

Annual Report 2023

Malformation Monitoring Centre
Saxony-Anhalt



SACHSEN-ANHALT

Ministerium für
Arbeit, Soziales, Gesundheit
und Gleichstellung

Annual Report 2023
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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Gender note:

For reasons of better comprehensibility, the annual report of the Malformation Monitoring Centre Saxony-Anhalt uses the masculine form. All persons and designations refer equally to all genders.

Introduction



Dear reader,

In order to record, analyze and reduce the incidence of congenital malformations in our state over a long term period, the Malformation Monitoring Centre Saxony-Anhalt has been an indispensable tool for many years. As an integral part of our health reporting, it documents the results of anonymous and continuous monitoring. It therefore provides a solid basis for preventive measures and targeted medical care. It also enables us to protect the health of our children and open up a good future for them. Together, we can help to ensure that more and more children are born healthy. The results of the Malformation Monitoring Centre also serve as a basis for scientific studies. By continuously analyzing the data, new discoveries can be made and innovative therapeutic approaches can be developed.

Congenital malformations are structural changes of the body that are present at birth and affect any part or parts of the body. Malformations can be accompanied by mild to severe functional impairment. This can range from changes of shape and size of organs up to the complete absence of organ systems. Congenital malformations are a significant cause of mortality of infants and young children as well as of chronic diseases and disabilities. Fortunately, congenital malformations are very rare: approximately one of 33 pregnancies in Europe is affected.

The Annual Report 2023 focuses on the coding and classification of congenital malformations. But what are classification models actually intended to achieve? The standardized classification of clinical findings makes a significant contribution to clearly identify each malformation and distinguish it from other diseases. This makes it possible to compare cases within and between different institutions, regions and countries.

The global outbreak of Mpox, known as “monkeypox”, is a current prime example of how the first cases could be identified quite quickly thanks to a well-established surveillance system. Early detection enabled the international community to respond quickly to the outbreak. The obtained data was evaluated using modern analysis methods to track the spread of the virus, identify risk groups and assess the effectiveness of measures.

An analysis of the risk factors is only possible with the help of standardized summaries. In order to improve the prognosis of pregnancies affected by malformations, various therapeutic and prophylactic approaches can be evaluated in clinical practice. The classification of new malformations is a complex process that is constantly evolving. There is no single, rigid method, as each malformation is unique and is quite often based on a combination of genetic, environmental and random factors.

But regardless of whether they are diagnosed prenatally or postnatally: Congenital malformations present parents with major challenges. Professional support from experienced midwives, nurses and doctors who can assist parents is helpful. I would therefore like to thank all those who support affected children and parents in their everyday work. I would also like to express my gratitude to all those who have contributed to the compilation of this report with their commitment.

Your sincerely

A handwritten signature in black ink, appearing to read 'Petra Grimm-Benne'.

Petra Grimm-Benne
Federal Minister of Labor, Social Affairs, Health
and Integration of the State of Saxony-Anhalt

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Abbreviations

AABR	automated auditory brainstem response	ICSI	intracytoplasmic sperm injection
ASD	atrial septal defect	IUGR	intrauterine growth restriction
AVSD	Atrioventricular septal defect	LB	Live birth(s)
ATC	Anatomical-Therapeutic-Chemical classification	MCA	Multiple congenital anomalies
AV-Block	atrioventricular block (= cardiac block)	NHS	Newborn hearing screening
bds.	bilateral	NIPT	non-invasive prenatal test (cell-free DNA-analysis)
BMI	Body-Mass-Index	NT	nuchal translucency
BP	basis prevalence	n. (o.) s.	not otherwise specified
(c)CMV	(connatal) cytomegalovirus infection	OR	odds ratio
CHD	Congenital Heart Defects	P	prevalence
CI	confidence interval	PDA	persistent ductus arteriosus
CNS	central nervous system	PFO	persistent foramen ovale
dB	Decibel	SA	spontaneous abortion
DIV	Double Inlet Ventricle	SB	Stillbirth(s)
DORV	Double Outlet Right Ventricle	SD	Standard deviation
DUP	dilated Urography	TEOAE	transistoric evoked otoacoustic emissions
EUROCAT	European Surveillance of Congenital Anomalies	TGV	transpositions of great vessels
ENT	ears, nose, throat	TORCH	Acronym made up of the first letters of important prenatal infections: Toxoplasmosis, other (other, e.g. syphilis, listeriosis), rubella, cytomegalovirus (CMV) and herpes simplex
FAS	fetal alcohol syndrome	VSD	Ventricular septal defect
FASD	fetal Alcohol Spectrum Disorder	WOP	Week of pregnancy
G-BA	Federal Joint Committee		
HLHS	hypoplastic left heart syndrome / left heart hypoplasia syndrome		
IA	Induced abortion(s)		
ICBDSR	International Clearinghouse for Birth Defects Surveillance and Research		

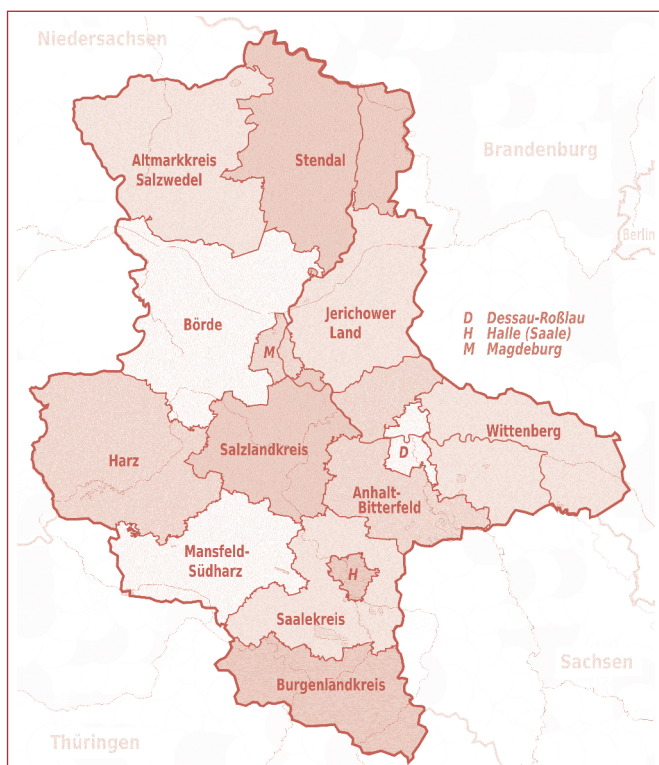
1 Births and fetuses 2023 in the registration region

Districts / major cities	Live births	Totgeburten*	Live births and stillbirths in total	Spontaneous abortions (> 16 WOG)‡	Terminations of pregnancy‡
Altmarkkreis Salzwedel	526	o. A.	527**	-	2
Anhalt-Bitterfeld	890	o. A.	891**	-	7
Börde	1,043	4	1,047	-	1
Burgenlandkreis	973	4	977	-	1
Dessau-Roßlau	498	4	502	-	4
Halle	1,897	4	1,901	-	4
Harz	1,142	7	1,149	4	7
Jerichower Land	485	o. A.	485**	-	-
Magdeburg	1,787	8	1,795	2	12
Mansfeld-Südharz	714	3	717	1	1
Saalekreis	1,140	3	1,143	-	4
Salzlandkreis	1,057	5	1,062	2	5
Stendal	682	o. A.	683**	1	2
Wittenberg	716	4	720	-	3
Landkreis in Sachsen-Anhalt o.n.A.	-	-	-	-	-
Saxony-Anhalt	13,550	49	13,599	10	53

* Source: © SStatistical Office Saxony-Anhalt, Halle (Saale), 2024

** extrapolated figure

‡ Data Malformation Monitoring Centre 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 2023

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

- AMEOS Klinikum Aschersleben
- Helios Klinik Jerichower Land Burg
- Städtisches Klinikum Dessau
- Altmark-Klinikum Krankenhaus Gardelegen
- AMEOS Klinikum Halberstadt
- Krankenhaus St. Elisabeth und St. Barbara Halle (Saale)
- Universitätsklinikum Halle (Saale) A.ö.R.
- Helios Klinik Köthen
- Herzzentrum Leipzig - Universitätsklinik für Kinderkardiologie (*outside of Saxony-Anhalt*)
- Klinikum Magdeburg
- Krankenhaus St. Marienstift Magdeburg
- Universitätsklinikum Magdeburg A.ö.R.
- Carl-von-Basedow-Klinikum Saalekreis Merseburg
- Altmark-Klinikum Krankenhaus Salzwedel
- Helios Klinik Sangerhausen
- Johanniter-Krankenhaus Stendal
- Harzklinikum Dorothea Christiane Erxleben Klinikum Wernigerode
- Evangelisches Krankenhaus Paul Gerhardt Stift Wittenberg
- SRH Klinikum Zeitz

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

- Dr. H. und C. Seidel, Fächärzte für Frauenheilkunde und Geburtshilfe, Dessau-Roßlau
- Dipl. Heilpädagogin Schlote, Glindenberg/Magdeburg
- Dr. Krull, Fachärztin für Kinder- und Jugendmedizin, Haldensleben
- Krankenhaus St. Elisabeth und St. Barbara Halle, Klinik für Geburtshilfe, Pränatale Ultraschalldiagnostik: CA Dr. Seeger, OÄ Dr. Radusch
- Universitätsklinikum Halle (Saale) A.ö.R., Universitätsklinik und Poliklinik für Geburtshilfe und Pränatalmedizin, Pränatale Ultraschalldiagnostik: OA Dr. Riemer
- Zentrum für Pränatale Medizin Halle: S. Riße, N. Manthey
- Labor Schenk/Ansorge, Genetikzentrum, Dr. Ababei, Fachärztin für Humangenetik, Magdeburg
- Dr. Blaschke, Fachärztin für Kinder- und Jugendmedizin, Magdeburg
- Dr. Karstedt, Facharzt für Kinder- und Jugendmedizin, Kinderkardiologie, Magdeburg
- Dr. Karsten, Facharzt für Frauenheilkunde und Geburtshilfe, Magdeburg
- Klinikum Magdeburg, Klinik für Frauenheilkunde und Geburtshilfe, Pränatale Ultraschalldiagnostik: OÄ Dr. Schleef
- Dr. Lüß, Facharzt für Kinder- und Jugendmedizin, Magdeburg
- Universitätsklinikum Magdeburg A.ö.R., Institut für Humangenetik
- Universitätsklinikum Magdeburg A.ö.R., Universitätsfrauenklinik, Pränatale Ultraschalldiagnostik: OÄ Dr. Gerloff
- Universitätsklinikum Magdeburg A.ö.R., Institut für Klinische Chemie, Screeninglabor
- Trackingstelle Neugeborenen-Hörscreening Sachsen-Anhalt, Magdeburg
- Dr. Welger, Fachärztin für Frauenheilkunde und Geburtshilfe, Magdeburg
- Dipl.-Med. Fiedler und Giesecke, Fachärzte für Orthopädie, Merseburg
- Altmark-Klinikum Krankenhaus Salzwedel, Klinik für Frauenheilkunde und Geburtshilfe, Pränatale Ultraschalldiagnostik: CA Dr. Müller
- Dr. Achtzehn, Dr. Adams, Fachärzte für Kinder- und Jugendmedizin, Wanzleben
- Harzklinikum Dorothea Christiane Erxleben Klinikum Wernigerode, Klinik für Gynäkologie und Geburtshilfe, Pränatale Ultraschalldiagnostik: OÄ Dr. Schulze

2.3 Pathological-anatomical institutes (ordered by location)

- Institut für Pathologie Dr. Bilkenroth, Dr. Irmscher, Dr. Lupatsch, Eisleben
- Universitätsklinikum Magdeburg A.ö.R., Institut für Pathologie

3 Malformation registration in Saxony-Anhalt

3.1 General information

The long-term regional recording of different congenital malformations makes it possible to recognize temporal accumulation or long-term trends of individual malformations. The presented data analysis of the birth cohort 2023, shows this on the basis of 37 exemplary selected congenital malformations.

At the beginning, we would therefore like to express our **thanks** for the continuation of interdisciplinary cooperation within the framework of the prospective recording of malformations, **to you as the sender**. We can only emphasize again and again that without this cooperation and participation in the project "Malformation Monitoring Saxony-Anhalt" of numerous colleagues from all healthcare professions the underlying database and thus the performed epidemiological analysis would not be possible.

In 2023, the birth rate decreased by 6.2 % compared to the previous year to 692,989 children across Germany (Federal Statistical Office). The number of births was at last below 700,000 children eleven years ago in 2013 (2013: 682 069). The decline was slightly lower than in 2022, with 7.1% fewer infants born compared to the previous year. Even though we are unfortunately seeing a further decline of the birth rate, this is reason enough to do everything to ensure that every child can grow up unharmed and can develop its full potential.

In this report we also include data for comparison from the European network of malformation registers (EUROCAT). EUROCAT can refer to data from 36 active malformation registries from 21 European countries. This monitoring, which records abortions after prenatal diagnosis as well as births and uses several sources as information input,

3.2 Registration and Analysis

Our present annual report contains data about children/fetuses with congenital malformations and chromosomal disorders of the Federal State of Saxony-Anhalt, whereby we refer to the place of residence of the mother during pregnancy respectively at the time of birth.

Basis of the annual prevalence calculations forms the total number of births, i.e. live and stillbirths, of Saxony-Anhalt. The prevalence of congenital malformations and anomalies as well as genetically caused diseases includes: live births, stillbirths, terminations of pregnancy (of all WOG) as well as spontaneous abortions from the 16th WOG.

The expected date of delivery is used as basis for analysing the termination of pregnancy, e.g. 2023 is considered the year of birth although some terminations of pregnancy after prenatal diagnostics took place at the end of 2022. 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 about live births and stillbirths is provided annually in mid-year by the Statistical Office Halle for the previous year. The shown percentages and prevalences are rounded values.

covers 29% of the European birth population. The Malformation Monitoring Centre Saxony-Anhalt has been working as a part of the EUROCAT network since 1992 (<https://eu-rdplatform.jrc.ec.europa.eu/eurocat>).

Also the, in the WHO associated organization, International Clearinghouse for Birth Defects Surveillance and Research (ICBDSR), which is an association of 42 birth defect registries from 38 countries around the world (www.icbdsr.com), the malformation monitoring program forms part since 1993. ICBDSR brings together malformation register from all over the world with the aim of investigating the occurrence of malformations and to reduce the impact of their consequences.

The comprehensive population-based recording of malformations in Saxony-Anhalt is only possible thanks to funding by the Ministry of Labor, Social Affairs, Health and Integration of the State of Saxony-Anhalt. Special thanks are extended to the head of the department Mrs. K. Müller. We are pleased and also thank for the good cooperation with Department 23 with Dr. med. A. Henze and Mr. M. Schiener.

We thank for the continued cooperation of the project "Congenital Malformation Monitoring" at the Medical Faculty of the Otto von Guericke University Magdeburg. We are pleased that the support under Prof. Dr. med. H.-J. Heinze, as Medical Director, Mr. M. Bohn, as Commercial Director could be continued in 2023. Our special thanks goes to the Dean Prof. Dr. rer. nat. D. C. Dieterich in particular for her support.

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 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 from 2011 to 2023. 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 2023 in comparison to the last 12 years (2011-2022). Here, **a total number of 202,461 births** forms basis for the **basis prevalence calculation 2011 to 2022**.

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 presented as well for the whole publishing time of the Annual Report (Chapter 10.38).

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 malformation monitoring receives information about newborns and fetuses from the maternity and pediatric clinics and from colleagues of pre and postnatal diagnostics (chapter 4.2). These are evaluated, coded and entered into the database of the malformation monitoring. Based on this data the annual report is compiled, scientific projects are processed and questions relating to malformations are resolved.

For the birth year 2023, the Malformation Monitoring Centre received 1,670 reports, 361 of those came from outpatient facilities. Reports were received for 23.9% of the children/fetuses from several senders. This increases the chance of reliably and to classify even rare or complex malformations which is an important prerequisite for high data quality. Since the publication of the last report, the number of data records of 2022 has increased from 1,600 to 1,636. All late registrations are included in the current report.

For the 2023 birth cohort, data of 1,304 children/fetuses was entered into the Malformation Monitoring database. Like the birth figures of Saxony-Anhalt, this number is also falling. Only 9.6% of the children and fetuses of Saxony-Anhalt in 2023 are recorded in the Malformation Monitoring database. This includes newborns and fetuses with congenital malformations and without malformations, which serve as a control group.

The informative value of the report depends to a large extent on the completeness and accuracy of the data. Important information is almost complete thanks to the excellent cooperation and the commitment of all contributors: Month of birth (100 %), country (99.5 %), gestational age (99.1 %), maternal age and gender (98.7 % each). However, in a total of 89 cases (14 times at live births) the birth weight which is important for the small for date- assessment was not specified. The indication of the head circumference for the assessment of microcephaly was missing in 23.4 % of the reported live births.

Every year, we ask all senders to inform us about every malformations, to indicate all accompanying malformations and to describe them as fully as possible. As unconfirmed findings are not included in the prevalence calculations or some clinics do not always think of malformation reporting, some malformations may appear more frequently than stated in the report.

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 basis 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 / or corresponding symptoms are important here.

Both documentation sheets are also available for download on our homepage www.angeborene-fehlbildung.com. It is possible to complete the sheet 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 some 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 2023

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

male	6,944 live births and stillbirths
female	6,655 live births and stillbirths
total	13,599 live births and stillbirths

Sex ratio m : f = 1.04

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

male	280 births
female	191 births
undetermined	1 birth
unknown	13 births
total	485 births

Sex ratio m : f = 1.47

Sex ratio of all births with only minor malformations and anomalies

male	114 births
female	115 births
total	229 births

Sex ratio m : f = 0.99

Since 2016, the number of live births in Saxony-Anhalt is declining. In the year 2023, 13,550 live births were recorded. 49 children were stillborn in 2023. The ratio of live births and stillbirths of the current year is slightly more in favor of live births than in the reporting period (2023: 276.5:1 vs. 2011-2022: 234.4:1).

For 2023, the sex ratio of all children is expected to be slightly in favor of boys (2023: m : f = 1.04; 2011-2022: m : f = 1.05). For stillbirths in 2023 with m : f = 1.72, a more boyish sex ratio can be seen than in the reporting period (2010-2021: m : f = 1.18).

Major malformations were detected in case of 485 children/fetuses in 2023, i.e. live births and stillbirths, medically induced abortions and spontaneous abortions from the 16th week of gestation. Their sex ratio shows a maximum androtropy for the reporting period (2011-2022) (2023: m : f = 1.47, minimum 2015: m : f = 1.17).

The sex ratio of the 229 children/fetuses reported in 2023 with only small malformations showed, as in 2022, a very slight gynecotropy (m : f = 0.99). During the reporting period, the gender ratio fluctuated only slightly between m : f = 0.88 (2017) and m : f = 1.38 (2014).

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

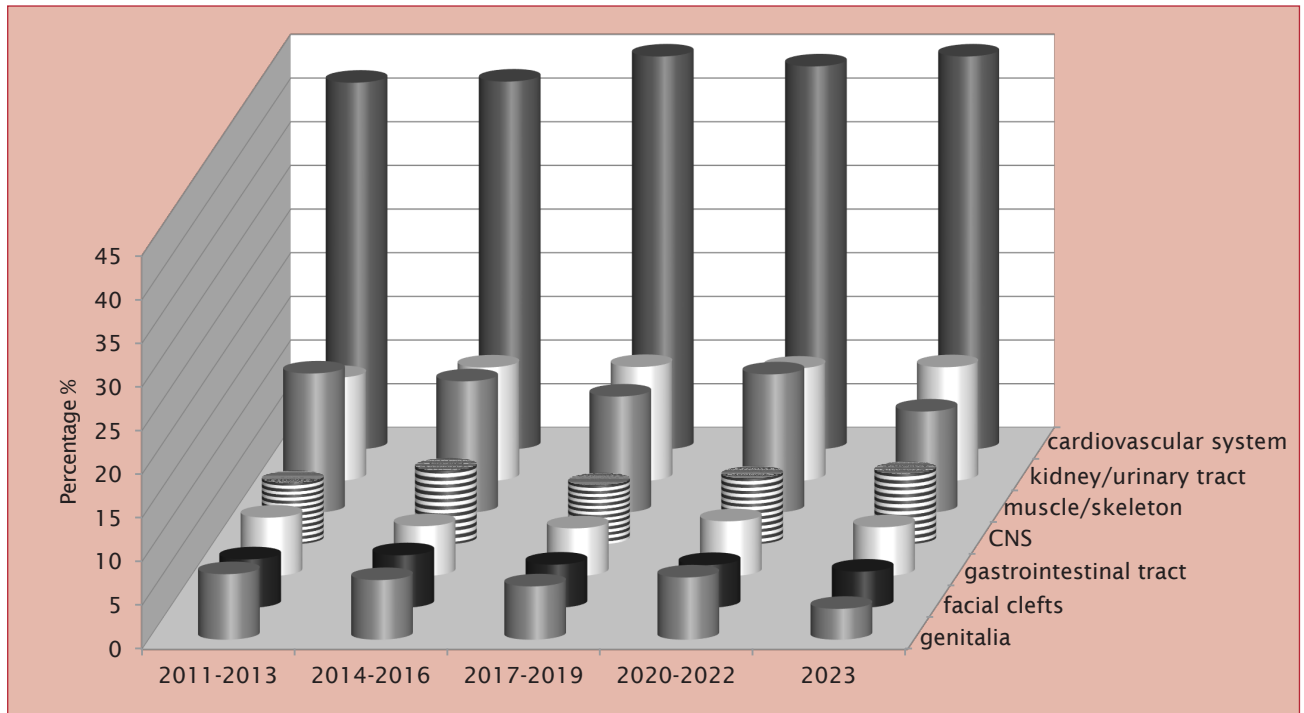


Fig. 5: Organ system involvement in major malformations (grouped)

The question which organ systems of children/fetuses are most affected by major malformations should be answered with the diagram shown above (Fig. 5). In four 3-year sections over the reporting period and separately for 2023, the incidence of malformations in seven of the most important organ systems is shown for all children/fetuses affected by major malformations (2011-2023: 7,846; 2023: 483) in Saxony-Anhalt.

Of the 485 children/fetuses born in 2023 with major malformations, multiple malformations were detected in 200 children/fetuses (41.2%). The percentage was 42.0% on average for the years 2011-2022. These children/fetuses with major malformations in more than one of the organ systems shown are included several times in the diagram.

The majority of malformations concern the cardiovascular system. In the reporting period 2011-2022: 48.3% of all children/fetuses with major malformations suffered from a cardiac malformation. In the current year, the share is significantly higher (2023: 47.6%).

Between 2011 and 2022, severe malformations of the musculoskeletal system were the second most common malformation (2011-2022: 14.6%). In the current year (2023), however, there was a significantly lower proportion (11.6%) of children/fetuses with a malformation of the musculoskeletal system. This proportion is still below the previous year's minimum proportion (2021: 12.4%).

Malformations of the kidneys and urinary tract are currently the second most common, with a proportion of 13.0% (2023) in the upper normal range of the proportion of children/fetuses with major malformations (2011-2022: 12.8%). At the beginning of the reporting period, large

fluctuations in the proportions (between 9.4% and 15.7%) were recorded.

The proportion of children/fetuses with malformations of the CNS (8.7%) lies in 2023 well above the average proportion of the years 2011-2022 (7.6%). Around 40% of CNS malformations are neural tube defects (2011-2022: 8.6 per 10,000 children/fetuses), which were observed significantly more frequently in 2023 (12.5 per 10,000 births) than during the whole reporting period (Chapter 10.1).

In 2023, 5.6% of children/fetuses with major malformations had malformations of the intestinal tract. The proportion corresponds to the normal percentage of children/fetuses with malformations of the digestive tract during the period of 2011-2022 (5.8%).

A facial cleft was observed in 4.1% of all children/fetuses with major malformations in 2023. This proportion is significantly lower than the average of the years 2011-2022 (5.2% of all children/fetuses with major malformations). Facial clefts include two indicator malformations, cleft lip with cleft palate (2023: 8.8 per 10,000 births) and cleft palate (2023: 4.4 per 10,000 births), both of which were registered very rarely in 2023 (Chapter 10.14, 10.15).

The proportion of children/fetuses with severe malformations of the genital system among children/fetuses with major malformations is also significantly lower in 2023 (3.5%) than expected (2011-2022: 6.6%). The current proportion represents a new minimum value of the reporting period. In 2011 and 2012, it was still over 7% and has been falling since then.

Most frequent single diagnosis 2023 (only major malformations)

	ICD-10	Diagnosis	Children/Fetuses 2023*		Children/Fetuses 2011-2022**	
			Number	Prevalence /10,000	Prevalence /10,000	Confidence interval (CI 95%)
1.	Q21.1	Atrial septal defect (without PFO)	135	99.3	105.6	101.2 - 110.2
2.	Q21.0	Ventricular septal defect	62	45.6	48.0	45.0 - 51.1
3.	Q90.	Down's syndrome (trisomy 21)	28	20.6	20.8	18.9 - 22.9
4.	Q62.3	Dilated uropathy grade II-IV/ureterocele	22	16.2	25.1	23.0 - 27.4
5.	H90.	Conductive and sensorineural hearing loss	21	15.4	24.8	22.7 - 27.1
	Q63.0	Accessory kidney / duplex kidney	21	15.4	8.2	7.0 - 9.6
6.	Q66.0	Pes equinovarus congenitus (clubfoot)	18	13.2	14.0	12.4 - 15.8
7.	Q54.	Hypospadias	15	11.0	22.6	20.6 - 24.8
8.	Q62.2	Megaureter	12	8.8	9.3	8.0 - 10.7
	Q21.2	Atrial and ventricular septum defect (AVSD/ASD I)	12	8.8	4.8	3.9 - 5.9
9.	Q25.1	Aortic valve stenosis	10	7.4	5.9	4.9 - 7.0
	Q79.2	Omphalocele	10	7.4	3.6	2.8 - 4.5
10.	Q69.	Polydactyly (pre- and postaxial)	9	6.6	11.6	10.2 - 13.2
	Q60.0	Renal agenesis, unilateral	9	6.6	5.5	4.5 - 6.6
	Q91.0-3	Edwards-syndrome (trisomy 18)	9	6.6	4.3	3.5 - 5.4
	Q20.3	Discordant ventriculoarterial connection (incl. complete TGA)	9	6.6	3.8	3.0 - 4.8
11.	Q37.	Cleft lip with cleft upper jaw and palate	8	5.9	9.9	8.6 - 11.3
	Q05.	Spina bifida	8	5.9	4.9	4.0 - 6.0
12.	Q61.4	Renal dysplasia	7	5.1	6.2	5.1 - 7.4
	Q25.4	Right-sided aortic arch	7	5.1	3.8	3.0 - 4.8
13.	Q65.3-5	Subluxation of the hip joint (unilateral/bilateral/w.o. Sidedness)	6	4.4	7.4	6.2 - 8.6
	Q25.0	Patent ductus botalli (PDA), hemodynamically effective	6	4.4	9.2	7.9 - 10.6
	Q02.	Micocephaly	6	4.4	4.3	3.5 - 5.4
	E03.	Hypothyroidism	6	4.4	2.3	1.7 - 3.1
	Q25.6	Stenosis of the pulmonary artery (peripheral pulmonary stenosis)	6	4.4	3.3	2.5 - 4.1
	Q23.0	Aortic valve stenosis/atresia	6	4.4	2.9	2.2 - 3.8
14.	Q22.1	Pulmonary valve stenosis	5	3.7	7.0	5.9 - 8.2
	Q35.	Gaumenspalte	5	3,7	4,6	3,8 - 5,7
	Q79.3	Gastroschisis	5	3,7	3,5	2,7 - 4,4
	Q00.	Anencephalie	5	3,7	2,5	1,9 - 3,3

* in reference to 13,599 births

** in reference to 202,461 births

The table above presents the most frequently observed major individual malformations in Saxony-Anhalt in 2023. Listed in order of frequency in 2023 are 30 major individual malformations. For each malformation, the number of affected children/fetuses in the year of birth 2023 and the associated current annual prevalence based on 13,599 births is shown, as well as the basis prevalence for the years 2011-2022 (population: 202,461 births) as a comparative figure.

By far the most common malformation detected in children/fetuses is regularly the atrial septal defect. It was diagnosed in the current year (2023) with a prevalence of 99.3 per 10,000 births, slightly less than normal (2011-2022: 105.6 per 10,000 births). During the reporting period, prevalence fluctuated between a minimum (2012) of 84.4 and a maximum (2017) of 133.9 per 10,000 births. Another cardiac malformation, ventricular septal defect, occurs about half as often, in one out of 209 children/fetuses. The current prevalence (2023: 45.6 per 10,000 births) lies at the usual level (2011-2022: 48.0 per 10,000 births).

In third to fifth place for years, although not always in the same order, are three very different major malformations. Down syndrome is calculated to have an unremarkable prevalence in the tolerance range of 2023 (20.6 per 10,000 births). Dilated uropathy II.-IV. degree/ureterocele (2023: 16.2 per 10,000 births; 2011-2022: 25.1 per 10,000 births) and congenital hearing disorders (2023: 15.4 per 10,000 births; 2011-2022: 24.8 per 10,000 births) occur often more common than Down syndrome. They were detected significantly less frequently than during the reporting period.

With an annual prevalence well above the normal level and not always included in the frequency list, accessory kidneys were detected this year (2023: 15.4 per 10,000 births; 2011-2022: 8.2 per 10,000 births). The prevalence has never been this high since the early 2000s.

The prevalence of clubfeet (2023: 13.2 per 10,000 births) is usually ranked sixth, in the middle of the basis prevalence range.

Hypospadias (2023: 11.0 per 10,000 births; 2023: 22.6 per 10,000 births) follows in seventh place, with an exceptionally low annual prevalence and a minimum value in the reporting period.

There was an annual prevalence of 8.8 per 10,000 births for two malformations in 2023. While the prevalence of megaureter corresponds to the usual occurrence, the annual prevalence of the defects of atrial and ventricular septum is above the upper limit of the confidence interval of the basis prevalence (2011-2022: 4.8 per 10,000 births).

In ninth place and significantly more than expected, two indicator malformations were registered in 2023 with an annual prevalence of 7.4 per 10,000 births, which are aortic isthmus stenosis (2011-2022: 5.9 per 10,000 births) and omphalocele (2011-2022: 3.6 per 10,000 births) (Chapter 10.13, 10.30).

Four malformations will rank in 2023 with a prevalence of 6.6 per 10,000 births in tenth place. This means that

the prevalence of polydactyly is currently even lower than in the previous year, far below the tolerance range of the basis prevalence (2011-2022: 11.6 per 10,000 births). Depending on the localization, it is classified as preaxial polydactyly (2023: 2.9 per 10,000 births; 2011-2022: 3.0 per 10,000 births; Chapter 10.27) and postaxial polydactyly (2023: 3.7 per 10,000 births; 2011-2022: 9.1 per 10,000 births). The preaxial form was seen within a normal range in 2023, postaxial polydactyly was seen significantly less frequently. The three malformations, unilateral renal agenesis (2011-2022: 5.5 per 10,000 births), Edwards' syndrome (2011-2022: 4.3 per 10,000 births) and d-TGA (2011-2022: 3.8 per 10,000 births), which all occurred in 2023 more frequently than in the previous year and far more frequently than usual, are only rarely seen in one of the top ten places on the frequency list of individual malformations.

In the current year, spina bifida (2023: 5.9 per 10,000 births) occurred in the usual frequency, with a prevalence just below the upper confidence limit of the basis prevalence. With the same annual prevalence, cleft lip and palate was again slightly more common than in the previous year (minimum since 2000: 4.8 per 10,000 births), but at the same time the prevalence lies also in the current year well below the confidence interval of the basis prevalence (2011-2022: 9.9 per 10,000 births). As cleft lip and palate is part of the indicator malformation cleft lip with cleft lip and palate (Chapter 10.14), this is also reflected in the prevalence development of cleft lip and cleft lip with cleft palate.

The annual prevalence of renal dysplasia in 2023 was determined 5.1 per 10,000 births, which is just still within the confidence interval at the lower limit. With the same value, the annual prevalence of the right aortic arch exceeds significantly the normal range (2011-2022: 3.8 per 10,000 births).

An annual prevalence (2023) of 4.4 per 10,000 births was calculated for six malformations. Subluxation of the hip joint (2011-2022: 7.4 per 10,000 births) and PDA (2011-2022: 9.2 per 10,000 births) occurred in lower numbers than expected in 2023. For microcephaly, the prevalence of 2023 is equal to the basis prevalence. Hypothyroidism (2011-2022: 2.3 per 10,000 births), stenosis of the pulmonary artery (2011-2022: 3.3 per 10,000 births) and aortic valve stenosis/atresia (2011-2022: 2.9 per 10,000 births) stood out in 2023 with unusually high prevalence rates. They are among the rare malformations which are diagnosed less than 5 times per 10,000 children/fetuses and which are usually not listed in the table of the most common individual malformations.

With a prevalence of 3.7 per 10,000 births (2023) four malformations complete this year's list. Pulmonary valve stenosis (2011-2022: 7.0 per 10,000 births) and cleft palate (2011-2022: 4.6 per 10,000 births) are otherwise a little higher up in the frequency list, but their prevalence in 2023 is expected to be significantly below the respective basis prevalence. Gastroschisis is found in the usual number. Significantly more frequently than normal (2011-2022: 2.5 per 10,000 births), anencephaly (Chapter 10.2) was seen in 2023. However, the maximum value in the reporting period (2014: 4.7 per 10,000 births) was not reached.

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. Synonyms: Spina bifida, anencephaly, NTD

2. Anencephaly:

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

3. Spina bifida:

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

4. Encephalocele:

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

5. Microcephaly:

is characterized by a too small occipito frontal skull circumference (two standard deviations below the norm, www.intergrowth21.ndog.ox.ac.uk according to Villar et al. Lancet 2014, chapter 10.5), relative to the gestational age- and sex-dependent normal distribution. Exclusive microcephaly associated with a neural tube defect.

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 prenatally or at birth. Not counted when present with a neural tube defect. Exclusive macrocephaly without dilatation of ventricular system, skull of macerated fetus, hydranencephaly, 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. Not counted when present

with a neural tube defect.

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 / Pentalogy:

a condition characterized by ventricular septal defect, overriding aorta, infundibular pulmonary stenosis, and often right ventricular hypertrophy. Included is Fallot pentalogy, which has an additional ASD.

11. Transposition of great vessels (TGV):

a cardiac defect where the aorta exits from the right ventricle and the pulmonary artery from the left ventricle, with or without other cardiac defects. Inclusive double outlet ventricle so called corrected transposition.

12. Hypoplastic left heart syndrome:

a complex 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). In addition, cleft lip and cleft lip and palate are excluded in arhin- and holoprosencephaly, respectively.

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. In addition, cleft palate is excluded in arhin- or holoprosencephaly.

16. Choanal atresia, bilateral:

congenital obstruction (membranous or osseous) of the posterior choana or choanae. Excludes choanal stenosis that does not require therapy.

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. In cases with an omphalocele or gastroschisis small intestine atresia/stenosis is excluded.

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. Inclusive penile, scrotal, and perineal hypospadias. Exclusive 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. Inclusive 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 and Roberts syndrome. 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 hypoplasia of abdominal muscles, skin covered 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. Excluded are aplasia or hypoplasia of the abdominal muscles, skin-enclosed umbilical hernia, and the 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 materials. 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 known as Ullrich-Turner syndrome or monosomy X, is caused by the partial or complete absence of one of the two X chromosomes in a girl (gonosomal monosomy). A mosaic or a gonosomal abnormality is possible.

37. Klinefelter syndrome/male gonosome abnormalities:

Klinefelter syndrome is caused by two or more X chromosomes in a male phenotype (Karyotype 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 basis prevalences (2011 to 2022) is based on a total number of 202,461 births.

The analysis of indicator malformations is made in reference 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 2011-2022 of the 36 Full-Member-Register of European Surveillance of Congenital Anomalies (EUROCAT) from 21 different European countries. The calculation of the EUROCAT prevalences is based on a total number of 8,264,784 births, which are indicated for the same reason with a range of 20,000 births. (Source: https://eu-rd-platform.jrc.ec.europa.eu/eurocat/eurocat-data/prevalence_en).

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

Saxony-Anhalt	Year of 2023		
	Number	Prevalence/ 10,000 births	Comparison to basis prevalence
	17	12.50	↑
EUROCAT (full members)	Reporting period 2011-2022		
	Basis prevalence/ 10,000 births	Confidence interval (CI 95 %)	
	8.64	7.41 - 10.02	
EUROCAT (full members)	Period 2011-2022		
	Prevalence/ 10,000 births	Confidence interval (CI 95 %)	
	10.4	10.2 - 10.7	

With 17 children/fetuses with neural tube defects and the therefore resulting third-highest **annual prevalence** in the reporting period (2023: **12.5 per 10,000 births**; maximum 2014: 14.6 per 10,000 births) the current annual prevalence exceeds the basis prevalence of Saxony-Anhalt (2011-2022: 8.6 per 10,000 births) significantly. Between 2014 and 2021, the prevalences decreased, but in 2022 and 2023 an increase can be observed. The trend analysis (Chapter 10.38) therefore shows a significantly non-linear proportion and the development of the prevalence of the indicator malformation (2010-2023) is classified as a non-linear change.

The three neural closure disorders anencephaly, spina bifida and encephalocele together form the group of neural tube defects. In chapters 10.2 to 10.4 these are assessed individually. Most children/fetuses with a neural tube defect are usually affected by spina bifida (2011-2022: 57.1% of neural tube defects). The significantly high prevalence value for neural tube defects in 2023 results from the relatively high number of children/fetuses with an encephalocele (4) or anencephaly (5), as the number of children/fetuses with spina bifida (8) in 2023 corresponded to a normal value.

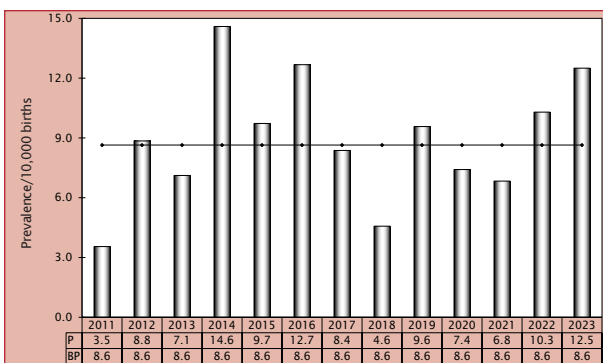


Fig. 6: Development of prevalence/10,000 births with neural tube defects in Saxony-Anhalt since 2011

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.

EUROCAT gives an overall prevalence for neural tube defects of 10.4 per 10,000 births (2011-2022). The prevalence interval of the basis prevalence of Saxony-Anhalt is just below the overall prevalence of the European malformation registers, however, this year's prevalence of Saxony-Anhalt is far above it.

additional information:

Pregnancy outcome	5 x live births 12 x termination of pregnancy
Sex	6 x male 7 x female 4 x no indication
Number of isolated malformations/MCA	10 x MCA 7 x isolated

Five children with neural tube defects were live births in 2023. Twelve times the pregnancy was terminated prematurely (2023: 70.6%; 2011-2022: 72.0% of children/fetuses with neural tube defects).

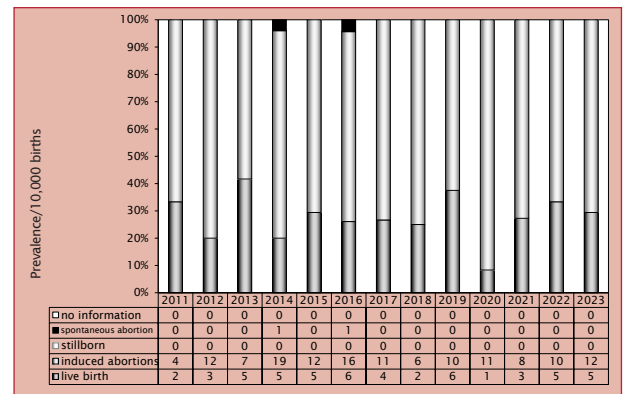


Fig. 7: Pregnancy outcomes of neural tube defects in Saxony-Anhalt since 2011

In 2023, one neural tube defect per 800 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*.

* Literature
Wegner C, Kancherla V, Lux A, Köhn A, Bretschneider D, Freese K, Heiduk M, Redlich A, Schleaf 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.)

Saxony-Anhalt	Year of 2023		
	Number	Prevalence/10,000 births	Comparison to basis prevalence
	5	3.68	↗
	Reporting period 2011-2022		
Basis prevalence/10,000 births		Confidence interval (CI 95 %)	
2.52		1.88 - 3.31	
EUROCAT (Full members)	Period 2011-2022		
	Prevalence/10,000 births	Confidence interval (CI 95 %)	
	4.2	4,1 - 4.4	

With five affected fetuses, the current **annual prevalence** (2023: **3.7 per 10,000 births**) for the indicator malformation anencephaly is slightly above the confidence interval of the basis prevalence of Saxony-Anhalt (2011-2022: 2.5 per 10,000 births). After three years with low prevalences at the beginning of the reporting period, we determined four times (2014, 2016, 2021, 2023) an annual prevalence above the upper confidence limit. The trend analysis in the last annual report for the period 2009-2022 showed a significant upward trend for anencephaly. The linear correlation of the period from 2010-2023 ($p = 0.0565$) is no longer detectable (Chapter 10.38).

Compared to the prevalence of the EUROCAT registers (2011-2022: 4.2 per 10,000 births), the Saxony-Anhalt basis prevalence for neural tube defects is considerably lower. The current annual prevalence (2023) of Saxony-Anhalt is also well below the European standard range.

additional information:

Pregnancy outcome	5 x termination of pregnancy
Sex	2 x male 3 x no indication
Number of isolated malformations/MCA	2 x MCA 3 x isolated

In four fetuses, the anencephaly or non-closure of the anterior neuroporus was detected between the 11th and 13th week of gestation during prenatal ultrasound screening.

Anencephaly was only discovered at an advanced stage of pregnancy, in the 21st week of pregnancy.

occured malformation combinations (MCA) or super-ordinate syndromes:

- Edwards' syndrome with: Omphalocele
- facial cleft

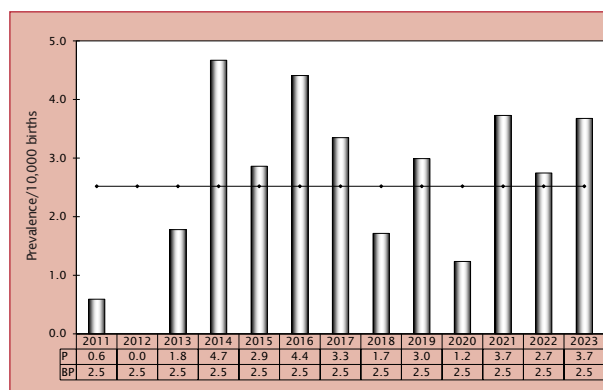


Fig. 8: Development of prevalence/10,000 births with anencephaly in Saxony-Anhalt since 2011

In 2023, one child/fetus with anencephaly was observed per 2,720 births in Saxony-Anhalt.

10.3 Spina bifida (Q05.)

Saxony-Anhalt	Year of 2023		
	Number	Prevalence/ 10,000 births	Comparison to basis prevalence
	8	5.88	↔
EUROCAT (full members)	Reporting period 2011-2022		
	Basis prevalence/ 10,000 births	Confidence interval (CI 95 %)	
	4.94	4.02 - 6.01	
EUROCAT (full members)	Period 2011-2022		
	Prevalence/ 10,000 births	Confidence interval (CI 95 %)	
	5.0	4.8 - 5.2	

In 2023, spina bifida was observed in eight children/fetuses in Saxony-Anhalt. The resulting **annual prevalence** (2023: **5.9 per 10,000 births**) lies within the confidence interval of the basis prevalence of Saxony-Anhalt (2011-2022: 4.9 per 10,000 births), just below the upper limit.

The basis prevalence of Saxony-Anhalt is close to the prevalence stated by EUROCAT for the years 2011-2022 (5.0 per 10,000 births), but due to the smaller population included, it has a much greater fluctuation range than the confidence interval of the European prevalence.

additional information::

Pregnancy outcome	3 x live births 5 x termination of pregnancy
Sex	3 x male 4 x female 1 x no indication
Number of isolated malformations/MCA	5 x MCA 3 x isolated

Most of the spina bifida cases were already seen prenatally. In case of one child, a spina bifida was discovered after an uncomplicated pregnancy after birth and in case of another child there is no information about prenatal examinations and the severity of the spina bifida. During the course of pregnancy, a hydrocephaly developed seven times. In five cases the pregnancy was terminated, one of these fetuses was affected by a thoracolumbar, three by a lumbosacral spina bifida, and one by a sacral spina bifida. Two children had lumbosacral spina bifida. In one case, a recent infection of the pregnant woman with *Toxoplasma gondii* in the first trimester can be assumed as the cause.

The proportion of live births with spina bifida falls insignificantly over the years of the reporting period. Their proportion corresponds in the year 2023 (38.0%) to the

average proportion of the years 2011-2022 (38,0 %). Stillbirths and spontaneous abortions did not occur during the entire period (2011-2023). Between 2011 and 2022, 62.0% of pregnancies of fetuses with spina bifida were terminated.

Malformation combinations (MCA) or superordinated syndromes detected:

- Omphalocele
- Pachygyria, syringomyelia, plexus cyst
- Scoliosis caused by bone malformations
- Knee joint dislocation, sickle foot on the right
- Toxoplasmosis

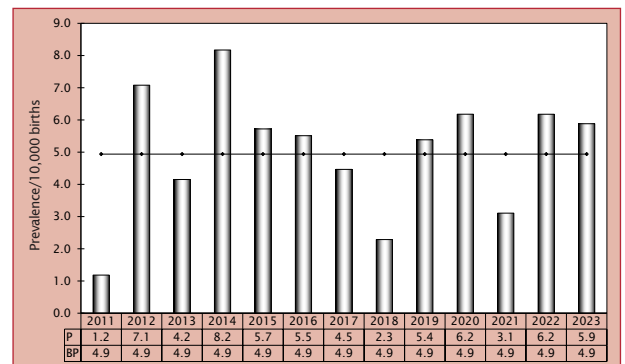


Fig. 9: Development of prevalence/10,000 births with spina bifida in Saxony-Anhalt since 2011

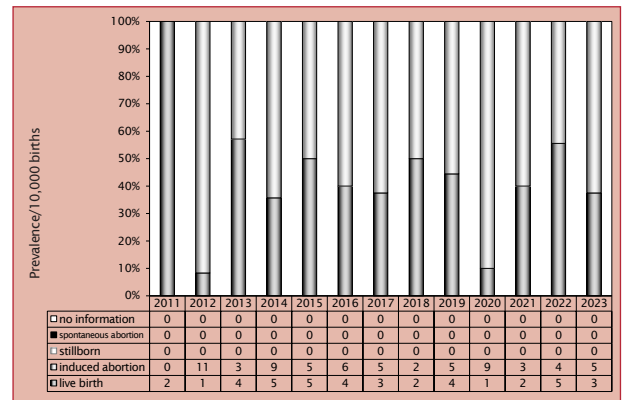


Fig. 10: Pregnancy outcomes of spina bifida in Saxony-Anhalt since 2011

In 2023, one child/fetus with spina bifida was observed per 1,700 births in Saxony-Anhalt.

10.4 Encephalocele (Q01.)

Saxony-Anhalt	Year of 2023		
	Number	Prevalence/10,000 births	Comparison to basis prevalence
	4	2.94	↑
	Reporting period 2011-2022		
Basis prevalence/10,000 births		Confidence interval (CI 95 %)	
1.19		0.76 - 1.76	
EUROCAT (Full members)	Period 2011-2022		
	Prevalence/10,000 births	Confidence interval (CI 95 %)	
	1.2	1.1 - 1.3	

For the year of birth 2023, four children/fetuses with encephalocele were registered. The **annual prevalence of 2.9 per 10,000 births** exceeds the previous highest value in the reporting period (2016: 2.8 per 10,000 births). This year's prevalence is considerably above the basis prevalence of Saxony-Anhalt (2011-2022: 1.2 per 10,000 births). However, the malformation is not seen in Saxony-Anhalt every year (2020, 2021). Due to the small numbers, the prevalences fluctuate strongly.

EUROCAT also shows an overall prevalence for the indicator malformation encephalocele of 1.2 per 10,000 births (2011-2022). The prevalence interval of the basis prevalence of Saxony-Anhalt is wider and spans that of the European malformation register due to the smaller numbers, but the value of prevalences is at the same level.

All encephaloceles were diagnosed prenatally, two occipital encephaloceles and one meningocele between the 19th and 22nd week of gestation and one nasofrontal encephalocele already at the 13th week of gestation.

additional information:

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

Malformation combinations (MCA) or superordinated syndromes detected:

- Edwards' syndrome with: Omphalocele
- facial cleft and left palpebral fissure anomaly, cranio-facial dysmorphism
- neuronal heterotype on the left

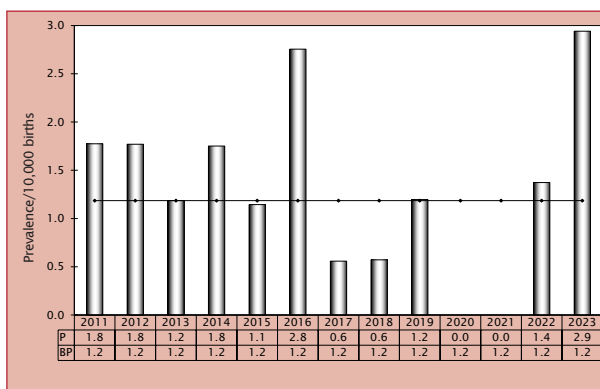


Fig. 11: Development of prevalence/10,000 births with encephalocele in Saxony-Anhalt since 2011

In 2023, one child/fetus with encephalocele was observed per 3,400 births in Saxony-Anhalt.

10.5 Microcephaly (Q02.)

Saxony-Anhalt	Year of 2023		
	Number	Prevalence/ 10,000 births	Comparison to basis prevalence
	6	4.41	↔
	Reporting period 2011-2022		
Basis prevalence/ 10,000 births		Confidence interval (CI 95 %)	
4.35		3.49 - 5.35	
EUROCAT (full members)	Period 2011-2022		
	Prevalence/ 10,000 births	Confidence interval (CI 95 %)	
	2.6	2.5 - 2.7	

In the 2023 birth cohort of Saxony-Anhalt, six children were registered with microcephaly. This year's **prevalence of 4.4 per 10,000 births** (2023) is inconspicuous within the range of the basis prevalence of Saxony-Anhalt (2011-2022: 4.3 per 10,000 births).

Taking into account gestational age and gender, three children were found to have head circumferences that deviated from normal by more than -2 SD. Microcephaly is often only detected in the course of the first year of life with the non-development of the brain and skull, as it was seen in case of three other children of the 2023 birth cohort. One child was also affected by complex malformations in several organ systems and another child was affected by pontocerebellar hypoplasia. The diagnosis of microcephaly is checked by the monitoring of congenital malformations using the international data provided by the INTERGROWTH 21st project study with the internationally percentile curves.

EUROCAT estimates the prevalence of microcephaly in Europe at a prevalence of 2.6 per 10,000 births (2011-2022). The confidence interval of the basis prevalence, as well as this year's value of the Saxony-Anhalt prevalence, are located above the confidence interval of the overall prevalence of the European register.

additional information:

Pregnancy outcome	6 x live births
Sex	3 x male 3 x female
Number of isolated malformations /MCA	3 x MCA 3 x isolated

Malformation combinations (MCA) or superordinated syndromes detected:

- HLHS, aortic isthmus stenosis, large bowel atresia, low-set ears
- Pontocerebellar hypoplasia type 1, peripheral cysts in the left cerebellum, craniofacial dysmorphism, blt. dysplastic ears, sickle foot on the right
- Pulmonary stenosis, PFO at full-term infant

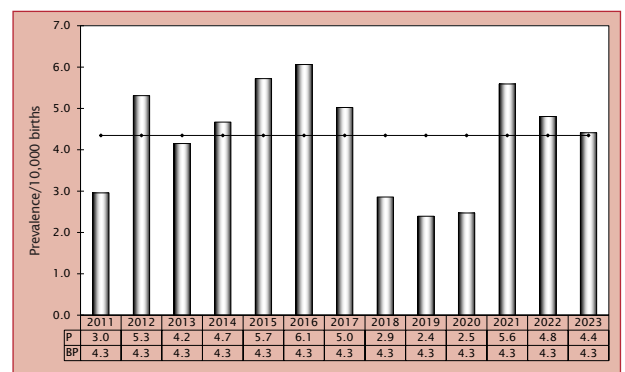


Fig. 12: Development of prevalence/10,000 births with microcephaly in Saxony-Anhalt in 2011

In 2023, one child/fetus with microcephaly was observed per 2,267 births in Saxony-Anhalt.

10.6 Congenital Hydrocephaly (Q03.)

Saxony-Anhalt	Year of 2023		
	Number	Prevalence/10,000 births	Comparison to basis prevalence
	3	2.21	↓
	Reporting period 2011-2022		
Basis prevalence/10,000 births		Confidence interval (CI 95 %)	
5.83		4.83 - 6.98	
EUROCAT (Full members)	Period 2011-2022		
	Prevalence/10,000 births	Confidence interval (CI 95 %)	
	5.1	4.9 - 5.2	

In the case of the indicator malformation hydrocephaly, only congenital hydrocephalies are considered, which have not developed in connection with a neural tube defect such as encephalocele (chapter 10.4).

Since the 1990s, the annual prevalence of congenital hydrocephaly was not as low as the **annual prevalence** of the current year with only three concerned children/fetuses (2023: **2.2 per 10,000 births**). This minimum value lies significantly below the normal range of the basis prevalence of Saxony-Anhalt (2011-2022: 5.8 per 10,000 births). In the reporting period, the prevalence reached its maximum value in 2017 (8.4 per 10,000 births) and has been falling since then.

When comparing the prevalences of Saxony-Anhalt with the European prevalence provided by EUROCAT (2011-2022: 5.1 per 10,000 births), this year's prevalence is far below, but both confidence intervals of the prevalences for the period of 2011-2022 have approximately the same level. The confidence interval of the basis prevalence of Saxony-Anhalt, however, spans a larger confidence interval due to smaller numbers.

additional information:

Pregnancy outcome	2 x live births 1 x termination of pregnancy
Sex	3 x male
Number of isolated malformations /MCA	2 x MCA 1 x isolated

One hydrocephaly was discovered prenatally as a concomitant malformation of Edwards' syndrome. This pregnancy was terminated prematurely.

Malformation combinations (MCA) or superordinated syndromes detected:

- Edwards' syndrome with: AVSD, blt. overlapping fingers
- Graves' disease, vitreous opacity of the right eye , DUP II. degree right and I. degree left, cholestasis

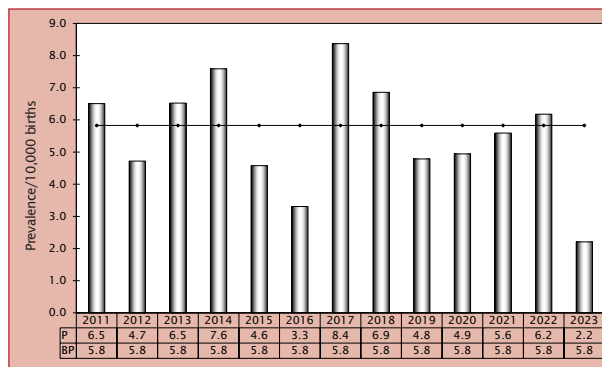


Fig. 13: Development of prevalence/10,000 births with congenital hydrocephalus in Saxony-Anhalt since 2011

In 2023, one child/fetus with congenital hydrocephalus was observed per 4,533 births in Saxony-Anhalt.

10.7 Arhinencephaly/Holoprosencephaly (Q04.1/Q04.2/Q87.3)

Saxony-Anhalt	Year of 2023		
	Number	Prevalence/10,000 births	Comparison to basis prevalence
	2	1.47	↔
	Reporting period 2011-2022		
Basis prevalence/10,000 births		Confidence interval (CI 95 %)	
1.48		1.00 - 2.12	
EUROCAT (full members)	Period 2011-2022		
	Prevalence/10,000 births	Confidence interval (CI 95 %)	
	1.7	1.6 - 1.8	

With two affected births in Saxony-Anhalt in 2023 by arhinencephaly/holoprosencephaly, this year's prevalence (2023: 1,5 per 10,000 births) corresponds to the basis prevalence (2011-2022: 1.5 per 10,000 births) of the not very common malformation. It was registered only 30 times in total during the years of the reporting period. Except in the years 2016 (3.9 per 10,000 births) and 2021 (3.7 per 10,000 births), there were always values within or below the confidence interval of the basis prevalence.

The confidence interval of the basis prevalence of Saxony-Anhalt is at a slightly lower level than the overall prevalence of the European malformation registers (2011-2022: 1.7 per 10,000 births). However, this is completely covered by the wider Saxony-Anhalt confidence interval. The Saxony-Anhalt annual prevalence for 2023 lies also within the range of the European average prevalence.

additional information:

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

In both cases of affected fetuses by holoprosencephaly, this was discovered during prenatal ultrasound screening, one time at the end of the first trimester and another time at the beginning of the second trimester. During the entire reporting period the two extremely rare malformations that count as indicator malformations arhinencephaly (2016) and cyclopia (2019) were only observed once each.

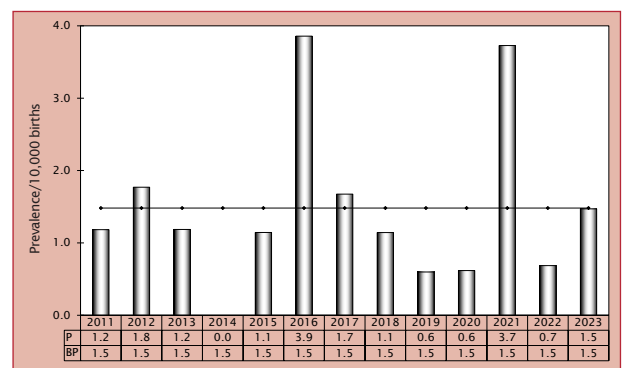


Fig. 14: Development of prevalence/10,000 births with arhinencephaly/holoprosencephaly in Saxony-Anhalt since 2011

In 2023, one arhinencephaly/holoprosencephaly per 6,800 births was registered in Saxony-Anhalt.

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

Saxony-Anhalt	Year of 2023		
	Number	Prevalence/10,000 births	Comparison to basis prevalence
	1	0.74	↔
	Reporting period 2011-2022		
Basis prevalence/10,000 births		Confidence interval (CI 95 %)	
0.99		0.60 - 1.53	
EUROCAT (Full members)	Period 2011-2022		
	Prevalence/10,000 births	Confidence interval (CI 95 %)	
0.9		0.9 - 1.0	

The indicator malformation anophthalmia/microphthalmia is one of the very rare malformations in Saxony-Anhalt with a basis prevalence of 1.0 per 10,000 births (2011-2022). With a total of 13,599 births in 2023 only one, maximum two cases were expected. After an unusually high prevalence in the last two years (2021: 1.9; 2022: 2.1 per 10,000 births), the **prevalence** of the current year lies with one affected fetus by anophthalmia/microphthalmia (2023: **0.7 per 10,000 births**) within the normal range.

The confidence interval of the basis prevalence of Saxony-Anhalt covers with clearly wider limits the confidence interval of the European prevalence which is indicated by EUROCAT (2011-2022: 0.9 per 10,000 births). Both prevalences are similarly high over the reporting period. The current annual prevalence of Saxony-Anhalt is estimated to be low, compared to that of EUROCAT.

additional information:

Pregnancy outcome	1 x live births
Sex	1 x female
Number of isolated malformations /MCA	1 x isolated

The child, who was born after an unremarkable pregnancy, suffered from agenesis of both eyes. No other malformations or chromosomal disorders were described.

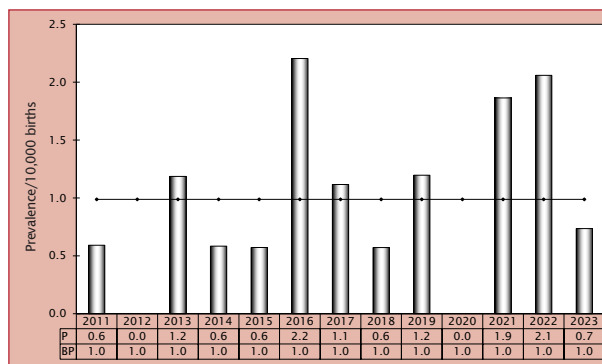


Fig. 15: Development of prevalence/10,000 births with anophthalmos/microphthalmos in Saxony-Anhalt since 2011

In 2023, one child/fetus with anophthalmia/microphthalmia was observed per 13,599 births in Saxony-Anhalt.

10.9 Microtie/Anotie (Q16.0/Q17.2)

Saxony-Anhalt	Year of 2023		
	Number	Prevalence/ 10,000 births	Comparison to basis prevalence
	6	4.41	↑
Reporting period 2011-2022			
Basis prevalence/ 10,000 births		Confidence interval (CI 95 %)	
2.82		2.13 - 3.65	
EUROCAT (full members)	Period 2011-2022		
	Prevalence/ 10,000 births	Confidence interval (CI 95 %)	
	not specified	not specified	

In 2023, the indicator malformation microtia/anotia occurred six times in Saxony-Anhalt. The calculated **prevalence of 4.4 per 10,000 births** lies significantly above the confidence interval of the basis prevalence (2011-2022: 2.8 per 10,000 births). Over the reporting period the prevalence of the indicator malformation microtia/anotia varied between a minimum of 0.6 per 10,000 births (2012) and a maximum of 6.1 per 10,000 births (2017).

European comparative values for the prevalence of the indicator malformation microtia/anotia are not available from EUROCAT. For grade IV auricular dysplasia (anotia) or atresia/stricture of the bony auditory canal EUROCAT determines a prevalence of 0.81 per 10,000 births (2011-2022; CI 0.75-0.88). When considering Saxony-Anhalt, a basis prevalence of 0.59 per 10,000 births (2011-2022; CI 0.30-1.04) can be determined.

additional information:

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

In 2023, no anotia was registered in Saxony-Anhalt. In case of two children bilateral dysplastic ears of grade II to III were observed. Two times, only the left and two times only the right ear was affected. In case of three children the microtia was combined with an atresia of the bony auditory canal and a sound conduction disturbance, once bilateral and in case of the two other children with a sound conduction disorder also on the side which was affected by microtia.

Malformation combinations (MCA) or superordinated syndromes detected:

- Epispadias, ventricular asymmetry on the left, blt. brachydactyly and clinodactyly of the 5th finger
- Treacher-Collins syndrome with: blt. sound conduction disorder with atresia of the bony auditory canals, mandibular retrognathia
- 2 x sound conduction disorder on the right at presence of atresia of the bony auditory canal
- Hereditary lymphedema, missing fingernails (Digit III, V), tetra-brachydactyly
- ASD II, blt. preauricular tag, skin tag at the left corner of the mouth, retarded hip maturation

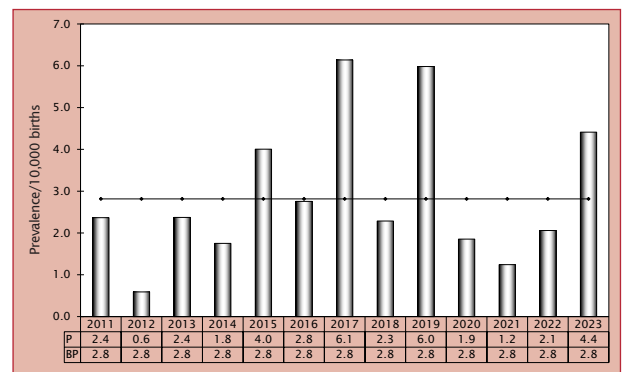


Fig. 16: Development of prevalence/10,000 births with microtia/anotia in Saxony-Anhalt since 2011

In 2023, one child/fetus with microtia/anotia was observed per 2,267 births in Saxony-Anhalt.

10.10 Tetralogy of Fallot (Q21.3/Q21.80)

Saxony-Anhalt	Year of 2023		
	Number	Prevalence/10,000 births	Comparison to basis prevalence
	4	2.94	↔
	Reporting period 2011-2022		
Basis prevalence/10,000 births		Confidence interval (CI 95 %)	
3.56		2.78 - 4.48	
EUROCAT (Full members)	Period 2011-2022		
	Prevalence/10,000 births	Confidence interval (CI 95 %)	
	3.8	3.6 - 3.9	

The malformation tetralogy of Fallot shows multiple cardiac malformations: Pulmonary stenosis, VSD, riding aorta and right heart hypertrophy are associated. The pulmonary circulation is reduced. The pentalogy of Fallot, which also belongs to the indicator malformation tetralogy of Fallot, shows additionally an ASD.

In Saxony-Anhalt, four children/fetuses born in 2023 were diagnosed with the indicator malformation tetralogy of Fallot (**2.9 per 10,000 births**). Therefore, the current years prevalence lies in the lower range of the basis prevalence (2011-2022: 3.6 per 10,000 births).

The confidence interval of the basis prevalence of Saxony-Anhalt covers, due to the smaller population included, the narrower confidence interval of the European prevalence (2011-2022: 3.8 per 10,000 births). The prevalence of Saxony-Anhalt of 2023 lies below the overall European prevalence.

The severe cardiac malformation was discovered prenatally in one child. It was transferred prenatally to a heart

center. Another child with an unknown pregnancy was only transferred to a university center after birth. In case of a twin pregnancy, after the affected fetus developed ascites, a selective feticide took place.

additional information:

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

Malformation combinations (MCA) or superordinated syndromes detected:

- Down's syndrome

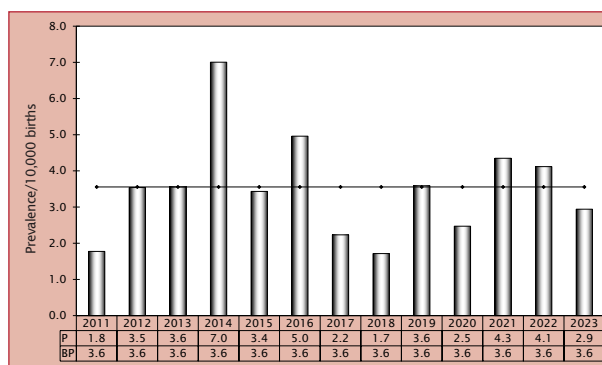


Fig. 17: Development of prevalence/10,000 births with Tetralogy of Fallot /Pentalogy in Saxony-Anhalt since 2011

In 2023, one child/fetus with tetralogy of Fallot was observed per 3,400 births in Saxony-Anhalt.

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

Saxony-Anhalt	Year of 2023			
		Number	Prevalence/ 10,000 births	Comparison to basis prevalence
	TGA	11	8.09	↑
	of which d-TGA	9	6.62	↑
	of which DORV	2	1.47	↔
	Reporting period 2011-2022			
		Basis prevalence/ 10,000 births		Confidence interval (CI of 95 %)
	TGA	5.19		4.24 - 6.28
	of which d-TGA	3.80		3.00 - 4.75
	of which DORV	1.58		1.08 - 2.23
EUROCAT (Full members)	Period 2011-2022			
		Prevalence/ 10,000 births	Confidence interval (CI of 95 %)	
	TGA	5.30	5.14 - 5.46	
	of which d-TGA	3.51	3.38 - 3.64	
	of which DORV	1.79	1.70 - 1.88	

One of the most severe congenital cyanotic cardiac malformations is the indicator malformation **transposition of the great arteries (TGA)**. In this case the outgoing vessels, aorta and pulmonary artery, are interchanged. If the aorta originates from the right ventricle and the pulmonary artery from the left ventricle, this is referred to as a **complete TGA (d-TGA, Q20.3)**. In case of a **double outlet right ventricle (DORV, Q20.1)**, the large arteries aorta and pulmonary artery originate together from the right ventricle.

For the 2023 birth cohort of Saxony-Anhalt, **TGA** was observed in eleven children/fetuses. The resulting **annual prevalence (2023: 8.1 per 10,000 births)** exceeds the basis prevalence (2011-2022: 5.2 per 10,000 births) significantly. However, the year 2021 (8.1 per 10,000 births) showed a similarly high value. While the rarer **DORV** in 2023 showed a prevalence within the interval of the basis prevalence (2023: 1.5 per 10,000 births; 2011-2022: 1.6 per 10,000 births), the **d-TGA** also shows a current annual prevalence far above the confidence interval of the basis prevalence (2023: 6.6 per 10,000 births; 2011-2022: 3.8 per 10,000 births).

	Regression coefficient B in %	Confidence interval (CI of 95 %)
d-TGA	4.54	-6.02 to 16.52
DORV	19.77	1.97 to 45.62

A trend analysis performed analogous to the trend analysis of indicator malformations in Chapter 10.38 (2-year prevalences from 2010-2023) results in the values listed above for the **d-TGA** and **DORV**. **DORV** shows a significant upward trend with a percentage change of 19.77 %, whereby the non-linear portion is ineffective ($p > 0.01$). It is conceivable that, due to more precise diagnostic

techniques since the middle of the reporting period, in case of multiple cardiac malformations the single malformation **DORV** is identified more frequently.

The confidence interval of the basis prevalence of Saxony-Anhalt for **TGA** (as well as for d-TGA and for DORV) encloses due to the smaller numbers the interval limits of the overall prevalence reported by EUROCAT for the European register (2011-2022: 5.3 per 10,000 births). The current prevalence value of **TGA** (2023) of Saxony-Anhalt is very high compared to the overall European prevalence.

additional information:

Pregnancy outcome	10 x live births 1 x termination of pregnancy
Sex	9 x male 2 x female
Number of isolated malformations /MCA	11 x MCA

One pregnancy was terminated prematurely after a suspected multiple cardiac malformation. Seven children were born in a specialized clinic. Three other children were transferred to a heart center after birth.

Malformation combinations (MCA) or superordinated syndromes detected:

- preductal aortic coarctation, VSD, biotinidase deficiency
- mitral valve stenosis, VSD
- endocardial cushion defect
- coronary sinus defect
- vascular ring through the anomalous right subclavian artery
- VSD, malformation of the coronary vessels, pulmonary valve stenosis, receding forehead, sunken nasal root, high palate, macroglossia, mandibular retrognathia
- 2 x VSD, malformation of the coronary vessels
- VSD, vascular ring of the large arteries
- VSD, left plexus cyst
- VSD

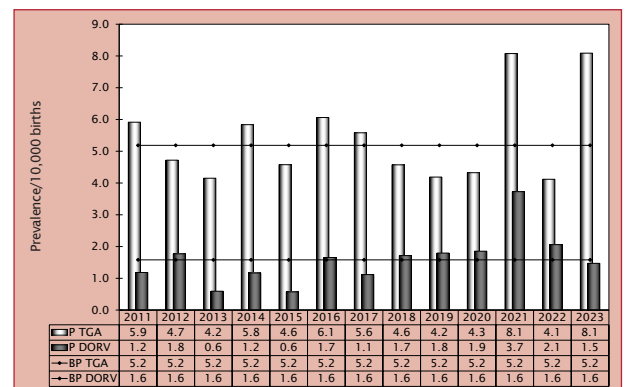


Fig. 18: Development of prevalence/10,000 births with transposition of great vessels in Saxony-Anhalt since 2011

In 2023, one child/fetus with transposition of the great arteries was observed per 1,236 births in Saxony-Anhalt.

10.12 Hypoplastic left heart syndrome (Q23.4)

Saxony-Anhalt	Year of 2023		
	Number	Prevalence/10,000 births	Comparison to basis prevalence
	3	2.21	↔
	Reporting period 2011-2022		
Basis prevalence/10,000 births		Confidence interval (CI 95 %)	
2.86		2.18 - 3.70	
EUROCAT (Full members)	Period 2011-2022		
	Prevalence/10,000 births	Confidence interval (CI 95 %)	
	2.8	2.7 - 2.9	

The indicator malformation hypoplastic left heart syndrome is a complex cardiac malformation in which several malformations of the heart and the aorta occur together. In this case, the left heart structures are underdeveloped.

In Saxony-Anhalt, three children/fetuses born in 2023 were registered with left heart hypoplasia. This determines a **prevalence of 2.2 per 10,000 births**, which is located in the lower confidence interval of the basis prevalence (2011-2022: 2.9 per 10,000 births).

The confidence interval of the basis prevalence of Saxony-Anhalt corresponds approximately to the overall prevalence of the European register (2011-2022: 2.8 per 10,000 births). However, the confidence interval of Saxony-Anhalt has a wider range than that of the European overall prevalence.

In case of all three affected children, the malformation hypoplastic left heart syndrome was already recognized during prenatal ultrasound. One child died on the third day of life. Thanks to improved surgical techniques and

treatment in specialized heart centers, there are now good treatment prospects for left heart hypoplasia and long-term prognoses, but not all children survive.

additional information:

Pregnancy outcome	2 x live births 1 x live birth deceased before 7 days of life
Sex	2 x male 1 x female
Number of isolated malformations /MCA	1 x MCA 2 x isolated

Malformation combinations (MCA) or superordinated syndromes detected:

- Microcephaly, aortic isthmus stenosis, large bowel atresia, low-set ears

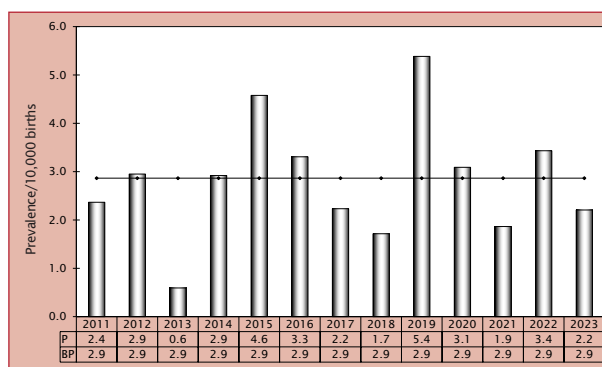


Fig. 19: Development of prevalence/10,000 births with hypoplastic left heart syndrome (Q23.4) in Saxony-Anhalt since 2011

In 2023, one child/fetus with hypoplastic left heart syndrome was observed per 4,533 births in Saxony-Anhalt.

10.13 Coarctation of aorta (Q25.1)

Saxony-Anhalt	Year of 2023		
	Number	Prevalence/ 10,000 births	Comparison to basis prevalence
	10	7.35	↗
EUROCAT (full members)	Reporting period 2011-2022		
	Basis prevalence/ 10,000 births	Confidence interval (CI 95 %)	
	5.93	4.91 - 7.09	
EUROCAT (full members)	Period 2011-2022		
	Prevalence/ 10,000 births	Confidence interval (CI 95 %)	
	4.1	4.0 - 4.3	

Ten children/fetuses from Saxony-Anhalt (**prevalence: 7.4 per 10,000 births**) were diagnosed in the birth cohort 2023 with the indicator malformation coarctation of aorta. This means that the current prevalence is slightly higher than expected and lies slightly above the tolerance range of the basis prevalence (2011-2022: 5.9 per 10,000 births).

The confidence interval of the overall prevalence of the European register (4.1 per 10,000 births) and the basis prevalence of Saxony-Anhalt do not overlap. The basis prevalence of Saxony-Anhalt is much higher. Compared with the overall European prevalence, the annual prevalence of Saxony-Anhalt for 2023 lies well above this.

additional information:

Pregnancy outcome	9 x live births 1 x termination of pregnancy
Sex	4 x male 6 x female
Number of isolated malformations /MCA	10 x MCA

Coarctation of aorta is a severe cardiac malformation, in which there is a narrowing or compression of the aorta in the area of the aortic arch. A preductal coarctation of aorta occurred in the context of a Shone complex. Five times, the coarctation of aorta was seen intrauterine. Three times other cardiac malformations were described prenatally, once only soft marker. One pregnancy with a Turner syndrome, coarctation of aorta and other malformations of different organ systems were detected during the 14th week of gestation, the pregnancy was terminated.

Malformation combinations (MCA) or superordinated syndromes detected:

- microcephaly, HLHS, atresia of the large intestine, low-set ears
- Turner syndrome with: bicuspid aortic valve, shield thorax, pterygium colli, blt. hypoplastic lungs, kidneys and ovaries, blt. pes calcaneovarus congenitus, laterally sloping eyelid axes, low-set and dysplastic ears, mandibular retrognathia, saddle nose, wide nipple spacing
- Turner syndrome with: Pulmonary valve stenosis, aortic hypoplasia, PFO at full term infant
- TGA, VSD, biotinidase deficiency
- Shone complex with: Bicuspid aortic valve, aortic valve and mitral valve stenosis, persistent left superior vena cava, PFO at full term infant, separate ASD II, DUP II. degree with duplex right kidney, blt. delayed hip maturation
- glandular hypospadias, ductus venous agenesis, left ventricular myocardial hypertrophy, cataracta congenita left, blt. hip joint dislocation, umbilical hernia, left inguinal hernia at preterm infant
- AVSD, mitral atresia, aortic hypoplasia, ASD II, persistent left superior vena cava
- AVSD, coronary sinus defect, brachycephaly, azygos-continuity of the inferior vena cava
- persistent left superior vena cava, stenosis of the pulmonary artery, ASD at full term infant
- bicuspid aortic valve

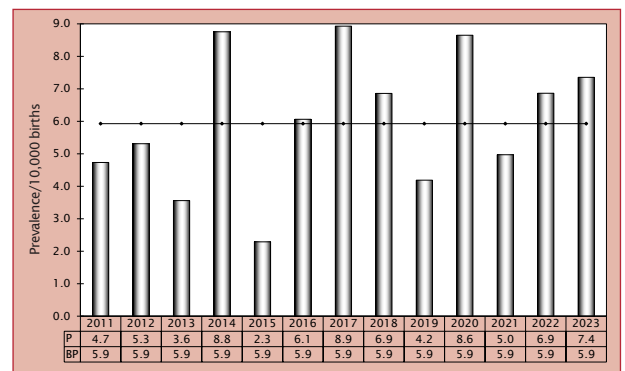


Fig. 20: Development of prevalence/10,000 births with coarctation of aorta in Saxony-Anhalt since 2011

In 2023, one coarctation of aorta per 1,360 births was registered in Saxony-Anhalt.

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

Saxony-Anhalt	Year of 2023		
	Number	Prevalence/10,000 births	Comparison to basis prevalence
	12	8.82	↓
	Reporting period 2011-2022		
Basis prevalence/10,000 births		Confidence interval (CI 95 %)	
12.64		11.14 - 14.29	
EUROCAT (Full members)	Period 2011-2022		
	Prevalence/10,000 births	Confidence interval (CI 95 %)	
	8.7	8.5 - 8.9	

In the reporting period, the birth rate of 2023 shows for the third time in a row with **8.8 per 10,000 births**, an **annual prevalence** significantly below the basis prevalence of Saxony-Anhalt (2011-2022: 12.6 per 10,000 births). A maximum prevalence value almost twice as high was registered in 2015 (16.6 per 10,000 births). In 2023, twelve children/fetuses were diagnosed with the indicator malformation cleft lip and cleft lip with cleft palate.

The indicator malformation includes all clefts of the upper lip with and without cleft alveolar ridge or the hard palate. Only the upper lip was affected four times, twice there was a very rare cleft lip and cleft jaw and six times a cleft lip with cleft palate was registered. Only once in 2023 a cleft lip was associated with a sound conduction disorder.

Four of the cleft lips and cleft lips with cleft palate occurred bilateral, seven times unilateral. Among the unilateral cases, the right side predominated (5 x), the left side was affected only once. In the case of one unilateral cleft lip, the side was not specified. Another cleft lip with cleft palate was reported without indicating the localization.

The Saxony-Anhalt basis prevalence of cleft lip and cleft lip with cleft palate is considerably higher than the Europe-wide overall prevalence provided by EUROCAT (2011-2022: 8.7 per 10,000 births). However, in the last three years, annual prevalence rates of Saxony-Anhalt were de-

termined twice to be close to the European overall prevalence (2021: 8.1 per 10,000 births; 2023: 8.8 per 10,000 births) and once (2022: 5.5 per 10,000 births) they were below the overall European prevalence.

additional information:

Pregnancy outcome	11 x live births 1 x termination of pregnancy
Sex	7 x male 4 x female 1 x no indication
Number of isolated malformations /MCA	4 x MCA 8 x isolated

Malformation combinations (MCA) or superordinated syndromes detected:

- Goldenhar syndrome with: Right facial cleft, arachnoid cyst, bilateral corneal opacity and preauricular tag, delayed hip maturation left
- AVSD, truncus arteriosus communis
- PFO at full term infant
- blt. sound conduction disturbance

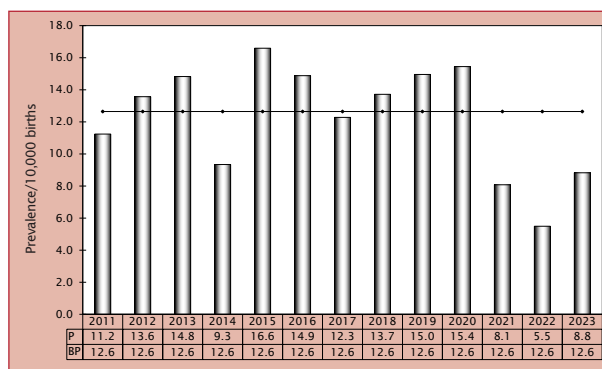


Fig. 21: Development of prevalence/10,000 births with cleft lip with or without cleft palate in Saxony-Anhalt since 2009

In 2023, one child/fetus with cleft lip and cleft lip and palate was observed per 1,133 births in Saxony-Anhalt.

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

Saxony-Anhalt	Year of 2023		
	Number	Prevalence/ 10,000 births	Comparison to basis prevalence
	6	4.41	↓
Saxony-Anhalt	Reporting period 2011-2022		
	Basis prevalence/ 10,000 births		Confidence interval (CI 95 %)
	7.41		6.27 - 8.69
EUROCAT (Full members)	Period 2011-2022		
	Prevalence/ 10,000 births		Confidence interval (CI 95 %)
	5.9		5.7 - 6.0

Cleft palates are clefts of the hard and soft palate in which there is no lip involvement. They occur in the 8th-10th week of gestation due to missing or insufficient fusion of the two paired palatal processes.

In case of six births in 2023, cleft palates were seen in Saxony-Anhalt. When calculating the **prevalence** of 2023 (**4.4 per 10,000 births**), this results in a minimum value of the reporting period. After a maximum prevalence in 2015 (10.3 per 10,000 births) values are predominantly falling. The current annual prevalence of 2023 is significantly below the normal range of the basis prevalence of Saxony-Anhalt (2011-2022: 7.4 per 10,000 births).

Compared to the average prevalence of EUROCAT (2011-2022: 5.9 per 10,000 births), the basis prevalence of Saxony-Anhalt is well above the normal range of the European register. The annual prevalence of Saxony-Anhalt of 2023 falls below the European prevalence provided by EUROCAT.

additional information:

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

Of the six children who were diagnosed with a cleft palate in 2023 two were affected by a bilateral cleft palate and three by a median cleft palate. In case of a submucosal cleft of the soft palate no localization was indicated. Twice a Pierre Robin sequence, once isolated and once with cardiac malformation, was diagnosed. Three children had impaired hearing, there was a sound conduction disorder present. Only once the cleft palate was known prenatally.

Malformation combinations (MCA) or superordinated syndromes detected:

- Down syndrome with: VSD, blt. sound conduction disorder
- ASD, stenosis of the pulmonary artery at full term infant
- double aortic arch, blt. sound conduction disorder, mandibular retrognathia
- blt. sound conduction disorder

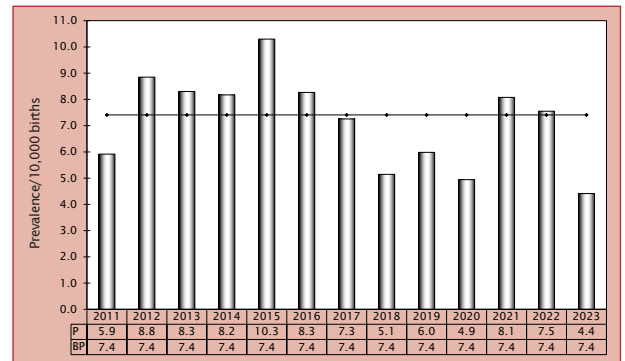


Fig. 22: Development of prevalence/10,000 births with cleft palate in Saxony-Anhalt since 2011

In 2023, one child/fetus with a cleft palate was observed per 2,267 births in Saxony-Anhalt.

10.16 Choanal atresia (Q30.0)

Saxony-Anhalt	Year of 2023		
	Number	Prevalence/10,000 births	Comparison to basis prevalence
	3	2.21	↔
	Reporting period 2011-2022		
Basis prevalence/10,000 births		Confidence interval (CI 95 %)	
2.57		1.92 - 3.37	
EUROCAT (Full members)	Period 2011-2022		
	Prevalence/10,000 births	Confidence interval (CI 95 %)	
	0.9	0.9 - 1.0	

Choanal atresia is characterized by the closure of the transition of the nasopharynx to the pharynx. The diagnosis is usually only made postnatally. The affiliation to the indicator malformation choanal atresia is limited to atresia and stenosis which require a treatment, low-grade stenoses are not included.

Three children/fetuses with choanal atresia were reported in the year of birth 2023. The calculated **annual prevalence (2.2 per 10,000 births)** for the indicator malformation lies in the middle of the normal range of the basis prevalence of Saxony-Anhalt (2011-2022: 2.6 per 10,000 births). The prevalences vary annually between very low values in 2011, 2012, 2018 and 2021, each with one or two affected births (maximum 0.6 per 10,000 births) and high prevalences in the middle of the of the reporting period (2014, 2015, 2016) with at least eight affected children/fetuses (maximum: 5.5 per 10,000 births). The trend analysis in Chapter 10.38 therefore shows a non-linear change that determines the trend over the years 2010-2023.

The confidence interval of the basis prevalence as well as the annual prevalence 2023 of Saxony-Anhalt are significantly above the interval of the average prevalence of the European register (2011-2022: 0.9 per 10,000 births).

additional information:

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

Malformation combinations (MCA) or superordinated syndromes detected:

- CHARGE-assoziation
- PFO at full term infant, retarded hip right

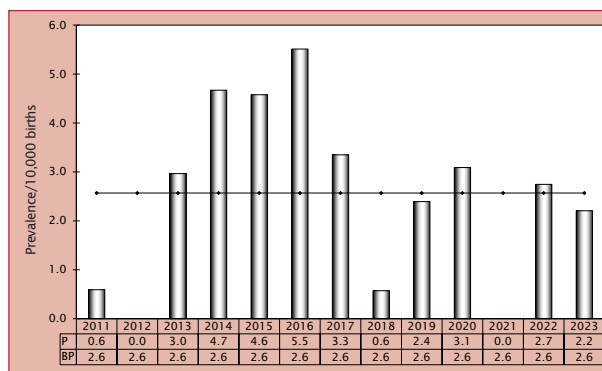


Fig. 23: Development of prevalence/10,000 births with choanal atresia in Saxony-Anhalt since 2011

In 2023, one child/fetus with choanal atresia was observed per 4,533 births in Saxony-Anhalt.

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

Saxony-Anhalt	Year of 2023		
	Number	Prevalence/ 10,000 births	Comparison to basis prevalence
	1	0.74	↓
EUROCAT (Full members)	Reporting period 2011-2022		
	Basis prevalence/ 10,000 births	Confidence interval (CI 95 %)	
	2.62	1.96 - 3.42	
EUROCAT (Full members)	Period 2011-2022		
	Prevalence/ 10,000 births	Confidence interval (CI 95 %)	
	2.7	2.6 - 2.8	

In 2023, only one child was born with an oesophageal atresia/stenosis/fistula in Saxony-Anhalt. The determined **annual prevalence** for the indicator malformation (2023: **0.7 per 10,000 births**) is very low and lies therefore also significantly below the basis prevalence (2011-2022: 2.6 per 10,000 births). The current annual prevalence does not quite reach the minimum prevalence of the reporting period (2014: 0.6 per 10,000 births).

When comparing the prevalence of the indicator malformation oesophageal atresia/stenosis/fistula of Saxony-Anhalt over the reporting period, as well as for the year 2023, with the prevalence of the European register provided by EUROCAT (2011-2022: 2.7 per 10,000 births), this lies well above the prevalence values of Saxony-Anhalt.

In case of one child with atresia of the oesophagus, there was a fistula (type Vogt III b) between the trachea and the lower esophageal pocket. The malformation, as well as a polyhydramnios, were found during prenatal ultrasound screening in the 22nd week of gestation.

additional information:

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

Malformation combinations (MCA) or superordinated syndromes detected:

- Hemangioma in the left lobe of the liver, blt. lacrimal duct stenosis

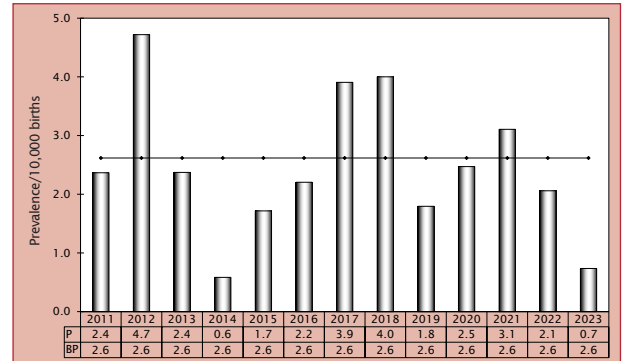


Fig. 24: Development of prevalence/10,000 births with oesophageal atresia/stenosis/fistula in Saxony-Anhalt since 2011

In 2023, one child with oesophageal atresia/-stenosis/-fistula per 13,599 births was registered.

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

Saxony-Anhalt	Year of 2023		
	Number	Prevalence/10,000 births	Comparison to basis prevalence
	1	0.74	↓
	Reporting period 2011-2022		
Basis prevalence/10,000 births		Confidence interval (CI 95 %)	
1.83		1.29 - 2.52	
EUROCAT (Full members)	Period 2011-2022		
	Prevalence/10,000 births	Confidence interval (CI 95 %)	
	0.9	0.8 - 0.9	

The indicator malformation small intestinal atresia/stenosis is not observed very frequently. After it did not occur at all in the previous year (2022), only one child was born with a stenosis of the small intestine in Saxony-Anhalt in 2023. The resulting **annual prevalence of 0.7 per 10,000 births** lies considerably below the range of the basis prevalence (2011-2022: 1.8 per 10,000 births).

Over the years 2010-2023 of the trend analysis (Chapter 10.38) we registered in four years (2010, 2014, 2022, 2023) prevalence rates below 0.8 and twice (2012, 2017) over 3.3 per 10,000 births in Saxony-Anhalt. Due to the fluctuating numbers, the non-linear change is significant when evaluating the trend.

The malformation is often only noticed postnatally. In the case of the child born in 2023 a colonic stenosis was suspected prenatally, and after birth a colonic atresia and multiple small bowel atresias (type IV) were diagnosed.

Compared to the European prevalence determined by EUROCAT (2011-2022: 0.9 per 10,000 births), Saxony-An-

halt's prevalence can be rated to be exceptionally high. However, the current annual prevalence is below the confidence interval of the overall European prevalence.

additional information:

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

Malformation combinations (MCA) or superordinated syndromes detected:

- large intestinal atresia, microcolon, diverticula of the intestine, corpus callosum hypoplasia, cholestasis

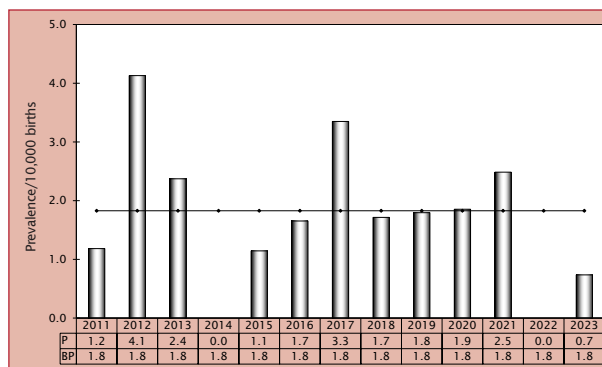


Fig. 25: Development of prevalence/10.000 births with small intestinal atresia/stenosis in Saxony-Anhalt since 2011

In 2023, one child/fetus with small bowel atresia/stenosis was observed per 13,599 births in Saxony-Anhalt.

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

Saxony-Anhalt	Year of 2023		
	Number	Prevalence/ 10,000 births	Comparison to basis prevalence
	3	2.21	↓
EUROCAT (full members)	Reporting period 2011-2022		
	Basis prevalence/ 10,000 births	Confidence interval (CI 95 %)	
	3.31	2.57 - 4.20	
EUROCAT (full members)	Period 2011-2022		
	Prevalence/ 10,000 births	Confidence interval (CI 95 %)	
	3.5	3.4 - 3.6	

With three cases of rectal and anal atresias, which occurred in 2023, the **annual prevalence** is calculated to be **2.2 per 10,000 births**, which lies below the lower confidence limit of the interval of the basis prevalence of Saxony-Anhalt (2011-2022: 3.3 per 10,000 births). It can be seen that since 2016 the annual prevalence rates can be located mostly well below the confidence interval (4 x) or in the lower segment (3 x) of the confidence interval of the basis prevalence. However, they are generally higher in the early years of the reporting period (with the exception of 2014). The result of the trend analysis (Chapter 10.38) is a downward trend with a percentage change of -12.62 % (CI -21.35 % to -1.22 %), whereby the non-linear portion is not effective ($p > 0.01$).

The confidence limits of the basis prevalence of Saxony-Anhalt are wider than those of the confidence interval of the Europe-wide prevalence provided by EUROCAT due to the smaller included population (2011-2022: 3.5 per 10,000 births). While the basis prevalence of Saxony-Anhalt and the European prevalence are roughly at the same level, the annual prevalence of Saxony-Anhalt of 2023 is considerably lower than the European overall prevalence.

As a rule, rectal and anal atresia, as in the case of the three children/fetuses in 2023, are detected only after birth. Rectal atresia did not occur at this time. The pregnancy of one fetus was diagnosed with severe malfor-

mations of the urinary transport system, pulmonary hypoplasia and anhydramnios. There was one anal atresia without fistula. Two other children had each an anal atresia with fistula.

additional information:

Pregnancy outcome	2 x live births 1 x termination of pregnancy
Sex	3 x male
Number of isolated malformations /MCA	2 x MCA 1 x isolated

Malformation combinations (MCA) or superordinated syndromes detected:

- blt. multicystic dysplastic kidneys, DUP and pulmonary hypoplasia, urethral valves, Meckel's diverticulum, megacystis, pelvic kidney on the right, low-set ears, mandibular micro- and retrognathia, epicanthus internus, hypertelorism, Potter facies, supination of the feet
- PFO at full term infant, right plexus cyst, DUP I. degree right

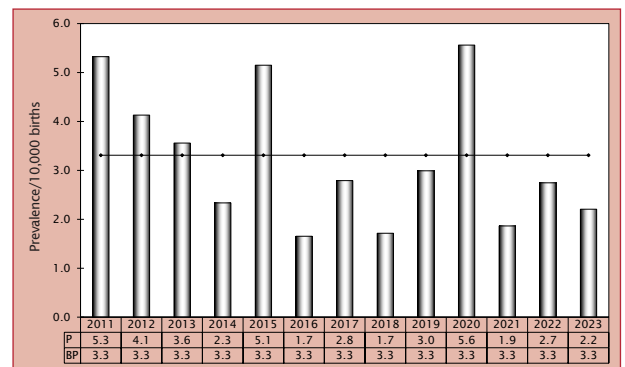


Fig. 26: Development of prevalence/10,000 births with anorectal atresia/-stenosis in Saxony-Anhalt since 2011

In 2023, one child/fetus with rectal and anal atresia/ stenosis was observed per 4,533 births in Saxony-Anhalt.

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

Saxony-Anhalt	Year of 2023		
	Number	Prevalence/10,000 births	Comparison to basis prevalence
	15	11.03	↓
	Reporting period 2011-2022		
Basis prevalence/10,000 births		Confidence interval (CI 95 %)	
22.62		20.60 - 24.79	
EUROCAT (Full members)	Period 2011-2022		
	Prevalence/10,000 births	Confidence interval (CI 95 %)	
18.7		18.4 - 19.0	

The indicator malformation hypospadias is one of the two most common indicator malformations in Saxony-Anhalt. This results in a basis prevalence of the reporting period of 22.6 per 10,000 births (2011-2022). Whereas the malformation occupied the first place in the first half of the reporting period (maximum value in 2016: 29.0 per 10,000 births), prevalence rates fell in the second half, so that from 2017 it generally took the second place. The trend analysis (Chapter 10.38) therefore shows a linear downward trend with a regression coefficient of -7.44 % (CI -11.18 % to -2.98 %), whereby the non-linear component is not effective ($p > 0.01$).

The **annual prevalence** reached in this year (2023) a level of only 15 affected and thus **11.0 per 10,000 births**, a prevalence far below the lower confidence limit of the normal range of the basis prevalence. With regard to 6,944 live and stillborn boys (2023), the calculated annual prevalence of 21.60 per 10,000 boys lies also considerably below the confidence interval of the basis prevalence (2011-2022: 43.30 per 10,000 boys; CI 39.43-47.45).

The confidence interval determined by EUROCAT of the years 2011-2022 (18.7 per 10,000 births) lies below the confidence interval of the basis prevalence of Saxony-Anhalt. This year's annual prevalence value is, however, far below the standard range of the European comparative values.

The mildest form of hypospadias, glandular hypospadias, was found in case of eleven boys. Two boys had coronary hypospadias and two boys were affected by penile hypospadias. The two very severe forms, penoscrotal and perineal hypospadias, did not occur in 2023.

additional information:

Pregnancy outcome	15 x live births
Sex	15 x male
Number of isolated malformations /MCA	6 x MCA 9 x isolated

All boys with hypospadias were born alive this year. One third of them was born before the 37th week of gestation, including two extremely small premature babies with a birth weight of less than 1000 grams.

Malformation combinations (MCA) or superordinated syndromes detected:

- Goltz-Gorlin syndrome with: Urinary bladder neck obstruction, ureterocele, blt. megaureter and DUP III. degree
- preductal aortic isthmus stenosis, ductus venous agenesis, left ventricular myocardial hypertrophy, cataracta congenita left, blt. hip joint dislocation, umbilical hernia, left inguinal hernia at preterm infant
- blt. megaureter and DUP IV. degree, urethral valves, megacystis, preputial apron, preauricular appendage left, PFO at preterm infant
- Megaureter and DUP III. degree left
- VSD, fistula of the lip, blt. DUP I. degree
- right: sound perception disorder, delayed hip maturation and hydrocele

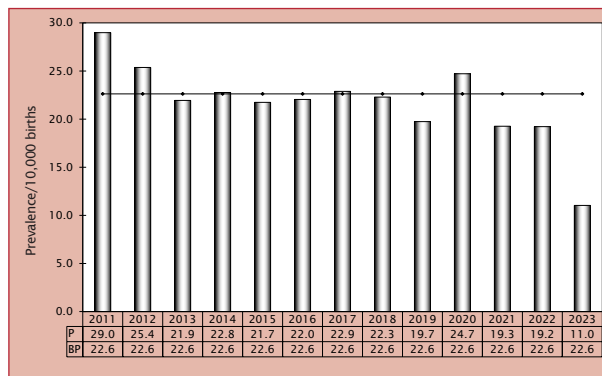


Fig. 27: Development of prevalence/10,000 births with hypospadias in Saxony-Anhalt since 2011

In 2023, one hypospadias per 907 births (463 boys) was registered in Saxony-Anhalt.

10.21 Epispadias (Q64.0)

Saxony-Anhalt	Year of 2023		
	Number	Prevalence/ 10,000 births	Comparison to basis prevalence
	1	0.74	↗
	Reporting period 2011-2022		
Basis prevalence/ 10,000 births		Confidence interval (CI 95 %)	
0.25		0.08 - 0.58	
EUROCAT (Full members)	Period 2011-2022		
	Prevalence/ 10,000 births	Confidence interval (CI 95 %)	
	no information	no information	

With one child and a **prevalence of 0.7 per 10,000 births** in 2023, the indicator malformation epispadias is one of the very rarely seen malformations. The maximum prevalence of the reporting period was 1.1 per 10,000 births in 2016 with two children. In the entire reporting period (2011-2022) this indicator malformation occurred only 5 times, which corresponds to a basis prevalence of 0.2 per 10,000 births (2011-2022).

The European malformation register EUROCAT does not provide separate prevalence data for the indicator malformation of epispadias.

additional information:

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

Malformation combinations (MCA) or superordinated syndromes detected:

- Microtia and ventricular asymmetry left, blt. brachydactyly and clinodactyly of the 5th finger

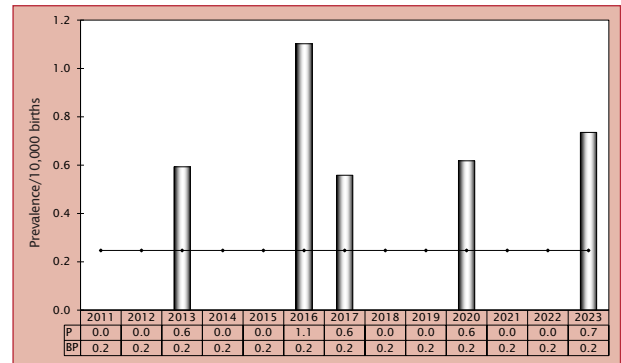


Fig. 28: Development of prevalence/10,000 births with epispadias in Saxony-Anhalt since 2011

In 2023, one child/fetus with epispadias was observed per 13,599 births (6,944 boys) in Saxony-Anhalt.

10.22 Indeterminate sex (Q56.)

Saxony-Anhalt	Year of 2023		
	Number	Prevalence/10,000 births	Comparison to basis prevalence
	1	0.74	↔
	Reporting period 2011-2022		
Basis prevalence/10,000 births		Confidence interval (CI 95 %)	
0.69		0.38 - 1.16	
EUROCAT (Full members)	Period 2011-2022		
	Prevalence/10,000 births	Confidence interval (CI 95 %)	
	0.5	0.4 - 0.5	

In 2023, one child was registered with the rare indicator malformation indifferent sex in Saxony-Anhalt. This results in an **annual prevalence of 0.7 per 10,000 births**. It lies inconspicuously within the range of the basis prevalence determined for Saxony-Anhalt (2011-2022: 0.7 per 10,000 births). The maximum prevalence of the reporting period with three children (1.7 per 10,000 births) was achieved in 2016. Between 2011 and 2022, there were only 14 affected children in total. The low numbers exclude a trend analysis.

The European-wide comparison shows, that the confidence interval of the overall prevalence given by EUROCAT (2011-2022: 0.5 per 10,000 births) lies in the lower range of the confidence interval of the Saxony-Anhalt basis prevalence for indifferent sex. Due to the larger population observed, the European confidence interval is narrower and it is covered at the same time by the interval of Saxony-Anhalt.

additional information:

Pregnancy outcome	1 x live birth deceased before the 7th day of life
Sex	1 x indeterminate
Number of isolated malformations /MCA	1 x MCA

A Potter sequence was known prenatally in case of the child with indifferent sex. It died a few hours after birth.

Malformation combinations (MCA) or superordinated syndromes detected:

- Potter sequence with: blt. pelvic kidney, clubfeet, hypertelorism, Potter facies, mandibular micround, retrognathia

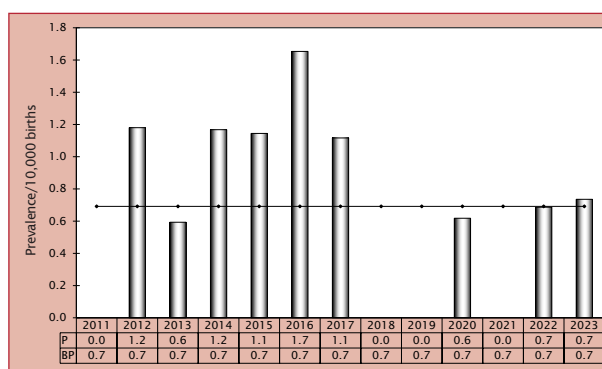


Fig. 29: Development of prevalence/10,000 births with indeterminate sex in Saxony-Anhalt since 2011

In 2023, one child/fetus with an indeterminate sex was observed per 13,599 births in Saxony-Anhalt.

10.23 Potter sequence (Q60.6)

Saxony-Anhalt	Year of 2023		
	Number	Prevalence/ 10,000 births	Comparison to basis prevalence
	3	2.21	↔
EUROCAT (full members)	Reporting period 2011-2022		
	Basis prevalence/ 10,000 births	Confidence interval (CI 95 %)	
	2.77	2.09 - 3.59	
EUROCAT (full members)	Period 2011-2022		
	Prevalence/ 10,000 births	Confidence interval (CI 95 %)	
	1.3	1.2 - 1.3	

Bilateral non-functional (polycystic/multicystic dysplastic) or non-functioning kidneys are characteristics of a Potter sequence. In the course of the pregnancy an oligohydramnios develops without functioning kidneys, as a result of which further malformations such as clubfeet and lung hypoplasia develop. The subsequent malformations are considered to be part of the Potter sequence and are therefore not presented separately in the report.

In 2023, three children/fetuses in Saxony-Anhalt were diagnosed with a Potter sequence. This results in an **annual prevalence** (2023: **2.2 per 10,000 births**), which lies in the lower quarter of the confidence interval of the basis prevalence (2011-2022: 2.8 per 10,000 births). Since a peak was reached in the reporting period (2016: 5.0 per 10,000 births), prevalence rates have always been within or below the normal range.

The basis prevalence of the Potter sequence of Saxony-Anhalt exceeds the prevalence value specified by EUROCAT (2011-2022: 1.3 per 10,000 births). At the same time the lower confidence limit of the basis prevalence of Saxony-Anhalt as well as the current annual value lies significantly above the European confidence interval.

The Potter sequence was detected in all three cases prenatally between the 18th and 20th week of gestation. A prematurely born child with non-functioning hypoplastic

kidneys only lived for a few hours. Two pregnancies were terminated prematurely after discovery of the Potter sequence and other malformations. On one occasion there was a bilateral renal agenesis and once the kidneys were non-functional. In case of one mother the intake of medication during pregnancy was documented, but this was not the cause of the malformation.

additional information:

Pregnancy outcome	1 x live birth deceased before 7 days of life 2 x termination of pregnancy
Sex	1 x male 1 x indeterminate 1 x no indication
Number of isolated malformations /MCA	3 x MCA

aufgetretene Fehlbildungskombinationen (MCA) oder übergeordnete Syndrome neben typischen Dysmorphien:

- intersexual genitalia, hypertelorism, mandibular micro- and retrognathia
- Aortic valve stenosis, tricuspid valve dysplasia
- Cerebellar hypoplasia, lateral neck cysts

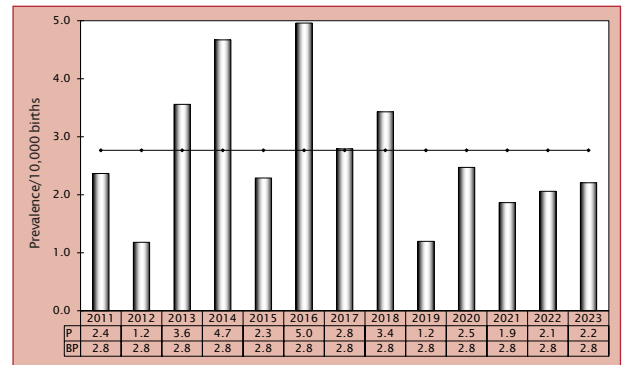


Fig. 30: Development of prevalence/10,000 births with Potter sequence in Saxony-Anhalt since 2011

In 2023, one Potter sequence per 4.533 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 trimester 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 fetal damage is an intrauterine oliguria. Since amniotic fluid production depends from the second trimester on mainly from fetal 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, limbs deformity, 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).

For further detailed information about this topic, please visit the website of the pharmacovigilance and advisory centre for embryonic toxicology (www.embryotox.de).

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

Saxony-Anhalt	Year of 2023		
	Number	Prevalence/ 10,000 births	Comparison to basis prevalence
	9	6.62	↗
	Reporting period 2011-2022		
Basis prevalence/ 10,000 births		Confidence interval (CI 95 %)	
5.48		4.51 - 6.60	
EUROCAT (Full members)	Period 2011-2022		
	Prevalence/ 10,000 births	Confidence interval (CI 95 %)	
	4.2	4.1 - 4.3	

In 2023, nine children/fetuses were diagnosed with unilateral renal agenesis in Saxony-Anhalt. This year's **prevalence** (2023: **6.6 per 10,000 births**) lies just above the upper confidence limit of the basis prevalence of Saxony-Anhalt (2011-2022: 6.6 per 10,000 births). In 2018, the annual prevalence rose to a maximum value of 9.4 per 10,000 births. A minimum value was recorded in 2016 (2.2 per 10,000 births).

A comparison with the prevalence provided by EUROCAT for 2011-2022 (4.2 per 10,000 births) suggests, that a prevalence value for Saxony-Anhalt in 2023 and during the reporting period was recorded far above the European average.

In 2023, five cases of right-sided and four cases of left-sided renal agenesis were registered. In case of one fetus with unilateral renal agenesis and reduction malformations of the arms and legs, the malformation was discovered at an advanced stage of pregnancy and the pregnancy was terminated prematurely.

additional information:

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

Malformation combinations (MCA) or superordinated syndromes detected:

- blt. radius aplasia, missing right fibula
- Embryofetopathy due to cannabis use by the mother, left duplex kidney and DUP I. degree
- Club feet, hyperplastic kidney right

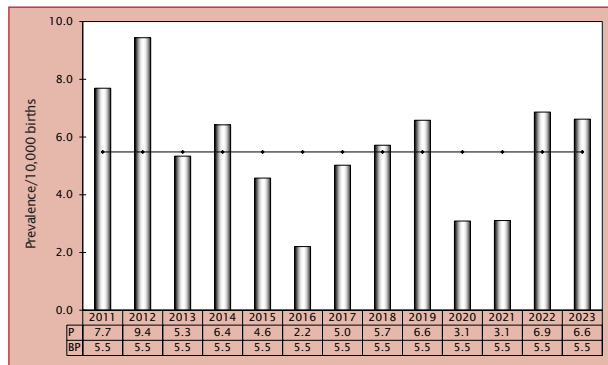


Fig. 31: Development of prevalence/10,000 births with unilateral renal agenesis in Saxony-Anhalt since 2011

In 2023, one child/fetus with unilateral renal agenesis was observed per 1,511 births in Saxony-Anhalt.

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

Saxony-Anhalt	Year of 2023		
	Number	Prevalence/ 10,000 births	Comparison to basis prevalence
	7	5.15	↓
	Reporting period 2011-2022		
Basis prevalence/ 10,000 births		Confidence interval (CI 95 %)	
7.11		6.00 - 8.37	
EUROCAT (Full members)	Period 2011-2022		
	Prevalence/ 10,000 births	Confidence interval (CI 95 %)	
	no information	no information	

Polycystic kidneys often appear in families and have a genetic cause. Many fluid-filled cysts gradually form in the kidneys, resulting in a renal insufficiency. Ultimately, the kidneys fail with severe degeneration.

After a maximum value of the annual prevalence in the last year (2022: 11.0 per 10,000 births), this year's **prevalence** of the indicator malformation cystic kidneys (2023: **5.1 per 10,000 births**) can be considered to be very low. The current annual prevalence (2023) is considerably lower than the basis prevalence (2011-2022: 7.1 per 10,000 births).

European-wide comparative values of the prevalence of cystic kidneys are not provided by EUROCAT.

additional information:

Pregnancy outcome	5 x live births 2 x termination of pregnancy
Sex	5 x male 2 x female
Number of isolated malformations /MCA	2 x MCA 5 x isolated

Cystic kidney degeneration occurred unilaterally six times (1 x right, 4 x left, once no indication of the affected side) and once both kidneys were affected. All cystic kidneys were discovered prenatally. In case of two fetuses prenatal signs of the cystic kidneys as well as severe malformations in other organ systems appeared. These pregnancies were terminated.

Malformation combinations (MCA) or superordinated syndromes detected:

- Anal atresia, urethral valves, blt. DUP and pulmonary hypoplasia, Meckel's diverticulum, megacystis, pelvic kidney right, low-set ears, mandibular micro- and retrognathia, internal epicanthus, hypertelorism, Potter facies, supination of the feet
- Megacisterna magna, mitochondriopathy

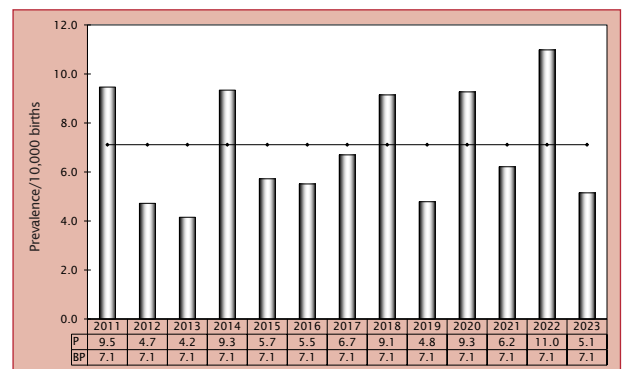


Fig. 32: Development of prevalence/10,000 births with cystic kidneys in Saxony-Anhalt since 2011

In 2023, one child/fetus with polycystic kidneys was observed per 1,943 births in Saxony-Anhalt.

10.26 Bladder Exstrophy (Q64.1)

Saxony-Anhalt	Year of 2023		
	Number	Prevalence/10,000 births	Comparison to basis prevalence
	0	0.00	↓
	Reporting period 2011-2022		
Basis prevalence/10,000 births		Confidence interval (CI 95 %)	
0.35		0.14 - 0.71	
EUROCAT (Full members)	Period 2011-2022		
	Prevalence/10,000 births	Confidence interval (CI 95 %)	
	no information	no information	

Exstrophy of the urinary bladder is a serious indicator malformation, in which there is an inhibition malformation of the anterior abdominal wall and the bladder. If epispadias occurs at the same time, this is considered to be part of the malformation bladder exstrophy.

Urinary bladder exstrophy is only observed very occasionally. In eight years of the reporting period, including the previous year and the current year (2022, 2023), it was not registered at all. Twice (2012, 2016), a maximum of two cases per year was observed. In both years, the upper normal range of the basis prevalence (2011-2022:

0.3 per 10,000 births) was exceeded by far. One case per year corresponds to the basis prevalence of Saxony-Anhalt.

For the indicator malformation exstrophy of the urinary bladder EUROCAT does not provide European-wide prevalence data, but for the bladder exstrophy-epispadias complex as a whole. For 2011- 2022, the prevalence of the European register is given with a value of 0.61 per 10,000 births (CI 0.56-0.67).

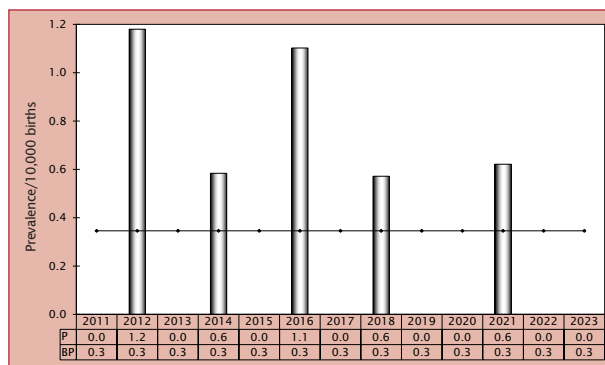


Fig. 33: Development of prevalence/10,000 births with bladder exstrophy in Saxony-Anhalt since 2011

In 2023, no bladder exstrophy was registered in Saxony-Anhalt.

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

Saxony-Anhalt	Year of 2023		
	Number	Prevalence/ 10,000 births	Comparison to basis prevalence
	4	2.94	↔
	Reporting period 2011-2022		
Basis prevalence/ 10,000 births		Confidence interval (CI 95 %)	
2.96		2.26 - 3.81	
EUROCAT (full members)	Period 2011-2022		
	Prevalence/ 10,000 births	Confidence interval (CI 95 %)	
	no information	no information	

Polydactylia at fingers or toes are formed for the most part postaxially. Only about one third of the polydactylia are found at thumbs or big toes. For 2023 a prevalence value is calculated for Saxony-Anhalt of 2.9 per 10,000 births, which lies in the middle of the confidence interval of the basis prevalence (2011-2022: 3.0 per 10,000 births).

When taking preaxial and/or postaxial polydactyly together (Chapter 9), this shows a **prevalence** of the current year of Saxony-Anhalt (2023) of **6.6 per 10,000 births**, which is far below the basis prevalence (2011- 2022: 11.6 per 10,000 births). The Saxony-Anhalt prevalence of polydactyly in total matches the average European prevalence, which EUROCAT estimates for 2011-2022 to be 10.86 per 10,000 births (CI 10.64-11.09). EUROCAT does not provide separate prevalence values for preaxial polydactyly.

additional information:

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

In case of all four children, the preaxial polydactyly occurred isolated. Twice the right thumb and once each time one right and one left big toe were created in duplicate.

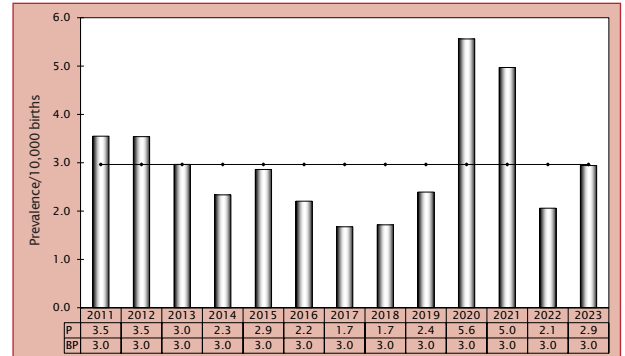


Fig. 34: Development of prevalence/10,000 births with preaxial polydactyly in Saxony-Anhalt since 2011

In 2023, one child/fetus with preaxial polydactyly was observed per 3,400 births in Saxony-Anhalt.

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

Saxony-Anhalt	Year of 2023		
	Number	Prevalence/ 10,000 births	Comparison to basis prevalence
	4	2.94	↓
	Reporting period 2011-2022		
Basis prevalence/ 10,000 births		Confidence interval (CI 95 %)	
8.00		6.82 - 9.33	
EUROCAT (Full members)	Period 2011-2022		
	Prevalence/ 10,000 births	Confidence interval (CI 95 %)	
5.0		4.9 - 5.2	

In 2023, a minimum prevalence of four cases was registered (**2.9 per 10,000 births**) and thus resulted in a current **annual prevalence** significantly below the confidence interval of the basis prevalence (2011-2022: 8.0 per 10,000 births). The highest rate of reduction malformations was seen in the second year of the reporting period, in 2012 (14.7 per 10,000 births). Since then, the prevalence values have been falling. Only once the value was above the confidence interval of the basis prevalence (2014: 11.1 per 10,000 births), 10 times it was either in or, as in 2016, 2018-2021 and 2023, below the confidence interval. This development is reflected in the trend calculation over the period from 2010-2023 (Chapter 10.38) in a significant downward trend with a percentage change of -10.47 % (CI -16.60 % to -2.75 %) with a non-effective non-linear proportion ($p > 0.01$).

When comparing the average prevalence given by EUROCAT for the years 2011-2022 (5.0 per 10,000 births) with the basis prevalence of Saxony-Anhalt, the latter is much higher. The annual prevalence 2023 of Saxony-Anhalt is significantly lower than the European overall prevalence, however.

additional information:

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

Both live births were affected by an unilateral reduction malformation of the extremities, three fingers were missing on the right hand and in another case toes were missing (digit II - V) on the left foot. One spontaneous abortion showed clumsy hands. In case of one fetus with prenatal bilateral radius aplasia, missing right fibula and with additional malformations, the pregnancy was terminated.

Malformation combinations (MCA) or superordinated syndromes detected:

- right renal agenesis
- blt. lung hypoplasia and sickle feet

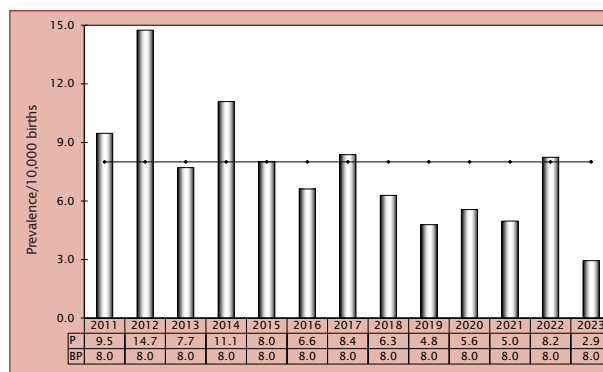


Fig. 35: Development of prevalence/10,000 births with limb reduction defects in Saxony-Anhalt since 2011

In 2023, one child/fetus with reduction malformations was observed per 3,400 births in Saxony-Anhalt.

10.29 Diaphragmatic hernia (Q79.0)

Saxony-Anhalt	Year of 2023		
	Number	Prevalence/ 10,000 births	Comparison to basis prevalence
	2	1.47	↓
EUROCAT (Full members)	Reporting period 2011-2022		
	Basis prevalence/ 10,000 births	Confidence interval (CI 95 %)	
	2.72	2.05 - 3.54	
EUROCAT (Full members)	Period 2011-2022		
	Prevalence/ 10,000 births	Confidence interval (CI 95 %)	
	3.0	2.9 - 3.1	

After three years (2020-2022) with very high prevalence rates (between 4.1 and 5.0 per 10,000 births), only two children were diagnosed with diaphragmatic hernia in 2023. This resulted in an **annual prevalence of 1.5 per 10,000 births**. The current annual prevalence is significantly below the confidence interval of the basis prevalence of Saxony-Anhalt for diaphragmatic hernia (2011-2022: 2.7 per 10,000 births). In the first half of the reporting period, lower average prevalence values were recorded than in the second half. An increasing trend for the linear proportion, however, is not yet detectable ($p = 0.0520$).

The current prevalence of diaphragmatic hernia of Saxony-Anhalt also falls below the European average (2011-2022: 3.0 per 10,000 births). Due to the smaller numbers, the confidence interval of the basis prevalence of Saxony-Anhalt is wider than the interval of the European overall prevalence and it covers the prevalence range of the EUROCAT register.

One child was found to have a large left-sided diaphragmatic hernia with effects on the entire abdominal cavity, the other child had only a small median fascial gap.

additional information:

Pregnancy outcome	1 x live births 1 x live births deceased until 7 days of life
Sex	1 x male 1 x female
Number of isolated malformations /MCA	2 x MCA

Malformation combinations (MCA) or superordinated syndromes detected:

- cardiac malposition, duodenal stenosis, lack of intestinal rotation with malformed intestinal fixation, pancreas anulare, malformation of liver and spleen, lung sequestration right
- persistent right aortic arch, blt. megaureter and DUP, gallbladder aplasia

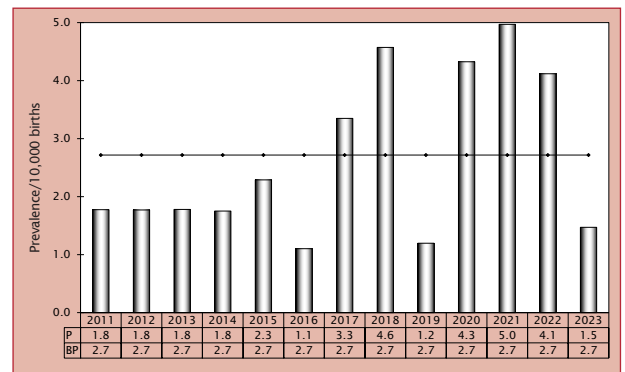


Fig. 36: Development of prevalence/10,000 births with diaphragmatic hernia in Saxony-Anhalt since 2011

In 2023, one child/fetus with diaphragmatic hernia was observed per 6,800 births in Saxony-Anhalt.

10.30 Omphalocele (Q79.2)

Saxony-Anhalt	Year of 2023		
	Number	Prevalence/ 10,000 births	Comparison to basis prevalence
	10	7.35	↑
	Reporting period 2011-2022		
Basis prevalence/ 10,000 births		Confidence interval (CI 95 %)	
3.61		2.83 - 4.53	
EUROCAT (Full members)	Period 2011-2022		
	Prevalence/ 10,000 births	Confidence interval (CI 95 %)	
	3.9	3.8 - 4.1	

In 2023, an unusually high number of ten children/fetuses were diagnosed with an omphalocele in Saxony-Anhalt. This results in a **prevalence (2023: 7.4 per 10,000 births)** which is far above all recorded prevalence values since the beginning of the 2000s and which exceeds significantly the basis prevalence (2011-2022: 3.6 per 10,000 births). The previous maximum value was reached in 2014 with 5.3 per 10,000 births.

The confidence interval of the basis prevalence of Saxony-Anhalt spans, due to smaller numbers, a larger confidence interval than the interval of the average prevalence of the European register (3.9 per 10,000 births). The basis prevalence of Saxony-Anhalt fits to the European prevalence. The current prevalence value however, lies far above this.

additional information:

Pregnancy outcome	3 x live births 2 x spontaneous abortion 5 x termination of pregnancy
Sex	5 x male 3 x female 2 x no indication
Number of isolated malformations /MCA	9 x MCA 1 x isolated

In case of six children/fetuses, the omphalocele was present in connection with a chromosomal disorder. 5 times omphalocele and malformations of the CNS or heart were detected sonographically between the 12th and 15th week of gestation. These pregnancies were terminated prematurely.

Malformation combinations (MCA) or superordinated syndromes detected:

- 4 x Edwards-Syndrom mit je 1 x:
 - exencephaly
 - nasofrontal encephalocele
 - AVSD
 - VSD
- lumbosacral spina bifida
- Wiedemann-Beckwith syndrome with: PFO at preterm infant
- dextrocardia, bicuspid aortic valve, PFO at fullterm infant
- blt. lung hypoplasia and triphalangeal thumbs, splenic malformation, myocardial hypertrophy, high philtrum, hypertelorism, broad nasal root, sandal gap left
- deletion of a chromosome segment

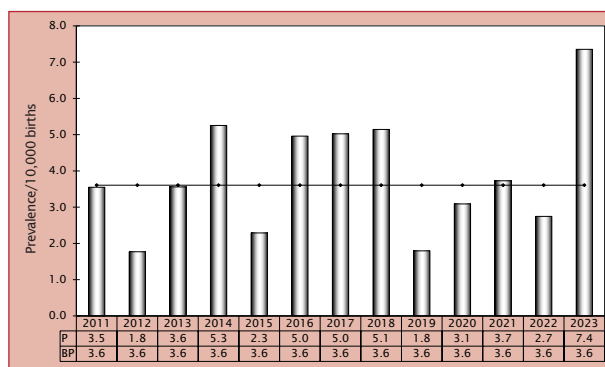


Fig. 37: Development of prevalence/10,000 births with omphalocele in Saxony-Anhalt since 2011

In 2023, one child/fetus with omphalocele was observed per 1,360 births in Saxony-Anhalt.

10.31 Gastroschisis (Q79.3)

Saxony-Anhalt	Year of 2023		
	Number	Prevalence/ 10,000 births	Comparison to basis prevalence
	5	3.68	↔
EUROCAT (Full members)	Reporting period 2011-2022		
	Basis prevalence/ 10,000 births	Confidence interval (CI 95 %)	
	3.46	2.70 - 4.37	
EUROCAT (Full members)	Period 2011-2022		
	Prevalence/ 10,000 births	Confidence interval (CI 95 %)	
	2.5	2.4 - 2.6	

After two years with very low prevalence rates (2021:1.2 per 10,000 births; 2022: 1.4 per 10,000 births) the Saxony-Anhalt prevalence of gastroschisis shows in 2023 again an **annual prevalence (3.7 per 10,000 births)**, which lies, in contrast to the basis prevalence (2011-2022: 3.5 per 10,000 births), inconspicuously within the normal range.

The confidence interval of the basis prevalence of Saxony-Anhalt for gastroschisis lies above the average prevalence provided by EUROCAT (2011-2022: 2.5 per 10,000 births). This year's prevalence value of Saxony-Anhalt is therefore also above the upper confidence limit of the prevalence stated by EUROCAT.

additional information:

Pregnancy outcome	5 x live births
Sex	3 x male 2 x female
Number of isolated malformations /MCA	1 x MCA 4 x isolated

Gastroschisis was seen four times during prenatal ultrasound screening at the beginning of the 2nd trimester. In one case it was immediately detected postnatally after an uncomplicated pregnancy.

Malformation combinations (MCA) or superordinated syndromes detected:

- VSD

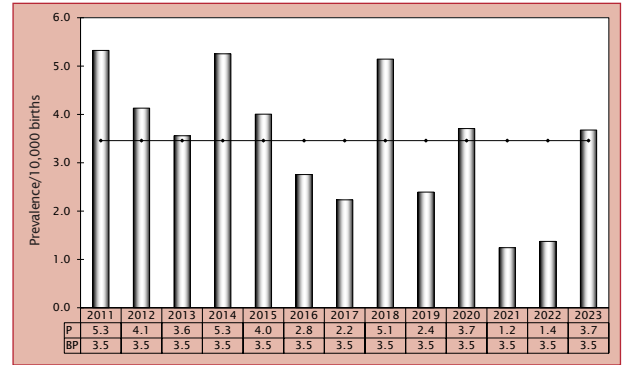


Fig. 38: Development of prevalence/10,000 births with gastroschisis in Saxony-Anhalt since 2011

In 2023, one child/fetus with gastroschisis was observed per 2,720 births in Saxony-Anhalt.

10.32 Prune-Belly syndrome (Q79.4)

Saxony-Anhalt	Year of 2023		
	Number	Prevalence/10,000 births	Comparison to basis prevalence
	0	0.00	↓
	Reporting period 2011-2022		
Basis prevalence/10,000 births		Confidence interval (CI 95 %)	
0.79		0.45 - 1.28	
EUROCAT (Full members)	Period 2011-2022		
	Prevalence/10,000 births	Confidence interval (CI 95 %)	
	0.1	0.1 - 0.2	

The prune-belly syndrome or sequence is a malformation that occurs only occasionally. Since the beginning of the reporting period the indicator malformation has only been registered 16 times. In the recent and in the current year (2022, 2023), it was not detected at all in Saxony-Anhalt. At the beginning of the 2000s, there was a maximum prevalence value registered of the prune-belly sequence (3.0 per 10,000 births). Later, prevalence rates of less than 1.3 per 10,000 births were always found in the reporting period. The normal range of the basis prevalence of 0.8 per 10,000 births (2011-2022) includes up to two cases per year, depending on the number of births.

A comparison of the confidence interval of the basis prevalence of Saxony-Anhalt with that of the European register (2011-2022: 0.1 per 10,000 births) shows, that this of Saxony-Anhalt is far above. However, the current prevalence lies below this.

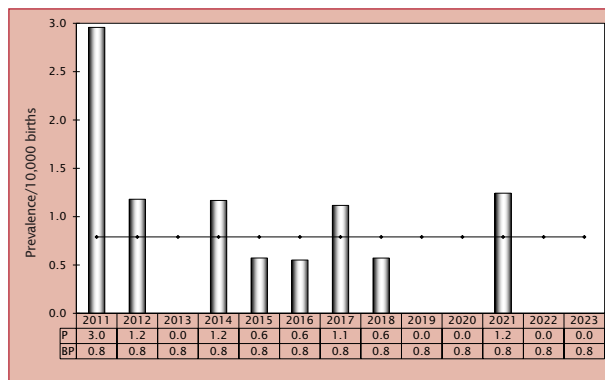


Fig. 39: Development of the prevalence/10,000 births with Prune belly syndrome in Saxony-Anhalt since 2011

In 2023, no children/fetuses with prune belly syndrome were observed in Saxony-Anhalt.

10.33 Down's Syndrom - Trisomy 21 (Q90.)

Saxony-Anhalt	Year of 2023		
	Number	Prävalenz/ 10.000 Geburten	Comparison to basis prevalence
	28	20.59	↔
	Reporting period 2011-2022		
Basis prevalence/ 10,000 births		Confidence interval (CI 95 %)	
20.84		18.90 - 22.93	
EUROCAT (full members)	Period 2011-2022		
	Prevalence/ 10,000 births	Confidence interval (CI 95 %)	
	25.0	24.6 - 25.3	

Down syndrome has a basis prevalence of 20.8 per 10,000 births (2011-2022), and is therefore one of the three most frequently occurring major malformations (Chapter 9). For the third year in a row, with 28 affected births (2023: **20.6 per 10,000 births**), an **annual prevalence** within the middle of the basis prevalence (2011-2022: 20.8 per 10,000 births) was calculated. The prevalence calculation only for the 422 live births during the reporting period (2011-2022) results in 9.5 per 10,000 live births. Of these children, 15 (3.6 %) died before their 6th birthday.

When comparing the basis prevalence of Down syndrome of Saxony-Anhalt with the European overall prevalence it can be seen that the confidence interval specified by EUROCAT (2011-2022: 25.0 per 10,000 births) is considerably higher than the interval of Saxony-Anhalt. Since the probability of the occurrence of trisomy 21 increases with the age of the pregnant women, it can be assumed that the higher European prevalence values result from the higher maternal age at birth (EU average 2013-2021: 30.7 years*) compared to the maternal age of Saxony-Anhalt (2013-2021: 29.6 years).

By the year of birth 2023, only around 40% of those affected by Down syndrome were live births (with an average 36.8 WOG; median 37.0 WOG) were born. 17 pregnancies were terminated on average at 17.1 WOG (median 17.0 WOG, minimum 12th WOG, maximum 17th WOG). The first diagnosis was made in case of the terminated pregnancies at Ø 14.9 WOG (median 15.0 WOG).

additional information:

Pregnancy outcome	11 x live births 17 x termination of pregnancy
Sex	15 x male 12 x female 1 x no indication
Number of isolated malformations /MCA	10 x MCA 18 x isolated

Malformation combinations (MCA) or superordinated syndromes detected:

- Tetralogy of Fallot
- blt. cleft of the hard and soft palate, VSD, blt. sound conduction disorder
- embryofetopathy due to addictive drugs, AVSD, ASD II, stenosis of the pulmonary artery at full term infant
- AVSD, ASD II, VSD, small tongue, prominent nuchal fold
- AVSD, VSD, Meckel's diverticulum, mandibular retrognathia
- AVSD, DUP blt.
- AVSD
- ASD II, persistent left superior vena cava, tricuspid insufficiency, pulmonary vein stenosis
- ASD II, broad nasal root
- duodenal stenosis

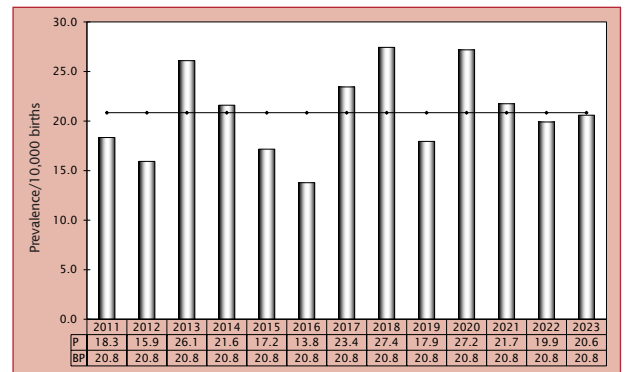


Fig. 40: Development of prevalence/10,000 births with Down's syndrome in Saxony-Anhalt since 2011

In 2023, one Down's syndrome per 486 births was registered in Saxony-Anhalt.

* Source: https://ec.europa.eu/eurostat/databrowser/view/DEMO_FORDAGEC_custom_8092017/default/table
eurostat-Titel: Live births by mother's age and birth order

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

Saxony-Anhalt	Year of 2023		
	Number	Prevalence/10,000 births	Comparison to basis prevalence
	2	1.47	↔
	Reporting period 2011-2022		
Basis prevalence/10,000 births		Confidence interval (CI 95 %)	
1.78		1.25 - 2.46	
EUROCAT (Full members)	Period 2011-2022		
	Prevalence/10,000 births	Confidence interval (CI 95 %)	
2.3		2.2 - 2.4	

Patau syndrome occurred with very high prevalence rates in the last two years (2021: 5.0 per 10,000 births; 2022: 4.1 per 10,000 births), and returned to a normal frequency in the current year. The **annual prevalence** (2023: **1.5 per 10,000 births**), which is calculated from two affected fetuses this year is similar to the basis prevalence of 1.8 per 10,000 births (2011-2022).

At the beginning of the reporting period, from 2011 to 2014, the prevalences are consistently below the basis prevalence, in the years 2015-2019 mostly in the medium normal range or just below the confidence interval of the basis prevalence. This is followed by the peak in the years 2021 and 2022. Over the following 14-year period (2010-2023), it results in a trend analysis (Chapter 10.38) which shows a significant upward trend with a percentage change of 21.26 (CI 4.85 % to 45.92 %) with a non-effective ($p > 0.01$) non-linear proportion. This trend remains under observation. It is possible that due to increasingly earlier diagnosis, improved diagnostic techniques (3D/4D ultrasound) or the increased use of new methods (NIPT), Patau syndrome will be diagnosed more frequently in the future.

The interval of the overall prevalence determined by EUROCAT of the European malformation register (2011-2022: 2.3 per 10,000 births) is narrower due to the observed, much larger population than the prevalence interval of the basis prevalence of Saxony-Anhalt and is covered by the upper edge of the wider interval.

additional information:

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

In two cases the amniocentesis in the 13th and 16th week of gestation revealed a trisomy of chromosome 13. The prenatal ultrasound screening showed serious malformations.

Malformation combinations (MCA) or superordinated syndromes detected:

- Megacisterna magna, tricuspid insufficiency, pulmonary valve stenosis

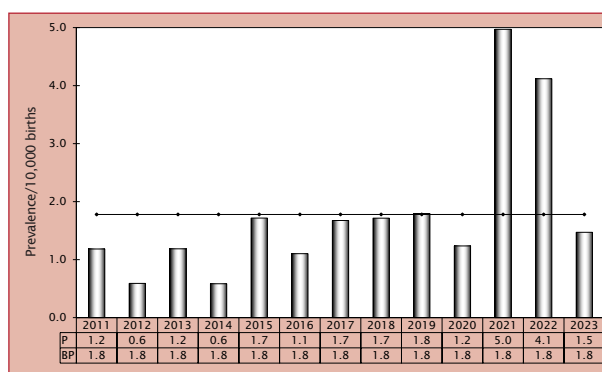


Fig. 41: Development of prevalence/10,000 births with a Patau syndrome in Saxony-Anhalt since 2011

In 2023, one child/fetus with Patau syndrome was observed per 6,800 births in Saxony-Anhalt.

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

Saxony-Anhalt	Year of 2023		
	Number	Prevalence/ 10,000 births	Comparison to basis prevalence
	9	6.62	↑
EUROCAT (Full members)	Reporting period 2011-2022		
	Basis prevalence/ 10,000 births	Confidence interval (CI 95 %)	
	4.35	3.49 - 5.35	
EUROCAT (Full members)	Period 2011-2022		
	Prevalence/ 10,000 births	Confidence interval (CI 95 %)	
	6.3	6.1 - 6.4	

The third most common chromosomal trisomy, Edwards' syndrome, was recorded nine times in Saxony-Anhalt in 2023. It was registered significantly more common than expected. The current **annual prevalence** (2023: **6.6 per 10,000 births**) of the indicator malformation does not quite reach the maximum value of the prevalence of 2018 (7.4 per 10,000 births), but exceeds the basis prevalence (2011-2022: 4.3 per 10,000 births) significantly.

The prevalence of Saxony-Anhalt is below the overall European prevalence reported by EUROCAT (2011-2022: 6.3 per 10,000 births). The very high annual prevalence of Saxony-Anhalt for Edwards' syndrome in 2023 is also high compared to the European prevalence.

additional information:

Pregnancy outcome	9 x termination of pregnancy
Sex	7 x male 2 x no indication
Number of isolated malformations /MCA	8 x MCA 1 x isolated

All nine fetuses were diagnosed between the 10th and 16th week of gestation during prenatal ultrasound examinations. Severe malformations such as omphalocele, AVSD or malformations of the CNS, but also soft markers which are typical of Edwards' syndrome, such as hygroma colli or hypoplastic nasal bone occurred.

Malformation combinations (MCA) or superordinated syndromes detected:

- 4 x omphalocele and 1 x each
 - exencephaly
 - nasofrontal encephalocele
 - AVSD
 - VSD
- Dandy-Walker syndrome with AVSD
- univentricular heart, ductus venosus agenesis, aortic valve stenosis
- VSD
- clubfoot

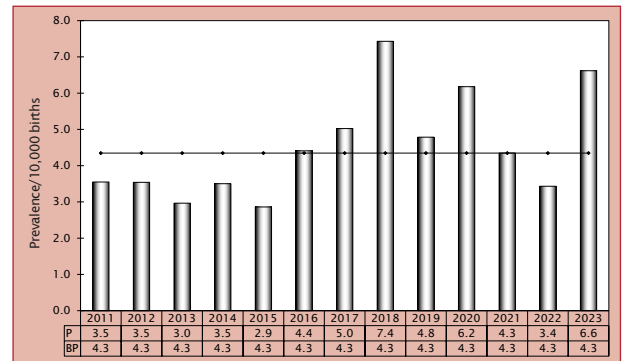


Fig. 42: Development of prevalence/10,000 births with Edwards syndrome in Saxony-Anhalt since 2011

In 2023, one Edwards syndrome per 1,511 births was registered in Saxony-Anhalt.

10.36 Turner syndrome (Q96.)

Saxony-Anhalt	Year of 2023		
	Number	Prevalence/10,000 births	Comparison to basis prevalence
	4	2.94	↔
	Reporting period 2011-2022		
Basis prevalence/10,000 births		Confidence interval (CI 95 %)	
2.22		1.62 - 2.97	
EUROCAT (Full members)	Period 2011-2022		
	Prevalence/10,000 births	Confidence interval (CI 95 %)	
	2.6	2.5 - 2.7	

As in the previous year, the indicator malformation Turner syndrome, also known as monosomy X occurred 4 times in Saxony-Anhalt in 2023. The resulting **annual prevalence** (2023: **2.9 per 10,000 births**) is slightly below the upper limit, but is still located within the confidence interval of the basis prevalence (2011-2022: 2.2 per 10,000 births).

The basis prevalence of Saxony-Anhalt for the years 2011-2022 and the European prevalence provided by EUROCAT (2011-2022: 2.5 per 10,000 births) are similarly high, whereby the Saxony-Anhalt confidence interval has a much wider range.

additional information:

Pregnancy outcome	1 x live birth 2 x spontaneous abortion 1 x termination of pregnancy
Sex	4 x female
Number of isolated malformations /MCA	2 x MCA 2 x isolated

The indication of Turner syndrome was found 4 times already prenatally. In two cases, which had developed hydrops fetalis, each of the pregnancies ended spontaneously in the 21st week of gestation. The live birth and the fetus of the terminated pregnancy were affected by severe cardiac malformations.

Malformation combinations (MCA) or superordinated syndromes detected:

- Preductal aortic isthmus stenosis, bicuspid aortic valve, shield thorax, pterygium colli, blt. hypoplastic lungs, kidneys and ovaries, blt. pes calcaneovarus congenitus, laterally sloping eyelid axes, low-set and dysplastic ears, mandibular retrognathia, saddle nose, wide nipple distance
- Preductal aortic isthmus stenosis, pulmonary valve stenosis, aortic hypoplasia, PFO at full term infant

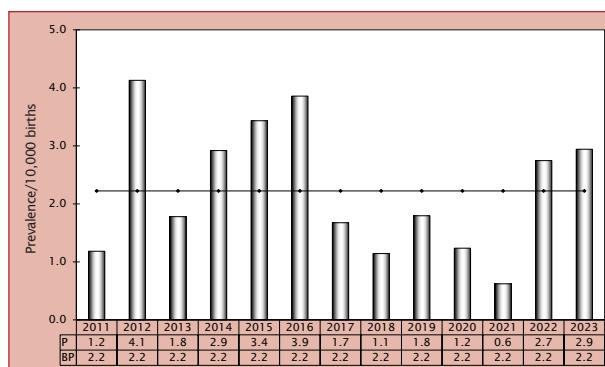


Fig. 43: Development of prevalence/10,000 births with Turner syndrome in Saxony-Anhalt since 2011

In 2023, one Turner syndrome per 3,400 births was registered in Saxony-Anhalt.

10.37 Klinefelter syndrome/male gonosome anomalies (Q98.)

Saxony-Anhalt	Year of 2023		
	Number	Prevalence/10,000 births	Comparison to basis prevalence
	0	0.00	↓
	Reporting period 2011-2022		
Basis prevalence/10,000 births		Confidence interval (CI 95 %)	
0.94		0.56 - 1.47	
EUROCAT (Full members)	Period 2011-2022		
	Prevalence/10,000 births	Confidence interval (CI 95 %)	
	no information	no information	

The indicator malformation Klinefelter syndrome/male gonosomal anomaly was not detected in Saxony-Anhalt in the current year (2023), similar to the majority of the years of the reporting period (2011-2022). Since 2011, a total of only 15 children and four fetuses have been diagnosed with Klinefelter syndrome or a male gonosomal anomaly. The maximum prevalence of the reporting period lies at a value of 2.4 per 10,000 births (2013).

Based on 105,770 live and stillborn boys (2011-2022), the calculation of the basis prevalence results in a value of 1.80 per 10,000 boys (CI 1.08-2.81).

EUROCAT does not provide European-wide prevalence values for the indicator malformation Klinefelter syndrome/male gonosomal anomaly.

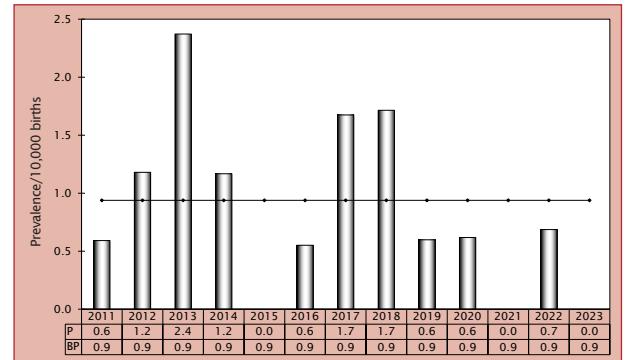


Fig. 44: Development of prevalence/10,000 births with Klinefelter syndrome/male gonosome anomalies in Saxony-Anhalt since 2011

In 2023, no children/fetuses with Klinefelter syndrome/male gonosome abnormalities were observed in Saxony-Anhalt.

10.38 Trend analysis of indicator malformations

Chapter 10.1 to 10.37 of the annual report are dealing with the absolute and relative frequency of indicator malformations as well as with the comparison of the current prevalences (2023) of Saxony-Anhalt with the basis values of the reporting period (2011-2022), both for the Federal State and European-wide. The definitions of the 37 indicator malformations, which are based on those of the ICBDSR (International Clearinghouse for Birth Defects Surveillance and Research) are presented in Chapter 10.0. In chapter 10.38, a trend analysis is used to assess the temporal development of the frequencies of the indicator malformations (2010 to 2023).

In case of 173 children/fetuses (1.27% of 13,599 births) of the 2023 birth cohort, at least one indicator malformation was detected, which means that the basis prevalence 2011-2022 of Saxony-Anhalt (1.42%, CI 1.37-1.48) is significantly undercut. 84 children/fetuses were only affected by one indicator malformation, 89 had other malformations (MCA), including 14 children/fetuses with two and three children/fetuses with three indicator malformations. During the period of 2011 to 2021, 73.9% of children/fetuses with indicator malformations were live births. In 2023, only 68.2% (118 children) were live

births. Three children died in the first three days of life in 2023. Five fetuses were spontaneously aborted. The pregnancies of 50 fetuses (28.6 %) were terminated prematurely. This proportion is higher than in the entire reporting period (2011- 2022: 23,5 %).

The aim of the below presented trend analysis is to visualize long-term developments with regard to the occurrence of malformations. The strength and orientation of the changes of the indicator malformation prevalences is examined over the period from 2010-2023.

The trend estimation is only carried out for indicator malformations that meet the basis requirement that, in the tested time period, the expected value for the malformation is at least five and the observed value is at least two. Indicator malformations belong, for the most part, to the rare diseases. In order to fulfill the precondition for the test of change in case of small frequencies, two years are combined into one interval and the trend is analyzed.

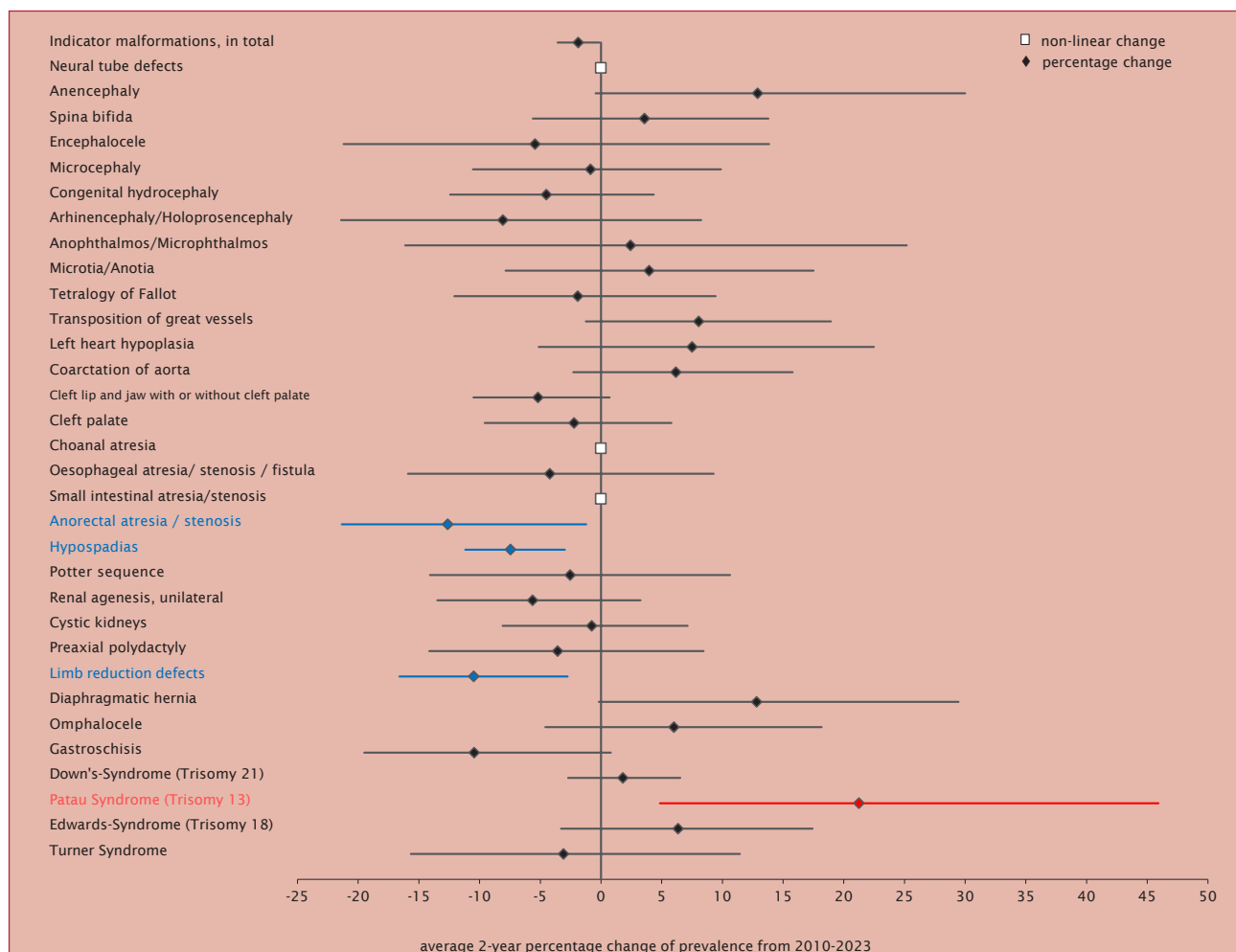


Fig. 45: Trend analysis 2009 to 2022 with average percentage change of two-year prevalence (95% CI)

Figure 45 on page 64 and the table on this page show the estimated average percentage changes in the two-year prevalence of the indicator malformations for which the above-mentioned initial conditions apply. 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, choanal atresia and small intestinal atresia/stenosis. 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 be observed for Patau syndrome (trisomy 13) 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, hypospadias and reduction malformations of the extremities.

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	-1.89	-3.58 to -0.13
Anencephaly	12.90	-0.44 to 30.00
Spina bifida	3.57	-5.61 to 13.79
Encephalocele	-5.43	-21.20 to 13.85
Microcephaly	-0.87	-10.55 to 9.88
Congenital hydrocephaly	-4.51	-12.43 to 4.34
Arhinencephaly/Holoprosencephaly	-8.09	-21.42 to 8.25
Anophthalmia/Microphthalmia	2.44	-16.14 to 25.19
Microtia/Anotia	3.97	-7.86 to 17.50
Tetralogy of Fallot	-1.92	-12.08 to 9.45
Transposition of great vessels	8.04	-1.26 to 18.94
Left heart hypoplasia	7.51	-5.13 to 22.48
Coarctation of aorta	6.18	-2.28 to 15.79
Cleft lip with cleft palate	-5.20	-10.50 to 0.70
Cleft palate	-2.22	-9.59 to 5.81
Oesophageal atresia/stenosis/fistula	-4.22	-15.90 to 9.28
Anorectal atresia/stenosis	-12.62	-21.35 to -1.22
Hypospadias	-7.44	-11.18 to -2.98
Potter sequence	-2.55	-14.10 to 10.63
Renal agenesis, unilateral	-5.63	-13.48 to 3.26
Cystic kidney	-0.77	-8.10 to 7.14
Preaxial polydactyly	-3.57	-14.15 to 8.44
Limb reduction defects	-10.47	-16.60 to -2.75
Diaphragmatic hernia	12.82	-0.19 to 29.46
Omphalocele	6.00	-4.59 to 18.18
Gastroschisis	-10.45	-19.51 to 0.81
Down's-Syndrome	1.80	-2.70 to 6.54
Patau Syndrome (Trisomy 13)	21.26	4.85 to 45.92
Edwards Syndrome (Trisomy 18)	6.35	-3.30 to 17.42
Turner Syndrome	-3.10	-15.66 to 11.44

13 Summary

The Monitoring of Congenital Malformations receives nationwide data about children and fetuses. In this way, 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 compiled every year from the data provided to the Monitoring of Congenital Malformations. The reported information is categorized and presented together with the official birth figures of the State Statistical Office of Saxony-Anhalt. In this current annual report, the focus lies on data of the years 2011 to 2022 and the most recent complete year 2023. To estimate the prevalences of Saxony-Anhalt, Europe-wide data of EUROCAT is shown. For years, Saxony-Anhalt has been the only Federal State in which comprehensive population-related malformation data is collected and analyzed.

The evaluations of the annual report are based on a population of 13,599 births in the year 2023 in Saxony-Anhalt (Chapter 1). In addition, data of 53 terminations of pregnancy and 10 spontaneous abortions from the 16th week of gestation are included into the analyses.

In 2023, an average of 37 children were delivered per day in Saxony-Anhalt. The number of live births (2023: 13,550) is the lowest since 1990. In the reporting period (2011-2022), there were 202,601 live births in total (Ø 16,883 children per year).

According to the Federal Statistical Office (www.destatis.de), 692,989 children were live births in Germany in 2023, 6.2% fewer than in 2022 (738,819). The birth rate fell to 1.35 children per woman. Around 2.0% of all newborns in Germany come from Saxony-Anhalt.

49 stillbirths, which are indicated by the State Statistical Office of Saxony-Anhalt for the year 2023 correspond to a ratio of one stillbirth to 277 live births. In the reporting period (2011-2022), the ratio is one stillbirth per 234 live births.

In 2023, 485 children/fetuses (3.57% of all births) are affected by major malformations. This shows a prevalence well below the confidence interval of the basis prevalence (2011-2022: 3.88%, CI 3.79-3.96%; 202,461 births). 423 children/fetuses with major malformations (87.2%) were live births. Seven died in the first year of life. In 10.9% of all children/fetuses with major malformations, the pregnancy was terminated. This proportion corresponds roughly to that of the years 2011-2022 (10,2%). Spontaneous abortions and stillbirths in children/fetuses with major malformations in 2023 represent a combined share of 1.8%. (Chapter 6).

The two cardiac malformations VSD and ASD are also the most common single diagnoses in 2023 (0.99% and 0.46% of births respectively). Place three to five are followed, as in the last three years, by Down syndrome (0.21% of births) with a frequency in the normal range. Dilated uropathy II.-IV. degree/ureterocele and hearing loss (Chapter 9) are following slightly lower.

Chapter 10 provides an overview about the occurrence of 37 clearly defined indicator malformations. In the year of birth 2023, 173 children/fetuses were affected by an in-

dicator malformation. Neural tube defects, encephalocele, microtia/anotia, TGA, omphalocele and Edwards syndrome show a higher prevalence than the corresponding basis prevalence. Lower annual prevalence rates result for hydrocephaly, cleft lip and cleft lip and palate, cleft palate, esophageal atresia/stenosis/fistula, small intestinal atresia/stenosis, rectal and anal atresia/stenosis, hypospadias, cystic kidneys, ectropomy of the urinary bladder, reduction malformations of the extremities, diaphragmatic hernia, prune-belly sequence and Klinefelter syndrome. For Patau syndrome, there is an increasing trend for 2010-2023 (B=21.26%).

In 2023, the Monitoring of Congenital Malformations registered 53 malformation-related terminations of pregnancy, which took place at Ø 18.0 WOG. The latest pregnancy was terminated in case of fetuses with multiple anomalies and other malformations (20.8%) at 20.4 weeks of gestation. In case of chromosomal aberrations (54.7%) the termination took place at Ø 16.4 weeks of gestation and in case of CNS malformations (24.5%) at Ø 19.5 weeks of gestation (Chapter 12).

Chapter 11 contains syndromes, multiple and complex malformations that were discovered in 106 children/fetuses born in 2023. Chromosomal aberrations were diagnosed 47 times, frequently Down syndrome (28 times). In 29 children/fetuses, genetically determined/co-determined diseases and microdeletions were diagnosed. Seven children/fetuses had a sequence, association or complex. 13 children were affected by a fetopathy, ten children/fetuses suffered from a congenital infection.

In the first part of the special topic (Chapter 14), the requirements of coding of congenital anomalies with a view to the future (ICD11) are presented. A comparison of the validity of existing congenital anomaly registrations is drawn. The second part shows the different results of an AI-supported query on the use of AI technology in the diagnosis of malformations, depending on diagnosis and treatment.

For the 2023 birth cohort, the monitoring of congenital malformations received 1,670 reports about 1,304 children/fetuses (chapter 4). In 485 children/fetuses, at least one major malformation was described, a further 229 children/fetuses had minor malformations or anomalies. Data about 590 children without malformations was registered. In addition to the data about children/fetuses with congenital malformations and anomalies as well as genetically caused diseases, data of children without malformations is important, as in scientifically based evaluations, risks can only be assessed by comparison (case-control study design).

With the help of many colleagues from different medical institutions who have been voluntarily and unselfishly reporting congenital malformations for many years, a solid database has been created, which also served as basis for the 2023 annual report.

We would therefore like to express our sincere thanks to all our „senders“, in the confidence that we will !

14. Focus theme

14.1 International compatibility of coding - recording of malformations with the background of the ICD-11 introduction

In order to achieve an internationally comparable data collection it is important to use a standardized classification system. The ICD code is a globally recognized system with which medical diagnoses are uniformly named. ICD stands for “International Statistical Classification of Diseases and Related Health Problems”, in simple terms: “International Classification of Diseases”. In addition to the current version ICD-10, the new version ICD-11 came into force in January 2022. For a transitional period of five years, both versions can be used. Until the ICD-11 is introduced in Germany, coding will continue according to ICD-10 [1].

The worldwide introduction of ICD-10 has shown that the coding guidelines provided with the classification can improve the comparability of the collected data. For medical statistics and epidemiologic data that follow clear coding guidelines and that are synchronized with an annual update cycle of the classification, the international comparability of the data is high. For morbidity coding with ICD-10, many countries introduced individual coding guidelines. Nevertheless, the need to adapt the coding to national requirements (language) has triggered the different coding guidelines for ICD-10 and shows the need for a national definition of coding with a “translated” classification system [2].

After the ICD-11 was adopted in May 2019 by the WHA72 (72nd World Health Assembly) it came into force on January 01, 2022. Since then, the member states of the World Health Organization (World Health Organization, WHO) have been able to report their mortality data ICD-11-coded to the WHO. However, the German website of the Federal Institute for Drugs and Medical Devices (BfArM) states the following about the 11th revision: “Since it came into force on 01.01.2022, the ICD-11 is generally usable, however, the draft version of the ICD-11 in German cannot yet be used for licensing reasons. It is cur-

rently not possible to download the draft version of the ICD-11 in German or to obtain it in any other way.” [3].

Effective coding is essential for the programs of monitoring epidemiological data about congenital malformations, as the subsequent use of the data depends on the storage and retrieval of cases by using codes. Therefore, the coding process must be carefully considered. The main objective of coding is to represent the malformations accurately, completely and precisely. Coding procedures must take into account the objectives of monitoring. For example, programs that focus on research require different coding procedures than those that focus on linking data in the healthcare system (billing data). The coding of congenital malformations is associated with several challenges, including the need to distinguish cases with multiple malformations and syndromes, those with isolated malformations. In addition, there is a need for strategies of coding suspected malformations for which there is no confirmation available. The selection of a coding system by program is very important in regard to the usefulness of the data collected. Most programs use a variation of systems based on the International Statistical Classification of Diseases and Related Diagnoses (ICD) [4].

The purpose of coding congenital anomalies in the European network of malformation registration EUROCAT is to summarize the non-standardized text in such a way that the data can be used for monitoring and research purposes. Registries can encourage the use of standard definitions, diagnostic tests and clinical follow-up, but rarely mandate it and the coding system must allow different levels of precision and accuracy of the information provided by clinicians [5].

The purpose of a “classification system” in the sense we use this term, is to group abnormalities that have etiological or clinical characteristics in common. A balance



must be found between a) the “grouping” heterogeneous groups of anomalies and “dividing them so finely” that there are only a few cases in each group, and b) creating groups on the basis of a high precision and accuracy of diagnosis and coding and creating groups that take into account what can be found realistically available in most cases in medical records and regional or national databases [6].

Electronic health databases are increasingly being used to study the epidemiology of congenital anomalies (CA), although there are concerns about their validity. In the EUROlinkCAT project, data of eleven EUROCAT register was linked to electronic hospital discharge databases. The coding of CA in electronic hospital databases was compared to (gold standard) codes in the EUROCAT re-

gisters. For the birth cohorts 2010-2014 all linked cases of live births with congenital anomalies and all cases identified in the hospital databases with a code for congenital anomalies children were analyzed. The registries calculated the sensitivity and the positive predictive value (positive predictive value (PPV) for 17 selected congenital anomalies. Afterwards, pooled estimates were then calculated for the sensitivity and PPV for each anomaly using random effects of meta-analyses. The remaining anomaly subgroup in the study showed low or heterogeneous sensitivity and PPV, suggesting that the information of the hospital database was incomplete and of varying validity. Electronic health databases cannot replace CA register but can be used as an additional source of data for CA register. CA register remain the most valid source of data for the epidemiological follow-up observation of CA [7].

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14.2 Advances in the detection of congenital anomalies: The integration of artificial intelligence into clinical applications

Introduction

Initial publications emphasize that the systematic analysis of important parameter and methods also in the field of classification of congenital malformations artificial intelligence (AI) has a high transformative potential to improve diagnostic accuracy and optimize clinical outcomes for patients [1]. Here is a first overview of the currently used AI techniques in conjunction with selected classifications of congenital anomalies. From device control to therapy recommendation and monitoring or in appointment communication everyday life is already being shaped by elements of AI in pediatric and adolescent radiology [2].

Congenital anomalies, defined as structural or functional abnormalities that are present at birth, regardless of when they are diagnosed (prenatal, postnatal, post mortem), represent a significant global health problem and contribute to high rates of infant morbidity and mortality [3]. These anomalies include a variety of diseases, including neural tube defects, cardiac malformations, cleft lip with cleft palate and genetic syndromes (EUROCAT Guide 1.5 https://eu-rd-platform.jrc.ec.europa.eu/eurocat/data-collection/guidelines-for-data-registration_en#in-line-nav-2) [4].

Early detection and accurate diagnosis are crucial for improving clinical outcomes and the development of effective treatment strategies. Recent advances in AI have also found their way into prenatal diagnostics and have presented innovative solutions to identify and assess congenital anomalies. Through the use of sophisticated algorithms and machine learning techniques, AI can analyze large amounts of data with remarkable speed and accuracy. This capability should support diagnostic precision and also risk stratification and personalized treatment planning [1, 5].

For this annual report, we ventured an experiment and asked AI about congenital malformations. We used the conversational search engine Perplexity AI. Citing used literature references and internet sources by the AI presents a problem. Therefore, references used here are added manually.



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AI techniques used in different categories of congenital anomalies

Categorie	Used AI techniques	Important results/outcomes
Neural tube defects	YOLOv3 CNN	AUC1 of up to 0.933 achieved; performance comparable to experienced sonographers [6, 7]
Congenital hydrocephalus	Deep Learning Model	Dice score ² of 0.901; provides rapid volumetric output for clinical decision making [8]
Ear anomalies	convolutional neural networks (CNN) ³	Accuracy rates of over 90 % of the severity classification of microtia [9]
Cardiac anomalies	Random forest model ⁴	showed strong predictive power for serious adverse cardiovascular events [10]
	Deep Learning Model ⁵	effective in ECG analysis for risk stratification [10]
	Support Vector Machines ⁶	high accuracy in identifying various cardiac abnormalities [11]
Craniofacial malformations	convolutional neural networks (CNN)	erzielte bis zu 95 % Genauigkeit bei der Diagnose von Lippen-Kiefer-Gaumenspalten (LKGS) [12]
	New AI approaches	Average efficiency of 81.6 % in the prenatal diagnosis of cleft palate [12]
Urogenital anomalies	Maschine learning model	high accuracy rates in the classification of the severity of hypospadias [13]
Chromosomenaberrationen	Maschine learning algorithms ⁷	Sensitivity rates of up to 99.2 % in the detection of trisomies 13, 18 and 21 [14, 15]

¹ AUC = AUC = Area Under the Curve, is a single scalar value between 0 and 1, which represents a snapshot of the model's performance.

² Dice Score, also known as Dice Similarity Coefficient, is a measure of the similarity between two data sets. The dice score ranges from 0, indicating no overlap, to 1, indicating perfect overlap.

³ Convolutional neural networks are a concept inspired by biological processes in the field of machine learning. CNNs are used in numerous artificial intelligence technologies, primarily in the machine processing of image and audio files.

⁴ Random forest is a commonly used machine learning algorithm that combines the result of multiple decision trees into a single result.

⁵ Deep learning models use artificial neural networks (e.g. CNN) to learn from data.

⁶ Support Vector Machines is a supervised machine learning algorithm that classifies data.

⁷ Machine learning models are already in clinical use with non-invasive prenatal testing (NIPT).

Case studies

Cerebral malformations

Neural tube defects (NRD) (including anencephaly, spina bifida, encephalocele), microcephaly, congenital hydrocephalus and arhinencephaly/holoprosencephaly are malformations that could be detected prenatally. Recent advances in AI technology have shown promising results in improving prenatal ultrasound diagnosis for these entities. Intelligent ultrasound systems can analyze the ultrasound images of the fetus to identify abnormalities more efficiently than traditional methods [1].

For example, the Prenatal Ultrasound Diagnosis AI Conduct System (PAICS) uses a YOLOv3 algorithm for convolutional neural networks (CNN) to detect patterns of fetal intracranial abnormalities. Macro-average AUCs (AUC = Area Under the Curve, is a single scalar value between 0 and 1 that represents a snapshot of the performance of the model) of 0.933 for internal validation and 0.902 for external validation were achieved. The performance was comparable to that of experienced sonographers, but required significantly less time per image (0.025 seconds versus 4.4 seconds) [7]. This study by Lin et

al. further supports the application of AI by demonstrating real-time detection of abnormal image patterns in standardized sonographic reference planes during screening for fetal intracranial malformations [7]. The particular challenges are fetal movements and the subtlety of some associated cerebral malformations. Current research is mainly focused on algorithmic performance; therefore, there is an urgent need for studies to explore the clinical utility of these AI models specifically for NRD detection [6]. Comprehensive models for integrating diagnostic imaging with clinical data are crucial for improving detection rates and ensuring accurate diagnoses. In the detection of hydrocephalus, a fully automated deep learning model for cerebral ventricle segmentation and volume calculation was developed, which achieved an overall Dice similarity coefficient⁸ of 0.901 and improved accuracy with external data (Dice score: 0.926). This model outperformed existing methods in terms of speed and accuracy and facilitated clinical decision making by providing fast and accurate volume calculations to assess ventricular shape [8, 16, 17].

Eye and ear anomalies

Ear malformations, such as microtia, are congenital anomalies ranging from minor structural irregularities of the pinna to the complete absence of the outer pinna (with or without atresia of the auditory canal). Microtia is characterized by the complexity of auricular anomalies. Despite their frequency, there is currently no reliable objective method of assessment and classification. Traditional classifications are often subjective and could lead to inconsistencies in diagnosis and treatment [18-20]. Recent advances in artificial intelligence, particularly through convolutional neural networks (CNNs), have shown promising results in improving diagnostic accuracy for congenital auricular anomalies. Studies have shown that different CNN models can effectively classify the severity of microtia based on clinical photographs [9, 21]. For example, CNN models, such as AlexNet and MobileNet, have achieved accuracy rates of over 90%, suggesting that CNN can provide objective assessments of microtia severity [22].

Cardiac malformations

Cardiac malformations present considerable challenges in early diagnosis and treatment due to their complexity and the risk of serious complications [11]. Tetralogy of Fallot belongs to the group of cyanotic vitia in which there is a mixing of the blood of the systemic and pulmonary circulation resulting in a bluish skin coloration [23]. Recent studies have used AI to improve the detection and classification of tetralogy of Fallot through modern imaging techniques, such as cardiovascular computed tomography (CT). A new neural network-based model (SOSPCNN) has been developed specifically for this purpose. This model is used to improve feature evaluation from complex image data. The SOSPCNN model showed impressive performance figures: Sensitivity 92.25 %, Specificity 92.75 %, Precision 92.79 %, Accuracy 92.50 % and an AUC value of 0.9587 [24]. These results show that the SOSPCNN method outperformed three modern approaches for the detection of tetralogy of Fallot and thus offers an improved diagnostic possibility [25]. In addition, AI models have been developed specifically for pediatric populations to predict serious adverse cardiovascular events associated with congenital cardiac malformations using routinely collected clinical data [10]. A random forest model⁹ trained on these pediatric data showed strong predictive power with AUC values of 0.81 for test datasets and 0.88 for training datasets [10].

Craniofacial malformations

Craniofacial malformations and cleft lip with cleft palate (LKGS) are complex congenital disorders that require precise diagnosis and treatment strategies, which should be customized to the individual patient. Deep learning algorithms have been used to improve the diagnosis of LKGS with high accuracy rates - up to 95% - in identifying cleft-specific features and severity levels through image analysis. Recent advances include new AI approaches with an average efficiency of 81.6% in the prenatal diagnosis of cleft palate through ultrasound images [12].

Genital anomalies

For genital anomalies, such as hypospadias (characterized by a false orifice of the urethra through the shortened urethra, a curvature of the penile shaft and an atypical, split, apron-like foreskin), machine learning models have been developed to classify severity based on clinical images with high accuracy rates [13, 26]. Subjectivity among examiners remains a challenge; therefore, standardization through AI can help reduce variability in assessments, while simultaneously diagnostic reliability is increased [13].

Renal anomalies

Renal anomalies, such as bilateral renal agenesis (Potter sequence or better oligohydramnios sequence) and unilateral renal agenesis (unilateral), can benefit from AI technologies that enable early detection through advanced imaging techniques [27]. Another promising area for the use of AI is acute kidney injury and the prediction of acute renal failure. Different AI models are used in prediction. The “area-under-the-receiver-operating-characteristic-curve” values (AUC value) achieved with these models diverge strongly and are influenced by various factors, such as the prediction period and the definition of acute renal failure. Most models show an AUC value between 0.650 and 0.900, with lower values for predictions further into the future and the application of the acute kidney injury network (AKIN) criteria. Although phenotyping has already succeeded in classifying patients into groups with different risks of increased mortality or need for renal replacement therapy, there is still a lack of etiologies and therapeutic consequences [28, 29].

Genetic syndromes

Genetic syndromes, such as Down syndrome (trisomy 21), Patau syndrome (trisomy 13), Edwards syndrome (trisomy 18) and Turner syndrome, will be increasingly analyzed using AI applications to evaluate genomic data associated with these diseases. Machine learning algorithms analyze genetic variants associated with these syndromes to identify effectively high-risk patients or populations [30, 31]. AI has demonstrated its potential through non-invasive prenatal testing methods (NIPT) using analysis of cell-free fetal DNA, showing sensitivity rates up to 99% in the detection of trisomies 13, 18 and 21 [14, 15]. Facial recognition algorithms have achieved an accuracy rate of up to 88% in recognizing Down syndrome characteristics based on facial features [15, 32, 33].

⁸ Dice Score, also known as Dice Similarity Coefficient, is a measure of the similarity between two data sets. The dice score ranges from 0, which means no overlap, to 1, which indicates a perfect overlap.

⁹ Random Forest is a commonly used machine learning algorithm that combines the result of multiple decision trees into one single result.



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Conclusion

Despite these promising advances in the applications of artificial intelligence to detect congenital anomalies, several challenges remain: The effectiveness of AI models depends on high-quality datasets that represent accurately diverse populations; many AI systems act as “black boxes”, making it difficult for clinicians to understand the decision-making process behind predictions. Continued

interdisciplinary collaboration between computer scientists and healthcare professionals is critical to overcome existing challenges and maximize the benefits of these technologies in clinical practice.

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16 Newborn Hearing Screening 2023

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 screening examination is the **Children's Directive of the Joint Federal Committee about the early detection of diseases at infants (Children's Directive)** with section **IV. Early detection of hearing disorders at newborns**.

The Children's 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
- 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's Directive **performance and results of the newborn hearing screening** as well as 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 2008):

- 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:

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Participating institutions

19 maternity clinics existed in Saxony-Anhalt in 2023. All these clinics offer a newborn hearing screening already for several years by TEOAE or AABR. These maternity clinics all participated in the newborn hearing screening in 2022.

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 midwives. 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 2023	Live births with screening ID in this period
AMEOS Klinikum Aschersleben	01.01.-31.12.2023	351
Helios Klinik Jerichower Land Burg	01.01.-31.12.2023	341
Städtisches Klinikum Dessau	01.01.-31.12.2023	813
Altmark-Klinikum Krankenhaus Gardelegen	01.01.-31.12.2023	145
AMEOS Klinikum Halberstadt	01.01.-31.12.2023	413
Krankenhaus St. Elisabeth und St. Barbara Halle (Saale)	01.01.-31.12.2023	1,693
Universitätsklinikum Halle (Saale)	01.01.-31.12.2023	1,223
Helios Klinik Köthen	01.01.-31.12.2023	393
Krankenhaus St. Marienstift Magdeburg	01.01.-31.12.2023	832
Klinikum Magdeburg	01.01.-31.12.2023	1,290
Universitätsklinikum Magdeburg	01.01.-31.12.2023	1,166
Carl-von-Basedow-Klinikum Saalekreis Merseburg	01.01.-31.12.2023	725
SRH Klinikum Naumburg	01.01.-31.12.2023	390
Altmark-Klinikum Krankenhaus Salzwedel	01.01.-31.12.2023	400
Helios Klinik Sangerhausen	01.01.-31.12.2023	563
Johanniter-Krankenhaus Stendal	01.01.-31.12.2023	685
Harzklinikum Dorothea Christiane Erxleben, Klinikum Wernigerode	01.01.-31.12.2023	922
Evangelisches Krankenhaus Paul Gerhardt Stift Wittenberg	01.01.-31.12.2023	611
SRH Klinikum Zeitz	01.01.-30.04.2023	83
Total number of live births with Screening-ID in Saxony-Anhalt		13,039
Further live births with Screening-ID: e.g. home births / births in a birthing centre resp., infants not born in Saxony-Anhalt	01.01.-31.12.2023	158
Tracked infants, in total		13,197

In total, **13,039 births** received a screening ID in their maternity clinic in Saxony-Anhalt in 2023 and data was transmitted to the tracking center. Therefore, these infants could participate in the hearing screening tracking. Furthermore, **158 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 **89 senders** in 2023.

Births with screening-ID and number of incoming results

2023	Infants with screening ID	Number of incoming results
Januar	1,109	2,417
Februar	1,053	914
März	1,109	1,958
April	1,002	1,131
Mai	1,132	1,301
Juni	1,097	1,379
Juli	1,221	1,422
August	1,170	1,453
September	1,169	1,464
Oktober	1,077	1,334
November	1,062	1,342
Dezember	996	1,062
total	13,197	17,177

Results (date October 2024)

All results that were reported to the hearing screening tracking centre about infants that were born in 2022 are included in our analyses 2023 of the newborn hearing screening:

10,616 infants out of **13,197 infants** with screening ID had an **unsuspicious newborn hearing screening result**. In **2,581 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 2,581 infants showed in **1,884 cases** an **unsuspicious result**. The remaining 697 infants had again a suspicious result.

249 of these 697 infants received a **complete paediatric audiological confirmation diagnostic**. According to our knowledge, **216 infants** did **not receive a confirmation diagnostic** and therefore are considered as **lost to follow-up**. In **18 cases**, the **further examinations** were **refused** by the parents.

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. 1,431 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, **2,513 letters resp. faxes** were forwarded in 2023 (one up to 11 letters/ faxes per infant). With reference to all infants with screening ID this corresponds to an average of 0.19 letters per infant. The tracking software also records telephone calls with the parents/legal guardians of the infants or with the treating doctors/practices/clinics as well as processing notes are logged. For the children with screening ID, which were born in 2022, a total of **1,448 telephone calls or log notes** were documented as part of the tracking measures (average 0.11 phone calls/log notes per infant).

148 infants did **not participate in the screening** (no reaction of parents to reminder letters or refusal of examination) and in **17 cases** the **status** is still **pending**, i.e. the examinations were not finished in Oktober 2024 or the tracking process still requires more time.

In **49 cases** the **tracking** was closed from our side **without any result**, because the parents could not be contacted, or the infant had died.

In total, the **follow up-examinations** of **262 infants** who were born in 2023 could be **completed** (confirmations diagnostics). Among 249 infants with a suspicious result, 13 infants had an unsuspicious first screening. Maybe these infants received a follow-up-examination due to present risk factors.

Within the follow-up examination, a **hearing disorder** could be **excluded** in **239 cases**. In **23 cases** a **hearing disorder was diagnosed** (13 x bilateral and 10 x unilateral hearing disorder) and the corresponding therapy was initiated. For instance, **12 infants** received a **hearing aid** (8 x hearing aids on both sides, 4 x hearing aid on one side).

17 Annual Report 2023 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

Cooperative direction of the screening-center:

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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.

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 distributed to the laboratories as it is presented in figure 1. The screening laboratory in Magdeburg handles the dry blood samples of all infants born in Saxony-Anhalt. Table 1 shows the frequencies 2021 of the screening target diseases in Germany¹ for a total number of 795,492 screened births.

Tab. 1: Frequency of diseases detected in screening in Germany 2021 (including mild forms)

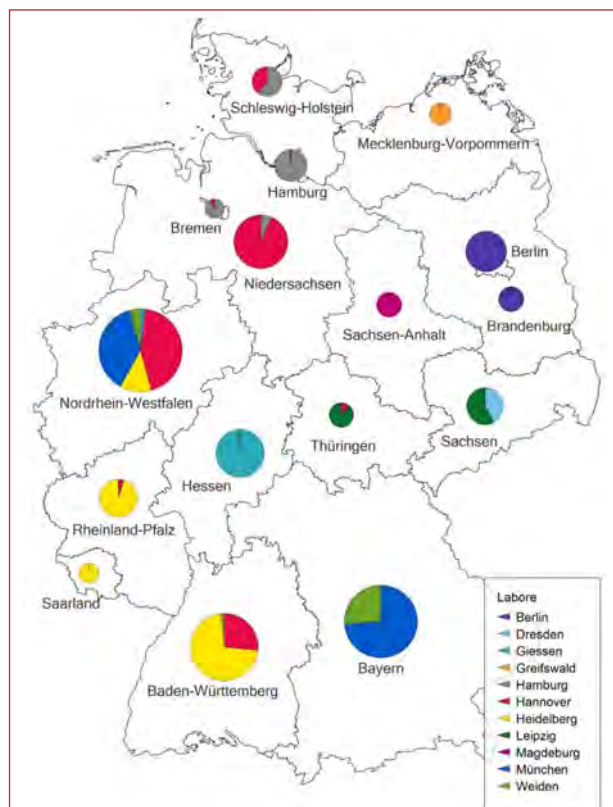


Fig. 1: Sample distribution of the screening centers in Germany¹

Disease	Confirmed cases	Prevalence
Congenital hypothyroidism (CH)	278	1 : 2,861
Congenital adrenal hypoplasia (CAH)	48	1 : 16,573
Biotinidase deficiency (incl. partial defects)	41	1 : 19,402
Galactosemia (classical)	11	1 : 72,317
Hyperphenylalaninemia (HPA) [of which phenylketonuria (PKU)]	120 [49]	1 : 6,629 [1 : 16,235]
Maple syrup urine disease (MSUD)	2	1 : 397,746
Medium-Chain-Acyl-CoA-Dehydrogenase deficiency (MCAD)	75	1 : 10,607
Long-Chain 3-OH-Acyl-CoA-dehydrogenase deficiency (LCHAD)	3	1 : 265,164
(Very-)Long-Chain-Acyl-CoA-dehydrogenase deficiency (VLCAD)	13	1 : 61,192
Carnitin-Palmitoyl-CoA-Transferase I deficiency (CPTI)	1	1 : 795,492
Carnitin-Palmitoyl-CoA-Transferase II deficiency (CPTII)	3	1 : 265,164
Carnitin-Acylcarnitin-Translocase deficiency (CACT)	-	
Glutaric aciduria type I (GA I)	8	1 : 99,437
Isovaleric acidemia (IVA)	9	1 : 88,388
Tyrosinemia type I	2	1 : 397,746
Cystic Fibrosis (CF) / CFSPID	164	1 : 4,851
Severe combined immunodeficiency	34	1 : 23,397
Spinal muscular atrophy (SMA) (from 10/2021)	29	
Sickle cell disease (as of 10/2021)	28	
total	826	1 : 915

Screening data 2023 of Saxony-Anhalt is outlined in the following:

Process quality

Process quality describes the process sequences and their evaluation by expert committees on the basis of predefined indicators.

Indicators of 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 must be examined further on
- confirmation diagnostics
 - diagnostics type
 - diagnostics period
- 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 infants 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. These blank cards should be sent to the laboratory to support the tracking process.

The coverage rates of Saxony-Anhalt were as following for the year 2023:

According to the Federal Statistical Office 13,550 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	13,053
Non-resident in Saxony-Anhalt	11
Screening of children living in Saxony-Anhalt	13,042

The discrepancy between the number of live births and screened infants with residence in Saxony-Anhalt amounts to 508.

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 re-

sidence. 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	412
Blank card: infant deceased/ stillbirth	6
Blank card: refusal of early taking	291
Blank card: transfer to another hospital	37
Blank card: screening refused by parents	37
Screening took place	323

As 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	First screening < 36h or < 32 WOG
Requested	359
Received at own laboratory	305

WOG = weeks of gestation

Examination numbers, recall rates and assured cases

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

Tab. 5: Recall-rate 2023 and diagnosed patients with a metabolic disease in reference to 13,053 screening examinations (includes also early withdrawal < 36 h and preterm births < 32 WOG), prevalence 1999-2022

Target disease incl. all forms of disease	Number of recalls* 2023	Assured cases 2023	Prevalence in Saxony-Anhalt 1999-2022
Hypothyroidism (CH)	54	8	1 : 4,142
Phenylketonuria (PKU/ HPA)	8	2	1 : 5,376
Galactosemia (classical)	1	1	1 : 126,325
Biotinidase deficiency	1	1	1 : 95,763
Adrenogenital syndrome (AGS) ^I	26	2	1 : 16,358 ^I
Medium-Chain-Acyl-CoA-Dehydrogenase deficiency ^{II} (MCAD) ^{II}	-	-	1 : 11,266 ^{II}
Long-Chain 3-OH-Acyl-CoA-dehydrogenase deficiency ^{II} (LCHAD) ^{II}	-	-	1 : 76,610 ^{II}
(Very-)Long-Chain-Acyl-CoA-dehydrogenase deficiency ^{II} (VLCAD) ^{II}	1	0	1 : 127,684 ^{II}
Maple syrup urine disease (MSUD) ^{II}	-	-	
Carnitin-Palmitoyl-CoA-Transferase I and II deficiency (CPTI) ^{II}	-	-	
Carnitin-Acylcarnitin-Translocase deficiency (CACT) ^{II}	-	-	
Glutaric aciduria type I (GA I) ^{II}	-	-	
Isovaleric acidaemia (IVA) ^{II}	3	-	
Mucoviscidosis ^{III}	11	2	1 : 5,361 ^{III}
Tyrosinemia type I ^{IV}	2	0	1 : 78,782 ^{IV}
Severe combined immunodeficiencies (SCID) ^V	11	0	
5q-associated spinal muscular atrophy (SMA) ^{VI}	3	2	1 : 30,000 ^{VI}
Sickle cell disease (SCD) ^{VI}	4	1	1 : 30,000 ^{VI}
Other ^{II}	-	-	

* 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 adrenogenital syndrome (AGS) since 1997

^{II} Enlarged screening (TMS) since 05/2001

^{III} Screening for mucoviscidosis since 09/2016

^{IV} Screening for tyrosinemia type I since 04/2017

^V SCID since 08/2019

^{VI} 5q-SMA and SCD since 10/2021

Process times

Point of taking blood samples

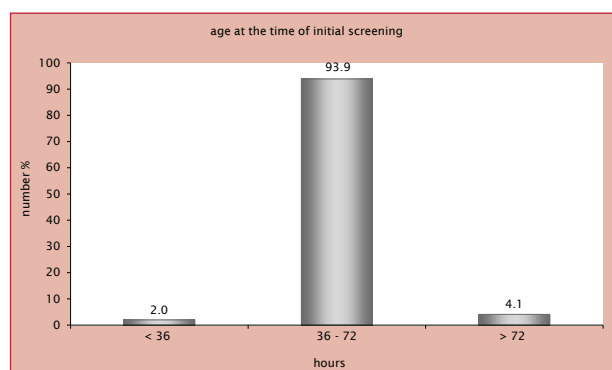


Fig. 2: Age at point of blood taking for first screening

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 93.9 % (2022: 93.5 %) of all cases. At a total number of 6.1%, the taking of blood samples took not place within the required period of time (2022: 6.7%).

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 19,5 % (2022: 19,6 %) of all transmittals reached the laboratory more than three days after the blood taking. On average, samples from 21 clinics reach the laboratory within the required time window (table 6). Postal transport times are longer than they were ten years ago, but they have not deteriorated further in the last three years.

Although there were dry blood cards that only arrived at the laboratory after more than ten days, the average transportation times were within the required range for all clinics.

Since every delayed blood collection or every prolonged postal route means a potential (life) risk for the concerned infants, the laboratory tries to improve the quality of the blood collection by means of training events (letters, training events) to sensitize hospitals about this important issue. The main cause is certainly the sending of dried blood samples via private mail carriers. We urgently recommend sending the samples directly to the screening laboratory mailbox by Deutsche Post. The following instructions should 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 as soon as possible
- do not send to the hearing screening tracking center

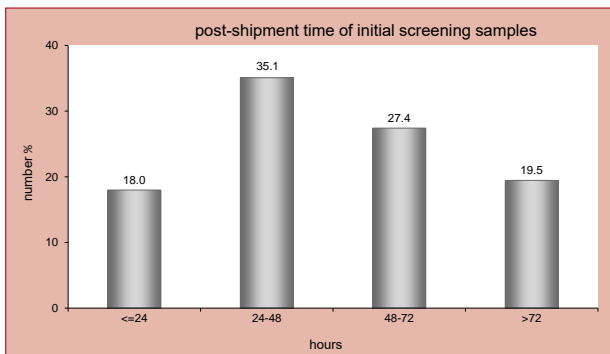


Fig. 3: Post-dispatch time of the dry blood cards (first screening) Time from blood collection to arrival at the laboratory

Transmission of Results

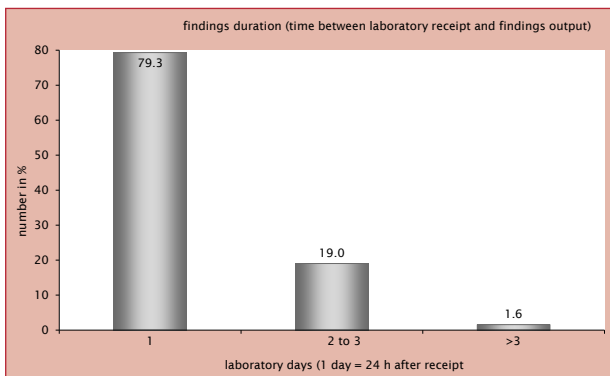


Fig. 4: Duration of findings transmission

Tab. 6: Post-dispatch time of dry blood cards per sending hospital (average value of all wards of a hospital), comparison 2023 to 2015

Maternity clinic	Average shipping time Shipping time (in hours)	
	2023	2015
Magdeburg St. Marienstift*	20	12
Magdeburg Universitätsklinikum*	20	29
Magdeburg Klinikum*	26	25
Stendal	45	46
Salzwedel	48	45
Halle St. Elisabeth und St. Barbara	49	50
Naumburg	50	41
Gardelegen	51	41
Zeitz	53	49
Aschersleben	56	50
Wernigerode	56	50
Köthen	57	49
Merseburg	59	51
Burg	59	44
Halle Universitätsklinikum	60	53
Sangerhausen	61	50
Dessau-Roßlau	65	44
Lutherstadt Wittenberg	69	56

*Clinic with a courier service

Figure 4 shows the duration of laboratory analysis of all initial screening examinations. 20,6% of all findings, that leave the laboratory after more than 24 hours, essentially reflect the prolonged duration of the findings due to the cystic fibrosis screening (3-stage screening including mutation analysis), internal repetition of analyses in case of implausibility and disruptions in the laboratory process (equipment maintenance, repairs, etc.).

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

Cystic fibrosis screening

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

	2023	2022
Screening, in total	13,053	13,974
CF screening included	100 %	99.8 %
CF screening positive	11	12
sweat test performed	11	12
CF confirmed	2	4

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 2023 no parent or guardian rejected the participation in the CF screening. 0.2 % 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 midwives and paediatricians/ maternity clinic works well. All children received a sweat test after a positive CF screening, which showed highly abnormal findings in 3 children. A genetic analysis subsequently confirmed the diagnosis of severe cystic fibrosis.

Confirmation diagnostics and therapy of screening-positive patients

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

Tab. 8: Diagnosis, confirmation diagnostics and therapy starting 2023

Diagnosis	Confirmation diagnostics	Age at start of therapy
8x Hypothyroidism	Serum-TSH sonography: athyreosis/severe dysplasia	5-29 days
3 x Phenylketonuria 2 x Hyperphenylalaninemia (HPA) 1 x classic PKU	Serum Phe, BH4 test, DHPR activity, pterins, partial mutation analysis	9 days HPA no therapy necessary
2 x 5q spinal muscular atrophy (SMA)	mutation analysis	9-16 days
2 x Adrenogenital syndrome (AGS)	Serum 17-OHP, mutation analysis	3-7 days
1 x sickle cell disease (SCD): SCD-S/S	Hb electrophoresis, mutation analysis	10 days
2 x cystic fibrosis 2 x compound heterozygous mutation	Sweat test, mutation analysis	28-51 days
1 x biotinidase deficiency	No feedback	No feedback

Summary

In 2023, there was a further decline compared to 2022 in the number of samples (a decrease of 921 samples).

There are two main reasons for this:

1. decline of number of births in Saxony-Anhalt
2. closure of the maternity clinic in Halberstadt

On March 2021, a new version of the Children's Directive came into force. The target diseases 5q-associated spinal muscular atrophy (SMA) and sickle cell disease (SCD) were added to the extended newborn screening. Since October 2021, every child born in Germany will be screened for SMA and SCD.

Accordingly, new information flyers were provided and 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 pre-analytical problems arose due to the introduction of the new laboratory method for the analysis of the SMN1 gene for SMA and haemoglobin S for SCD. The SMN1 gene is analysed by means of qPCR and tolerates no additives such as heparin or EDTA. The senders have been trained to fulfil the required criteria for the collection of dry blood samples from the heel strictly:

- 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 analysis of haemoglobin variants for SCD led to the following findings:

- Children with previous transfusion are in most cases not reported to the screening centre and only become apparent during Hb analysis

The Gene Diagnostics Act also applies to cystic fibrosis screening and is the overarching law with penalty paragraphs. Midwives are only allowed to take blood from newborns for the cystic fibrosis screening after permission by a paediatrician. Forms can be found on our homepage (www.stwz.ovug.de).

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

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 screening¹).

We thank all maternity clinics/ ambulances and midwives 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 DGNS1 is available on the Society's own website (<http://screening-dgns.de>) two years after the respective period of time.

¹ Source: Deutsche Gesellschaft für Neugeborenen-Screening e.V. (DGNS) (German Society of newborn screening): National screening report Germany 2021 https://www.screening-dgns.de/Pdf/Screeningreports/DGNS-Screeningreport-d_2021.pdf

