevalence /10,000 births	Confidence interval (CI 95%)	
	0.58	0.53 - 0.64	

The indicator malformation indifferent sex belongs to the rarely seen malformations with a basis prevalence of 0.7 per 10,000 births (2007-2018) in Saxony-Anhalt. On average, one or two cases are counted per year in Saxony-Anhalt. In some years, the malformation is not diagnosed at all, as is the case in 2019.

EUROCAT gives an overall prevalence of 0.6 per 10,000 births (2007- 2018) for indifferent sex. The prevalence interval of the basis prevalence of Saxony-Anhalt is wider and exceeds the value of the European malformation registers due to the smaller numbers, but the value of the prevalences is of a similar height.

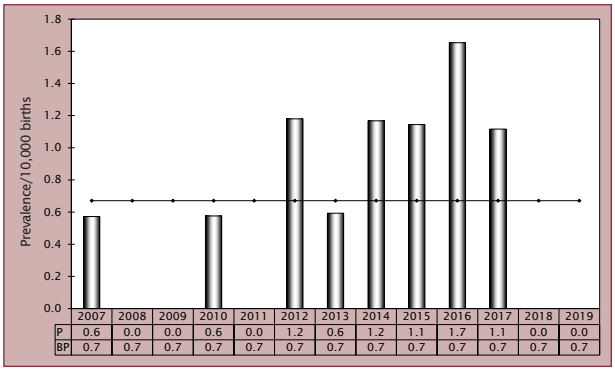


Fig. 29: Development of prevalence/10,000 births with indeterminate sex in Saxony-Anhalt since 2007

In 2019, no birth with indeterminate sex was registered in Saxony-Anhalt.

10.23 Potter sequence (Q60.6)

	Year 2019		
Saxony-Anhalt	Number	Prevalence /10,000 births	Comp. to basis prevalence
	2	1.20	↓
	Reporting period 2007-2018		
	Basis prevalence /10,000 births	Confidence interval (CI 95%)	
	2.83	2.15 - 3.65	
EUROCAT (Full members)	Period 2007-2018		
	Basis prevalence /10,000 births	Confidence interval (CI 95%)	
	1.26	1.19 - 1.34	

A Potter sequence was diagnosed in only two cases in Saxony-Anhalt in 2019. In case of the unfavourable prognosis, the pregnancies were terminated prematurely two weeks after diagnosis in each case. The **prevalence** of **1.2 per 10,000 births** determined for the current birth year is to be considered very low. However, the prevalence will not fall below the minimum (2007: 0.6 per 10,000 births) in 2019. The current annual prevalence is far below the confidence interval of the basis prevalence (2.8 per 10,000 births). In the years 2013 to 2018, annual prevalences were always above or within the range of the basis prevalence. The increasing trend that emerged in the trend analysis of the last report did not continue in 2019. The development remains to be observed.

This year's prevalence shows up in the lower range of EUROCAT's overall prevalence across Europe. The confidence interval of the basis prevalence of Saxony-Anhalt lies above the interval of the European registers (2007-2018: 1.3 per 10,000 births).

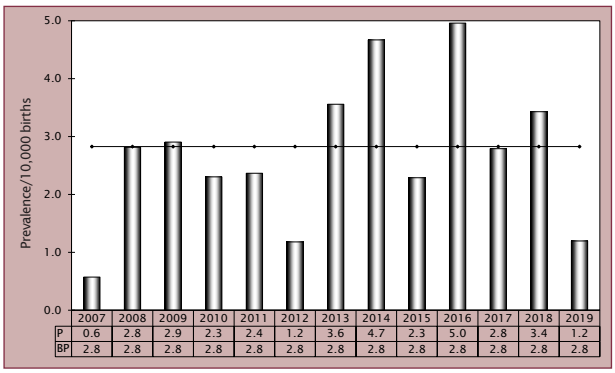
additional information:

Pregnancy outcome	2 x termination of pregnancy
Sex	2 x male
Number of isolated malformation/MCA	1 x MCA 1 x isolated

One fet, who already had a sibling affected by a Potter sequence, suffered from an unilateral renal agenesis and the other kidney was hypoplastic and non-functional. The second fet had bilateral non-functional polycystic kidneys. Bilateral renal agenesis was not found this year. In both cases, no information about medication intake of the mother was submitted to the malformation monitoring.

Malformation combinations (MCA) or superordinated syndromes detected:

- bilateral cleft lip and palate, broad nasal root, low-set ears, Potter facies



	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019
P	0.6	2.8	2.9	2.3	2.4	1.2	3.6	4.7	2.3	5.0	2.8	3.4	1.2
BP	2.8	2.8	2.8	2.8	2.8	2.8	2.8	2.8	2.8	2.8	2.8	2.8	2.8

Fig. 30: Development of prevalence/10,000 births with Potter sequence in Saxony-Anhalt since 2007

In 2019, one Potter sequence per 8,359 births was registered in Saxony-Anhalt.

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).

10.24 Renal agenesis, unilateral (Q60.0/Q60.2)

	Year 2019		
Saxony-Anhalt	Number	Prevalence /10,000 births	Comp. to basis prevalence
	11	6.58	↔
	Reporting period 2007-2018		
	Basis prevalence /10,000 births	Confidence interval (CI 95%)	
	5.99	4.99 - 7.14	
EUROCAT (Full members)	Period 2007-2018		
	Basis prevalence /10,000 births	Confidence interval (CI 95%)	
	no information	no information	

Eleven children/fetuses with unilateral renal agenesis were registered in Saxony-Anhalt in 2019. The **prevalence** calculated from this data for 2019 (**6.6 per 10,000 births**) lies within the middle range of the confidence interval of the basis prevalence (2007-2018: 6.0 per 10,000 births). During the reporting period, the prevalence of unilateral renal agenesis ranged from a minimum of 2.2 per 10,000 births (2016) to a maximum of 9.6 per 10,000 births (2008).

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

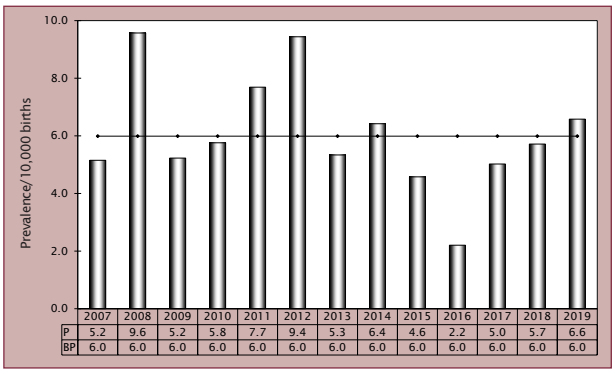
additional information:

Pregnancy outcome	9 x live births 1 x live birth, deceased up to 7th day 1 x termination of pregnancy
Sex	8 x male 3 x female
Number of isolated malformation/MCA	3 x MCA 8 x isolated

As usual, the left kidney was absent more often (7x) than the right kidney (3x) in the cases of children/fetuses with unilateral renal agenesis (2007-2018: left 53.2 %). On one occasion, the laterality was not indicated. Eight of ten live births had no other malformations beside the unilateral renal agenesis. One child with unilateral renal agenesis in the context of a caudal regression syndrome died on the first day of life. In one case, the pregnancy was terminated prematurely after 20 weeks of gestation at presence of renal and CNS malformations.

Malformation combinations (MCA) or superordinated syndromes detected:

- Caudal regression syndrome with: Spina bifida with hydrocephaly, tetralogy of Fallot, unilateral multicystic dysplastic
- Arnold-Chiari syndrome with: lumbosacral spina bifida, duplex kidney left
- DUP grade II left



	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019
P	5.2	9.6	5.2	5.8	7.7	9.4	5.3	6.4	4.6	2.2	5.0	5.7	6.6
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

Fig. 31: Development of prevalence/10,000 births with unilateral renal agenesis in Saxony-Anhalt since 2007

In 2019, one renal agenesis, unilateral per 1,520 births was registered in Saxony-Anhalt.

10.25 Cystic kidney (Q61.1-Q61.9)

	Year 2019		
Saxony-Anhalt	Number	Prevalence /10,000 births	Comp. to basis prevalence
	8	4.79	↓
	Reporting period 2007-2018		
	Basis prevalence /10,000 births	Confidence interval (CI 95%)	
	7.28	6.17 - 8.54	
EUROCAT (Full members)	Period 2007-2018		
	Basis prevalence /10,000 births	Confidence interval (CI 95%)	
	no information	no information	

Various forms of cystic kidneys, excluding isolated cysts, are summarised under the indicator malformation cystic kidneys (Chapter 10.0). With a **prevalence** of **4.8 per 10,000 births** and eight affected children, it was observed less frequently than usual in 2019. The basis prevalence (2007-2018: 7.3 per 10,000 births) is higher than the annual prevalence, although the prevalences of the individual years range between a minimum (2008) of 3.9 per 10,000 births and a maximum (2010) of 11.5 per 10,000 births during the reporting period.

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

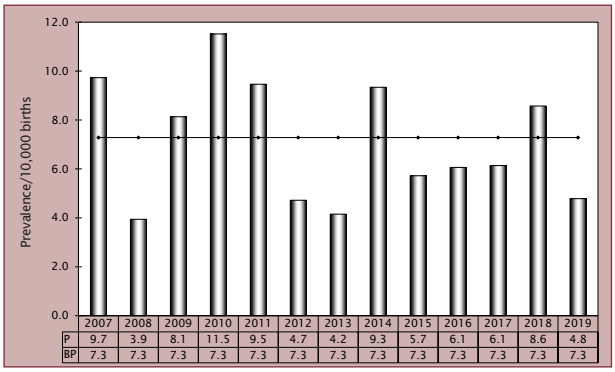
additional information:

Pregnancy outcome	7 x live births 1 x live birth, deceased up to 7th day
Sex	5 x male 3 x female
Number of isolated malformation/MCA	2 x MCA 6 x isolated

Two children showed a bilateral cystic kidney degeneration in 2019. In one case of a child with unilateral cystic kidney the second kidney was missing. It was affected by a caudal regression syndrome and had other severe CNS and cardiac malformations. Six children had unilateral findings, three on the left and two on the right side. In one case, the side was not specified.

Malformation combinations (MCA) or superordinated syndromes detected:

- Caudal regression syndrome with: Spina bifida with hydrocephaly, tetralogy of Fallot, unilateral renal agenesis
- DUP grade III and left ureteral outlet stenosis



	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019
P	9.7	3.9	8.1	11.5	9.5	4.7	4.2	9.3	5.7	6.1	6.1	8.6	4.8
BP	7.3	7.3	7.3	7.3	7.3	7.3	7.3	7.3	7.3	7.3	7.3	7.3	7.3

Fig. 32: Development of prevalence/10,000 births with cystic kidneys in Saxony-Anhalt since 2007

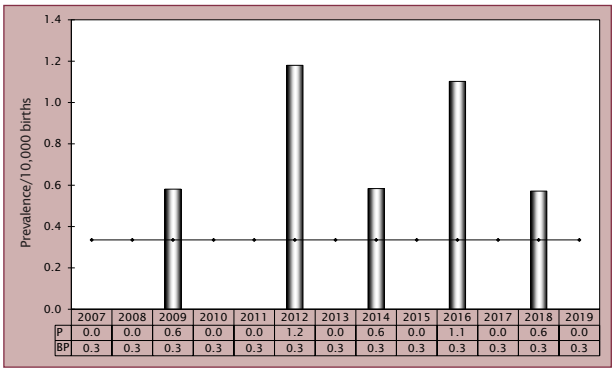
In 2019, one child with cystic kidney per 2,090 births was registered in Saxony-Anhalt.

10.26 Bladder exstrophy (Q64.1)

	Year 2019		
Saxony-Anhalt	Number	Prevalence /10,000 births	Comp. to basis prevalence
	0	0.00	↓
	Reporting period 2007-2018		
	Basis prevalence /10,000 births	Confidence interval (CI 95%)	
	0.34	0.13 - 0.69	
EUROCAT (Full members)	Period 2007-2018		
	Basis prevalence /10,000 births	Confidence interval (CI 95%)	
	no information	no information	

The indicator malformation exstrophy of the urinary bladder is very rare. It is only recorded as an isolated occurrence. During the reporting period (2007-2018), it was diagnosed in a total of only six children and one termination of pregnancy. In seven years of the reporting period and also in 2019, no urinary bladder exstrophy was recorded in Saxony-Anhalt. The basis prevalence of urinary bladder exstrophy is therefore very low and amounts to only 0.3 per 10,000 births.

EUROCAT does not provide any data of comparison for bladder exstrophy.



	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019
P	0.0	0.0	0.6	0.0	0.0	1.2	0.0	0.6	0.0	1.1	0.0	0.6	0.0
BP	0.3	0.3	0.3	0.3	0.3	0.3	0.3	0.3	0.3	0.3	0.3	0.3	0.3

Fig. 33: Development of prevalence/10,000 births with bladder exstrophy in Saxony-Anhalt since 2007

In 2019, no birth with a bladder exstrophy was registered in Saxony-Anhalt.

10.27 Preaxial polydactyly (Q69.1/Q69.2)

	Year 2019		
Saxony-Anhalt	Number	Prevalence /10,000 births	Comp. to basis prevalence
	3	1.79	↓
	Reporting period 2007-2018		
	Basis prevalence /10,000 births	Confidence interval (CI 95%)	
	3.74	2.95 - 4.66	
EUROCAT (Full members)	Period 2007-2018		
	Basis prevalence /10,000 births	Confidence interval (CI 95%)	
	no information	no information	

After a maximum value of the annual prevalence of 8.0 per 10,000 births in 2007, the indicator malformation preaxial polydactyly has always been observed in Saxony-Anhalt in the lower range of the basis prevalence (2007-2018: 3.7 per 10,000 births) or totally below since 2011. Also in 2019, the annual **prevalence** (**1.8 per 10,000 births**) lies far below the lower limit of the confidence interval of the basis prevalence. The trend calculation over the period of 2006-2019 (Chapter 10.38) logically shows a significantly declining trend for preaxial polyactyly with a percentage change of -21.24 % (CI -26.63 % to -10,89 %).

Regarding all polydactylies (2007-2018: 12.4 per 10,000 births), about one third of the cases involve the thumb or big toes, about two thirds are postaxial. Unlike preaxial polydactylies, the postaxial polydactylies do not show a trend. In 2019, the prevalence for all polydactylies (10.8 per 10,000 births) was only slightly below the normal range (Chapter 9).

Comparative EUROCAT data for preaxial polydactyly is not available.

additional information:

Pregnancy outcome	3 x live births
Sex	2 x male 1 x female
Number of isolated malformation/MCA	1 x MCA 2 x isolated

All three children showed accessory thumbs in 2019, once on the right and twice on the left side. In one case, the preaxial polydactyly and other malformations of the skeletal system and the urinary tract system were caused by a chromosomal aberration.

Malformation combinations (MCA) or superordinated syndromes detected:

- Male gonosome anomaly with: clubfoot left, bilateral DUP grade III, dominant forehead

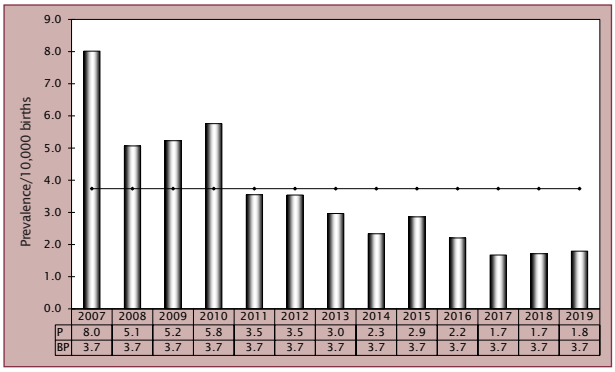


Fig. 34: Development of prevalence/10,000 births with preaxial polydactyly in Saxony-Anhalt since 2007

In 2019, one preaxial polydactyly per 5,572 births was registered in Saxony-Anhalt.

10.28 Limb reduction defects of both upper and lower limbs (Q71./Q72./Q73.)

Saxony-Anhalt	Year 2019		
	Number	Prevalence /10,000 births	Comp. to basis prevalence
	8	4.79	↓
	Reporting period 2007-2018		
	Basis prevalence /10,000 births	Confidence interval (CI 95%)	
	8.62	7.41 - 9.98	
EUROCAT (Full members)	Period 2007-2018		
	Basis prevalence /10,000 births	Confidence interval (CI 95%)	
	5.29	5.14 - 5.44	

In 2019, only eight children/fetuses in Saxony-Anhalt showed a limb reduction defect. This results in an annual **prevalence** of **4.8 per 10,000 births**, which is significantly below the normal range of the basis prevalence (2007-2018: 8.6 per 10,000 births) and currently represents the minimum value of the reporting period. A similar low prevalence was registered recently in 2006 (4.7 per 10,000 births). A maximum value was recorded in 2012 with 14.2 per 10,000 births.

The confidence interval of the total prevalence of the European malformation registers (2007-2018) is smaller and lies at the same time below the basis prevalence of Saxony-Anhalt. The Saxony-Anhalt prevalence for 2019 is also low compared to the overall prevalence across Europe.

additional information:

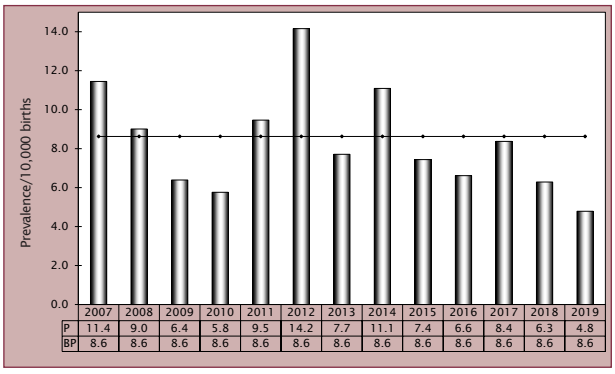
Pregnancy outcome	7 x live births 1 x termination of pregnancy
Sex	2 x male 5 x female 1 x no indication
Number of isolated malformation/MCA	1 x MCA 7 x isolated

The indicator malformation limb reduction defects includes malformations that have a similar appearance but different causes or whose aetiology is not yet known. In almost all cases (7x) the upper extremities were affected, only once a peromelia was seen on the left leg. The ratio of laterality is balanced, the malformations occurred three times only on the right or left side and twice on both sides.

The peromelia was detected in the 12th week of gestation during prenatal sonography and the pregnancy was terminated.

Malformation combinations (MCA) or superordinated syndromes detected:

- Vascular ring through the anomalous right subclavian artery, intestinal malrotation, bilateral clubfeet, subluxation of the hip joints, low-set ears and laterally rising lid axes, facial asymmetry, craniofacial dysmorphia



	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019
P	11.4	9.0	6.4	5.8	9.5	14.2	7.7	11.1	7.4	6.6	8.4	6.3	4.8
BP	8.6	8.6	8.6	8.6	8.6	8.6	8.6	8.6	8.6	8.6	8.6	8.6	8.6

Fig. 35: Development of prevalence/10,000 births with limb reduction defects in Saxony-Anhalt since 2007

In 2019, one limb reduction defect per 2,090 births was registered in Saxony-Anhalt.

10.29 Diaphragmatic hernia (Q79.0/Q79.1)

	Year 2019		
Saxony-Anhalt	Number	Prevalence /10,000 births	Comp. to basis prevalence
	3	1.79	↘
	Reporting period 2007-2018		
	Basis prevalence /10,000 births	Confidence interval (CI 95%)	
	2.64	1.99 - 3.43	
EUROCAT (Full members)	Period 2007-2018		
	Basis prevalence /10,000 births	Confidence interval (CI 95%)	
	2.93	2.82 - 3.05	

We registered a very high prevalence in the previous year, which was the maximum value of the whole reporting period (2018: 4.6 per 10,000 births). This year, only three births with diaphragmatic hernia were registered which corresponds to a rather low **prevalence** of **1.8 per 10,000 births**. The value lies slightly below the range of the basis prevalence of Saxony-Anhalt (2019: 2.6 per 10,000 births).

In comparison with the overall European prevalence (2.9 per 10,000 births), Saxony-Anhalt's basis prevalence is at a similar level, but with a larger random range due to the much smaller numbers. The European prevalence will also not be reached by the Saxony-Anhalt annual prevalence in 2019.

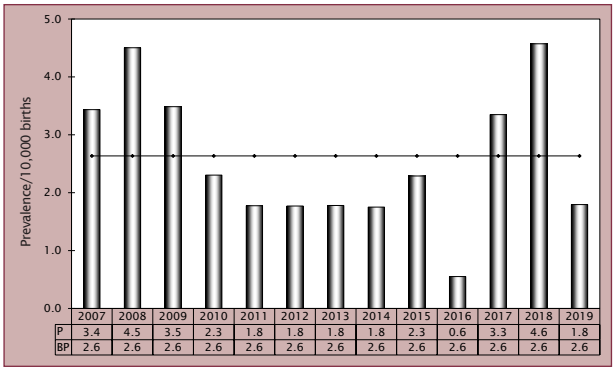
additional information:

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

One birth suffered from a right-sided diaphragmatic hernia. This malformation develop between the 8th and 10th week of gestation. Two fetuses were diagnosed with diaphragmatic hernia (1 x bilateral, 1 x without indication of the extent) and multiple malformations in the 18th and 20th week of gestation. Both pregnancies were terminated prematurely.

Malformation combinations (MCA) or superordinated syndromes detected:

- Omphalocele, VSD, ASD II, hypothyroidism, malrotation of the colon, hernia inguinalis at premature infant on the right, sacral dimple
- bilateral anopthalmia, synechiae of the eyelids and lung hypoplasia, cardiac malformation
- cardiac malformation, bilateral deformity of toes and feet



	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019
P	3.4	4.5	3.5	2.3	1.8	1.8	1.8	1.8	2.3	0.6	3.3	4.6	1.8
BP	2.6	2.6	2.6	2.6	2.6	2.6	2.6	2.6	2.6	2.6	2.6	2.6	2.6

Fig. 36: Development of prevalence/10,000 births with diaphragmatic hernia in Saxony-Anhalt since 2007

In 2019, one diaphragmatic hernia per 5,572 births was registered in Saxony-Anhalt.

10.30 Omphalocele (Q79.2)

Saxony-Anhalt	Year 2019		
	Number	Prevalence /10,000 births	Comp. to basis prevalence
	3	1.79	↓
	Reporting period 2007-2018		
	Basis prevalence /10,000 births	Confidence interval (CI 95%)	
	3.50	2.74 - 4.40	
EUROCAT (Full members)	Period 2007-2018		
	Basis prevalence /10,000 births	Confidence interval (CI 95%)	
	3.48	3.35 - 3.60	

The increasing trend of frequency of the indicator malformation omphalocele, which was noticeable in 2018, stopped in the current year. In 2019, an omphalocele was only seen three times in Saxony-Anhalt. The resulting annual **prevalence** of **1.8 per 10,000 births** is clearly below the lower confidence limit of the basis prevalence of 3.5 per 10,000 births.

The basis prevalence of Saxony-Anhalt is similar to the European basis prevalence reported by EUROCAT (2007-2018: 3.5 per 10,000 births), but covers the smaller confidence interval of the European prevalence due to the smaller population included. This is also undercut by the annual prevalence in 2019.

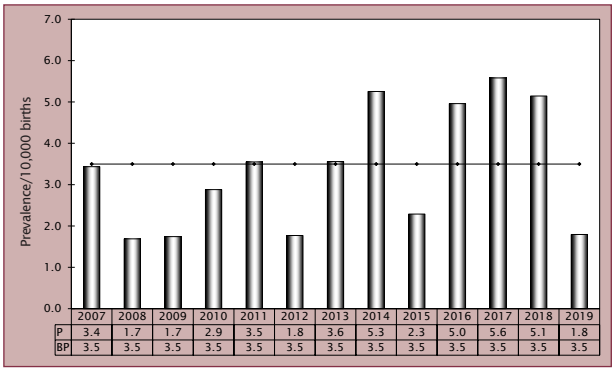
additional information:

Pregnancy outcome	1 x live birth 1 x live birth, deceased up to 7th day 1 x spontaenous abortion
Sex	1 x male 2 x female
Number of isolated malformation/MCA	3 x MCA

If the physiological umbilical hernia does not regress before the 10th week of gestation, an omphalocele develops. At one fet with Patau syndrome and at one with OEIS complex, an omphalocele and other severe malformations were discovered prenatally. Both pregnancies ended spontaneously in the 20th and 12th week of gestation. In two cases of the live births, the omphalocele and a ventricular septal defect had also been seen during prenatal ultrasound in the 12th and 16th week of gestation. One extremely premature baby died on the first day of life. The other child was born after 34 weeks of gestation and was operated at the age of three months.

Malformation combinations (MCA) or superordinated syndromes detected:

- Patau syndrome with: holoprosencephaly, bilateral cleft lip and palate, malformation of the heart
- Right diaphragmatic hernia, VSD, ASD II, hypothyroidism, malrotation of the colon, inguinal hernia at preterm infant on the right side, sacral dimple
- VSD



	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019
P	3.4	1.7	1.7	2.9	3.5	1.8	3.6	5.3	2.3	5.0	5.6	5.1	1.8
BP	3.5	3.5	3.5	3.5	3.5	3.5	3.5	3.5	3.5	3.5	3.5	3.5	3.5

Fig. 37: Development of prevalence/10,000 births with omphalocele in Saxony-Anhalt since 2007

In 2019, one omphalocele per 5,572 births was registered in Saxony-Anhalt.

10.31 Gastroschisis (Q79.3)

	Year 2019		
Saxony-Anhalt	Number	Prevalence /10,000 births	Comp. to basis prevalence
	3	1.79	↓
	Reporting period 2007-2018		
	Basis prevalence /10,000 births	Confidence interval (CI 95%)	
	3.74	2.95 - 4.66	
EUROCAT (Full members)	Period 2007-2018		
	Basis prevalence /10,000 births	Confidence interval (CI 95%)	
	2.76	2.65 - 4.87	

Gastroschisis was found only three times in Saxony-Anhalt in 2019. The resulting **prevalence** of **1.8 per 10,000 births** is the lowest registered value for this abdominal wall defect in the reporting period. A similar low annual prevalence was observed for the last time in 2000 (1.6 per 10,000 births). The basis prevalence (2007-2018: 3.7 per 10,000 births) is significantly higher than this year's prevalence.

The confidence intervals of the total prevalence of the European malformation registers (2.8 per 10,000 births) and the basis prevalence of Saxony-Anhalt do not overlap. Saxony-Anhalt has a higher prevalence, which can be classified in the upper third of the prevalences of all EUROCAT centres. Compared to the overall European prevalence, Saxony-Anhalt's annual prevalence for 2019 is lower.

additional information:

Pregnancy outcome	3 x live births
Sex	2 x male 1 x female
Number of isolated malformation/MCA	1 x MCA 2 x isolated

In all three live births, the gastroschisis was discovered prenatally between the 11th and 16th week of gestation and the children were delivered by caesarean section in the 33rd or 34th week of gestation. The first operation was performed in each case on the first day of life.

Malformation combinations (MCA) or superordinated syndromes detected:

- Intestinal malrotation, intact urachus, colonic atresia, left inguinal hernia at preterm infant

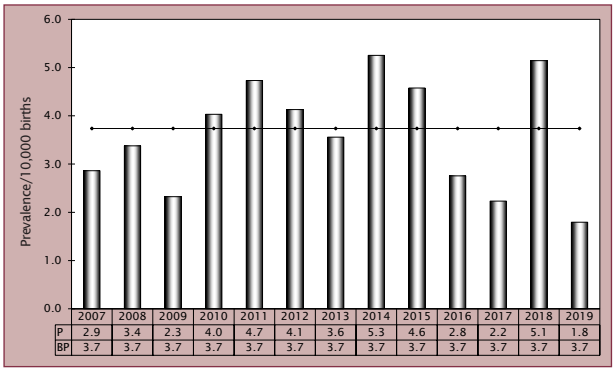


Fig. 38: Development of prevalence/10,000 births with gastroschisis in Saxony-Anhalt since 2007

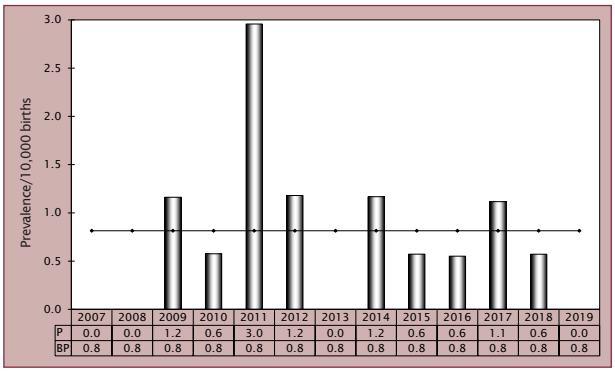
In 2019, one gastroschisis per 5,572 births was registered in Saxony-Anhalt.

10.32 Prune-Belly syndrome (Q79.4)

Saxony-Anhalt	Year 2019		
	Number	Prevalence /10,000 births	Comp. to basis prevalence
	0	0.0	↓
	Reporting period 2007-2018		
	Basis prevalence /10,000 births	Confidence interval (CI 95%)	
	0.81	0.47 - 1.30	
EUROCAT (Full members)	Period 2007-2018		
	Basis prevalence /10,000 births	Confidence interval (CI 95%)	
	no information	no information	

One of the rarest indicator malformations is the prune-belly sequence. There are always years, including 2019, in which this malformation does not occur at all in Saxony-Anhalt. In the reporting period, it was never seen more than twice a year, except for the outlier in 2011 (5x). The basis prevalence (2007-2018) lies at 0.8 per 10,000 births.

EUROCAT does not provide an overall European prevalence for comparison.



	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019
P	0.0	0.0	1.2	0.6	3.0	1.2	0.0	1.2	0.6	0.6	1.1	0.6	0.0
BP	0.8	0.8	0.8	0.8	0.8	0.8	0.8	0.8	0.8	0.8	0.8	0.8	0.8

Fig. 39: Development of the prevalence/10,000 births with Prune-belly syndrome in Saxony-Anhalt since 2007

In 2019, no Prune-Belly syndrome was registered in Saxony-Anhalt.

10.33 Down syndrome - Trisomy 21 (Q90.)

	Year 2019		
Saxony-Anhalt	Number	Prevalence /10,000 births	Comp. to basis prevalence
	27	16.15	↓
	Reporting period 2007-2018		
	Basis prevalence /10,000 births	Confidence interval (CI 95%)	
	19.21	17.38 - 21.19	
EUROCAT (Full members)	Period 2007-2018		
	Basis prevalence /10,000 births	Confidence interval (CI 95%)	
	23.85	23.53 - 24.18	

Down syndrome occurred less frequently in Saxony-Anhalt in 2019 with 27 births and a resulting **prevalence** of **16.2 per 10,000 births**. Last year, many more cases were observed (2018: 25.1 per 10,000 births). The basis prevalence of Saxony-Anhalt (2007-2018) lies at 19.2 per 10,000 births. This means that Down syndrome is one of the five most common malformations (Chapter 9) and is by far the most common chromosomal aberration.

When comparing the basis prevalence of Saxony-Anhalt with the prevalence given by EUROCAT for all European registries, it is noticeable that the basis prevalence of Saxony-Anhalt has a lower level. The risk of having a child with Down syndrome increases with higher maternal age. For the prevalence comparison, it should be taken into account that the maternal age in Saxony-Anhalt is even lower compared to the EU average (2017: 28.7 years vs. 29.1 years*).

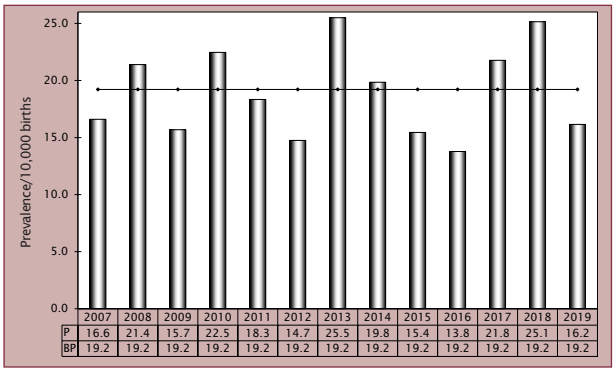
additional information:

Pregnancy outcome	10 x live births 1 x live birth, deceased after 7th day 16 x termination of pregnancy
Sex	13 x male 11 x female 3 x no indication
Number of isolated malformation/MCA	13 x MCA 14 x isolated

In a mean of 16 cases, the pregnancy was terminated prematurely after prenatal diagnosis of a Down syndrome at 18.0 weeks of gestation (median 18.0 weeks of gestation). The earliest termination was at 12 weeks of gestation and the latest at 26 weeks of gestation.

Malformation combinations (MCA) or superordinated syndromes detected:

- Duodenal stenosis, pancreas anulare, ASD II, bilateral sound perception disorder
- DUP grade III and megaureter on the left side, underdeveloped nose, cutis laxa
- AVSD, DIV, ASD II, bilateral sound conduction disorder
- 2 x AVSD (1 x clubfoot, 1 x clubfoot left)
- 2 x AVSD
- VSD, ASD II
- VSD, PFO at fullterm infant, sound perception disorder and preauricular tag left, bilateral cataracta congenita
- VSD, PFO at preterm infant
- VSD
- ASD II
- Endocardial cushion defect



	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019
P	16.6	21.4	15.7	22.5	18.3	14.7	25.5	19.8	15.4	13.8	21.8	25.1	16.2
BP	19.2	19.2	19.2	19.2	19.2	19.2	19.2	19.2	19.2	19.2	19.2	19.2	19.2

Fig. 40: Development of prevalence/10,000 births with Down syndrome in Saxony-Anhalt since 2007

In 2019, one Down syndrome (trisomy 21) per 619 births was registered in Saxony-Anhalt.

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

10.34 Patau syndrome - Trisomy 13 (Q91.4-Q91.7)

	Year 2019		
Saxony-Anhalt	Number	Prevalence /10,000 births	Comp. to basis prevalence
	3	1.79	↗
	Reporting period 2007-2018		
	Basis prevalence /10,000 births	Confidence interval (CI 95%)	
	1.15	0.74 - 1.71	
EUROCAT (Full members)	Period 2007-2018		
	Basis prevalence /10,000 births	Confidence interval (CI 95%)	
	2.22	2.12 - 2.32	

Patau syndrome was genetically detected in three cases in Saxony-Anhalt in 2019, once after a positive NIPT in the 14th week of gestation and twice after prenatal pathological ultrasound in the 19th/20th week of gestation. This results in a **prevalence** of **1.8 per 10,000 births** for Saxony-Anhalt in 2019, slightly above the confidence interval of the basis prevalence (2007-2018: 1.1 per 10,000 births). Since 2000, when the malformation monitoring system began to survey malformations in the entire Federal State of Saxony-Anhalt, a maximum of four (2006: 2.4 per 10,000 births) and a minimum of no case (2007-2018: 1.8 per 10,000 births) of Patau syndrome (2004) was registered.

The overall European prevalence given by EUROCAT for Patau syndrome lies at 2.2 per 10,000 births. The basis prevalence of Saxony-Anhalt as well as the annual prevalence for 2019 can be found below the confidence interval of the overall European prevalence and in the lower third of the other malformation centres in a European comparison. The probability of the occurrence of a trisomy increases with maternal age. The average age of mothers in Saxony-Anhalt compared to the higher average age of mothers in the EU is reflected in the different prevalence levels.

additional information:

Pregnancy outcome	1 x spontaneous abortion 2 x termination of pregnancy
Sex	3 x female
Number of isolated malformation/MCA	3 x MCA

Malformation combinations (MCA) or superordinated syndromes detected:

- Holoprosencephaly, omphalocele, bilateral cleft lip and palate, cardiac malformation
- Hydrocephalus internus at Dandy-Walker syndrome, cleft lip and palate, brachycephaly
- Cleft lip and palate, cardiac malformation

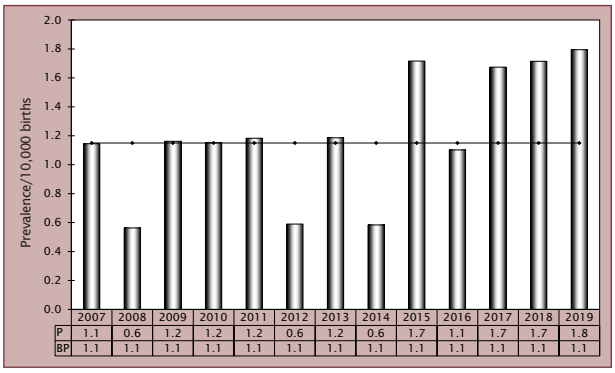


Fig. 41: Development of prevalence/10,000 births with a Patau syndrome in Saxony-Anhalt since 2007

In 2019, one Patau syndrome (trisomy 13) per 5,572 births was registered in Saxony-Anhalt.

10.35 Edwards syndrome - Trisomy 18 (Q91.0-Q91.3)

	Year 2019		
Saxony-Anhalt	Number	Prevalence /10,000 births	Comp. to basis prevalence
	8	4.79	↔
	Reporting period 2007-2018		
	Basis prevalence /10,000 births	Confidence interval (CI 95%)	
	4.31	3.47 - 5.30	
EUROCAT (Full members)	Period 2007-2018		
	Basis prevalence /10,000 births	Confidence interval (CI 95%)	
	5.80	5.64 - 5.96	

Edwards syndrome is the second most common trisomy diagnosis. In 2019, this chromosomal aberration was verified prenatally 8 times in Saxony-Anhalt. This means that the **prevalence** in the current year lies at **4.8 per 10,000 births**, after a very high value in last year (2018: 7.4 per 10,000 births) and at the same time it lies conspicuously in the range of the basis prevalence (2007-2019: 4.3 per 10,000 births).

In the Europe-wide comparison, the basis prevalence of Saxony-Anhalt for Edwards syndrome, just as for the two trisomies Down`s syndrome and Patau syndrome, appears below the respective overall prevalence determined by EUROCAT. It can be found in the lower third of the average prevalences of the European registers.

additional information:

Pregnancy outcome	1 x live birth, deceased after 7th day 7 x termination of pregnancy
Sex	3 x male 4 x female 1 x no indication
Number of isolated malformation/MCA	4 x MCA 4 x isolated

Malformation combinations (MCA) or superordinated syndromes detected:

- AVSD, anal atresia with fistula, skeletal malformation, bilateral hearing loss, plexus cyst
- Tetralogy of Fallot, cleft lip, plexus cyst
- Clubfoot, urinary bladder neck obstruction, bilateral missing ribs (one on the right, two on the left), plexus cyst, megacystis
- VSD, horseshoe kidney, membranous syndactyly

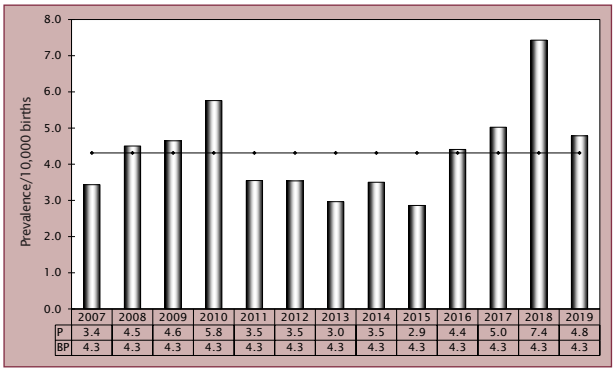


Fig. 42: Development of prevalence/10,000 births with Edwards syndrome in Saxony-Anhalt since 2007

In 2019, one Edwards syndrome per 2,090 births was registered in Saxony-Anhalt.

10.36 Turner syndrome (Q96.)

	Year 2019		
Saxony-Anhalt	Number	Prevalence /10,000 births	Comp. to basis prevalence
	3	1.79	↔
	Reporting period 2007-2018		
	Basis prevalence /10,000 births	Confidence interval (CI 95%)	
	2.11	1.53 - 2.83	
EUROCAT (Full members)	Period 2007-2018		
	Basis prevalence /10,000 births	Confidence interval (CI 95%)	
	2.49	2.39 - 2.60	

Turner syndrome is presented as an indicator malformation for the first time in this report. It is the most common form of gonadal dysgenesis. In Saxony-Anhalt, Turner syndrome was prenatally diagnosed in three cases in 2019. The diagnosis was made between the 10th and 17th week of gestation. The pregnancies were terminated prematurely.

The 2019 **prevalence** for Turner syndrome lies at **1.8 per 10,000 births**, inconspicuously within the confidence interval of the basis prevalence (2007-2018: 2.1 per 10,000 births). The confidence intervals of Saxony-Anhalt's basis prevalence and the prevalence reported by EUROCAT for the European malformation centres overlap each other. The annual prevalence of Saxony-Anhalt can be located below the overall European prevalence.

additional information:

Pregnancy outcome	3 x termination of pregnancy
Sex	3 x female
Number of isolated malformation/MCA	1 x MCA 2 x isolated

Malformation combinations (MCA) or superordinated syndromes detected:

- bilateral pulmonary hypoplasia, funnel chest, low-set ears

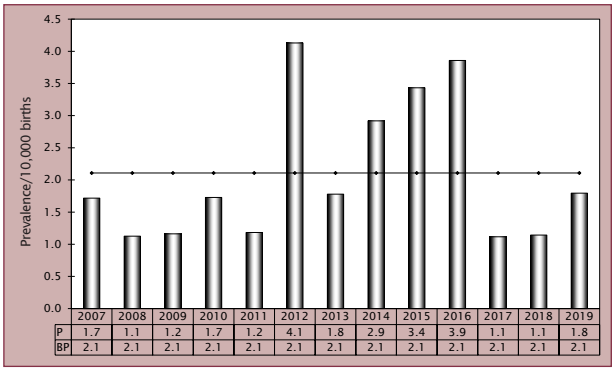


Fig. 43: Development of prevalence/10,000 births with Turner syndrome in Saxony-Anhalt since 2007

In 2019, one Turner syndrome per 5,572 births was registered in Saxony-Anhalt.

10.37 Klinefelter syndrome/male gonosome anomalies (Q98.)

	Year 2019		
Saxony-Anhalt	Number	Prevalence /10,000 births	Comp. to basis prevalence
	1	0.60	↘
	Reporting period 2007-2018		
	Basis prevalence /10,000 births	Confidence interval (CI 95%)	
	1.10	0.70 - 1.65	
EUROCAT (Full members)	Period 2007-2018		
	Basis prevalence /10,000 births	Confidence interval (CI 95%)	
	no information	no information	

The indicator malformation Klinefelter syndrome/male gonosomal anomalies, which was newly included into the annual report 2019, was diagnosed in only one case in Saxony-Anhalt this year. This corresponds to a **prevalence** of **0.6 per 10,000 births**. The annual prevalence lies slightly below the basis prevalence determined for the reporting period (2007-2019: 1.1 per 10,000 births).

A prevalence of 0.9 per 10,000 births is calculated for Klinefelter syndrome (Q98.0-Q98.4) in Saxony-Anhalt for the reporting period 2007-2018. EUROCAT shows a similar prevalence (2007-2018) of 0.7 per 10,000 births.

additional information:

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

Malformation combinations (MCA) or superordinated syndromes detected:

- accessory right thumb, clubfoot left, bilateral DUP III. degree, prominent forehead

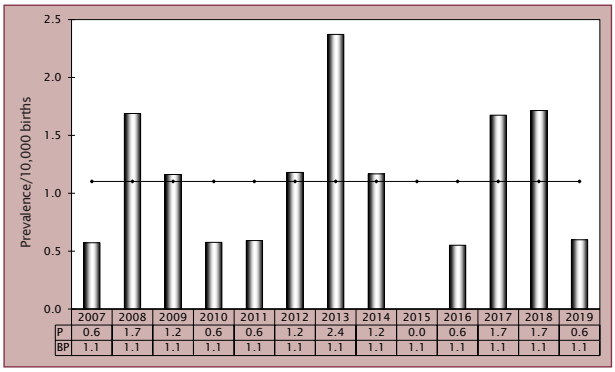


Fig. 44: Development of prevalence/10,000 births with Klinefelter syndrome/male gonosome anomalies in Saxony-Anhalt since 2007

In 2019, one Klinefelter syndrome/male gonosome anomalie per 16.717 births was registered in Saxony-Anhalt.

10.38 Trend analysis of indicator malformations

The monitoring of malformations has the task to identify clusters or trends in the occurrence of malformations. Each of the previous chapters 10.1 to 10.37 of the annual report deals with one of the indicator malformations that are clearly described by the ICBDSR (International Clearinghouse for Birth Defects Surveillance and Research) (chapter 12.0) and internationally used. It is reported how far the currently observed frequency of the malformation can be classified temporally and spatially. Chapter 10.38 is dedicated to the frequency development of all indicator malformations over the **years 2006 to 2019**.

At least one indicator malformation was detected in 201 births in Saxony-Anhalt in 2019. A total of 224 (up to four indicator malformations per child/ fet) were diagnosed. Only 144 children with indicator malformations (71.6%) were live births. In the reporting period (2007-2018), the proportion of live births, with a downward trend, amounted to an average of 74.1% of all affected cases. Four stillbirths and two spontaneous abortions from the 16th week of pregnancy showed indicator malformations. Together, they represent 3.0% of the children/fetuses with indicator malformations in 2019. The proportion of terminations of pregnancies amounts to an average of 23.2% from 2007 to 2018. After a maximum value in the previous year (2018: 29.4%), the proportion for 2019 resulted to 25.4 %.

1.2% of all births in Saxony-Anhalt were diagnosed with one of the 37 indicator malformations in 2019. The prevalence falls below the lower confidence limit of the basis prevalence which was determined over the years 2007-2018 (1.42%, CI 1.37-1.47).

The aim of the following trend analysis is to present long-term trends in the occurrence of malformations. In the current report, the strength and orientation of the changes in the indicator malformation prevalences are examined over the period 2006-2019.

The trend estimation has been an integral part of the annual report for the recent 10 years. Condition for the trend analysis is that we expect each malformation to appear at least five times or that we registered at least two cases of the corresponding malformation. If in each case values from individual years are considered, the initial requirement is not met for about one third of the indicator malformations, depending on the frequency. In order to be able to carry out the test for changes even in the case of indicator malformations with a lower frequency, 2-year intervals are formed and tested for the first time in this report.

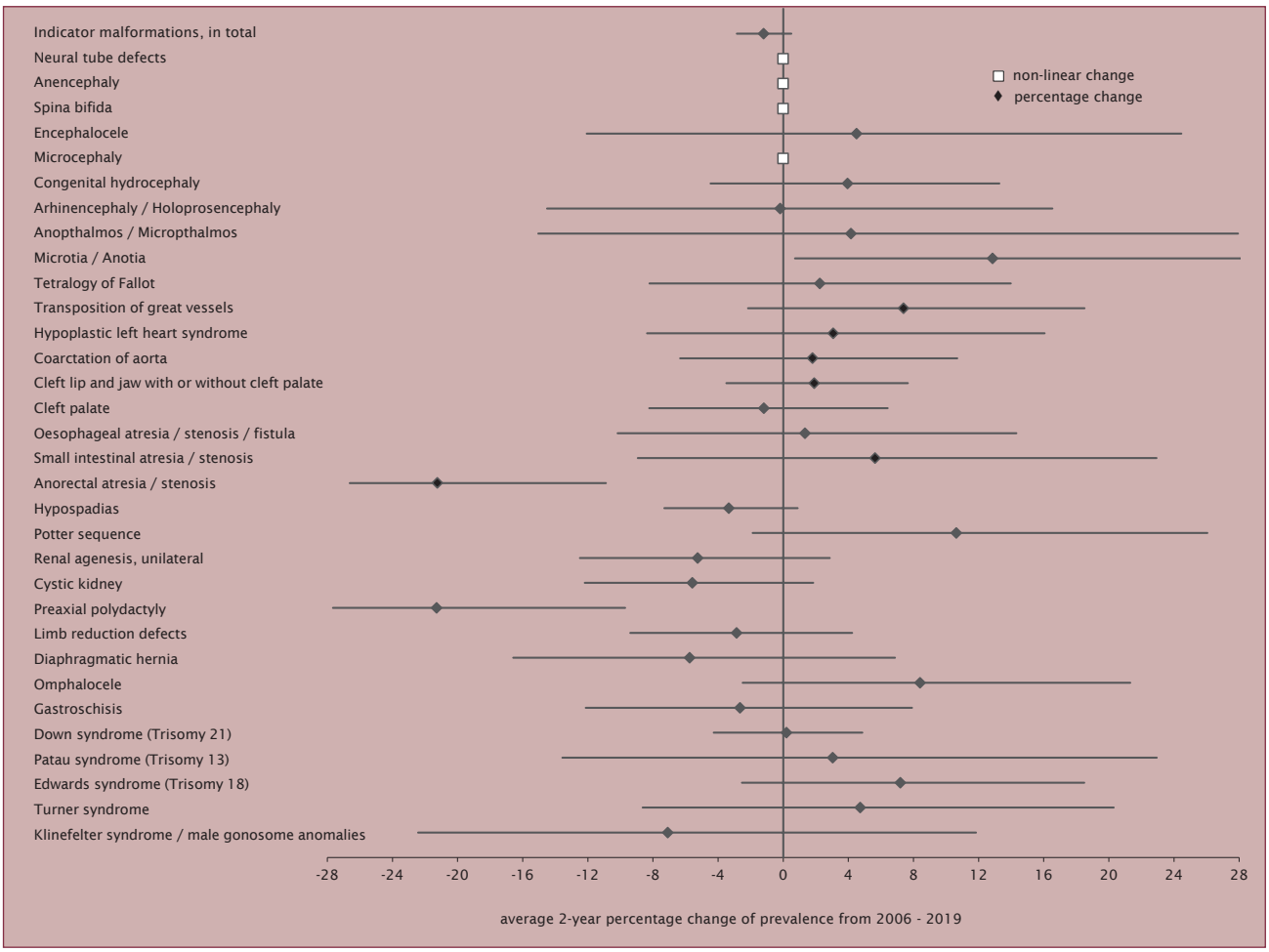


Fig. 45: Trend analysis 2006 to 2019 with average percentage change of annual prevalence (95% CI)

Figure 46 on page 64 and the table on this page show the estimated average percentage changes in the 2-year prevalence of the indicator malformations for which the above-mentioned initial conditions applies. The mathematical basis of the analysis is binary logistic regression based on the maximum likelihood method.

The measure of the strength and direction of the percentage annual change is the regression coefficient B. In the case of a significantly increasing trend characterised by a positive regression coefficient, this is entered into the diagram on the right side of the ordinate axis, including the CI of 95%. In case of a decreasing trend, the regression coefficient can be found on the left side of the axis (in the negative range). The shown 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 to neural tube defects, anencephaly, spina bifida and microcephaly.

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 increasing trend** can only be observed for microtia/anotia (+12.86%, CI 0.72 to 28.40) during the reporting period. A **significant decreasing trend**, according to a negative regression coefficient B and a non-effective non-linear component, is observed for rectal 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 a trend evaluation.

	Regression coefficient B in %	Confidence interval (CI of 95%)
Indicator malformations, in total	-1.20	-2.85 to 0.49
Encephalocele	4.51	-12.07 to 24.45
Congenital hydrocephaly	3.95	-4.46 to 13.28
Arhinencephaly / Holoprosencephaly	-0.19	-14.50 to 16.53
Anopthalmos / Micropthalmos	4.16	-15.05 to 27.94
Microtia / Anotia	12.86	0.72 to 28.40
Tetralogy of Fallot	2.25	-8.22 to 13.97
Transposition of great vessels	7.39	-2.17 to 18.51
Hypoplastic left heart syndrome	3.08	-8.36 to 16.05
Coarctation of aorta	1.81	-6.33 to 10.68
Cleft lip with or without cleft palate	1.91	-3.49 to 7.65
Cleft palate	-1.18	-8.23 to 6.42
Oesophageal atresia/stenosis/fistula	1.33	-10.18 to 14.33
Small intestinal atresia	5.64	-8.94 to 22.93
Anorectal atresia/stenosis	-21.24	-26.63 to -10.89
Hypospadias	-3.35	-7.30 to 0.89
Potter sequence	10.63	-1.88 to 26.05
Renal agenesis, unilateral	-5.26	-12.48 to 2.86
Cystic kidney	-5.59	-12.19 to 1.84
Preaxial polydactyly	-21.30	-27.66 to -9.71
Limb reduction defects	-2.86	-9.4 to 4.23
Diaphragmatic hernia	-5.75	-16.58 to 6.86
Omphalocele	8.40	-2.49 to 21.31
Gastroschisis	-2.66	-12.16 to 7.92
Down syndrome (Trisomy 21)	0.19	-4.27 to 4.86
Patau syndrome (Trisomy 13)	3.04	-13.56 to 22.94
Edwards syndrome (Trisomy 18)	7.20	-2.54 to 18.49
Turner syndrome	4.72	-8.64 to 20.30
Klinefelter syndrome / male gonosome anomalies	-7.10	-22.42 to 11.84

13 Summary

The annual report of the Federal State of Saxony-Anhalt about the frequency of congenital malformations and anomalies as well as genetically caused diseases is based on data reported to the malformation monitoring from 2007 to 2019. The nationwide malformation data received by the malformation monitoring is evaluated, sorted and under application of the number of births population-based and 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 currently no comparative data from Germany in any other Federal State.

After an interim peak of the number of births in Saxony-Anhalt in 2016 (18,092), the birth figures given by the State Statistical Office are declining. In 2019, only **16,618 live births** were registered, less than the average of the years 2007-2018 (17,322.3).

According to the State Statistical Office, **99 stillbirths** were registered in 2019. There was one stillbirth for every 168 live births this year. In the reporting period (2007- 2018), the ratio was one stillbirth to 250 live births. An influence of the amended §31 PStV of 2018 can be assumed.

According to the Federal Statistical Office (Destatis), 778,090 children were live births in Germany in 2019, slightly less than in 2018 (787,523). Around 2.1 % of all newborns in Germany are from the Federal State of Saxony-Anhalt.

In addition to data of live and stillbirths, the prevalences that are presented in the annual report 2019 are based on data of **63 terminations of pregnancy** and **16 spontaneous abortions after 16 WOG`s**. The statistical calculation of the report is therefore based on a **total number of 16,717 births** in 2018 (chapter 2).

581 births (3.48 % of all births) showed a **major malformation** in 2019. The malformation rate had been above the basis prevalence for three years (2007-2018: 3.63%, CI 3.55 to 3.71%), but in 2019, the prevalence was slightly below the confidence interval of the basis prevalence. In total, 514 live births with major malformations were registered in 2019. Of these, 18 children (3.5%) died in the first year of life. Terminations of pregnancy amount to 10.3% of all births with major malformations in the usual range in 2019 (Chapter 6).

Continuously, and also in 2019, the two cardiac malformations VSD and ASD are the **most frequent individual diagnoses**. ASD was detected more frequently than normal in 1.13% of all births in 2019 and VSD in 0.51% of births with usual frequency. Dilated uropathy II.-IV. degree/ureterocele, hearing loss and clubfoot, following in the frequency ranking, appeared within the expected range (Chapter 9).

In 2019, 201 births showed one of the 37 clearly defined **indicator malformations** (Chapter 10). A **higher prevalence** than the respective basis prevalence was observed for microtia/anotia and hypoplastic left heart syndrome. **Lower prevalences** were recorded for microcephaly, arhincephaly/holoprosencephaly, aortic valve stenosis, oesophageal atresia/stenosis/fistula, rectal and anal atresia/stenosis, hypospadias, epispadias, indifferent sex, Potter sequence, cystic kidneys, urinary bladder exstrophy, preaxial polydactyly, limb reduction malformations, omphalocele, gastroschisis, Prune-belly sequence and Down syndrome.

The monitoring of congenital malformations received information about **60 malformation caused terminations of pregnancy** in 2019. On average, the pregnancies were terminated at 18.8 weeks of gestation. The latest termination of pregnancy was at 20.2 weeks of gestation among births with multiple anomalies and other malformations (30.0 %). In cases of births with chromosomal aberrations (50.0 %), an abruption occurred at an average of 18.3 weeks of gestation, and in the case of CNS malformations (20.0 %) at an average of 17.7 weeks of gestation (Chapter 12).

A **genetically caused/corelated disease or microdeletion** was detected at 29 births in 2019. A **sequence, association or complex** was detected at 8 births. Five infants showed a **fetopathy**, three births suffered from the results of a **congenital infection**. Also in this year, at more than half of the 49 births with a **chromosomal aberration**, a Down syndrome (27 x) was diagnosed (chapter 11).

Based on the example of the bar malformations agenesis and hypoplasia of the corpus callosum, Chapter 14.1 provides information about the development, possible causes, frequency and prenatal diagnosis of CNS malformations. The prevalences of Saxony-Anhalt (2000-2019) and European-wide are presented and discussed. The very current topic of COVID-19 and the risk of infection for pregnant women is discussed in Chapter 14.2.

The monitoring of congenital malformations received in 2019 **1,898 reportings** about 1,738 births. These include data from children and fetuses with at least one major malformation (581) and data from children/ fetuses with minor malformations or anomalies (268). In addition to data from births with congenital malformations or anomalies as well as genetic diseases, collection of data from children without malformations is important, as risks can only be assessed in scientifically based evaluations by comparison.

With the help of many colleagues from different medical institutions who have been reporting congenital malformations for many years, a solid database has been created which also served as basis for the 2019 annual report. **We would therefore like to express our sincere thanks to all our „senders", in the confidence that we will continue to work successfully together, and we look forward to continue our interdisciplinary cooperation!**

14. Focus theme

14.1 Prenatal diagnostics and CNS malformations

Due to their high clinical relevance, malformations of the central nervous system (CNS) are the subject of numerous scientific analyses and publications and belong to the major malformations. CNS malformations cover a wide range of known clinical pictures. The proportion that is detected via prenatal diagnostics is very large [1].

The diagnosis of a structural or functional anomaly is highly distressing for the expectant parents at any stage of pregnancy. But quite a few, such as the structural anomalies of the bar (corpus callosum), are only detected in the course of the child's development or as incidental finding in a CNS imaging diagnosis at a later stage. However, a postnatal cranial sonography screening at the time of U1/U2 has not been established nationwide.

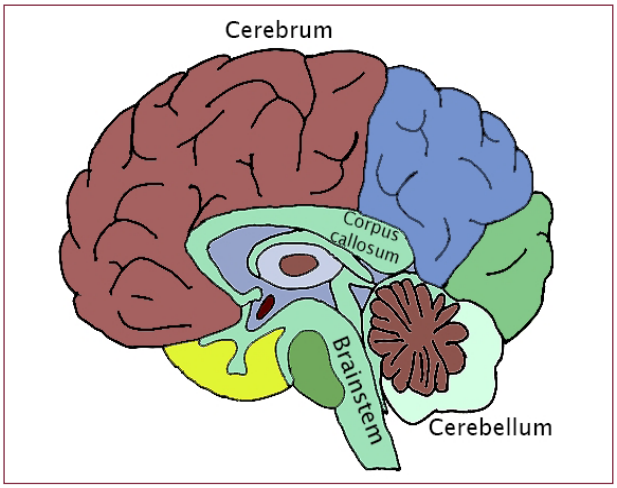


Fig. 49: Cross-section of the brain (own representation)

Corpus callosum malformations

Development:

The corpus callosum forms a connection between the two cerebral hemispheres and consists of about 190 million axons. It develops in humans in the 7th week of pregnancy [2] with the expansion of the dorsal part of the lamina terminalis, later also called lamina reuniens [3, 4]. In the 12th week of gestation, the first fibres start to cross into the area of the primordial hippocampus. Axons begin to cross the median line and at the same time the meninx primitiva, the commissura primitiva, the commissura anterior, the bar and the commissura posterior start to develop. The process is mediated by axonin-I and cell adhesion molecules [3].

Widening in both directions, the anterior part of the bar forms until 14-15 weeks of gestation and the posterior part until 18-19 weeks of gestation. The maturation of the corpus callosum takes time. By the process of myelination in the 4th month of life the cerebral hemispheres connect and at the age of 11, 90% of the fibres are aligned. At the age of 20, about 90% of the fibres are myelinated [4].

Function:

Transfer and coordination of information to the other cerebral hemisphere takes place by means of the bar fibres [5]. They have mainly excitatory, information integrating, but also inhibitory tasks. Depending on the quality of the nerve fibre and the localisation of the junction, information of sensory integration, motor and visual information processing and higher cognitive functions, linguistic requirements or language processing can be transmitted via the bar fibres [6].

Structure and direction:

The fibres of the corpus callosum show a topographical organisation. Anatomically, from ventral to dorsal, the genus, truncus, (isthmus), splenum and rostrum can be designated. The structural anomalies of the bar have a marker function, since this connection of the two cerebral hemispheres, which consists of the four large areas, does not form separately from further developmental steps of the brain. If a malformation is detected in this area, further abnormalities should be investigated. This enables a chronological classification of the time of disorder [3].

Disorders and frequencies:

A part of the CNS malformations (defined in the ICD-10 WHO section Q04. as „Other congenital malformations of the brain") are calculated from the EUROCAT data for the period 2005 to 2014 with a prevalence of 9.8 per 10,000 births. For this purpose data from 29 malformation registers from 15 European countries with approx. 1.7 million births per year (this comprises 29% of the birth population of the European Union) was analysed. Across Europe significant variations of the prevalence of the combined CNS malformations, depending on the proportion that can be prenatally diagnosed, have been recorded [7].

A part of the CNS malformations (defined in ICD-10 WHO section Q04. as „Other congenital malformations of the brain") are calculated from the EUROCAT data for the period 2005 to 2014 with a prevalence of 9.8 per 10,000 births. Agenesis of the corpus callosum is also reported in other cohorts with a prevalence of 1.8-2.5 per 10,000 births. Among patients with a neurological developmen-

tal disorder, corpus callosum agenesis cab be found in 230-600 per 10,000 births [8].

In principle, all fibres of the corpus callosum are present at time of birth in a non-dysfunctional system. Anatomical disorders can range from total absence, agenesis of the corpus callosum, hypoplasia with topographically regular formation but thinner expression and dsygenesis/ partial agenesis of the corpus callosum up to the absence of individual parts. Hyperplasia is also detected and results from postnatal synapse deletion [4, 6].

Associated malformations and syndromes:

Accompanying extracerebral anomalies are found in 81% of affected individuals in the following organ systems: eyes (e.g. hypertelorism), cardiovascular system, gastrointestinal tract, muscles, urinary tract and cleft lip, jaw and palate [4, 6]. Additional malformations of the nervous system are found in 46-83 % of affected persons with bar anomalies [4]. More than 200 syndromic diseases also show bar anomalies [9].

Causes:

Genetic factors are assumed to be causative in the majority of cases (30-45% of cases), including all modes of inheritance. The rate of bar malformations associated with chromosomal anomalies is up to 10% and genetic syndromes are described for 20-35% [4, 10]. Higher prevalences of bar agenesis of genetic origin are reported with increasing maternal age [6]. Other external factors contributing to the development may be fetal alcohol exposure (fetal alcohol syndrome: prevalence of bar agenesis 6.8%) and prenatal infections. Vascular prenatal processes additionally influence bar formation (primary or secondary) [4].

Diagnostics:

Prenatal imaging of the corpus callosum is currently offered in Germany from 18+0 to 21+6 weeks of gestation according to the guidelines of the Federal Joint Committee (G-BA). The maternity guidelines apply for a 2nd screening (biometry with fetal morphology) [11]. However, prenatal sonographic diagnosis of balk agenesis is difficult. In the majority of cases, a complete absence of the bar can be diagnosed during a second screening by an expert within the course of a neurosonographic examination, but an exact description of possible anatomical defects is difficult in general. These can be determined by a fetal MRI, in particular additional peripheral defects of the CNS can be better visualised [12].
Nevertheless, during standard prenatal ultrasound examination of a pregnancy without a risk constellation, a visualisation of the bar is not required and the disease can only be suspected by the presence of indirect findings (ventriculomegaly or a lack of visualisation of the cavum septi pellucidi) [13].

The most urgent question for expectant parents is related to the prognosis if abnormalities were seen prenatally. Fetal MRI imaging often provides additional information in this regard. A description of the abnormality that is as precise as possible must be achieved in order to be able to make a statement about the risk of a postnatal developmental disorder [12].
The fetal MRI scan allows direct visualisation of the corpus callosum. This is important because the diagnosis of the corpus callosum agenesis by ultrasound has been associated in studies with a false positive rate between 0% and 20% [14, 15].
The association of bar agenesis with other cerebral anomalies increases the likelihood of subsequent neurological impairment; therefore, fetal MRI examination should also be part of the antenatal assessment as an adjunct, particularly in fetuses with apparently isolated corpus callosum agenesis.

Prognosis:

Prenatal statements regarding the prognosis remain difficult. Recent studies suggest that chromosomal abnormalities are rare in cases of isolated bar hypoplasia and agenesis. Nevertheless, postnatal follow-up studies show that about 15% of cases that were considered prenatally as isolated showed associated abnormalities after birth.
The outcome of neurological development at presence of an isolated bar agenesis has recently been studied in a systematic review and the results indicate age-appropriate development in about 65-75% of all cases. However, the results must be considered in light of the various limitations of existing studies in terms of study design, selection bias, differences in definitions and imaging protocols, ascertainment bias and lack of control groups. These uncertainties mean that prenatal counselling is very difficult and further large prospective studies are needed [13].

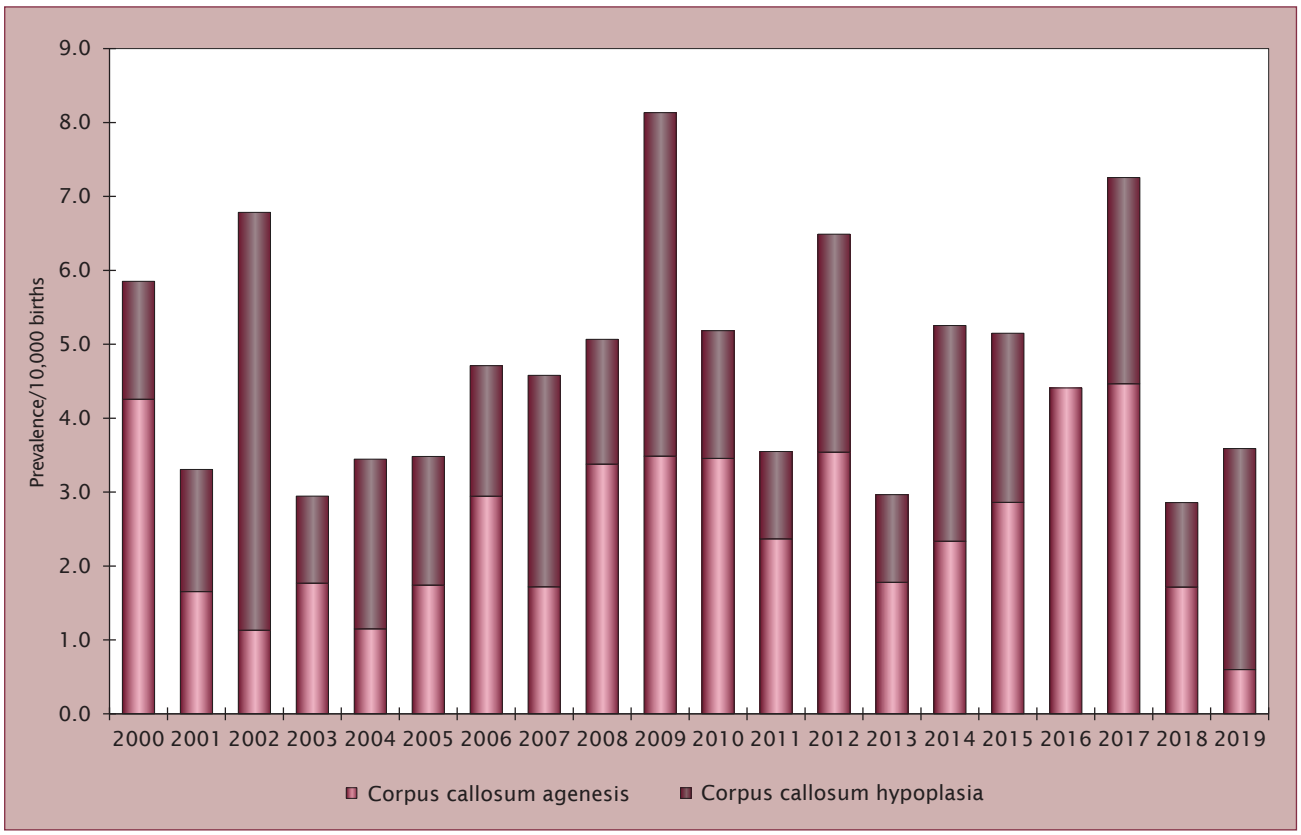


Fig. 50: Prevalence of corpus callosum agenesis and hypoplasia
Data of malformation monitoring, birth cohorts 2000 to 2019 (with a total of 438,659 births in the registration region)

Figure 51 shows data of the malformation monitoring Saxony-Anhalt from 2000 to 2019. 166 cases which were diagnosed by the end of the 1st year of life could be included into the analysis. All pregnancy outcomes (live births, stillbirths, spontaneous abortions from the 16th week of gestation and terminations of pregnancy after prenatal diagnosis during all weeks of gestations) were included into the analysis.

Pregnancy outcomes of congenital malformations of the corpus callosum are shown in Figure 52 (data of malformation monitoring, birth cohorts 2000 to 2019).

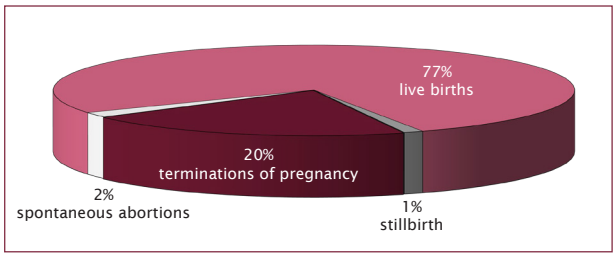


Fig. 51: Pregnancy outcome of congenital malformations of the corpus callosum
(Q 04.0 incl. agenesis of corpus callosum)

Despite similar genetically disorders of the corpus callosum, the clinical expression of neurodevelopmental disorders can vary significantly. Similarities up to identical overlapping of clinical symptoms are seen in agenesis and hypoplasia/dysgenesis [10].

Isolated corpus callosum agenesis does not seem to affect the development of affected children in 75% of the cases. However, 12% show various neurological deficits/developmental delays, and 15% even show severe impairments. Palmer and Mowat point out that it is still unclear why a total or partial absence can cause similar clinical pictures. They see a possible influence of neuronal plasticity, genetic background, developmental disorders and concomitant diseases [6].

Affected children with corpus callosum agenesis may show deficits concerning higher language functions, complex processing of information, complex attention, retentiveness and their mathematical abilities. Epilepsy may occur. In particular, social interactions cause problems for the patients, up to and including behaviours from the autism spectrum have been described, as well as schizophrenias and attention deficit disorders (ADHD) [6, 10]. The Probst bundle (atypical fibre bundles, running parallel to the interhemispheric gap), which is often present in the complete absence of the corpus callosum, seems to create compensatory connections to the other half of the brain; the more, the better this patients succeeds in social integration [4].

Other congenital malformations of the brain in 29 EUROCAT registries from 2005 -2014, modified according to Morris et al. 2019 2019 [7]

ICD 10 Code[1]	Q04.2	Q04.1	Q04.4	Q04.5	Q04.3	Q04.0	Q04.8	Q04.6	Q04.9	Q04
Malformation	Holopro-sencephaly syndrome	Arhinencephaly	Septooptical dysplasia	Megalen-cephaly	Other cereb-ral reduction deformities	Congenital malformations of the corpus callosum, cor-pus callosum agenesis	Other speci-fied congeni-tal cerebral malformations	Congenital cerebral cysts (porencepha-ly, schizen-cephaly)	Congenital cerebral mal-formations, not otherwise specified	Cases, in total
Number of cases	865	33	94	49	1,409	1,476	383	375	243	4,927
Number of diagnosis[2]	865	46	99	49	1,464	1,748	550	555	273	5,649
Prevalence/ 10,000 births (CI 95%)[3]	1.55 (1.37 - 1.77)	0.04 (0.01 - 0.07)	0.19 (0.11 - 0.26)	0.08 (0.05 - 0.11)	2.92 (2.51 - 3.35)	3.25 (2.72 - 3.82)	0.75 (0.53 - 1.01)	0.69 (0.49 - 0.93)	0.39 (0.29 - 0.52)	9.78 (8.5 - 11.16)
Live births n (%)	155 (18)	2 (6)	90 (96)	33 (67)	792 (56)	975 (66)	259 (68)	302 (81)	112 (46)	2,720 (55)
Fetal deaths n (%)	34 (4)	1 (3)	0 (0)	1 (2)	55 (4)	37 (3)	12 (3)	6 (2)	18 (7)	164 (3)
TOPFA[4] n (%)	676 (78)	30 (91)	4 (4)	15 (31)	562 (40)	464 (31)	112 (29)	67 (18)	113 (47)	2,043 (41)
Non-genetic/ chromosomal cases n (%)	539 (62)	12 (36)	91 (97)	43 (88)	1,119 (79)	1,156 (78)	307 (80)	325 (87)	192 (79)	3,784 (77)
Average mater-nal age (years)	30 (30 - 31)	32 (30 - 34)	23 (22 - 24)	30 (28 - 32)	30 (30 - 30)	30 (30 - 31)	30 (30 - 31)	29 (28 - 30)	29 (29 - 30)	30 (30-30)
Live births pre-mature births (< 37 weeks of gestation) n (%)	62 (40)	1 (50)	17 (19)	5 (17)	229 (29)	208 (22)	79 (31)	113 (38)	34 (32)	748 (28)
Prenatal dia-gnosis n (%)	811 (94)	32 (97)	32 (34)	27 (55)	962 (68)	1038 (70)	207 (54)	182 (49)	157 (65)	3,448 (70)
Male cases n (%)	316 (37)	14 (42)	52 (55)	29 (59)	684 (49)	749 (51)	198 (52)	196 (52)	114 (47)	2,352 (48)

[1] ICD-10, International Classification of Diseases, 10th Revision
[2] The number of diagnoses will be higher than the number of cases, as each case may have more than one different diagnosis of a cerebral anomaly
[3] Adjusted for potential underreporting of the different registries by means of a random-effects meta-analysis
[4] TOPFA = termination of pregnancy for fetal anomaly after prenatal diagnosis

The table on page 78 shows the data analysis for all cases of „other congenital cerebral malformations“ coded in chapter Q04 (ICD-10, International Classification of Diseases, 10th Revision). Data of 29 EUROCAT malformation registers was analysed with a total of 1.7 million births (overview of 29 % of births in the European Union) of the birth cohorts 2005-2014.
A total of 4,927 cases were analysed with the diagnosis of a cerebral malformation up to the end of the 1st year of life. All pregnancy outcomes were included into this analysis (live births, stillbirths, spontaneous abortions from the 20th WOG, terminations of pregnancy after prenatal diagnosis of all WOG).

When cases showed combinations of cerebral anomalies classified within chapter Q04 (ICD10), they were hierarchically assigned to a group in a way that all cases were assigned to one main diagnosis. The diagnoses on the left side had priority over those on the right side. The diagnoses of single cerebral cysts, arachnoid and plexus cysts and abnormalities of the septum pellucidum can be found on the EUROCAT list of minor malformations that are excluded. Therefore, a case is not included if it was described as the only cerebral abnormality of the patient.

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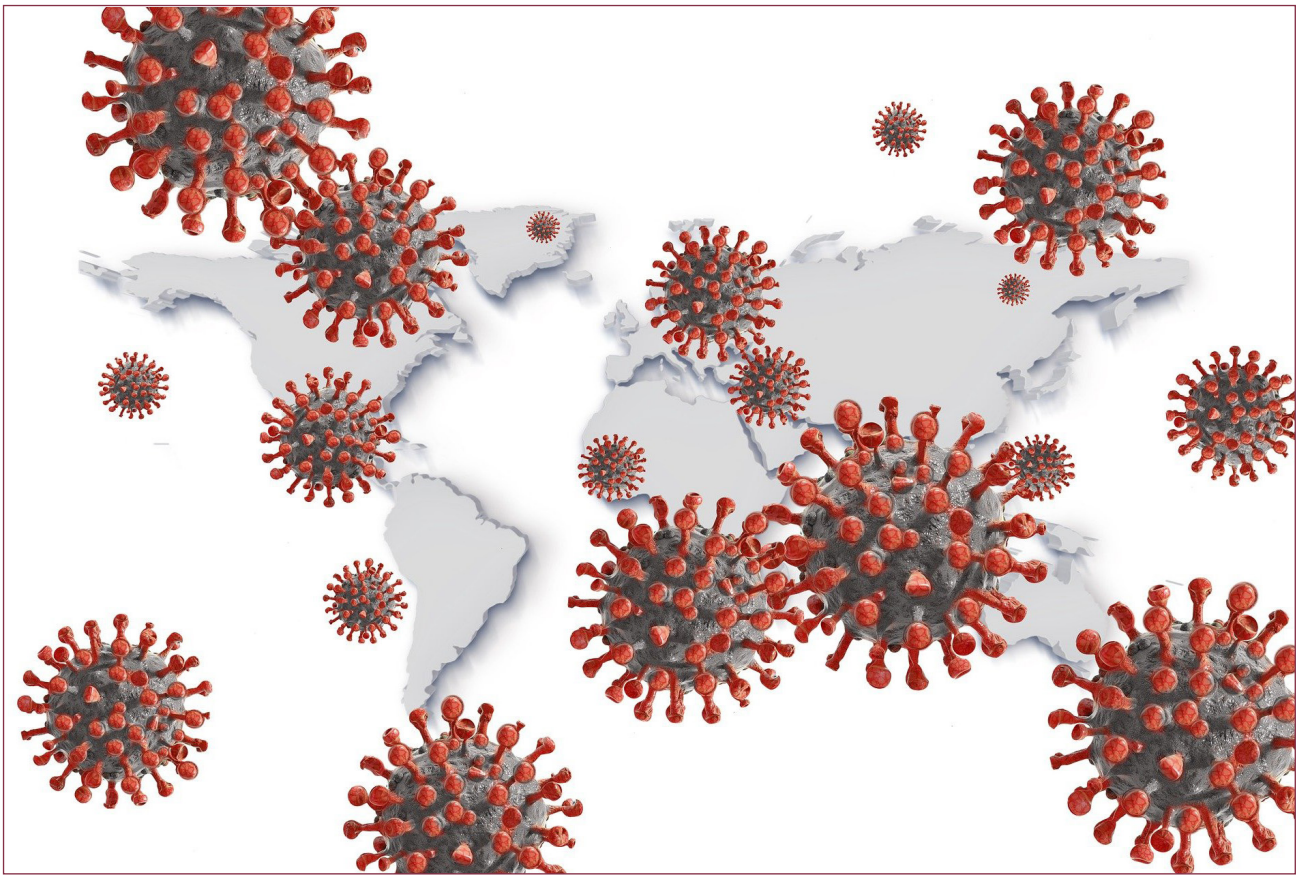
14.2 COVID-19 infection risk for pregnant women



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We are aware of the tense situation when someone who is working in the health sector is pregnant. To the best of our knowledge, pregnant health professionals are no more susceptible to the virus or its complications than their non-pregnant colleagues [1]. The World Health Organisation (WHO) [2], the European Centre for Disease Prevention and Control (ECDC) [3] and the Robert Koch Institute (RKI) in Germany [4] all agree in their risk assessment that pregnant women are not at higher risk of COVID-19 infection. In this context, the general measures for infection prevention and the current recommendations of the RKI under „Prevention and management in health care facilities“ (https://www.rki.de/DE/Content/InfAZ/N/Neuartiges_Coronavirus/nCoV.html) are valid.

The appearance of SARS-CoV-2 as a new infection from the end of December 2019 and its spread to a pandemic poses unique challenges for the healthcare system worldwide. The infection does not even stop at pregnant women and newborns. It is known from embryology that the first trimester carries the greatest risk for miscarriage and fetal developmental abnormalities. In the late second and third trimesters, there is an increased likelihood of developing maternal diseases, such as gestational diabetes and hypertension, which can contribute to maternal morbidity and preterm birth [1, 5].

There is no reliable evidence of vertical transmission (intrauterine transplacental, peripartum or breast milk transmitted infection) of the SARS-CoV-2 virus from the data available so far [6]. Ten births (one twin pregnancy) are reported from the neonatology department of Wuhan University Hospital (PR China). Among these nine pregnant women with confirmed 2019-nCoV-infection, clinical symptoms occurred in four cases before delivery, in two cases on the day of delivery and in three cases after delivery. Among these births, „severe illness“ was reported (respiratory distress (6x), pneumothorax (1x), haemorrhage (2x), growth retardation (2x), premature birth (6x) and death on one occasion) [7]. In another retrospective observation, nine births were reported to do better. Four premature infants and two infants showed a growth retardation. All had oxygen requirements and received antibiotics [8]. However, it is not clear whether these diseases are related to the mother‘s infection or a vertical transmission of the virus during pregnancy is possible.

There is no epidemiological data yet from Europe on SARS-CoV-2 exposure in early pregnancy, but with possible vertical transmission, exposure in early pregnancy could be a problem.

According to the meta-analyses available so far, there is a risk of fetal growth restriction (growth retardation) or prematurity (rates between 15-39%) if the pregnant woman became severely ill with COVID-19 infection [1, 9, 10].

The recommendations of the German Society for Perinatal Medicine on pregnancy, birth and the postnatal period were renewed in June and explicitly state that breastfeeding should be made possible in SARS-CoV-2 positive mothers. Figure 53 shows the course of the disease in relation to antibody detection. Individual cases of virus detection in breast milk do not outweigh the numerous advantages of breastfeeding (additional passive immune protection possible). In order to minimise the risk of horizontal transmission during breastfeeding, appropriate specific hygiene rules and measures are recommended [10].

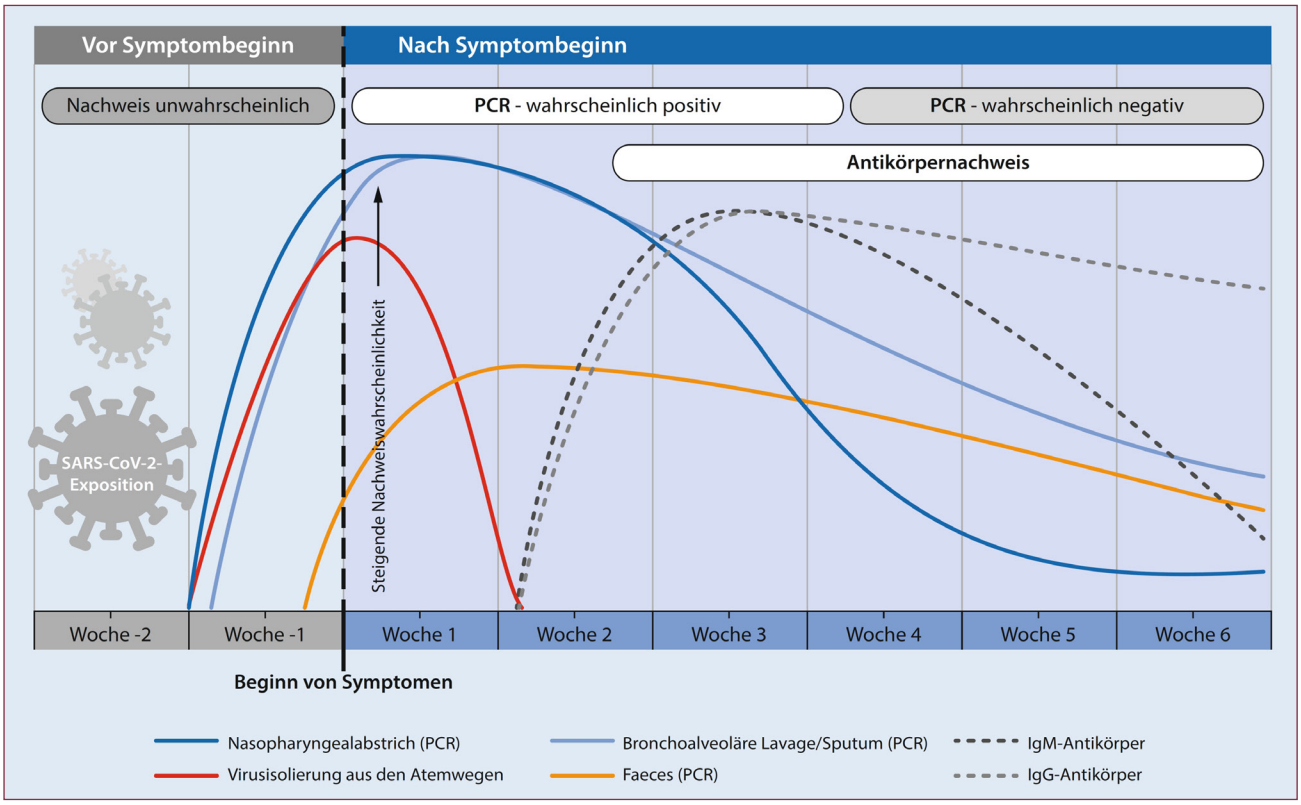

Fig. 52: Disease progression in correlation to PCR (polymerase chain reaction) and Ig(immunoglobulin)-serology from Hagenbeck et al. 2020 [9]

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16 Newborn Hearing Screening 2019

Introduction

Every newborn is entitled to receive a general newborn hearing screening which belongs as from 1st January 2009 to the recommended early detection examinations after birth of a child.
Aim of the newborn hearing screening (NHS) is **to detect congenital hearing disorders at an early stage (up to the 3rd month of life)** and **to initiate the corresponding therapies (up to the 6th month of life)**.

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

The Children Directive determines the **process of the newborn hearing screening** in the following way:
- measurement of each ear by TEOAE or AABR up to the 3rd day of life (outside of hospital by no later than early detection examination 2 (U2))
- AABR examination is mandatory for children with increased risk for a hearing disorder
- examinations of premature infants by no later than calculated date of delivery and examinations of not healthy 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 Directive **performance and results of the newborn hearing screening as well as** a possible **confirmation diagnostics** have to be **recorded** in the **"yellow book of examination" of every child**. The responsible paediatrist resp. ENT physician can evaluate by reading this information if the required diagnostics resp. therapy in case of a hearing disorder was initiated.
The Monitoring of Congenital Malformations Saxony-Anhalt cooperates with the Centre for Newborn Hearing Screening Saxony-Anhalt since 2006 as **tracking centre for the newborn hearing screening** (Federal State specific screening centre).

The Newborn Hearing Screening Directive stipulates that the hearing screening should be performed via AABR at **children with an increased risk for congenital hearing disorders**.
The following overview outlines in extracts possible **indications for the performance of an AABR examination** due to an increased risk of hearing disorders (modified according to JCIH 2007):
- positive family history regarding hearing disorders
- clinical suspicion of hearing disorder/deafness
- premature birth, birth weight under 1500 g
- neonatal intensive care (> 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

22 maternity clinics existed in Saxony-Anhalt in 2019. All these clinics offer a newborn hearing screening already for several years by TEOAE or AABR. These maternity clinics all participated 2019 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 86 gives an overview about the single maternity clinics and number of births with a screening ID.

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

Maternity Clinic	Tracking period 2019	Live births with screening ID in this period
AMEOS Klinikum Aschersleben	01.01.-31.12.2019	452
Gesundheitszentrum Bitterfeld/Wolfen	01.01.-31.12.2019	423
HELIOS Klinik Jerichower Land Burg	01.01.-31.12.2019	388
Städtisches Klinikum Dessau	01.01.-31.12.2019	804
Altmark-Klinikum Krankenhaus Gardelegen	01.01.-31.12.2019	345
AMEOS Klinikum Halberstadt	01.01.-31.12.2019	508
Krankenhaus St. Elisabeth und St. Barbara Halle	01.01.-31.12.2019	1,983
Universitätsklinikum Halle (Saale)	01.01.-31.12.2019	1,298
HELIOS Klinik Köthen	01.01.-31.12.2019	417
Krankenhaus St. Marienstift Magdeburg	01.01.-31.12.2019	1,047
Klinikum Magdeburg	01.01.-31.12.2019	1,342
Universitätsklinikum Magdeburg	01.01.-31.12.2019	1,195
Carl-von-Basedow-Klinikum Saalekreis Merseburg	01.01.-31.12.2019	920
Saale-Unstrut Klinikum Naumburg	01.01.-31.12.2019	448
Harzklinikum Dorothea Christiane Erxleben, Klinikum Quedlinburg	01.01.-31.12.2019	501
Altmark-Klinikum Krankenhaus Salzwedel	01.01.-31.12.2019	424
HELIOS Klinik Sangerhausen	01.01.-31.12.2019	625
AMEOS Klinikum Schönebeck	01.01.-31.12.2019	488
Johanniter-Krankenhaus Genthin-Stendal	01.01.-31.12.2019	766
Harzklinikum Dorothea Christiane Erxleben, Klinikum Wernigerode	01.01.-31.12.2019	744
Evangelisches Krankenhaus Paul Gerhardt Stift Wittenberg	01.01.-31.12.2019	746
Georgius-Agricola Klinikum Zeitz	01.01.-31.12.2019	363
Total number of live births with Screening-ID in Saxony-Anhalt		**16,227**

Further live births with Screening-ID: e.g. home births / births in a birthing centre resp., infants not born in Saxony-Anhalt	01.01.-31.12.2019	130

Tracked infants, in total	**16,357**

In total, **16,227 births** received a screening ID in their maternity clinic in Saxony-Anhalt in 2019.
In this way, these infants could participate in the hearing screening tracking.

Furthermore, **130 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 **94 senders** in 2019.

Births with screening-ID and number of incoming result

2019	Infants with screening ID	Number of incoming results
January	1,336	1,757
February	1,195	1,612
March	1,260	1,586
April	1,332	1,782
May	1,383	1,852
June	1,382	1,791
July	1,543	1,971
August	1,497	1,905
September	1,453	1,846
October	1,371	1,761
November	1,280	1,605
December	1,325	1,649
total	**16,357**	**21,117**

The previous 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. 1,760 reports can be expected, however in some cases we received multiple reports 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, **2,336 letters resp. faxes** were forwarded in 2019 (one up to eight letters per infant). With reference to all infants with screening ID this corresponds to an average of 0.14 letters per infant. Additionally, the parents and attending physicians of the infants born in 2019 were contacted by telephone. In total, **154 calls** were made in connection with the hearing screening tracking (one up to six calls per infant).

Results (November 2020)

All results that were reported to the hearing screening tracking centre about infants that were born in 2019 are included in our analyses 2019 of the newborn hearing screening:

14,115 infants out of **16,357 infants** with screening ID had an **unsuspicious newborn hearing screening result**. In **2,242 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 2,242 infants showed in **1,541 cases** an **unsuspicious result**. The remaining **701 infants** had again a **suspicious result**.
315 of these 701 infants received a **complete paediatric audiological confirmation diagnostic**.
According to our knowledge, **189 infants** did **not receive a confirmation diagnostic** and therefore are considered as **lost to follow-up**.

168 infants did **not participate in the screening** (no reaction of parents to reminder letters or refusal of examination) and in **15 cases** the status is still **pending**, i.e. the examinations were not finished in November 2020 or the tracking process still requires more time. In **14 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 **350 infants** who were born in 2019 could be **completed (confirmations diagnostics)**. Among 315 infants with a suspicious result, 35 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 314 cases**. In **36 cases** a **hearing disorder was diagnosed** (25x bilateral and 11x unilateral hearing disorder) and the corresponding therapy was initiated. For instance, **26 infants** received a **hearing aid** (20x hearing aid bilateral, 6x hearing aid unilateral).

17 Annual Report 2019 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

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Kompetenznetz Neugeborenen-Screening
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Introduction

The Newborn screening is a population-based preventive measure with the aim of a complete and early detection as well as quality-assured therapy of all newborns with severe, congenital metabolic disorders (Tab. 1).
The Directive of the Joint Federal Committee about the early detection of childhood diseases (Children's Directive) 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 statistical processing of the screening data is based on the quality criteria defined in the Directive for the implementation of NGS and CF screening in Germany.

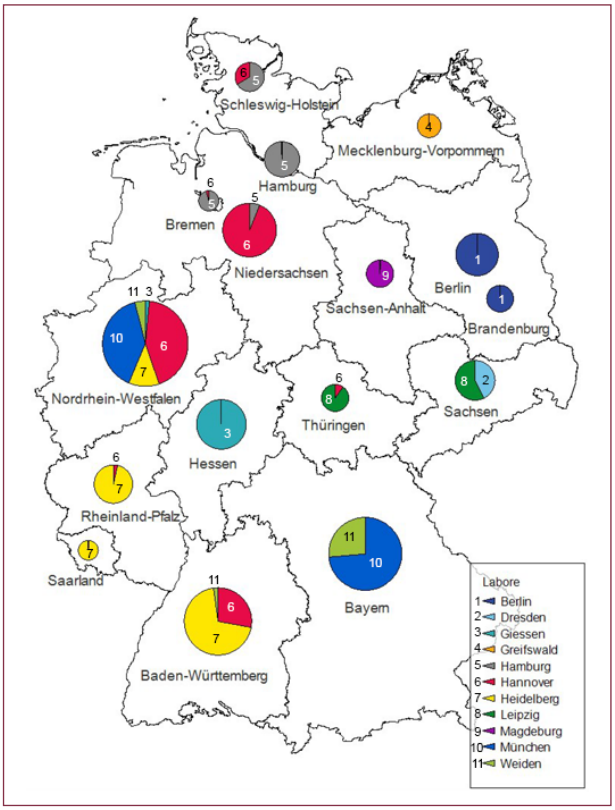

Fig. 1: Sample distribution of the screening centres in Germany[1]

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 Germany1 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	Confirmed cases	Prevalence
Congenital hypothyroidism (CH)	279	1 : 2,813
Congenital adrenal hyperplasia (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
Cystische fibrosis (CF) / CFSPID	160	1 : 4,906
total	**786**	**1 : 999**

Screening data 2019 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 Directive 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 Directive the obstetric clinics have to document on a blank test card the total refusal of screening, the refusal of an early blood taking within the screening, the transfer to specialised institutions or death of the newborn. The test card 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 2019:
According to the Federal Statistical Office 16,618 children were live births in Saxony-Anhalt
(data according to the place of maternal residence).

Tab. 2: Initial examinations according to the place of maternal residence

	Number
First screening in Magdeburg, in total	16,312
Non-resident in Saxony-Anhalt	796
Screening of children living in Saxony-Anhalt	**15,516**

The discrepancy between the number of live births and screened infants with residence in Saxony-Anhalt amounts to 1102.

Basis for the data of the State Statistical Office are the births that are reported by the birth centres to the registry offices, 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	**324**
Blank card: infant deceased/stillbirth	69
Blank card: refusal of early taking	199
Blank card: transfer to another hospital	16
Blank card: screening refused by parents	13
Screening took place	223

As a result of follow-up (telephone calls, faxes, letters), only 1% of the blank cards sent in remained 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	84	412
Received at own laboratory	84	376
Deceased before control examination	-	4
Received at another laboratory	-	32

WOG = weeks of gestation

Examination numbers, recall rates and assured cases

ITable 5 shows recall rates of the single parameter and assured cases. A total of 134 control examinations had to be carried out in 2019.

Tab. 5: Recall-rate 2019 and diagnosed patients with a metabolic disease in reference to 16,312 screening examinations (includes also early withdrawal < 36 h and preterm births < 32 WOG), prevalence 1992-2019

Target disease incl. all forms of disease	Number of recalls* 2019	Assured cases 2019	Prevalence in Saxony-Anhalt 1992-2019
Hypothyroidism (CH)	57	2	1 : 4,034
Phenylketonuria (PKU/HPA)	4	3	1 : 5,286
Galactosemia (classical)	1	-	1 : 114,981
Biotinidase deficiency	4	-	1 : 112,559
Congenital adrenal hyperplasia (CAH)	38	-	1 : 18,871[I]
Medium-Chain-Acyl-CoA-Dehydrogenase deficiency (MCAD)	2	1	1 : 10,552[II]
Long-Chain-3-OH-Acyl-CoA-Dehydrogenase deficiency (LCHAD)	2	1	1 : 67,535
(Very-)Long-Chain-Acyl-CoA-Dehydrogenase deficiency (VLCAD)	2	-	1 : 168,838
Maple syrup urine disease (MSUD)	-	-	
Carnitin-Palmitoyl-CoA-Transferase I and II deficiency (CPTI/CPTII)	-	-	
Carnitin-Acylcarnitin-Translocase deficiency (CACT)	-	-	
Glutaric aciduria type I (GA I)	-	-	
Isovaleric acidaemia (IVA)	2	-	
Cystic fibrosis	15	4	1 : 5,681[III]
Tyrosinemia type I[IV]	-	-	
Severe combined immunodeficiencies (SCID)[V]	1	-	
Other	9	-	

* Recall: Request of a new blood sample at suspicious screening result at first examination.
Shown here the number inclusive early blood withdrawal (<36 h) or premature infant (< 32 WOG)
I Screening to detect congenital adrenal hyperplasia syndrome (since 1997)
II Enlarged screening (TMS) since 05/2001
III Screening for mucoviscidosis since 09/2016
IV Screening for tyrosinemia since 04/2017
V Severe combined immunodeficiencies SCID since 08/2019

Process times

Point of taking blood samples

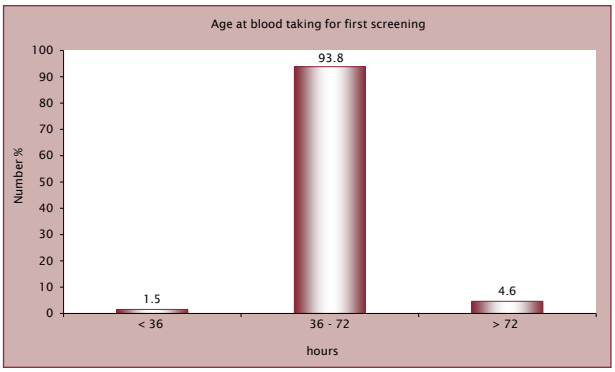

Fig. 2: Age at point of blood taking for first screening

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 93.8% of all cases (2018: 93.5%). At a total number of 6.2% the taking of blood samples took not place within the required period of time (2016: 7.6%). We regard this trend as slightly positive in comparison to the previous years.

Note: Only newborns were included in the analysis if all required information was available (date and time of birth and blood collection date 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 18.6% (2017: 18.0%) 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 2019. 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 (letters, training events). The main reason for this is surely the dispatch via private mail deliverers. We recommend urgently shipping the samples therefore with the Deutsche Post directly to the screening mailbox. The following advices 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
- do not send to the hearing screening tracking center

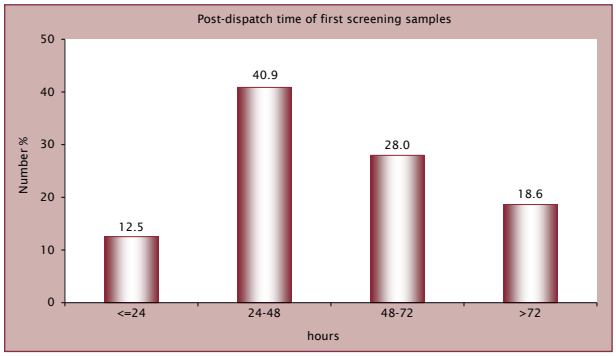

Fig. 3: Post-dispatch time of the dry blood cards (first screening) Time from blood collection to arrival at the laboratory

Tab. 6: Post-dispatch time of dry blood cards per sending hospital (average value of all wards of a hospital), comparison 2019 and 2015

Maternity clinic	Average shipping time (hours)	
	2019	2015
Magdeburg St. Marienstift*	22.6	12.1
Magdeburg Universitätsklinikum*	29.3	28.9
Magdeburg Klinikum*	37.9	25.4
Gardelegen	40.3	41.5
Quedlinburg	41.5	44.1
Zeitz	44.5	49.2
Salzwedel	45.7	45.1
Bitterfeld-Wolfen	45.8	55.5
Schönebeck	46.7	40.8
Wernigerode	48.6	49.8
Halle St. Elisabeth und St. Barbara	48.9	50.1
Aschersleben	51.2	49.7
Naumburg	51.4	40.9
Merseburg	54.8	50.5
Lutherstadt Wittenberg	55.8	56.0
Stendal	57.8	46.0
Halle Universitätsklinikum	60.0	53.4
Sangerhausen	61.2	49.6
Köthen	66.8	48.8
Dessau-Roßlau	70.1	44.0
Burg	83.7	44.2
Halberstadt	97.8	62.1

* Clinic with a courier service

Transmission of Results

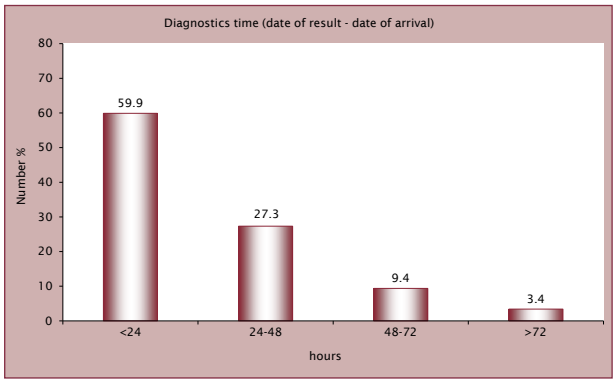

Fig. 4: Duration of findings transmission

Figure 4 shows the duration of laboratory analysis of all initial screening examinations. Findings that are finished after more than 24 hours are caused by the following: Repetition of analyses and stages 2 and 3 of CF screening. 12.8 % (2016: 11.1 %) of all findings that left the laboratory after more than 48 hours mainly reflect the extended finding duration due to cystic fibrosis screening (3-stage screening incl. mutation analysis) and disruptions in the laboratory workflow (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

	2019	2018
Screening, in total	16,312	16,987
CF screening included	99.7 %	99.7 %
CF screening positive	17	8
sweat test performed	16	7
CF confirmed	4	2

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 attend 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 2019 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 a positive CF screening. In the case of the

birth with a conspicuous CF screening, we unfortunately did not receive any feedback from the maternity clinic if the former premature baby received a sweat test, even after repeated requests.

Confirmation diagnostics and therapy of screening-positive patients

Eleven suspected screening cases could be confirmed by confirmation diagnostics and provided with a therapy:

Tab. 8: Diagnosis, confirmation diagnostics and therapy starting

Diagnosis	Confirmation diagnostics	Age at start of therapy
2 x Hypothyroidism	Serum TSH, fT3, fT4, sonography, thyroid antibodies	5-26 days
3 x Phenylketonuria 0 x Hyperphenylalanemia	Serum-Phe, BH4 test, DHPR activity, pterins, mutation analysis	4-12 days
1 x MCAD deficiency	Organic acids in urine	No information
1 x LHCAD deficiency	Organic acids in urine, mutation analysis	5 days
4 x cystic fibrosis (2 x classical homocygotic mutation)	Sweat test mutation analysis	16-20 days

Summary

A new version of the Children's Directive became effective in February 2019. The screening for severe combined immunodeficiencies - SCID was included.
Accordingly, new information flyers were provided and the senders were informed about this innovation. As before, parents have the option to have the screening for cystic fibrosis performed independently from the extended newborn screening or to decline it (checkbox on the dry blood card). CF screening can take place up to the 4th week of life of the newborn. The analysis of all target diseases of the Extended Newborn and Cystic Fibrosis Screening can be performed from one blood sample, provided that sufficient blood has been dripped.
Here, new preanalytical problems arose due to the introduction of a new laboratory method for the analysis of TREC for the disease of SCID. This T-cell typical cyclic DNA is analyzed by qPCR and does not tolerate any additives such as heparin. Therefore, senders were trained to strictly meet the required criteria for the collection of dry blood samples from the heel:

- Do not use EDTA, heparin or coated capillaries
- Recommendation: use lancets with cutting blades, they provide optimal blood flow (e.g. Safety-Lancet Neonatal Blade or Safty-Heel Neonatal by Sarstedt, BD QuikHeel™ safety incision lancet)
- Disinfect heel with 70-80% alcohol and allow to dry thoroughly before puncture. Do not use hand sanitizers or similar, as they will interfere with the analysis
- Soak all 4 circles completely

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, the intensive cooperation with pediatricians for endocrinology and metabolism 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. Since 2019, the laboratory has a qPCR, which is currently used for the screening for SCID. It is likely that two new target diseases will be introduced to the Advanced Newborn Screening in the coming year 2021: Sickle Cell Disease (SCD) and Spinal Muscular Atrophy (SMA).

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).

We thank all medical centres and ambulances for the good and smooth collaboration.

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 senders, 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 the Societys 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